

Department of Pharmaceutical Sciences and Natural Products
Scheme of Programme
Ph.D. in Medicinal Chemistry (W.E.F 2018)

Duration of the Course: 3-5 Years

Eligibility: Master's degree in Chemistry/Medicinal chemistry/Pharmaceutical Chemistry or equivalent with 55% marks from a recognized Indian or Foreign university

SEMESTER 1 (Course Work)

S. No.	Paper Code	Course Title	L	T	P	Cr
1	CMC.701	Research Methodology	4			4
2	CMC.702	Biostatistics	2			2
3	CMC.703	Computer Applications	2			2
*Opt any two of the following courses						
4	*CMC.704	Natural Products in Drug Discovery and Development: Recent Advances	3	-	-	3
5	*CMC.705	Recent Advances in Medicinal Chemistry of Nucleic Acids	3			3
6	*CMC.706	Emerging Trends in Green Synthesis and Drug Discovery	3			3
7	*CMC.707	Trends in Molecular Modelling for Drug Design	3			3
8	XXX.YYY [#]		3			3
Seminar at Department level						
9	CMC.797	Seminar	-			2
		Total	14			16

^{##} Any other relevant course offered by faculty member of the same department or other department/School-
To be decided by the respective supervisor.

E: Total Marks

L: Lectures T: Tutorial P: Practical Cr: Credits

Course Title: Research Methodology

L	T	P	Credits
4	-	-	4

Paper Code: CMC.701

Learning Outcomes:

Students who successfully complete this course will be able to:

1. Select and define an appropriate research problem and parameter
2. Understand, design and set the objectives based on the literature search.
3. Grasp the knowledge of protecting the research work through patent or copyright or trademarks.

Unit 1

15 hours

General principles of research: Meaning and importance of research, Critical thinking, Formulating hypothesis and development of research plan, Review of literature, Interpretation of results and discussion.

Bibliographic index and research quality parameters- citation index, impact factor, h index, i10 index, etc. Research engines such as google scholar, Scopus, web of science, etc.

Unit 2

15 hours

Technical writing: Technical & Scientific writing - theses, technical papers, reviews, electronic communication, research papers, etc., Poster preparation and Presentation and Dissertation. Reference Management using various softwares such as Endnote, reference manager, Refworks, etc. Communication skills – defining communication; type of communication; techniques of communication, etc..

Library: Classification systems, e-Library, Reference management, Web-based literature search engines

Unit-3

15 hours

Plagiarism: Plagiarism, definition, Search engines, regulations, policies and documents/thesis/manuscripts checking through softwares, Knowing and Avoiding Plagiarism during documents/thesis/manuscripts/scientific writing

Unit-4

15 hours

Intellectual Property Rights: Intellectual Property, intellectual property protection (IPP) and intellectual property rights (IPR), WTO (World Trade Organization), WIPO (World Intellectual Property Organization), GATT (General Agreement on Tariff and Trade), TRIPs (Trade Related Intellectual Property Rights), TRIMS (Trade Related Investment Measures) and GATS (General Agreement on Trades in Services), Nuts and Bolts of Patenting, Technology Development/Transfer Commercialization Related Aspects, Ethics and Values in IP.

Suggested Readings:

1. Gupta, S. (2005). *Research methodology and statistical techniques*, Deep & Deep Publications (p) Ltd. New Delhi. ISBN 10: 9327248198
2. Kothari, C. R. (2008.) *Research methodology(s)*, New Age International (p) Limited. New Delhi
3. Best J. W., Khan J. V. (Latest Edition) *Research in Education*, Prentice Hall of India Pvt. Ltd.
4. *Safe science: promoting a culture of safety in academic chemical research*; National Academic Press, www.nap.edu.
5. Copyright Protection in India [website: <http://copyright.gov.in>].
6. World Trade Organization [website: www.wto.org].
7. Wadedhra B.L. Law Relating to Patents, Trademarks, Copyright Design and Geographical Indications. Universal Law Publishing, New Delhi. Latest Edition. ISBN-10: 8175343826

Course Title: Biostatistics

L	T	P	Credits
2	-	-	2

Paper Code: CMC.702

Learning Outcomes:

Students who successfully complete this course will be able to:

1. Understand basic descriptive and inferential statistics including the concepts and principles of research design and statistical inference.
2. Perform and interpret descriptive and inferential statistical techniques including the Construction of tables and graphs, t-tests, Chi-square tests, and regression analysis.
3. Use appropriate software packages to solve analytical problems.

