COURSE DESCRIPTION
APPLIED PHARMACEUTICAL CHEMISTRY

SSD: FARMACEUTICO TECNOLOGICO APPLICATIVO (CHIM/09)

DEGREE PROGRAMME: CORSO DI LAUREA MAGISTRALE IN CHIMICA E TECNOLOGIA FARMACEUTICHE (M46)
ACADEMIC YEAR 2022/2023

COURSE DESCRIPTION

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GENERAL INFORMATION ABOUT THE COURSE

INTEGRATED COURSE: NOT APPLICABLE
MODULE: NOT APPLICABLE
CHANNEL: A-Z
YEAR OF THE DEGREE PROGRAMME: IV
PERIOD IN WHICH THE COURSE IS DELIVERED: SEMESTER II
CFU: 12

REQUIRED PRELIMINARY COURSES

None

PREREQUISITES

Knowledge of basic chemistry, elementary skills of mental calculation

LEARNING GOALS

The main objective of the course is to provide students with the principles and logic of preformulation activities, with a view to the preparation and control of conventional and unconventional pharmaceutical dosage forms. In particular, the necessary tools to understand the relationships between the chemical-physical characteristics of the active molecules and/or excipients, the route of administration and bioavailability will be provided.

EXPECTED LEARNING OUTCOMES (DUBLIN DESCRIPTORS)

Knowledge and understanding

The student must demonstrate knowledge and understanding of the problems relating to preformulation; moreover, he/she must be able to discuss the relationships between biological needs and the properties of the active ingredients and materials used in the production of pharmaceutical dosage forms, starting from the notions learned regarding the concepts of hydrophilicity/lipophilicity, cellular transport and material science addressed during the course. The training course aims to provide students with the knowledge and essential methodological tools necessary to learn the cultural bases for preformulation. Such tools will allow students to recognize the implications of combining different materials in producing traditional and innovative pharmaceutical forms.

Applying knowledge and understanding

The student must demonstrate that he/she is able to identify and solve problems relating to the administration of drugs, with a special focus on the problems relating to the preparation of pharmaceutical forms. The course is aimed at providing suitable skills and operational tools needed to apply the acquired knowledge.

COURSE CONTENT/SYLLABUS

DRUGS AND PHARMACEUTICAL FORMS: definitions; routes of administration; development of pharmaceutical products.

METROLOGY: international system of units; determination of a given amount.

BIOPHARMACEUTICAL: drug administration; LADME scheme, Noyes-Whitney equation; absolute and relative bioavailability, bioequivalence; absorption of drugs through biological membranes; passive transport of drugs, Fick's law; active transport, endocytosis, efflux pump; factors influencing passive transport: distribution, Henderson-Hasselbalch equation; absorption of drugs with respect to routes of administration; physicochemical properties of drugs and absorption: crystallinity, polymorphism; external factors that affect absorption: wettability, complexation, adsorption; conventional/modified release pharmaceutical dosage forms; drug absorption/elimination patterns; biopharmaceutical classification scheme.

GRANULOMETRIC ANALYSIS OF POWDERS: definitions, fundamental and derivative properties of powders; average diameters and distributions of diameters; powder classification techniques: sieves, Andreasen's pipette and Stokes's equation, microscopy techniques; shape of powders; Coulter counter; laser light scattering; porosity of powders, apparent volume test, Carr index, flowability.

MIXING OF POWDERS: definitions of positive, negative, neutral mixture; homogeneity of the mixtures; mixing mechanisms; stability of powder mixtures; mixing indices; mixing of small quantities of powders, geometric dilution; rotating body and fixed body mixers.

GRINDING: effects and mechanisms of grinding, Hooke's law; properties affecting grinding: hardness, adhesiveness, glass transition temperature, moisture content, plasticity; mechanisms involved in grinding; grinding; crushers, dry and wet mills, air jet mills, ball mills, hammer mills, blademills, cylinder mills; colloidal mills; criteria for equipment choice.

