FIFTH SEMESTER

PHAR 311 Medicinal Chemistry I (60 hours)

Unit- 1: Physicochemical parameters, transducer mechanism, biotransformation & prodrug – (8hrs)

1.1 Solubility, Partition coefficient, pKa & degree of ionization, Isomerism (Geometrical, Optical) & bioactivity, Bioisosterism (classical/non classical)
1.2 Types of Drug-receptor interaction, transduction mechanism (G-protein coupled receptor, ligand gated ion receptor, tyrosine kinase receptor, intracellular receptor)
1.3 Biotransformation (phase I and Phase II - conjugation)
1.4 Prodrug

Unit- 2: Principles of Drug Design (Theoretical Aspects): (7 hours)

2.1.Quantitative Structure Activity Relationship: Introduction, QSAR Parameters, QSAR Methods, Linear & nonlinear relationship between Log P and Biological activity, Electronic parameters, Steric substituent constant,effect of electronic and steric parameters on lipohilicity, Experimental determination of partition coefficients, Methods used in QSAR studies, achievements & limitation of QSAR and introduction to molecular modeling. Introduction to Computer aided drug designing (CADD).

2.2.Introduction to Hansch equation, Craig plot, Topliss scheme & Free-Wilson approach

Study of the following classes of compounds including their chemical classification, structure and nomenclature, physicochemical properties, mechanism of action, structure activity relationship (SAR),uses and outline of synthesis (of compounds with star).

Unit- 3: Cholinergic receptors and Drug Affecting Cholinergic Neurotransmission (8 hours).

3.1 Cholinomimetics: Cholinergic receptors, Acetylcholine – biosynthesis and release, SAR, Classification of Cholinomimetics, Structure, Synthesis, property and use of Methacholine*, Neostigmine, Physostigmine, Pyridostigmine*, Donepezil, Organophosphate Poisoning and reactivation of phosphorylated Cholinestarase.

3.2 Anticholinergics: Natural Belladonna alkaloids (Atropine sulphate), Semi synthetic alkaloids (Ipratropium bromide), Synthetic substitutes –Tropicamide*, Dicyclomine*, Trihexyphenidyl HCl* and Pirenzepine. Drotaverine as antispasmodic.

Unit- 4: Adrenergic receptors and Drug Affecting Adrenergic Neurotransmission (8 hours).

4.1 Adrenomimetics- Adrenoreceptors, Dopamine, Epinephrine*, Phenylephrine, Terbutaline, Salmeterol, Isoproterenol, Resorcinol, Metaproterenol, Albuterol*(Salbutamol), Phenylephrine, indirect acting (Amphetamine, L-(+)-Pseudoephedrine,), adrenergics with mixed mechanism of action (Ephedrine, phenylpropanolamine). Nasal Decongestant – Phenylpropanolamine, Phenylepherine, Oxymetazoline, Xylometazoline.

4.2 Antiadrenergics: α- Adrenergic blockers (ergometrine, Prazosin, Terazosin and Tamsulosin). β- Adrenergic blockers: Propranolol*, Atenolol**.**

Unit- 5: Antihistaminic and Antiulcer (4 hours)

5.1 H1 receptors antagonist –Diphenhydramine*, Tripelennamine, Methapyrilene, Chlorcyclizine, Promethazine, Terfenadine; Astemizole; Loratadine, Triprolidine, Cetirizine, Chlorpheniramine Maleate*; Cyproheptadine Hydrochloride.

5.2 H2 receptors antagonist- structure, Cimetidine, Ranitidine and Famotidine.

5.3 Proton Pump Inhibitors; structure, Omeprazole, Pantoprazole and Esmoprazole.Sucralfate and Bismuth salts.

Unit- 6: Non-steroidal anti-inflammatory Agents and Neuromuscular blockers: (4 hours)

6.1.Salicylate, Arylacetic acids, Propionic acids, Fenamic Acid, Pyrazoles and Enolic acid, Aspirin, Mefenamic acid, Indomethacin, Ibuprofen*, Ketoprofen, Diclofenac, Naproxen, Piroxicam, Ketorolac, Acetaminophen*, Mefenamic acid, Phenylbutazone.

6.2.Skeletal Muscle relaxants: Tubocurarine chloride, Succinylcholine*, Pancuronium, Baclofen, Danthroline, Tizanidine and Chlorzoxazone.

Unit- 7: Oxytocics and Prostaglandin (2 hours)

Structure, property and uses of - Oxytocin**,** Ritodrine, Isoxsuprine.Prostaglandins F2, Prostaglandin E2, Prostaglandin E1, Carboprost, Misoprostol, Bimatoprost.

Unit – 8: Steroids (4 hours)

Cortisone, Hydrocortisone, Beclomethasone, Budesonide, Prednisolone*, Methylprednisolone, Triamcinolone, Dexamethasone, Fluticasone and Mometasone. **E**strogens (Estradiol, Diethylstilbistrol), Progesterone, Testesterone,

Unit-9: CVS Drugs (11 hours).

