Title: Drug Discovery and Development   [3-0-0-3]

Content *:*
Identification of target or drug leads associated with a particular disease by a number of different techniques including combinations of molecular modeling, combinatorial libraries and high-throughput screening (HTS); Conceptualizing the automation of the HTS process and the importance of bioinformatics and data processing in identification of lead compounds; Rational drug design, based on understanding the three-dimensional structures and physicochemical properties of drugs and receptors; Modelling drug/ receptor interactions with the emphasis on molecular mechanisms, molecular dynamics simulations and homology modelling; Conformational sampling, macromolecular folding, structural bioinformatics, receptor-based and ligand-based design and docking methods, in silico screening of libraries, semi-empirical and ab-initio methods, QSAR methods, molecular diversity, design of combinatorial libraries of drug-like molecules, macromolecular and chemical databases.

Identification of relevant groups on a molecule that interact with a receptor and are responsible for biological activity; Understanding structure activity relationship; Structure modification to increase potency and therapeutic index; Concept of quantitative drug design using Quantitative structure–activity relationship models (QSAR models) based on the fact that the biological properties of a compound are a function of its physicochemical parameters such as solubility, lipophilicity, electronic effects, ionization, stereochemistry, etc.; Bioanalytical assay development in support of in vitro and in vivo studies (LC/MS/MS, GC/MS and ELISA).

Principles of drug absorption, drug metabolism and distribution - intestinal absorption, metabolic stability, drug-drug interactions, plasma protein binding assays, metabolite profile studies, Principles of toxicology, Experimental design for preclinical and clinical PK/PD/TK studies, Selection of animal model; Regulatory guidelines for preclinical PK/ PD/TK studies; Scope of GLP, SOP for conduct of clinical & non clinical testing, control on animal house, report preparation and documentation Integration of non-clinical and preclinical data to aid design of clinical studies.

Requirements of GMP implementation, Documentation of GMP practices, CoA, Regulatory certification of GMP, Quality control and Quality assurance, concept and philosophy of TQM, ICH and ISO 9000; ICH guidelines for Manufacturing, Understanding Impurity Qualification Data, Stability Studies.

Objectives of Phase I, II, III and IV clinical studies, Clinical study design, enrollment, sites and documentation, Clinical safety studies: Adverse events and adverse drug reactions, Clinical PK, pharmacology, drug-drug interaction studies, Statistical analysis and documentation.

Global Regulatory Affairs and different steps involved, Regulatory Objectives, Regulatory Agencies; FDA guidelines on IND and NDA submissions, Studies required for IND and NDA submissions for oncology, HIV, cardiovascular indications, On-label vs. off-label drug use GCP and Requirements of GCP Compliance, Ethical issues and Compliance to current ethical guidelines, Ethical Committees and their set up, Animal Ethical issues and compliance.

Texts / References:
1. Krogsgaard-Larsen et al. Textbook of Drug Design and Discovery. 4th Edition. CRC Press.
2. Kuhse, H. (2010). Bioethics: an Anthology. Malden, MA: Blackwell.
3. Nally, J. D. (2006) GMP for Pharmaceuticals. 6th edition. CRC Press
4. Brody, T. (2016) Clinical Trials: Study Design, Endpoints and Biomarkers, Drug Safety, and FDA and ICH Guidelines. Academic Press.