COURSE (TITLE): Design and Synthesis of bioactive compounds.

LECTURER:

YEAR and SEMESTER: 2nd year, 1st semester

CREDITS (CFU): 8

SECTOR (SDS): CHIM/06, CHIM/08

ACADEMIC YEAR:

ASSESSMENT: Oral exam

LOCATION: Department of Environmental, Biological and Pharmaceutical Sciences and Technologies, Via Vivaldi 43 Caserta

COURSE OBJECTIVES/OUTCOMES: The aim of this course is to provide the basic knowledge of the fundamental principles regarding: i) the structure activity relationships (SARs) studies, ii) the design of bioactive molecules and iii) the main computational tools applied in the pharmaceutical field. Moreover, the student will be provided with the essential elements to design peptides and proteins.
Moreover, the student will acquire the ability to analyse the structure and plan the chemical synthesis of bioactive molecules such as nucleic acids, peptides and their analogues.

SYLLABUS (overview): Molecular interactions, the structure-activity relationships, pharmacophore and bioisostery. Computational methods for the design of biologically active molecules. Amino acids, peptides and proteins: Chemical and conformational properties. Design of helical peptides. Design of beta sheet peptides.
Structure of natural oligonucleotides. Oligonucleotide analogues: structure and functions. Chemical synthesis of oligonucleotides and analogues. Purification of characterization methods for oligonucleotides and analogues. Synthesis of peptides. Principles of combinatorial chemistry approach.

SYLLABUS (Detailed description):
Chemical features of standard and non-standard amino acids. The peptide bond. Structural features of molecular recognition. Structural features of helicoidal peptides. Stability criteria of α-helices. Tools for the stabilization of α-helices. Examples of peptide α-helices design. Drug-receptor interactions. Electrostatic interactions. Bond implicated in the drug-receptor interactions: covalent bond, ionic bond, H-bond, charge-transfer interactions. Representation of the 3D molecular structures and of the associated properties. Visualization of molecular structures at the computer. Calculation and visualization of molecular surfaces, volumes and properties (electron density, electrostatic potential). Calculation of the geometry and energy minimization of a molecule. Quantum mechanics and molecular mechanics. Molecular conformational analysis and molecular dynamics.
Rational drug design, pharmacophore search. Quantitative structure-activity relationships (QSAR). Ligand-based drug design. Privileged structures. De novo ligand design. Structure-based drug design.

Structure of natural oligonucleotides. Nucleotide analogues: structure and functions. Linear, convergent and divergent synthetic strategies, evaluation criteria of a synthesis, retrosynthetic analysis, synthetic objectives. Activating agents, Solution synthesis. Solid-phase synthesis. Polymeric supports in solid-phase synthesis. Support functionalization. Oligonucleotide synthesis: phospho diester, phosphoro threester, phosphoramidite, H-phosphonate methods. Analogues synthesis: peptide nucleic acid synthesis. Oligonucleotide purification and characterization methods. Peptide solid-phase synthesis. Peptide purification and characterization. Principles of combinatorial chemistry.

TEXTBOOKS:

ADDITIONAL READING: