M.TECH. - NANOMEDICAL SCIENCES

The M.Tech. in Nanoscience and Technology is a course designed for students to explore in depth the application of nanotechnology to the biomedical area. Such applications include new implant technologies, regenerative engineering, new nanomedicines to combat cancer and drug resistance, targeted medicines for treatment with reduced side effects, diagnostic technologies using nanomaterials etc. To gain strength in this new area the course covers in depth nanomaterials and their properties, nanosystems design, the physics and chemistry of nanomaterials and applications of nanotechnology to the biomedical area,including engineering of scaffolds and the engineering of devices at the nanoscale for diagnostics and treatment.

The program also offers clinical exposure in one of the many operation theatres of the hospital to help students develop an understanding of the medical applications of nanotechnology. In short, this is a pioneering program that aims to develop an all-round scientist and technologist with interdisciplinary specialization in three areas -- nanotechnology, biotechnology and medical sciences.

CURRICULUM

First Semester

Course Code	Type	Course	LTP	Credits
16NS601	FC	Research Methodology and Statistics	101	2
16NS602	SC	Science and Properties of Nanomaterials	300	3
16MM601	FC	Cell Biology and Human Physiology	400	4
16MM602	FC	Clinical Biochemistry and Proteomics	300	3
16MM604	SC	Biochemistry, Cell Culture Lab and Animal Lab	103	4
16HU601	HU	Cultural Education*		P/F
		Total Credits		**16**

*Non-credit Course

Second Semester

Course Code	Type	Course	LTP	Credits
16NS603	SC	Nanomaterials – Chemistry and Design	310	4
16NS604	SC	Nanotoxicology and Nanomedicine	400	4
16NS605	SC	Bionanomaterials and Regenerative Engineering	400	4
16NS606	SC	Characterization of Nanomaterials	300	3
16NS607	SC	Nanomaterials Lab	102	3
		Total Credits		**18**

Third Semester

Course Code	Type	Course	LTP	Credits
16MM603	FC	Microbiology and Immunology	400	4
16MM611	SC	Pharmacokinetics and Drug Delivery	400	4
16HU602	HU	Technical Writing and Presentation*		P/F
16NS798	P	Dissertation		10
		Total Credits		**18**

*Non-credit Course

Fourth Semester

Course Code	Type	Course	LTP	Credits
16NS799	P	Dissertation		12
		Total Credits		**12**

List of Courses
Foundation Core

Course Code	Course	L T P	Cr
16NS 601	Research Methodology and Statistics	1 0 1	2
16MM 601	Cell Biology and Human Physiology	4 0 0	4
16MM602	Clinical Biochemistry and Proteomics	3 0 0	3
16MM603	Microbiology and Immunology	4 0 0	4
			Total credits: 13

Subject Core

Course Code	Course	L T P	Cr
16NS602	Science and Properties of Nanomaterials	3 0 0	3
16MM604	Biochemistry, Cell Culture Lab and Animal Lab	1 0 3	4
16NS603	Nanomaterials – Chemistry and Design	3 1 0	4
16NS604	Nanotoxicology and Nanomedicine	4 0 0	4
16NS605	Bionanomaterials and Regenerative Engineering	4 0 0	4
16NS606	Characterization of Nanomaterials	3 0 0	3
16NS607	Nanomaterials Lab	1 0 2	3
16MM611	Pharmacokinetics and Drug Delivery	4 0 0	4
			Total credits: 29

Project Work

Course Code	Course	L T P	Credits
16NS 798	Dissertation		10
16NS 799	Dissertation		12
			Total credits: 22

Total credits for course: 64

16NS 601 RESEARCH METHODOLOGY AND STATISTICS 1-0-1-2

Introduction to Biostatistics-Need for Statistical Methods in Medicine, Public Health, Biology, Biotechnology & Nano Sciences –Their uses and Misuses, Types of Variables, Data collection Methods, Population and Sample.

Basics of Mathematics- (a) Differential & Integral Calculus Differentiation – Derivative of a function, Integration as the inverse operation of Differentiation, Methods of Integration. (b) Linear Algebra – Set Theory, Matrix Algebra (i) Set Theory- Sets and their operations. (ii) Matrix Algebra- Special type of Matrices, Determinants.

Study Designs-Prevalence and incidence studies, Case control and Cohort studies, Experimental studies – randomization.

