European University Cyprus

Doc. 300.1.2

Higher Education Institution's Response

Date: 20/6/2023

- **Higher Education Institution:**
  European University Cyprus (EUC)
- **Town: Nicosia**
- **Programme of study - Name (Duration, ECTS, Cycle)**

  In Greek:
  "Φαρμακευτικές Βιοεπιστήμες και Ανάπτυξη Φαρμάκων (18 Μήνες/90 ECTS, Μεταπτυχιακό)"-Εξ Αποστάσεως

  In English:
  "Drug Biosciences and Pharmaceutical Development (18 Months/90 ECTS, Master of Science)"-E-learning
- **Language(s) of instruction:** English and Greek
- **Programme's status:** New
- **Concentrations (if any):**

  In Greek: Concentrations
  In English: Concentrations

The present document has been prepared within the framework of the authority and competencies of the Cyprus Agency of Quality Assurance and Accreditation in Higher Education, according to the provisions of the "Quality Assurance and Accreditation of Higher Education and the Establishment and Operation of an Agency on Related Matters Laws" of 2015 to 2021 [L.136(I)/2015 – L.132(I)/2021].

A. Guidelines on content and structure of the report

- *The Higher Education Institution (HEI) based on the External Evaluation Committee's (EEC's) evaluation report (Doc.300.1.1 or 300.1.1/1 or 300.1.1/2 or 300.1.1/3 or 300.1.1/4) must justify whether actions have been taken in improving the quality of the programme of study in each assessment area. The answers' documentation should be brief and accurate and supported by the relevant documentation. Referral to annexes should be made only when necessary.*

- *In particular, under each assessment area and by using the 2nd column of each table, the HEI must respond on the following:*

    - *the areas of improvement and recommendations of the EEC*
    - *the conclusions and final remarks noted by the EEC*

- *The institution should respond to the EEC comments, in the designated area next each comment. The comments of the EEC should be copied from the EEC report **without any interference** in the content.*

- *In case of annexes, those should be attached and sent on separate document(s). Each document should be in *.pdf format and named as annex1, annex2, etc.*

1. Study programme and study programme's design and development
(ESG 1.1, 1.2, 1.7, 1.8, 1.9)

Areas of improvement and recommendations **by EEC**	Actions Taken by the Institution	For Official Use ONLY
1.1 EUC must manage student expectations regarding the option of hybrid teaching with practice elements in the lab. This should be explicit in all materials to clarify that on-campus research project is an option.	We agree with the Committee that the availability of on-campus research projects should be communicated to our prospective students as early as possible. At the moment, this information is available on page 2 of the Master Thesis syllabus and page 13 of the Master Thesis Study Guide (**Appendix I**). Upon program accreditation, the opportunity to conduct an on-campus research project during the 'Thesis' semester (Semester 3) will also be communicated: a) via the program's EUC website, and b) during the registration process, i.e., before students' enrolment in the program. To further help students plan and manage their expectations, clear timelines for deciding on a preferred mode of carrying out the Thesis will be provided through the LMS platform Blackboard Learn Ultra and emphasized via teleconference. Detailed description of available Thesis projects will be available to students by the end of Semester 2.	Choose level of compliance:
1.2 We recommend that the project module does not offer 'literature review' as an online student alternative for a 'wet lab' project, but rather that it would be replaced with: a) 'dry lab' (computational research) with data collection or b) systematic review (with clear methodology, e.g., PRISMA). This would enable ALL students to meet the learning outcomes of the Masters thesis.	We again align with the EEC recommendations. Hence, the option to conduct a 'literature review' has now been removed from both the Syllabus and the Master Thesis Study Guide and has been replaced with a systematic review or a 'dry-lab' project (**Appendix I,** please see pages 2-3 of the Master Thesis syllabus and pages 13 & 18 of the Master Thesis Study Guide). Thus, as the EEC notes, this will enable all students to meet the learning outcomes of the Master Thesis, particularly in relation to the collection and analysis of scientific data.	Choose level of compliance:

1.3 The number of elective subjects should be increased, to give students the possibility to get acquainted with topics covering a broader drug life-cycle perspective. One could consider existing courses in other programs, e.g., public health, medicine or (health) law. In addition to a research methods elective for those students who choose the research project option.	We completely agree that the provision of additional electives will complement our program, extending its focus to include topics covering the broader perspective of a drug's life-cycle, well beyond the early phases of drug development. Therefore, to provide students with a more comprehensive understanding of Drug Biosciences and Pharmaceutical Development, we have included the following elective courses into the curriculum: • From the 'Public Health' E-learning Master program, we have included the course of 'Biostatistics (PHE610)', to provide our students with theoretical and practical knowledge of the essential statistical methods that are required for conducting a Master Thesis project. • The courses 'Principles and Practice of Clinical Trials (DBP670)', and • 'Biological Drugs and Bio-technological Product Development (DBP680)' are novel and have been included in the curriculum to cover broader and more current aspects of drug development. The syllabi of the new electives are shown in **Appendix II** and **Table 1**. Please note that a minimum of five students will be required to initiate the 'opening' of an elective course, as this will ensure interactivity between students and the course content, communication among participants, and the effective delivery of high-quality educational material.	Choose level of compliance:

1.4 The literature dedicated to "Drug Design and small molecule synthesis" course presented in course description is rather old, from the end of the twentieth century. In opinion of EEC should be updated. The proposal is: R. Hill "Drug Discovery and Development" 3rd Ed. 2021, Elsevier; EH Kerns "Drug-like Properties. Concept, Structure Design, and Methods" 2016, Academic Press ; S. Hongmao "Practical Guide to Rational Drug Design" 2015 Elsevier Science & Technology.	We thank the EEC for providing detailed information on the bibliography of the DBP610-Drug Design and Small Molecule Synthesis course. We have replaced the outdated material with the suggested literature, in both the course description and the Study Guide (please see **Appendix III**, highlighted in yellow).	Choose level of compliance:
1.5 The professional software for Drug design should be explicitly incorporated into modules (as appropriate) to map to support for dry project.	We thank the EEC for its recommendation. In **Appendix III,** we present the updated Study Guide for the course DBP610-Drug Design and Small Molecule Synthesis, which now explicitly incorporates drug design software to fulfil the course's educational requirements. Specifically, we use the **SeeSAR** software for drug design, which is introduced during Week 4 (please see page 17 of the Study Guide). **ChemDraw** is used throughout the course, to enable students to become proficient in drawing known and novel chemical structures. Computational tools to evaluate the molecular and pharmacokinetic properties of chemical compounds include **Molinspiration** and **admetSAR**, respectively (please see Week 3, page 14). For the needs of the "dry lab" thesis project we intend to use **Gaussian** and **GOLD CCDC** software for geometry optimisations, prediction of molecular properties and docking studies.	Choose level of compliance:

2. Student – centred learning, teaching and assessment *(ESG 1.3)*

Areas of improvement and recommendations **by EEC**	Actions Taken by the Institution	For Official Use ONLY
2.1 Safeguarding measures require development for online activities.	EUC employs two main tools to safeguard the integrity of the online activities and exams in its E-learning programs. When written assignments are submitted, these are automatically checked for plagiarism by **Turnitin**, a software that performs similarity checks across a wide range of available databases. Instructors may also use Turnitin as a pedagogical tool to help students improve the final draft of their assignment before the submission to the Blackboard Learn Ultra platform. Flags for instances of similarity constitute opportunities for formative feedback and revision during the writing process. For the online/e-Proctoring implementation of the final exams of E-Learning courses, the LockDown browser platform **Respondus** is used. This tool allows students to undertake their exams in a proctored environment. Before starting the exam, the students are asked to use their University IDs to identify themselves. Exam recorded videos are stored on GDPR compliant Amazon Web Services (AWS Servers) and are automatically deleted every two (2) months. Up until students have submitted their final answers, the software 'locks' their computer, not allowing them to perform any other actions on their PCs, other than their final examination, until they have submitted their final answers. The software uses the camera and microphone of the student's PC to	Choose level of compliance:

	monitor their movements, sounds, conversations, etc. and produces reports of student activity at the time of the examination. If potential transgressions are detected by the software, the instructor is alerted accordingly (i.e., the software flags specific snapshots and then the instructor when reviewing the recording can view those points more cautiously). The instructor, who is the only one with access to the recording, can access the video to review the reasons for a high alert. If deemed necessary, the student is interviewed and explanations for the alert are requested. If the information is not sufficient, further actions are taken based on the University's regulation on academic dishonesty. In addition to using specialized software for safeguarding the integrity of the online assessment, EUC implements secure login processes, user authentication methods, and access controls, to prevent unauthorized access to its online platforms and activities. Moreover, the course instructors monitor user-generated content to prevent sharing of inappropriate or harmful material and are responsible for maintaining and moderating online behavior, prohibiting activities such as bullying, harassment, or discrimination. These policies are also communicated to our students via appropriate rubrics (see criteria for Professional communication in **Appendix V**).	
2.2 Align module learning objectives (LOs) to EQF terminology. For example, for Masters study too many LOs are 'describe' or 'list', consider greater focus on 'evaluate' or 'apply'.	We thank the EEC for pointing this out. We have aligned the Learning Outcomes of the program's courses to the EQF terminology, as recommended. In specific, where appropriate, we have included verbs from higher levels of Bloom's	Choose level of compliance:

	Taxonomy to accurately reflect the cognitive complexity associated with the learning objectives of our program (please refer to Syllabi in **Appendix II & Appendix IV**). Please note that we have employed a scaffolding approach in crafting our learning objectives, and thus a certain degree of 'understanding', 'describing' and 'listing' is required to support our learning outcomes.	
2.3 The EEC has not seen relevant assessment documents, including grading criteria, marking guides and rubrics. The EUC should develop these.	We confirm to the EEC that the bulk of this material is already in place, and we apologise for not sharing/highlighting this information during the accreditation meetings. A description of EUC's grading system, along with representative marking guides and rubrics, are presented in **Appendix V**.	Choose level of compliance:
2.4 The team has been using VLE learning analytics tools to monitor student attendance and progression. There is a need for clearly articulated expectations of engagement and cut off point for support structures to be initiated.	EUC's student support structure includes: a) providing up-to-date information and program-specific expectations to all students, namely undergraduate and postgraduate, Conventional and E-Learning. b) ensuring that students are aware of the role of GPA and the impact of low GPA on the progress of their studies. c) increasing the support provided at the Program, Department and School level when this is deemed appropriate. d) implementing the procedures suggested by the Student Advising Centre. In the case of students with low GPA, the following steps are followed for both conventional and e-learning programs: **1.** The Department of Enrolment provides Schools at the beginning of each academic semester (e.g., third week of October and February,	Choose level of compliance:

	respectively) with a list of their students with a low GPA (for postgraduate courses: below 2.5). **2.** The School (this concerns all undergraduate and postgraduate Conventional and Distance Learning Programs of Study): A. For first year students at the end of the 1st semester of their studies or for students included in the list for the first time: Each affected student is called by the Program Coordinator, to ensure that students are aware of the concern of the Department and School, and that students are indeed properly informed that the Department is available to provide support [specifically, students are informed about the role and importance of the GPA, the possible reasons and causes of the low GPA, and ways for improvement of the situation, which may either involve the student (e.g., further effort) or the Department and School]. B. For new students, which continue to be in the same situation at the end of the second semester of their studies or for students appearing in the list for a second time: The process presented in Item A is repeated in the presence of the Chairperson of the Department, for further discussion and enhancement of the process, aiming at the most tangible academic targets and the procedures involved. If needed, the Chairperson of the Department and the Program Coordinator will request the presence of the Dean. C. For students who exhibit the phenomenon on a continuous basis: The possibility of sending a letter from the Dean to the student (registered, in	

	the home address) is considered (A detailed description of the EUC Low GPA Policy with "Sample" letters appear attached in **Appendix VI**). **3.** The Department of Enrolment: Each Student Advisor: A. Contacts/communicates with students and ensures that each student is well-informed and advised about the University's grading system and the role of GPA. B. In the case of students not passing a course, the advisor re-registers them to the same course in order to immediately delete the received F, and thus avoid accumulation of Fs. This takes places in the exact following semester in case the affected course is a prerequisite to other courses, to avoid F accumulation. C. Student advisors are in constant communication with the Program Coordinators in order to streamline this process. In addition to EUC's policy for the support of students with low GPA (described above), clear expectations of engagement are set between the students and the instructors at the teleconferences preceding the initiation of each course. Moreover, student engagement expectations are detailed on a weekly basis in the Study Guides and relevant rubrics. In the case where a student fails to submit exercises, the instructor sends reminders emphasizing the importance of timely delivery and reminding any upcoming deadlines. In the case where a student *repeatedly* fails to submit	

	exercises, the instructor reaches out to inquire about the reasons for the lack of submission. Based on the outcome of this communication and the circumstances of the student, deadline extensions, penalties or provision of additional resources can be provided to support the student's efforts.	

3. Teaching staff
(ESG 1.5)

Areas of improvement and recommendations **by EEC**	Actions Taken by the Institution	For Official Use ONLY
3.1 Any continuous professional development staff activities should benefit from embedding in internal and external recognised professional frameworks (e.g. Advance HE) and providing certification to be used for career progression.	We appreciate this suggestion and are actively taking steps towards ensuring that the growth and development of our personnel is internationally recognized. We joined Advance HE as an international member in November 2021. This academic year (F2022-S2023), the 'New to Teaching' Professional Learning Program by Advance HE was incorporated into our continuous professional development (CPD) curriculum. Moreover, a 'Connect Benefit Series' of webinars and informational material has become available to all faculty members on our CPD platform, offering guidance on how to benefit from EUC's membership with Advance HE. In addition to taking steps towards embedding our CPD in externally recognized professional frameworks, our staff members complete at least 35 h of compulsory educational training at the beginning of their employment. This training focuses on e-learning, particularly the use of communication technologies for effective teaching and learning. The training period is internally recognized by the award of a certificate, which describes the courses attended/successfully completed by the participant. We are thus committed to enhancing the pedagogical knowledge and skills of our instructors, as we understand that this will ultimately contribute to the overall	Choose level of compliance:

	improvement of the educational experience for our students.	
3.2 The team would benefit from increased research resources.	While EUC provides valuable support to the program through access to various online research resources, databases, and thesis-project funding, we recognize that the inclusion of additional resources, especially during the "Thesis" semester, would greatly benefit both our students and us. To address the need for increased research resources, we are routinely applying for competitive research grants and funding, and leverage our ongoing partnerships with other institutions, organizations, and researchers, to facilitate resource-sharing and collaborative research. Importantly, our team recognizes that additional opportunities for research growth lie within EUC's Department of Life Sciences. By improving our collaborative decision-making processes and fostering synergies, we aim to enhance resource utilization and unlock new avenues for research at EUC, a transformative and ongoing process that we believe will benefit our Institution as a whole.	Choose level of compliance:
3.3 Allocation of personal tutors for each student should also be the norm for the e-learning cohort, including pastoral and academic support.	Personal tutoring at EUC is facilitated by our Student Advisors. Upon registration to the program, every E-learning student is assigned a personal student advisor, who provides tailored support and guidance. The advisors play a vital role in assisting students with study planning, monitoring their progress, and resolving any challenges that may arise during their academic journey. Working both independently and in collaboration with course instructors, the advisors ensure that	Choose level of compliance:

	students receive comprehensive and individualized support throughout their studies. They provide a safe space for students to express their concerns, and offer guidance on managing stress, anxiety, or other emotional challenges. Moreover, they serve as a bridge between students and the institution, facilitating communication, addressing students' queries and concerns, and fostering a sense of engagement with the EUC community. In other words, we fully understand the importance of personalized support for our E-learning students and implement it via our dedicated student advisors. The advisors are an integral part of our three-pillar student-support structure, which also includes the academic instructors and members of the Distance Education Unit (DEU), which provides administrative support. Additional details of the available support for E-learning programs are shown in **Appendix VII,** page 7.	

4. Student admission, progression, recognition and certification *(ESG 1.4)*

Areas of improvement and recommendations **by EEC**	Actions Taken by the Institution	For Official Use ONLY
4.1 There should be further clarity about the language requirements in order to register for this program. This will have a positive effect on the program teams' recruitment strategy. In the documentation the EEC has seen, this is described as both in Greek and English.	Thank you for emphasizing the importance of language requirements for program registration. Proof of English language proficiency is required for admission, as will be presented on the program's website upon accreditation of the program. This is essential, not only for accommodating students that do not speak Greek and want to be admitted in the program, but also because the majority of the reading material is in the English language. The language admission criteria appear below: 1. Proof of English language proficiency: applicants are required to have certification for "Very Good Knowledge" of English at level B2-C1 of the Common European Framework of Reference for Languages (CEFR) by submitting one of the following: - Proof that undergraduate instruction and coursework has been done in English - Test of English as a Foreign Language (TOEFL) examination with a minimum score of 550 (paper-based total) or 213 (Computer based total) or 72 and above in IBT - IELTS with a score equalling to Band 5.5-6.5 and above	Choose level of compliance:

	- English IGCSE (GCE) O' Level with grade of "C" or above - Password Plus test with grade 6 or above. - In case that the above English language requirements cannot be met for practical reasons, a student shall take the English Placement Test of European University Cyprus. The minimum level for the student to be admitted to the program is ENL102 Advanced English. 2. Proof of Greek language proficiency (only for applicants who apply for the Greek version of the program): applicants are required to have certification of Greek language proficiency by submitting one of the following: - School-leaving certificate (Απολυτήριο) of a recognized six-year secondary education school in Greece or in Cyprus, provided that the principal language of instruction is Greek; - C (or higher) at a Modern Greek GCE/A-level; - Certificate of success at the Ministry of Education and Culture examination for Greek language proficiency.	
4.2 Clear student career pathways should be provided to enhance the employability of the students completing the program.	Our program aims to equip students with the necessary knowledge, skills, and experience to succeed in the pharmaceutical industry, as well as to prepare them for further specialization in the field of Drug Biosciences and	Choose level of compliance:

	Pharmaceutical Development. We provide a curriculum that combines theoretical foundations with practical training, and strive to foster critical thinking, problem-solving abilities, and a deep understanding of the drug development process, particularly during its early phases. Therefore, the career pathway of our graduates is designed to lead them towards the discovery, R&D and regulatory sectors of pharmaceutical industry or towards pursuing higher studies, e.g., PhD. To further enhance these employability prospects, we actively collaborate with leading pharmaceutical companies and research institutions. These partnerships provide valuable opportunities for common research projects and industry placements, allowing our students to gain real-world experience and network with professionals in the field. Additionally, we offer career counseling services, workshops, and networking events to help our students explore career options, develop job search strategies, and connect with potential employers. These initiatives are supported by the personalized assistance and guidance provided by EUC's career centre and advisors to our students and alumni. In the future, based on the employability data collected by the School's Program Committee and/or the developing needs of the local industry for specialized personnel, we may also consider offering tracks for students especially interested in either drug discovery, R&D, or regulatory affairs.	

	Overall, our aim with this program is to provide a comprehensive understanding of the drug development process, ensuring that our graduates are well-prepared to succeed in the challenging environment of drug development.	

5. Learning resources and student support
(ESG 1.6)

Areas of improvement and recommendations **by EEC**	Actions Taken by the Institution	For Official Use ONLY
5.1 The program should develop the learning materials on the program VLE well ahead of the starting date of the program, according to the descriptions of activities and content in the program study guides.	We confirm that all the learning materials of the program, as described in the Study Guides, will be uploaded to Blackboard Learn Ultra in the first week of September, i.e. the VLE will be ready approximately one month before the start of the academic semester (October 2nd).	Choose level of compliance:
5.2 MSc assessment (exam) should focus more on authentic assessment and scenario / problem-based examination. The exam papers should be reviewed and updated to reflect mode of assessment (online) as well as level.	We agree that it is important to align the methods of assessment with both the E-Learning mode of program delivery and the desired learning outcomes of the specific M.Sc. program. Compared to the undergraduate exam sample papers presented upon request to the EEC, which were designed for face-to-face assessment at the B.Sc. level, the M.Sc. papers will contain a greater proportion of simulation and case-based assessments, to reflect the complexity and depth of skills and knowledge expected at the M.Sc. level. Please find examples of discipline-specific authentic assessment that have been included in the M.Sc. program in **Appendix VIII**. Representative topics include designing the synthesis of a commercially available drug (DBP610), analyzing real-world toxicology data (DBP630), and evaluating real-world clinical trial results (DBP640).	Choose level of compliance:

5.3 Course leaders and library colleagues could collaborate more effectively in provision of the most up to date materials online.	We agree with EEC's suggestion. It is the policy of the University and the EUC Library to purchase all the book titles that are suggested as required or recommended reading on each course syllabus (including the updated titles suggested by the Committee). The Library purchases three (3) copies of every mandatory textbook and two (2) copies of each recommended book title, all of which are placed on the Reserve Shelf. The Library, in an effort to ensure that all titles are available, rechecks all syllabuses and confirms availability to the faculty once a new programme of study is launched or re-accredited. Also, it would be useful to inform the EEC that the Library subscribes to the Curriculum Builder Tool. The Tool is an add-on service for the Library's EBSCO Discovery Service (EDS) and part the university's LMS platform. The Tool gives the faculty the ability to search from within the LMS platform all the Library's paid services (such as databases, e-books and e-journals). Furthermore, it allows the faculty to search online for any Open Educational Resources and Open Textbooks and then directly use them in their courses. Any material found (such as web links to archives, free primary sources, e.g., government documents, pamphlets, texts of laws, poems, literary works, book chapters, and so on) can then be used to create reading lists, be used for student assignments, etc.	Choose level of compliance:

	Finally, on a regular basis, the Library sends out emails to the faculty and provides guides on how to take advantage of online resources paid and free as part of the open access policies adopted by publishers.	

6. Additional for doctoral programmes

(ALL ESG)

N/A

7. Eligibility (Joint programme)
(ALL ESG)

N/A

B. Conclusions and final remarks

Conclusions and final remarks **by EEC**	Actions Taken by the Institution	For Official Use ONLY
Major recommendations		
EUC must manage student expectations regarding the option of hybrid teaching with practice elements in the lab. This should be explicit in all materials to clarify that on-campus research project is an option.	We agree with the Committee that the availability of on-campus research projects should be communicated to our prospective students as early as possible. At the moment, this information is available on page 2 of the Master Thesis syllabus and page 13 of the Master Thesis Study Guide (**Appendix I**). Upon program accreditation, the opportunity to conduct an on-campus research project during the 'Thesis' semester (Semester 3) will also be communicated: a) via the program's EUC website, and b) during the registration process, i.e., before students' enrolment in the program. To further help students plan and manage their expectations, clear timelines for deciding on a preferred mode of carrying out the Thesis will be provided through the LMS platform Blackboard Learn Ultra and emphasized via teleconference. Detailed description of available Thesis projects will be available to students by the end of Semester 2.	Choose level of compliance:
We recommend that the project module does not offer 'literature review' as an online student alternative for a 'wet lab' project, but rather that it would be replaced with: a) 'dry lab' (computational research) with data collection or b) systematic review (with clear methodology, e.g. PRISMA) This would enable ALL students to meet the learning outcomes of the Masters thesis.	We again align with the EEC recommendations. Hence, the option to conduct a 'literature review' has now been removed from both the Syllabus and the Master Thesis Study Guide and has been replaced with a systematic review or a 'dry-lab' project (**Appendix I,** please see pages 2-3 of the Master Thesis syllabus and pages 13 & 18 of the Master Thesis Study Guide). Thus, as the EEC notes, this will enable all students to meet the learning outcomes of the Master Thesis,	Choose level of compliance:

	particularly in relation to the collection and analysis of scientific data.	
The number of elective subjects should be increased, to give students the possibility to get acquainted with topics covering a broader drug life-cycle perspective. One could consider existing courses in other programs, e.g. public health, medicine or (health) law. In addition to a research methods elective for those students who choose the research project option.	We completely agree that the provision of additional electives will complement our program, extending its focus to include topics covering the broader perspective of a drug's life-cycle, well beyond the early phases of drug development. Therefore, to provide students with a more comprehensive understanding of Drug Biosciences and Pharmaceutical Development, we have included the following elective courses into the curriculum: • From the 'Public Health' E-learning Master program, we have included the course of 'Biostatistics (PHE610)', to provide our students with theoretical and practical knowledge of the essential statistical methods that are required for conducting a Master thesis project. • The courses 'Principles and Practice of Clinical Trials (DBP670)', and • 'Biological Drugs and Bio-technological Product Development (DBP680)' are novel and have been included in the curriculum to cover broader and more current aspects of drug development. The syllabi of the new electives are shown in **Appendix II** and **Table 1**. Please note that a minimum of five students will be required to initiate the 'opening' of an elective course, as this will ensure interactivity between students and the course content, communication among participants, and the effective delivery of high-quality educational material.	Choose level of compliance:

Clear student career pathways should be provided to enhance the employability of the students completing the program.	Our program aims to equip students with the necessary knowledge, skills, and experience to succeed in the pharmaceutical industry, as well as to prepare them for further specialization in the field of Drug Biosciences and Pharmaceutical Development. We provide a curriculum that combines theoretical foundations with practical training, and strive to foster critical thinking, problem-solving abilities, and a deep understanding of the drug development process, particularly during its early phases. Therefore, the career pathway of our graduates is designed to lead them towards the discovery, R&D and regulatory sectors of pharmaceutical industry or towards pursuing higher studies, e.g., PhD. To further enhance these employability prospects, we actively collaborate with leading pharmaceutical companies and research institutions. These partnerships provide valuable opportunities for common research projects and industry placements, allowing our students to gain real-world experience and network with professionals in the field. Additionally, we offer career counseling services, workshops, and networking events to help our students explore career options, develop job search strategies, and connect with potential employers. These initiatives are supported by the personalized assistance and guidance provided by EUC's career centre and advisors to our students and alumni. In the future, based on the employability data collected by the School's Program Committee and/or the developing needs of the local	Choose level of compliance:

	industry for specialized personnel, we may also consider offering tracks for students especially interested in either drug discovery, R&D, or regulatory affairs. Overall, our aim with this program is to provide a comprehensive understanding of the drug development process, ensuring that our graduates are well-prepared to succeed in the challenging environment of drug development.	
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Align module learning objectives (LOs) to EQF terminology. For example, for Masters study too many LOs are 'describe' or 'list', consider greater focus on 'evaluate' or 'apply'.	We thank the EEC for pointing this out. We have aligned the Learning Outcomes of the program's courses to the EQF terminology, as recommended. In specific, where appropriate, we have included verbs from higher levels of Bloom's Taxonomy to accurately reflect the cognitive complexity associated with the learning objectives of our program (please refer to Syllabi in **Appendix II & Appendix IV**). Please note that we have employed a scaffolding approach in crafting our learning objectives, and thus a certain degree of 'understanding', 'describing' and 'listing' is required to support our learning outcomes.	
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	have been included in the M.Sc. program in **Appendix VIII**. Representative topics include designing the synthesis of a commercially available drug, analyzing real-world toxicology data, and evaluating real-world clinical trial results.	
Minor recommendations		
The literature dedicated to "Drug Design and small molecule synthesis" course presented in course description is rather old, from the end of the twentieth century. In opinion of EEC should be updated. The proposal is: R. Hill "Drug Discovery and Development" 3rd Ed. 2021, Elsevier ; EH Kerns "Drug-like Properties. Concept, Structure Design, and Methods" 2016, Academic Press ; S. Hongmao "Practical Guide to rational Drug Design" 2015 Elsevier Science & Technology.	We thank the EEC for providing detailed information on the bibliography of the DBP610-Drug Design and Small Molecule Synthesis course. We have replaced the outdated material with the suggested literature, in both the course description and the Study Guide (please see **Appendix III**, highlighted in yellow).	
The EEC has not seen relevant assessment documents, including grading criteria, marking guides and rubrics. The EUC should develop these.	We confirm to the EEC that the bulk of this material is already in place, and we apologise for not sharing/highlighting this information during the accreditation meetings. A description of EUC's grading system, along with representative marking guides and rubrics, are presented in **Appendix V**.	
The team has been using VLE learning analytics tools to monitor student attendance and progression. There is a need for clearly articulated expectations of engagement and cut off point for support structures to be initiated.	EUC's student support structure includes: a) providing up-to-date information and program-specific expectations to all students, namely undergraduate and postgraduate, Conventional and E-Learning. b) ensuring that students are aware of the role of GPA and the impact of low GPA on the progress of their studies. c) increasing the support provided at the Program, Department and School	

	level when this is deemed appropriate. d) implementing the procedures suggested by the Student Advising Centre. In the case of students with low GPA, the following steps are followed for both conventional and e-learning programs: **1.** The Department of Enrolment provides Schools at the beginning of each academic semester (e.g., third week of October and February, respectively) with a list of their students with a low GPA (for postgraduate courses: below 2.5). **2.** The School (this concerns all undergraduate and postgraduate Conventional and Distance Learning Programs of Study): D. For first year students at the end of the 1st semester of their studies or for students included in the list for the first time: Each affected student is called by the Program Coordinator, to ensure that students are aware of the concern of the Department and School, and that students are indeed properly informed that the Department is available to provide support [specifically, students are informed about the role and importance of the GPA, the possible reasons and causes of the low GPA, and ways for improvement of the situation, which may either involve the student (e.g., further effort) or the Department and School]. E. For new students, which continue to be in the same situation at the end of the second semester of their studies or for students appearing in the list for a second time:	

	The process presented in Item A is repeated in the presence of the Chairperson of the Department, for further discussion and enhancement of the process, aiming at the most tangible academic targets and the procedures involved. If needed, the Chairperson of the Department and the Program Coordinator will request the presence of the Dean. F. For students who exhibit the phenomenon on a continuous basis: The possibility of sending a letter from the Dean to the student (registered, in the home address) is considered (A detailed description of the EUC Low GPA Policy with "Sample" letters appear attached in **Appendix VI**). **3.** The Department of Enrolment: Each Student Advisor: D. Contacts/communicates with students and ensures that each student is well-informed and advised about the University's grading system and the role of GPA. E. In the case of students not passing a course, the advisor re-registers them to the same course in order to immediately delete the received F, and thus avoid accumulation of Fs. This takes places in the exact following semester in case the affected course is a prerequisite to other courses, to avoid F accumulation. F. Student advisors are in constant communication with the Program Coordinators in order to streamline this process. In addition to EUC's policy for the support of students with low GPA (described above), clear expectations	

	of engagement are set between the students and the instructors at the teleconferences preceding the initiation of each course. Moreover, student engagement expectations are detailed on a weekly basis in the Study Guides and relevant rubrics. In the case where a student fails to submit exercises, the instructor sends reminders emphasizing the importance of timely delivery and reminding any upcoming deadlines. In the case where a student *repeatedly* fails to submit exercises, the instructor reaches out to inquire about the reasons for the lack of submission. Based on the outcome of this communication and the circumstances of the student, deadline extensions, penalties or provision of additional resources can be provided to support the student's efforts.	
Any continuous professional development staff activities should benefit from embedding in internal and external recognised professional frameworks (e.g., Advance HE) and providing certification to be used for career progression.	We appreciate this suggestion and are actively taking steps towards ensuring that the growth and development of our personnel is internationally recognized. We joined Advance HE as an international member in November 2021. This academic year (F2022-S2023), the 'New to Teaching' Professional Learning Program by Advance HE was incorporated into our continuous professional development (CPD) curriculum. Moreover, a 'Connect Benefit Series' of webinars and informational material has become available to all faculty members on our CPD platform, offering guidance on how to benefit from EUC's membership with Advance HE. In addition to taking steps towards embedding our CPD in externally recognized professional frameworks,	

	our staff members complete at least 35 h of compulsory educational training at the beginning of their employment. This training focuses on e-learning, particularly the use of communication technologies for effective teaching and learning. The training period is internally recognized by the award of a certificate, which describes the courses attended/successfully completed by the participant. We are thus committed to enhancing the pedagogical knowledge and skills of our instructors, as we understand that this will ultimately contribute to the overall improvement of the educational experience for our students.	
The team would benefit from increased research resources.	While EUC provides valuable support to the program through access to various online research resources, databases, and thesis-project funding, we recognize that the inclusion of additional resources, especially during the "Thesis" semester, would greatly benefit both our students and us. To address the need for increased research resources, we are routinely applying for competitive research grants and funding, and leverage our ongoing partnerships with other institutions, organizations, and researchers, to facilitate resource-sharing and collaborative research. Importantly, our team recognizes that additional opportunities for research growth lie within EUC's Department of Life Sciences. By improving our collaborative decision-making processes and fostering synergies, we aim to enhance resource utilization and unlock new avenues for research at EUC, a transformative and ongoing process that we believe will benefit our Institution as a whole.	

Allocation of personal tutors for each student should also be the norm for the e-learning cohort, including pastoral and academic support.	Personal tutoring at EUC is facilitated by our Student Advisors. Upon registration to the program, every E-learning student is assigned a personal student advisor, who provides tailored support and guidance. The advisors play a vital role in assisting students with study planning, monitoring their progress, and resolving any challenges that may arise during their academic journey. Working both independently and in collaboration with course instructors, the advisors ensure that students receive comprehensive and individualized support throughout their studies. They provide a safe space for students to express their concerns, and offer guidance on managing stress, anxiety, or other emotional challenges. Moreover, they serve as a bridge between students and the institution, facilitating communication, addressing students' queries and concerns, and fostering a sense of engagement with the EUC community. In other words, we fully understand the importance of personalized support for our E-learning students and implement it via our dedicated student advisors. The advisors are an integral part of our three-pillar student-support structure, which also includes the academic instructors and members of the Distance Education Unit (DEU), which provides administrative support. Additional details of the available support for E-learning programs are shown in **Appendix VII,** page 7.	
There should be further clarity about the language requirements in order to register for this program. This will have a positive effect on the program teams'	Thank you for emphasizing the importance of language requirements for program registration. Proof of English language proficiency is required for admission, as will be	

recruitment strategy. In the documentation the EEC has seen, this is described as both in Greek and English.	presented on the program's website upon accreditation of the program. This is essential, not only for accommodating students that do not speak Greek and want to be admitted in the program, but also because the majority of the reading material is in the English language. The language admission criteria appear below: 3. Proof of English language proficiency: applicants are required to have certification for "Very Good Knowledge" of English at level B2-C1 of the Common European Framework of Reference for Languages (CEFR) by submitting one of the following: - Proof that undergraduate instruction and coursework has been done in English - Test of English as a Foreign Language (TOEFL) examination with a minimum score of 550 (paper-based total) or 213 (Computer based total) or 72 and above in IBT - IELTS with a score equalling to Band 5.5-6.5 and above - English IGCSE (GCE) O' Level with grade of "C" or above - Password Plus test with grade 6 or above. - In case that the above English language requirements cannot be met for practical reasons, a student shall take the English Placement Test of European University Cyprus. The minimum level for the student to be	

	admitted to the program is ENL102 Advanced English. 4. Proof of Greek language proficiency (only for applicants who apply for the Greek version of the program): applicants are required to have certification of Greek language proficiency by submitting one of the following: - School-leaving certificate (Απολυτήριο) of a recognized six-year secondary education school in Greece or in Cyprus, provided that the principal language of instruction is Greek; - C (or higher) at a Modern Greek GCE/A-level; - Certificate of success at the Ministry of Education and Culture examination for Greek language proficiency.	
Course leaders and library colleagues could collaborate more effectively in provision of the most up to date materials online.	We agree with EEC's suggestion. It is the policy of the University and the EUC Library to purchase all the book titles that are suggested as required or recommended reading on each course syllabus (including the updated titles suggested by the Committee). The Library purchases three (3) copies of every mandatory textbook and two (2) copies of each recommended book title, all of which are placed on the Reserve Shelf. The Library, in an effort to ensure that all titles are available, rechecks all syllabuses and confirms availability to the faculty once a new programme of study is launched or re-accredited. Also, it would be useful to inform the EEC that the Library subscribes to the Curriculum Builder Tool. The Tool is an add-on service for the Library's	

	EBSCO Discovery Service (EDS) and part the university's LMS platform. The Tool gives the faculty the ability to search from within the LMS platform all the Library's paid services (such as databases, e-books and e-journals). Furthermore, it allows the faculty to search online for any Open Educational Resources and Open Textbooks and then directly use them in their courses. Any material found (such as web links to archives, free primary sources, e.g., government documents, pamphlets, texts of laws, poems, literary works, book chapters, and so on) can then be used to create reading lists, be used for student assignments, etc. Finally, on a regular basis, the Library sends out emails to the faculty and provides guides on how to take advantage of online resources paid and free as part of the open access policies adopted by publishers.	

C. Higher Education Institution academic representatives

Name	*Position*	*Signature*
Dr. Athanasios Metaxas	Program Coordinator	
Dr. Anastasios Theodorou	Chairperson of the Department of Life Sciences	
Prof. Panagiotis Papageorgis	Dean of the School of Sciences	

Date: 20/6/2023

TABLE 1: STRUCTURE OF THE PROGRAMME OF STUDY

PROGRAMME REQUIREMENTS	**ECTS**
All students pursuing the Master of Science in **Drug Biosciences and Pharmaceutical Development** program must complete the following requirements:	
Compulsory Courses	50
Elective Course	10
Master Thesis	30
Total Requirements	**90**

Compulsory Courses		**50**
Code	**Course Title**	**ECTS**
DBP600	Natural Medicinal Products: Discovery and Characterization	10
DBP610	Drug Design and Small Molecule Synthesis	10
DBP620	Drug Formulation, Quality Assurance and Quality Control	10
DBP630	Preclinical Development: Pharmacological and Toxicological Evaluation	10
DBP640	Regulatory Aspects of Drug Development	10
Elective Courses **Students choose one (1) from the following courses:**		**10**
DBP650	Bioanalysis in Drug Development	10
DBP660	Health Economics and Pharmacoeconomics	10
DBP670	Principles and Practice of Clinical Trials	10
DBP680	Biological Drugs and Biotechnological Product Development	10
PHE610	Biostatistics	10
Master Thesis		**30**
DBP690	Master Thesis	30

APPENDIX I

Course title	Master Thesis				
Course code	DBP690				
Course type	Compulsory				
Level	Master (2nd Cycle)				
Year / Semester	2nd Year/1st Semester				
Teacher's name	Dr. Constantinos Nikiforou				
ECTS	30	**Lectures/ week**	–	**Laboratories/ week**	Up to 6
Course purpose and objectives	The ultimate purpose of the Master thesis is the critical analysis and/or solution - at a theoretical and/or practical level - of one or more problems associated with Drug Biosciences and Pharmaceutical Development. The thesis introduces students to research methodology, training them in the planning, organization, and implementation of a scientific study, as well as in the adequate analysis, documentation, and presentation of its content. The preparation of the M.Sc. thesis offers students the opportunity to deepen, synthesize and apply the knowledge acquired during their studies. For the preparation of the thesis, students carry out independent research under the oversight of an academic supervisor. The area of the research subject is agreed upon in collaboration with the academic supervisor, prior to conducting the thesis. The project assignment may involve applied research or a systematic review of a research question. The writing of a thesis, as well as its public oral defence before a three-member Evaluation Committee, are required for the completion of the Master thesis project.				
Learning outcomes	Upon completing this course, students should be able to: • Organize and implement a scientific research project. • Identify sources of information related to the topic under study, through bibliographic search in academically valid databases. • Compose a systematic review of the literature, critically approaching the available scientific information on a given subject. • Plan, organize and implement an experimental research project in the subjects of Drug Biosciences and Pharmaceutical Development, according to academic standards. • Formulate hypotheses and clearly present the problem, purpose, methodology and the results that stem from the analysis of data. • Discuss findings, contrasting them with the findings of other studies, identifying areas for further study and suggesting ways to address problems. • Evaluate and discuss issues related to research ethics.				

