28/08/2012

RAJIV GANDHI PROUDHYOGIKI VISHWAVIDYALAYA

M. Pharm (Pharmaceutical Chemistry)

III Semester Elective Course Contents

ELECTIVE I

MPY- 301 PCh : DRUG DESIGN & DISCOVERY

Unit I

Software overview: Introduction to computational chemistry software, brief information on commercial software like Schrodinger, Sybyl, MOE, Open Eye programmes, Drug Discovery Studio, Hyperchem, ChemBioOffice , Gold, Auto-Dock, V-Life MDS with special attention to the basic approaches utilized in their working like- energy minimization approaches and parameters, force fields, quantum mechanics, scoring functions used and their relative efficiency.

Unit II

Introduction to chemoinformatics: Cheminformatics tools for drug discovery, chemical structure representation (SMILE & SMART),chemical databases: CSD, ACD, WDI, ChemBank, hazardous chemical database,PUBCHEM, Various format of small molecules like mol, mol2 ,sdf, mae.

Unit III

Combinatorial Library Design, Molecular Similarity, and Diversity Applications – Introduction, Molecular Similarity/Diversity, Combinatorial Library Design, Subset Selection and Screening Set Enrichment, Example Approaches, Conclusions and Future Directions.

Unit IV

Virtual Screening - : Introduction, Techniques for known receptor active site or inferred active sites like receptor-based design, automated shape matching, artificial intelligence and site-directed design, automated detection of receptor binding regions, Putative receptor site. Techniques for unknown receptor site like: deducing the pharmacophore (and the receptor) from binding drugs, Active analogue approach, Crippen's distance geometry, Ensemble approach, site modeling. Drug-likeliness screening, ligand base virtual screening, structure base virtual screening, application of virtual screening in drug discovery, examples.

Unit V

The FDA and Regulatory. Issues

Caveat, Introduction, Chronology of Drug Regulation in the United States, FDA Basic Structure, IND Application Process, Drug Development and Approval Time Frame, NDA Process, U.S. Pharmacopeia and FDA,CDER Freedom of Information Electronic Reading Room, Conclusion,

Unit VI

Intellectual Property in Drug Discovery and Biotechnology: Introduction, Patent Protection and Strategy, Requirements for Patents, Enforcement of Patents, Worldwide Patent Protection, Trademarks, Trade Secrets, Other Forms of Protection, Conclusion.

Books and references recommended:

1. Smith HJ, Williams H, eds, "Introduction to the principles of Drug Design" Wright Boston.
2. Silverman R.B. "The organic Chemistry of Drug Design and Drug Action" Academic Press New York.
3. Robert GCK, ed., "Drug Action at the Molecular Level" University Prak Press Baltimore.
4. Martin YC. "Quantitative Drug Design" Dekker, New York.
5. Lien EJ. SAR "Side effects and Drug Design" Dekker, New York.
6. William H, Malick JB "Drug Discovery and Dovelopment" Humana Press Clifton.
7. Delgado JN, Remers WA eds "Wilson & Gisvolds's Text Book of Organic Medicinal & Pharmaceutical Chemistry" Lippincott, New York.
8. Foye WO "Principles of Medicinal chemistry" Lea & Febiger.
9. Wolf ME, ed. "The Basis of Medicinal Chemistry, Burger's Medicinal Chemistry" John Wiley & Sons, New York.
10. Ariens EJ "Drug Design" Academic Press New York.
11. Olson EC "Computer Assisted Drug Design" American Chemical Society ACS Symposium Series 112.
12. Roberts SM, Price B.J.Eds. "Medicinal Chemistry. The Role of Organic Chemistry in Drug Research "Academic Press New York.
13. Patrick Graham, L., An Introduction to Medicinal Chemistry, Oxford University Press.
14. Fischer Janos, Ganellin C. Robin "Analogue-based drug Discovery, Wiley-VCH Verlag Gmb H & Co. KG &A.
15. Pandi, Veerapandian "Structure based drug design New York Marcel Dekker, inc., 1997.
16. Wermuth GC, "The Practice of Medicinal Chemistry" Second edition, Academic Press, Elsevier
17. P.K. Larsen, Tommy and U. Madsen, Textbook of Drug Design and Discovery.
18. T.J. Perun and C.L. Propst, Computer Aided Drug Design.
19. Alfred Burger, Donald J. Abraham - Burger's Medicinal Chemistry and Drug Discovery. Volume 1: Drug Discovery (6th edition) , Publisher: Wiley-Interscience | 2003-01-17 | ISBN: 0471270903

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M. Pharm (Pharmaceutical Chemistry)

III Semester Elective Course Contents

ELECTIVE I

MPY- 302 PCh : SYNTHETIC ORGANIC CHEMISTRY

Unit I

RETROSYNTHETIC ANALYSIS: Disconnections and reliability of reactions, synthons: Donor and acceptor, functional group interconversions, one group carbon-heteroatom and carbon–carbon disconnections, two group carbon-heteroatom and carbon-carbon disconnections, chemo-, regio- and stereoselectivity considerations, natural reactivity .

