MEDICINAL CHEMISTRY II

Code number: ΝΠ18-40
Cycle: Undergraduate
Semester: sixth
Course type

	Background/General knowledge
X	Scientific area (pharmacy)

Credit Units (ECTS): 6
Lectures (hours/week): 3
Tutorial (hours/week): -
Laboratory work (hours/week): 2
Course coordinator: Vasilis Dimopoulos, Professor
Tutor (s):
Vasilis Dimopoulos, Professor
Room 408A & 409B, 4th floor Biology/Pharmacy building
Collaboration with students: Every day 1 -2 p.m
Communication: e-mail (vdem@pharm.auth.gr)
Ioannis Nicolaou, Assistant Professor
Room 404, 4th floor Biology/Pharmacy building
Collaboration with students: Every day 12 -1 p.m.
Communication: e-mail (inikolao@pharm.auth.gr)
Dimitra Hadjipavlou-Litina, Professor
Room 408/B & 410, 4th floor Biology/Pharmacy building.
Collaboration with students: Every day 11-12 a.m.
Communication: e-mail (hadjipav@pharm.auth.gr)
Assisting personnel:
Dr Antonis Gavalas, RTL'S
Aims of the course:

-Relationship between structure, physicochemical properties and activity of drug molecules
- Chemical-molecular mechanism of activity of drug molecules
- Chemical stability of drug molecules
- Biotransformations of xenobiotics

- Representative synthetic strategy-Chemical quantitative identification of drug molecules

Skills:

Practical application a) oxidation reaction, b) reduction reaction, c) esterification. Gradual alternation of acid-base conditions for purification of organic drug molecules. Qualitative identification and purity of drug molecule using thin layer chromatography (T.L.C.), or quantification by colorimetry (based on Lambert-Beer law) by diazotization and coupling (azo color formation). Clarification of characteristic fingerprints of organic drug molecules in nuclear magnetic resonance (NMR) spectra.

Teaching methods:

Lectures, theoretical and practical laboratory exercises.

Contents of the course:

Vasilis Dimopoulos

Synthetic strategy, origin - isolate, structure clarification, analysis, molecular mechanism of activity, molecular structure-activity relationships (SAR), selectivity, pharmacochemical aspect of activity and ADMET in the body of diuretics. Use of various molecular simulation and statistical processing programs in the field of pharmacochemistry

Ioannis Nicolaou

Pharmacochemical approach [such as design, synthesis, physicochemical properties, molecular action, interactions with molecular targets, structure & activity relationships (SAR), pharmacochemical explanation of toxicity, metabolism] of the following groups of drugs: Drugs acting on the renin-angiotensin system, drugs as dual inhibitors of renin-angiotensin system and the enzyme neprilysin for the treatment of heart failure, vasopressin antagonists for the treatment of heart failure, calcium channel blockers & Levosimendan as the first clinical agent of a new class of inotropic drugs, inhibitors of Nitric oxide donors & Ivabradine as the first selective If channel inhibitor in the sinus node for the treatment of angina symptoms, drugs for the treatment of pulmonary hypertension (I. Endothelin receptor antagonists, II. Stimulators and Activators of Soluble Guanylate Cyclase III. Prostacyclin receptor IP agonists), drugs used in Diabetes & anti-obesity drugs, inhibitors of platelet aggregation, local anesthetics.

Dimitra Hadjipavlou-Litina,

Synthetic strategy, origin - isolation, structure clarification, analysis, molecular mechanism of activity, molecular structure-activity relationships, selectivity, pharmacochemical aspect of activity and ADMET in the body of the following groups of drugs: acetylcholine agonists, acetylcholinesterase inhibitors, acetylcholine antagonists (in parasympathetic transmembrane terminals, in neuromuscular synapses, in the autonomic ganglia), sympathomimetic drugs as α- and β-receptor agonists, sympatholytic drugs as α- and β-receptor antagonists, anticoagulants, serine protease inhibitors, anti-hyperlipidemic drugs (statins as HMG-CoA reductase inhibitors).

