

Centre for Pharmaceutical Sciences and Natural Products
Scheme of Programme
Ph.D. in Medicinal Chemistry

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

S. No.	Paper Code	Course Title	L	T	P	Cr	E
1	MCL.701	Research Methodology	2			2	50
2	MCL.702	Biostatistics	2			2	50
3	MCL.703	Computer Applications	2			2	50
*Opt any three of the following courses							
4	*MCL.704	Natural Products in Drug Discovery and Development: Recent Advances	4			4	100
5	*MCL.705	Recent Advances in Medicinal Chemistry of Nucleic Acids	4			4	100
6	*MCL.706	Emerging Trends in Green Synthesis and Drug Discovery	4			4	100
7	*MCL.707	Trends in Molecular Modeling for Drug Design	4			4	100
8	XXX.YYY#		4			4	100
9	MCS.799	Seminar	-			2	50
		Total	18			20	500

#Any other relevant course offered by other Centre/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	Marks
2	-	-	-	50

Paper Code: MCL.701**Learning Outcomes:**

Students who successfully complete this course will be able to:

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

Unit 1**10 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.

Technical writing: Scientific writing, Writing research paper, Poster preparation and Presentation and Dissertation.

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

Unit-2**10 hours**

Entrepreneurship and business development: Importance of entrepreneurship and its relevance in career growth, Characteristics of entrepreneurs, Developing entrepreneurial competencies, Types of enterprises and ownership (large, medium SSI, tiny and cottage industries, limited, public limited, private limited, partnership, sole proprietorship), Employment, self-employment and entrepreneurship, Financial management-importance and techniques, Financial statements-importance and its interpretation,

Unit-3**16 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.
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.

Course Title: Biostatistics

L	T	P	Credits	Marks
2	-	-	-	50

Paper Code: MCL.702**Learning Outcomes:**

Students who successfully complete this course will be able to:

- Understand basic descriptive and inferential statistics including the concepts and principles of research design and statistical inference.
- Perform and interpret descriptive and inferential statistical techniques including the construction of tables and graphs, t-tests, Chi-square tests, and regression analysis.
- Communicate with statisticians and other professionals about the planning, implementation, and interpretation of analytic studies.
- Use appropriate software packages to solve analytical problems.

Unit 1**10 hours**

Overview of biostatistics: Difference between parametric and non-parametric statistics, Univariate and multivariate analysis, Confidence interval, Errors, Levels of significance, Hypothesis testing.

Descriptive statistics: Measures of central tendency and dispersal, Histograms, Probability distributions (Binomial, Poisson and Normal), Sampling distribution, Kurtosis and Skewness.

Unit 2**5 hours**

Experimental design and analysis: Sampling techniques, Sampling theory, Various steps in sampling, collection of data-types and methods.

Unit 3**12 hours**

Comparing means of two or more groups: Student's t-test, Paired t-test, Mann-Whitney U-test, Wilcoxon signed-rank, One-way and two-way analysis of variance (ANOVA), Critical difference (CD), Least Significant Difference (LSD), Kruskal-Wallis one-way ANOVA by ranks, Friedman two-way ANOVA by ranks, χ^2 test.

Unit 4**9 hours**

Regression and correlation: Standard errors of regression coefficients, Comparing two regression lines, Pearson Product-Moment Correlation Coefficient, Spearman Rank Correlation Coefficient, Power and sampling size in correlation and regression.

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: MCL.703

L	T	P	Credits	Marks
2	0	0	2	50

Learning Outcomes:

Students who successfully complete this course will be able to:

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

Unit 1

18 hours

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

Application software: Spreadsheet applications, Word-processing applications, Presentation applications, Internet browsers, Reference Management, and Image processing applications.

Unit 2

18 hours

Computer language: Basic DOS commands, AutoHotKey scripting language, HTML and basic structure of a webpage, Designing websites.

World wide web: Origin and concepts, Latency and bandwidth, Searching the internet, Advanced web-search using Boolean logic, Cloud computing.

Suggested Readings:

1. Gookin, D. (2007). *MS Word 2007 for Dummies*. Wiley.
2. Harvey, G. (2007). *MS Excel 2007 for Dummies*. Wiley.
3. Johnson, S. (2009). *Windows 7 on demand*. Perspiration Inc.
4. Norman, G. and Streiner, D. (3rd edn) (2008). *Biostatistics: The Bare Essentials*. Decker Inc., Canada.
5. 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.
6. Thurrott, P. and Rivera, R. (2009). *Windows 7 Secrets*. Wiley.

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

L	T	P	Credits	Marks
4	1	0	4	100

Paper Code: MCL.704

Learning Outcomes:

Students who successfully complete this course will be able to:

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

Unit 1

14 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

14 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

16 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

16 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.

Unit 5

12 hours

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

Suggested references

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
Paper Code: MCL.705
Credits Hours: 4

L	T	P	Credits	Marks
4	-	-	4	100

Learning outcomes:

Students who successfully complete this course will be able to:

- Understand, design of new inhibitors of nucleic acid drug targets in diseases like cancer and others.

Unit 1 **18 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 **18 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 **18 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 **18 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. Nogardy, 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: MCL.706
Credits Hours: 4

L	T	P	Credits	Marks
4	-	-	4	100

Learning outcomes:

Students who successfully complete this course will be able to:

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

Unit 1

18 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

18 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

18 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

18 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 Reading:

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. Unique versatility of Ionic liquids as clean and efficient decarboxylation catalyst: A metal and quinoline free paradigm towards synthesis of Indoles, Styrenes, Stilbenes and Arene derivatives under microwave in aqueous condition, Abhishek Sharma, Rakesh Kumar, Naina Sharma, Vinod Kumar and Arun K. Sinha, *Adv. Synth. Catal.*, 2008, 350, 2910-2920.
9. A Chemoselective Hydrogenation of the Olefinic Bond of α , β -Unsaturated Carbonyl Compounds in Aqueous Medium Under Microwave Irradiation; Anuj Sharma, Vinod Kumar and A. K Sinha, *Adv. Synth. Catal.*, 2006, 348, 354-360.
10. Remarkable Synergism in Methylimidazole-Promoted Decarboxylation of Substituted Cinnamic acids in basic water medium under Microwave Irradiation: A Clean Synthesis of Hydroxylated (*E*)-Stilbenes; Vinod Kumar, Abhishek Sharma, Anuj Sharma and Arun K. Sinha, *Tetrahedron*, 2007, 63, 7640-7646.
11. 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

Course Title: Trends in Molecular Modeling for Drug Design**Paper Code: MCL.707****Credits Hours: 4**

L	T	P	Credits	Marks
4	-	-	4	100

Learning outcomes:

Students who successfully complete this course will be able to:

- How a small change in substituents effect the biological activity of drugs?
- How molecular modeling can increase efficiency?
- Pharmacophore and receptor based rational drug design.

Unit 1**18 hours**

QSAR: Introduction, history, applications, various descriptors used in QSARs: lipophilicity, electronic, stearic 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**18 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**18 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**18 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.

Recommended Books:

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.