<table>
<tr><td></td><td colspan="3">Compose and present scientific work in both written and oral forms, and present this work in front of an audience.
Demonstrate thorough knowledge of the subject under investigation, expertise in applying basic scientific methods, and ability to contribute to scientific knowledge.</td></tr>
<tr><td>Prerequisites</td><td>Successful completion of all Year 1 compulsory and elective courses.</td><td>Co-requisites</td><td>None</td></tr>
<tr><td>Course content</td><td colspan="3">Supervision and guidance
Meetings are held between students and their supervisor at least every two weeks. The meetings aim to provide general guidance to the students, helping them organize their methodological and research approach, the analysis of collected data and/or discuss any activity that is required to successfully complete the Master Thesis.
Students receive regular feedback on the progress of their work.
Implementation of research project – systematic review
This type of thesis can be undertaken entirely off-campus.
The students thoroughly study the literature to determine the nature of the review project.
The students collaborate with the supervisor to choose the research methodology to be applied (search words, databases, exclusion criteria).
The students carry out independent work to identify primary sources related to the subject under investigation.
The students examine the identified studies, qualitatively and/or quantitatively (meta-analysis), and evaluate, interpret, and discuss their findings.
The students compose the Master Thesis in written form, according to the instructions provided in the Master's thesis guide.
Implementation of research project – ‘dry-lab’ project
This type of thesis can be undertaken entirely off-campus.
The students thoroughly study the literature to comprehend the topic of the research project.
The students collaborate with the supervisor to Identify the specific data analysis techniques, software, or tools that will be utilized.
The students collaborate with the supervisor to determine the data sources required for the project. This may include existing datasets, public databases, or simulated data. The students collect and organize the data in a suitable format for analysis.
The students examine the data applying statistical methodologies to evaluate, interpret and discuss the findings of the study.
The students compose the Master Thesis in written form, according to the instructions provided in the Master's thesis guide.
Implementation of research project – ‘wet-lab’ project
Students are expected to be physically present for this type of thesis.</td></tr>
</table>

	• The students thoroughly study the literature to comprehend the topic of the research project. • The students collaborate with the supervisor to choose and explicitly describe the experimental methodology to be followed. • The students are trained in experimental techniques related to the subject under investigation, to apply them independently for data collection. • The students examine the data applying statistical methodologies to evaluate, interpret and discuss the findings of the study. • The students compose the Master Thesis in written form, according to the instructions provided in the Master's thesis guide. **Master thesis presentation** • After submitting the thesis to a three-member advisory body, students are informed of the date of the oral presentation of their work. • After the oral defence of the master's thesis, the students submit the final form of their dissertation to the Department Secretariat, and receive a grade for the course. A detailed description of the content and prerequisites of the course are provided in the "Master Thesis Preparation Guide".
Teaching methodology	E - Learning
Bibliography	*Cochrane Handbook for Systematic Reviews of Interventions*, Second Edition, Higgins J.P.T., Thomas J., Chandler J., Cumpston M., Li T., Page M.J., Welch V.A. (Eds), 2020, Chichester (UK): Wiley, eISBN:9781119536604. *How to Write a Master's Thesis*, Third Edition, Bui W.N., 2019, SAGE Publications, ISBN-13: 978-1506336091. Selected scientific journal articles, in PDF format. Master Thesis Preparation Guide, Department of Life Sciences, European University Cyprus.
Assessment	Master Thesis 70% Oral defence 30% *It is noted that success in the Master thesis course requires being successful in each of the above individual assessments.*
Language	Greek and English

European University Cyprus

SCHOOL OF SCIENCES
DEPARTMENT OF LIFE SCIENCES

Drug Biosciences and Pharmaceutical Development (M.Sc.)

MASTER THESIS STUDY GUIDE

1st Version:

Nicosia, 2022

In lieu of a Preface…

The Master thesis contributes significantly to the development of the search and learning skills in the aspiring graduate's subject area. The drafting and completion of the thesis gives a sense of accomplishment in developing and creating. Over time, other people, including students, teachers, researchers, etc. will go through and read the works previously prepared, in order to complete their own search and broaden their knowledge.

In the process of submitting a Master thesis in a University, elegant and accurate writing is as important as the comprehensiveness and originality of the research. This "Master Thesis Writing Guide" has been prepared by the academics of the Departments of Life Sciences to assist students in achieving an outstanding result.

This Master thesis Guide is not an exhaustive manual but can provide substantial assistance in preparing an acceptable Thesis. The faithful application of the rules of the Guide is essential and will offer quality support to the entire effort. Moreover, attention to the various details and suggestions will help save valuable time. Students are therefore urged to read this manual thoroughly before embarking on the process of preparing the Master Thesis.

We also recommend and wish to draw your attention to the fact that you should not use other templates which may be incorrect, or follow instructions that are in conflict with the provisions of this Guide. An older Master Thesis or a Thesis from other Institutions may not have been drafted according to the writing rules included in this manual.

We wish you all the best!

Table of Contents

INTRODUCTION

The Master Thesis is considered to be the capstone of the student's educational process, being a key prerequisite for completing the studies and obtaining the Master's Degree.

The Master Thesis has both a formal and substantial status and is distinguished for its contribution to scientific knowledge, as it enables the student to explore the subject of study in depth and apply a systematic and scientific approach towards achieving the goal, whilst reflecting the quality of the application of his/her Program of Study.

The Master Thesis is a creative, independent and scientific search. It is the outcome of the student's capability to analyse and synthesize and his/her ability to use the entire spectrum of knowledge and skills acquired throughout the Program of Study.

A high-quality Master Thesis is a reflection of continuous study and assimilation, as well as the application of knowledge, on condition that it meets the requirements in order to verify the student's professional maturity in addressing sophisticated applications of greater complexity and developing the skill of assessing and making good use of bibliography sources. It provides the proof that the student has the ability to apply his/her knowledge and skills, whilst learning how to function and work in a methodical way, using combinatorial thinking and documentation.

This "Master Thesis Guide" was prepared in order to thoroughly describe the process of writing the Thesis and the guidelines for its completion.

It describes in particular the process of choosing the subject, the specifications in terms of writing, the structure, content, special methodological instructions for writing the key parts of the Master Thesis, its scientific documentation, the time frames relating to the completion, submission, consideration and assessment, the assessment criteria and the student's obligations throughout the preparation of the Master Thesis.

Information which is not clearly covered by this Guide in relation to the writing of the Master Thesis, as well as any problems which may arise during the process, will be addressed by the Supervising Professor in collaboration with the person in charge of the Course and the competent committee of the Department of Life Sciences. It is also recommended to use manuals on the Methodology of Research and Statistics, where this is deemed useful by the Supervising Professor in collaboration with the student.

The ongoing collaboration between the student and the Supervisor becomes necessary and essential and the student must fulfill his/her obligations without fail. The preparation of the Master Thesis in an entirely interactive process between the student and the Supervisor throughout its duration, in the sense that the Supervisor provides ongoing and progressive feedback on the development of the Thesis.

Students must study the Guide carefully from the time they declare the Master Thesis through to its oral defense, in order to avoid any mistakes, omissions and delays.

The academic personnel guides and facilitates the ongoing collaboration with the students, with a view to completing the Thesis within the prescribed time frame.

OBJECTIVE AND LEARNING OUTCOMES

OBJECTIVE

The objective of the Master Thesis is to enable students to study in depth a topic within their chosen discipline, consisting of a dynamic combination of scientific significance and practical interest (connection with the student's main studies or his/her professional pursuits) through the mental process of analysis and synthesis and the use of critical thinking, as it derives from current scientifically and empirically documented knowledge.

LEARNING OUTCOMES

Upon completion of their Master Thesis students are expected to:

i. clearly identifies the process of learning through the study and investigation of a topic and the application of a systematic and scientific approach to acquire new knowledge relevant to their discipline,
ii. search for and explore a subject area in depth and make use of current literature on the subject in a critical and synthesizing way that adds value and substantiates the subject, thus creating a new original work,
iii. organize and use time to complete a scholarly project within a given time frame,
iv. present and investigate the causes of a problem, propose solutions and present the findings of the investigation,
v. design and conduct original research by testing ideas and theories with data and conclusions,
vi. develop the ability to critically review publications and research papers,
vii. identify and integrate the specific study into the epistemological field of their discipline,
viii. apply in practice the principles of research and the methodology of handling research data and documenting results,
ix. identify how the results of their scientific investigation are related to and used in the application of their science.

THESES COMMITTEES

COMMITTEE OF MASTER THESIS OF THE DEPARTMENT (INFORMAL)

The "informal" Committee of Master Thesis of the Departments comprises the professor in charge of the course and one representative (member of the Teaching and Research Personnel – TRP) from each Program of Study. The purpose of the Committee is to address issues regarding the review of the "Thesis Writing Guide", examine important issues arising from the execution of the Thesis by students, such as violation of academic ethics and morals (e.g., plagiarism) or other issues not foreseen or covered by this version of the Thesis Writing Guide, and inform students on current developments.

COMMITTEES OF MASTER THESES (INFORMAL)

There is a Three-member Master Theses Committee comprising from the Thesis supervisor, one member of the Program's Teaching Personnel and the professor in charge of the course. The purpose of this Committees is to coordinate and supervise the process of assigning Master Theses and plan and organize the procedure for their presentation and assessment through to their final submission with the Secretariat of the Department. This Committee is also responsible for addressing and tackling issues of minor importance which may arise.

RIGHT TO CONDUCT A MASTER THESIS

The right to conduct and Master thesis have:

i. students who have completed the courses up to semester 2 (1st year of studies) or have complete 60 ECTS,

ii. students with a GPA greater than or equal to 2.00.

DETERMINATION OF THE THESIS TOPIC – MASTER THESIS SUPERVISION - STUDENT GUIDANCE

The supervision of the Master Thesis is undertaken by the Department's teaching personnel amongst holders of PhD (members of the TRP or Scientific Associates) or PhD candidates (Special Teaching Personnel, Clinical Trainers, Laboratory Assistants) or holders of Master's degrees upon the relevant approval of the Department's Committee of Master Theses. The responsibility for the allocation of the Theses per Supervisor lies with the Committees of Master and Graduate Theses of the Department of Life Sciences. Each member of the TRP undertakes the supervision of a maximum of five (5) of different scope. The maximum number of Master Theses allocated per Supervisor is determined by the needs of the Program and of the Department in general and may vary.

APPOINTMENT OF SUPERVISING PROFESSOR

The Supervising Professor (proposer) is appointed by the Committee of Master Theses of the Program within 10 working days from the expiry of the deadline for the submission of applications. The criteria for the selection of the Supervising Professor are his subject area and research interests. Any preferences of the student for a

specific supervisor are taken into consideration only in research and original topics and provided there is availability in the specific period of time. Following the announcement of the proposers by the Committee of Master Theses of the Program, students must contact the Supervising Professor in order to specify and analyze the topic of the Master Thesis they have undertaken and proceed to the preparation and presentation of their research proposal.

CHANGE OF SUPERVISING PROFESSOR

Once a supervisor has been designated, he/she may not change without the prior submission of a justified request to the Committee of Master Theses of the MSc Applied Dietetics and Nutrition program. In this case, if the Committee of Master Theses finds that the student is not at fault for the delay, it may extend the deadline for completing the Thesis by up to 6 months.

SUPERVISION – EXECUTION OF THE MASTER THESIS

STUDENT SUPERVISION – GUIDANCE

During the execution of the Master Thesis, the student has weekly 30-60 minute meetings with his/her supervisor, as determined between them (either in person or by teleconference), in order to receive feedback on the progress of the Thesis, plan together the next stages of execution and verify his/her progress. They may also communicate through other electronic means or in any other way as determined by the Supervisor. At the initial meeting, the time frames for the progress of the Master Thesis are set and discussed and the skeleton to be followed by the student for the completion of the Master Thesis is defined.

Collaboration between the student and the Supervisor is essential and plays a key role in his/her final grade. In case, at any stage of the execution of the Thesis, more than three weeks elapse without any contact between the student and the proposer, the Supervising Professor reports the fact to the Committee of Master Theses of the respective Program and the student is called to justify this lack of contact in writing. If such justification is deemed inadequate, the Supervisor has the right to terminate the collaboration, in which case it is considered that the student has failed the course and receives an "**F**" (Fail) grade. Students have the obligation and must submit to their supervisor parts of their Thesis at regular intervals in accordance with the set time frame (see pages 8-9). The delivery of the completed Thesis to the Supervisor, before or after the deadline for submission, without previous submission and correction by the Supervisor in parts, will not be accepted and the Master Thesis will be rejected, resulting in the student's failure. Moreover, Supervisors are not obliged to hold meetings and make corrections during holidays (Christmas, Easter, August).

ANNOUNCEMENT – ALLOCATION OF THESIS TOPICS

The topics of the Master Theses are sent by the coordinator of the MSc Drug Biosciences and Pharmaceutical Development program to the professor in charge of the course for approval and are posted by the latter on the Blackboard Learn platform, together with the respective application forms. Once the topics are posted, the professor notifies the students using their University email address, they choose the topic that interests them and submit it online within the prescribed time frames announced at the same time as the topics.

APPLICATIONS FOR UNDERTAKING A THESIS TOPIC

During the summer of the semester preceding the semester in which the Master Thesis course is offered, applications are accepted on the Blackboard Learn platform by students who satisfy the criteria to conduct a Master Thesis, in view of undertaking a relevant topic.

CHOICE OF TOPICS

The students state on the standardized form, on a priority basis (see Annex on page 34) up to 5 (five) Thesis titles from amongst the topics to be announced by the Program of Studies of the Department of Life Sciences which they are attending.

ALLOCATION OF A THESIS TOPIC

The determination and assignment of a topic to the student falls within the competence of the Committees of Master Theses of the Programs of the Departments of Health or Life Sciences. More specifically, after the expiry of the deadline for the submission of topics by the students, the respective Committee of Master Theses of each Program of Studies of the Departments of Life Sciences meets and examines the applications, allocating students to Supervising Professors. As a rule, for applications submitted within the deadline, topics and Supervisors are assigned on a priority basis in accordance with the following criteria:

The overall grade of each student (GPA)

The availability of Supervisors.

For example, in case 2 (two) or more students happen to have chosen the same topic, priority is given to the student who has submitted his/her application within the deadline. In case two or more students have chosen the same topic and have both submitted their application within the deadline, the topic is allocated to the student with the highest overall grade (GPA) up until the third year of studies (in the case of a group Thesis the GPA of all collaborating students is taken into consideration). Finally, topics proposed by a supervisor are allocated to students up until the maximum number of Theses that he/she can supervise. When the said number is reached, interested students are obliged to choose any other topic from amongst those remaining available on the list. It is the Departments' intention to satisfy the interests of all students, however for various reasons (availability of infrastructure, personnel, topic covered by other students) this may not be possible. As a result, a new topic and type of Master Thesis may be assigned to students.

MODIFICATION – CHANGE OF THESIS TOPIC

Following the allocation of the Thesis topic, no modification is permitted without the prior submission of a well-substantiated application to the Committee of Master Theses of the respective Program, on condition that serious reasons for doing so apply.

DURATION OF THE THESIS

As a rule, the total duration of the execution of the Master Thesis is one (1) academic semester.

In the MSc Drug Biosciences and Pharmaceutical Development program the Master thesis is presented and submitted during the third semester. This can be extended up to 2 additional academic semesters. In this case, the student receives an "**I**" (Incomplete). If, after the end of the two subsequent semesters, the Master Thesis has not been completed, the student receives an "F" (Fail) and enrolls again for the course in the next semester in which it is offered.

The ECTS academic units for the declaration of the Thesis are granted to the student in one semester only, and specifically in the semester in which the Master Thesis is declared. In case of failure, the student must enroll again in the course and will be granted the ECTS units again. The student is also granted the credit units corresponding to the course.

ASSESSMENT OF THESIS

The final deadline for the submission of the Final Master Thesis for preliminary check is set at two weeks before the end of the normal duration of semester courses (Fall, Spring) and one week before the end of the normal duration of Summer semester, provided that the corrections in the various sections have been made during the supervision of the Master Thesis in the semester of execution. The process preceding the presentation is set out in the time frame below.

	Time frame	**Prior to the Presentation ***		
		Round 1	**Round 2**	**Round 3**
		Spring	Fall	Summer
1	Dispatch of Final Thesis by the student to the Supervisor	5 weeks	5 weeks	4 weeks
2	Dispatch of the Thesis back to the student and final corrections.	4 weeks	4 weeks	3 weeks
3	Submission of Thesis via the Blackboard Learn platform by the student	3 weeks	3 weeks	2 weeks
4	Corrections and marking by Members 2 and 3 (Professor in charge of the course plus one more member) and dispatch of comments and grade to the proposer and the professor in charge If members fail to send comments, this amounts to positive acceptance of the Thesis as is (without this releasing the members from the obligation to send a grade)	2 weeks	2 weeks	1 week

5	The student makes any changes and corrections to the Thesis based on the feedback and thereafter submits the final text to the proposer for purposes of final confirmation. If the student fails to make any changes / corrections / improvements, the supervisor may decide either to accept the Thesis as is or reject it with an F grade (Fail).	10 days	10 days	5 days
6	The Supervisor reads the final text, marks it and grants the student the final approval that the Thesis is ready.	7 days	7 days	3 days
7	The student completes the Thesis (if necessary) and submits it to Blackboard Learn for archiving.	5 days	5 days	2 days
8	The student proceeds to the oral defense of his/her Thesis.	Day of the presentation	Day of the presentation	Day of the presentation

* Public holidays are not taken into consideration in the above time frame.

As a rule, the Master Theses are presented in the week following the end of the final June examinations (for submission in the Spring Semester) or the week after the end of the final January examinations (for submission in the Fall Semester) or the week after the end of the final July examinations (for submission in the Summer Semester).

SUBMISSION OF THESIS FOR CORRECTIONS

In case the Master Thesis is not delivered within the set time frame, the process of assessment and presentation is postponed, automatically and without derogations, until the next academic semester (Fall, Spring or Summer), again subject to the set time frames.

The Master Thesis is delivered online (MS Word<20Mb file) and via the online platform Blackboard Learn. It is pointed out that the student can **in no case submit** the text in print form as this does not facilitate the follow-up of the corrections and comments, whilst resulting in unnecessary and needless financial cost.

The correction and marking of the single text of the Master Thesis by the members of the Committee will take place as follows:

i. **Member 1 (Chair of the Committee):** Within 1 week from receiving the Thesis.
ii. **Member 2 (Member):** Within 1 week from receiving the Thesis
iii. **Member 3 (Supervisor):** Within 2 days from receiving the Thesis.

The written text of the Master Thesis is corrected electronically using the "Review/Track Changes" option in MS Word where corrections are made and any

comments are inserted using the “New Comment” option. Once corrections are completed, the electronic file is forwarded by the Supervisor to the student for the necessary adjustments after explaining to him/her orally the full range of the corrections/remarks.

If the above time frame is respected, the preliminary corrections to the Thesis will have been completed precisely at the end of the exam period of the academic semester in question, and thereafter the student will be granted 10 days (in the Fall and Spring period) to make the corrections received in order to submit his/her text for marking to the proposer, and then proceed to the final submission via Blackboard Learn and to the oral defense of his/her Master Thesis.

PRESENTATION OF THE THESIS

Once the check has been completed and the Supervisor verifies that the modifications to the text have been made, the student prepares for the oral defense on the set date.

Theses which, according to the Committee of Master Theses of the MSc Drug Biosciences and Pharmaceutical Development program, do not satisfy the requirements for oral defense, will be returned to the Supervisor with comments and their defense will be postponed until the next period of presentations within the following academic semester, provided all requirements have been satisfied.

APPOINTMENT OF THREE-MEMBER ASSESSMENT COMMITTEE

The Committee of Master Theses of the MSc Blackboard Learn program appoints the Three-member Assessment Committees which comprise the Supervising Professor (as member) and 2 independent examiners from the program’s Faculty.

The assessment of the Master Thesis comprises two stages. The first one regards the assessment of the written text and is carried out before the presentation and the second regards the oral defense of the Thesis and is carried out at the time of the presentation. The marking forms are prepared by the supervisor together with the remuneration forms (for both Members) and are placed in the locker of the Professor in charge of the course for approval, who will in turn verify and send the student’s grade to the Secretariat.

MARKING OF THE THESIS

WRITTEN TEXT

The assessment and marking of the written text is a key prerequisite for the oral defense of the Master Thesis. Only when the Thesis is considered adequate, even with recommendations for minor corrections by the Three-member Assessment Committee and provided it receives a minimum pass grade (35/70), will the student be given permission to proceed to the oral defense of the Thesis. The written text of the Thesis is assessed using the “Review / Track Changes” option in MS Word, where corrections are made to the text, whilst any comments are inserted using the “New Comment” option. The assessment is based on clearly defined criteria laid down in the relevant form (see Annex page 38).

The grade assigned by each member of the Three-member Assessment Committee to the written text of the Master Thesis has a different weight and is allocated as follows:

i. **Member 1 (Chair of the Committee):** 30/70
ii. **Member 2:** 20/70
iii. **Member 3 (Supervisor):** 20/70

On completion of the assessment of the written text, the relevant marking forms are collected by the Proposer who brings them to the oral presentation for completion and signing. Three (3) working days before the oral presentation, the Committee of Master defense of the Thesis and makes all necessary arrangements (reservation of room, provision for electronic means and technical support). He/she then informs accordingly by email the members of the Three-member Assessment Committee and the student who, under the responsibility of his/her supervisor, has the obligation to post a relevant announcement on the Department's announcement board (see Annex page 37). The program of presentations of the Theses will also be posted on the page of the course on the Blackboard Learn platform under the responsibility of the Professor in charge of the course.

ORAL DEFENSE OF THE THESIS

The defense of the Master Thesis through an oral presentation by the student is carried out using "powerpoint" or a similar software program. The presentation takes place in a University room, as arranged by the Committee of Master Theses of the Program, and lasts **15-30 min**. After the presentation, students are examined by the Three-member Assessment Committee for not more than **20 min**. On completion of the examination, the Committee meets in the absence of the student to determine the final grade as it arises from the presentation, whilst making relevant comments/remarks on the presentation which are announced to the student forthwith.

The guidance and supervision of the preparation of the Thesis presentation by the student are part of the Supervisor's obligations. The process of presentation and examination of the Master Theses are open to the public and anyone wishing to attend is welcome to do so, but has no right to comment, unless the Chair of the Three-member Assessment Committee decides otherwise. In any case, comments made by the public follow the examination and marking by the members of the Three-member Assessment Committee and are therefore not taken into consideration in determining the grade. The oral defense of the Master Thesis is assessed based on clearly defined criteria laid down in the relevant form (see Annex page 39).

The grade assigned by each member of the Three-member Assessment Committee during the oral defense of the Thesis is of equal weight and is allocated as follows:

i. **Member 1 (Chair of the Committee):** 15/30
ii. **Member 2:** 7.5/30
iii. **Member 3 (Supervisor):** 7.5/30

Each member of the Three-member Assessment Committee must attend the defense of the Thesis, either as Proposer or as Examiner. In case the Proposer or the Chair of the Committee is prevented from attending, the Committee of Master Theses of the MSc Applied Dietetics and Nutrition program must be notified in writing at least 5 days prior to the date of the examination in order to be able to set a new date.

OUTCOME OF THE THESIS

The Three-member Assessment Committee of the Thesis assesses and accepts or rejects the student's Thesis in accordance with the criteria stated in the form of assessment of the written text (see Annex page 38). The Committee has the right:

- **i.** To accept the Thesis as is and proceed with the presentation;
- **ii.** To accept the Thesis after recommending to the student minor corrections and modifications, to be made in fixed short period of time (10 days) and checked by the Supervising Professor and proceed with the presentation;
- **iii.** Not to accept the Thesis as is, but recommend broad modifications and corrections. Once these are completed within a fixed period of time (30 days), the Thesis will be submitted again for defense and assessment by the same Committee, at a time set by the Committee of Master Theses of the Program;
- **iv.** Not to accept the Thesis, but recommend substantial modifications and improvements to be made within a fixed period of time (60 days), followed by a new submission for assessment by the same Committee;
- **v.** To reject the Thesis and consider that the student has failed the course ("F": Fail), in which case the student must repeat the process from the beginning.

ENTRY OF COURSE GRADE

SUBMISSION OF GRADE TO THE SECRETARIAT

Once the examination is complete, the Proposer places within 3 (three) working days in the locker of the Professor in charge of the course, the marking forms relating to the written text and the oral defense of the Thesis as well as the remuneration forms (Member A, Member B and Member C) for further processing.

ISSUANCE OF GRADE

On completion of the above process, it is considered that the student has fulfilled his/her obligations in relation to the course and therefore the Professor in charge checks and forwards the markings forms to the Secretariat for the issuance of the grade and the remuneration forms to the Chair of the Department.

DESCRIPTION OF THE STRUCTURE OF THE DIFFERENT TYPES OF THESES

TYPES AND LENGTH OF THESES

The Thesis may be in the form of a "**Systematic Review**", a "**Dry-lab Research Thesis**", or an experimental, "**Wet-lab Research Thesis**", all projects requiring the collection and processing of data. Although the choice to conduct wet-lab research is optional, students who select this type of work are required to be physically present on-site to conduct their experiments.

The length of the Thesis, which relates only to the Main Part of a Thesis is determined as follows:

1. **Systematic Review:**
   i. One person: 8,000 – 12,000 words.
   ii. Two persons: 12,000 – 16,000 words
2. **Research Thesis (Dry-lab or Wet-lab):**
   i. One person: 8,000 – 12,000 words.
   ii. Two persons: 12,000 – 16,000 words.

Once completed, the Thesis must respect the specific structure presented in detail below, depending on its type.

FINAL LAYOUT OF THESIS

Once the Thesis is completed and before its submission to the Supervisor for corrections, great care must be taken by students to ensure that it complies with the proper structure and development and is easy to read and accurate. The pagination of the Thesis must follow the order below:

Cover

Preliminary Pages

- Title Page
- Copyright Page
- Assignment of Copyright Page
  - **→given by the Professor in charge at the Blackboard Learn under the name Front_Pages.docx**
- Abstract
- Preface (optional)
  - Acknowledgements Section
  - Dedication Section
- Table of Contents, with reference pages
- List of Tables, with titles and reference page
- List of Figures, with titles and reference page
- List of Illustrations, with titles and reference page
- List of Photographs, with titles and reference page

Main Part of the Thesis

- Introduction Chapter

- Brief presentation of bibliography and articles
- Purpose
- Objectives
- Research and statistical hypotheses
- Key requirements
- Limitations
- Abbreviations
- Symbols

Methodology Chapter

- Research design
- Material (Location and time of conduct of the study, Sample, Tools)
- Data collection method
- Statistical analysis and processing of data (where applicable)
- Ethical issues

Results Chapter*

Discussion Chapter*

Conclusions Chapter*

Proposals

**Please note that these chapters can be presented in any way (e.g. as Results - Discussion chapter, Discussion - Conclusions chapter).*

Bibliography (referencing system of Harvard Anglia Ruskin University or National Library of Medicine - NML style)

Annexes (if any).

The following information should be included in the Thesis:

PRELIMINARY PAGES

COVER

The cover includes:

the logo of the University,

the School, the Department and the student's Program of Study,

the title of the Thesis,

the name of the student or students and their University registration number,

the name and title of the Supervising Professor,

the place where the thesis was conducted and the date of acceptance.

TITLE PAGE

The title page of the Thesis must contain the following:

The title of the Thesis, positioned in the centre, 5 cm from the top of the page. The title must be clear and concise and present the substance of the study pursued.

In case the Thesis is a bibliographical review, the two words "bibliographical review" must be stated at the end.

The name of the student, positioned in the centre, 2.5 cm under the title.

The following statement, inside full margins, positioned 2.5 cm under the author's name: Thesis submitted to the body of professors in partial fulfillment of the requirements for the Integrated Master of Pharmacy… (enter the respective name of the Program, e.g. Pharmacy) of the Department of Life Sciences, of the School of Sciences of European University Cyprus.

The following words are positioned in the lower half of the page, in the centre: Nicosia? 20… (The year on the title page must refer to the location where the study was conducted and the year of acceptance of the Thesis).

The following words are stated on the right: Approved by: …The names of the Three member Examining Committee are stated in the lines below.

COPYRIGHT PAGE

In case the student wishes to copyright the Thesis, the copyright page must be included, after the title page, with the following information written in the center, in the lower half of the page:

© Year, Full Name
ALL RIGHTS RESERVED

ASSIGNMENT OF COPYRIGHT PAGE

With this page, European University Cyprus is granted permission to use the Thesis for purposes of the University, as well as to print and make copies available to the public on a non-profit making basis, in case copies are not available in any other way.

ABSTRACT

The abstract follows the title page (and the copyright page, if any) and must be included in the Table of Contents.

The word "ABSTRACT" of the Thesis is typed in 1½ line spacing, Arial 12 font, in fully justified formatting. It is positioned centrally, at a distance of 5 (five) cm from the top of the page. It is followed by the name of the student and the title of the Thesis. In brackets, in the centre under the title, follows the phrase (Under the supervision of

_____) which states the name of the Supervising Professor. This is followed by an empty line and the text of the abstract, in 1½ line spacing. The abstract must be printed on one side of the page only and in one single paragraph. The margins of the abstract must comply with the relevant instructions stated in the Annex to this Guide. The abstract of the Thesis must not exceed 500 words. It is written in Greek and optionally in English.

The title of the abstract must follow the same formatting as that of the title page. In general, the inclusion of mathematical formulas, diagrams and illustrations in the abstract is avoided. The abstract is a brief description of the Thesis and must be accurate and comprehensive so as to reflect the purpose and the content of the research, whilst lengthy explanations and personal views must be avoided. Also, the abstract must be self-contained, i.e., it must describe all the parts of the research. The

abstract must help the reader understand in a few sentences what has been studied, the reason why it has been studied and the conclusions that arise. The abstract is structured and contains the following sections:

Introduction
Purpose
Methodology
Results
Conclusions.

At the end of the abstract the keywords are stated (up to 8), which offer a more general description of the Thesis topic. In the case of a review, the keywords do not refer to the keywords to be used in the bibliography search.

PREFACE

The preface follows the abstract and is typed in 1½ line spacing, Arial 12 font, in fully justified formatting. The heading is titled "PREFACE" and is positioned in the centre, 5 (five) cm from the top of the page. The preface is an *optional part* of the Thesis and consists in a general reference to what is included in each chapter of the Thesis in relation to the topic addressed. This part also contains separate pages for dedication and acknowledgments, if any.

TABLE OF CONTENTS

The table of contents follows the abstract (and the preface, if any). The heading is titled "TABLE OF CONTENTS" and is positioned in the centre, five (5) cm from the top of the page.

The table of contents must include all the parts of the Thesis, including the preliminary pages (title page, abstract, preface, copyright page, acknowledgments page, dedication page). In the table of contents, the preliminary pages are numbered in Latin numerals while the pages of the main part of the Thesis are numbered in Arabic numerals. It also includes the bibliography section and all the annexes to the Thesis.

If the Thesis contains sub-titles of one and/or more levels, these must be included in the table of contents. The sub-title(s) must begin in a paragraph 3 (three) to 5 (five) tabs to the right of the margin for the titles of the chapters. The titles set out in the table of contents referring to the various chapters must accurately reflect the titles of the chapters contained in the body of the Thesis.

The page numbers in the table of contents must be positioned in the right margin, while the empty space between the title or the sub-title and the page number must be covered by a straight continuous or dotted line.

The spacing between two chapters must be double, the sub-titles within a chapter must have a 1½ line spacing and if the reference to the corresponding sub-title extends to more than one line, it is interrupted at three quarters of the line and continues on the following line but with a single space.

LIST OF TABLES

Each table of the Thesis is defined with an Arabic numeral (for example Table 1, Table 2, etc.) or is defined with two parts of an Arabic numeral where the first digit refers to the chapter in which it is included, followed by a full stop, and the second digit indicates

its sequence in the chapter (for example Table 3.2 refers to the second table of the third chapter).

The heading for the list of tables must be positioned at a distance of 2.5 cm from the top of the page, in the centre, and the phrase “LIST OF TABLES” must be written in capitals. Between the heading and the first title there must be an empty line. The line spacing between the titles must be double.

The number of each table (Arabic) and its title must be positioned in the left margin. The numbers of the pages (Arabic) are positioned exactly inside the right margin. The space between the tab and the page number is covered with a stippled line. The space between the table and its title is single while the space between the titles is double. If the title requires more than one line, this is interrupted at three quarters and continues below on a second line, with a single space. The number of the table and its title in the list of tables must accurately reflect those contained in the body of the Thesis.

LIST OF FIGURES

The heading for the list of figures must be positioned at a distance of 2.5 cm from the top of the page, in the centre, and the phrase “LIST OF FIGURES” must be written in capitals. The instructions set out above on the list of tables also apply to the list of figures.

LIST OF ILLUSTRATIONS

The heading for the list of illustrations must be positioned at a distance of 2.5 cm from the top of the page, in the centre, and the phrase “LIST OF ILLUSTRATIONS” must be written in capitals. The instructions set out above on the list of tables also apply to the list of illustrations.

LIST OF PHOTOGRAPHS

The heading for the list of photographs must be positioned at a distance of 2.5 cm from the top of the page, in the centre, and the phrase “LIST OF PHOTOGRAPHS” must be written in capitals. The instructions given above on the list of tables also apply to the list of photographs.

RESEARCH TYPE THESIS
(DRY LAB OR WET LAB)

MAIN PART

The main part of the Thesis is typed in 1½ line spacing, Arial 12 font, in fully justified formatting. It must include the following sections.

INTRODUCTION

The text begins with the word "Introduction" and the title of the research as title of the first chapter written in bold letters. In the introduction, the student guides the reader towards an understanding of the topic, taking a shortcut. This chapter describes sufficiently any information regarding the topic and acquaints and prepares the reader for the more clarifying information that will follow in the main body of the Thesis. More specifically, the Introduction presents the problem whose resolution will be later attempted through the research, presents the purpose, the specific objectives, the research hypotheses (if any), states the requirements, the boundaries and the limitations of the research, which may be related to the sampling, the research design, the tools used for the collection of the data and, in general, the adopted methodology which may affect the generalization of the results. Finally, it sets out the functional definitions and explains the abbreviations and symbols (where necessary).

In brief, the Introduction:

- Presents the problem and the research approach;
- Provides a sufficient overview and presentation of the bibliography related to the problem**;
- States the most relevant research on the topic of the Thesis;
- Refers to the importance of the research;
- Presents the purpose of the research;
- Accurately states, in 4-5 lines, the objectives of the specific research;
- Sets out the research and null hypotheses of the research (applies primarily to wet-lab studies),
- States the key requirements, the limitations and the boundaries of the research;
- Also states the theoretical and functional definitions of key terms;
- Finally, it sets out the abbreviations and explains the symbols which may be included in the Thesis.

**The review of the bibliography includes an extensive reference to relevant contemporary bibliography. The number of bibliography sources analyzed in the Introduction chapter varies depending on the type of the Thesis as follows:

i. **Research Thesis**: ≥ 12 - 17 (1 person) - ≥ 20 - 28 (2 persons) primary research sources.

It is noted that the above sources **do not include the material deriving from secondary sources** (books, review articles) usually used to present basic knowledge, e.g., anatomical information, physiological information, etc.

The bibliography review of original papers represents a complex mental processing of primary data and its usefulness lies in the ability to inform the student on recent

research developments in his/her field of study and enhance pre-existing knowledge related to the theory and exercise of evidence-based practice. Through the bibliography and article review, the student is called to study and analyze all contemporary developments on the topic under investigation, present comparisons and differences between them and recompose the existing knowledge, in order to present an original written work which will bear his/her personal stamp. In essence, a bibliography review is a form of organising information on a subject area, of systematic recording and drawing conclusions.

During the introductory bibliography review, special care must be taken to focus on the topic under investigation and limit the inclusion of studies with more general conclusions. In analyzing bibliography sources, insignificant details must be avoided whilst emphasis must be given to the relevant findings, the relevant methodological issues and the most important conclusions. The progression of the text follows a logical sequence between the older and more recent research, as well as between research with a different theoretical and conceptual basis. The problem is developed in such a way that it can be understood by the broader scientific public and not only by experts in the field under investigation. It is desirable to approach the research in question from a critical point of view and to address controversial conclusions fairly.

Primary sources must be analyzed extensively (whilst secondary sources are only listed), in stand-alone paragraphs of approximately 8-12 lines, forming part of homogeneous sections. The stand-alone descriptions of the experimental research must be linked between them and, at the end of each section, a critical summary of the conclusions arising therefrom must be set out.

In particular, the development and presentation of the primary sources must take into consideration the following:

Recording of information in chronological order
Classification based on their thematic sections
Classification based on the year's publication
Classification based on convergent or divergent views.

It is noted in particular that:

- The evidence set out must be valid and supported by evidence-based research.
- Information is strictly selected based on its relevance to the topic and publications of questionable origin and information from research involving corporate interests etc. are not included.
- Quotation marks must be used whenever information is copied or set out verbatim or paraphrased, although it is recommended that the student carries out the processing and systematic synthesizing of the information himself/herself. In case a piece of information is paraphrased, the student must be absolutely certain that he/she has reproduced precisely what the researcher meant in the relevant work.
- The third person must compulsorily be used in developing the texts. Nouns should not become subjects (for example instead of the phrase "the study showed that…." It is preferable to say "it was shown by the study that….").
- In all types of research, the bibliography review is written in the past tense.
- Both genders must be used (for example "he/she").

- Each section begins with a brief presentation of the topic to follow and ends with a summary of the information previously presented, focusing on the most important points.

METHODOLOGY

The title of the chapter is written in the middle of the page. The text begins below with a tab and usually includes the following sub-chapters which are written in small bold and italic letters, using one tab, and justified to the left. In this part, the student justifies his/her decisions relating to the methodology used and also states how he/she has addressed ethical issues of concern in the execution of the Thesis (permission from the Department's Committee of Ethics and Morals, permission from specific services, consent of participants in the research).

This part states the criteria and the mode of selection of the sample, the means and the equipment used, the procedures and the method followed and the statistical analysis. A detailed description allows other scholars-researchers to understand the entire process, verify the results and reproduce them if they wish.

Research design

The research design used in the Thesis, e.g., correlation study or prospective study or "patients-controls" study or randomized, experimental double-blind study is stated.

Material

a) Location and Time of conduct of the study

Brief description of the characteristics of the location of the study, its accessibility and the time of conduct. In case the study was conducted in a General Hospital, reference must be made to the necessary approvals obtained from the Research Promotion Committee of the Ministry of Health.

b) Participants sample

Sampling strategy and sample size, method of approach and process of informed consent. Criteria of inclusion in the protocol and exclusion from the study.

c) Tools

Description of tools used for measuring the variables (e.g., questionnaires, scales, lab equipment), justification and psychometric characteristics. Reference to the empirical evidence of their validity and reliability.

Data collection method

Brief but accurate description of all the procedures followed from the beginning of the study until the completion of data collection.

Statistical analysis and data processing (where applicable)

Brief but accurate description of the statistical tests used with reference to the specific hypotheses and/or research questions.

Ethical issues

After the end of the methodology, it is very important to state how the rights and anonymity of the subjects will be protected as well as the process of their written consent. In case the study required approval in terms of bioethical issues, the authority which has granted the approval must be mentioned (e.g., National

Bioethics Committee, Office of the Commissioner for Personal Data Protection).

RESULTS

The title is positioned in the center of the page like in the previous chapters. The results are then classified and written in a clear and comprehensible manner. Graphs, summary tables and mathematical formulas are set out in all detail. The illustration of a statistically or non-statistically significant difference allows the person studying the Thesis to identify what is being addressed. When the presentation of the results includes tables, the word "Table", justified to the left and in bold letters, must appear above the table, e.g., **Table 3.1**, followed by the title of the table (not in bold). In the case of figures, there must be a sub-title under the illustration, justified to the left, indicating the number of the figure and its explanation, e.g., **Figure 3.1** Blood pressure variation rates following the administration of hypertension medication. Illustrations are marked in the same way as the figures. **Attention:** Both the text and the tables / figures / illustrations must be understandable to the reader and present the finding that you consider important. For this reason, the text must describe every table / figure / illustration and its main finding. On the other hand, each table / figure / illustration must be presented in such a way that the text is not necessary in order for the reader to be fully informed. In other words, the title must be self-explanatory, and the structure and content must be understandable. Therefore, if a reader does not read the text, he/she should be able to understand the main finding from the table / figure / illustration alone. The table / figure / illustration is used when they serve the scientific presentation of the results, otherwise their use is not meaningful. It is also possible to set out the annexes at the end of the Thesis, if the tables or the graphs take up a lot of space in the flow of the text.

More specifically, this chapter includes the following:

- **i.** Presentation of the demographic characteristics of the sample (e.g. gender, age, educational level) in a table and description thereof within the text.
- **ii.** Description of the statistical analyses for each one of the null hypotheses (e.g. the ANOVA analysis of variance was used to reject or accept null hypothesis No. 3).
- **iii.** Presentation of the statistical results. In case the results of statistical tests are presented (e.g. t-test for independent samples, ANOVA test, χ^2 test) the reader must be provided with the relevant information on the degree or value of the statistical test, the degrees of freedom and the level of statistical significance. For example, the results of the ANOVA statistical test are presented in the text ι as follows: $F_{(5,150)}= 5.75$, $p>0.05$. If a table presents evidence of a statistical analysis, the necessary statistical evidence must be set out under the table so that the reader can assess the test used. Tables of results from a statistical package are not acceptable for presentation in your Thesis unless they are properly processed. The appropriate results from these tables must be collected and presented in a new table written in Greek, which must bear an explanatory title and its structure and content must be understandable to the reader.