Estimation of Minimum Sample size in Different Designs of Studies and Sampling Methods.

Descriptive Data Analysis Methods- Statistical Tables, Diagrams & Graphs, Measures of Averages, Measures of Dispersion, Correlation Analysis Methods, Regression Analysis Methods.

Theory of probability and Standard Distributions- Probability: Random experiment, Sample space, Events, Mutually exclusive and exhaustive events, Frequency and classical definition of probability, Axiomatric definition of probability, Addition and multiplication theorems, Conditional probability and independence , Bye's theorem Random Variables and Probability Distributions :- Definition of discrete and continuous random variables, Probability density functions and distribution functions, Standard univariate discrete distributions – Binomial, poisson & Negative Binomial, Standard univariate continuous distributions – Normal, Log normal & Exponential. Sampling distributions – Chi- square distribution and F & 't' distributions. Logic of Statistical Inference- Concept of 'statistic' and 'parameter', Estimators and its properties, point and Interval estimation of parameters, Confidence intervals, concepts of standard error Principles of test of significance, Bayesian Inference Methods.

Methods of tests of Significance of Significance of Statistical Hypotheses- Concept of Statistical Hypotheses –Null and Alternative hypotheses, Type I and Type II errors, Significance level, Critical region and Power of a test , P- value and its interpretation; Large and Small Sample Test – Normal test, Student's 't' test, Chi-square tests, Analysis of variance & Non parametric methods.

Statistical methods in planning and analysis of clinical trials;

Statistical aspects of diagnostic tests.

Nonparametric methods-Non-parametric methods for estimation, Methods for tests of significance for the independent and correlated samples, Nonparametric Methods for more than two populations.

Multivariate analysis Methods- Principles of Multivariate analysis, Multivariate regression analysis, Multivariate logistic regression analysis.

Practicals- (Statistical Software to be used: SPSS & SAS): (i) Practicals in Descriptive Data Analysis Methods, (ii)Practicals in Study Designs, (iii) Practicals in Sampling Theory, (iv) Practicals in Biostatistical Inference, (v) Practicals in Testing of Hypotheses, (vi) Practicals in Nonparametric Methods, (vii) Practicals in Clinical Trials, (viii) Practicals in Multivariate Regression Analysis.

TEXT BOOKS/REFERENCES:

1. *Applied Statistical modeling , Byron J T Morgan, 2000, Arnold Publishers.*
2. *Statistical Techniques for data Analysis: J.K. Taylor & Cheryl C, 2004 Chapman & Hall (CRC).*
3. *Data Analysis for SPSS: Manija J. Norusis, 1987.*
4. *Medical Statistics-Principles & Methods: Sundaram KR, Dwivedi SN, Sreenivas V.B Publishers, Delhi, 2009.*

5. *Biostatistics: A Foundation for Analysis in the Health Sciences : Daniel, Wayne W 8th Ed. , 2005.*
6. *An introduction to Medical Statistics: Martin Bland, 2000, Oxford university press.*
7. *Epidemiology – Study, Design & Analysis: Mark Woodward. Chapman & Hall (CRC Series).*

16NS 602 SCIENCE AND PROPERTIES OF NANOMATERIALS 3-0-0-3

Materials classification by bonding, amorphous and crystalline materials, crystal lattices, Miller Indices, Bragg's Law, Defects in crystal structure, principles of dislocations, theory of diffusion, mechanical properties, phase diagrams, polymeric materials, composite materials, corrosion, electrical and optical properties, types of nanomaterials, surfaces and particle size, surface energy and surface tension and relation to size, phase transformations in nanomaterials, specific heat and heat capacity of nanomaterials, mechanical propertiesof nanomaterials, optical properties of nanomaterials, electrical and magnetic properties of nanomaterials, carbon-based nanomatertials.

TEXTBOOK/REFERENCES

1. Materials Science and Engineering, William D. Callister, Jr., John Wiley
2. Nanomaterials – An Introduction to Synthesis, Properties and Applications, Dieter Vollath, Wiley-VCH, Second Edition, 2013

16MM 601 CELL BIOLOGY AND HUMAN PHYSIOLOGY 4-0-0-4

CELL BIOLOGY

Cell: the chemical components of a cell; Classification and properties of cell; Membranes: structure and function; membrane transport of small molecules and electrical properties of membranes; Intracellular compartments: structure and function; energy conversion by mitochondrion; Intracellular vesicular traffic: endocytosis; exocytosis; Mechanisms of cell communication: general principles and strategies of cell signaling; Cytoskeleton: organization of cytoskeleton; cytoskeleton and cell motility; Cell cycle: cell division; cell growth; control of cell division and growth; Apoptosis: programmed cell death; Cell junctions, cell adhesion and extracellular matrix: cell junctions; passageways from cell-to-cell; extracellular matrix; Germ cells: Characteristics of germ cells; Cell division and growth.