Unit II

CHEMISTRY OF PROTECTING AND DEPROTECTING GROUPS: Protection for alcohols, carbonyl (aldehyde and ketone), carboxylic groups and amino groups. With special consideration to the reagents used for the protection and deprotection like tertiary butly carbamates (BOC), p-toluenesulfonyl (TOS), methyl sulfonylethoxycarbonyl (MSC), Silanyl ethyl ethers, propargylchloraformate, Thioacetate, Fmoc, tetrathiomolybdate,etc.

Unit III

FUNCTIONAL GROUP TRANSFORMATIONS:

OXIDATION AND REDUCTION: Oxidation of Alcohols to Aldehydes and Ketones, Reagents and Procedures for Alcohol Oxidation, Chemoselective Agents for Oxidizing Alcohols, Oxidation of Acyloins, Oxidation of Tertiary Allylic Alcohols, Oxidative Procedures to Carboxylic Acids, Allylic Oxidation of Alkenes, Terminology for Reduction of Carbonyl Compounds, Nucleophilic Reducing Agents, Electrophilic Reducing Agents, Regio- and Chemoselective Reductions, Diastereoselective Reductions of Cyclic Ketones, Inversion of Secondary Alcohol Stereochemistry, Diastereofacial Selectivity in Acyclic Systems, Enantioselective Reduction

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FUNCTIONAL GROUP TRANSFORMATIONS:

THE CHEMISTRY OF CARBON-CARBON π-BONDS AND RELATED REACTIONS: Reactions of Carbon-Carbon Double Bonds, Reactions of Carbon-Carbon Triple Bonds

FORMATION *of* CARBON-CARBON SINGLE BONDS VIA ENOLATE ANIONS:

1,3-Dicarbonyl and Related Compounds, Direct Alkylation of Simple Enolates, Cyclization Reactions-Baldwin's Rules for Ring Closure, Stereochemistry of Cyclic Ketone Alkylation, lmine and Hydrazone Anions, Enamines, The Aldol Reaction, Condensation Reactions of Enols and Enolates, Robinson Annulation

FORMATION OF CARBON-CARBON BONDS VIA ORGANOMETALLIC REAGENTS:

Organolithium Reagents, Organomagnesium Reagents,Organotitanium Reagents,Organocerium Reagents,Organocopper Reagents, Organochromium Reagents, Organozinc Reagents,Organoboron Reagents,Organosilicon Reagents, Palladium-Catalyzed Coupling Reactions.

FORMATION OF CARBON-CARBON π –BONDS: Formation of Carbon-Carbon Double Bonds, Formation of Carbon-Carbon Triple Bonds

Unit IV

Green chemistry: Principles, metrics, perspective of pharmaceutical industries; Green discoveries

a. Greener reactions including water as solvent, ionic liquids, supercritical liquids, supported reagents and catalysts, Solvent free reactions catalysis,

b. Greener technologies : Microwave and Ultrasound assiated synthesis

c. Sustainable synthesis of pharmaceuticals.

Books and references recommended:

1. Burger, Drug discovery and development, wiley interscience publishers.
2. Jerry March, Advanced Organic Chemistry.
3. Solomons, G.T.W., Organic chemistry.

4. Kevin Burgess, Solid-Phase Organic Synthesis wileys publication.
5. SAUL PATAI, The chemistry of the amino group. Interscience publishers.
6. John A. Joule and Keith Mills, Hetrocyclic chemistry, wileys publication.
7. E. J. Corey and Xue min chang, The logic of chemical synthesis. Wileys publications.
8. Jurgon Fuhrhop and Gustav Penzalin, Organic synthesis- concept, method and starting material. VCH publishers.
9. Peter G. M. Buts and Theodora W. Greene, Protective groups in organic synthesis. Wileys publications.
10. Ledinicer: Organic Drug synthesis Vol. 1,2,3,4 .John Wiley &. Sons N.Y publications.
11. Stuart Warren : Organic Synthesis – The Disconnection Approach , John Wiley & Sons publications.
12. Modern organic synthesis: an introductionIGeorge S. Zweifel, Michael H. Nantz, W. W. FREEMAN AND COMPANY.