9.1 Cardiac glycosides (Digoxin), Glyceryl nitrate, Propranolol.

9.2 Antihypertensive agents: Reserpine, Prazosin, Terazosin, Clonidine, Hydralazine*, Sodium Nitroprusside*, Minoxidil, Captopril, Enalapril, Losartan, Nifedipine.

9.3 Diuretics: Acetazolamide*, Hydrochlorothiazide*, Frusemide, Spironolactone and Mannintol.

9.4 Anticoagulants: Heparin and Warfarin.

9.5 Antiplatelate drugs: Aspirin, Dipyridamol, Streptokinase.

Unit – 10: Local anti-infective agents (2 Hours)

Ethyl Alcohol, isopropyl alcohol, formaldehyde,: phenols, cresol, hydrogen peroxide, povidine iodine, halozone, Chlorhexidine gluconate, Gentian violet, Nitrofurazone, Merbromin. Salicylic acid and benzoic acid.

Unit-11: Sulphonamides (2 Hours)

General structure of sulphonamides, and MOA, Classification and SAR, Sulphamethoxazole and trimethoprim combination (MOA and uses), Sulphadimethoxin, Sulfacetamide and silver sulphadiazine.

PHAR 311 Lab Medicinal Chemistry II Practical [30 hours]

(Minimum 8 experiments)

Synthesis & pharmacopoeial analysis of some medicinal compounds:

- Hexamine
- Dibenzalacetone
- Barbituric acid from Diethyl Malonate
- Benzoic acid from Benzyl chloride
- Benzimidazole from o-phenylenediamine (Phillip's Reaction)
- Acetanilide from acetophenone
- P-amino benzoic acid (P-ABA) from P-nitrobenzoic acid
- Benzocaine from para- nitro benzoic acid
- Benzyl alcohol by Cannizoro's reaction
- Benzoylglycine from Benzaldehyde
- Benzoyl Alanine from Benzoyl Chloride.

Books nd other resources recommended:

1. Block JH, Beale JM, editor. Wilson and gisvold's textbook of organic medicinal and pharmaceutical chemistry. 11th ed. Baltimore: Lippincott Williams & Wilkins; 2004.
2. Lemke TL, Williams DA, editor. Foye's principles of medicinal chemistry. 6th ed. New Delhi: Wolters Kluwer and Lippincott Williams & Wilkins; 2008.
3. Kadam Dr. SS et al. – Principles of Medicinal Chemistry Vol. I and II.Nirali Prakashan, India.
4. Abraham DJ, editor. Burger's Medicinal Chemistry and Drug Discovery, 6th ed. Vol 1-6. New Jersey: John Wiley & Sons; 2007.
5. Hansch C, editor. Hansch's comprehensive medicinal chemistry, Delhi: Rajkamal Electronic Press; 2005.
6. Ariens EJ, editor. Drug design vol. I-X. Noida: Academic Press; 2009.
7. Roth HJ, Kleemann A. Pharmaceutical Chemistry. Vol-I. Drug synthesis. New York: Ellis Horwood Limited; 1988.
8. Lednicer D, Mitscher LA, The organic chemistry of drug synthesis, Volume-1-6. New York: A wiley-interscience publication; 2005.
9. Remington: The science and practice of pharmacy. 21st ed., vol. I & II, Lippincatt Willams & Wilkings, New Delhi, 2005.

10. Smith & Williams. Introduction to principles of drug design-Harwood academic press.

PHAR 312 Pharmaceutical Technology I (45 hours)

Unit- 1. Liquid Dosage Forms: (13 hrs)

Liquid dosage forms and route of administration, advantages and disadvantages of liquid dosage forms. **(0.5 hrs)**

Solutions: Solvents, Buffers, Viscosicity enhancers and density modifiers, Antioxidants, Reducing agents, Flavors and Fragrance, Isotonicity modifiers, Types of Oral solutions, General method of solution manufacturing. **(3.5 hrs)**

Suspension: Ideal properties of pharmaceutical suspension, Types, Theory of suspension, Theory of sedimentation, Electrical double layer and Zeta potential, DLVO theory of colloidal stability, flocculated and deflocculated suspension, Method of floccules formation, controlled flocculation, structured vehicle formulation, Wetting agents, suspending and thickening agents. Dispersing agents, flocculating agents. Taste mask of oral suspension. Quality control and pharmacopeial tests. Recent advances in suspension formulation – Sustain released suspension, Nanosuspension. **(6 hrs)**

Emulsion: Type, test for identification of emulsion type, emulsifying agents, stability of emulsion, preservation of emulsion, method of preparation, quality control including pharmacopeial tests. **(3 hrs)**

Unit- 2: Semisolid Dosage Forms (8 hrs):
Ideal properties of semisolid dosage forms, Types (Ointment, Cream, Gels- hydrogel, organo gel, oleo gel, stimuli responsive hydrogel, poultices, suppositories and passerines, Trans dermal patch). Precutaneous absorption, Factors affecting precutaneous absorption, Physiological and pathological condition of skin, formulation of semisolids, Bases types and gelling agents, method of manufacturing. Permeation enhancement (Physical and chemical permeation enhancers) and quality controls including pharmacopeial tests.