Proposed literature:

Vasilis Dimopoulos

- Richard B. Silverman "The Organic Chemistry of Drug Design and Drug Action", Academic Press, 2004, ISBN-10: 0126437327
- Annual Reports in Medicinal Chemistry, http://www.sciencedirect.com/science/bookseries/00657743
- Joseph J. Cannon "Pharmacology for Chemists", Oxford University Press, 2007, ISBN-10: 0841239274
- E. J. Corey, B. Czako, L. Kurti "Molecules and Medicine", Wiley, 2007, ISBN-10: 0470227494

Ioannis Nicolaou

- *Journal* of Medicinal *Chemistry* (ACS Publications)
- *Bioorganic & Medicinal Chemistry Letters* - Elsevier
- *Bioorganic & Medicinal Chemistry* (ISSN 0968-0896)
- The *Journal* of Biological *Chemistry*
- *Chemical* Research in *Toxicology* (ACS Publications)
- *Drug Metabolism and Disposition*

Dimitra Hadjipavlou-Litina,

- Medicinal Chemistry Principles and Practice, Ed. F.D.King. 1994, The Royal Society of Chemistry, ISBN 0-85186-494-5
- Contemporary Drug Synthesis Li J.J, Johnson D., Sliskovic D., Roth B. Wiley-

Interscience,2004, ISBN 0-471-21480-9

- New Trends in Synthetic Medicinal Chemistry, Ed. F. Gualtieri, Wiley –VCH, Vol. 7, 2000
- Annual Reports in Medicinal Chemistry, Academic Press
- **Journal** of Medicinal **Chemistry** (ACS Publications)
- **Bioorganic & Medicinal Chemistry Letters** - Elsevier
- **Bioorganic & Medicinal Chemistry** (ISSN 0968-0896)
- "Practical Pharmaceutical Chemistry part I, II) The Athlone Press 1975
- "Principles of Medicinal Chemistry" W.O. Foye, ed. Lea & Febiger, 1995
- "Remington's Pharmaceutical Sciences", Osol A. ed. Mack Publishing Co., 1980
- « Goodman & Gilman's The Pharmacological Basis of Therapeutics » Goodman a., Hardman

J., Limbird L., eds MacMillan Publishing Co 2001

- "Strategies for Organic Drug Synthesis and Design" Lednicer, D., ed. Wiley J. & Sons 2000
- "Essentials of Pharmacology" Theocharidis T. Little, Brown & Company 2nd edition, 1999

• Drug Actions, Basic Principles and Therapeutic Aspects, Mutschler/Devendorf □ Archiv.Pharm 317, 183-185, 1984 □ Arch Pharm 325, 483-90, 1992.

• Arch Pharm 328, 689-698, 1995

• Intensive Care Med. 18, 449-454, 1992

• Greenblatt et al. (1999) FEBS Letters **463**, p321

• Dvir et al. (2003) JACS **125**, p363

• Bar-On et al. (2002) Biochemistry **41**, p3555.

• Kryeger et al.,(1997) Structure 7,297

• Raves et al. (1997) Nature Structural Biology 4, p57

• National Prescription 2007, National Drug Organization

Educational activities:

Lectures, discussion with the students in every lecture and practical laboratory exercises.

Evaluation process and methods:

The evaluation of the knowledge and skills acquired by the students from the teaching of the course is done:
With written exams (80% of the final grade + 20% of the laboratory grade), conducted in the examination periods. The written exams include an average of ten (10) conceptually complex topics that correspond to the total material that makes up the course.
The grade is proportionally distributed per teacher, based on the program of their respective lectures.
The exams take place on the dates and places announced by the Department.
Exam time is 3.5 hours in total for the three teachers.
It is possible to take a progressive examination, with conditions that will be defined after consultation between teachers and students and which will be announced in a timely manner on the department's website.