Unit 1

8 hours

Descriptive Statistics: Meaning, need and importance of statistics. Attributes and variables. Measurement and measurement scales. Collection and tabulation of data. Diagrammatic representation of frequency distribution: histogram, stem and leaf plot, pie chart.

Unit 2

7 hours

Measures: Measures of central tendency, dispersion (including box and whisker plot), skewness and kurtosis. Linear regression and correlation (Karl Pearson's and Spearman's) and residual plots.

Unit 3

7 hours

Discrete and continuous random variables. Discrete Probability distributions like Binomial, Poisson and continuous distributions like Normal, F and student-t distribution.

Unit 4

8 hours

Differences between parametric and non-parametric statistics. Confidence interval, Errors, Levels of significance, Hypothesis testing

Parametric tests: Test for parameters of Normal population (one sample and two sample problems) z-test, student's t-test, F and chi-square test and Analysis of Variance (ANOVA).

Non-Parametric tests: One sample: Sign test, signed rank test, Kolmogrov-Smirnov test, run test, Kruskal-Wallis one-way ANOVA by ranks, Friedman two-way ANOVA by ranks.

Suggested Readings:

1. Norman, G. and Streiner, D. (3rd edn) (2008). *Biostatistics: The Bare Essentials*. Decker Inc., Canada.
2. Sokal, R.R. and Rohlf, F.J. (1994). *Biometry: The Principles and Practices of Statistics in Biological Research*, W.H. Freeman and Company, New York.
3. Bolton, S., & Bon, C. (2009). *Pharmaceutical statistics: practical and clinical applications*. CRC Press.

Course Title: Computer Applications
Paper Code: CMC.703

L	T	P	Credits
2	0	0	2

Learning Outcomes:

Students who successfully complete this course will be able to:

1. Use and search various search engines for literature survey their research work.
2. Type, cite and edit the references of their thesis/dissertation work

Unit 1

8 hours

Fundamentals of computers: Parts of computers, Hardware, BIOS, Operating systems, Binary system, Logic gates and Boolean algebra.

Unit 2

7hours

MS Word (Word Processing, Creating and Saving Documents, Text Formatting, Tables, Document Review Option, Inserting Table of Contents), Power point, Excel Sheet.

Unit 3

7hours

Scientific information retrieval and web browsing: Introduction to various search engines such as Protein Data Bank, PubMed, NISCAIR, ACS, RSC, Elsevier, SciFinder, Google Scholar, Google patent, Espacenet, Beilstein databases, etc.

Unit 4

8hours

Bibliography management and research paper formatting using reference software EndNote and reference manager. Sketching of molecules using ChemBio Draw, ChemSketch, etc. .

Suggested Readings:

Gookin, D. (2015). Word 2013 for dummies. John Wiley & Sons.

1. Gookin, D. (2013). Word 2013 for dummies. John Wiley & Sons.
2. Harvey, G. (2016). Excel 2016 for dummies. John Wiley & Sons.
3. Sinha, P. K., & Sinha, P. (2010). Computer fundamentals (Vol. 4). BPB publications.
4. Bott, E., Siechert, C., & Stinson, C. (2009). Windows 7 inside out. Pearson Education.
5. Goel, A., & Ray, S. K. (2012). Computers: Basics and Applications. Pearson Education India.

Course Title: Natural Products in Drug Discovery and Development: Recent Advances

L	T	P	Credits
3	-	0	3

Paper Code: CMC.704

Learning Outcomes:

Students who successfully complete this course will be able to:

1. Be familiar with the prospects of natural products
2. Understand the role of natural products in living organisms, their biosynthesis and medicinal properties
3. Understand the role of natural products in drug discovery and development

Unit 1

11 hours

Prospects of Natural Products research in the 21st Century: - Introduction, use of natural products in traditional medicines, Marine natural products, Use of herbal remedies and the potential of drug development from natural products and novel drug templates: paclitaxel, podophyllotoxin, artemisinin etc.

Unit 2

11 hours

Recent development in the research on naturally occurring polyphenolic compounds: - Introduction, Recently reported flavonoids, flavonoids as drug candidates, Biological and Pharmacological activities of flavonoids (Antioxidant activity, cyto-toxic activity, anticancer and anti-microbial activity), Biosynthetic pathway.

Unit 3

11 hours

Alkaloids: - General methods of structure elucidation, degradation, classification based on nitrogen heterocyclic ring, role of alkaloids in plants, Structure, stereochemistry, synthesis and biosynthesis of the following: Ephedrine, Nicotine and Morphine, Recent developments in medicinal aspects- Antimicrobial activity, antioxidant and anti-inflammatory activities of alkaloids.