DISCUSSION

This chapter examines, interprets and classifies the results and sets out in brief the main results. Particular emphasis is given to the theoretical repercussions of the results, but also to the validity of the conclusions. The discussion begins with a rewording of the purpose of the research and the research hypotheses, whilst stating clearly whether the results support the original hypotheses or not. Then follows a description of how the data support the answer(s) to the research question(s). Any similarities or differences between the results and other research clarify and confirm the conclusions. By comparing the findings of this study with those of other researchers, new and important elements are highlighted. The strengths and limitations of the study are presented (based on the methodology followed). The section ends with a clear statement (for example the consequences of the findings of the research) or with reflections based on the answer(s) to the research hypothesis(es).

CONCLUSIONS

The title is positioned in the middle of the page and the following must be included:

- **I.** One conclusion for each hypothesis.
- **II.** A brief correlation of the results with the results of other research.
- **III.** Recommendations for practical implementation.
- **IV.** Recommendations for future research.

RECOMMENDATIONS

The recommendations identify omissions, record deficiencies, suggest ideas, set out both the weak and firm views of the review whilst also recommending new aspects for investigation arising from the findings of the research approach which has been applied.

BIBLIOGRAPHY LIST

It sets out the list of bibliographical references used in drafting the Thesis in accordance with the referencing system of Harvard Anglia Ruskin University or of the Library of Medicine - NML style.

SYSTEMATIC REVIEW THESIS

MAIN PART

The main part of the Thesis is typed in 1½ line spacing, Arial 12 font, in fully justified formatting. It must include the following sections:

Title (up to 20 words)

The title must be clear and concise and present the substance of the study pursued. The words "systematic review" are stated at the end.

Abstract (200-300 words)

The abstract of your Thesis must help the reader understand in a few sentences what you have studied, the reason you have studied it and the conclusions you have reached. The abstract is structured and contains the following sections: **Introduction, Purpose, Methodology, Results, Conclusions**. At the end of the abstract the keywords are stated (up to 8), offering a more general description of the topic of the Thesis. The keywords do not refer to the keywords to be used in the bibliography search.

Introduction

i. Theoretical background

The topic is presented based on international bibliography. Also, relevant definitions are briefly described, concepts are clarified and epidemiological evidence is presented (where applicable).

ii. Existing knowledge

Describe what is generally known for the topic to date from studies in the bibliography, without going into great detail and without merely listing articles. An effort must be made to group conclusions of previous studies (primary and mandatorily of reviews {if any}), referring to the corresponding articles of the researchers. (The concealment of bibliographical reviews, whether deliberate or not, is considered to be an inappropriate approach and the topic automatically becomes a bibliographical review).

iii. Description of the problem

The need to conduct a systematic review of the research bibliography on the specific topic is explained (e.g., summary of existing scientific knowledge, identification of contradictions or gaps in the bibliography, absence of guidelines).

iv. Purpose and specific objectives

The purpose and specific objectives of the systematic review are clearly stated.

v. Enhancement of existing knowledge – Added value and benefit

State why this study is important for the specific population, how it will contribute with new knowledge to the promotion of the discipline, its significance for the practice and/or theory of the discipline with special reference to the specific subject area of the Program of Studies for which the Thesis is conducted.

Methodology

In this section you will describe the method and the means you have used to achieve the purpose and objectives of your study.

i. Description of search strategy

You will describe the search strategy, in other words you will mention:

a) All the databases in which you have searched for the articles;

b) The keywords you have used in your search, as well as their combination.

Your search strategy must be presented in a table for all the databases (see relevant example in page 27, Table 1).

ii. Study inclusion – exclusion criteria

State the inclusion or exclusion criteria of a study from the review with detailed references.

iii. Final selection of studies to be included in the systematic review

State the number of studies which have been checked and verified in terms of the fulfillment of the inclusion criteria in each stage, as well as the final number of studies included in the review. It would also be appropriate to briefly justify the reasons for which the studies were excluded from the review. This information will be presented in brief in a flow chart (see example in page 28 Illustration 1).

iv. Assessment of the quality of the studies (compulsory)

The quality of the information provided by the studies included in the review is assessed. This can usually be done with the assignment of a quality score for each separate study. In this case, state the scale of the quality score used in the assessment of the studies (depending on the Program). The scale of the quality score can be based on the following information regarding the study:

1) Selection of the study population and sample;
2) Method of design of the study;
3) Participation and duration of follow-up (repeat tests for prospective studies);
4) Method of assessing the exposure;
5) Method of determining the outcome;
6) Adjustments during the analysis.

Use the past tense when referring to the methodology you have followed for conducting the study as well as to your results.

Results

This section includes a presentation of the results of the research studies which have been reviewed. We usually begin with a general description of the search results.

In general, the results must include the following:

i. One table divided in sections (and/or more sections depending on the thematic presentation), presenting in brief and usually in chronological order, the main characteristics of the studies (e.g., year of publication and country of conduct, type of

the study, population – characteristics of participants, assessment of exposure and outcome, key findings, etc.) described in detail in the text (see example in page 29 Table 2).

ii. Detailed presentation and description of the studies in the text, attempting a combination of indications from different research. This can be done after grouping research results or types of studies.

iii. The structure of the text in sections is always done based on the research question and the various specific issues, whilst each section begins with an introductory sentence and ends with a conclusion.

iv. The methodological quality of each study is assessed separately based on criteria set with the use of an assessment scale which assigns a quality score to each study. This information can be presented in brief in a table setting out the score of the methodological quality of the studies (see example in page 30 Table 3).

It must be perfectly clear which of the studies were used in previous reviews, in order to highlight the work done by the student himself/herself.

Discussion

This section begins with a summary of the key findings, followed by comments, comparisons and interpretations of the results of the studies reviewed. In drawing conclusions, important issues that may relate to methodological problems of the research, contradictions in the findings and gaps that may have been identified, are addressed. The presentation can, again, be on a thematic basis, with regard to the main issues that require attention. It is noted that, contrary to the previous chapter where references are limited to the studies included in the review, here we can extend to related matters to substantiate views, positions and conclusions, with references to the broader international and Greek bibliography, giving examples of research and other studies not included in the review. This section sets out the strengths and limitations of the Thesis.

Conclusions

In general, conclusions include the following:

i. Research conclusions
ii. Significance for your discipline
iii. Orientation for future research, practice, dissemination of the results, information, health policy, clinical orientations.

Bibliography

Bibliography forms an integral part of the Thesis. It sets out the list of bibliographical references which have been used in writing the Thesis in accordance with the referencing system of Harvard Anglia Ruskin University or the National Library of Medicine – NLM style.

Table 1: Search strategy and keywords used in the identification of studies investigating the relationship between central obesity and dementia.

	Keywords	**Database 1**	**Database 2 etc.**
Central obesity – Exposure	1. central obes*		
	18. abdominal obes*		
	19. waist circumference		
	20. waist to hip ratio		
	21. waist-to-hip		
	22. waist-to-hip-ratio		
	23. WHR		
	24. Sagittal Abdominal Diameter		
25. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8			
Dementia – Outcome	**26.** Alzheimer's disease		
	11. Alzheimer disease		
	12. vascular dementia		
	13. dementia		
14. **#10 OR #11 OR #12 OR #13**			
Research design of the study	15. cohort		
	16. prospective		
	17. longitudinal		
	18. follow-up		
	19. incidence		
	20. risk		
	21. rate		
22. **#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21**			
24. **#9 AND # 14 AND # 22**			
Total			

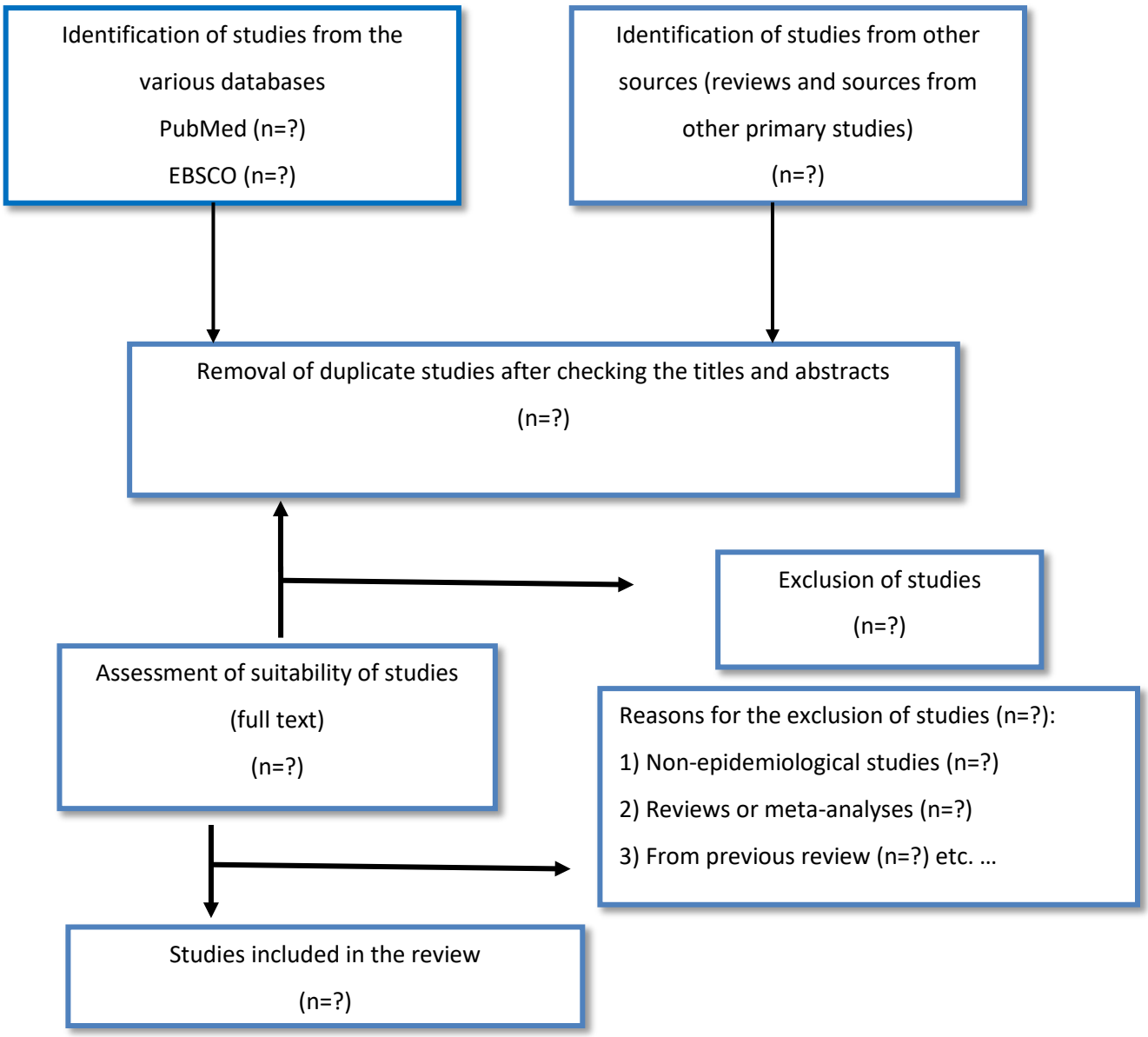

Illustration 1: Diagram illustration of the flow of results of the systematic search

Table 2: Characteristics of studies

STUDY	COUNTRY	STUDY POPULATION NUMBER (N) GENDER (G) AGE (A) Characteristics (Char.)	TYPE OF INTERVENTION	INTERVENTION SETTING (HOSPITAL, INSTITUTION, WORKPLACE)	DURATION	EFFICACY	
						CLINICAL SYMPTOMS	NEUROPHYSIO-LOGICAL PARAMETRES
Harter, et al. (1992) Retrospective study	USA	N: 265 G: 43%M / 57%F (114F / 151A) A (median and range: 45 yrs (20-90) S:49 yrs (median) C:42 yrs (median)	Surgery (77) (95 wrists) Vs Conservative treatment with various interventions[1] (188)	N/A	54 months	S: Yes C: Yes[2]	S: Yes C: We don't know
Seror (1992) Prospective observational study	France	N: 125 wrists G: S: 76%F / 24%M C:81%F / 19%M N.T: 79%F / 21%M A (median and range) in years: S: 57,5 (30-88) C: 58,6 (28-87) N.T.: 57,6 (28-87) Char.: Duration of symptoms (months) S: 23,3 C: 22,9 N.T.: 20,9	Surgery (33 wrists) Vs 1-3 doses of steroid injections (56 wrists) Vs No treatment (N.T.) (36 wrists)	Investigation laboratory	52 months	N/A	S: Yes C: No N.T.: slow deterioration

S= Surgical intervention, C= Conservative treatment, N.T.= No treatment, N/A= Not Stated

Table 3: Methodological quality score of the studies under review***

Study	Selection				Comparability		Result			Total
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	
Anderson, Johnson & Batal, 2005	*	*	-	*	*	-	*	*	*	**7**
MacDorman et al. 1997 (a)	*	*	-	*	-	*	*	*	*	**7**
MacDorman et al. 1997 (b)	*	*	-	*	-	*	*	*	*	**7**
Malloy Hoffman & Peterson, 1992	*	*	*	*	*	*	*	*	*	**9**
Pollack, 2001	*	*	*	*	*	*	*	*	*	**9**
Schellscheidt, Oyen & Jorch, 1997	*	*	-	*	-	-	*	*	*	**6**
Shah, Sullivan & Carter, 2006	*	*	-	*	*	*	*	*	*	**8**
Wisborg et al. 2000	-	*	*	*	-	*	*	*	*	**7**

Notes: 1. Representative sample of exposure, 2. Selection of non-exposed, 3. Ascertainment of exposure, 4. The outcome did not exist prior to the commencement of the study, 5. Adjustment for educational level, 6. Adjustment for additional (secondary) confounding factor, 7. Assessment of exposure, 8. Adequate follow-up time, 9. Non-attrition bias.

***Other methods of assessment can also be used depending on the Program of Studies. (Vantulder, Pedro, Furlan, Jadad, etc.).

GENERAL INSTRUCTIONS ON TEXT FORMATTING

TITLES OF CHAPTERS, SUB-CHAPTERS AND SECTIONS

It is advisable not to number the chapters and sub-chapters of the Thesis, but to escalate them based on the position and the way the headings are written, in the following order:

TITLE OF CHAPTER: In bold capital letters (e.g., METHOD, RESULTS, etc.); centrally justified; followed by an empty line.

Title of Sub-chapter: Bold, Italics, to the left, one tab in (e.g., Measurement Process). The text begins on the following line.

Title of Section: To the left, one tab in, italics (e.g., Test 1). The text begins after this title (on the same line).

NUMBERING

In case you need to use numbering in the text, this will be done first by using letters, e.g. a), b) etc. If each of these "a)"s and "b)"s must be further numbered, this will be done using numbers "1)", "2)", and if within these numbers, further numbering must be inserted then use Latin numbers. i.e., "i)", "ii)".

LETTER FONT

The letter font must be legible (Arial 12) and the contrast between the ink and the paper in the final printed text must be significant in order to ensure a clear and legible printout. Also, the spacing between the letters of the words must be adequate. Similarly, line spacing must also be adequate (1.5 spacing). The main text must be written in font 12 while the footnotes must be no more than two numbers smaller than the font used in the main text and can also be single-spaced.

UNDERLININGS

To underline, use one single continuous line, which must be the same throughout the text.

PHOTOGRAPHS AND ILLUSTRATIONS

The photographs and illustrations used in the Thesis must be of satisfactory quality, but not large in size, e.g., more than 200KB each.

MARGINS

In order to avoid problems after the book-binding, all the copies and the original of the Thesis must have the following margins:

I. Left

All the margins of the Thesis, from the first to the last page, must be at least 3 (three) cm. This margin allows enough space for book-binding.

II. Right

All the right margins must be at least 2.5 (two and a half) cm.

III. Bottom

The bottom margin must be at least 2.5 (two and a half) cm.

IV. Top

The top margin must be at least 2.5 (two and a half) cm, including the following pages: Copyright, Lists of Tables, Figures, Illustrations, Photographs, Bibliography, Annexes. The only exceptions (to the 2.5 margin) are the Title Page, the Abstract, the first page of the Preface (if any), the first page of the Table of Contents and the first page of each Chapter (including the Introduction), which must begin 5 cm from the top.

PRINTING, SPACING AND INDENTS

The Thesis must be printed only on one side of each page and the main text must be fully justified on each page. The spacing must be 1½ (one and a half), except in the case of references, notes, chapter titles, sub-titles and large headings, which will be single-spaced with an empty line between the topics. Paragraph indents must have five to ten spaces throughout the Thesis. References must have a distance of at least four spaces from the left and the right margin. The indent of the first row of a separate paragraph must have a minimum distance of four spaces.

PAGINATION

Each page of the Thesis must correspond to one number. The first page on which a number will appear will be page “ii” (Copyright page). The title page is deemed to be page “I” but it has no number. Arabic numerals (1, 2, 3, etc.) are used to number the rest of the pages of the text, illustrations, annexes, notes, list of references or bibliography. Page numbers must not appear on the first page of the main text or the first page of each new chapter. Numbers containing letters, hyphens, periods or parentheses [for example 1a, 1-2, -1-, I., and (I)] are avoided. The positioning of the page numbers must be the same throughout the Thesis, including the introduction, the text, the annexes and the bibliography. Given that the text is printed on one side only, page numbers must be positioned in one of the following three ways:

i. On the top right corner of the page, 3 (three) cm (4 lines) from the top and 2.5 (two and a half) cm from the right end.
ii. On the bottom in the centre, 3 (three) cm (4 lines) from the bottom of the page.
iii. As close to the positions described in i or ii as the word processor allows.

OTHER PROVISIONS

COPYRIGHT

The copyright of the Thesis belongs to the student and the Supervisor as they are the ones who have contributed to its execution. In case the material of the Thesis will be announced at a conference, the first name to appear will be that of the person giving the speech. In case the material of the Thesis is published in a journal, the author first named is the person who has the main responsibility for drafting the article and responding to any questions of the journal's editorial committee In any event, none of the copyright holders will undertake any publication activities without informing and involving his/her associate.

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BIOETHICAL ASSESSMENT OF RESEARCH THESIS

In the case of a research Thesis (clinical trials, case study, questionnaires, etc.), the student has the obligation, in collaboration with his/her supervisor, to submit an application to the University's Committee of Ethics and Morals for guidance / advice on the further steps until the submission of the complete research proposal to the National Bioethics Committee of the Republic of Cyprus, as determined in the relevant legislation. The collection of data and the remaining experimental procedures can only begin once the official approval of the National Bioethics Committee has been obtained.

AVOIDANCE OF PLAGIARISM

Both the student and his/her Supervisor must take all necessary measures to strictly avoid plagiarism, which is a serious academic but also criminal offence. Plagiarism is defined as the reproduction of verbatim texts or the paraphrasing of sections either from papers drafted by others or from books or scientific articles, without using quotation marks and references and without mention of the authors of the primary source. The Supervisor must thoroughly check the student's Thesis for phenomena of plagiarism and in case such phenomena are observed, the student is initially referred to the Department's Committee of Theses which drafts a relevant report. In this case, the student fails the course and the provisions laid down in the University's statute take effect.

ANNEX

European University Cyprus

SCHOOL OF SCIENCES
DEPARTMENT OF LIFE SCIENCES

MASTER THESIS

APPLICATION FOR DECLARATION OF THESIS TOPICS

NAME OF STUDENT	
REGISTRATION NO.	
PROGRAM OF STUDY	

DECLARATION OF TOPICS

1.	
TOPIC NO.	
TITLE	
2.	
TOPIC NO.	
TITLE	
3.	
TOPIC NO.	
TITLE	
4.	
TOPIC NO.	
TITLE	
5.	
TOPIC NO.	
TITLE	

Date: _____ Signature: _____

For Official Use

Application received on: _____

Decision of the Committee of Master Theses

Approval of Topic No.: _____

Supervising Professor: _____

Re-submission of Topic: Yes ____ No ____

European University Cyprus

SCHOOL OF SCIENCES
DEPARTMENT OF LIFE SCIENCES

MASTER THESIS

APPLICATION TO CHANGE THESIS TITLE

Student Name	
Registration Number	
Program of Study	

Current title

Title Number	
Title	

New title

Title Number	
Title	

Justification

(continue at back of page if needed)

Date: _____ Signature: _____

For Departmental Use

Date Application Received*:* _____

Decision of Master Thesis Committee

Approval of new title numbered: _____

Supervisor: _____

Re-submission of title: Yes____ No____

European University Cyprus

SCHOOL OF SCIENCES
DEPARTMENT OF LIFE SCIENCES

MASTER THESIS

APPLICATION TO CHANGE SUPERVISOR

Student Name	
Registration Number	
Program of Study	

Current title

Title Number	
Title	
Supervisor	

Justification

(continue at back of page if needed)

Date: _____ Signature: _____

For Departmental Use

Date Application Received: _____

Decision of Master Thesis Committee

Approval of new title numbered: _____

Supervisor: _____

Re-submission of title: Yes____ No____

European University Cyprus

SCHOOL OF SCIENCES
DEPARTMENT OF LIFE SCIENCES

ANNOUNCEMENT OF PUBLIC PRESENTATION AND EXAMINATION OF MASTER THESIS

Student Name	
Registration Number	
Program of Study	

TOPIC OF MASTER THESIS

TITLE	
SUPERVISOR	

Presentation Date: _____

Time: _____

Room: _____

WRITTEN TEXT ASSESSMENT CRITERIA

EUROPEAN UNIVERSITY CYPRUS

School of Sciences
Department of Life Sciences
Program of Pharmacy

THESIS ASSESSMENT

Name of student: …… Registration No.: ……..

Topic of Thesis:

Chair of the Committee
Member 1:

Scale of Assessment of Written Study

	ASSESSMENT CRITERIA	Grade*		
		Chair (30%)	**Member 2** (20%)	**Member 3** (20%)
1	Method and completeness in addressing the topic *Comments:*			
2	Organisation of material *Comments:*			
3	Documentation of information and data *Comments:*			
4	Originality of topic – inspiration *Comments:*			
5	Scientific background (correct terms and concepts) *Comments:*			
6	Thesis layout *Comments:*			
7	Language, spelling, correlation of concepts, clarity of written language *Comments:*			
8	Completeness and recording of bibliography *Comments:*			
***Attention**: Each assessor assesses each criterion out of 100%. Normalization is performed automatically using mathematical formulas.	**Total**			
Date 12/12/2022	**Grade of written text**			
The three-member Assessment Committee	**Final grade of Thesis**			

The three-member Assessment Committee

Chair of the Committee Signature:
Member 2 Signature:
Member 3 Signature:

ORAL PRESENTATION ASSESSMENT CRITERIA

EUROPEAN UNIVERSITY CYPRUS

School of Sciences
Department of Life Sciences
Program of Pharmacy

THESIS ASSESSMENT

Name of student: ……

Registration No.: ……..

Topic of Thesis:

Chair of the Committee
Member 1:

Scale of Assessment of Oral Presentation of Study

	ASSESSMENT CRITERIA	Grade*		
		Chair (15%)	**Member 2** (7.5%)	**Member 3** (7.5%)
1	Method and completeness in addressing the topic *Comments:*			
2	Documentation of information and data *Comments:*			
3	Originality of topic – inspiration *Comments:*			
4	Knowledge and assimilation of the topic *Comments:*			
5	Scientific background (correct terms and concepts) *Comments:*			
6	Organisation of material *Comments:*			
7	Time management *Comments:*			
8	Quality of oral communication *Comments:*			
***Attention**: Each assessor assesses each criterion out of 100%. Normalization is performed automatically using mathematical formulas.				
	Total			
Date 12/12/2022	**Grade of oral presentation**			
The three-member Assessment Committee	**Final grade of Thesis**			

The three-member Assessment Committee

Chair of the Committee	Member 2	Member 3
Signature:	Signature:	Signature:

European University Cyprus

DECLARATION OF ASSIGNMENT OF THESIS RIGHTS

NAME OF STUDENT	
REGISTRATION NO.	
PROGRAM OF STUDY	
TITLE OF THESIS	

I, the aforementioned student, unreservedly declare that this Thesis is the product of my own exclusive effort and work, save where the text includes references to other authors, and that it has not been submitted elsewhere as part of any academic requirement or other purposes.

In the framework of the assessment of the Thesis, I have no objection whatsoever to the following:

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- Provision of the electronic file of the Thesis to a competent service for purposes of establishing the offence of plagiarism and the preservation of a copy in the records of the relevant service for purposes of future consideration of the offence of plagiarism.

I hereby declare that I have thoroughly studied, understood and fully complied with the internal regulations of European University Cyprus regarding Academic Ethics, Morals and Student Discipline.

Date: _____

DECLARATION OF ASSIGNMENT OF COPYRIGHT BY THE THREE-MEMBER COMMITTEE

We hereby declare that this Thesis has been conducted under our supervision and guidance and relates to original work. We have no objection to the assignment of the copyright of the Thesis to European University Cyprus as detailed above.

Capacity of Member of the Assessment Committee	**Chair**	**Member 2**	**Member 3**
Electronic signature			
Name			
Date	/ /	/ /	/ /

METHODOLOGICAL APPROACH TO SYSTEMATIC REVIEWS

DEFINITION OF SYSTEMATIC REVIEW

A systematic review is defined as the process of review of the indications (exhibits) in available research bibliography in connection with a clearly formulated research question, using a systematic and well-defined methodological process. This process aims to identify, select and assess appropriate primary research studies, but also record and analyze the data of the studies to be included in the review.

STAGES LEADING TO THE COMPLETION OF A SYSTEMATIC REVIEW

i. FORMULATION OF A RESEARCH QUESTION

The most important step of a systematic review is the clear formulation of a research question regarding the relationship between the identifier to be studied and the frequency of appearance of an outcome in a given population. It is also very helpful to accurately define the method of measuring both the identifier to be studied and the outcome.

ii. ESTABLISHMENT OF THE INCLUSION AND EXCLUSION CRITERIA OF A STUDY

The establishment of the inclusion or exclusion criteria of a study is another key step in the review. These criteria may be specific, such as the type or types of studies to be researched (e.g. intervention studies, cross-sectional studies, epidemiological prospective studies, qualitative studies with the use of a standardized questionnaire), the characteristics of the participants (e.g. specific age groups), the place of conduct of the study (e.g. community, school, hospital), the types of intervention (e.g. training programme), the outcome variables, but also general, such as the language of publication (e.g. publications only in English and Greek), time frame (e.g. studies conducted over the last decade), country of origin (e.g. European or other economically developed countries). The criteria must be selected carefully so that the articles are not too general, resulting in a multitude of information, or too specific, therefore missing important research work.

iii. BIBLIOGRAPHY SEARCH

This stage defines the search strategy (where and how to look) and includes an extensive bibliography review in all relevant sources (this is mostly done in selected online bibliography reference databases) in order to find appropriate studies, whilst an analytical algorithm of the keyword combinations (and synonymous phrases) used in the search must be maintained. The main online databases where a bibliography search may be conducted are Medline, Scopus, Embase, ISI web of science, Cinahl. A search may also be conducted in records of conference abstracts, of private and state research organizations, as well as of pharmaceutical companies.

iv. SELECTION OF STUDIES

In this stage, the studies are examined and it is decided whether they satisfy the inclusion – exclusion criteria. Some studies are rejected immediately upon reading the titles and abstracts, while for some others we must first find and read the full text, before we can decide whether or not to include them. The number of studies checked and assessed for completeness of the inclusion criteria in each stage, as well as the final number of studies included in the review can be presented in a flow chart (page 43, Illustration 2). This flow chart can also justify, in brief, the reasons for which studies have been excluded from the review.

v. RECORDING OF THE MAIN CHARACTERISTICS OF THE STUDIES

The main characteristics of the studies to be included in the review are identified and briefly described in a table (e.g., page 44, Table 4). Depending on the research question, the table may include for each research the details of the researchers, the year of publication, the size of the sample and its characteristics (e.g. age and gender), the type and methodology of the study, the type of intervention, the type of exposure and outcome, the key findings, etc. In case of missing data in some studies, an effort is made to contact the researchers in order to try and obtain the relevant information.

vi. ASSESSMENT OF THE METHODOLOGICAL QUALITY OF THE STUDIES

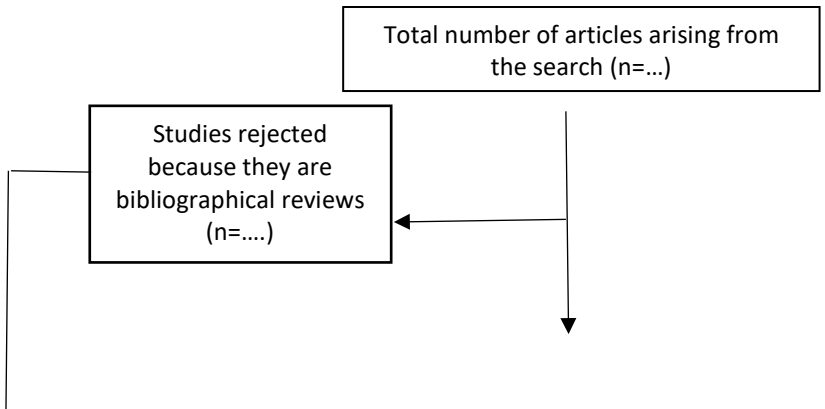
This process includes the assessment of the methodological quality of each separate study based on set criteria which depend on the type of the study included in the review (e.g. for randomized controlled studies some of these criteria may be the random allocation of treatment measures, the concealment of allocation, the blinding of participants, whilst for cohort studies criteria may include the ascertainment of exposure, the representativeness of the exposed cohort, the adequacy of follow-up cohorts, etc. The criteria are usually set out in a list, stating which of them are satisfied in each study. This information can be briefly presented in a table such as Table 5 (page 44), which shows the results of the assessment of the methodological quality of randomised controlled studies.

vii. SUMMARY OF THE INDICATIONS (EXHIBITS) AND INTERPRETATION OF THE RESULTS

This stage includes the analysis and interpretation of the results of the studies to be included in the review, whilst where data allows this, it is appropriate to use methods of statistical synthesis of the results (meta-analysis). Otherwise, the synthesis of the results can be done in a narrative (descriptive) manner.

viii. CONCLUSIONS ARISING FROM THE SYSTEMATIC REVIEW

The interpretation of the results of the studies included in the review leads to conclusions which may include recommendations and suggestions for future research and/or public health policies, clinical practice, etc.



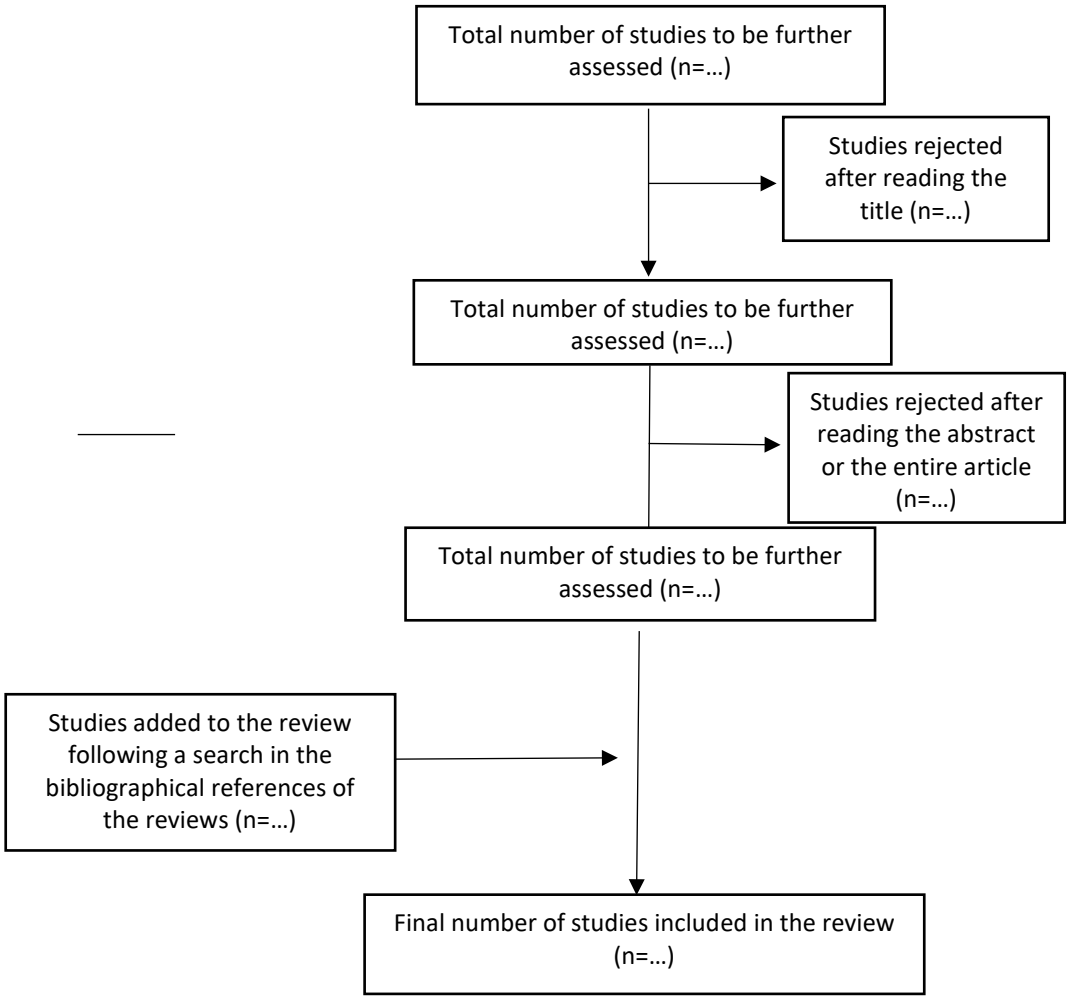


Illustration 2: Illustration of the results of the search strategy (Source – Patelarou, E., Brokalaki, H. (2010). Methodology of systematic review and meta-analysis. Nosileftiki, 49(2): 122-130)

Table 4: Summary of the main characteristics of the studies assessing the efficacy of smoking cessation interventions in patients with coronary disease (Source – Tziallas, D., Kastanioti, A., Skapinakis, P. (2009). Systematic review of smoking cessation interventions in patients with coronary disease, Nosileftiki, 48(1): 30-36)

Study	***Country***	***Study population***	***Type of intervention***	***Intervention setting***	***Duration***	***Efficacy %***
Quist-Paulsen P et al.	Norway	240 smokers <76 years old	Advice and written material. Follow-up for five months.	Hospital and community	5 months	57% after the first year
Reid R et al.	Canada	254 smokers	Mixed (nicotine patches and brief instructions).	Hospital and community	3 months	53% (at 3 months, 39% (in the first year)
Murchie P et al.	England	1,343 patients <80 years old	Advice and check of: blood pressure – hyperlipidaemia – nutrition – medication Intervention provided by nurses.	Community	12 months	No statistically significant difference observed between the two methods of intervention
Bolman C et al.	Denmark	789 patients	Advice provided by nurse.	Hospital and community	12 months	No statistically significant difference observed between the two methods of intervention
Hajek P et al.	England	540 patients - Smokers	20-30 min. counselling intervention by nurses – contact with other people with the same motive.	Hospital and community	Duration of treatment	No statistically significant difference observed between the two methods of intervention
Feeney GF et al.	Australia	198 patients - Smokers	Two different intervention programs.	Hospital and community	Duration of treatment	39% after one year

Table 5: Assessment of the quality of randomized controlled trials using five criteria (Source – Devereaux et al. (2005). How strong is the evidence for the use of perioperative beta blockers in non-cardiac surgery? Systematic review and meta-analysis of randomized controlled trials, BMJ, 331: 313-321)

Trials	Concealment of randomisation in the allocation of treatment measures	Short duration of conduct of the trial	Concealment of treatment measures from patients	Concealment of treatment measures from healthcare providers	Concealment of treatment measures from the assessors of the outcome
Liu	No	No	Yes	Yes	Yes
Stone	Yes	No	No	Yes	Yes
Polderman	Yes	Yes	No	No	Yes
Zaugg	Yes	No	No	No	Yes
Urban	Yes	Yes	No	No, with the exception of the anesthesiologists	Yes

APPENDIX II

Course title	Principles and Practice of Clinical Trials				
Course code	DBP670				
Course type	Elective				
Level	Master (2nd Cycle)				
Year / Semester	1st Year/2nd Semester				
Teacher's name	TBA				
ECTS	10	**Lectures/ week**	Up to 6 Teleconferences	**Laboratories /week**	–
Course purpose and objectives	Clinical trials are prospective studies, in which one or more human subjects are prospectively assigned to receive one or more interventions, including drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioral treatments and preventive care. Clinical trials aim to evaluate the safety and efficacy of the aforementioned interventions on health-related biomedical or behavioral outcomes. They are carefully designed, reviewed, and completed, and need to be approved before they can start. The purpose of this course is to provide students with a comprehensive understanding of the fundamental principles of designing, conducting and overseeing a clinical trial. The main objective is to familiarize students with the methodologies, ethical aspects and practical considerations related to clinical trials, preparing them to contribute effectively to the implementation of a clinical research study.				
Learning outcomes	Upon completing this course, students should be able to: • Explain basic clinical trial concepts. • Compare and contrast different types of clinical studies. • Evaluate benefits of different clinical trial designs and their practical implications, including decisions to alter or end a trial before termination. • List participants' roles and obligations during a clinical trial. • Understand the ethical requirements underpinning the conduct of a clinical trial. • Analyze the basic statistical methods used in clinical research. • Critically evaluate various aspects of quality in clinical trial results.				
Prerequisites	None		**Co-requisites**	None	
Course content	• Introduction to clinical trials • Clinical phases of drug development • Considerations in designing and conducting a clinical trial • Overview of trial designs				

	• Statistical aspects of clinical trials • Bias considerations • Ethics in clinical trials • Consent forms • The clinical trial protocol • Patient enrolment • Documentation of clinical study • Aspects of quality management • Interpretation and dissemination of results
Teaching methodology	E - Learning
Bibliography	***Educational Handbook:*** *Principles and Practice of Clinical Trials,* (2020), Piantadosi Steven, Meinert L. Curtis (Eds), Springer. ***Recommended Readings:*** *Clinical Trials* (2nd edition), (2020), Timothy M. Pawlik, Julie A. Sosa (Eds), Springer. *New Drug Development. An Introduction to Clinical Trials: Second Edition*, (2010), J. Rick Turner, Springer. European Patient's Academy on Therapeutic Innovation (EUPATI), Clinical Development
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course Title	Biological Drugs and Biotechnological Product Development				
Course Code	DBP680				
Course Type	Elective				
Level	Master (2nd Cycle)				
Year/Semester	1st Year/2nd Semester				
Teacher's name	TBA				
ECTS	10	**Lectures/ week**	Up to 6 Teleconferences	**Laboratories/ week**	None
Course, Purpose and Objectives	The aim of this course is to increase students' theoretical knowledge of fundamental concepts in molecular biology and biotechnology (including genetic engineering, gene therapy, synthetic biology, and transgenic organisms). The impact of modern biotechnology on health will be examined, with a particular emphasis on the use of advanced therapy medical products (ATMPs) in the prevention and treatment of disease. Finally, the course seeks to deepen students' understanding of bioinformatics, as well as to build skills and competences needed for the use of laboratory, biotechnology procedures (through dry-lab simulations).				
Learning outcomes	Upon completing this course, students should be able to: • Summarize the main applications of Biotechnology relating to animals, plants and microorganisms, mainly for application in medicine, food and environment. • Explain basic principles and molecular processes involved in the technology of recombinant DNA, nucleic acids analyzing methods and PCR technology. • Understand the principles of cloning and protein expression. • Define biotechnology applications in medicine, regarding disease prevention, treatment and diagnosis. • Evaluate the process of biologic drug design. • Know the most innovative biotechnology strategies regarding gene therapy, cell therapies, regenerative medicine, protein therapy, etc. • Classify advanced therapy medical products (ATMPs) and understand the GMP requirements for their clinical application US and Europe • Apply experimental approaches for drug production using enzymes, genes, genetically modified microorganisms and plants. • Employ bioinformatics for high-edged biotechnology approaches. • Create critical thinking about bioethics, regarding innovative biotechnological applications.				