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M. Pharm (Pharmaceutical Chemistry)

III Semester Elective Course Contents

ELECTIVE I

MPY- 303 PCh : IMPURITY PROFILING

Unit I

Impurity synthesis: Defination, classification, synthesis, purification, standardization, and quantification of impurities of active drug substances. Origin of impurities, types of impurities: process impurities, degradation impurities, and contamination impurities etc. Pharmacopoeial limits of impurities in active drug substances. Impurity-drug interaction.

Unit II

Application of analytical techniques in impurity profiling: Application of HPLC, preparative chromatography, flash chromatography, column chromatography, gas chromatography; UV/Visible, FTIR, Raman, NIR, MS, NMR spectroscopy; LC-MS, LC-MS-MS, GC-MS, TLC-MS, CE-MS, MEKC-MS, CEC-MS, LC-NMR, LC-IR in impurity profiling.

Unit III

Structure elucidation: Introduction of systematic approaches for structure elucidation of unknown impurities and metabolites. Case studies for identification and structure elucidation of impurity and metabolites.

Unit IV

Designing and optimization of synthetic route: Designing and optimization of different routes for synthesis of impurities.

References

1. R.J. Smith, M. L. Webb, *Analysis of Drug Impurities,* Blackwell Publishing.
2. M.V.N. Kumar Talluri, *Impurity Profiling of Drugs and Pharmaceuticals,* Lambert Academic Publishing.
3. ICH harmonized tripartite guideline, *Impurities in new drug products Q3B(R2)*
4. ICH harmonized tripartite guideline*, Impurities: guideline for residual solvents Q3C(R3)*
5. USFDA, Guidance for Industry ANDAs: *Impurities in Drug Products.*
6. USFDA, Guidance for Industry ANDAs: *Impurities in Drug Substances.*
7. USP

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M. Pharm (Pharmaceutical Chemistry)

III Semester Elective Course Contents

ELECTIVE I

MPY- 304 PCh : BIOANALYSIS

1. **Introduction**

   Bioanalysis, pharmacokinetics and drug metabolism (BPDM), The role of BPDM in drug discovery and drug development.

2. **The importance of the physicochemical properties of drugs to drug metabolism**

   Introduction , The physicochemical nature of drug molecules, The structure of the cell membrane and its implications for drug disposition, Drug partitioning across membranes, The ionisation of drugs, The pH environment of the body and how it affects drug bsorption and distribution, The importance of the physicochemical properties of drugs to their metabolism and excretion, Chirality and its effects on drug absorption, metabolism and excretion, The importance of physicochemical properties to the analysis of drugs.

3. **Sample preparation in Bioanalytical techniques**

   Introduction, Sample preparation techniques, Instrumentation, Bioanalytical automation strategy, Future development

4. **High-performance liquid chromatography in pharmaceutical bioanalysis**

   Introduction, A brief look at the theory of chromatographic separation in HPLC, The basic equipment comprising a modern HPLC system, modes of liquid chromatography , High-throughput bioanalysis, Chiral HPLC, Future trends in HPLC.

5. **Mass spectrometry and quantitative bioanalysis**

   Introduction, The instruments, Analytical interfaces, Ionisation, Mass analysers, Use of MS in quantitative LC–MS, Developing an LC–MS assay method

6. In vitro techniques for investigating, drug metabolism

Introduction, Preparation of liver subcellular fractions and hepatocytes, Use of subcellular fractions, hepatocytes and liver, slices to study drug metabolism, In vitro–in vivo correlations, Advantages and disadvantages of the in vitro systems used to study drug metabolism, The study of drug interactions using in vitro systems

7. Identification of drug metabolites in biological fluids using qualitative spectroscopic and chromatographic techniques

Introduction, Mass spectrometry, Sample preparation, Phase I & Phase II , NMR spectroscopy, Characterisation of metabolites by ^{1}H NMR, ^{19}F NMR metabolite profiling, Conclusions

8. Regulatory Guidelines for bioanalytical method development.

Refrences

1. A Handbook of Bioanalysis and Drug Metabolism, Edited by Gary Evans, CRC Press, 2004.
2. FDA Guidance (draft) : Analytical Procedures and Methods Validation
3. FDA Policy guide: Requesting Methods Validation for Abbreviated New Drug Applications (ANDAs)
4. FDA Guidance: Bioanalytical Method Validation
5. FDA Guidance: Mass, Spectrometry for Confirmation of the Identity of Animal Drug Residues, Draft
6. FDA Guidance: Guideline for Submitting Samples and Analytical Data for Methods Validation