SYSTEMS PHYSIOLOGY

Systems Physiology: General introduction to systems physiology. Homeostasis, function, and common pathological conditions in various human organ systems including: Cardiovascular and circulatory system, nervous system, renal system, gastrointestinal and hepatobiliary system, reproductive system, skin, pulmonary system, vision and auditory systems, ear, nose and throat, and the musculoskeletal system.

TEXT BOOKS / REFERENCES:

1. *Gerald Karp, "Cell and Molecular Biology", Fifth Edition, John Wiley, 2008*
2. *Alberts B, Johnson A, Lewis J, Raff M, Roberts K and Walter P, "Molecular Biology of the Cell", Fifth Edition, Garland Publishing Inc. 2008.*
3. *Kim E, Barrett, Susan M, Barman, Scott Boitano, and Heddwen Brooks, "Ganong's Review of Medical Physiology", 24th Edition, McGraw-Hill Medical, 2012*

16MM 602 CLINICAL BIOCHEMISTRY AND PROTEOMICS 3-0-0-3

Overview of Metabolism: Integration of Metabolism—the Provision of Metabolic Fuels; Carbohydrates of Physiological Significance; Lipids of Physiological Significance Bioenergetics: The Role of ATP; Biologic Oxidation; Glycolysis & the Oxidation of Pyruvate; Citric Acid Cycle; Respiratory Chain & Oxidative Phosphorylation; Metabolism of Carbohydrates & Lipids: Glycogen catabolism; Gluconeogenesis & Control of the Blood Glucose; The Calvin Cycle and the Pentose Phosphate Pathway; Biosynthesis of Fatty Acids; Oxidation of Fatty Acids: Ketogenesis; Protein chemistry, amino acid and amino acid metabolism, protein post-translational modifications Medicine Enzymes: Basic Concepts and Kinetics; Regulation of Activities; Biosynthesis of Membrane Lipids; Lipid Transport & Storage; Cholesterol Synthesis, Transport, & Excretion; What is proteome and proteomics, different types of proteomics, mass spectroscopy, protein identification using mass spectrometry. Clinical proteomics.

TEXT BOOKS / REFERENCES:

1. *Harper's, "Illustrated Biochemistry" Sixteenth Edition, McGraw Hill Medical Publishing, July 2009*
2. *Stryer's " Biochemistry" Fifth Edition, W.H.Freeman & Co Ltd, 2002.*
3. *D.L. Nelson and M.M. Cox , "Lehninger's Principles of Biochemistry",W.H.Freeman, 2005*
4. *D. Voet and J.G. Voet, "Fundamentals of Biochemistry", Wiley, 2008*

16MM 604 BIOCHEMISTRY, CELL CULTURE LAB AND ANIMAL LAB 1-0-3-4

- Using balances and pipettes
- Making of solutions of given normality
- Knowing pH meters: Preparation of buffers, determination of pKa values and
- dissociation constant of a given acid, Titration of amino acids
- Spectrophotometry: Determination of concentration of proteins, Recording absorption
- spectra of a given protein and chromophore, Difference spectra
- Cell culture and extraction of proteins
- Centrifugation and ultracentrifugation
- Protein estimation: Lowry, BCA and Bradford methods

- Protein fractionation: Salting-in and salting-out
- Enzyme assays
- Chromatography: Gel filtration; Ion exchange; affinity; high performance liquid
- chromatography (HPLC)
- Electrophoresis, western blotting.
- Cell culture techniques – mammalian cell culture, MTT assay, Live-dead cell assay;
- Animal handling techniques – animal feed, gavage, injection, ethical treatment of animals, Institutional Animal Ethics Committee

TEXT BOOKS / REFERENCES:

1. *Lab Manuals*

16NS603 NANOMATERIALS - CHEMISTRY AND DESIGN 3-1-0-4

Module I:

Basics of the Chemistry of Solids; Chemical Bonding – Orbital concept; Elementary Thermodynamics – First and Second laws of thermodynamics; Entropy and Gibb's Free Energy; Phase transition – Thermodynamics of Phase transitions; Thermodynamics of Nanoscale Growth; Crystalline phase transitions in nanocrystals with respect to grain size dependence; Concept of Surface Free Energy; Stabilization mechanisms in nanomaterials – electrostatic, steric and electrosteric stabilization; Controlling Nucleation, Growth and Aggregation in Nanomaterials.