Unit 4

12 hours

Terpenoids: - Old secondary metabolites with new therapeutic properties- Introduction, general biosynthesis of terpenoids, Ecological role of terpenoids and terpenoids in herbal medicines.

Essential Oils:- Introduction, manufacturing process, processing of essential oils, uses of essential oils and composition of essential oils, Pharmacological applications.

Steroids: Structure determination and synthesis of cholesterol, partial synthesis of Testosterone and Progesterone, Chemical tests for steroids, Medicinal applications of steroids.

Suggested Readings:

1. Bhat, S.V.; Nagasampagi, B.A.; Meenakshi, S. (2009). Natural Product Chemistry & Applications. Publisher: Narosa Publishing House, New Delhi.
2. Finar, I.L. (2006) Organic Chemistry: Stereochemistry and the Chemistry of Natural Products. 5th edn, Dorling Kindersley (India) Pvt. Ltd., New Delhi.
3. Bhat, S.V.; Nagasampagi, B.A.; Sivakumar, M. (2005) Chemistry of Natural Products. Publisher: Narosa Publishing House, New Delhi.

4. Butler, M.S. (2005) Natural products to drugs: natural product derived compounds in clinical trials. *Natural Product Report*, 22, 162-195.5.
5. Butler, M.S. (2008) Natural products to drugs: natural product derived compounds in clinical trials. *Natural Product Report*, 25, 475-516.
6. Butler, M.S.; Blaskovich, M.A.; Cooper, M.A. (2013) Antibiotics in the clinical pipeline in 2013. *The Journal of Antibiotics*, 66, 571-591.
7. Blunt, J.W.; Copp, B.R.; Keyzers, R.A. (2013) Marine Natural Products. *Natural Product Report*, 30, 237-323.

Course Title: Recent Advances in Medicinal Chemistry of Nucleic Acids

L	T	P	Credits
3	-	-	3

Paper Code: CMC.705

Learning outcomes:

Students who successfully complete this course will be able to:

1. Understand, design of new inhibitors of nucleic acids
2. Drug targets in diseases like cancer and others.

Unit 1

11 hours

Nucleic acids: Introduction, central dogma, biosynthesis, structure (conformation, size, shape, bending, supercoiling etc.) and functions (transcription, post transcriptional modifications and translations) and damage and repair. Genetic polymorphism.

Unit 2

11 hours

Protein-nucleic acid interactions: proteins involved in the biosynthesis of nucleic acids, enzymes in replications, transcription and translation. Damage and repair enzymes and epigenetic factors (HDAC/nucleosomes/HATs/MTs).

Unit 3

11 hours

Drug design and synthesis: Drugs targeting nucleic acids conformations, drugs targeting associated proteins, drugs mimicking, drugs targeting replication/transcription/translation and the proteins mentioned in unit 2. Drugs affecting gene expression (kinase inhibitors etc.)

The SAR and *in silico* and pharmacokinetic approaches: to be discussed wherever possible in above mentioned topics.

Unit 4

12 hours

Nucleic acids in R&D and diseases: Diseases associated with nucleic acids (such as SNPs and chromosomal inversions etc.). Anti-nucleic acid therapies and naturally occurring small antisense RNAs (Si/micro RNA). Therapies of nucleic acids in stem cells. Vehicles mediated targeted delivery.

Suggested Readings:

1. Zhang, L.-H., Xi, Z., Chattopadhyaya, J. (2011), *Medicinal Chemistry of Nucleic Acids*, Wiley, 1 edition.
2. Mayer, G. (2010), *The Chemical Biology of Nucleic Acids*, Wiley, 1 edition.
3. Bloomfield, V. A., Crothers, D. M., Tinoco, I., Hearst, J. E., Wemmer, D. E., Killman, P. A., Turner, D. H. (2000) *Nucleic Acids: Structures, Properties, and Functions*, University Science Books; 1 edition.
4. Delgado, J. N. and Remers W A, Ed. (2010). *Wilson & Gisvold's Textbook of Organic and Pharmaceutical Chemistry*, J. Lippincott Co., 7th edition, Philadelphia.
5. Foye, W. C. (2008). *Principles of Medicinal Chemistry*, Publisher: Lea and Febiger, 6th edition, Philadelphia.
6. Neidle, S. (2007), *Principles of Nucleic Acid Structure*, Academic Press; 1 edition.
7. Blackburn, G. M., Gait, M. J., Loakes, D., Williams; D. (2006), *Nucleic Acids in Chemistry and Biology*, Royal Society of Chemistry; 1 edition.