Use of TIC / Electronic distribution of the lectures

Vasilis Dimopoulos

Course lectures, notes, announcements, etc. are posted on a website (https://users.auth.gr/vdem

Ioannis Nicolaou

Course lectures, notes, announcements, etc. are posted on a website (http://inikolao.webpages.auth.gr/)

Dimitra Hadjipavlou-Litina,

Course lectures, notes, announcements, etc. are posted on a website https://users.auth.gr/hadjipav/

Teaching:

Teaching of this course is accomplished through lectures:

Lecture	Title	Tutor

1-3	Diuretics, chemical biology of pharmacodynamic and pharmacokinetic properties, synthetic strategy & physicochemical identification	**Vasilis** **Dimopoulos**
4	Drugs that interfere with renin angiotensin system	**I.Nicolaou**
5	Inhibitors of the renin-angiotensin system & the enzyme neprilysin for the treatment of heart failure	**I.Nicolaou**
6	Vasopressin and vasopressin antagonists (vaptans) for the treatment of heart failure	**I.Nicolaou**
8	Calcium Channel Blockers & Levosimendan as the first clinical agent of a new class of inotropic drugs, a calcium sensitizers for the treatment of heart failure	**I.Nicolaou**
9	Nitrate esters as donors of nitric oxide & Ivabradine as the first selective inhibitor of If channels in the sinus node for the treatment of angina symptoms	**I.Nicolaou**
10-11	Drugs for the treatment of pulmonary hypertension: I. Endothelin receptor antagonists, II. Stimulators and Activators of Soluble Guanylate Cyclase, III. Prostacyclin receptor IP agonists	**I.Nicolaou**
11-15	Drugs used in mellitus diabetes & anti-obesity drugs	**I.Nicolaou**
16-17	Inhibitors of platelet aggregation	**I.Nicolaou**
18	Local anesthetics.	**I.Nicolaou**
19-20	Peripheral Nervous System - Cholinergic Drugs-synthetic strategy & molecular structure-activity relationships	**D. Hadjipavlou-Litina**

21-23	Acetylcholine Antagonists - Anticholinesterases – Organophosphates, Antiglaucoma agents - synthetic strategy & molecular structure-activity relationships	**D. Hadjipavlou-Litina**
24	Acetylcholine antagonists- depolarizing & anti-depolarizing, synthetic strategy & molecular structure - activity relationships	**D. Hadjipavlou-Litina**
25	Anti-Alzheimer agents - synthetic strategy & molecular structure - activity relationships	**D. Hadjipavlou-Litina**
26-27	Adrenergic drugs - synthetic strategy & molecular structure - activity relationships	**D. Hadjipavlou-Litina**
28	α- receptor agonists- synthetic strategy & molecular structure-activity relationships	**D. Hadjipavlou-Litina**
29	Sympathomimetic amines - Aliphatic amines with adrenergic action - synthetic strategy & molecular structure-activity relationships	**D. Hadjipavlou-Litina**
30	α- and β- receptor antagonists (alpha & beta blockers) - synthetic strategy & molecular structure-activity relationships	**D. Hadjipavlou-Litina**
31-32	Anticoagulants, serine protease inhibitors	**D. Hadjipavlou-Litina**
33-34	Anti-hyperlipidemic drugs (statins as HMG-CoA reductase inhibitors)	**D. Hadjipavlou-Litina**

Laboratory work:

Laboratory work	**Title**	**Tutors**

1-4	First step of benzocaine synthesis	**V.Dimopoulos,** **D.Hadjipavlou-Litina,** **I. Nicolaou**
5-8	Second step of benzocaine synthesis	**V.Dimopoulos,** **D.Hadjipavlou-Litina,** **I. Nicolaou**
9-11	Third step of benzocaine synthesis	**V.Dimopoulos,** **D.Hadjipavlou-Litina,** **I. Nicolaou**
12-13	Qualitative identification and purity of drug molecule using thin layer chromatography (T.L.C.) or quantification by colorimetry (based on Lambert-Beer law) by diazotization and coupling (azo color formation)	**V.Dimopoulos,** **D.Hadjipavlou-Litina,** **I. Nicolaou**