Module II:

Classification of Nanomaterials – Zero, One and Two Dimensional Materials; Fabrication Methods of Nanomaterials: Top down and bottom up approaches; Top down methods: Milling, Lithography; Bottom up methods – Synthesis of zero dimensional metal, metal oxides, semiconductor nanoparticles by different routes – Colloidal method, Sol-gel, Electrodeposition, Micellar growth; Synthesis of one dimensional nanosystems by different routes – VLS and SLS methods; Synthesis of two dimensional nanosystems – Vapor phase deposition methods – CVD, PVD, MBE, MOCVD, ALD; Spray Pyrolysis; Special Nanomaterials – Core/shell structures, Carbon based Nanomaterials, Polymeric Nanomaterials

Text Books:

1. Physical Chemistry – Gordon and Barrow, 5th Edition, McGraw Hill Company
2. C. Brechignac P and Houdy M Lahmani, Nanomaterials and Nanochemistry, Springer Verlag 2007.
3. G. Cao, Nanostructures and Nanomaterials – Synthesis, Properties and Applications, Imperial College Press 2006.
4. Nano: The Essentials, T. Pradeep, McGraw Hill Publications, 2008

16NS 604 NANOTOXICOLOGY AND NANOMEDICINE 4-0-0-4

Origin of nanotoxicology: Classification of nanoparticles based on size, shape, surface properties and composition and its interconnectivity with toxicity properties, Nanotoxicity evaluation methods: Cellular up-take mechanisms of nanoparticles, Cell toxicity mechanisms: Cell viability, MTT/Alamar Blue, Reactive oxygen species (DCFH Assay, Risorufin, singlet oxygen assay), Lipid peroxidation, Apoptosis, PI/Annexin V, Necrosis, LDH leakage, Mitochiondrial damage, Genotoxicity: Comet assay and micronuclear disintegration. Case studies: Toxicity effect of important nanoparticles: ZnO, TiO2, Quantumdots, CNT and Graphene. Blood contact properties of nanoparticles; In vivo nanotoxicology concepts:

Biology of cancer: Benign and malignant tumors, characteristics of malignant cancer cells. Types of cancers-cell and tissue type that give rise to cancer (carcinomas, sarcomas, haematopoeitic tumors). Mechanisms of progression in Cancer: Cellular trafficking, Cancer invasion, Migration, Angiogensis and Metastasis. Details of some important cancers staging.

Cancer Nanomedicine: Rational design of nanomedicine based on cancer biology: human cancer-types. molecular mechanisms of cancer, cancer diagnosis methods: computed tomography, positron emission topography, MRI, fluorescence imaging, nanoparticles for optical, CT, MRI and nuclear imaging of cancer. Cancer Therapy: existing therapeutic modalities: radiation & chemotherapy; nanomaterials for chemotherapy, active & passive targeting concepts, nanoparticles for radiation therapy, photodynamic and nanoscintilation therapy, photothermal therapy, magnetic hyperthermia, radio-frequency ablation therapy, nanotheragnostics: concept and applications.

TEXT BOOKS /REFERENCES:

1. Molecular Mechanisms of Cancer Georg F. Weber University of Cincinnati Academic Health Center Cincinnati, Ohio USA 2007(springer)
2.Manzoor Amiji, "Nanotechnology for Cancer Therapy", First Edition, CRC Press, 2007
3.Challa Kumar, "Nanomaterials for Medical Diagnosis and Therapy", First edition, Wiley-VCH, 2007
4.Challa Kumar, "Nanomaterials for Cancer therapy", First edition, Wiley-VCH, 2006
5.Challa Kumar, "Nanomaterials for Cancer Diagnosis", First edition, Wiley-VCH, 2007

16NS 605 BIONANOBIOMATERIALS AND REGENERATIVE ENGINEERING

4-0-0-4

Natural and Synthetic Biomaterials-Silicone biomaterials, Hydrogels, Bioresorbable and Bioerodible Materials, Natural Materials-Chitin, Alginate, Hyluronic acid, Collagen, Metals, Ceramics, Glasses, composites.