Prerequisites	None	**Co-requisites**	None
Course content	**Basics of biotechnology:** • Introduction and historical perspective of the use of Biotechnology since ancient times. Comparison with modern Biotechnology • Recombinant DNA technology -Fermentation -Enzymatic reactions -Use of microorganisms in Biotechnology • Animals and Biotechnology • Plants and Biotechnology, genetic modification, classical genetic improvement • Bioreactors and microbiotic production of secondary metabolites • Biotechnology based drugs, medical devices. **Molecular biology applications in biotechnology:** • Cloning and gene expression for protein production, Restriction enzymes • PCR method and its applications • Nucleic acids analyzing methods: Electrophoresis, Hybridization of nucleic acids, Blotting, Sequencing • Microarrays and comparative genomics • Protein expression systems (bacteria, fungi, plant cells, eukaryotic cells) • Production and purification issues during protein expression (protein folding and functionality) • Gene delivery: viral and non-viral methods • Intracellular Transduction of Recombinant Proteins – Protein Transduction Technologies **Biotechnology in medical field:** • Disease prevention – vaccines: conventional vaccines, purified antigen vaccines, recombinant vaccines. DNA vaccines, In vitro transcribed mRNA technology • Disease treatment – Products from recombinant organisms, interferons, growth factors, antisense nucleotides as therapeutic agents, monoclonal antibodies. • Disease Diagnosis – Probes, monoclonal antibodies and detection of genetic disease • Biologic drug designing • Pharmacogenomics • Regenerative medicine and artificial tissues/organs • Gene therapy: drug delivery and targeting • Protein and enzyme replacement therapy • Cellular Therapies (CAR T-cell therapy, cloning somatic cells, embryonic stem cells, induced pluripotent stem cells) • Advanced therapy medical products (ATMPs) classification, • ATMPs manufacturing processes, GMP requirements and quality attributes. • The major differences between GMP for ATMPs and conventional therapies. • ATMPs regulatory, cost, and sustainability.		

	• Bioethics in Biotechnology **Bioinformatics:** • Introduction to the basic concepts, methods and applications of bioinformatics • The most common bioinformatics tools e.g. FASTA, BLAST, BLAT, RASMOL and databases GENBANK, PubMed, PDB. • Introduction to Biological Databases such as NCBI, DDBJ and EMBL. • Introduction to sequences and arrays (e.g. pairwise arrays using BLAST and FASTA algorithms and multiple sequence arrays using Clustal W algorithm) • Evolutionary models. Construction and evaluation of phylogenetic trees. • Computational biology and prediction tools. • Fundamentals of large-scale molecular biology data through genome sequencing (i.e. next-generation sequencing (NGS), protein sequencing (e.g. mass spectrometry), gel electrophoresis, NMR spectroscopy, X-ray diffraction and microarray. **Dry-lab simulations:** • Principles for PCR experimental procedure and agarose gel electrophoresis • Blotting procedures • Cloning in plasmid vectors and restriction enzyme reactions • Restriction Fragment Length Polymorphism (RFLP) Analysis • Bacteria transformation and protein expression procedure Finding homologous sequences for any nucleotide and protein query sequence using BLAST and FASTA. Search and retrieval of nucleotide sequences from GenBank database, retrieval of protein sequences from "SWISS-PROT" database and protein structure data using Entrez software and protein deconvolution software. Use of different online nucleotide and protein alignment tools (Pairwise and Multiple sequence alignment).
Teaching methodology	E - Learning
Bibliography	**English Bibliography** • Godbey, W.T(2015). An Introduction to Biotechnology. The Science, Technology and Medical Applications, Academic Press, ISBN: 978-1-907568-28-2. • Suresh, K.G, Joginder, Duhan, J.S, Salar,R.K, Siwach,P Suresh, K., Pawar, K, (2018) Advances in Animal Biotechnology and its Applications, Springer, ISBN: 978-981-10-4702-2. • Brahmachari, G. (2017), Biotechnology of Microbial Enzymes, Production, Biocatalysis and Industrial Applications Academic Press, ISBN: 978-0-12-803725-6. • Choudhuri S., (2014), Bioinformatics for Beginners: Genes, Genomes, Molecular Evolution, Databases and Analytical Tools Academic Press, ISBN: 978-0-12-410471-6.

	• Papachristodoulou, D, Snape, A, Elliot, W. E. (2014) Biochemistry and Molecular Biology, 5th edition, OUP Oxford, ISBN: 978-0199609499. • Miliotou, AN, Papadopoulou, LC (2018). CAR T-cell Therapy: A New Era in Cancer Immunotherapy. Current pharmaceutical *biotechnology* 19 (1), 5-18. • Moody, S.A. (2014), Principles of Developmental Genetics Academic press, ISBN: 978-0-12-405945-0. • Issaq, H.J & Veenstra, T.D (2013) Proteomic and Metabolomic Approaches to Biomarker Discovery, ISBN: 978-0-12-394446-7. • Ed. By Cabral, Joaquim M.S & De Silva, C (2016), Stem Cell Manufacturing, Elsevier, ISBN: 978-0-444-63265-4. **Greek Bibliography** • Lesk, Arthur M. (2017) Εισαγωγή στη γονιδιωματική, Utopia, ISBN: 978-618-5173-18-0. • Τριανταφυλλίδης, Κωνσταντίνος Δ. (2017) Οικονομία - δίκαιο στη Βιολογία: Έμφαση στη βιοτεχνολογία, Εκδόσεις Κυριακίδη, ISBN: 978-960-599-017-6. • Lieberman, Daniel E. (2015) Η ιστορία του ανθρώπινου σώματος: υγεία, ασθένεια, και φυσική επιλογή: το νέο εξελικτικό πεδίο της ιατρικής, Κάτοπτρο, ISBN: 978-618-5111-41-0
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course title	Biostatistics				
Course code	PHE610				
Course type	Elective				
Level	Master (2nd Cycle)				
Year / Semester	1st Year/2nd Semester				
Teacher's name	TBA				
ECTS	10	**Lectures/ week**	Up to 6 Teleconferences	**Laboratories /week**	–
Course purpose and objectives	This course aims to combine theory and practice of essential statistical methods (such as graphical methods, descriptive summary measures, confidence intervals and statistical tests) and advance statistical methods in Public Health (such as linear, logistic and Poisson regressions to adjust for potential confounders simultaneously and time-to-event analysis including Kaplan-Meier estimation and Cox' proportional hazards model for confounder adjustment). This course develops a critical understanding and evaluation of statistical methods applied in Public Health and it is giving a particular emphasize on the appropriate interpretation and communication of the statistical results. Finally, it prepares students to critically explore and apply statistical methods in real Public Health data.				
Learning outcomes	Upon completing this course, students should be able to: • Critically appraise and evaluate statistical methodology that has been used in epidemiological and Public Health studies and interpret tables and figures that are presented in such studies. • Explore numerical and graphical summary techniques, estimate confidence intervals and apply hypothesis testing. • Critically explore and apply appropriate statistical methods for one variable and two variables with continuous and categorical data. • Choose and then apply an appropriate regression model, and interpret the results from this model, for the analysis of case-control studies, cohort studies, cross-sectional surveys, and randomised trials, using appropriate computer software. • Plan a strategy of analysis to answer an epidemiological research question, using an appropriate choice and order of statistical analyses to control for confounding and account for interaction. • Autonomously undertake own statistical analysis and interpret and communicate properly the results and findings of statistical methods.				
Prerequisites	None		**Co-requisites**	None	

Course content	• Introductory concepts and type of data • Describing data with frequency tables • Describing data with diagrams • Describing data with summary measures of location and variance • Distribution of sample mean • Estimating confidence interval for a population mean • Estimating confidence interval for the difference and the ratio of two population parameters • Statistical test for the difference between population means, the statistical test t for independent means and the ANOVA test • Statistical test for the ratio of two population parameters and x2 statistical test for the independence of two categorical variables • Estimating the correlation between two numerical variables • Linear, Logistic and Poisson regression to adjust for potential confounders simultaneously • Survival analysis including Kaplan-Meier estimation and Cox' proportional hazards model for confounder adjustment The theoretical concepts will be specialized in the context of the weekly computer laboratory, where students will process and analyse data by means of a statistical software, so that upon completion of the course they will be able to process data, prepare tables and charts and produce statistical results in their own scientific work.
Teaching methodology	E - Learning
Bibliography	**Educational Handbook:** Bowers, D. Medical Statistics from Scratch. An Introduction for Health Professionals. John Wiley & Sons. Latest edition. Kirkwood, B. and Sterne, J. Essential Medical Statistics. Blackwell Science. Latest edition. **Recommended reading:** Sullivan, L. (2017). Essentials of Biostatistics in Public Health. John and Bartletts Learning. Nikulin, M.S., Commenges, D, Huber-Carol, K. (2006). Probability, Statistics and Modelling in Public Health.
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

APPENDIX III

Course title	Drug Design and Small Molecule Synthesis				
Course code	DBP610				
Course type	Compulsory				
Level	Master (2nd Cycle)				
Year / Semester	1st Year/1st Semester				
Teacher's name	Dr. Andreas Kalogirou and Dr. Eleni Moushi				
ECTS	10	**Lectures / week**	Up to 6 Teleconferences	**Laboratories /week**	–
Course purpose and objectives	The course "Drug Design and Small Molecule Synthesis" aims to present the fundamental methods and available tools (i.e., molecular modeling software) used in the design of new drugs. Both traditional and modern methods for the synthesis of organic and inorganic drug molecules are presented. Emphasis is given to the use of retrosynthesis, catalysis, asymmetric synthesis, use of organometallic reagents and protecting groups, and the synthesis of metal complexes. Issues related to intellectual property in the early stages of drug development are also presented.				
Learning outcomes	Upon completing this course, students should be able to: • Explain the basic principles of drug discovery, design and development. • Use molecular modeling software for the design of new drug molecules. • Search, evaluate and use the scientific literature in order to explain the practices of drug design. • Plan the synthesis of organic drug molecules. • Plan the synthesis of metal complexes with pharmaceutical applications. • Apply the use of protecting groups in the synthesis of organic target molecules. • Apply retrosynthetic analysis in planning the synthesis of academically and commercially important organic target molecules. • Determine the reagents and strategies for the stereoselective synthesis of chiral molecules.				
Prerequisites	None	**Co-Requisites**	None		
Course content	• Introduction, historic overview, the pre-regulation era. Natural products. Synthetic products. The need for regulation and development of a regulatory framework. Intellectual property. Use of chemical structure drawing software (ChemDraw).				

	• The stages of drug design and development. The cost of new drug development. Opportunities and challenges. Drug design strategies: Target based design, phenotype-based design and mixed approach. • Drug design and metabolism: prodrugs, ADME. Use of SMILES and the Molinspiration software. Introduction to molecular interactions and dynamic binding. Structure and molecular diversity, molecule libraries. Multicomponent reactions and their use for the generation of molecule libraries. ADMETSAR software. • Lead discovery. Drug design using the techniques SBDD, LBDD, FBDD, CADD. Lead optimization. Design of new molecule binders using the SeeSAR software. • Introduction to organic synthesis. Characteristic reactions of alkenes, halogenoalkanes, aromatics and carbonyl compounds. Mechanisms of the reactions of nucleophilic substitution, electrophilic addition to unsaturated compounds, electrophilic aromatic substitution, cycloaddition. Chemo- and regioselectivity. • Retrosynthesis. Classic functional group transformations (oxidation, reduction). Use of protecting groups in synthesis. Design of a synthetic route using these strategies. • Chemistry of boron, silicon and tin in synthesis: Hydroboration, Baeyer–Villiger rearrangement, silyl ethers, arylic and vinylic silanes, organotin compounds. • Synthesis and reactions of heterocyclic compounds: 5-membered rings (furan, thiophene, pyrrole), 6-membered rings (pyridine, pyrimidine), bicyclic systems (indole, quinoline, quinazoline). • The importance of stereochemistry in pharmacy. Enantiomers and diastereoisomers. Asymmetric synthesis: Sharpless epoxidation, Mitsunobu reaction, enantioselective hydrogenation, organocatalysis. • Introduction to inorganic chemistry. Basic principles of inorganic chemistry. Definition of metal complexes, metal/ligand interactions using the donor-acceptor and HSAB theories. Design of metal complexes with correct illustrations of coordination and geometry. • Synthesis and characterization of metal complexes with pharmacological activity. • Transition metal organometallic chemistry: Palladium (C-C and C-N couplings: Suzuki, Stille, Sonogashira, Negishi, Heck and Buchwald reactions), Ruthenium (Grubs metathesis).

	• Selected syntheses of organic drug molecules: β-lactam synthesis, steroid chemistry, sugar chemistry, alkaloid synthesis. New developments in organic synthesis: C-H bond activation.
Teaching methodology	E - Learning
Bibliography	*An introduction to Medicinal Chemistry,* 5th Edition, Graham L. Patrick, 2013, Oxford University Press, ISBN: 978-0-19-969739-7. *Organic Chemistry*, 2nd Edition, Clayden J., Greeves N., Warren S., 2012, Oxford University Press, ISBN: 9780199270293.*e art of drug synthesis*, Johnson D.S., Li J.J. (Eds), 2007, Wiley. ISBN 978-0-471-75215-8. *Advanced Inorganic Chemistry*, 6th Edition, Murillo C. A., Bochmann M., Cotton F. A., Wilkinson G., 1999, ISBN: 978-0-471-19957-1. *Metals in Medicine*, 2nd edition, Dabrowiak J.C., 2017, Wiley, ISBN: 978-1-119-19137-7. *Drug Discovery and Development*, 3rd edition, Hill R.G & Richards D, 2021, Elsevier, ISBN: 9780702078040. *Drug-like Properties: Concept, Structure Design, and Methods*, Kerns E.H. & Di L., 2016, Academic Press, ISBN: 9780123695208. *Practical Guide to Rational Drug Design*, Hongmao S., 2015, Elsevier Science & Technology, ISBN: 9780081000984. *Smith and Williams' Introduction to the Principles of Drug Design and Action*, Smith H.J. (Ed), 2004, Taylor and Francis, ISBN 9780415288774. Added sources of information: www.ema.europa.eu, www.fda.gov
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

THE CYPRUS AGENCY OF QUALITY ASSURANCE AND ACCREDITATION IN HIGHER EDUCATION

European University Cyprus

FORM: 200.1.3

STUDY GUIDE

COURSE: DBP610 – Drug Design and Small Molecule Synthesis

Institution	European University Cyprus		
Program of Study	Drug Biosciences and Pharmaceutical Development – M.Sc.; E-Learning		
Course	DBP610	Drug design and synthesis	
Level	Undergraduate ☐	Postgraduate (master) ☒	
Language of Instruction	English		
Course Type	Compulsory ☒	Elective ☐	
Number of Teleconferences	Total: Up to 6	Face to face: -	Teleconferences: Up to 6
Number of assignments	Total number of graded items: 3 Two (2) individual assignments (2 x 10% = 20% of total grade) & one (1) group assignment (30% of total grade)		
Assessment	Assignments 50%	Final examination 50%	
Number of ECTS Credits	10		

Study Guide drafted by:	Dr. Andreas Kalogirou Dr. Eleni Moushi
Editing and Final Approval of Study Guide by:	Dr. Athanasios Metaxas
Study Guide Review (current lecturer):	Dr. Andreas Kalogirou Dr. Eleni Moushi

CONTENTS

1ST TELECONFERENCE/GRUP CONSULTATION MEETING: INTRODUCTION

Program Presentation

Brief description and objectives

The journey of a drug from bench to bedside is a long and complicated process, which requires cooperation among specialized and quite different scientific disciplines. The Master of Science (M.Sc.) in 'Drug Biosciences and Pharmaceutical Development' is an interdisciplinary program designed to equip students with the necessary theoretical knowledge and practical experience to understand and participate in the production stages of a new pharmaceutical product. It is aimed at students who want to acquire the required skills to work in the pharmaceutical industry, in public and private research organizations, as well as in the drug regulatory authorities of the European Union (EU) countries.

In particular, the program aims to:

- Offer specialized knowledge of Pharmacognosy, Pharmaceutical Chemistry & Analysis, Formulation of Medicines, Pharmacology and Toxicology, with a focus on the application of this knowledge at different stages during the life cycle of a pharmaceutical product.
- Promote a comprehensive and proactive understanding of the drug development process, which considers the regulatory and commercial aspects of the licensing and marketing of a new drug.
- Create scientists capable of understanding, coordinating, and supporting the range of research activities involved in the drug development process.
- Enable students to acquire skills in laboratory practice and production of primary scientific data.
- Cultivate the necessary skills for the critical evaluation and synthesis of the scientific literature, as well as for the discussion and communication of international bibliography.

Expected learning outcomes

Graduates of this Program are expected to be able to:

- Analyze the process of discovery, development, and approval of new drugs, and understand the connections between the individual stages of this process.
- Describe the challenges presented during the development of a pharmaceutical product, and implement strategies to address them.
- Evaluate the role of natural products as lead compounds for the discovery, design and development of new drugs.
- Use molecular modelling software, and apply specialized strategies to design active pharmaceutical ingredients.
- Develop conventional and innovative pharmaceutical forms, according to the intended therapeutic goal and the appropriate route of administration of the preparations.

- Understand the importance of implementing management systems and quality control in the development, manufacture and supply of different dosage forms of medicines.
- Choose the appropriate pharmacological and toxicological methods to ascertain the efficacy and safety of a pharmaceutical product during development.
- Follow the appropriate regulatory procedures for the approval and marketing of a new pharmaceutical product for human use in the EU.
- Contribute to the creation of new knowledge in the field of drug research and development, by combining the theoretical and practical knowledge acquired during their studies.

Presentation of the Course through the Study Guide

Brief description and Objectives

The course “Drug Design and Small Molecule Synthesis” aims to present the basic methods and available tools (i.e., molecular modeling software) used for the design of new drugs. The classic and modern methods for the synthesis of organic and inorganic drug molecules are presented. Emphasis is given to the use of retrosynthesis, catalysis, asymmetric synthesis, use of organometallic reagents and protecting groups and to the synthesis of metal complexes. Issues related to intellectual property in the early stages of drug development are also presented.

Expected learning outcomes

Upon completion of the course, students are expected to be able to:

- Understand the basic principles of drug discovery, design and development.
- Use molecular modeling software and apply it for designing new drug molecules.
- Search, evaluate and use the scientific literature in order to explain the practices of drug design.
- Plan the synthesis of organic drug molecules.
- Plan the synthesis of metal complexes with pharmaceutical applications.
- Apply the use of protecting groups in the synthesis of organic target molecules.
- Apply retrosynthetic analysis in the planning of the synthesis of academically and commercially important organic target molecules.
- Determine the reagents and strategies for the stereoselective synthesis of chiral molecules.

Recommended student work time

Approximately 5 h (including reviewing the Study Guide)

TITLE: Introduction to drug design

(1st Week)

Summary

This chapter introduces and gives a brief historical overview of drug design, starting from the pre-regulatory period and reaching to the modern era of drug discovery. Common sources of natural drug products and synthetic compounds are cited, while intellectual property and protection issues are explained.

Introductory Remarks

Medicinal chemistry or pharmaceutical chemistry is the science that deals with the discovery of new drugs based on the relationship between chemical structures and their biological action. Our introduction to the subject of drug discovery begins with a historical overview of the evolution of this process from ancient times, through the 19th and 20th centuries, to the present day.

In ancient times, nature was the source of most medicines. The earliest evidence for the medicinal use of plants is from the cultures of China, India, the Mediterranean, and the Mayans of Central America. Notable examples from this era are the Chinese Emperor Shen Nung's description of two medicines, Chang Shan for treating fever and Ephedra sinica as a cardiotonic and anti-cough medicine. Some medicinal substances known in antiquity are hemp, opium, cocaine, quinine and digitalis glycosides.

In the 19th century, active substances were isolated in pure form, examples being the isolation of morphine from opium in 1806, caffeine in 1820 and salicylic acid from willow in 1874. The progress of organic chemistry enabled the synthesis of active compounds with a typical example being the synthesis of aspirin from salicylic acid in 1899 by Bayer.

From the 20th century and until today, the world has witnessed the development of modern pharmaceutical industry, and the emergence of multinational pharmaceutical companies. Due to the breakthroughs in biology, drug screening experiments are now done on animals, organs, cells, enzymes and membranes, before actually being tested in humans. The development of technology and the emergence of techniques such as X-ray crystallography, NMR spectroscopy, mass spectrometry, HPLC, etc. have further contributed to the progress of pharmaceutical science. More recent developments are the use of combinatorial chemistry and compound libraries and the development of biological products. New pharmacomolecular screening systems have also been developed, such as high-throughput screening (HTS) on human proteins.

If we focus on synthetic drugs, we will see that the first ones appeared as accidental discoveries, as for example acetanilide and penicillin. Gradually, however, scientists began to use information from nature to discover new drugs, such as the development of local anesthetics based on the structure of

cocaine. The contribution of P. Ehrlich was very important, as he recognized the importance of the binding of drug molecules to targets which led to the discovery of antimicrobial "sulfa drugs".

With the development of the pharmaceutical industry came the need for regulation and the development of a regulatory framework, which was demonstrated by the sulfanilamide tragedy. The use of the toxic substance diethylene glycol to make a sulfanilamide elixir for children resulted in hundreds of deaths and led to the establishment/strengthening of the Food and Drug Administration (FDA) and the tightening of drug laws.

In addition, the development of new drugs by pharmaceutical companies created a need for invention protection, most importantly protection of the structure of each active drug molecule. Such discoveries, which are the intellectual property of the inventor, are protected by patenting. Patents give inventors, i.e., the pharmaceutical companies, the exclusive commercial exploitation of their discovery for a defined period of time. An example of the value of patents is the case study on ranitidine, which will be presented in this chapter.

Finally, in this chapter, students will become familiar with drawing and modifying chemical structures using the molecular design software ChemDraw. A user guide to this important software will be provided.

Aims/Objectives

The purpose of this introductory chapter is for students to understand the historical of context of drug development, and to familiarize themselves with the difficulties and challenges it had to face. Students will also be introduced to finding and understanding pharmaceutical patents, as well as designing chemical structures on a computer, by using appropriate software.

Learning Outcomes

Upon completion of week 1, students should be able to:

- Recognize modern challenges in the pharmaceutical industry, as well as the fields of science involved in its success.
- Discuss patents and recognize the chemical structures of the drug molecules they describe.
- Use molecular design software to describe chemical molecules and reactions.

Keywords

Drug discovery	Natural products	Synthetic products	Intellectual property

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 1, Dr. Andreas Kalogirou, European University Cyprus.
Here you will find a description of the introduction to this course.

ChemDraw user guide, Dr. Andreas Kalogirou, European University Cyprus.
A guide to the use of this software, with examples and exercises.

An introduction to Medicinal Chemistry, 5th Edition, Graham L. Patrick, 2013, Oxford University Press, ISBN: 978-0-19-969739-7.
Study chapter 15.2 (Patenting and regulatory affairs) for a description of the basic principles of patenting and the role of regulatory agencies.

- **Supplementary Sources/Material**

Taste of Raspberries, Taste of Death; The 1937 Elixir Sulfanilamide Incident. FDA Consumer magazine, 1981.
An article by FDA about the tragedy of sulfanilamide.

Video: Discovery of new drugs: is it such a big deal?
A video on the process of drug discovery and development.

Drug Discovery and Development, 3rd edition, Hill R.G & Richards D, 2021, Elsevier, ISBN: 9780702078040.
Study chapter 1 (The development of the pharmaceutical industry) for a description of the history of the pharmaceutical industry.

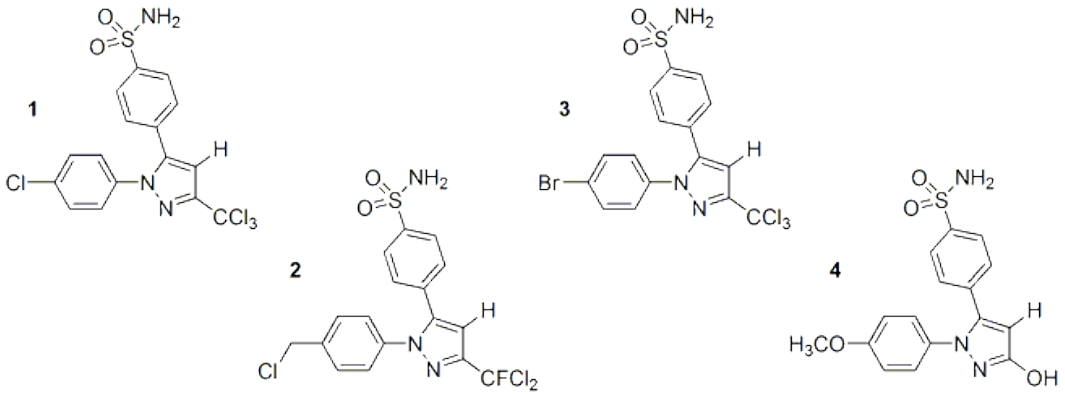
Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 1.1

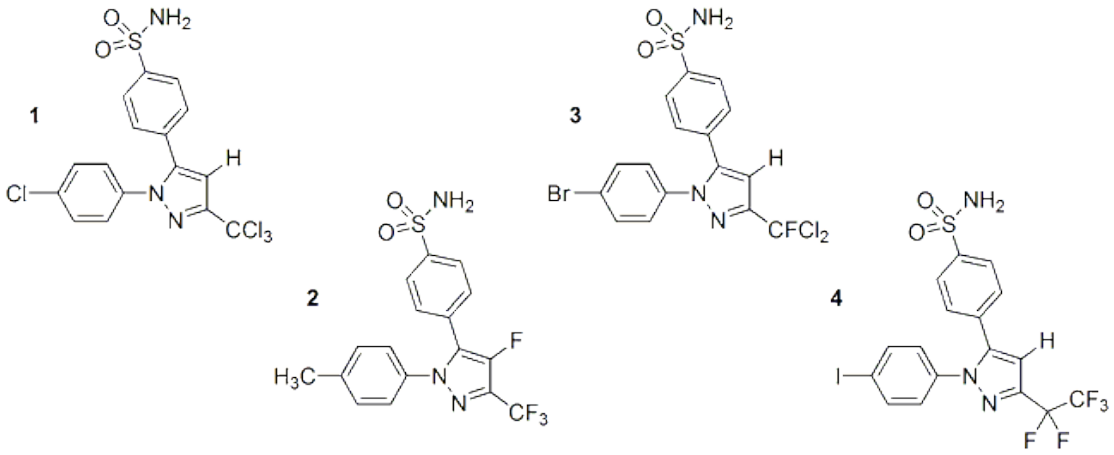
In the following link you can find the patent for the drug Celecoxib:
https://patents.google.com/patent/WO1999022720A2/en

Read the patent document and answer the following questions.

a) Which of the following structures is not covered by the patent?



b) Which of the following structures is covered by the patent?



Recommended student work time: approximately 10 h

TITLE: The stages of drug design and development

(2nd Week)

Summary

This chapter provides an overview of the stages of designing and developing a new drug and an explanation of the costs involved in this process. Three drug design strategies are mentioned: target-based design, phenotype-based design and the mixed approach.

Introductory Remarks

After many years of progress, drug development today follows a standardized process that takes, on average, more than 10 years. In this process, we begin with thousands of candidate compounds and end up with an approved drug. The process consists of the research (or discovery) phase, the preclinical phase, the clinical trial phases (typically phase I to III) and finally the approval and marketing of the drug.

Drug development is a process that involves large costs, currently estimated at around 2.5 billion Euros per drug. The high cost is mainly due to the significant failure rate during the clinical trial phase, where the probability of finding a safe and effective new drug is low (<10% from phase I to marketing). In addition, part of the cost in clinical trials comes from the costs of health services, which involve the participation/payment of human subjects in clinical trials and the expensive analyses carried out at this stage.

The challenge that the pharmaceutical industry faces is the reduction of costs, which has led to the meticulous analysis of the reasons for the failure of a drug candidate to enter the market. The most common reasons of failure include the poor pharmacokinetic behavior of the compound under study, its low efficacy and safety, as well as the reduction of the drug's market due to competition. A strategy used to reduce the cost of drug development is to "fail fast, fail cheap", which aims in finding the potential efficacy and safety problems of a drug molecule as fast as possible during the development process, during the preclinical phase if possible. For example, various tests as well as computational tools are used in the preclinical phase to study the pharmacokinetics of candidate compounds, while the increased use of phenotypic controls helps to document early drug efficacy.

In the first stage of the drug development process, the discovery phase, there must be a way to design and study drug candidates. This can be done with three strategies, either target-based, phenotype-based, or both (intermediate or mixed approach).

Target-based design focuses on targeting a specific protein that is important in the disease we want to treat. The course of planning in this method is as follows: finding a target protein by studying the biochemical processes of the disease,

developing a biochemical control method of observing the binding of molecules to this protein (assay), studying the binding of potential drug molecules to this protein for finding "hits" and optimizing the binding ability of drug molecules by synthesizing chemical analogs, until the most strongly binding molecules (leads) are found. The disadvantages of this strategy are that it often leads to drug molecules with low efficiency (since strong binding does not always imply high activity) and that it is sometimes difficult to find the exact protein target of a disease.

An alternative method of drug discovery is based on phenotype (phenotype-based design), which aims to find drug molecules that affect the phenotype (i.e., observable characteristics) of a living organism, tissue or cell. The process is often initiated by a "lead compound" known to have an effect on the phenotype of the test organism. The lead compound is then optimized to find more active compounds. This method is based on *in vivo* assays in living organisms or cells, so it is a slower process than the simple binding assay done in target-based discovery, yet it is a method that demonstrates greater efficiency.

The mixed approach of drug design is the intermediate of the target- and phenotype-based approaches and can be performed in several ways. For example, we can start with the protein target and a study to find active compounds through a biochemical screening assay. The most promising active molecules are selected and chemically modified to optimize them. Then the efficacy of drug candidates can be directly ascertained through phenotypic tests in animals. If a molecule with good binding properties is also active *in vivo* then its therapeutic value is confirmed.

Finally, in this chapter, an analysis of the concepts of agonist, competitor, potency and efficacy is made.

Aims/Objectives

The purpose of this chapter is for students to understand the basic stages of drug design and development, and to recognize the main steps involved in this process, as well as the challenges. Emphasis is given to the three drug design strategies as well as the advantages/disadvantages of each.

Learning Outcomes

Upon completion of week 2, students should be able to:

- Recognize the stages of drug development process, as well as the challenges it faces.
- Explain select methods of drug discovery.
- Research, evaluate and use publications from the scientific literature to understand practices in drug discovery.

Keywords

Target based drug design	Phenotype based drug design	Mixed approach drug design

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 2, Dr. Andreas Kalogirou, European University Cyprus.
Here you will find a description of the steps of drug development.

An introduction to Medicinal Chemistry, 5th Edition, Graham L. Patrick, 2013, Oxford University Press, ISBN: 978-0-19-969739-7.
Study chapter 15.1.4 (Clinical trials) for a description of the structure and role of clinical trials.

- **Supplementary Sources/Material**

Video: The Drug Development Process
A short description of the steps of drug development.

Video: Laboratory Automation, High Throughput Screening and Drug Discovery
A video on the use of the methods of high throughput screening (HTS) in target based drug discovery.

Video: Basics of Phenotypic Screening
A video on phenotype-based drug discovery.

Drug Discovery and Development, 3rd edition, Hill R.G & Richards D, 2021, Elsevier, ISBN: 9780702078040.
Study chapter 4 (The drug discovery process) for a description of the general principles of drug discovery and some related case histories.

David C. Swinney, Chapter 1: Phenotypic Drug Discovery: History, Evolution, Future, In: Phenotypic Drug Discovery, 2020, pp. 1-19
An article on phenotype-based drug discovery.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 2.1 (Individual assignment, graded 10%)

Study the article by Hassan Al-Ali, Stephan C. Schürer, Vance P. Lemmon, John L. Bixby, Chemical Interrogation of the Neuronal Kinome Using a Primary Cell-Based Screening Assay; *ACS Chem. Biol*. 2013, 8: 1027−1036 (https://pubs.acs.org/doi/10.1021/cb300584e).

Write your comments in the relevant discussion forum describing the research objective, the procedure used, and the results of the research described in the manuscript (<200 words).

Read and comment on a colleague's posts. Commenting will take place in the context of an online discussion, the goal of which is to submit your own thoughts. Your post is expected to be <100 words long.

Recommended student work time: approximately 15 h

TITLE: Drug design and metabolism

(3rd Week)

Summary

This chapter is a brief introduction to pharmacokinetics and its impact on drug design. The value of molecular libraries in drug discovery and some methods for their creation are explained. Finally, we provide an introduction to molecular interactions and dynamic binding.

Introductory Remarks

Pharmacokinetics describes the journey of the drug molecule through the body; therefore, its study is important in drug design. Pharmacokinetics consists of four stages: absorption, distribution, metabolism and excretion of the drug from the body (ADME). The oral (*per os*) administration of drugs has special pharmacokinetic requirements, which are determined by the specific physicochemical properties of candidate drug molecules. These properties typically have a narrow range, called the physicochemical space of pharmaco-similarity.

An important factor in the action of a drug administered in solid form is its solubility. Improving the solubility of candidate drug molecules is important to enable their use as drugs. The solubility of ionizable compounds is related to the pH and their pKa, while for non-ionizable substances it can be calculated as a function of logP and melting point.

Absorption of drugs from the gastrointestinal (GI) tract requires a proper balance of water solubility and lipophilicity of the drug molecule. A set of simple rules for predicting a drug's ability to cross cell membranes and, by extension, be absorbed by the GI into the bloodstream is "Lipinski's rule of five" published in 1997 by Chris Lipinski of Pfizer. This rule was an attempt to link structural or physical properties of molecules (molecular markers) to their behavior as drugs. The four molecular parameters included in this rule are molar mass, lipophilicity, and the number of hydrogen bond acceptors and donors.

The distribution of the drug in the body is again related to various properties of the drug molecule, with its binding to plasma proteins being especially important. This interaction can lead to poor behavior of the drug in the body, as well as create interactions with other drugs.

Metabolism is one of the most important processes affecting the action of a drug. Metabolic reactions are mainly carried out by enzymes and are divided into two categories, phase I reactions (mainly oxidation, reduction and hydrolysis) and phase II reactions (conjugation with small polar molecules). It is important to be able to predict the metabolites of a potential drug molecule, in order to avoid toxicity issues that may arise from their generation. Moreover, genetic heterogeneity in the function of the liver enzymes in some patients can lead to abnormalities in drug metabolism. The case study on cimetidine (a liver

enzyme inhibitor) shows how important is the effect of some drugs on the metabolism of other drugs.

One way of using metabolism to improve the action of a drug is with prodrugs. These are molecules with good pharmacokinetic properties, which are an inactive form of the drug and which are metabolized to the active drug form within the body.

Computational tools can help us study the pharmacokinetic properties of a molecule under study. Some tools that are presented here are the software Molinspiration, which shows key molecular properties of any given compound, and the online software admetSAR, which can predict possible problems with absorption and metabolism.

From a pharmacodynamics perspective, this chapter introduces molecular interactions and molecular dynamic binding. The binding of two molecules (target and drug molecule) has a binding constant, the value of which tells us how strong the connection is and the change in the value of free energy by the binding. The latter depends on both intermolecular forces (ΔH) and hydrophobic interactions (ΔS).

Stereochemistry is an important factor influencing the binding of the drug molecule to its target. The size, but also the shape of a molecule in 3D is often the determining factor in the appearance of biological activity. The presence of asymmetric centers as well as the number of rotatable bonds are important factors. The latter increase the conformational flexibility of a molecule and reduce the possibility of functional groups meeting those of the binding site.

All these different molecular properties that have been mentioned above reveal the specific requirements that a molecule must have in order to become a drug. But the number of possible molecules that can have these conditions is large, and even larger is the number of possible molecules that can exist or be synthesized. Therefore, in the search for a new drug for a disease, among the large number of possible organic molecules, those that have a therapeutic effect on the disease must be found. This is achieved by the use of molecular libraries, which are large collections of molecules with different structures that can be studied by pharmaceutical companies to find promising "hits" that can then develop into drugs. The greater the molecular variability of the molecules in the library, the greater the probability of finding a hit.

One way to synthesize libraries of organic molecules is by using combinatorial chemistry, which is a method of synthesizing new molecules using combinations of reagents in simple and often automated steps. One class of reactions that can be used are multicomponent reactions that can give a multitude of products by combining different analogs of the reactants. An example of such a reaction is the Passerini reaction, presented here in a case study.

Aims/Objectives

The aim of this chapter is for students to understand the basic principles of pharmacokinetics and to familiarize themselves with metabolic reactions and ways to improve the pharmacokinetic behavior of drug molecules. Emphasis is given to the calculation of pharmacokinetic properties of molecules using online

tools. Finally, the purpose of this chapter is to introduce the importance of stereochemistry and the use of molecular libraries in drug development.

Learning Outcomes

Upon completion of week 3, students should be able to:

- Propose structures of prodrugs or drug molecules with optimal pharmacokinetic properties.
- Predict the potential metabolites of drug molecules.
- Recognize the importance of stereochemistry in drug-target interactions.
- Propose reactions for the synthesis of molecular libraries.

Keywords

Pharmacokinetics	ADME	Metabolism	Molecular libraries

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 3, Dr. Andreas Kalogirou, European University Cyprus.
Here you will find a description of the methods of drug design and metabolism.

An introduction to Medicinal Chemistry, 5th Edition, Graham L. Patrick, 2013, Oxford University Press, ISBN: 978-0-19-969739-7.
Study chapter 11 (Pharmacokinetics and related topics) for a description of the basic principles of pharmacokinetics.

Smith and Williams' Introduction to the Principles of Drug Design and Action, Smith H.J. (Ed), 2004, Taylor & Francis, ISBN 9780415288774.
Study chapter 1 (Processes of Drug Handling by the Body) for a description of the basic principles of pharmacokinetics.

- **Supplementary Sources/Material**

Organic Chemistry Portal, Multicomponent Reactions
In this website you can find information on multicomponent reactions.

Video: Drug Metabolism Made Simple
Video: Pharmacokinetics 4 - Metabolism
Two short videos on drug metabolism.

Practical Guide to Rational Drug Design, Hongmao S., 2015, Elsevier Science & Technology, ISBN: 9780081000984.
Study chapter 1 (Structures, Limitations, and Pitfalls) for a description of the general principles of drug design.

Drug-like Properties: Concept, Structure Design, and Methods, Kerns E.H. & Di L., 2016, Academic Press, ISBN: 9780123695208.

Study the chapters 11 (Metabolic Stability) and 15 (Cytochrome P450 Inhibition) for a description of these important topics regarding pharmacokinetics.

Jiankun Lyu, Sheng Wang, Trent E. Balius, Isha Singh, Anat Levit, Yurii S. Moroz, Matthew J. O'Meara, Tao Che, Enkhjargal Algaa, Kateryna Tolmachova, Andrey A. Tolmachev, Brian K. Shoichet, Bryan L. Roth, John J. Irwin, Ultra-large library docking for discovering new chemotypes, 2019, Nature, 566: 224-229.
An article on the use of virtual molecular libraries in drug discovery.

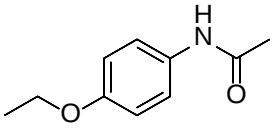
Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 3.1

Sigma-Aldrich is a chemical reagent vendor and has 1,800 carboxylic acids, 1,200 aldehydes, and 70 isonitriles available on its website. Of these compounds, 80% of the acids, 80% of the aldehydes and all the isonitriles are suitable for the Passerini reaction. How many products of the reaction can be synthesized from a combination of these reagents? Give your answers in the group forum of week 3.

Exercise 3.2

Suggest the products of two phase I metabolic reactions and one phase II reaction for the drug molecule that is shown below. Submit your answer to the corresponding assignment in Blackboard.



Recommended student work time: approximately 17 h

TITLE: Lead discovery

(4th Week)

Summary

In this chapter, we present methods to discover and optimize a lead compound during drug development. Various strategies used in lead discovery are explained, such as SBDD, LBDD, FBDD, and CADD. Finally, an introduction is made to SeeSAR, a software that is used to design candidate compounds with pharmaceutical activity.

Introductory Remarks

In the previous chapter, the initial steps of the drug development process were studied, including the discovery and screening of active compounds (hits). In this chapter, we will study the transition from hit to lead, i.e., finding the lead compounds, which are the most promising chemical structures that will lead to the final drug molecule.

The basic strategies for finding the lead compound are:

- LBDD (ligand-based drug design): It is based on knowledge of which compounds bind to the target and of the pharmacophore structure.
- FBDD (fragment-based drug design): Study of the joining of fragments for development of active compounds.
- SBDD (structure-based drug design): It is based on knowledge of the structure of the target biomolecule.
- CADD (computer-aided drug design): Use of a computer to simulate target binding.

The LBDD and SBDD techniques have already been presented in the previous chapter, where target-based and phenotype-based drug candidate discovery techniques were analyzed.

The FBDD strategy is based on the use of molecular libraries to find active candidate compounds. However, these libraries consist of molecular fragments, i.e., molecules smaller in size than typical drug molecules. Fragments are made of 10-15 atoms and have an Mr of 150-250 g/mol. Their advantage is that due to their smaller size they are also fewer in number, since the possible combinations of atoms are few. In fragment-based discovery (FBDD), a library of only a few thousand fragment-sized molecules is screened for binding to the protein under study.