DRYING: definition; heat transfer by conduction, convection, radiation; equilibrium humidity; external, structural and adsorption water; convection drying: stoves and cabinets; microwave and fluidized bed drying; spray-drying; freeze-drying.
STERILIZATION. Definition; sterility assurance level; time of sterilization and decimal reduction; rate of microbial destruction, Z value; dry heat sterilization: direct flame, stoves; moist heat sterilization: autoclave; sterilization by UV radiation, ionizing radiation, ethylene oxide; preparation in asepsis: clean rooms, sterile hoods.
WATER FOR PHARMACEUTICAL USE. Classification of water: levels I-IV; distillation: definition, Clausius-Clapeyron law; deionized, distilled, deionized water; basic and thermocompression distiller; bi-distillation of soluble binary mixtures: Raoult's law, azeotropic mixtures; simple co-current and counter-current distillation: fractionation; azeotropic distillation; reduced pressure distillation; molecular distillation; steam distillation.
PREFORMULATION. Definition; solubility of a p.a., determination of solubility; intrinsic solubility; cyclodextrins: synthesis, inclusion complexes, stoichiometry of the complexes, phase solubility diagrams; solubility/degree of ionization - pH profiles; pH - intrinsic solubility relationship; pka determination for weak acids and weak bases; thermal characterzation of substances: Young's modulus, glass transition and fusion; differential scanning calorimetry (DSC): definition and principle of operation; heating rates and thermograms: definition, peaks, inflections; thermo gravimetric analysis: operating principle, integral and derivative thermogram; effect of the heating rate; preformulation program; salification and criteria of selection of salts; solubility and crystallinity of salts; dissolution rate; physical stability: hygroscopicity; quantitative measurement of hygroscopicity; tolerability; alternative solvents to water: cosolvents and oils.
LIQUID PREPARATIONS. Solutions, strong and weak electrolytes; definition of dispersed systems, interfacial phenomena; surface tension; surfactants and wetting agents; critical micellar concentration; hydrophilic/lipophilic balance; classification of surfactants: anionic, cationic, amphoteric, non-ionic; Span, PEG, pluronic; suspensions: definition, aggregation phenomena; strategies to increase suspension stability: electrolytes, surfactants, colloids; zeta potential: London forces; emulsions: definitions; emulsifiers and mechanism of action; instability phenomena of emulsions: creaming, flocculation, coalescence.
EXCIPIENTS. Definition, requirements, purposes, effects of excipients; classification of excipients: diluents, binders, disintegrants, lubricants, glidants, preservatives, antioxidants.
POLYMERS. Definition, nomenclature and classification; copolymers, polyelectrolytes; structure of polymers and copolymers: linear, branched, cross-linked polymers; tacticity in polymers; number average and weight average molecular weights; molecular weight distributions, polydispersity index; semicrystalline polymers: crystallinity models: fringed micelle, lamellae, spherulites; factors affecting crystallinity; degree of crystallinity.
STABILITY AND STABILIZATION OF MEDICINES. Definition and criteria; chemical, physical, microbiological, therapeutic, toxicological stability; degradation in pharmaceutical forms; physical degradation; chemical degradation: hydrolysis, oxidation, photochemical degradation, isomerization; microbiological stability: pharmacopoeia requirements, preservatives; zero-order and first-order degradation kinetics; stability studies: stress tests on the active ingredient, accelerated stability studies, effect of pH on the degradation of active ingredients.

READINGS/BIBLIOGRAPHY

P. Colombo, A. Gazzaniga, E. Vidale, “Principi di Tecnologia Farmaceutica”. Casa Editrice Ambrosiana. ISBN: 9788808186720 H.C. Ansel, S.J. Stockton
“Principi di calcolo farmaceutico”. Editore Edra, 2017. ISBN 9788821443947
The professor is available to provide clarifications on the topics of the program, after an email appointment. Course slides will also be provided.

TEACHING METHODS OF THE COURSE (OR MODULE)

Lessons in presence

EXAMINATION/EVALUATION CRITERIA

a) Exam type

- [ ] Written
- [x] Oral
- [ ] Project discussion
- [ ] Other

In case of a written exam, questions refer to

- [ ] Multiple choice answers
- [ ] Open answers
- [ ] Numerical exercises

b) Evaluation pattern