Polymers-Basic concepts of polymer science-Classification of polymers-s-chain polymerization-mechanism of free radical, cationic, anionic and co-ordination polymerization-Techniques of polymerization-bulk, solution, emulsion, suspension, interfacial, solid state and melt polycondensation-Amorphous and crystalline polymers-Factors affecting Tg and crystallinity of polymers. Determination of Tg and Tm-TGA, DTA and DSC of polymers-Determination of Molecular weight.

Polymeric Nanobiomaterials-Preparation of Polymeric Nanofibers, Nanogels, Nanoparticles, Nanocomposite scaffolds - Applications of polymeric nanobiomaterials in drug delivery, tissue engineering, wound healing and other biomedical applications.

Principles of Tissue engineering; Significance of Extracellular matrix; Biocompatibility, Major physiological systems of current interest to biomedical engineers; Biomaterial aspect of Tissue engineering; Types of scaffold and its fabrication; Properties of mesenchymal stem cells; Growth factors and its impact in tissue regeneration; Techniques to evaluate tissue-engineered construct; Bioreactors; Animal models for tissue engineering with case studies; Case studies of tissue engineering (bone, cartilage; ligament, pancreas etc).

References

1. John P. Fisher, Antonios G. Mikos, Joseph Bronzino, "Tissue Engineering", CRC Press, Taylor and Francis group, 2006.
2. Robert Lanza, Robert Langer and Joseph Vacanti. Principles of Tissue Engineering (Third Edition) Copyright © 2007 Elsevier Inc.

16NS 606 CHARACTERIZATION OF NANOMATERIALS 3-0-0-3

Characterization of Nanomaterials: Structural characterization – XRD, Reciprocal lattice, Bragg's law, Ewald's construction, XRD of nanolayers, Grazing incidence diffraction, texture and stress measurements with x-ray diffraction, SEM: scattering of electrons, secondary and backscattered electrons, electron gun, lenses and apertures, imaging modes in SEM, TEM: Interaction of electrons with matter, elastic and inelastic scattering, electron sources, lenses, apertures and resolution, TEM instrument, Forming diffraction patterns and images, selected area and convergent beam electron diffraction patterns, Kikuchi diffraction, Imaging and contrast in TEM, HRTEM, Electron energy loss spectrometry, SPM: Principle of operation, instrumentation and probes, contact and non-contact AFM, low temperature SPM, dynamic force microscopy, molecular recognition force microscopy, magnetic force microscopy, Gas adsorption, Chemical Characterization – Optical Spectroscopy, Electron spectroscopy, Ionic spectroscopy, IR spectroscopy: vibrational modes, theory of IR spectroscopy, infrared spectrometers, IR correlation diagrams, single and group frequencies, advantages of FTIR, Force spectroscopy with AFM, Nuclear magnetic resonance, Near field scanning optical microscopy (NSOM), Dielectrophoresis

TEXT BOOKS / REFERENCES:

1. *Harold P. Klug and Leroy E. Alexander, "X-Ray Diffraction Procedures: For Polycrystalline and Amorphous Materials", Second Edition, Wiley-Interscience, 1974*
2. *David B. Williams and C. Barry Carter, "Transmission Electron Microscopy: A Textbook for Materials Science", Second Edition, Springer, 2009*
3. *Ray F. Egerton, "Physical Principles of Electron Microscopy: An Introduction to TEM, SEM, and AEM", Second printing edition, Springer, 2008*
4. *Bharat Bhushan, "Springer handbook of Nanotechnology", Second Revised and Extended Edition, Springer, 2007*

16NS 607 NANOMATERIALS LAB 1-0-2-3

- Preparation of alginate based nano and microparticles; fibers and films
- Characterization of nanoparticles using DLS and Zeta Potential
- Chemical modification of chitosan to carboxy methyl chitosan and its evaluation using Fourier Transform Infrared Spectroscopy
- Preparation of carboxy methyl chitosan nanoparticles and its evaluation using DLS and Zeta potential
- Thermal characterization of chitosan and carboxymethyl chitosan using TG/DTA and DSC
- Preparation of aqueous PVA solution and its characterization using viscometry; Electrospinning of PVA nanofibers and its characterization using Scanning Electron Microscopy
- Preparation of Nylon using Compounding and Injection Moulding and its mechanical characterization using MTS.

