Course Title	**Advanced Topics in Design, Discovery and Development of Drugs**				
Course Code	**PHA420**				
Course Type	Pharmacy Elective				
Level	MPharm (Level 2)				
Year / Semester	4th year / 8th semester				
Teacher's Name	Dr G Papagiouvannis				
ECTS	6	Lectures / week	3	Laboratories/week	-
Course Purpose	The aim of this course is to present a historical background of drug discovery, the methods used up to about 1940, the presentation and contribution to drug discovery of Alchemy, the relationship to iatrochemistry and synthetic dyes to pharmacotherapeutic agents and the approaches used during the modern era. Aim is also to familiarise the students with terms like lead compound, pharmacophore discovery, lead optimisation, bioisosterism, biofunctional groups, and rational drug design. Further aim is the relationship of properties such as pKa, lipophilicity, molecular volume, and drug action. An introduction is made to computational methods in drug action, molecular modeling and graphics. Further, the presentation of advanced modern approaches in contemporary drug design, exploiting the pathobiochemistry of the disease, the molecular mechanisms of drug action, drug metabolism, as well as tools such as molecular graphics, receptor mapping, drug receptor fitting and docking, energy calculations, conformational analysis and molecular shape analysis. Lipophilicity, electron distribution and molecular volume, in relation to pharmacokinetics and pharmacodynamics are studied. The phenomenon of drug targeting and (Q)SAR relationships are analysed. Toxicity studies, as well as clinical studies before the clinical phases (I, II, II and pharmacovigilance) are presented. Another aim is to present examples of the discovery of currently introduced, in pharmacy practice, molecules, for various diseases (atheromatosis, autoimmune and neurodegenerative diseases). Thus, the main purpose is to present and discuss the prospects of future and current advances in the field of drug design and development.				
Learning Outcomes	**By the end of this course, the students should be able to:** • Explain the basics of the historical perspectives of drug discovery; the difference in discovering drugs in antiquity, serentipity, the try-and-error- method, the iatrochemistry era, that of synthetic dyes, massive pharmacological testing and antibiotics; • Analyse the meaning and use of lead compound, pharmacophore, lead optimisation, drug receptor-fitting and docking, molecular graphics, receptor mapping; • Explain the exact meaning, applications, profitable use of lead compound, pharmacophore, lead optimisation; • Identify the meaning and use of important bases of rational drug design;				

	• Distinguish and apply theoretical calculations, pKa, lipophilicity (log P) and topological polar surface area (TPSA) of bioactive molecules; • Explain the docking of molecules to the active site of receptors and the meaning of receptor targeting and QSAR; • Distinguish the contribution of clinical phases I, II, III and pharmacovigilance; • Analyse advantages of the massive pharmacological screening and the approach of rational drug design and have a fair idea on the prospects for the future in the field of drug discovery and development. • Critically review the current evolutions on the field of drug design, development and discovery. • Analyse and apply the techniques for drug targeting, development and optimising of current and novel pharmaceutical compounds.		
Prerequisites	PHA301 PHA307	Corequisites	-
Course Content	Historical presentation of drug discovery. The isolation and identification of active ingredients of medicinal plants, The “try and see” method, Serendipity, Ethnopharmacy - Ethnopharmacology - Therapeutics, Massive pharmacological examination. Lead compound, pharmacophore discovery, lead optimization. The notions of bioisosterism and biofunctional groups. Structural modifications. Physicochemical properties important for drug activity, lipophilicity-partition coefficient, ionization-pKa, molecular volume, their determination and calculation. Computational prediction of important physicochemical properties of pharmaceutical compounds and membrane permeability of biological barriers. Advanced topics of relationship of structure, physicochemical properties and activity, using conventional and computational techniques. Numerical analysis. Applications of programming in medicinal chemistry problems. Statistical analysis and plotting of pharmacochemical data using statistical programmes for Medicinal Chemistry. Molecular modelling and graphics. Exploitation of Rational Drug Design, pathobiochemistry of the disease, chemical mechanism of drug action, drug metabolism, the assistance of molecular graphics, receptor mapping, drug-receptor fitting and docking. Energy calculations, conformational analysis, molecular shape analysis. Lipophilicity, electron distribution, molecular volume in relation to pharmacokinetics and pharmacodynamics. Drug targeting. Quantitative structure-activity relationships (QSAR). Computational QSAR methods using relevant software packages: applications in specific pharmaceutical categories, such as ACE and AchE inhibitors Cellular degeneration and radical attack, atheromatosis, diabetic complications, neurodegeneration (Parkinson’s, Alzheimer’s diseases). Cellular death, apoptosis, biologic stress, diseases caused by biologic stress. Rheumatoid diseases and other autoimmune conditions. Preclinical tests, clinical investigations, phases I, II and III, pharmacovigilance. Revision and critical analysis on current articles in the field. Perspectives in drug discovery. Advanced lectures in specific topics of drug design, development and discovery by experts in various areas of the field, such as the polymeric, antioxidant, anti-inflammatory and diagnostic drugs.		