After finding fragments that bind to the protein under study, two strategies can be followed to convert them into hits: the strategy of growth and the strategy of linking. Structural growth of the fragment involves the stepwise addition of functional groups or substituents to the structural core of the fragment in order to maximize favorable interactions with the binding site. An example of the use of this strategy is the discovery of inhibitors of the enzyme pantothenic acid synthase of the Mycobacterium tuberculosis. In the linking strategy, fragments

attached to the protein at different binding sites are then linked by carbon atoms and the ideal length of the chain that will join the two fragments is designed.

The two challenges of FBDD are the low solubility of the fragments at the concentrations required for the activity assay and the sensitivity of the process to the presence of impurities that can give a false indication of bioactivity.

In CADD, a virtual screening is essentially performed, i.e., a study of the binding of compounds to a protein binding site using a computer. This study requires an accurate knowledge of the target structure (SBDD) as well as the use of the necessary software that will calculate the binding energies for each member of an electronic library of chemical molecules to the binding site. The advantage of this technique is that the compounds studied are virtual, so there is no need to synthesize them, while there are also no limits to the possible structures of the compounds. The activity of virtual "hits" can only be confirmed by synthesizing them and submitting them to an *in vitro* test.

We will use the software SeeSAR to carry out such a study. Students will gain access to this software and by performing an exercise they will learn how to load entries from the protein data bank, design molecules that bind to a specific binding site on the protein and study their binding energy. An example that will be studied in teleconference is finding cyclooxygenase-2 (COX2) inhibitors, followed by homework on the design of H1 antagonists (Exercise 4.1).

The selection of hits after a high throughput screening is a necessary step in the drug discovery process. Initially, a simple visual inspection of the structures is performed and those containing problematic functional groups are rejected. A group of such compounds that are called "PAINS" (pan assay interference compounds) contain strong electrophiles and tend to bind to all proteins. Other compounds to be discarded are those that we expect to have toxic metabolites, such as anilines.

Various molecular markers can be used to evaluate hits such as ligand efficiency (LE) and ligand lipophilicity efficiency (LLE). In addition to these indicators, some experimental tests are also used that aim to study the mode of metabolism, the possible action as an inhibitor of metabolic enzymes, the binding to plasma proteins and the cellular permeability of the candidate compounds.

Optimizing the lead compound is the last step before finding the structure of the drug molecule. This is usually done by minor chemical modifications to the structure of the lead compound, usually involving additions or changes of functional groups to improve pharmacokinetic properties, as well as improve binding to the target. Some strategies used for lead optimization are homologation, use of bioisosterism and peptidomimetics.

Aims/Objectives

The purpose of this chapter is to familiarize students with the basic ways of discovering and optimizing lead compounds during the development of new drugs. Students will gain experience in applying different lead compound discovery strategies, as well as using the software SeeSAR to design binding molecules for given protein structures.

Learning Outcomes

Upon completion of week 4, students should be able to:

- Recognize the strategies of lead compound discovery in drug development.
- Research, evaluate and use publications in the scientific literature to understand and justify drug discovery practices.
- Use molecular modeling software and apply it to the designing of new drugs.

Keywords

Lead discovery	Lead optimization	Molecular docking software

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 4, Dr. Andreas Kalogirou, European University Cyprus.
Here you will find a description of the main methods of lead discovery and optimization in drug development.

An introduction to Medicinal Chemistry, 5th Edition, Graham L. Patrick, 2013, Oxford University Press, ISBN: 978-0-19-969739-7.
Study chapter 12 (Drug discovery: finding a lead) focusing on section 12.4 (finding a lead compound) that gives a good analysis of the materials covered this week.

- **Supplementary Sources/Material**

SeeSAR software
In this website, you will find information about the SeeSAR software, as well as a user guide.

Video: Lead discovery in drug development
A video on lead discovery.

Drug-like Properties: Concept, Structure Design, and Methods, Kerns E.H. & Di L., 2016, Academic Press, ISBN: 9780123695208.
Study chapter 20 (Lead-like Compounds) for a description of the main properties of lead compounds.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 4.1

On SeeSAR load the file 3RZE_1 describing the H1 receptor with the bound molecule doxepin. You are asked to modify this compound and suggest two compounds with improved binding to the receptor. Your compounds must be

chemically correct and have a reduced ability to cross the blood-brain barrier (BBB). Upload your answers to the discussion forum of exercise 4.1 in Blackboard. Try to give structures that are different than those of your colleagues.

Recommended student work time: approximately 15 h

TITLE: Introduction to organic synthesis

(5th Week)

Summary

This chapter provides fundamendal knowledge in organic synthesis. Basic reactions of the main homologous series of organic chemistry (alkenes, alkynes, alcohols, carbonyls, aromatics, halogenoalkanes, and amines) are covered. Knowledge of these reactions is necessary for the remaining chapters on the organic synthesis of drug molecules.

Introductory Remarks

Organic reactions are classified based on their mechanisms into addition, elimination, substitution, redox and rearrangement reactions. Redox reactions, in particular, are divided into reduction and oxidation reactions. Reduction reactions include hydrogenation reactions (with H_2/Pd or Zn/HCℓ), reactions with hydride compounds such as $LiAℓH_4$ and $NaBH_4$, and electron transfer reactions (with Li in liquid ammonia). Oxidation reactions include reaction with non-metallic oxidizing reagents, such as ozone or metals with high oxidation numbers, such as the reagents $KMnO_4$ και $K_2Cr_2O_7$.

Another classification distinguishes organic reactions based on the homologous series to which the organic reactants or their products belong.

One of the main homologous series is that of alkenes. Alkenes are synthesized by elimination reactions, such as the dehydration of alcohols and the dehydrohalogenation of alkyl halides. The characteristic reactions of alkenes are those of addition, hydrogenation and oxidative cleavage. Addition reactions include the addition of halogens, hydrogen halides, water (oxymercuration/reduction or hydroboration/oxidation), and carbenes. Emphasis is given to the regioselectivity of these reactions (Markovnikov and anti-Markovnikov addition) and their mechanisms.

Another homologous series with similarities to alkenes is that of alkynes, whose characteristic reactions again include addition and redox reactions, but also acetylenic hydrogen replacement reactions.

One of the most useful groups of organic molecules are the alkyl halides, which can undergo nucleophilic substitution (S_N1 and S_N2 mechanisms) and elimination (E1 and E2 mechanisms) reactions, as well as give Grignard reagents after reaction with magnesium.

Aromatic hydrocarbons are another important group of organic molecules. Their reactions focus mainly on electrophilic aromatic substitution reactions. Knowledge of the mechanisms of these reactions is essential for understanding their regioselectivity.

Alcohols are characterized by cleavage reactions to form alkenes, oxidations of primary and secondary alcohols, and reactions to convert the hydroxyl group to a good leaving group.

Carbonyl compounds are one of the largest groups of organic compounds and are characterized by four categories of reactions that have distinct mechanisms. These reactions are nucleophilic addition to aldehydes/ketones (addition of Grignard and Gilmann reagents, formation of acetals, diols, imines, Wittig reaction, conjugate addition to α,β-unsaturated carbonyls), nucleophilic acyl substitution in carboxylic acid derivatives (formation and reactions esters, amides, carboxylic acids, acid anhydrides and acyl halides), α-substitution (formation of enolic ions with bases and their reaction with electrophiles, malonic and acetoacetic ester synthesis) and carbonyl condensation (Aldol, mixed aldol, Claisen and Dickman cyclization).

Finally, in the homologous series of amines, important reactions are the formation of amines by reductive amination, the reactions of amines as nucleophiles, the Hoffmann elimination and the Sandmeyer reactions of anilines.

Aims/Objectives

The purpose of this charter is to familiarize students with the basic categories of organic reactions, and the main ways of converting one organic molecule into another. Knowledge of the reagents, as well as the conditions and the chemo- and regio-selectivities they exhibit, is essential in designing the synthesis of drug molecules.

Learning Outcomes

Upon completion of week 5, students should be able to:

- Recognize the structures of molecules and the basic reactions of organic chemistry.
- Propose reactions to convert one organic molecule into another.
- Predict the chemo- and regio-selectivity of specific reagents based on knowledge of the corresponding chemical reaction mechanism.

Keywords

Chemical reaction	Reaction mechanism	Homologous series	Chemoselectivity	Regioselectivity

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 5, Dr. Andreas Kalogirou, European University Cyprus. *Here you will find a summary of the main organic transformations, their reagents and mechanisms.*

Jonathan Clayden, Nick Geeves, Stuart Warren Organic Chemistry (2nd Edition), 2012, Oxford University Press.

Study chapter 5 (Organic reactions) and chapter 23 (Chemoselectivity and protecting groups). These chapters contain a good analysis of the chemistry presented in this week.

- **Supplementary Sources/Material**

Video: Organic Chemistry Reactions Summary
A video on organic reactions.

Organic Chemistry Portal, Organic Synthesis Search
A website with information on organic reactions.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 5.1

Visit webpage https://www.organic-chemistry.org/synthesis/ and propose which reagent you would use to make the conversions below. Give your answers in the group forum of week 5 (Blackboard). State whether or not you agree with the reagents suggested by your fellow students and try to propose alternatives.

An indicative selection is the following conversions:

Alkyne → Alkene

Alkene → Alcohol

Alcohol → Alkene

Primary alcohol → Aldehyde

Primary alcohol → Carboxylic acid

Nitroalkane → Amine

Aniline → Bromobenzene

Note: Selected examples of molecules would be given for the above transformations.

Recommended student work time: approximately 17 h

TITLE: Retrosynthesis

(6th Week)

Summary

This chapter covers the basic principles of retrosynthesis. Examples of the syntheses of known drug substances along with their retrosynthesis will be studied.

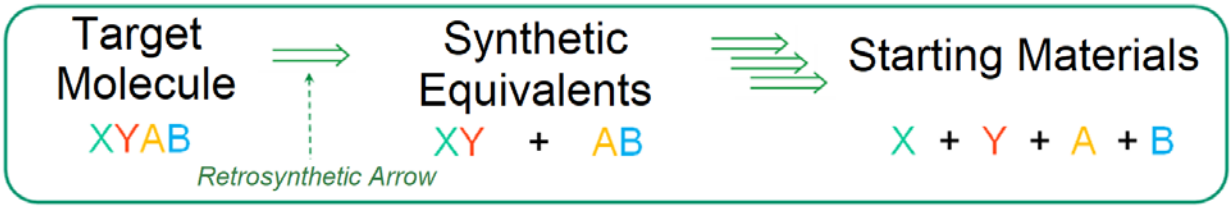
Introductory Remarks

The field of chemistry that deals with the preparation of organic compounds is organic synthesis. Through organic synthesis, an organic molecule can be prepared by selected and appropriate organic reactions, which in several cases may involve several steps (multi step synthesis) to achieve the desired molecule.

Organic synthesis can be divided into two major categories: a) total synthesis and b) asymmetric synthesis or otherwise enantioselective or stereoselective synthesis. In total synthesis, complex organic molecules are synthesized from natural or simple, commercially available precursors. Asymmetric synthesis includes one or more enantiomeric elements (new and desired). In the field of pharmaceuticals, asymmetric synthesis is very important, since the enantiomeric or diastereomeric forms of many drugs show different properties. Asymmetric synthesis will be covered in week 9.

One strategy of synthesis design involves the sequential degradation of the target molecule into precursor molecules, until the starting reagents from which the desired molecule is synthesized are found. This strategy is called *Retrosynthesis* or *Retrosynthetic analysis* and can be characterized as the reverse course of an organic synthesis, where from the target molecule we end up with the starting materials (Fig. 1).

Figure 1: Representation of a retrosynthesis pathway.



When performing a retrosynthesis, it is necessary to choose the appropriate synthetic route and the student must focus on how specific bonds can be efficiently cleaved. It is generally accepted that the majority of reactions take place in the functional groups, which also characterize the activity of the molecules. Functional groups must be detached with relative ease and converted into new groups through reactions that can be reversed, recreating the original functional group. Common conversions of functional groups are C–X/C–OH (X= Cℓ, Br), CHO/CH_2OH, NO_2/NH_2, CH_3/COOH. Thus, the student should first identify the functional group on the target molecule and study how

to synthesize it, while the proposed bond breaking must be based on known and reliable reactions. This procedure is repeated until the initial reagents are obtained. The bonds that are often broken during a retrosynthesis are C–OH, C–X (X = Br, Cℓ) and C–C. When possible, the cleavage preferably takes place in the middle of the molecule and/or at the points where there are branches in chains or rings. The most widely used reactions of this class are the reactions of aldehydes/ketones, alcohols, and carboxylic acids. In addition, in some cases, protective groups may also be used.

When a researcher wishes to apply retrosynthetic analysis, he/she should be familiar with basic terminologies such as:

a) The molecule whose synthesis is desired is called the target molecule (TM).

b) The initial reagents are characterized as Readily Available Starting Materials (RASM) and must be commercially available and preferably low cost.

c) The reverse synthesis course, which involves the hypothetical breaking of a bond to form "synthons" is characterized as a *disconnection*.

d) The product resulting from bond breakage is usually an ion and is designated as a *synthon*. In most reactions, it has no real meaning, but it helps in choosing the correct reactants (Fig. 2).

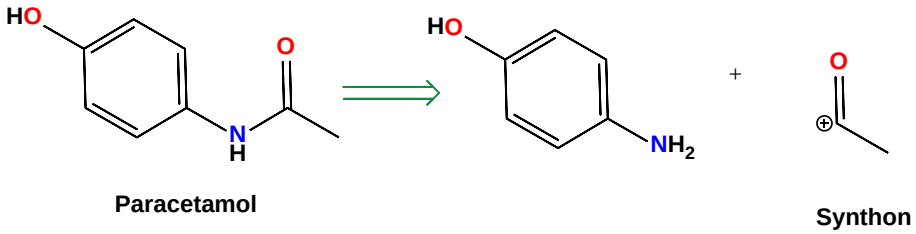


Figure 2: Retrosynthetic analysis of paracetamol.

A retrosynthesis example is that of the ethyl ester precursor of cetaben, a drug that can be used to lower blood lipid levels. As seen in Fig. 3, the molecule contains an amine group, which is the functional group that will undergo the first disconnection. This leads to the formation of an alkyl bromide and an aromatic amino ester (ethyl p-amino benzoate). The alkyl bromide is commercially available, but the amino ester is not. Thus follows a 2nd step aimed at dissociating the precursor compound. Observing Fig. 3, we conclude that the best disconnection choice is the cleavage of the C – O bond between the carbonyl group and the -OEt group. This leads to p-amino benzoic acid and ethanol. Based on all of the above, it appears that the synthesis of the target molecule is a two-step synthesis.

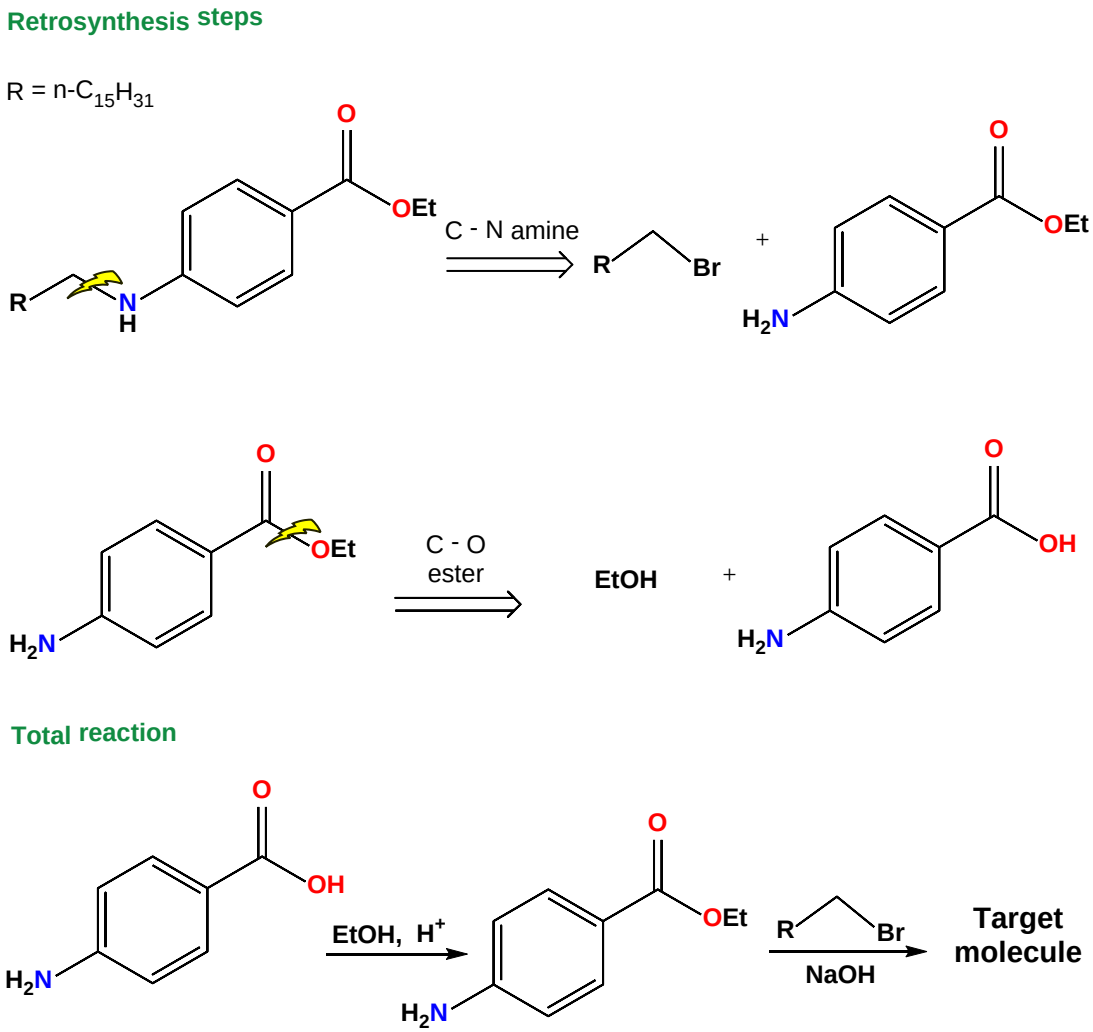


Figure 3: Retrosynthetic analysis of the ethyl ester precursor of cetaben.

Aims/Objectives

The purpose of this chapter is for students to understand the basic principles of retrosynthesis. An additional goal is for students to be able to predict the synthesis of simple pharmaceutical molecules through retrosynthetic analysis.

Learning Outcomes

Upon completion of week 6, students should be able to:

- Describe retrosynthesis.
- Identify the functional groups that can undergo dissociation in a retrosynthesis.
- Describe the synthesis of simple drug molecules through retrosynthetic analysis.

Keywords

Retrosynthesis	Retrosynthetic analysis	Functional group	Synthon

Annotated Bibliography

- **Basic Sources/Material**

Jonathan Clayden, Nick Geeves, Stuart Warren Organic Chemistry (2nd Edition), 2012, Oxford University Press.
Study chapter 28 (Retrosynthetic analysis), which provides a detailed explanation of the use of retrosynthesis.

- **Supplementary Sources/Material**

Video: Retrosynthetic Analysis
Video: Organic Chemistry - Retrosynthetic Analysis
Video: Chapter 30: Retrosynthetic Analysis | Organic Chemistry by Clayden - Greeves - Warren
A series of videos explaining retrosynthesis.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 6.1 (individual graded exercise, 10% weighting)

Use the Reaxys database to study the retrosynthesis of a drug that you will be given e.g., Lorlatinib or Vibegron (these drugs are indicative).

Then upload your retrosynthesis and proposed forward synthesis to the discussion forum of exercise 6.1 in Blackboard.

Each student must comment on a retrosynthesis proposed by a fellow student and state whether they agree or disagree, and if it is possible to suggest a second synthetic path.

Recommended student work time: approximately 20 h

TITLE: Boron, silicon and tin chemistry in organic synthesis

(7th Week)

Summary

This chapter examines the chemistry of boron, silicon and tin, three inorganic elements that find many uses in organic synthesis. Many well-known reactions such as silicon-Bayer-Villinger and Stille coupling are based on organic reagents containing these elements.

Introductory Remarks

Although typical organic molecules found in living organisms are composed of very few elements, there is a large number of elements that can form the basis of reagents, catalysts, and reactive intermediates in organic reactions. Metals will be studied in week 12 (organometallic chemistry), while this week we will study three p-domain elements, which form covalent bonds with carbon and are usually removed at the end of the synthesis as their presence in the final product is not desired.

Starting with boron, it is important to note that it can form compounds with 6 or 8 electrons in its outer shell. The classical reactions by which it is introduced into organic molecules are the hydroborations of alkenes or alkynes with borane or its derivatives. Hydroboration is a regioselective reaction as it is a syn-addition with anti-Markovnikov regiochemistry. The organoborate product can be converted to an alcohol by reaction with hydrogen peroxide under alkaline conditions. The use of sterically hindered mono- or dialkylboranes in hydroboration reactions results in increased selectivity and selective addition of one borane molecule over two. Carbon-boron bonds can be converted to C-O, C-N or C-C bonds with increased stereoselectivity upon reaction with appropriate nucleophiles. The mechanism of these transformations is quite similar to that of the Bayer-Villinger reaction, due to the presence of a positive charge on the alkyl group that is transferred.

Allyl and crotyl boranes react as nucleophiles through their double bond via a six-membered cyclic transition state. These reactions are stereoselective and lead to allylic products.

The chemistry of silicon is similar to carbon with some differences being the large strength of the Si-O bond and the smaller strength of the Si-Si bond. Trialkylsilanes are widely used as protecting groups for alcohols as silyl ethers, while they also give useful compounds with carbon. Two useful reagents that react via nucleophilic substitution are chlorotrimethylsilane and trimethylsilane triflate. Alkynylic silanes can be used as a protection to acetylenic hydrogen, but also to activate the alkyne in reactions with electrophiles by stabilizing the positive charge that results on the β carbon after addition of the electrophile. Aryl silanes can undergo ipso substitution with electrophiles to give useful products. Allyl silanes can also react with electrophiles giving intermediate stable β-cations which can, after loss of silicon, re-form an alkene.

Organosilicon compounds can also form stable carbanions, which can act as nucleophiles. Finally, silicon transfer from carbon to oxygen has been widely observed, for example in the Brook and sila-Pummerer rearrangements.

In organotin compounds tin occurs in oxidation number +4. Their chemistry is dominated by the transfer of alkyl groups from tin to other reagents. Organotins can be synthesized from Grignard reagents and tributyltin oxide or hydrostannilation of alkenes, and their chemistry is similar to that of organosilanes. Organotin crotylates react with aldehydes with good stereoselectivity to give allylic alcohols.

Aims/Objectives

The purpose of this chapter is to acquaint students with the basic reactions of organoboron, silane and tin compounds, as well as with their methods of preparation. Knowledge of the mechanisms of these reactions is essential for predicting their regio- and stereo-selectivity.

Learning Outcomes

Upon completion of week 7, students should be able to:

- Propose reactions for the synthesis of organic molecules using the chemistry of boron, silicon and tin.
- Predict the chemo- and regioselectivity of specific reagents based on knowledge of the corresponding chemical reaction mechanism.

Keywords

Hydroboration	Aryl silanes	Allyl silanes	Organotin compounds

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 7, Dr. Andreas Kalogirou, European University Cyprus.
Here you will find a description of the basic reactions of organic boron, silicon and tin compounds, their reagents and their mechanisms.

Jonathan Clayden, Nick Geeves, Stuart Warren Organic Chemistry (1st Edition), 2000, Oxford University Press.
Chapter 47 (Organo main group chemistry 2: boron, silicon and tin) offers a good analysis of the chemistry covered this week. You will find this chapter along with the lecturer notes in the relevant literature link of week 7.

- **Supplementary Sources/Material**

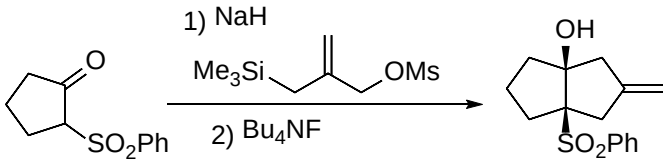
Video: Stoichiometric Organometals V: Organoboron Compounds; Allylations, Prof. Reiser, Lecture 6.
An informative video-lecture on the chemistry of born on YouTube.

Organic Chemistry Portal, Organic Synthesis Search
A website with information on the organic reactions covered in this chapter.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 7.1

Suggest a mechanism for the following reaction. Upload your answer to the discussion forum of week 7 in Blackboard. State whether or not you agree with the reagents suggested by your fellow students and try to propose alternatives.



Recommended student work time: approximately 15 h

TITLE: Synthesis and reactions of heteroaromatics

(8th Week)

Summary

In this chapter, we will focus on the chemistry of heterocyclic compounds with an emphasis on heteroaromatic compounds. These compounds find applications in a multitude of drug molecules, for example quinine, cimetidine and timolol. The basic groups of heteroaromatic compounds, containing five- or six-membered rings or bicyclic systems will be studied. The synthesis of heteroaromatic rings as well as the typical reactions of these systems will be covered.

Introductory Remarks

A large number of heteroaromatic compounds are available and these are separated based on the size of the ring and the number and type of heteroatoms. In this chapter, we study selected heterocyclic compounds.

The most important five-membered heteroaromatic compounds are furan, thiophene and pyrrole. The synthesis of these three compounds can be performed by starting from an acyclic 1,4-dicarbonyl compound with introduction of the heteroatom and subsequent cyclization. In the case of furan, this heteroatom is the oxygen already present in the dicarbonyl, in thiophene the sulfur comes from treatment with P_2S_5, while in pyrrole the nitrogen comes from an amine.

The activity of these three compounds is characterized by electrophilic aromatic substitution reactions with positions 2 and 5 being the most reactive towards substitution.

Among the six-membered compounds, the most well known are pyridine and pyrimidine. Pyridine can be synthesized from a 1,5-dicarbonyl and an amine or ammonia and subsequent oxidation of the resulting 1,4-dihydropyridine. Alternatively, the Hantzsch synthesis can be used, where two ketoesters, an aldehyde and ammonia are condensed. The pyrimidine can be synthesized from a condensation of 1,3-dicarbonyls and amidines.

Pyridines and pyrimidines are electron-poor compounds and are mainly characterized by nucleophilic substitution reactions that take place mainly in positions 2, 4 and 6. This activity is enhanced by the stabilization of the negative charge on the nitrogen atoms.

Two important bicyclic systems are indole and quinoline. The best known synthesis of indoles is the Fischer synthesis from arylhydrazines and ketones involving a [3,3]-sigmatropic rearrangement. Quinolines can be synthesized from the condensation of anilines and 1,3-diketones.

The chemistry of indoles is more similar to that of pyrroles since they react mainly with electrophilic aromatic substitution reactions mostly at position 3. In

contrast, the chemistry of quinolines resembles that of pyridines since they react with nucleophiles mainly at positions 2, 4, 6 and 8.

Aims/Objectives

The purpose of this chapter is to familiarize students with the basic categories of heteroaromatic compounds, and to render them capable of designing their synthesis and describe their chemical reactivity. Knowledge of reagents, conditions, and the chemo- and regioselectivity they exhibit is essential for the design of syntheses of drug molecules containing heterocyclic rings.

Learning Outcomes

Upon completion of week 8, students should be able to:

- Recognize the structures of basic heteroaromatic compounds and their chemical reactivity.
- Propose reagents and strategies for the synthesis of heteroaromatic molecules.
- Design a course of reactions for the synthesis of target heteroaromatic compounds.

Keywords

Heterocycles	Furan	Pyridine	Pyrimidine	Quinoline

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 8, Dr. Andreas Kalogirou, European University Cyprus.
Here you will find a description of the chemistry of heterocyclic compounds.

Jonathan Clayden, Nick Geeves, Stuart Warren Organic Chemistry (2nd Edition), 2012, Oxford University Press.
Study chapters 29 (Aromatic heterocycles 1: reactions) and 30 (Aromatic heterocycles 1: synthesis) that give a good analysis of the chemistry covered this week.

- **Supplementary Sources/Material**

Video: Aromatic Compounds & Heterocycles - Nucleophilic & Electrophilic Aromatic Substitution Reactions
An informative YouTube video on the material covered this week.

Vitaku E, Smith DT, Njardarson JT; Analysis of the Structural Diversity, Substitution Patterns, and Frequency of Nitrogen Heterocycles among U.S. FDA Approved Pharmaceuticals. *J. Med. Chem.* 2014, 57 (24): 10257−10274. DOI: 10.1021/jm501100b.
An article showing the main heterocyclic systems in FDA-approved drugs.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 8.1

Study the article by Sharma GVM, Reddy KL, Lakshmi PS, Krishna PR, 'In situ' Generated 'HCl' - An Efficient Catalyst for Solvent-Free Hantzsch Reaction at Room Temperature: Synthesis of New Dihydropyridine Glycoconjugates, *Synthesis*, 2006 (1): 55-58.

Suggest a synthesis for the drug molecule nifedipine, along with its reaction mechanism.

Upload your answer to the discussion forum of week 8 in Blackboard.

Recommended student work time: approximately 15 h

TITLE: Stereoselective synthesis

(9th Week)

Summary

With most drug molecules having asymmetric carbons and defined stereochemistry, the great importance of stereochemistry in pharmaceuticals should be clear. It is important to understand the different types of stereochemistry (enantiomers, diastereomers, etc.) and how a synthesis can selectively give a product of certain stereochemistry. In this chapter, some stereoselective reactions that are used in both research laboratories and the pharmaceutical industry will be studied.

Introductory Remarks

Starting with the topic of diastereoselectivity, we will study how we can synthesize compounds as a single diastereomer. The reactions we will study are either stereospecific (the stereochemistry of the reactants determines that of the products based on the reaction mechanism) or stereoselective (when one stereoisomer is mainly formed that follows the reaction pathway with the lower energy).

Two stereospecific reactions are the S_N2 nucleophilic substitution and the E2 elimination. The former always leads to an inversion of stereochemistry, while the latter requires a planar transition state thereby the stereochemistry of the reactant determines that of the alkene product. Many addition reactions to alkenes such as bromination and iodolactonization, are also stereospecific. Epoxides also react stereospecificaly, since their stereochemistry is determined by that of the original alkene from which they are prepared, while their opening occurs by an S_N2 mechanism. Other stereospecific reactions include nucleophilic attack on six-membered cyclic ketones and alkylation of cyclic enolate ions.

One important stereoselective reaction, is the nucleophilic addition to carbonyls bearing adjacent asymmetric carbons in the molecule. The major diastereomer of the product can be predicted using Newman projections and applying the Felkin–Anh model. Although this model is based on steric strain (functional group size), the effect of electronegativity is also important with electronegative groups choosing to be away from the attacking nucleophile. The formation of ion complexes with metal cations of reagents can also affect the outcome in nucleophilic addition reactions.

Also of interest, is the epoxidation of unsymmetrical alkenes where we can use Houk's model to predict the stereochemistry of the product. Another stereoselective reaction is that of an aldehyde with an enolate ion that takes place via a cyclic transition state that takes the shape of a chair structure and thus prefers bulky groups to occupy equatorial positions.

Continuing with the topic of enantioselectivity, asymmetric synthesis can also be done using natural chiral molecules (chiral pools), chiral auxiliaries and asymmetric reagents and catalysts.

A low-cost method of enantioselective synthesis is the use of chiral compounds that exist in nature (chiral pool) that can be converted into the target molecule. Such natural molecules are sugars and amino acids, and there are many examples of applications of this strategy, such as the synthesis of the insect pheromone S-ipsenol. This method is however limited by the availability of natural asymmetric molecules.

A more convenient method is the use of chiral auxiliaries, which are molecules that are attached to one of the reagents, determine the stereoselectivity of the reaction, and are then removed and reused. An example of this strategy is the asymmetric Diels-Alder reaction, where an acrylamide derivative of alanine is used to determine the stereochemistry of the reaction.

Finally, more modern is the technique of asymmetric synthesis using asymmetric reagents and catalysts. This creates two mechanistic pathways for the reaction that give a different enantiomeric product and have different activation energy. Consequently, the enantiomer originating from the pathway with the lowest activation energy is mainly produced. Examples are asymmetric hydrogenation catalyzed by a ruthenium complex containing an asymmetric ligand, asymmetric Sharpless epoxidation, and asymmetric hydroxylation.

Aims/Objectives

After the completion of this chapter, the students should comprehend the basic stereoselective reactions and be able to describe the conversion reactions of one organic molecule into another with specific stereochemistry. The knowledge of the mechanistic explanation of the selectivity of these reactions and the ability to apply them to syntheses of target molecules is essential in the design of stereoselective syntheses of drug molecules.

Learning Outcomes

Upon completion of week 9, students should be able to:

- Identify reagents and strategies for the stereoselective synthesis of asymmetric molecules.
- Predict the result of stereospecific reactions based on the knowledge of the corresponding chemical reaction mechanism.
- Explain the outcome of stereoselective reactions using the Felkin–Anh and Houk models.

Keywords

Enantiomers	Diastereoisomers	chiral pool	Sharpless epoxidation	Enantioselective hydrogenation

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 9, Dr. Andreas Kalogirou, European University Cyprus.
Here you will find a description of the main stereoselective reactions.

Jonathan Clayden, Nick Geeves, Stuart Warren Organic Chemistry (2nd Edition), 2012, Oxford University Press
Study chapters 33 (Diastereoselectivity) and 41 (Asymmetric synthesis), which give a good analysis of the chemistry covered this week.

- **Supplementary Sources/Material**

Jonathan Clayden, Nick Geeves, Stuart Warren Organic Chemistry (2nd Edition), 2012, Oxford University Press.
Study chapter 14 (Stereochemistry) for a reminder of the elements of stereochemistry (in case this is needed).

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 9.1

Study the article by Andrew C. Flick, Hong X. Ding, Carolyn A. Leverett, Robert E. Kyne, Jr., Kevin K. -C. Liu, Sarah J. Fink, Christopher J. O'Donnell, Synthetic Approaches to the New Drugs Approved During 2015, *J. Med. Chem.* 2017, 60 (15): 6480–6515.

Focus on the synthesis of the drug Sacubitril.

Explain the following regarding the reaction of the synthesis of molecule 49 (Scheme 7):

a) Why is the Mitsunobu used in the synthesis of compound 45 considered stereospecific?

b) Why does the reduction of the double bond give a single stereoisomer?

Upload your response in the relevant discussion forum of week 9.

Exercise 9.2 (Group assignment, graded 30%)

For this exercise, students are divided into groups of three. Each student in the group will undertake one of the following objectives (research in Reaxys, retrosynthesis, synthesis course). Then the group will meet to discuss and join together all the information, preparing a final report that will be posted on the course platform.

You will be given a target drug molecule for which you must study its retrosynthesis after you first searching its synthesis on the Reaxys database.

You must then give a partial or complete synthesis of at least four steps involving at least one of the following reactions:

- Synthesis or chemistry of a heterocycle (Week 8),
- Boron, silicon or tin chemistry (Week 7)
- Stereoselective synthesis (Week 9).

Upload your answer in pdf form in the corresponding assignment of week 9.
The reagents required for your synthesis must be commercially available.
All chemical structures must be drawn using the ChemDraw software.

Recommended student work time: approximately 25 h

TITLE: Introduction to inorganic chemistry

(10th Week)

Summary

In this chapter, reference is made to the basic theories concerning metal complexes. More specifically, the general principles regarding the coordination of ligands to metal ions are presented. Emphasis is given to bond theories for metal complexes.

Introductory Remarks

In 1893, the Swiss chemist Alfred Werner published the widely accepted coordination theory. In fact, the discovery of this theory was also the reason why he was awarded the Nobel Prize in 1913, as a result of which he is rightly described as the father of coordination chemistry.

The coordination compounds or otherwise coordination complexes form a group of chemical compounds. This means that their structure is described by the theories and concepts that apply to all compounds, while their activity is linked to their structure.

A metal complex consists of a central atom or ion that joins with one or more molecules or ions (ligands) that act as Lewis bases, forming cordination bonds with the central atom or ion that acts as a Lewis acid (Fig. 4). Ligand atoms that bond directly to the central atom or ion are called donor atoms. These atoms are usually oxygen (O), nitrogen (N), sulfur (S), halogens (F, Cℓ, Br, I) and phosphorus (P).

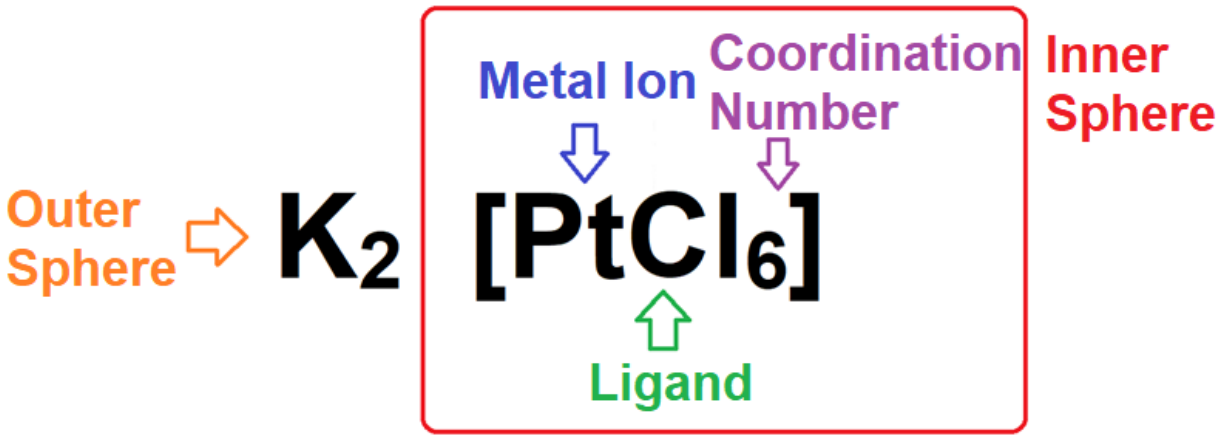


Figure 4: The molecular formula with emphasis on the inner and outer spheres of a complex.

Three bonding theories are used to explain the structure and properties of complexes. These are a) the valence-bond theory (VB), b) the crystal field theory (CFT) and c) the molecular orbital theory (MO).

The valence bond theory was developed by Pauling in the 1930s and considers the formation of a molecule as the result of the coming together of atoms which, when they interact, largely retain their original character. Although nowadays it is not used in the study of complexes (mainly d-transition metals), the terminology and several of its ideas have been preserved, while some knowledge of this theory remains essential. In summary, VB theory explains the geometrical structure and some properties (mainly magnetic properties) of complexes. In transition metal complexes, the central atom has a number of empty orbitals, equal to the number of ligands, which undergo hybridization. The resulting hybrid orbitals have the same energy and defined directions in the three dimensions of space. For the formation of the molecular bond, the pair of electrons occupying the empty orbitals of the central atom comes from the ligand, resulting in the creation of a dative covalent bond. This results in the creation of two categories of metal complexes, namely a) outer orbital-complexes or high-spin or spin-free complexes and b) inner orbital-complexes or low-spin complexes orbital, low-spin or spin paired-complexes. However, there are contradictions between the actual data and the bond-valence theory. This is due to the fact that the VB theory assumes molecular bonds are formed between metal and ligand, while in reality the electrostatic forces between them also play a very important role.

Around the same time that Pauling was developing VB theory, Hans Bethe, John van Vleck, and Leslie Orgel were developing crystal field theory. This theory is an electrostatic model that predicts that the d-orbitals in a metal complex are not degenerate. The splitting of d-orbitals depends on the crystal field, which is determined by the arrangement and type of ligands. The ligands are considered as point charges and there are no covalent metal-ligand interactions. This theory explains phenomena such as the color of various complexes and the magnetic properties of transition elements. In addition, the crystal field theory presents some advantages over the VB theory. In principle, it is more complete and can be applied to ionic crystals, which is due to the assumption that the ligands are negative point charges and interact with the central metal only electrostatically. Also, it enables quantitative estimations as well as prediction of stereostructure and properties of the complexes (e.g., magnetic properties).

Another approach to understanding bonding in metal complexes is molecular orbital (MO) theory, which was developed by Hund and Mulliken in 1932. In contrast to crystal field theory, molecular orbital theory views the bonds between ligands and a central metal ion as covalent. In particular, the MO theory distributes the electrons in molecular orbitals formed by the partial overlap of orbitals. In complexes the molecular orbitals are formed by overlapping the appropriate orbitals of the central atom/ion with appropriate orbitals of the ligands. This is how σ-bonds (LCAO-Linear Combination of Atomic Orbitals) and π-bonds are formed.