8. King, F. D. (2003). *Medicinal Chemistry Principles and Practice*, Royal Society of Chemistry, 2nd Edition, London.
9. Nogard, T. and Weaver D F (2005). *Medicinal Chemistry: A Molecular and Biochemical Approach*, Oxford University Press, 3rd edition, New York.
10. Patrick, G.L. (2009). *An Introduction to Medicinal Chemistry*, Oxford University Press, 4th edition. UK.
11. Singh, H., Kapoor, V.K. (Latest Edition). *Medicinal and Pharmaceutical Chemistry* Vallabh Prakashan, Delhi.
12. Wermuth, C.G. (2009). *The Practice of Medicinal Chemistry*, Academic Press (Elsevier), 3rd edition.
13. Wolff, M E, Ed., (2010). *Burger's Medicinal Chemistry and Drug Discovery*, John Wiley and Sons, New York.

**Course Title: Emerging Trends in Green Synthesis and Drug
Discovery**
Paper Code: CMC.706

L	T	P	Credits
3	-	-	3

Learning outcomes:

Students who successfully complete this course will be able to:

1. Understand the mechanism of microwave assisted organic transformation
2. Conduct ionic liquids, solid supported organic reactions under MW and conventional conditions
3. Utilize metal and organocatalysts for various C-C and C-N bond formation reactions
Apply recent tools in drug discovery and developments

Unit 1

11 hours

Microwave Assisted Organic synthesis (MAOS): Heating effects of microwaves: (i) Dipolar polarization and (ii) Ionic conduction, Synthesis of target molecules under solventless conditions and on solid support, Microwave and stereoselectivity, Recent advancement in aqueous reaction conditions and microwave.

Unit 2

11 hours

Synthesis of Bioactive molecules using Ionic Liquids: Ionic liquids as green solvents, Replacement of volatile organic solvents and environmental impact, Ionic liquids as catalyst, Designer solvents, Ionic liquids and asymmetric synthesis.

Unit 3

11 hours

Developments in metal catalysis and organocatalysis

New developments in the palladium catalyzed chemistry for C-C bond formation reaction, copper catalyzed C-N bond formation reactions, metal catalyzed reactions under microwave conditions, Solid supported reactions, Organic catalytic systems

Unit 4

12 hours

Recent Trends in Drug Discovery: Computer in drug designing, Natural product based drug design, Identification of target molecules, Lead candidate and lead optimization, Ligands with multi receptor affinity profile, Diversity oriented synthesis in drug discovery, Nano drug delivery systems.

Suggested Readings:

1. Mann and Saunders. (2009). *Practical organic chemistry*, Pearson, 4th edition, UK.
2. Anastas, P.T.; Warner J. C. (2000). *Green chemistry, Theory and Practical*. Oxford University Press, 1st edition, US.
3. Paul, M.D. (1997) *Medicinal Natural Products: A Biosynthetic Approach*, John Wiley & Sons., New York.
4. Walton, N.J., Brown, D.E. (1999) *Chemicals from Plants: Perspectives on Plant Secondary Products*, Imperial College Press, London.
5. Gang, D.R., Wang, J., Dudareva, N., Nam, K.H., Simon, J.E., Lewinsohn, E., Pichersky, E. *Plant Physiol.*, **2001**, 125, 539.
6. Rubenstein, K., (2009), *Medicinal Chemistry for Drug Discovery: Significance of Recent Trends*, Insight Pharma Reports.
7. King, F. D. (2003). *Medicinal Chemistry Principles and Practice*, Royale Society of Chemistry, 2nd Edition, London.