Teaching Methodology	The teaching methodology includes lectures on the theory and laboratory exercises to better apprehend the basic concepts of Drug Design, Discovery and Development. The lesson uses PowerPoint detailed notes and images to better understand the principles of modern Drug Design. Includes tutorials, case studies and demonstrations. Methods such as discussion, questions/answers, pros/cons, brainstorming, debates and cooperative learning are used to enhance student's participation. Recent research findings are included in the course content and article summaries and / or bibliographic reviews. Computer programs like HyperChem, AutoDock Vina and Pymol etc. are also incorporated as part of the practical teaching method and relevant assignments are given to the students.
Bibliography	**Textbooks:** 1. «Βασικές Αρχές Σχεδιασμού και Ανάπτυξης Φαρμάκων», Βασίλης Δημόπουλος, Άννα Τσαντίλη-Κακουλίδου, Ελληνικά Ακαδημαϊκά Ηλεκτρονικά Συγγράμματα και Βοηθήματα, www.kallipos.gr, 2015. 2. «Οργανική Φαρμακευτική Χημεία, Θέματα Φαρμακοχημείας-Σχεδιασμού φαρμάκων», Ε.Α. Ρεκκα, Π.Ν. Κουρουνάκης, Εκδ. Φ. Χατζηπάντου, Θεσσαλονίκη 2010. 3. "Textbook of Drug Design and Discovery", P. Krogsgaard-Larsen, K. Stromgaard, U. Madsen, CRC Press; 5th edition, 2016. 4. "Drug Discovery and Development", R.G. Hill, D. Richards, Elsevier: 3rd edition, 2021. 5. Articles on the field from the current literature. **References:** 1. «Σχεδιασμός Φαρμάκων», Ε.Α. Ρεκκα, Π.Ν. Κουρουνάκης, Γραφικές τέχνες, Θεσσαλονίκη 1992. 2. Lecture notes
Assessment	• Mid Term Exam and exercises **40%** • Final Examination **60%** Course evaluation is done by: (a) a written examination and exercises assigned to students during the semester account for 40% of the total grade (b) a final written examination which examines all modules of the course material and it accounts for 60% of the total grade. Students are prepared for the above written exams over the theoretical and practical background in the classroom and with additional exercises given to them for further practice. For the better comprehension of the subject frequent revisions are performed at regular intervals. Questions of gradual difficulty apply to the evaluation of the mid-term and final examination. There may be multiple choice or right/wrong questions with justification of the answers or issue analysis and problem solving questions may be applied in order to evaluate the knowledge and perception of the student on the subject.

	The above criteria and assessment tools, as well as their weight, are communicated to the students, and are formulated in such a way in order to maximize the expected learning outcomes as well as the quality of the course.
Language	Greek, English