The most modern and complete of the three theories is the MO theory, the other two can be considered special cases, because they are simpler and easier to

use than the MO theory. In particular, VB theory can be used to explain the geometry of complexes, but not phenomena related to antibonding orbitals, such as light absorption. Crystal field theory assumes that substituents are point charges and thus interact only electrostatically with the central metal. This fact is an oversimplification, because metal-ligand bonds can have a small or large percentage of molecular bonding. Therefore, this particular theory can be used to explain the absorption of light, but not chemical bonds.

Aims/Objectives

The purpose of this chapter is for students to understand the three main theories that explain the formation of coordination complexes. An additional goal is for students to understand that many of the properties of complex compounds can be predicted and interpreted through specific theories.

Learning Outcomes

Upon completion of week 10, students should be able to:

- Recognize a chemical compound as a coordination complex.
- Describe what the molecular formula of a complex consists of.
- Describe the formation of a complex according to valence-bond, crystal field and molecular orbital theories.

Keywords

Complexes	Valence-bond theory	Crystal field theory	Molecular orbital theory

Annotated Bibliography

- **Basic Sources/Material**
  Mark Weller, Tina Overton, Jonathan Rourke, Fraser Armstrong (2018). Inorganic Chemistry 7th Edition, Oxford University Press (chapter 7, pages 216 – 243).
  The above chapter is an introduction to coordination compounds and explains the basic principles of the three theories that explain the creation of bonds in coordination complexes.

- **Supplementary Sources/Material**

Video: Transition metal complexes

Video: Electron Configurations of Coordination Complexes

Video: Crystal Field Theory

Video: Valence Bond Theory, Hybrid Orbitals, and Molecular Orbital Theory

The above videos describe what transition metal complexes are and the basic principles of the three theories that explain the formation of bonds in inclusion complexes.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 10.1

Watch the video «High spin and Low spin Complexes».

Post in the discussion forum of week 10 a paragraph on the differences between the two classes of complex compounds based on the content of the video (<200 words), and give two examples of complexes, one high and one low spin.

Comment on the post of one of your colleagues (<100 words).

Recommended student work time: approximately 15 h

TITLE: Synthesis and characterization of metal complexes with medicinal properties

(11th Week)

Summary

This section describes typical examples of complex compounds that are currently used as drugs in various diseases. More specifically, reference is made to the synthesis, structure and the mechanism of action of cis-platin and Auranofin.

Introductory Remarks

Inorganic medicinal chemistry is a field of great importance, in both therapeutics and diagnostics. This is due to the fact that it offers potential for the design of new therapeutic and diagnostic agents which often lead to a better understanding and treatment of diseases that are currently incurable. The role of inorganic medicinal chemistry in medicine is also strengthened by the fact that many organic molecules for their action either a) can be activated or biotransformed by metal ions, or b) have a direct or indirect effect on the metabolism of various metal ions.

The discovery and development of cis-platin played a prominent role in the establishment of the field of inorganic medicinal chemistry. In particular, cis-platin is the first platinum complex to be used as an antineoplastic drug. This particular complex inhibits DNA synthesis in the cell cycle, thus causing the death of cancer cells. It is used in specific types of cancer, such as testicular, bladder, esophagus, cervix, breast, lung cancer and many others. The treatment is limited, however, by several side effects, such as nephrotoxicity, emetogenesis, and neurotoxicity.

Cis-platin according to IUPAC is called cis-diamminodichloroplatinum (II) and has the molecular formula **$[Pt(NH_3)_2Cl_2]$** (Fig. 5).

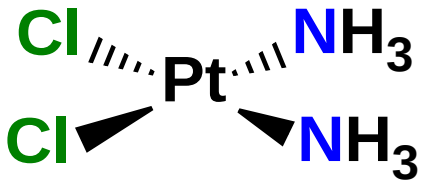


Figure 5: The structure of complex cis-platin.

The synthesis of the complex is relatively simple and is based on the controlled reduction of potassium hexachloroplatinate (IV) (starting material) with hydrazine hydrochloride ($N_2H_4 \cdot 2HCl$) to the corresponding potassium tetrachloroplatinate (II) $K_2[PtCl_4]$. This is then reacted with a mixture of NH_3 - NH_4Cl to give the desired complex, according to the reactions:

$$2K_2[PtCl_6] + N_2H_4 \cdot 2HCl \longrightarrow 2K_2[PtCl_4] + N_2 + 6HCl \quad \textit{Equation 1}$$

$$2K_2[PtCl_4] + 2NH_3 \xrightarrow{NH_4Cl} \textbf{cis-}[Pt(NH_3)_2Cl_2] + 2KCl \quad \textit{Equation 2}$$

Because some trans-complex is inevitably formed, in another preparation method the tetrachlorocomplex $K_2[PtC\ell_4]$ is initially converted to the tetraiodocomplex, $K_2[PtI_4]$ with excess KI, due to the smaller trans-effect of iodides compared to that of chloride ions. Regarding the structure, as shown in Fig. 5, the Pt(II) cation is arranged in a square planar geometry in which two ammonia molecules and two $C\ell^-$ anions are placed in a cis-configuration.

A second complex with important applications in pharmaceuticals is auranofin (Fig. 6).

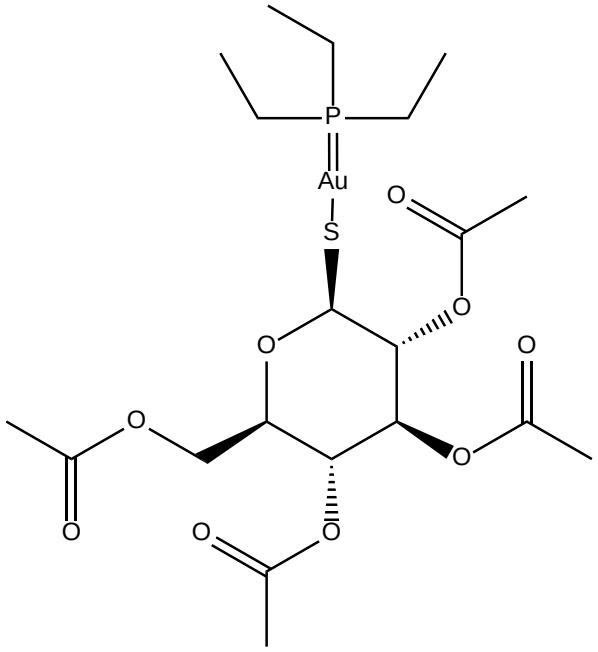


Figure 6: The skeletal structure of auranofin.

Auranofin exhibits anti-arthritic, anti-inflammatory and immunoregulatory properties. In fact, some of these properties are unique and contribute to the therapeutic response. The most important property of auranofin is that it is a disease-modifying antirheumatic drug (DMARD) that has been found to limit or prevent joint damage, especially if given in the early stages of the disease. The main mechanism of action of auranofin is through the inhibition of reduction/oxidation (redox) enzymes necessary to maintain intracellular levels of reactive oxygen species. Inhibition of these enzymes leads to cellular oxidative stress and endogenous apoptosis.

Auranofin is a neutral gold complex in the oxidation state I, where the metal ion has a linear geometry and is joined by two substituents (Fig. 6). Specifically, it joins with a triethylphosphine molecule that acts as a neutral electron donor and with a tetra-acetyl-pyranosyl-thiouronium molecule where in the complex formed the thiol acts as an anionic donor.

The synthesis of auranofin is carried out by the reaction of triethylphosphine-chlorogold (I) with tetra-acetyl-pyranosyl-thiouronium. This specific substituent is obtained from β-D-glucopyranose, while the synthesis of triethylphosphine-gold (I) chloride is carried out in ethanol by mixing triethylphosphine and tetrachlorogold (III) anion (Fig. 7).

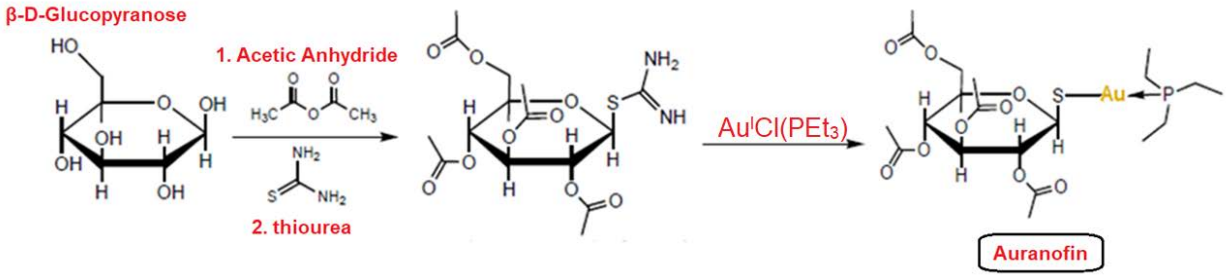


Figure 7: The synthesis of Auranofin.

Aims/Objectives

The purpose of this chapter is for students to understand the importance of complex compounds in medicine. An additional objective is for students to be able to study recent literature and refer to the synthesis, structure and mechanism of action of a complex compound with medicinal properties.

Learning Outcomes

Upon completion of week 11, students should be able to:

- Describe the synthesis of complex compounds with medicinal properties.
- Describe the structure of complex compounds with medicinal properties.
- Describe the mechanism of action of complex compounds with medicinal properties.

Keywords

Metal complexes in medicine	Platinum complexes and cancer	Ruthenium complexes and cancer	Copper complexes in medicine	Zinc complexes in medicine	Metal complexes with pharmaceutical properties

Annotated Bibliography

- **Basic Sources/Material**

Metals in Medicine, 2nd edition 2017, by James C. Dabrowiak, Wiley. ISBN: 978-1-119-19137-7 May 2017.
In the following chapters you can find information on complexes of platinum (chapter 3) and gold (chapters 4.3, 6) with pharmaceutical properties.

- **Supplementary Sources/Material**

Pattan SR, Pawar SB, Vetal SS, Gharate UD, Bhawar SB, 2012, The scope of metal complexes in drug design – a review, *Indian Drugs*; 49 (11): 5-12.
An article on the scope of metal complexes used in drug design.

Mjos KD. Orvig C, 2014, Metallodrugs in Medicinal Inorganic Chemistry, Chemical Reviews 114: 4540-4563.
An article which makes a historical review of metal-containing drugs.

Video: The Mechanism of Cisplatin
A video describing the mechanism of action of cis-platin.

Video: AURANOFIN
A video on the mechanism of action of Auranofin.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 11.1

Study the article by Ariana C. F. Santos, Luís P. G. Monteiro, Adriana C. C. Gomes, Fátima Martel, Teresa M. Santos, Bárbara J. M. Leite Ferreira, 2022, NSAID-Based Coordination Compounds for Biomedical Applications: Recent Advances and Developments, *International Journal of Molecular Sciences*; 23:2855, which is a literature review referring to coordination complexes with non-steroidal anti-inflammatory drugs (NSAIDs).

Each student must choose one of the complexes mentioned in the article and study it (find the original references regarding synthesis, structure and properties).

Then, each student must report in the relevant discussion forum of week 11, the synthesis and structure of the complex of their choice (100-200 words).

Recommended student work time: approximately 12 h

TITLE: Transition metal organometallic chemistry

(12th Week)

Summary

This chapter discusses some aspects of organometallic chemistry, emphasizing the types of bonding and reactions encountered in this class of compounds. Special reference is then made to reactions of organometallic compounds of palladium (Pd).

Introductory Remarks

The field of Organometallic Chemistry developed around the 1950s and deals with the chemistry of compounds containing metal-carbon bonds. It includes a large number of compounds and reactions, where substituents interact with σ- and π-bonds with metals and metal ions. In addition, organometallic compounds exhibit a variety of coordination geometries and metal oxidation numbers, which combine with carbon atoms of various substituents, leading to additional bond types not found in other types of compounds. This results in the extremely rich and at the same time complex chemistry of organometallic compounds. [Compounds of certain elements (semimetals) e.g., boron, silicon and arsenic containing carbon bonds, are not typically characterized as organometallics].

In organometallic chemistry, we find five (5) types of bonds:

a. The ionic bond: found in compounds of highly electropositive metals (alkali, alkaline earth, lanthanides and actinides, with electronegativity values of ~ 1 or less).
b. The covalent σ-bond: found in compounds where the carbon atom is attached to the metal by a normal covalent bond. They are generally formed from most elements with electronegativity values greater than 1.
c. The synergistic bond: is the type of bond in which electron density is simultaneously offered and accepted. It can be characterized as the most representative bond in organometallic compounds.
d. The electron-poor bond: is the type of bond in which the valence electrons available for bond formation are not sufficient to fill all the bonding orbitals with electron pairs, resulting in the formation of polycentric bonds.
e. Delocalized metal bonds: is the type of bond in which delocalization of the metal charge is observed in an extended orbital system.

The stability of organometallic compounds depends on whether the metals belong to the s or p domain or whether they are transition metals (d metals). In the first case, the bond is relatively simple and is adequately described only by σ-bonds. In the case of d organometallic compounds, a variety of bonds are observed and often have a total of 16 or 18 valence electrons around the metal/metal ion (18 electron rule). This limitation is due to the strength of π-bonding interactions between the carbon-containing substituents and the metal. In addition, organometallic compounds have a variety of coordination numbers

(CN), the most common being 6-, while quite often we find complexes with CNs of 7-, 8- and 9-. The geometries observed in these complexes are those generally encountered in Inorganic Chemistry, i.e., linear, planar trigonal, tetrahedral, planar tetragonal, trigonal bipyramidal, octahedral, trigonal prismatic, etc.

An additional very important chapter of organometallic chemistry are the types of organometallic reactions. The most important of these are oxidative addition, reductive elimination, and transmetalation (Fig. 8). During the oxidative addition to a metal, which is oxidized by two units, the metal is bonded to two other atoms by insertion into a bond, either an X – Y single bond, or a multiple bond by reduction in the order of the multiple bond and formation of a cyclic metal compound, or a C – H bond in an orthometalation step. Reductive elimination is the opposite of oxidative addition, i.e., the substituents join and detach from the metal center, which is reduced by two units. Transmetalation reactions can be thought of as replacement reactions. In these, a compound of a relatively inert metal is treated with a more reactive metal, with the result that the latter takes the place of the former in the compound.

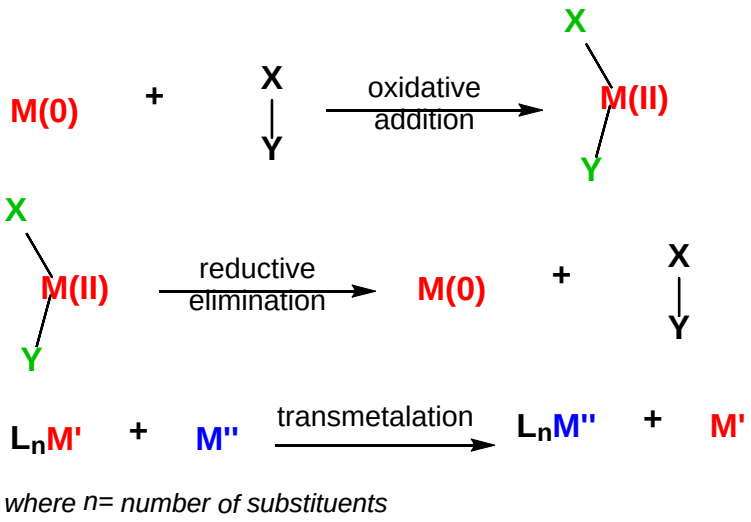
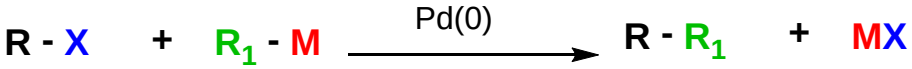


Figure 8: Types of organometallic reactions.

All of the above form the basis for the organometallic chemistry of the transition metals and are the same regardless of which metal is combined with the various substituents. This section focuses on the chemistry of one of the most important transition metals, palladium, as it is one of the most widely used metals in industry and research. It is worth noting that most syntheses of large organic molecules today involve palladium compounds in one and/or more basic steps. Examples of (cross-coupling) reactions catalyzed by palladium are Suzuki-Miyaura (1979), Stille (1978), Negishi (1977), Sonogashira (1975) and Heck (1968). These reactions are named after the researcher who discovered them. The general reaction of the above is as follows:



These reactions can be represented by the general catalytic cycle shown in Figure 9:

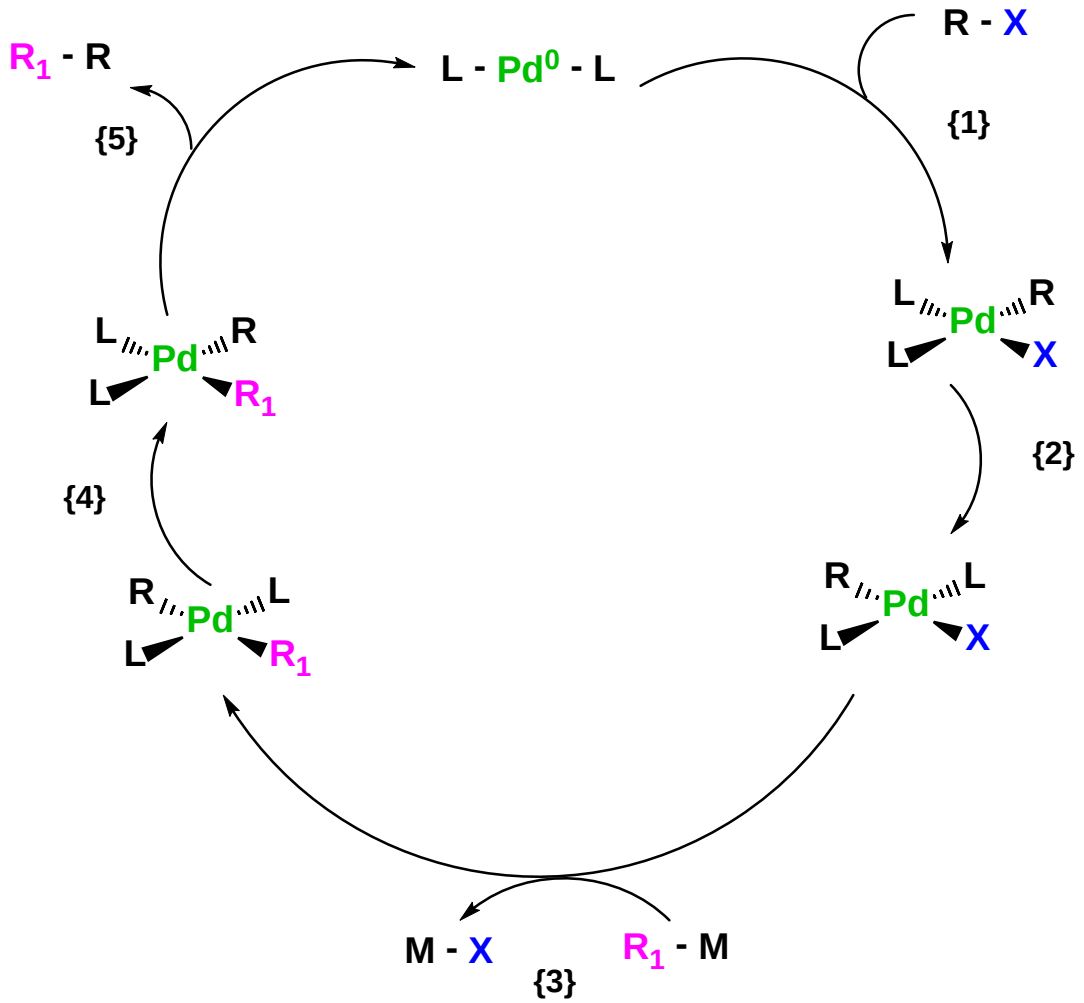


Figure 9: The general catalytic cycle of Pd cross coupling reactions.

During step {1} oxidative addition of RX (where R= alkyl, aryl) to a Pd(0) complex takes place resulting in the formation of a planar Pd(II) complex. If the new complex is of a cis-conformation, then very fast cis-trans isomerization takes place (step {2}) to avoid having a good σ donor (L) opposite a strong R donor in a trans position. In step {3} a transmetalation takes place, where the nucleophile (R_1) is transferred from the organometallic reagent to the palladium, while the counterion X (where X = halide) is transferred to the metal M. In step {4} a second cis-trans isomerization takes place (if the transmetalation product is in the trans form), since in step {5} reductive cleavage of a C-C bond takes place, which requires the cis arrangement of R and R_1. It is worth noting that the identity of M is what determines the type of reaction.

Aims/Objectives

The purpose of this chapter is for students to understand the importance of organometallic compounds in the field of pharmaceutics. An additional goal is

for students to study and understand basic organic syntheses that involve the use of palladium organometallic compounds as catalysts.

Learning Outcomes

Upon completion of week 12, students should be able to:

- Describe organometallic compounds.
- Describe the basic types of reactions carried out by organometallic compounds.
- Describe basic catalytic reactions, using organometallic palladium complexes as the catalyst.

Keywords

Organometallic chemistry	Organometallic compounds	Reactions of organometallic compounds		
Suzuki-Miyaura coupling	Stille coupling	Negishi coupling	Sonogashira coupling	Heck coupling

Annotated Bibliography

- **Basic Sources/Material**

Jonathan Clayden, Nick Geeves, Stuart Warren Organic Chemistry (2nd Edition), 2012, Oxford University Press
Study chapter 40 (Organometallic chemistry), that offers a good analysis of the chemistry covered this week.

- **Supplementary Sources/Material**

Video: Transmetalation
An interesting video on transmetalation.

Video: Oxidative addition and Reductive elimination
An interesting video on oxidative addition and reductive elimination.

Video: Organometallics 5: Suzuki Reaction
An interesting video on the mechanism of the Suzuki-Miyaura coupling.

Video: Organometallics 6: Stille Reaction
An interesting video on the mechanism of the Stille coupling.

Video: Negishi cross-coupling reaction
An interesting video on the mechanism of the Negishi coupling.

Video: Sonogashira Coupling Reaction Mechanism
An interesting video on the mechanism of the Sonogashira coupling.

Video: Organometallics 3: Heck Reaction
An interesting video on the mechanism of the Heck coupling.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 12.1

Study the review article by Buskes MJ, Blanco MJ, titled Impact of Cross-Coupling Reactions in Drug Discovery and Development, 2020, *Molecules*; 25: 3493, which refers to the impact of cross-coupling reactions on new drug discovery and development.

Each student is asked to describe the mechanism of synthesis of a drug, which has resulted from a cross-coupling reaction in the relevant forum of week 12 (<200 words).

After submission, students will be asked to comment and rate the work of one of their fellow students.

Exercise 12.2

Study the article by Andrew C. Flick, Hong X. Ding, Carolyn A. Leverett, Robert E. Kyne Jr., Kevin K.C. Liu, Sarah J. Fink, Christopher J. O'Donnell, 2017, Synthetic Approaches to the New Drugs Approved During 2015, Med. Chem.; 60 (15): 6480–6515.

Propose the mechanism for the first step of the synthesis of Ozenoxacin (Scheme 4).

Upload your answer in the relevant discussion forum of week 12.

Recommended student work time: approximately 18 h

TITLE: Selected syntheses of organic drug molecules

(13th Week)

Summary

The synthesis of drug molecules is one of the most important applications of synthetic organic chemistry. This chapter is a recap of the entire course as it uses knowledge gained in most chapters such as retrosynthesis and asymmetric synthesis. Selected syntheses of drug molecules such as benzocaine, salbutamol, thyroxine and dofetilide will be studied as well as syntheses of compound groups of pharmaceutical interest such as β-lactams, alkaloids and sugars. Finally, the more complex synthesis of the anti-HIV drug Crixivan will complete the content of the course.

Introductory Remarks

Some drug molecules are products that occur in nature in very small amounts, so chemists must develop synthetic methods to prepare the large amounts needed to treat patients. Other drugs are the result of design, using the techniques discussed in the first four weeks, so they again require efficient synthetic methods to produce them. This week, we will study in detail some of the synthetic methods used in the preparation of important drug molecules.

The synthesis of the local anesthetic benzocaine is one of the simplest examples, since it uses classical aromatic chemistry and some functional group conversions. Similarly, the synthesis of the antiasthmatic salbutamol uses Friedel-Crafts acylation as well as selective carbonyl reduction in the presence of protecting groups. Synthesis of the hormone thyroxine uses different chemistry since it involves a nucleophilic aromatic substitution reaction.

The synthesis of the antiarrhythmic dofetilide is more diverse, since it includes a multitude of functional group conversions and different mechanisms, such as nucleophilic attack on epoxide and reductive amination.

Many drug molecules have carbohydrate moieties; therefore, carbohydrate synthesis is important. An example of carbohydrate synthesis is that of ribonucleotides starting from ribose. The synthesis presented involves protection of ribose functional groups, nucleophilic substitution at the anomeric position and a phosphate ester formation reaction.

An important class of antibacterials are the β-lactams. In addition to biosynthetic methods, β-lactam can also be prepared by [2+2]-cycloadditions of an imine and a ketene. The regiochemistry of this reaction depends on the substituents on the imine nitrogen.

A class of pharmacologically active natural products are alkaloids. The synthesis of alkaloids often mimics the reactions of their preparation by biological systems using reactions such as the coupling of radicals resulting from the oxidation of phenols. Two classic examples of alkaloid synthesis are the synthesis of papaverine and morphine.

Finally, the synthesis of the anti-HIV drug Crixivan is a process that incorporates much of the knowledge gained in this course. It includes a detailed retrosynthesis and design of the reaction pathway followed for the assembly of the molecule. The synthesis involves several asymmetric synthesis steps, such as Sharpless epoxidation and asymmetric hydrogenation.

Aims/Objectives

The purpose of this chapter is to familiarize the students with the basic methods of drug molecule synthesis and render them able to design and describe the course of reactions for the synthesis of target drug molecules. For this purpose, it is important to know the reagents, the conditions and the chemo- and regio-selectivity of each reaction.

Learning Outcomes

Upon completion of this chapter, students should be able to:

- Design the synthesis of target organic drug molecules.
- Apply strategic use of protecting groups in the synthesis of complex molecules.
- Apply retrosynthetic analysis to the design of the synthesis of academically and commercially important organic target molecules.

Keywords

β-lactam synthesis	Steroid synthesis	Sugar synthesis	Alkaloid synthesis

Annotated Bibliography

- **Basic Sources/Material**

Course notes for week 13, Dr. Andreas Kalogirou, European University Cyprus. *Here you will find some examples of the syntheses of biologically active compounds.*

Organic Chemistry, 2nd Edition 2012, by Jonathan Clayden, Nick Geeves, Stuart Warren, Oxford University Press: *Chapter 43 (Organic chemistry today)*. *In this chapter we are interested only in the synthesis of the anti-HIV drug Crixivan.*

- **Supplementary Sources/Material**

Jonathan Clayden, Nick Geeves, Stuart Warren Organic Chemistry (2nd Edition), 2012, Oxford University Press
Chapter 34 (Pericyclic reactions 1: cycloadditions). In this chapter we are interested only in the synthesis of β-lactam.

Weekly Self-Assessment & Interactive Exercises/Activities

Exercise 13.1

Study the retrosynthesis of Ozenoxacin and propose a synthesis of at least three steps. Upload your answer in the relevant discussion forum of week 13.

You can see the structure of the drug molecule in the following website:

https://go.drugbank.com/drugs/DB12924

Recommended student work time: approximately 20 h

FINAL TELECONFERENCE/GROUP CONSULTATION MEETING

During this final teleconference, students are informed about the format of the final exam (e.g., multiple-choice questions, short or long answers, case studies, etc.) and if the exam will be open-book or not.

TITLE: Final exams

(14th Week)

Date of final exams: TBA

Time: TBA

Recommended number of work hours for the student: Approximately 50 h

INDICATIVE ANSWERS FOR WEEKLY SELF-ASSESSMENT & INTERACTIVE EXERCISES/ACTIVITIES

Exercise 1.1

α) Structure 4 is not covered by the patent.

β) Structures 1, 2 and 3 are covered by the patent.

Exercise 2.1

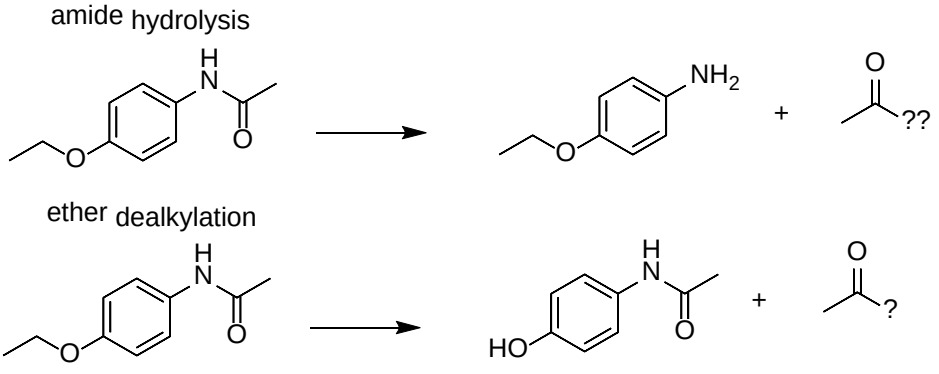
The goal of the research by the Miami Project to Cure Paralysis was to find drug molecules that stimulate the growth of axons in order to recreate the lost connections between neurons. The researchers used a phenotypic cell screening procedure using nerve cells from the hippocampus of rats. The study was limited to 240 small molecules with known activity as kinase inhibitors. Cells were placed in 96-well plates and then a solution of each compound under study was added. After some incubation time the cells were observed. Hits are neurons that showed a >25% increase in axon length compared to blank (DMSO only). Search results: 40 hits were found. The classes of active compounds are isoquinolines, indolinomaleimides and anilinoquinazolines.

Exercise 3.1

Answer: (1,800*0,8)*(1,200*0,8)*70 = 96,8 million compounds.

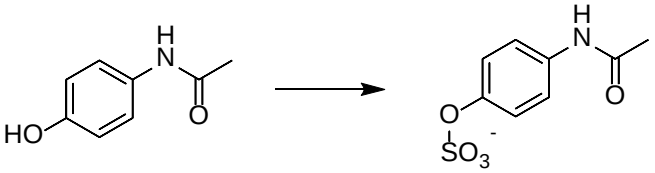
Exercise 3.2

Products from two phase I reactions:



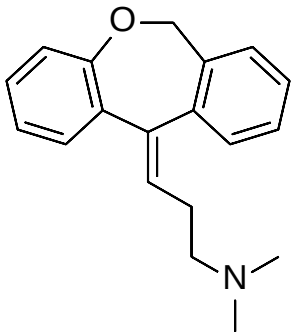
Products from a phase II reaction:

Coupling with a sulfate group

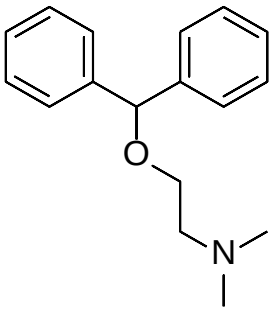


Exercise 4.1

There are many correct answers. The ideal is drug diphenhydramine.



Doxepine



Diphenhydramine

Exercise 5.1

The reagents required are the following:

Alkyne → Alkene: H_2, Lindlar catalyst.

Alkene → Alcohol: It can be done in two ways, oxymercuration/reduction (originally with $Hg(OAc)_2$ and water and then with $NaBH_4$) or hydroboration/oxidation (initially with BH_3 in THF and then H_2O_2, KOH).

Alcohol → Alkene: It could be done with H_2SO_4 and heating for tertiary alcohols, but with $POCl_3$ and pyridine for primary and secondary alcohols.

Primary alcohol → Aldehyde: Oxidation with PCC.

Primary alcohol → Carboxylic acid: Oxidation can occur with various reagents like $KMnO_4$ in water, CrO_3 ή $K_2Cr_2O_7$.

Nitroalkane → Amine: Reduction with H_2, Pd/C.

Aniline → bromobenzene: A Sandmeyer reaction occurs: firstly the aniline is converted to a diazonium salt with $NaNO_2$, H_2SO_4 and it is subsequently reacted with CuBr, HBr.

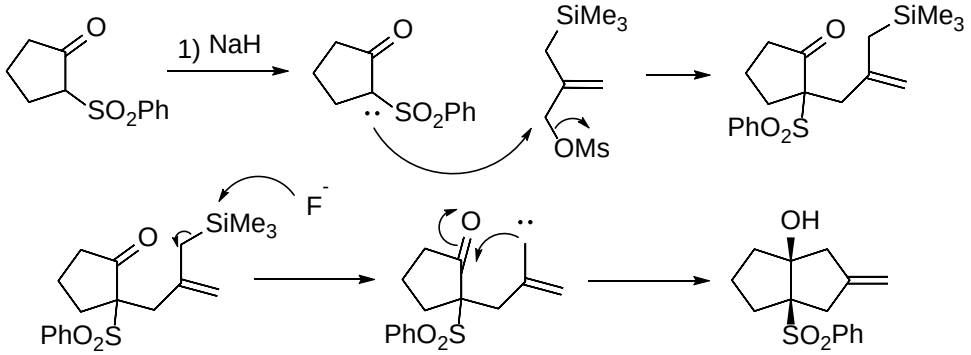
Exercise 6.1

Students are expected to report that they will search and post a synthetic route of a drug via retrosynthesis. In addition, they should comment on a retrosynthesis of another student.

Exercise 7.1

This exercise is a reminder of the ability of sulfones to stabilize anions in the adjacent carbon as well as the ability of fluoride to attack silicon.

Mechanism: Sodium hydride deprotonates the proton next to the sulfone to form an enolate ion. This performs a nucleophilic substitution of the mesylate ion. The product then reacts with silicon to give an allyl ion which then adds to the ketone giving a 5/5 bicyclic system with the necessary cis stereochemistry



Exercise 8.1

The synthesis of nifedipine is described in the following article:

https://www.tandfonline.com/doi/full/10.1080/00397911.2010.528289

The general mechanism of Hantzsch reactions is given in the website:

https://www.organic-chemistry.org/namedreactions/hantzsch-dihydropyridine-synthesis.shtm

Exercise 9.1

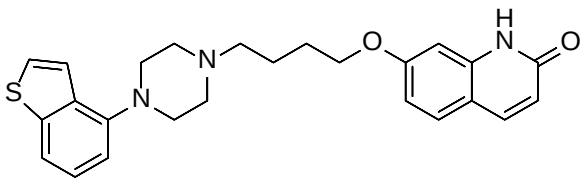
A) The Mitsunobu reaction is stereospecific as it involves an S_N2 nucleophilic substitution. The mechanism of this reaction is given in the website:

https://www.organic-chemistry.org/namedreactions/mitsunobu-reaction.shtm

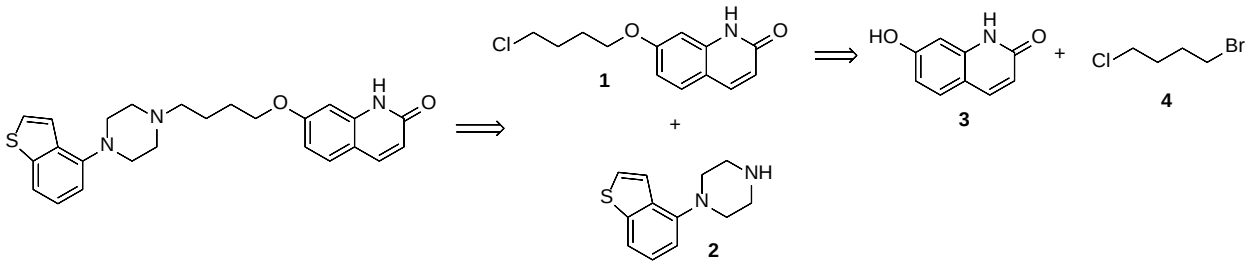
B) Reduction of the double bond using a ruthenium catalyst in the presence of an asymmetric substituent gives a single stereoisomer (compound 48). The binding of the double bond and the substituent on ruthenium gives an asymmetric intermediate in which addition of the hydrogen to the double bond occurs selectively on the side with the least steric hindrance.

Exercise 9.2

An example of a target drug molecule is Brexpiprazole given below.

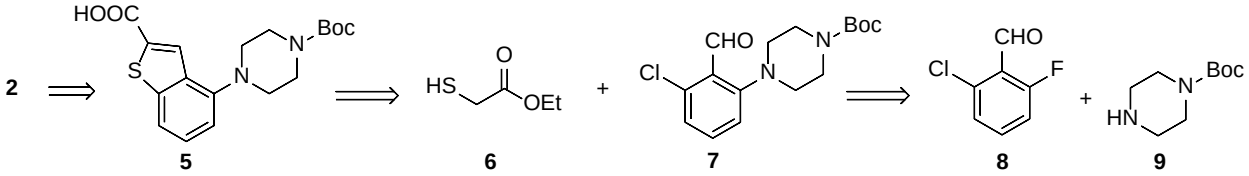


A suggested retrosynthetic pathway is the following:

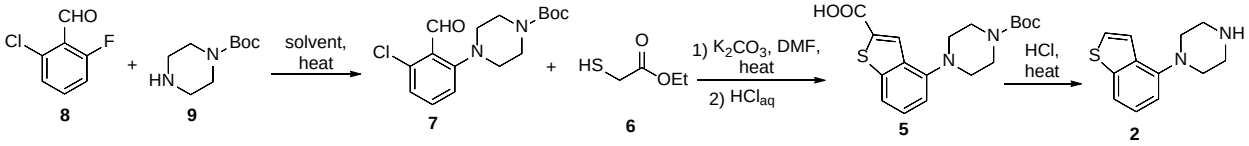


The first disconnection is that of the piperazine bond to the alkyl group giving chloride **1** and piperazine **2**. The ether in chloride **1** can be formed by a Williamson reaction of phenol **3** with halide **4**. Compounds **3** and **4** are commercially available.

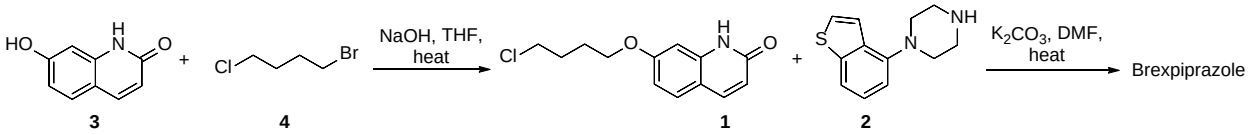
Regarding the synthesis of fragment **2**, it is proposed to prepare the thiophene ring from aldehyde **7** and thiol **6**. This results in the presence of carboxylic acid and Boc groups in thiophene **5**. Aldehyde **7** can be synthesized by nucleophilic aromatic substitution of piperazine **9** on benzaldehyde **8**. Compounds **6**, **8** and **9** are commercially available.



Below you can see the synthesis of the drug molecule starting from the preparation of fragment **2** which includes a heterocyclic ring synthesis. Nucleophilic substitution on aldehyde **8** by the protected piperazine **9** gives compound **7**. Condensation with thiol **6** gives thiophene **5** after hydrolysis of the ethyl ester group. Heating under acidic conditions leads to deprotection of the Boc group and decarboxylation of the carboxylic acid leading to thiophene **2**.



Subsequently, for the synthesis of chloride **1**, the Williamson reaction between phenol **3** and halogenoalkane **4** in the presence of NaOH base is proposed. The synthesis of the final drug molecule is done by the alkylation of piperazine **2** with chloride **1** in the presence of the base K_2CO_3.



Exercise 10.1

Students are expected to report that:

a) when strong field substituents are present in a complex (π.χ. CO, CN^-, NO_2 etc.), these cause a large splitting between the d orbitals of the metal resulting in the creation of a *low spin complex*. In these cases, inner shell orbitals are used for hybridization and the complex is called a complex of inner orbitals.

b) when in a complex there are weak field substituents (e.g. OH^-, H_2O etc.), they cause a small splitting between the d orbitals of the metal, resulting in the creation of a *high spin complex*. In these cases, outer shell orbitals are used to hybridize the orbitals of the metal ion, the complex is called a complex of outer orbitals and is *high spin*.

(weak field) $I^- < Br^- < S^{2-} < SCN^- < Cl^- < NO_3^- < N_3^- < F^- < OH^- < C_2O_4^{2-} \approx H_2O <$

$NCS^- < CH_3CN <$ py $< NH_3 <$ en $<$ bipy $<$ phen $< NO_2^- < PPh_3 < CN^- \approx$ CO *(strong field)*

Typical examples of low spin complexes are $[Co(NH_3)_6]^{3+}$, $[Ni(CN)_4]^2$, $Cr(CO)_6$

Typical examples of low spin complexes are $[CoF_6]^{3-}$, $[Co(H_2O)_6]^{3+}$, $[Cr(NH_3)_6]^{2+}$, tris(acetylacetonato)iron (III) (Tris(acetylacetonato)iron(III)).

Exercise 11.1

Each student must choose a complex to describe. He/She must find the original articles that refer to synthesis and structure (there may be more than one article), study them and make a summary of them.

Exercise 12.1

Each student must choose a drug that has resulted from a cross-coupling reaction and describe its synthesis mechanism.

Exercise 12.2

This is a Buchwald-Hartwick reaction. The general mechanism of such reactions is given in the website:

https://www.organic-chemistry.org/namedreactions/buchwald-hartwig-reaction.shtm

Exercise 13.1

You can see the synthesis of the drug molecule Ozenoxacin in the following article:

Synthetic Approaches to the New Drugs Approved During 2015 (https://doi.org/10.1021/acs.jmedchem.7b00010).

APPENDIX IV

<table>
<tr><td>Course title</td><td colspan="5">Natural Medicinal Products: Discovery and Characterization</td></tr>
<tr><td>Course code</td><td colspan="5">DBP600</td></tr>
<tr><td>Course type</td><td colspan="5">Compulsory</td></tr>
<tr><td>Level</td><td colspan="5">Master (2nd Cycle)</td></tr>
<tr><td>Year / Semester</td><td colspan="5">1st Year/1st Semester</td></tr>
<tr><td>Teacher’s name</td><td colspan="5">Dr. Constantinos Nikiforou and Dr. Ioannis Stavrou</td></tr>
<tr><td>ECTS</td><td>10</td><td>Lectures / week</td><td>Up to 6 Teleconferences</td><td>Laboratories / week</td><td>–</td></tr>
<tr><td>Course purpose and objectives</td><td colspan="5">The main goal of this course is to introduce postgraduate students to the traditional and modern sources of natural bioactive compounds with therapeutic applications, as well as with the methods used for their qualitative and quantitative characterization. Additionally, the objectives of the course are for postgraduate students to acquire in-depth knowledge in modern and advanced techniques of discovery, isolation, characterization, identification and quantification of natural products and plant extracts, with the aim of using them in the pharmaceutical industry.</td></tr>
<tr><td>Learning outcomes</td><td colspan="5">Upon completing this course, students should be able to:
Describe a variety of drug sources of natural origin.
Identify main important chemical classes of bioactive compounds of natural origin, their biological roles, and the therapeutic effects of their action on the human body.
Evaluate a series of modern and advanced techniques for the discovery, isolation, identification and analysis of natural pharmaceutical products.
Apply this knowledge to the design of a pharmaceutical product of natural origin.
Appreciate the role of natural products as driver molecules for the design and development of new drugs.</td></tr>
<tr><td>Prerequisites</td><td colspan="2">None</td><td>Co-Requisites</td><td colspan="2">None</td></tr>
</table>

Course content	• Natural sources of pharmaceuticals: bacteria, fungi, animals and plants. • Discovery and identification of plant-derived bioactive molecules. • Techniques for the extraction and isolation of natural products. Structure characterization, qualitative and quantitative analysis. • Extracts and essential oils as medicinal products: Regulatory requirements and quality control. • Clinical trials and approval of ingredients of natural origin to create pharmaceutical formulations.
Teaching methodology	E - Learning
Bibliography	*Textbook of Pharmacognosy and Phytochemistry*, Shah B., Seth A., 2009, Elsevier India, e book ISBN: 9788131232606. *Fundamentals of Pharmacognosy and Phytotherapy* (Third Edition), Heinrich M., Barnes J., Prieto-Garcia J., Gibbons S., Williamson E., 2018, Elsevier, ISBN: 9780702070082. *Drugs of Natural Origin: A Treatise of Pharmacognosy* (Sixth Edition), Samuelson G., Bohlin L., 2010, Swedish Pharmaceutical Press, ISBN: 978-91-976510-5-9. *Pharmaceutical Analysis: A Textbook for Pharmacy Students and Pharmaceutical Chemists,* Watson D.G., Elsevier, 2020, eBook ISBN: 9780702078095. *Natural Products Analysis: Instrumentation, Methods, and Applications*, Havlicek V., Spizek J. (Eds), 2014, Wiley, eBook ISBN: 978-1-118-87602-2. *Recent Advances in Natural Products Analysis*, Nabavi S.M., Saeedi M., Nabavi S.F., Sanches Silva A. (Eds), 2020, Elsevier, eBook ISBN: 9780128175194. *Metabolomics Tools for Natural Product Discovery*, Roessner U., Dias D.A. (Eds), 2013, Humana Totowa, NJ, Springer Science + Business Media, LLC, eBook ISBN: 978-1-62703-577-4.
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course title	Drug Design and Small Molecule Synthesis				
Course code	DBP610				
Course type	Compulsory				
Level	Master (2nd Cycle)				
Year / Semester	1st Year / 1st Semester				
Teacher's name	Dr. Andreas Kalogirou and Dr. Eleni Moushi				
ECTS	10	**Lectures / week**	Up to 6 Teleconferences	**Laboratories / week**	–
Course purpose and objectives	The course "Drug Design and Small Molecule Synthesis" aims to present the fundamental methods and available tools (i.e., molecular modeling software) used in the design of new drugs. Both traditional and modern methods for the synthesis of organic and inorganic drug molecules are presented. Emphasis is given to the use of retrosynthesis, catalysis, asymmetric synthesis, use of organometallic reagents and protecting groups, and the synthesis of metal complexes. Issues related to intellectual property in the early stages of drug development are also presented.				
Learning outcomes	Upon completing this course, students should be able to: • Explain the basic principles of drug discovery, design and development. • Use molecular modeling software for the design of new drug molecules. • Search, evaluate and use the scientific literature in order to explain the practices of drug design. • Plan the synthesis of organic drug molecules. • Plan the synthesis of metal complexes with pharmaceutical applications. • Apply the use of protecting groups in the synthesis of organic target molecules. • Apply retrosynthetic analysis in planning the synthesis of academically and commercially important organic target molecules. • Determine the reagents and strategies for the stereoselective synthesis of chiral molecules.				
Prerequisites	None		**Co-Requisites**	None	
Course content	• Introduction, historic overview, the pre-regulation era. Natural products. Synthetic products. The need for regulation and development of a regulatory framework. Intellectual property. Use of chemical structure drawing software (chemdraw).				

	• The stages of drug design and development. The cost of new drug development. Opportunities and challenges. Drug design strategies: Target based design, phenotype-based design and mixed approach. • Drug design and metabolism: prodrugs, ADME. Use of SMILES and the Molinspiration software. Introduction to molecular interactions and dynamic binding. Structure and molecular diversity, molecule libraries. Multicomponent reactions and their use for the generation of molecule libraries. ADMETSAR software. • Lead discovery. Drug design using the techniques SBDD, LBDD, FBDD, CADD. Lead optimization. Design of new molecule binders using the SeeSAR software. • Introduction to organic synthesis. Characteristic reactions of alkenes, halogenoalkanes, aromatics and carbonyl compounds. Mechanisms of the reactions of nucleophilic substitution, electrophilic addition to unsaturated compounds, electrophilic aromatic substitution, cycloaddition. Chemo- and regioselectivity. • Retrosynthesis. Classic functional group transformations (oxidation, reduction). Use of protecting groups in synthesis. Design of a synthetic route using these strategies. • Chemistry of boron, silicon and tin in synthesis: Hydroboration, Baeyer–Villiger rearrangement, silyl ethers, arylic and vinylic silanes, organotin compounds. • Synthesis and reactions of heterocyclic compounds: 5-membered rings (furan, thiophene, pyrrole), 6-membered rings (pyridine, pyrimidine), bicyclic systems (indole, quinoline, quinazoline). • The importance of stereochemistry in pharmacy. Enantiomers and diastereoisomers. Asymmetric synthesis: Sharpless epoxidation, Mitsunobu reaction, enantioselective hydrogenation, organocatalysis. • Introduction to inorganic chemistry. Basic principles of inorganic chemistry. Definition of metal complexes, metal/ligand interactions using the donor-acceptor and HSAB theories. Design of metal complexes with correct illustrations of coordination and geometry. • Synthesis and characterization of metal complexes with pharmacological activity. • Transition metal organometallic chemistry: Palladium (C-C and C-N couplings: Suzuki, Stille, Sonogashira, Negishi, Heck and Buchwald reactions), Ruthenium (Grubs metathesis).

	• Selected syntheses of organic drug molecules: β-lactam synthesis, steroid chemistry, sugar chemistry, alkaloid synthesis. New developments in organic synthesis: C-H bond activation.
Teaching methodology	E - Learning
Bibliography	*An introduction to Medicinal Chemistry,* 5th Edition, Graham L. Patrick, 2013, Oxford University Press, ISBN: 978-0-19-969739-7. *Organic Chemistry*, 2nd Edition, Clayden J., Greeves N., Warren S., 2012, Oxford University Press, ISBN: 9780199270293.*e art of drug synthesis*, Johnson D.S., Li J.J. (Eds), 2007, Wiley. ISBN 978-0-471-75215-8. *Advanced Inorganic Chemistry*, 6th Edition, Murillo C. A., Bochmann M., Cotton F. A., Wilkinson G., 1999, ISBN: 978-0-471-19957-1. *Metals in Medicine*, 2nd edition, Dabrowiak J.C., 2017, Wiley, ISBN: 978-1-119-19137-7. *Drug Discovery and Development*, 3rd edition, Hill R.G & Richards D, 2021, Elsevier, ISBN: 9780702078040. *Drug-like Properties: Concept, Structure Design, and Methods*, Kerns E.H. & Di L., 2016, Academic Press, ISBN: 9780123695208. *Practical Guide to Rational Drug Design*, Hongmao S., 2015, Elsevier Science & Technology, ISBN: 9780081000984. *Smith and Williams' Introduction to the Principles of Drug Design and Action*, Smith H.J. (Ed), 2004, Taylor and Francis, ISBN 9780415288774. Added sources of information: www.ema.europa.eu, www.fda.gov
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course title	Drug formulation, Quality Assurance and Quality Control				
Course code	DBP620				
Course type	Compulsory				
Level	Master (2nd Cycle)				
Year / Semester	1st Year / 1st Semester				
Teacher's name	Dr. Panoraia Siafaka and Dr. Ioannis Stavrou				
ECTS	10	**Lectures / week**	Up to 6 Teleconferences	**Laboratories / week**	–
Course purpose and objectives	The quality of a pharmaceutical product is determined by the raw materials, the equipment and the technical knowledge applied during its production and packaging. This specific course gives students the opportunity to obtain a broad overview of the production process of a pharmaceutical product, from the formulation stage to market authorisation. Various pharmaceutical dosage forms are examined. The pre-formulation and formulation studies of drug dosage forms, the scaling-up process, aspects of quality, such as Good Manufacturing Practices (GMP), as well as relevant quality guidelines are discussed.				
Learning outcomes	Upon completing this course, students should be able to: • Define the different types of pharmaceutical dosage forms. • Analyze differences in formulations according to their administration route. • Describe the manufacturing process, the use of excipients and quality controls of pharmaceutical forms. • Analyze the role and specifications of packaging materials. • Provide an overview of how a drug is tested in animals, in humans, and formulated as the final drug product. • Evaluate the challenges related to the transportation of a drug product in a controlled way (for a human study and to the final consumer). • Understand the importance of QA/GMP/QC during development, manufacture, and supply of drug dosage forms. • Explain how Good x Practice (GxP) laws/guidelines are implemented within a company, and describe the role of regulatory bodies in licensing medicaments and manufacturers. • List the Good Manufacturing Practices applied in Pharmaceutical Industry. • Apply tools to ensure ongoing compliance with GxP laws/guidelines. • Review the latest trends in formulation, quality management, process control and regulatory perspectives of drug dosage forms.				

Prerequisites	None	**Co-Requisites**	None
Course content	**<u>Drug Formulation</u>** • Introduction to pharmaceutical industry, formulation during the life cycle of a drug product. • **Pre-formulation and Formulation**: Pharmaceutical pre-formulation, excipient selection and formulation of conventional and innovative dosage forms for various drug administration routes. Process optimization and validation during the development process of pharmaceutical formulations by applying Design of experiments, Quality by Design and statistical analysis (e.g. ANOVA, Plackett-Burman, first-order designs etc.). **<u>Quality Assurance (QA) and Quality Control (QC)</u>** • **Introduction to Quality Systems: Basics of Quality and a Quality system.** Introduction to international legislation GxP Introduction to the role of European Medicines Agency (EMA), Food and Drug Administration (FDA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). • **International GMP specifications. Design and implementing of Pharmaceutical clean areas.** Quality control and standard operating procedure requirements. GMP guidelines for Active Pharmaceutical Ingredient (API) and Investigational Medicinal Product (IMP) manufacturers, Medical devices legislation, Patent life management. • **Pharmaceutical Analysis/Analytical Testing.** Analytical Techniques Used in the GMP Laboratory, Development and Validation of Analytical Procedures. Stability Testing, Physicochemical testing of drug dosage forms. *In vitro* and in vivo studies.		
Teaching methodology	E - Learning		
Bibliography	*Quality Systems and Controls for Pharmaceuticals*, Sarkar D.K., 2008, Wiley, ISBN: 978-0-470-05692-9. *Analytical Testing for the Pharmaceutical GMP Laboratory*, Huynh-Ba K. (Ed), 2022, Wiley, ISBN: 978-1-119-12091-9 Aulton's pharmaceutics: The design and manufacture of medicines (5th edition), Aulton M.E., Taylor K. (Eds), 2017, Edinburgh: Churchill Livingstone/Elsevier, ISBN: 9780702070013. *Pharmaceutical Manufacturing Handbook: Production and Processes*, Gad S.C., 2008, Wiley, ISBN: 978-0-47025-981-8.		

	The Certified Pharmaceutical GMP Professional Handbook (2nd Edition), Durivage M.A., 2016, Quality Press, ISBN: 978-0-87389-933-8. *Essentials of Pharmaceutical Preformulation*, Gaisford S., Saunders M., 2013, Wiley, ISBN: 978-1-11842-322-6. *Pharmaceutical Formulation: The Science and Technology of Dosage Forms*, Tovey G.D., 2018, Royal Society of Chemistry, ISBN: 978-1-5231-2289-9.
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course title	Preclinical Development: Pharmacological and Toxicological Evaluation				
Course code	DBP630				
Course type	Compulsory				
Level	Master (2nd Cycle)				
Year / Semester	1st Year / 2nd Semester				
Teacher's name	Dr Malamati Kourti and Dr Athanasios Metaxas				
ECTS	10	**Lectures / week**	Up to 6 Teleconferences	**Laboratories / week**	–
Course purpose and objectives	In recent decades, research and development (R&D) units of pharmaceutical companies have incorporated the systematic evaluation of the pharmacodynamic, pharmacokinetic and toxicological effects of drug candidates in the preclinical phases of drug development. Information from these early studies is used to both decide whether a drug under development will advance to the clinical trial stage, as well as to optimally design a clinical trial. The course 'Preclinical development: Pharmacological and Toxicological Evaluation' provides students with essential knowledge of the early/non-clinical stages of drug development, focusing on the most common practices for characterizing the pharmacological and toxicological profile of a drug candidate. Its ultimate purpose is to highlight the importance of preclinical drug evaluation in increasing the success of subsequent clinical trials.				
Learning outcomes	Upon completing this course, students should be able to: • Recognize the stages of preclinical development of new drug molecules. • Assess the types of non-clinical studies required to evaluate the pharmacokinetic, pharmacodynamic and toxicological behaviour of drug candidates. • Describe and compare different approaches for evaluating the toxicological activity of drug candidates, for different types of toxicity. • Explain the differences between the preclinical development of small molecule drugs and biopharmaceuticals. • Explain the basic methods of *in vitro* and *in vivo* evaluation of new drugs. • Evaluate the results of preclinical tests and apply them to make decisions regarding clinical trials.				
Prerequisites	None		**Co-requisites**	None	

Course content	• Preclinical development in the life cycle of a medicinal product. • Pharmacodynamic studies: primary and secondary, *in vitro* and *in vivo*, systematic screening of compounds, biological activity tests, pharmacodynamic interactions. • Pharmacokinetic studies: absorption, distribution, metabolism, excretion. • Safety pharmacology: central nervous, respiratory and cardiovascular system, necessity/need to study additional systems. • Toxicological assessment: single-dose toxicity and repeated dose toxicity, genotoxicity, carcinogenicity, reproductive/developmental toxicity, local tolerance, immunotoxicity. • Toxicological evaluation of biological products. • The use of laboratory animals in preclinical research and development. • Comparison of preclinical development programs of small and large pharmacomolecules: studies, materials, costs, choice of experimental animals. • Comparison of preclinical development programs of small molecule and biological drugs: studies, materials, costs, choice of experimental animals. • Bridging preclinical and clinical development: the role of pharmacokinetic/ pharmacodynamic modeling, translational research and biomarkers, dose determination for first-in-human studies, risk-benefit analysis.
Teaching methodology	E - Learning
Bibliography	*Evaluation of Drug Candidates for Preclinical Development: Pharmacokinetics, Metabolism, Pharmaceutics, and Toxicology* Han C., Davis C.B., Wang B. (Eds), 2010, Wiley, ISBN: 9780470574881. *Preclinical Drug Development*, 2nd edition, Rogge M., Taft D.R. (Eds), 2016, Taylor and Francis (Informa Healthcare), ISBN: 9781420084733. *A Comprehensive Guide to Toxicology in Preclinical Drug Development*, Faqi A.S. (Ed), 2012, Elsevier, ISBN: 9780123878168. *Preclinical Safety Evaluation of Biopharmaceuticals*, Cavagnaro J.A. (Ed), 2008, Wiley, ISBN: 9780470292532. *New Drug Development*, 2nd edition, Turner J.R., 2010, Springer, ISBN: 9781441964182. *Current Topics in Nonclinical Drug Development*, Sahota P.S., Bentley P., Wojcinski Z. (Eds), 2020, CRC Press, ISBN: 9780429651137. *Dose Optimization in Drug Development*, Krishna R. (Ed), 2006, Taylor and Francis, ISBN: 978-1574448085

Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course title	Regulatory Aspects of Drug Development				
Course code	DBP640				
Course type	Compulsory				
Level	Master (2nd Cycle)				
Year / Semester	1st Year / 2nd Semester				
Teacher's name	Dr. Athanasios Metaxas, Dr. Kyriakos Kypreos				
ECTS	10	**Lectures / week**	Up to 6 Teleconferences	**Laboratories / week**	–
Course purpose and objectives	The course provides a concise and comprehensive description of the legislation governing the development, licensing, and marketing of pharmaceutical products. Its purpose is to provide students with knowledge and skills in the field of drug regulation, highlighting the most important elements in the interaction of pharmaceutical companies with drug regulatory authorities during the development of different types of pharmaceutical products.				
Learning outcomes	Upon completing this course, students should be able to: • Analyze the institutional framework and basic regulatory principles that govern the development and circulation of pharmaceutical products. • Summarize the purpose, role and operation of selected national and supranational regulatory organizations. • Evaluate the quality requirements applied at different stages of the development of a pharmaceutical product. • Understand the importance of the Common Technical Document in assessing the benefit-risk relationship of a medicinal product under development. • Plan and apply the correct licensing procedure for the circulation of a pharmaceutical product in the EU countries. • Describe the post-authorisation surveillance procedures for maintaining the marketing authorization of a medicinal product.				
Prerequisites	None		**Co-requisites**	None	
Course content	• The legal framework governing the life cycle of a medicinal product. • Drug regulatory authorities and organizations. • Pharmaceutical legislation and related guidelines.				

	• Good Practices (GxP) during the development of a pharmaceutical product. • Pharmaceutical product licensing procedures. • Marketing authorization applications (full, summary and special cases). • Product license amendments and relevant procedures. • Risk management, supervision and Pharmacovigilance. • Intellectual property and drug marketing exclusivity.
Teaching methodology	E - Learning
Bibliography	*Regulatory Affairs in the Pharmaceutical Industry*, Ali J., Baboota S. (Eds), 2021, Elsevier, eBook ISBN: 9780128222232. *Global New Drug Development: An Introduction*, Rosier J.A., Martens M.A., Thomas J.R., 2014, Wiley, ISBN: 978-1-118-41485-9. *Medical Product Regulatory Affairs*: *Pharmaceuticals, Diagnostics, Medical Devices* Tobin J.J., Walsh G., Wiley, ISBN: 978-3-527-31877-3. *Medical Regulatory Affairs, An International Handbook for Medical Devices and Healthcare Products*, 3rd Edition, Wong J., Tong R.K.Y. (Eds), 2022, Taylor and Francis, ISBN: 9789814877862. Additional Sources of Information: EudraLex - EU Legislation: EudraLex (europa.eu) EMA: European Medicines Agency | (europa.eu) FDA: U.S. Food and Drug Administration (fda.gov)
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course title	Bioanalysis in Drug development				
Course code	DBP650				
Course type	Elective				
Level	Master (2nd Cycle)				
Year / Semester	1st Year / 2nd Semester				
Teacher's name	Dr. Ioannis Stavrou				
ECTS	10	**Lectures / week**	Up to 6 Teleconferences	**Laboratories / week**	–
Course purpose and objectives	The main objective of the course is for students to obtain a detailed understanding of the specialized techniques that are used for the identification, characterization and quantification of small molecules and macro-molecules in biological matrices. The course offers specialized knowledge in the areas of biopharmaceutical analysis, -omics technologies, as well as therapeutic drug monitoring.				
Learning outcomes	Upon completing this course, students should be able to: • Define major biological matrices, identify and address problems they may cause during analysis (e.g., macromolecule interactions, macromolecule-drug interactions). • Describe the most basic sample preparation techniques used in bioanalysis and their applications. • Evaluate the main analytical techniques used in bioanalysis, such as immunochemical, chromatographic, as well as advanced coupled analysis techniques. • Explain the principles and applications of -*omics* technologies and biomarker analysis. • Understand the role and applications of bioanalysis in the various stages of drug development.				
Prerequisites	None	**Co-Requisites**	None		
Course content	• Introductory concepts of bioanalysis – Biomolecules. • Biological matrices – Sampling. • Modern sampling techniques and Sample processing techniques. • Analytical Methods in Bioanalysis: Immunochemical analysis techniques, spectroscopic methods, chromatographic techniques and coupled techniques (LC-MS, LC-MS/MS, HRMS).				

	• Analysis of drug molecules, peptide and protein drugs in biological fluids – Applications. • Validation of Bioanalytical methods. • Systems biology – *omics* technologies. • The role of bioanalysis in drug discovery process.
Teaching methodology	E - Learning
Bibliography	*Understanding Bioanalytical Chemistry: Principles and Applications*, Gault V.A., McClenaghan N.H., 2013, Wiley, eBook ISBN: 978-1-118-68489-4. *A Handbook of Bioanalysis and Drug Metabolism*, Evans G. (Ed), 2004, CRC Press, ISBN-13: 978-0415275194. *Therapeutic Drug Monitoring*, Dasgupta A., 2012, Academic Press, eBook ISBN: 9780123854681. *Βιοαναλυτική Χημεία*, Θεοδωρίδης Γ. (κύριος συγγραφέας), Γηρούση Σ., Ζαχαριάδης Γ., Ζώτου Α.Σ., Σαμανίδου Β., 2015, ΣΥΝΔΕΣΜΟΣ ΕΛΛΗΝΙΚΩΝ ΑΚΑΔΗΜΑΪΚΩΝ ΒΙΒΛΙΟΘΗΚΩΝ, Εθνικό Μετσόβιο, Πολυτεχνείο, Ηρώων Πολυτεχνείου 9, 15780 Ζωγράφου, www.kallipos.gr
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course title	Health Economics and Pharmacoeconomics				
Course code	DBP660				
Course type	Elective				
Level	Master (2nd Cycle)				
Year / Semester	1st Year / 2nd Semester				
Teacher's name	Dr. Panagiotis Petrou				
ECTS	10	**Lectures / week**	Up to 6 Teleconferences	**Laboratories / week**	–
Course purpose and objectives	In addition to obtaining marketing authorization from the regulatory authorities, market access is seen by the pharmaceutical industry as an important goal for drug development. Health Economics and Pharmacoeconomic analysis are pivotal in opening or hindering market access for many innovative products. The purpose of the course is to acquaint students with the fundamental principles and approaches of health economics, which are used in public health for the evaluation of a new technology/medicine. The main objective of the course is for students to understand health from the market perspective, and to be able to make informed decisions based on cost and effectiveness data.				
Learning outcomes	Upon completing this course, students should be able to: • Comprehend economic theories as they relate to the health care market, and propose measures to enhance efficiency. • Appraise the major causes of demand and supply in health care. • Appreciate the array of health provider reimbursement mechanisms. • Analyse the phenomena of 'moral hazard' and 'adverse selection', which impair the function of health insurance. • Understand the surging fiscal pressures on the health market and the underlying reasons that fuel them. • Analyse the confluence of health system and health costs. • Explain productivity theory. • Understand the range and applicability of cost-containment methods. • Evaluate decision-making strategies based on pharmacoeconomic studies.				
Prerequisites	None	**Co-requisites**	None		
Course content	• Health market and the principal-agent relationship • Induced demand • Moral Hazard				

	• Health production • Health System-Health financing • Cost-containment approaches • Reimbursement approaches for health providers • Willingness to pay thresholds • Quality adjusted life years • Efficiency • Discounting • Economic evaluations – Pharmacoeconomics • Economic models
Teaching methodology	E - Learning
Bibliography	***Educational Handbook:*** *Health Economics: Core Concepts and Essential Tools,* Bernell Steph (2016). Chicago: HAP/AUPHA/Health Administration Press. ***Recommended Readings:*** Guinness, Lorna, Wiseman, Virginia, Wonderling, David (2011). *Introduction to Health Economics Second edition.* London School of Hygiene and Tropical Medicine: Open University Press Alastair M. Gray, Philip M. Clarke, Wolstenholme L Jane, Wordsworth L. Sarah (2011). *Applied Health Economics for Public Health Practice and Research.* Oxford: Oxford University Press. Sherry, Glied and Smith C. Peter (2011). *The Oxford Handbook of Health Economics.* Oxford: Oxford University Press. Drummond, M.F., Sculpher, M.J., Torrance, G.W. O'Brien, B., Stoddart, G.L. (2005). *Methods for the economic evaluation of health care programmes.* 3rd ed. Oxford: Oxford University Press.
Assessment	Final Exam 50% Assignments/On-going evaluation 50%
Language	Greek and English

Course title	Master Thesis				
Course code	DBP690				
Course type	Compulsory				
Level	Master (2nd Cycle)				
Year / Semester	2nd Year / 1st Semester				
Teacher's name	Dr. Constantinos Nikiforou				
ECTS	30	**Lectures / week**	–	**Laboratories / week**	Up to 6
Course purpose and objectives	The ultimate purpose of the Master thesis is the critical analysis and/or solution - at a theoretical and/or practical level - of one or more problems associated with Drug Biosciences and Pharmaceutical Development. The thesis introduces students to research methodology, training them in the planning, organization, and implementation of a scientific study, as well as in the adequate analysis, documentation, and presentation of its content. The preparation of the M.Sc. thesis offers students the opportunity to deepen, synthesize and apply the knowledge acquired during their studies. For the preparation of the thesis, students carry out independent research under the oversight of an academic supervisor. The area of the research subject is agreed upon in collaboration with the academic supervisor, prior to conducting the thesis. The project assignment may involve applied research or a systematic review of a research question. The writing of a thesis, as well as its public oral defence before a three-member Evaluation Committee, are required for the completion of the Master thesis project.				
Learning outcomes	Upon completing this course, students should be able to: • Organize and implement a scientific research project. • Identify sources of information related to the topic under study, through bibliographic search in academically valid databases. • Compose a systematic review of the literature, critically approaching the available scientific information on a given subject. • Plan, organize and implement an experimental research project in the subjects of Drug Biosciences and Pharmaceutical Development, according to academic standards. • Formulate hypotheses and clearly present the problem, purpose, methodology and the results that stem from the analysis of data. • Discuss findings, contrasting them with the findings of other studies, identifying areas for further study and suggesting ways to address problems. • Evaluate and discuss issues related to research ethics. • Compose and present scientific work in both written and oral forms, and present this work in front of an audience.				

<table>
<tr><td></td><td colspan="3">Demonstrate thorough knowledge of the subject under investigation, expertise in applying basic scientific methods, and ability to contribute to scientific knowledge.</td></tr>
<tr><td>Prerequisites</td><td>Successful completion of all Year 1 compulsory and elective courses.</td><td>Co-requisites</td><td>None</td></tr>
<tr><td>Course content</td><td colspan="3">
Supervision and guidance

Meetings are held between students and their supervisor at least every two weeks. The meetings aim to provide general guidance to the students, helping them organize their methodological and research approach, the analysis of collected data and/or discuss any activity that is required to successfully complete the Master Thesis.
Students receive regular feedback on the progress of their work.

Implementation of research project – systematic review

This type of thesis can be undertaken entirely off-campus.
The students thoroughly study the literature to determine the nature of the review project.
The students collaborate with the supervisor to choose the research methodology to be applied (search words, databases, exclusion criteria).
The students carry out independent work to identify primary sources related to the subject under investigation.
The students examine the identified studies, qualitatively and/or quantitatively (meta-analysis), and evaluate, interpret, and discuss their findings.
The students compose the Master Thesis in written form, according to the instructions provided in the Master's thesis guide.

Implementation of research project – ‘dry-lab’ project

This type of thesis can be undertaken entirely off-campus.
The students thoroughly study the literature to comprehend the topic of the research project.
The students collaborate with the supervisor to Identify the specific data analysis techniques, software, or tools that will be utilized.
The students collaborate with the supervisor to determine the data sources required for the project. This may include existing datasets, public databases, or simulated data. The students collect and organize the data in a suitable format for analysis.
The students examine the data applying statistical methodologies to evaluate, interpret and discuss the findings of the study.
The students compose the Master Thesis in written form, according to the instructions provided in the Master's thesis guide.

Implementation of research project – ‘wet-lab’ project

Students are expected to be physically present for this type of thesis.

</td></tr>
</table>

	• The students thoroughly study the literature to comprehend the topic of the research project. • The students collaborate with the supervisor to choose and explicitly describe the experimental methodology to be followed. • The students are trained in experimental techniques related to the subject under investigation, to apply them independently for data collection. • The students examine the data applying statistical methodologies to evaluate, interpret and discuss the findings of the study. • The students compose the Master Thesis in written form, according to the instructions provided in the Master's thesis guide. **Master thesis presentation** • After submitting the thesis to a three-member advisory body, students are informed of the date of the oral presentation of their work. • After the oral defence of the master's thesis, the students submit the final form of their dissertation to the Department Secretariat, and receive a grade for the course. A detailed description of the content and prerequisites of the course are provided in the "Postgraduate Thesis Preparation Guide".
Teaching methodology	E - Learning
Bibliography	*Cochrane Handbook for Systematic Reviews of Interventions*, Second Edition, Higgins J.P.T., Thomas J., Chandler J., Cumpston M., Li T., Page M.J., Welch V.A. (Eds), 2020, Chichester (UK): Wiley, eISBN:9781119536604. *How to Write a Master's Thesis*, Third Edition, Bui W.N., 2019, SAGE Publications, ISBN-13: 978-1506336091. Selected scientific journal articles, in PDF format. Master Thesis Preparation Guide, Department of Life Sciences, European University Cyprus.
Assessment	Master Thesis 70% Oral defence 30% *It is noted that success in the Master thesis course requires being successful in each of the above individual assessments.*
Language	Greek and English

APPENDIX V

The grading system for E-Learning courses according to EUC regulations appears in the table below:

MASTER's DEGREES (POSTGRADUATE PROGRAMMES)			
Grade	**Description**	**ECTS**	**Percentage**
A	Excellent	4.0	90+
B+	Very Good	3.5	85-89
B	Good	3.0	80-84
C+	Fairly Good	2.5	75-79
C	Average	2.0	70-74
D+	Below Average	0	
D	Poor	0	
F	Failure	0	
I	Incomplete	0	
W	Withdrawal	0	
P	Pass	0	
AU	Audit	0	
TR	Course from transfer	0	

(a) The grade **"I"** is awarded where a student has maintained a satisfactory level of performance but was unable to complete a major portion of course work (e.g. term paper or final exam), for reasons deemed acceptable by the instructor. It is the responsibility of the student to justify any failure to complete work required, and to reach an agreement as to how remaining course requirements will be satisfied. Following the award of an "I" mark and in consultation with the course instructor, the student is responsible for fulfilling any outstanding course requirements within the first 4 weeks of the following semester. In exceptional cases, the instructor may extend the existing incomplete grade to the next semester. Failure to complete work within a specified period will result in an **"F",** which will be recorded as the final grade.

(b) A grade of **"W"** indicates withdrawal from a course, occurring within a time period specified in the withdrawal policy.

(c) The **"P"** grade is not counted in the G.P.A. but is counted against credit units.

(d) The **"F"** grade is calculated in the G.P.A.

(e) Students enrolling for a course on an **"AU"** Audit basis must indicate their intention to do so at the time of registration. Students registering for a course on an Audit basis receive no ECTS, but they will be charged the respective tuition fees.

(f) Courses transferred from another academic institution are not included in the calculation of the G.P.A.

Students prepare and deliver their work, including the final exam, aiming to accumulate a grade of at least 70% to pass an individual graduate class. Weekly objectives and learning outcomes are clearly stated in all Study Guides, allowing students to self-assess progress by reflecting on their grasp of target concepts and knowledge.

The grading criteria are specific to each assignment. Below, we present an indicative grading rubric for an online discussion assignment (10% of total grade):

Criteria	Exemplary	Proficient	Limited	Unsatisfactory
Critical Analysis	Discussion postings display an excellent understanding of the required readings and underlying concepts, including correct use of terminology. Postings integrate a resource or relevant research, to support critical points. Sources are cited appropriately **(3.5 points).**	Discussion postings display an understanding of the required readings and underlying concepts, including correct use of terminology **(3 points).**	Discussion postings repeat and summarize basic, correct information, but do not link reading to outside references or relevant research, and do not consider alternative perspectives or connections between ideas. Sources are not cited **(2 points).**	Discussion postings show little or no evidence that readings were completed or understood. Postings are largely personal opinions or feelings, without supporting statements from the readings, outside resources, relevant research, or specific real-life situation **(0 points).**
Participation as member of the learning community	Discussion postings actively stimulate and sustain further discussion by building on peers' responses, including building a focused argument around a specific issue or asking a new relevant question or making an oppositional statement supported by related research or experience. Consistently responds to peers' postings within 24 h **(3.5 points).**	Discussion postings contribute to the class' ongoing conversations as evidenced by affirming statements or references to relevant research or asking related questions or, making an oppositional statement supported by related research or experience. Respond postings to peers take place within 48 h **(3 points).**	Discussion postings sometimes contribute to ongoing conversations as evidenced by affirming statements or references to relevant research or asking related questions or, making an oppositional statement supported by related research or experience. Respond postings to peers occur more than 48 h after the initial discussion **(2 points).**	Discussion postings do not contribute to ongoing conversations or respond to peers' postings. There are no replies to questions or comments. Discussion points are not posted or only posted on the last day of the assignment **(0 points).**
Professional communication	Written interactions on the discussion forum display respect and sensitivity to peers' beliefs. Responses are free of grammatical, spelling and punctuation errors. The writing style invites and facilitates communication. **(3 points).**	Written interactions on the discussion forum show respect and interest in the viewpoints of others. Written responses are largely free of grammatical, spelling or punctuation errors. The writing style generally facilitates communication **(2.5 points).**	Some of the written interactions on the discussion forum show respect and interest in the viewpoints of others. Written responses include some grammatical, spelling or punctuation errors that distract the reader **(2 points).**	Written interactions on the discussion forum show disrespect for the viewpoints of others. Written responses contain numerous grammatical, spelling or punctuation errors. The style of writing does not facilitate effective communication **(0 points).**

Rubric adapted from similar evaluation tools developed by the University of Hawaii and Northwestern University (USA).

The assessment criteria for the written text of the Master thesis are presented in the table below and can also be found in the Postgraduate Thesis Study Guide.

Scale of Assessment of Written Study

	ASSESSMENT CRITERIA	Grade*		
		Chair (30%)	**Member 2** (20%)	**Member 3** (20%)
1	Method and completeness in addressing the topic *Comments:*			
2	Organisation of material *Comments:*			
3	Documentation of information and data *Comments:*			
4	Originality of topic – inspiration *Comments:*			
5	Scientific background (correct terms and concepts) *Comments:*			
6	Thesis layout *Comments:*			
7	Language, spelling, correlation of concepts, clarity of written language *Comments:*			
8	Completeness and recording of bibliography *Comments:*			
***Attention**: Each assessor assesses each criterion out of 100%. Normalization is performed automatically using mathematical formulas.	**Total**			
Date 12/12/2022	**Grade of written text**			
The three-member Assessment Committee	**Final grade of Thesis**			

The assessment criteria for the oral defence of the Master thesis are presented in the table below and can also be found in the Postgraduate Thesis Study Guide.

Scale of Assessment of Oral Presentation of Study

ASSESSMENT CRITERIA		Grade*		
		Chair (15%)	**Member 2** (7.5%)	**Member 3** (7.5%)
1	Method and completeness in addressing the topic *Comments:*			
2	Documentation of information and data *Comments:*			
3	Originality of topic – inspiration *Comments:*			
4	Knowledge and assimilation of the topic *Comments:*			
5	Scientific background (correct terms and concepts) *Comments:*			
6	Organisation of material *Comments:*			
7	Time management *Comments:*			
8	Quality of oral communication *Comments:*			
***Attention**: Each assessor assesses each criterion out of 100%. Normalization is performed automatically using mathematical formulas. **Total**				
Date 12/12/2022	**Grade of oral presentation**			
The three-member Assessment Committee	**Final grade of Thesis**			

APPENDIX VI

INTERNAL REGULATION ON

"EUC"s PROCEDURES FOR SUPPORTING STUDENTS WITH LOW GRADE POINT AVERAGE (GPA)"

71st Senate Decision: 7 February 2020

Aiming to develop a proposal/framework on the process and actions to be taken, in order to address and reduce the phenomenon of students' low G.P.A. and its effects, the actions to be taken in order to help reduce the phenomenon, are:

- the provision of correct information to all students, namely undergraduate, postgraduate, Conventional and Distance Learning;
- ensure that students are aware of the role of GPA and the impact of low GPA on the progress of their studies;
- increase of the support provided at the Program, Department and School level;
- proper implementation of procedures by the Student Advising Centre.

These actions are additional to the efforts/support that each individual instructor provides to each student and aim for a timely and early enough diagnosis of the phenomenon in order to facilitate an effective, early intervention.

The following steps will be followed for all students (both conventional and distance education):

1. **The Department of Enrollment** provides the Schools at the beginning of each academic semester (e.g. third week of October and February, respectively) with a list of their students with a low GPA (for undergraduate courses: below 1.80 except for the School of Medicine where the threshold has been set to 2.0; for postgraduate courses: below 2.5; for Ph.D. courses the issues concern late progress in completing the Ph.D-see sample letter attached).

2. **The School** (this concerns all undergraduate and postgraduate Conventional and Distance Learning Programs of Study)**:**
   (1) ***For first year students at the end of the 1st semester of their studies or for students included in the list for the first time****:*
   Each affected student is called by the Program Coordinator, in order to ensure that, students are aware of the concern of the Department and School, and that

students are indeed properly informed that the Department is available to provide support (e.g. Specifically, students are informed about the role and importance of the GPA, the possible reasons and causes of the low GPA, and ways for improvement of the situation, which may either involve the student (e.g. further effort) or the Department and School).

(2) ***For new students, which continue to be in the same situation at the end of the second semester of their studies or for students appearing in the list for a second time***:
The process presented in Item 1 above is repeated in the presence of the Chairperson of the Department, for further discussion and enhancement of the process, aiming at the most tangible academic targets and the procedures involved. If needed, the Chairperson of the Department and the Program Coordinator will request the presence of the Dean.

(3) ***For students who exhibit the phenomenon on a continuous basis****:*
The possibility of sending a letter from the Dean <u>to the student</u> (registered, in the home address) is considered (see attached "Sample" letters).

<u>For the School of Medicine (undergraduate degrees) in more specific</u>: The students with a GPA lower than 2.0 receive a “Letter of Probation” before the beginning of the second academic year of their studies (September). Students who received a “Letter of Probation” and still maintain an unacceptably low GPA will be given only one last opportunity to correct their GPA during the coming semester (Spring). At the end of the Spring semester of their second year of studies,, these students (e.g. those who have already received a letter of warning in the past), and continue to maintain a very low GPA will receive a “Letter of Dismissal”, with the option to either change their program of study (e.g. transfer to biology) or to withdraw from the School. Those students who, on the other hand, have not yet received a “Letter of Probation” in the past, but perform unsatisfactorily, will receive a “Letter of Probation” at the end of the Spring semester of their second year of studies, with subsequent consequences should their performance not improve. This option will be provided this one and only time to those students with failures; no other opportunity will be provided to improve “F” grades. Each student will be notified accordingly, depending on their status.

3. The Department of Enrollment:

Each Student Advisor:

(1) Contacts/communicates with students and ensures that each student is well informed and advised about the University’s grading system and the role of GPA ;

(2) In the case of students not passing a course, the advisor re-registers them to the same course in order to immediately delete the received F, and thus avoid accumulation of F's. This takes places in the exact following semester in case the affected course is a prerequisite to other courses, in order to avoid accumulation of F’s;

(3) Student advisors are in constant communication with the Program Coordinators in order to secure this process.

Encl.: (1) Sample Letters (Greek and English version)
(2) Sample Letter of Probation (School of Medicine)
(3) Sample Letter of Dismissal (School of Medicine)
(4) Sample Letter for Ph.D. Students (Department of Enrollement)

..... 2020

Προς
.....

Θέμα: Χαμηλός Μέσος Όρος Βαθμολογίας (G.P.A.)

Αγαπητή/έ.....,

Σε συνέχεια της αναφοράς του/της Προέδρου του Τμήματος και του/της Συντονιστή/τριας του Προγράμματος που παρακολουθείτε κατά το περασμένο ακαδημαϊκό εξάμηνο, παρακαλώ σημειώστε ότι ο μέχρι τώρα μέσος όρος της βαθμολογίας σας (G.P.A.) είναι .....

Θα ήθελα να σας υπενθυμίσω, επί του προκειμένου, τους κανονισμούς του Πανεπιστημίου μας αναφορικά με τις προϋποθέσεις απόκτησης πτυχίου, οι οποίοι προβλέπουν μέσο όρο βαθμολογίας (G.P.A.) 2.00 και άνω.

Ο/η Πρόεδρος του Τμήματος και ο/η Συντονιστής/τρια του Προγράμματος που παρακολουθείτε μπορούν να σας δώσουν περισσότερες πληροφορίες και σχετική υποστήριξη.

Ελπίζω ότι, κυρίως με την αναβάθμιση των δικών σας προσπαθειών, θα καταστεί δυνατή τόσο μια ποιοτική συνέχιση των σπουδών σας, όσο και η τελική επίτευξη των στόχων σας.

Με εκτίμηση,

.....
Κοσμήτορας,
Σχολή .....

Κοιν.:
-Συντονιστής/τρια Προγράμματος Σπουδών
-Πρόεδρος Τμήματος

European University Cyprus
6 Diogenous str, 2404 Engomi,
P.O.Box 22006, 1516 Nicosia, Cyprus
Telephone: +35722559514
Fax: +357 22559515

Date XXX

Student's Name: xxxxx
ID: xxxx
Program: Doctor of Medicine, MD

Re: Letter of Probation for G.P.A. of less than 2.0

Dear [Name of Student],

I regret to inform you that, due to your low cumulative Grade Point Average (GPA), you are being placed on academic probation. You will remain on probation and will be subject to dismissal until your cumulative GPA reaches or exceeds 2.00.

Academic Probation status is serious. You must raise your cumulative GPA to 2.00 to return to good standing and to receive your degree. According to European University Cyprus bylaws and the decision outlined by the EUC 48th Senate, students with a GPA lower than 1.7 at the end of their second year (year 2) are subject to dismissal (termination).

The School of Medicine is committed to helping you improve your academic performance so that you can return to good standing and make progress toward your degree. We will provide you with the services and activities to help you achieve academic success. In return, you must commit yourself to work diligently. It is my sincere hope that you will be successful next semester.

Sincerely,

Professor Elizabeth O. Johnson
Acting Dean
School of Medicine
European University Cyprus

CC: Professor Ioannis Patrikios, Chair, Department of Medicine
Professor Loizos Symeou,Vice-Rector of Academic Affairs
Dr. Christos Tsiappas, Director of Enrollment

European University Cyprus
6 Diogenous str, 2404 Engomi,
P.O.Box 22006, 1516 Nicosia, Cyprus
Telephone: +35722559514
Fax: +357 22559515

Date XXX

Student's Name: xxxxx
ID: xxxx
Program: Doctor of Medicine, MD

Re: Letter of Dismissal
Dear [Name of Student],

As you are aware, on [date of probation letter] you were placed on academic probation because your cumulative Grade Point Average (GPA) was below 2.00.

After careful review of your academic performance, the School of Medicine must regrettably inform the Rectorate and Director of Admissions that you have not made satisfactory progress and are recommended for dismissal from the Doctor of Medicine, MD, program.

According to European University Cyprus bylaws and the decision outlined by the EUC 48th Senate, students with a GPA lower than 2.0 will not be eligible for graduation.

While you are being dismissed from the program of Doctor of Medicine, you may wish to explore your options of transferring to another program in Life Sciences, such as Biology, offered by European University Cyprus. We will be happy to assist you in this process. We wish you the best in your future endeavors.

Sincerely,

Professor Elizabeth O. Johnson
Acting Dean
School of Medicine
European University Cyprus

CC: Professor Ioannis Patrikios, Chair, Department of Medicine
Professor Loizos Symeou,Vice-Rector of Academic Affairs
Dr. Christos Tsiappas, Director of Enrollment

..... 2020

Προς
.....

Αγαπητή κα,

Με την παρούσα επιστολή θα ήθελα να σας ενημερώσουμε για τα παρακάτω:

Η διάρκεια των διδακτορικών σπουδών του Πανεπιστημίου είναι 3-6 χρόνια με τη δυνατότητα χορήγησης αναστολής φοίτησης μέχρι και ένα (1) ακαδημαϊκό έτος.

Είστε εγγεγραμμένη στο πρόγραμμα διδακτορικών σπουδών στις ……. από το Φθινοπωρινό Εξάμηνο 201…., και συνεπώς αναμένεται να ολοκληρώσετε τις σπουδές σας μέχρι το τέλος του Εαρινού Εξαμήνου 202….. Αυτό σας δίνει περιθώριο ακόμη τεσσάρων (4) εξαμήνων φοίτησης. Δείτε αναλυτικά τη σχετική αναλυτική σας βαθμολογία στο συνημμένα.

Επιπρόσθετα, θα ήθελα να σημειώσω ότι είστε εγγεγραμμένη στάδιο υποστήριξης πρότασης διατριβής (PHD801) για έξι (6) συνεχή εξάμηνα (από το S20….).

Με βάση τα πιο πάνω δεδομένα, και επειδή μας προβληματίζει η καθυστέρηση που παρατηρείται στην πρόοδό σας στο Πρόγραμμα, σας ενημερώνω ότι για την εντός του εναπομείναντα χρόνου ολοκλήρωση των διδακτορικών σας σπουδών, απομένουν οι εξής επιλογές:

(α) Μέχρι το επίσημο τέλος του τρέχοντος εξαμήνου (Φθινοπωρινό 20…), θα πρέπει να ολοκληρώσετε επιτυχώς το μάθημα PHD801. Στη συνέχεια θα έχετε στη διάθεσή σας ακόμη τρία (3) εξάμηνα για να ολοκληρώσετε το στάδιο συλλογή και ανάλυση δεδομένων (PHD802) και συγγραφή και υποστήριξη διδακτορικής διατριβής (PHD803).

β) Εάν τυχόν δεν ολοκληρώσετε επιτυχώς το μάθημα PHD801 μέχρι το τέλους του Φθινοπωρινού Εξαμήνου 20…, το Πανεπιστήμιο θα προχωρήσει στην καταχώρηση βαθμολογίας F. Θα μπορείτε να επανεγγραφείτε στον ίδιο κωδικό μαθήματος το επόμενο εξάμηνο με επιπρόσθετο κόστος 1.500 ευρώ. Στη συνέχεια θα έχετε ακόμη τρία (3) εξάμηνα για να ολοκληρώσετε τα μαθήματα PHD801, PHD802, PHD803.

Τέλος, σε περίπτωση που τα πιο πάνω δεν μπορούν να εφαρμοστούν, θα σας δοθεί η δυνατότητα, μετά από υποβολή αίτησης στο Τμήμα Εγγραφών και κοινοποίηση στο/την Πρόεδρο του Τμήματος ……., να επιλέξετε να μετεγγραφείτε από το διδακτορικό στο οποίο φοιτάτε σε ένα μεταπτυχιακό του Ευρωπαϊκού Πανεπιστημίου Κύπρου με αντιστοίχιση μαθημάτων που έχετε ήδη παρακολουθήσει και παρακολούθηση των μαθημάτων που υπολείπονται.

Βασική επιδίωξη του Πανεπιστημίου είναι η στήριξη των φοιτητών και φοιτητριών μας με απώτερο σκοπό την ακαδημαϊκή τους πρόοδο και επιτυχή αποπεράτωση των σπουδών τους.

Τόσο εγώ, όσο και η επόπτριά σας, ο συντονιστής του διδακτορικού προγράμματος και ο/η Πρόεδρος του Τμήματος ….. παραμένουμε στη διάθεσή σας για οτιδήποτε περαιτέρω.

Χρίστος Τσιάππας

Διευθυντής Τμήματος Εγγραφών

European University Cyprus

APPENDIX VII

The EUC E-Learning Programmes of Study

A Note on this Document

This document is intended primarily for all academic staff involved in course design and teaching on the E-Learning programmes of study at European University Cyprus (EUC). The document introduces the essential elements of the pedagogical principles and teaching philosophy employed on all E-Learning courses at EUC. The document breaks down into the following sections:

1. Introduction to e-learning at EUC
2. The Distance Education Unit
3. The EUC e-learning pedagogical model
4. The main principles of e-learning:
    a. Learner-centred learning design
    b. Inclusive design
    c. Co-design
    d. Interactive and collaborative learning
5. Support for e-learning at EUC
    a. Learning resources
    b. Academic guidance and support
    c. Administrative support
6. The fundamental structure of EUC's E-Learning Courses
    a. Course structure
    b. Synchronous meetings
    c. Asynchronous communication
    d. Course assignments
    e. Final exams
7. Student assessment in E-Learning courses
8. Programmes' quality assurance

1. Introduction to e-learning at EUC

European University Cyprus (EUC) has always met the differing educational needs of society by using the most up-to-date tools. As part of this mission, since 2013, EUC has offered fully recognized E-Learning Bachelor's (undergraduate) and Master's (postgraduate) programmes of study. The aim is to provide access to education for as many people as possible, particularly those who may not have had otherwise the chance to attend a programme of study.

Academic staff of the Departments and Schools teaching on E-Learning programmes of study have prolonged experience of instruction in tertiary education and research in their fields of study. All instructors receive ongoing professional development and training in e-learning, particularly in the use of communication technologies for teaching and learning. This combination of instructors' proficiency in their discipline, prolonged experience in e-learning, combined with the modern infrastructure of EUC, is what guarantees the quality of EUC's E-Learning programmes of study.

2. The Distance Education Unit

The Distance Education Unit (DEU) provides the administrative support for the E-Learning programmes of study of EUC. The Unit supports both students and academic staff of EUC's E-Learning programmes of study, by ensuring quality access to educational materials and technological resources. Students receive initial instruction in the use of the educational platform from the DEU, as well as ongoing advice, and if they have issues with the technology or delivery of their courses (not the academic content) then they bring these up with the DEU. The Unit also helps coordinate the production of training materials and courses, as well as coordinating with other administrative elements of the University, such as the Office of the Vice-Rector of Academic Affairs, the Department of Information Systems and Operations, the Department of Enrollment, and the Registrar's Office. Its mission is to ensure that e-learning is a vital element in all aspects of the University's academic and administrative policies and actions.

3. The EUC e-Learning Pedagogical Model

E-learning at EUC works according to a flexible pedagogical model that considers the needs of the student, the requirements of the discipline, and the technological infrastructure. It promotes best practice in instructional design and educational delivery, and provides useful guidelines against which instructors can assess their own educational practices.

This model follows the latest pedagogical guidelines and recommendations for the design and development of E-Learning programmes of study distributed by the Cyprus Agency of Quality Assurance and Accreditation in Higher Education (CY.Q.A.A.), including announcements of CY.Q.A.A. on 29.4.2020 and 4.5.2020 on E-Learning programmes of study, Study Guides and e-learning interactive activities. The model is regularly updated to ensure compliance with all requirements of the national framework. The EUC pedagogical model also takes into consideration the requirements and special characteristics of the legislation of countries other than Cyprus from which EUC E-Learning programmes of study have a large number of students (e.g. Greece), as well as the fundamental

functioning principles of the Open University of Cyprus, the Hellenic Open University, and other international Open Universities.

The **Blackboard Learn Ultra platform** is the environment that provides access to learning resources and content and supports the students' interaction with the material, their instructors and their classmates.

4. The main principles of e-learning

The EUC Pedagogical Model is based on the following learning principles:

- Learner-centred learning design
- Inclusive design
- Co-design
- Interactive and collaborative learning

Each of these principles are described below.

a. Learner-Centred learning design

The student holds a predominant position in the EUC pedagogical model. The entire process revolves around designing areas and resources to enable the student's learning. Information related to the E-Learning programmes of study are publicly available and objectives and expected learning outcomes of the courses as well as grading policies are available to all students and potential students. At the beginning of each semester, during the first meeting with students in courses, each instructor goes through her/his course outline and discusses with students the course content, learning process, activities and assignments. Students have the opportunity to make suggestions and customizations, bearing in mind that the fundamental content and objectives of the course cannot be altered as these were accredited by CY.Q.A.A. Meaningful learned-centred learning is also achieved by taking account of students' background, professional and prior education experiences, as well as taking advantage of opportunities for customization of the e-learning experience and learning activities based on students' own needs and interests. Finally, towards the end of each semester, students are asked to evaluate each of their courses online. Submission is anonymous and the time it takes to fill out the evaluation form is around 10-15 minutes. The survey pertains all aspects of the course and the overall learning experience of the student (hence named the Survey on 'Student Feedback on their Learning Experience' -SFLE), such as the course structure and content, the faculty performance, the facilities involved, the administrative support, etc. The information received are forwarded to faculty to review and act accordingly. The Chairperson of the Department also reviews the aggregated information per course and makes recommendations where needed.

b. Inclusive design

The inclusive design implementation of Universal Design for Learning (UDL) principles is one of the main concerns of the programme design and development

of all EUC programmes of study. The UDL principles in EUC's E-Learning programmes of study are implemented as shown in the table below:

UDL Principles	Activities and Course Design	Means, Technology and Tools
Provide options for Engagement	-Organisation of the course in weeks/themes/units with indicative timeframe for study -Facilitation of self-paced learning/study -Regular contact with instructor in a variety of ways -Assignments and learning activities linked to personal experiences, background, professional status, etc. (e.g. variations of practical experience, assignments linked to own experiences and work environment) -Compulsory and optional activities -Opportunity to choose some graded activities over others. -Options for individual and group activities and assignments -Options for authentic work (e.g. conducting small research projects in activities, assignments that avoid reproduction of literature but entail practical/implementation sections) -Variety in assessment methods (e.g. projects, portfolios, quizzes, open-ended questions, public dialogue discussions, discussion forum)	-LMS Blackboard Learn Ultra with accessibility features -Study guides available in various forms (word document, pdf) as well as content structured on platform follows the study guides -LMS build-in communication tools (e.g. discussion forums, chat options and messaging) -Options for communication off platform (e.g. blogs, personal IM, social network closed groups, video channels)
Provide options for Representation	-Alternative options of introduction of new knowledge and content (e.g. readings, teleconferencing, slide notes, pre-recorded videos, links to external content) -Both English and Greek literature (for programmes offered in Greek) -Uses of Glossary (in some courses that terminology is especially important) -Use of synchronous and asynchronous content connection activities (e.g. wikis, presentations, mind-mapping)	-Videos (accessible where possible) -Text on platform (online documents) -Visuals (e.g. diagrams, images, mind-maps) -Hyper-titles where possible -Recorded teleconferencing meetings available to all
Provide options for Action and Expression	-Synchronous and asynchronous options for interaction (student-student, student-instructor, student-content, student-platform) though various channels -Variety in assessment methods (e.g. projects, portfolios, quizzes, open-ended questions, public dialogue discussions, discussion forum)	-Interactive videos -Interactive (user-controlled) content (e.g. though authoring tools such as H5P) -Alternative accepted modes of communication (e.g. email, IM, discussion forum, chat, social media closed groups) -Alternative accepted modes of class participation (e.g. written, auditory, video presentations)

	-Variety of types of questions in final exams (by regulation all need to be written exams) -Creative assignments (e.g. presentations, repositories of resources, peer review activities) -Assignments broken in consecutive sections/parts during the semester (one building on the other)	-Access to Assistive Technology and reasonable adaptations through the Committee for the Support of Students with Disabilities and/or Special Educational Needs (Ε.Φ.Ε.Ε.Α.)

In addition to the above, inclusive e-learning design takes into consideration the students' workload (including assignments, examinations, learning outcomes and course literature) calculated in accordance with the ECTS of each course, and involves a variety of assessment methods that enable students to engage with and practice diverse skills and meet varying challenges. Various forms of written and oral examinations and assignments support the learner's general competencies. These include both individual and group work.

Where appropriate and possible, in order to ensure interconnections between theories and practice, syllabi comprise both theoretical and practical content; in particular, instructors are encouraged to develop assignments and examinations where students are required to use their experience gained from practice, in order to connect theory with practice. Finally, instructors provide support adjusted to students' individual abilities, learning needs and learning opportunities.

The University's annual Faculty Development Programme provides development training activities in inclusive design, as well as in differentiation and UDL in higher education.

c. Co-design

The instructors and the course coordinators, under the supervision and guidance of each program coordinator, regularly update their study guides to incorporate insights from ongoing training in learner-centred and inclusive design. Moreover, at the beginning and around the middle of the semester the program coordinator invites the instructors to a meeting to exchange opinions on students' issues and course delivery.

d. Interactive and collaborative learning

E-learning at EUC is designed in ways to promote interaction in various levels (learner-learner, learner-instructor, learner-content, learner-technology). The ultimate goal is to enhance the interaction between students and the learning that can only occur among motivated individuals working together. Interactive learning is a hands-on/real life approach to education founded upon building student engagement through guided social interaction connected with existing knowledge and their own experience and interests, with carefully designed and structured activities to facilitate learning in groups and challenge students to develop practical skills.

Interactive learning seeks to enhance the interaction between learners and:

1. the course materials
2. the instructor
3. their peers

Interactive learning emphasizes the active engagement of the learner in enrichment activities which aim at the practical and critical application of the theoretical knowledge. When interactive learning takes place within the contexts of student-material interaction, the student should be able to receive immediately feedback during her/his interaction with the course materials, and thus interactive learning will provide self-assessment opportunities. Interactive learning is, thus, a hands-on, real-life approach to education founded upon building activities to facilitate learning individually and/or in groups, challenging students to develop and apply practical scientific-specific skills and knowledge which are meaningful, connected to their existing theoretical knowledge, personal experiences, interests and (academic and professional) goals. The focal point of interactivity is always on the skills of learners, not the capabilities of the technology that seeks to facilitate learning.

Self-assessment and interactive exercises/activities are presented on a weekly basis. Such activities uphold the interest of students, motivate consistent participation and long-term engagement. Examples of such interactive exercises are the following:

- role playing
- simulations
- real-life scenarios
- learning tools
- online discussions for debating
- the use of visualization tools to come to a specific outcome
- brainstorming activities for answering a theoretical question
- problem-solving questions in groups
- preparing group PowerPoint presentations (e.g. after watching a video or studying a specific source)
- answering quizzes and peer reviewing assignments of other students, etc.

Gamification strategies are also embedded in EUC's E-Learning programmes of study. In addition, great emphasis is placed on communities of learning and collaboration. Learning collaboratively refers to using teamwork, through communication and discussion with the instructor and other student mates, to solve problems, develop projects, create products, either independently or jointly, etc. The construction of new knowledge is combined with the professional and personal experience of students, individual and group research processes and activities, knowledge management via the Blackboard Learn Ultra tools, etc. Collaboration is intertwined, supplemented and complemented with independent and autonomous learning, a necessary and needed condition of deep learning which is combined in a flexible way with other methodological approaches.

5. EUC support for e-learning:

Through guidance and support, each student receives personalized attention according to their needs, from the first day of their enrolment in an E-Learning programme of study. EUC supplies the following supportive structures and resources for students on their e-learning courses:

a. Learning resources

This can include educational materials expressly designed to support and convey the learning content, but it might also include other types of open educational resources and tools (either text, media, multimedia, digital documents, e.g. audible content, motion pictures, spreadsheets, photos, pdfs, graphics, etc. or material created by the students themselves), etc. EUC's pedagogical model is flexible and can be adapted to the special characteristics and objectives of each course.

b. Academic guidance and support

Students are guided and supported in all their academic activities by the instructors teaching in the E-Learning programmes of study. Course instructors provide tutoring and mentoring on the content of student's courses and their evaluation and assessment. The course instructor is the person in charge for the teaching and learning process of each course. They provide students with all the necessary information and resources for the delivery of the course. They are the persons responsible for the students' evaluation, as well as for the management of the learning content.

In addition, in alignment with relevant CY.Q.A.A. guidelines and respective open university international practices, for each course a Course Coordinator is appointed. Their role is to coordinate the course in case there are more than one sections regarding issues of content, design and elaboration of the learning activities, procedures and student evaluation.

The Program Coordinator is the person in charge of the structure and the content of each program, as well as for resolving conflicts between instructors and the students or between the students and the administrative services of the University.

c. Administrative support

Students are also supported by Student Advisors and the members of the Distance Education Unit who counsel them on administrative related issues, the planning of their study, problem resolution, and decision-making issues (e.g. course selection and enrolment, the registration and payment of tuition fees, etc.).

6. The fundamental structure of EUC E-Learning Courses

a. Course structure

Each course is carried out over 13 weeks, followed by a final exam week. Throughout the 13-week teaching period, up to six synchronous teleconferences are organised. The first of these is always scheduled for the first week of the semester after the orientation/familiarisation week (during which students become familiar with the **Blackboard Learn Ultra platform** and spend time studying the Course Outline and Study Guide of their courses); and the last is always scheduled in the last two weeks of the semester (always before the final examination week).

The rest of the synchronous teleconference dates are set by the instructor of each course in coordination with the students in order to best accommodate their availability and needs. Though Study Guides and the Course Outlines are structured in weeks, instructors are free to design and present their course content and activities in any way they consider useful to facilitate students' organization of their self-paced study, as well as to help students follow the Course Outline and learning objectives as communicated to them at the beginning of the course. This may maintain the weekly format, or follow a thematic organisation structure. In the case of thematic organisation, instructors should provide an indication of estimated week(s) of study, as well as matching with learning objectives and milestones of activities and course requirements during the semester.

b. Synchronous meetings

Teleconferences are set up using **Blackboard Collaborate** which is an embedded e-learning collaboration tool of the Blackboard Learn Ultra LMS platform. This virtual classroom tool enables instructors to create an engaging and pedagogically innovative environment for students fostering e-learning. During the teleconferences, the instructor, as facilitator and moderator, presents the main points of the topic under discussion, discusses with students related fundamental issues and provides guidance as to the content and materials to be studied at home by the students over the following weeks. Teleconference sessions may also include opportunities for synchronous group or individual work by students. All material is provided beforehand on the **Blackboard Learn Ultra platform**, so that students have a chance to study it, prepare questions on the content and activities of the specific weeks, and discuss these during the synchronous session that follows. The assignments and activities that are to be conducted asynchronously (approximate weekly study time is estimated at 10 hours – excluding assignment preparation time), are also discussed in these synchronous teleconferences. More importantly, through these teleconferences, interaction between the students and the instructor is achieved as students are given, among other things, the opportunity to ask questions or share reflections with other students and their instructor. The instructor also prepares interactive activities (please see relevant section above) to be prepared for and conducted during the synchronous teleconferences.

c. Asynchronous communication

During the semester, students communicate between themselves and with the instructor through the Blackboard Learn Ultra platform in an asynchronous form. The most common methods of asynchronous communication are by message, short chats and discussion forums. Messages are personal or group, sent through the platform and delivered as an email message to recipients' email inbox. Short chat discussions in Blackboard Ultra are enabled over assignments or other tasks assigned on the platform, and provide an opportunity for students to asynchronously exchange informal comments and ideas on any course item. Discussion forums can be either for general discussions (e.g. course inquiries), or assignment focused (graded or non-graded). For the latter, as appropriate per week or theme, students are engaged is collaborative activities and interaction such as discussion of particular course material. This material might have been

either independently studied, or presented and discussed in a videoconference synchronous learning meeting with the instructor.

d. Course assignments

For each course, students need to carry out individual and group assignments which are graded. The type and nature of each assignment is presented to students at the start of the semester through multiple avenues of communication on the platform, such as in the Course Outline and course Study Guides. It is also explained and discussed during the synchronous teleconferences (as described above). These graded assignments may require preparing an answer to a theoretical question (for instance, discussion of a quote from an academic article or judgment/position or discussion) which involves extended research, rational analysis, critical thinking and evaluation. Other graded assignments may include responding to a focus/problem question, which involves comprehensive understanding of focal content issues.

To increase student motivation and engagement, collaborative and interactive tools are used, such as Padlet for group participation and group projects, Flashcards, game-based learning (e.g. Kahoot & Archy Learning, Simulations, etc.), interactive videos and other interactive activities (e.g. though H5P integrated in the learning platform). This kind of assignments are used mainly for formative evaluation and aim to enrich student's knowledge and skills on the learning objectives of the topic. Specific assignment topics for each course are described in detail in the Study Guide of each course and posted on the Blackboard Learn Ultra platform, alongside evaluation rubrics for assignments including the grade weighting attached to each one. Through assignments, students conduct research on a specific topic using the online databases of the University library as well as other electronic resources, either individually and/or in groups (thus interacting with each other, with the material of the course, and with the instructor).

Apart from presenting their findings in a written form, students might elaborate on these during short oral presentations. These oral presentations are usually conducted asynchronously to be shared on the Blackboard Learn Ultra platform. There they can be viewed and commented on by fellow classmates, and evaluated by the instructor, as they form part of the overall grade ascribed to their assignments.

Even though variations across programmes of study exist, the approximate time for an individual assignment preparation is approximately 20 hours, for a group assignment preparation is approximately 15 hours and for preparing an oral presentation is approximately 5 hours.

When written assignments are submitted, these are automatically checked through Turnitin for plagiarism through performing a similarity check in available databases. Instructors may use also Turnitin as a pedagogical tool to help students improve the final draft of their assignment before the submission on the Blackboard Learn Ultra platform. Flags for instances of similarity constitute opportunities for formative feedback and opportunities for revision during the writing process.

Instructors proceed promptly (within 15 days at the latest) in providing the assignment grade as well as detailed feedback that the student needs to take into

consideration in a formative mode of assessment for his/her better preparation of the final exam. Feedback can be given either on an individual basis (especially for individual assignments), on a group basis (e.g. in the case of group assignments) or a whole class basis.

Blackboard analytics are also helpful for an evidence-based approach to teaching and learning, because they provide instructors greater insight into the factors that affect their students' performance. Analytics also provide a snapshot of what students know, what they should know and what can be done to meet students' academic needs.

During the semester, students are requested to work both individually and in groups in order to conduct their self-assessment and interactive exercises/activities, which are described in detail in the Study Guide of each course on the platform, and are presented on a weekly basis. At least three to five of such interactive activities/exercises are graded by the instructor (allocated a percentage of 10-15%). This element of the course further allows the students to engage in asynchronous interactive learning at three levels presented in the respective section above (approximate time for activities/exercises preparation is estimated at 30 hours).

e. Final exams

After the 13-week learning period is completed, students take the final exam for each of their courses (allocated percentage at 50%). The final exam assesses in a comprehensive way the level at which students have acquired the theoretical knowledge covered in the course, as well as the degree to which they have developed the skills in critical analysis aimed at by the course (approximate time for exam preparation 50 hours).

For the online/e-Proctoring implementation of the final exams of E-Learning courses, the LockDown browser platform **Respondus** is used. This tool allows the students to undertake their exams in a proctored environment. Before starting the exam, the students are asked to use their University IDs to identify themselves. Exam recorded videos are stored on GDPR compliant Amazon Web Services (AWS Servers) and are automatically deleted every two (2) months. Up until students have submitted their final answers, the software 'locks' their computer, not allowing them to perform any other actions on their PCs, other than their final examination, until they have submitted their final answers. The software uses the camera and microphone of the student's PC to monitor their movements, sounds, conversations, etc. and produces reports of student activity at the time of the examination. If potential transgressions are detected by the software, the instructor is alerted accordingly (i.e. the software flags specific snapshots and then the instructor when reviewing the recording can view those points more cautiously). The instructor, who is the only one with access to the recording, can access the video to review the reasons for a high alert. If deemed necessary, the student is interviewed and explanations for the alert are requested. If the information is not sufficient, further actions are taken based on the University's regulation on academic dishonesty. The University policy on penalties related to academic dishonesty is presented on instructors' Course Outlines for each course.

A video presentation of the semester delivery of a typical E-Learning course appears here:

MA_Ed_Sciences_SpecialandInclusive_DL_video.mp4

7. Student assessment in E-Learning courses:

The Study Guides provided at the beginning of the semester contain specific instructions, resource guidance, rubrics for grading, assigned grade value for graded activities, and timelines. Students prepare and deliver their work, including the final exam, aiming to accumulate a grade of at least 60% to pass an undergraduate class, or 70% to pass a graduate class. The grading system of E-Learning courses according to EUC regulations appears in the table below:

BACHELOR's DEGREES (UNDERGRADUATE PROGRAMMES)					MASTER's DEGREES (POSTGRADUATE PROGRAMMES)			
Grade	**Description**	**ECTS**	**Percentage**		**Grade**	**Description**	**ECTS**	**Percentage**
A	Excellent	4.0	90+		A	Excellent	4.0	90+
B+	Very Good	3.5	85-89		B+	Very Good	3.5	85-89
B	Good	3.0	80-84		B	Good	3.0	80-84
C+	Fairly Good	2.5	75-79		C+	Fairly Good	2.5	75-79
C	Average	2.0	70-74		C	Average	2.0	70-74
D+	Below Average	1.5	65-69		D+	Below Average	0	
D	Poor	1.0	60-64		D	Poor	0	
F	Failure	0			F	Failure	0	
I	Incomplete	0			I	Incomplete	0	
W	Withdrawal	0			W	Withdrawal	0	
P	Pass	0			P	Pass	0	
AU	Attendance	0			AU	Attendance	0	
TR	Course from transfer	0			TR	Course from transfer	0	

For every week the objectives and learning outcomes are clearly stated in all Study Guides, allowing students to self-assess progress by reflecting on their grasp of target concepts and knowledge. Based on each assignment specific criteria, an indicative grading rubric is included in the Study Guides. An example of a rubric for a group research paper in a research methodology course appears below:

Group Assignment Evaluation	Criterion	Maximum points possible	Points Earned
Names:			
Literature review and theoretical framework	• adequate presentation of basic theoretical tools • adequate presentation of local and international literature on the topic • presentation of researcher's epistemological paradigm • justification of necessity and importance of study	4	
Methodology	Justified presentation and bibliographic documentation of the	8	

	methodological choices concerning all parts of the methodological design: • appropriate research problem statement and research questions • data collection methods • participant profile • sampling and recruitment method • data analysis method • data collection duration • ethics issues • validity and reliability strategies		
Analysis-interpretation	• adequate interpretation and presentation of the findings • with documentation with original excerpts from the data, and • documentation from the literature	8	
Conclusions	• link of basic conclusions to the literature • comprehensive discussion of basic conclusions	3	
General	• proficient use of language • appropriate use of APA • general presentation-appearance of the work	2	
Total points		**25**	

8. Programmes' quality assurance

In order to improve the learning experience for the students, EUC has established a Standing Committee under the University's Committee of Internal Quality Assurance (C.I.Q.A.) named the "Pedagogical Planning of E-Learning Programmes of Study Standing Committee". The Committee is involved in all internal quality assurance procedures and decisions related to the University's E-Learning programmes of study. The Committee's aim is to improve the learning experience of E-Learning students through its active and qualitative support of the University's E-Learning programmes of study and is responsible for supporting Schools in:

- monitoring and evaluating the existing E-Learning programmes of study;
- the pedagogical planning of new E-Learning programmes of study;
- the design and evaluation of educational material for E-Learning programmes of study;
- the support and feedback processes to the students;
- the pedagogical use of technology, internet and digital information;
- the technical training and support of the instructors of E-Learning programmes of study;
- the interaction between academic staff and students in the E-Learning programmes of study.

The composition of the Pedagogical Planning of E-Learning Programmes of Study Standing Committee for the academic years 2022-2024 is the following:

Chair	
Members: School representatives	
School of Humanities, Social and Education Sciences	Dr. Constantina Demetriou, Lecturer (Psychology, B.Sc.)
	Dr. James Mackay, Assistant Professor (English Studies, B.A.)
	Dr. Georgia Petroudi, Associate Professor (Byzantine Music, B.A.)
	Dr. Monica Shiakou, Associate Professor (Child and Adolescence Mental Health, M.Sc.)
	Dr. Maria Papazachariou-Christoforou, Assistant Professor (Music, M.Mus)
	Dr. Constadina Charalambous, Assistant Professor (Education Sciences: Special and Inclusive Education, M.A.)
	Dr. Chrystalla Papademetri-Kachrimani, Assistant Professor (Education Sciences)
	Prof. Christos Kassimeris, Professor (Public Administration, M.P.A.)
	Dr. Panos Christodoulou, Assistant Professor (Hellenic Studies, M.A.)
	Dr. Nicos Drosos, Assistant Professor (Career Guidance and Counselling, M.A.)
School of Sciences	Dr. Yianna Danidou, Lecturer (Cybersecurity, M.Sc.)
	Dr. Konstantinos Giannakou, Lecturer (Public Health, M.Sc.)
	Dr. Marianna Christodoulou-Devledian, Lecturer (Speech Language Pathology, M.Sc.)
School of Business Administration	Dr. Christakis Sourouklis, Assistant Professor (Business Studies, B.B.A.)
	Dr. Lycourgos Hadjiphanis, Assistant Professor (Business Administration, M.B.A.)
School of Medicine	Dr. Violetta Raffay, Assistant Professor (Medical Education, M.Sc.)
School of Law	Dr. George Chloupis, Lecturer (Criminal Law, L.L.M.)
	Dr. Charalampos Stamelos, Lecturer (International Commercial Law and Public Law, L.L.M.)
Ex-officio Members:	
Director of Distance Education Unit	Dr. Paraskevi Chatzipanagiotou, Assistant Professor
Chair of Digitally Enhanced Learning (D.e.L.) Ad-Hoc Committee	Dr. Loucas Louca Associate Professor
Chair of Faculty Professional Development Standing Committee	Dr. Louiza Voniati Assistant Professor

APPENDIX VIII

Examples of discipline-specific authentic assessment

DBP610, Drug Design and Small Molecule Synthesis:

Search for the synthesis of N-(1-napthyl)-N'-(3-ethylphenyl)-N'-methylguanidine (cerestat) on the Reaxys database and design its retrosynthesis. You must present a partial or complete synthesis of at least four steps involving at least one of the following reactions:

- Synthesis or chemistry of a heterocycle
- Boron, silicon or tin chemistry
- Stereoselective synthesis

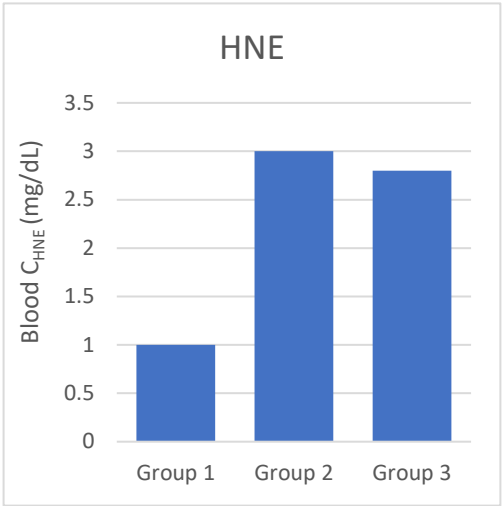
DBP630, Preclinical Development: Pharmacological and Toxicological Evaluation

A study was conducted to assess the utility of substance X as an antidote for substance A poisoning, and the results of the study are shown in diagrams I-IV below.

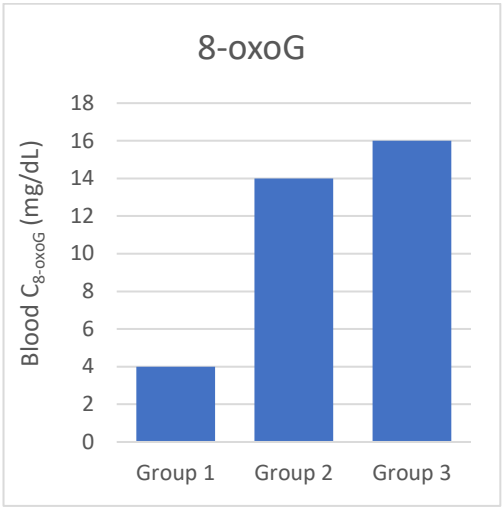
Each group received:

- Group 1 (control) physiological saline, i.p.
- Group 2 (A) substance A, 0.5 g/kg, i.p.
- Group 3 (A+X) substance A, 0.5 g/kg i.p., followed one 1h later by substance X (100 mg/kg i.p.).

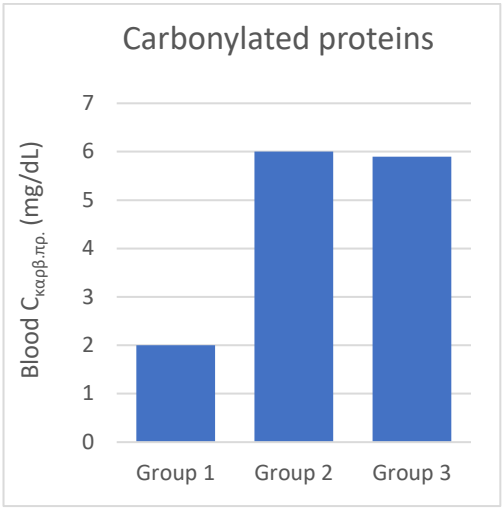
I. Effect of substance X on blood levels of 4-hydroxynonenal (HNE) in mice 24h after administration of substance A



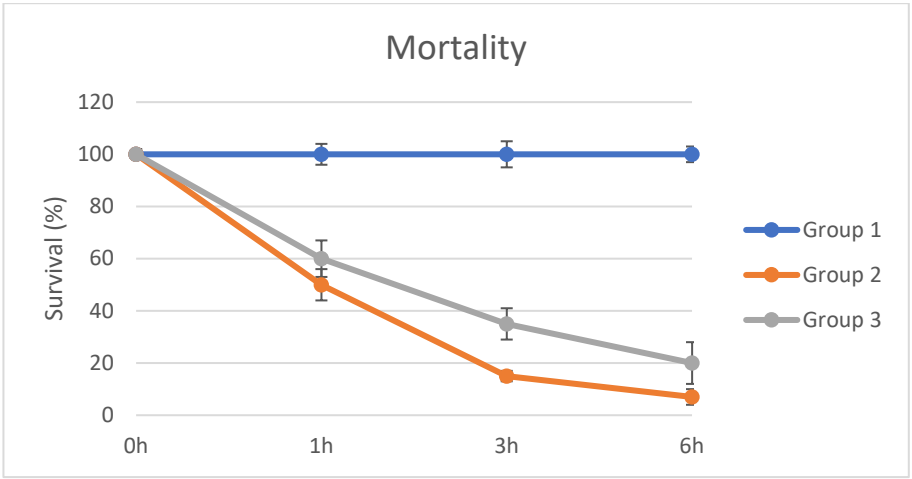
II. Effect of substance X on blood levels of 8-hydroxyguanine (8-oxoG) in mice 24h after administration of substance A



III. Effect of substance X on blood levels of carbonylated proteins in mice 24h after administration of substance A



IV. Effect of substance X on the mortality of mice after administration of substance A (n=10 in each group)



A. Why were concentrations of HNE, oxoG, and carbonylated proteins tested in this study? Explain in detail.

B. Is substance X actually useful as an antidote to substance A poisoning?

DBP640, Regulatory Aspects of Drug Development:

Read the article by Sumant Khanna, Eduard Vieta, Benjamin Lyons, Fred Grossman, Mariëlle Eerdekens and Michelle Kramer entitled “Risperidone in the treatment of acute mania”, 2005, *The British Journal of Psychiatry*, (187) 3; pp. 229-234. DOI: 10.1192/bjp.187.3.229.

Are there any concerning ethical issues with the clinical trial described in the Khanna et al., 2005 article?