8. Sharma, A., Kumar, R., Sharma, N., Kumar, V., & Sinha, A. K. (2008). Unique Versatility of Ionic Liquids as Clean Decarboxylation Catalyst Cum Solvent: A Metal-and Quinoline-Free Paradigm towards Synthesis of Indoles, Styrenes, Stilbenes and Arene Derivatives under Microwave Irradiation in Aqueous Conditions. *Advanced Synthesis & Catalysis*, 350(18), 2910-2920.
9. Sharma, A., Kumar, V., & Sinha, A. K. (2006). A Chemoselective Hydrogenation of the Olefinic Bond of α , β -Unsaturated Carbonyl Compounds in Aqueous Medium under Microwave Irradiation. *Advanced Synthesis & Catalysis*, 348(3), 354-360.
10. Kumar, V., Sharma, A., Sharma, A., & Sinha, A. K. (2007). Remarkable synergism in methylimidazole-promoted decarboxylation of substituted cinnamic acid derivatives in basic water medium under microwave irradiation: a clean synthesis of hydroxylated (E)-stilbenes. *Tetrahedron*, 63(32), 7640-7646.
11. Sinha, A. K., Joshi, B. P., Sharma, A., Kumar, V., & Acharya, R. (2007). Microwave-assisted mild conversion of natural dihydrotagetone into 5-isobutyl-3-methyl-4, 5-dihydro-2 (3H)-furanone, an analogue of whisky lactone. *Australian journal of chemistry*, 60(2), 124-127.
12. Microwave-assisted Mild Conversion of Natural Dihydrotagetone into 5-Isobutyl-3-methyl-4,5-dihydro-2(3H)-furanone: an Analogue of Whisky Lactone; Arun K. Sinha, Bhupender P. Joshi, Anuj Sharma, Vinod Kumar and Ruchi Acharya, *Aust. J. Chem.*, 2007, 60, 124-127.

Paper Code: CMC.707

L	T	P	Credits
3	-	-	3

Learning outcomes:

Students who successfully complete this course will be able to:

1. How a small change in substituents effect the biological activity of drugs.
2. How molecular modelling can increase efficiency.
3. Pharmacophore and receptor based rational drug design.

Unit 1 **12 hours**

QSAR: Introduction, history, applications, various descriptors used in QSARs: lipophilicity, electronic, steric based descriptors. Regression analysis, significance and validity of QSAR regression equations, case study – on pyranenamine, partial least squares (PLS) analysis, multi linear regression analysis. Use of genetic algorithms, neural networks and principle components analysis in the QSAR equations.

Unit 2 **11 hours**

2D QSAR: 2D QSAR techniques like Free-Wilson Analysis, Ban-Fujita modification, Topliss operational scheme, Craig Plot, Cluster Analysis and Hansch analysis and their applications.

Unit 3 **11 hours**

3D QSAR: COMFA – 3D QSAR techniques like Comparative molecular field analysis, CoMSIA- Comparative Molecular Similarity Indices Analysis, CoMSA-Comparative Molecular Surface Analysis, SOMFA - Self-organizing molecular field analysis and their applications.

Unit 4 **11 hours**

Virtual Screening and Molecular docking: Drug likeness screening, Concept of pharmacophore mapping and pharmacophore based Screening, **Molecular docking:** Rigid docking, flexible docking, manual docking; Docking based screening, *De novo* drug design.

Suggested Readings:

1. Thomas, G. (2007). *Medicinal Chemistry-An Introduction*. John Wiley and sons Ltd., IInd edition, New York.
2. Nogrady, T., Weaver, D. F. (2005). *Medicinal Chemistry: A Molecular and Biochemical Approach*, OXFORD University Press Inc., 3rd edition, New York.
3. Krosggaard-Larsen, P., Strogaard, K., Madsen, U. (2009). *Textbook of Drug Design and Discovery*, Fourth Edition, CRC Press, United States.
4. Silverman, R. B., Holladay, M. W., (2014). *Organic Chemistry of the Drug Design and Drug Action*, Academic Press, 3rd edition, Waltham, MA 02451, USA.
5. Foye, W. C. (2008). *Principles of Medicinal Chemistry*, Publisher: Lea and Febiger, 6th edition, Philadelphia.
6. Delgado, J. N. and Remers, W. A., Ed. (2010) *Wilson and Gisvolds Text book of Organic and Pharmaceutical Chemistry*, J. Lipincott Co., 7th edition, Philadelphia.
7. Patrick, G. L. (1995). *An introduction to Medicinal Chemistry*, Oxford University Press Inc., New York.

Course Title: Seminar

Paper Code: CMC.797

L	T	P	Credits
	-	-	2

Learning outcome: Students who successfully complete this course will be able to

- Perform literature review on a given topic
- Prepare a report on a given topic
- Prepare a power point presentation on a given topic

Presentation:

Power Point Presentation on Recent Trends in Drug Discovery, Bioorganic and Bio-inorganic Chemistry, Medicinal Chemistry, Natural Products Chemistry.

Evaluation of the presentation is based on the following contents and criteria:

- Literature survey/background information
- Organization of content
- Physical presentation
- Questions and answers
- Report evaluation