16MM603 MICROBIOLOGY AND IMMUNOLOGY 4-0-0-4

Bacteria-fungus-Virus-parasite general information; Spread and control of diseases: Sterilization, pasteurization and Disinfecion; Anti-microbial agents; Microbial nutrition and growth; Control of microbes by physical and chemical agents; DNA structure; Replication; Transcription; Translation; DNA repair, Conjugation; Transduction; Transposon, Mutation; Bacterial protein secretion; Recombinant DNA technology; Operons; Bacteriophages; Molecular mechanism of drug resistance; Biofilm and quorum sensing; Human diseases caused by bacteria and virus: Staphylococcus, Mycobacterium, Salmonella, Pseudomonas, Streptococcus, Neisseria, Vibrio, Helicobacter, HIV, Hepatitis, HBV, Dengueetc; Vaccines; Basic concepts; Cells and organs of the immune system; Host recognition of antigens; Innate and adaptive immune systems; Complement systems; Acquired immune systems; Recognition of antigens; Antigen recognition by B-cell and T-cell receptors; Generation of lymphocyte antigen receptors: Generation of diversity in immunoglobulins and T cell receptor gene rearrangement; Antigen presentation to T lymphocytes; Signaling through immune system receptors; Development and survival of lymphocytes; T-cell mediated immunity; Humoral immune response; Adaptive immunity to infection, Autoimmunity, Transplantation, Manipulations of immune response, Immunologists toolbox.

TEXT BOOKS / REFERENCES:

1. Presscott, harley and Klein's Microbiology, 7th edition, McGraw Hill Companies.
2. Alcamo's fundamentals of Microbiology, Jeffery C Pommerville, 9th edition, Jones and bartlett Publishers.
3. Ken Murphy, Paul Travers, Mark Walport , "Janeway'sImmunobiology", 7th edition, Garland science publishing, 2007.
4. Immunology, I. Roitt, 7th edition, Mosby Inc.

16MM 611 PHARMACOKINETICS AND DRUG DELIVERY 4-0-0-4

Significance of plasma drug concentration measurement; Compartment models: Definition and scope; Pharmacokinetics of drug absorption – Zero-order and First-order absorption rate constants using Wagner-Nelson and Loo- Riegelman methods; Volume of distribution and distribution coefficients; Compartmental Kinetics – One-compartment and Two-compartment models, Physiologically Based Pharmacokinetic (PBPK) model; Determination of pharmacokinetic parameters from plasma and urine data after drug administration by intravascular and oral routes; Curve fitting (Method of residuals) and Regression methods; Concept of Clearance; Mechanism of renal clearance, clearance ratio, determination of renal clearance; Extraction ratio; Hepatic clearance; Biliary excretion. Extrahepatic circulation; Non-linear pharmacokinetics with special reference to One-compartment model after Intravenous drug administration; Michalis-Menton kinetics; Detection of Non-linearity (saturation kinetics); Current trends in pharmacokinetics and pharmacodynamics.

Nanomedicine Development**:** Methods of preparation of drug nanoparticles, Structures of drug nanoparticles, Lipid based pharmaceutical nanoparticles, Targeted, non-targeted delivery-Absorption, Bioavailability, Distribution, Elimination; controlled drug release; Transdermal drug delivery; exploiting novel delivery routes using nanoparticles-Nano hydrogels for drug delivery-intelligent, ionic, thermo responsive, biohybrid, imprinted hydrogels.

TEXT BOOKS / REFERENCES:

1. *Rang MP, Dale MM and Ritter JM "Pharmacology", Churchill Livingston, 1999.*
2. *Lawrence DR and Bennett PN, "Clinical Pharmacology" Churchill Livingstone, 1980.*
3. *Gibaldi, Milo, Marcel Dekker Series, "Biopharmaceutics and Clinical Pharmacokinetics" Publisher: Lea & Febiger; 4th Sub edition (January 1991).*
4. *Shargel, "Applied Biopharmaceutics and Pharmacokinetics", McGraw-Hill Medical; 5th edition (August 19, 2004).*
5. *Rowland and Tozer, "Clinical Pharmacokinetics : Concepts and Applications", Lippincott Williams & Wilkins; Third edition (January 15, 1995).*