Medicinal chemistry

The main objectives of this master in medicinal chemistry are:

1- Understanding of the basic biological and pharmacological interactions by using both natural products and total synthesis of bioactive molecules

2- Use of corresponding knowledge for the development of biologically and clinically active drugs.

It will include advanced courses in natural products, organic synthesis, medicinal chemistry; fundamentals of cell biology, molecular biology, drug design, and analytical methods.

Total credits: 55

- General education knowledge : 11 ETC
- Fundamental and Core courses: 29 ETC
- Thesis: 15 ETC

Available curriculum:

No.	Code	Subject	Credits	Credit hours			Prerequisite
				Lecture	*Practice*	*Self-study*	
I		**General education knowledge**	**11**				
1	PHI5001	*Philosophy*	04	45	0	0	
2	ENG5001	*General English*	04	45	0	0	
3	ENG5002	*English for Academic Purposes*	03	60	0	0	
II		**Fundamental and Core courses**	**29/48**				
II.1		***Required***	***10***				
4	CHE6218	*Chemistry of natural products*	02	30	0	0	
5	CHE6215	*Chemistry of Hecterocyclic compounds*	02	30	0	0	
6	CHE6220	*Chemistry of peptides and proteins*	02	30	0	0	
7	CHE6216	*Organotransition metalic chemistry*	02	30	0	0	
8	CHE6221	*(Steriochemistry of organic compounds)*	02	30	0	0	
II.2		***Elective***	***19/38***				
9	CHE6222	*Molecular design and modelling*	02	30	0	0	
10	CHE6217	*Enzymes in organic synthesis*	02	30	0	0	
11	CHE6219	*Quantum chemistry*	03	45	0	0	
12	CHE6211	*From the Research Lab to the Industrial Processes*	02	30	0	0	
13	CHE6212	*Examples of Synthesis of*	02	30	0	0	

No.	Code	Subject	Credits	Credit hours			Prerequisite
				Lecture	*Practice*	*Self-study*	
		Commercially Drugs					
14	CHE6214	*Cell Biology*	02	30	0	0	
15	CHE6209	*Toxicology*	02	30	0	0	
16	CHE6210	*Bibliographical work*	03	45	0	0	
17	CHE6213	*From Nucleic acids to Proteins*	02	30	0	0	
18	CHE6200	*Asymmetric Synthesis for the preparation of bioactive compounds*	02	30	0	0	
19	CHE6201	*Catalysis for the synthesis of bioactive compounds*	02	30	0	0	
20	CHE6202	*Bioactive product from Vegetal Sources*	02	30	0	0	
21	CHE6203	*Bioactive Products from Non Vegetal Sources*	02	30	0	0	
22	CHE6204	*Strategies in Total Synthesis of Bioactive Natural Products*	02	30	0	0	
23	CHE6205	*Drugs Target for Organic Chemists*	02	30	0	0	
24	CHE6206	*Pharmacomodulations*	02	30	0	0	
25	CHE6207	*Molecular Modelling for Medicinal Chemistry*	02	30	0	0	
26	CHE6208	*Analytical Methods for Bioactive Compounds*	02	30	0	0	
III		**Graduate thesis**	**15**				
		Graduate thesis	15				
		Total	**55**				

UE 1- Organic Chemistry of Bioactive Compounds (4 ECTS : 36h Rennes +24h VietNam)

Objectives: knowledge in tactics and strategies for synthesis in medicinal chemistry

UE 1.1 Asymmetric Synthesis for the preparation of bioactive compounds

-Fundamentals of chirality and tools for preparation of chiral (enantiopure) bioactive compounds

- Fundamentals of chirality and conformational analysis

- Stereoselective addition to carbonyl compounds: the Felkin-Anh model, diastereoselective allylation reactions (Zimmerman-Traxler model, allylboronates and allyltin).

- Diastereoselective addition to enolates: enolate formation, diastereoselective alkylations (Evans oxazolidinones, Oppolzer N-acylsultams, Meyers oxazolines, RAMP and SAMP)

- Diastereoselective aldol reactions: Zimmerman-Traxler model, aldolisation with α-chiral aldehydes, Evans oxazolidinones - Oxidation of alkenes: allylic alcohol oxidations (Sharpless epoxidation and kinetic resolution),

-Jacobsen's salen catalysts (oxirane formation and enantioselective opening of meso oxiranes), Shi's system epoxidation, enantioselective cis-dihydroxylation (α and β-AD-mix)

- Reduction of alkenes: enantioselective hydrogenation, hydroboration of alkenes (Masamune and Brown's systems)

- Reduction of prochiral ketones: boranes and CBS catalyst

UE 1.2 Catalysis for the synthesis of bioactive compounds

-Transition metal catalysis, organocatalysis and biocatalysis: modern approaches for medicinal chemistry

- Transition metal catalysis: fundamentals of transition metals for organic chemists (structure and bonding, reaction mechanisms), oxidation and reduction reactions, palladium-catalyzed cross-coupling reactions (Heck, Suzuki, Sonogashira etc.), rhodium-catalyzed reactions, ruthenium and molybdenum

catalyzed metathesis of alkenes and other metathesis reactions.

- Organocatalysis: phase transfer catalysis, enamine catalysis, non-covalent organocatalysis.

- Biocatalysis: enzymatic processes in organic synthesis, kinetic resolution.

UE 2- Natural Bioactive Compounds

Objectives: knowledge on active compounds from natural sources (isolation, characteristics, uses, templates for chemically optimised drugs)

UE 2.1 Bioactive Products from Vegetal Sources

Overview of natural sources, main classes of natural products and main metabolites used in medicinal chemistry

- Overview of natural sources: origins and specific analytical requirements for drug quality

- Main classes of natural products according to biogenesis (Shikimate - polyketide-acetate - amino-acids pathways)

- Main metabolites used in pharmacy (sugars, polysaccharides and heterosides - polyketides, anthraquinones, orcinols - terpenoids and steroids - essential oils, iridoids, pyrethrins – phenols, lignans, coumarins, flavonoids, anthocyans and tanins – alkaloids)

- Extraction and main separative processes applied to the vegetal

UE 2.2 Bioactive Products from Non Vegetal Sources

Overview of the sources, main classes of compounds and main metabolites of interest

- Overview of the sources (animals, microorganisms + marine and fungal (including lichens) sources)

- Biotechnological processes

- Main classes of compounds related to biogenesis pathways

- Main metabolites of interest (Antibiotics: penicillins, cephalosporins, aminosides, macrolides, cyclins, rifamycins - Antifungal antibiotics – Immunomodulators: ciclosporine, tacrolimus - Ergot derivatives -

- Heparins, hirudins and related compounds) - Examples for structural identifications and hemisynthesis

UE 2.3 Strategies in Total Synthesis of Bioactive Natural Products

Fundamentals in retrosynthetic analysis and examples of total synthesis of bioactive natural products and drugs.

- Fundamentals in retrosynthetic analysis

- Examples of the total synthesis of natural products (taxol, epothilones, etc.)

UE3- Medicinal Chemistry – Part I Objectives: Background and fundamentals in medicinal chemistry

UE 3.1 Drugs Target for Organic Chemists

Relationship between a xenobiotic and the human body can be studied at different levels. Thus, can be studied the whole body (clinical study, study of populations….), the organ (studies of functions….), the cell (cell biology…) and/or molecule (molecular biology…). This part of the course could be divided into different major points:

` INTRODUCTION: Human body organization With definition of systems, apparatus, organs, tissus, cellule…

PART 1: basic physiology of organs Humans are continuously exposed (willingly or not) to a multitude of xenobiotics in environment in

which it operates. The major routes of entry of xenobiotics in the human body are inhalation, oral and dermal. We can studied in this program

- An overview of the physiology concerning intestine, liver, lungs, skin, kidney, cardiovascular system.

- Notion of barrier (intestinal barrier, blood-brain barrier…)

PART 2: General organization of the cell

The cell is the basic unit of tissue. In the research world, cell models are thus models of choice. Thus, in this program can be studied an overview of general organization of the cell.

PART 3 :

Today, toxicology studies have developed technology allowing high-throughput screening. Thus we can analyze influence of one or more molecules on the expression of many genes or on a set of proteins. This point of view can be addressed through examples: genomics, proteomics, metabolomics.

UE 3.2Pharmacomodulations

Drug discovery, from lead to drug and description of essential therapeutic agents

- General aspects of medicinal chemistry

- Molecular mechanism of drug actions (enzymes, receptors and nucleic acids)

- Strategies of lead compounds research

- Structure-activity relationships

- Prodrugs - Description of some essential therapeutic families

UE4- Medicinal Chemistry – Part II

Objectives : Medicinal chemistry in Industry

UE 4.1 From the Research Lab to the Industrial Processes

Development of hits and leads from an industrial perspective

Patent and rules, an industrial point of view in medicinal chemistry

UE 4.2Molecular Modelling for Medicinal Chemistry

Fundamentals and tools in molecular modelling for drug design

UE 4.3Examples of Synthesis of Commercially Drugs

Industrial synthesis of commercially drugs

UE5- Biochemistry and Molecular Biology

Objectives : Knowledge of the structure, function and dynamics of nucleic acid-protein interactions. Development of new drugs targeting the process of translation in pro- and eucaryotes.

UE 5.1 From Nucleic acids to Proteins

Fundamentals, protein structure and function, protein-nucleic acid interactions

- Nucleic Acids. DNA/RNA: what makes the difference?

- Protein structure and function.

- Protein/Nucleic Acid interactions.

- Methods in studying ribonucleo protein complexes.

- The ribosome as an example of a large macromolecular ribonucleoprotein complex: structure-activity relationships.

- The bacterial ribosome as a target for the development of new antibiotics.

- The eukaryotic ribosome as a target for the development of new antiviral drugs.

UE 5.2 Cell Biology

Cell structure and organization, cell cycle, pharmacological approach of cell cycle and cancer

- Cell structure and organization: introduction on cell organization and cell compartiment, membranes structure and function, organization and function of the genetic information, cytosol and cytoskeleton, organite and energy in the cell.

- Cell cycle: description and molecular aspect of cell cycle, protein kinases and cell cycle, protein degradation and cell cycle, adherent molecules and signaliting transduction, tensegrity and cell cycle.

- Methodological approach of the cell cycle analysis

- Pharmacological approach of cell cycle and cancer.

UE6 Bioactive Compounds

UE 6.1 Analytical Methods for Bioactive Compounds

The aim is to present a variety of the most frequently used methods for the isolation and characterisation of bioactive organic compounds (from extractive or synthetic sources)

- Overview of the Extraction processes : Material preparation, solvents used, techniques (maceration, lixiviation, Soxhlet process, High pressure solvent extraction, supercritical fluid extraction, liquid-liquid extraction, filtration)

- Overview of different analytical methods for isolation (column chromatography, MPLC, HPLC, OPLC,

Circular centrifugal chromatography, Centrifugal Partition Chromatography….) with a focus on specific supports (LH20, Hydrophobic resins, reversed phases…)

- Examples of structural identification of compounds by various methods (NMR, MS, IR, UV…)

UE 6.2 Toxicology

Generalities, mechanism of action of toxins and cellular consequences

- Generalities: principles of toxicology (introduction, classification of toxic agents, dose responses, variation in toxic responses)

- Disposition of toxicants: absorption, distribution and elimination of toxicants, Biotransformation of xenobiotics (Phase I, Phase II)

- Mechanism of action of toxins and cellular consequences: non-organ-directed toxicity (chemical carcinogenesis and developmental toxicology), toxic responses of the respiratory system and other organs

- Major toxicants (heavy metals and organic compounds)

- Assessment of toxic effects

UE 7- Bibliographical work (3 ECTS)

A personal bibliographical work on a subject selected in advance (for example: total synthesis of a natural product, discovery and development of a drug, traditional medicinal chemistry etc.)

UE 8- Non disciplinary lectures (3 ECTS)

Course of French with a final examination