Unit -3: Suppositories (3 hrs):
Type, uses, Type of bases, Factor affecting drug absorption from rectal and vaginal suppositories ideal suppository base, Methods of manufacturing, , quality control including pharmacopeial tests.

Unit-4: Extraction and Galenical products (3 hrs):
Scope, importance, theory of extraction process, infusion, decoction. Digestion, maceration, Percolation. Factors affecting extraction process.

Unit- 5: Pharmaceutical aerosols (3 hrs)
– Advantage, component of aerosol, Manufacturing methods, filling (Cold filling, Pressure filling, compressed gas filling), stability testing, Quality control and pharmacopeial tests.

Unit- 6: Ophthalmic preparations (7 hrs):

Challenges of ocular drug delivery, pharmacokinetic consideration, formulation consideration, Physiochemical properties of drug used in ophthalmic dosage form, Buffer capacity, pH and isotonicity, instillation volume, Osmotic pressure, formulation approach, Classical dosage forms (solution, suspension, ointments). Introduction to polymeric delivery system (viscosity enhancing polymers, Mucoadhesive polymer in situ gelling system), Introduction to colloidal drug delivery system (Nanoparticles, liposome, niosomes, microparticles), Introduction to delivery approach (Prodrug, penetration enhancers, cyclodextrin and ocular inserts).

Unit- 7: Cosmetology (8 hrs):

Definition (general and medical cosmetics), Types of cosmetics, Organ wise and body site wise cosmetics, Introduction to skin types. Sunscreens (mention UVA , UVB, drugs That Sensitize the Skin to Sunlight, mention ingredients, factors affecting the sunscreen the effectiveness of preparations), Moisturizers(methods of use, ingredients, toners(ingredients. Lipistics (ingredients and just idea of manufacturing). Hair (growth cycle and function, Shampoo and its ingredients, mention hair cream, dye and gel). Dentifrice (Defination, types- Tooth powder, Tooth paste, Mouth wash, and their ingredients).
Introduction to Manicure and Pedicure products.

PHAR 312 Lab Pharmaceutical Technology I Practical [30 hours]

1. Preparation, evaluation and packaging of liquid orals like solutions, suspensions and emulsions, ointments, suppositories, aerosols, eye drops, eye ointments etc.
2. Preparation of pharmacopoeial extracts and galenical products utilizing various methods of Extraction.
4. Formulation of various types of cosmetics preparations.

Books Recommended

1. Aulton, M.E. Pharmaceutics- The Science of Dosage Form Design. ELBS/Churchill Livingstone.
2. Lachman, L., Lieberman, H.A., and Kanig, J.L. The Theory & Practice of Industrial Pharmacy. Lea & Febiger, Philadelphia.
3. Sagarin & Balsam, M.S. Cosmetic Science & Technology. Vol. 1-3 2nd ed. John Wiley.
4. Poucher's Cosmeticology.
5. Ansel, H.C. Introduction to Pharmaceutical Dosage Forms. V.M. Verghese & Co., Mumbai.
6. Banker, G.S. and Rhode, C.T. Modern Pharmaceutics. Marcel Dekker.
7. Carter, S.J. Cooper & Gunn's Tutorial Pharmacy. CBS Publishers, Delhi.
8. Jellinek, J.S. Formulation and Function of Cosmetics. John Wiley & Sons.
5. Kac Chensney, J.C. Packaging of Cosmetics and Toiletries. Newness Butter Worth, London.
6. Pharmaceutical Dosage Forms and Drug Delivery Systems. Lea and Febiger, Philadelphia.
7. Rawlins, E.A. Bentley's Textbook of Pharmaceutics. ELBS.

PHAR 313 Pharmaceutical Biotechnology (45 hours)

Unit 1: Immunology and Immunological Preparations (10 hours)

Principles, antigens and haptens, immune system, cellular humoral immunity, immunological tolerance, antigen-antibody reactions and their applications. Hypersensitivity, Active and passive immunization; Vaccines- their preparation, standardization and storage.

Unit 2: Genetic Recombination (8 hours)

Transformation, conjugation, transduction, protoplast fusion and gene cloning and their applications. Development of hybridoma for monoclonal antibodies. Study of drugs produced by biotechnology such as Activase, Humulin, Humatrope, and HB.

Unit 3: Antibiotics (15 hours)

Historical development of antibiotics. Antimicrobial spectrum and methods used for their standardization. Screening of soil for organisms producing antibiotics, fermentetor, its design, and control of different parameters. Isolation of mutants, factors influencing rate of mutation. Design of fermentation process. Isolation of fermentation products with special reference to penicillin, streptomycin tetracycline and vitamin B.

Unit 4: Microbial Transformation (6 hours)

Introduction, types of reactions mediated by microorganisms, design of biotransformation processes, selection of organisms, biotransformation process and its improvements with special reference to steroids.

Unit 5: Enzyme immobilization (6 hours)

Techniques of immobilization, factors affecting enzyme kinetics. Study of enzymes such as hyaluronidase, penicillinase, streptokinase and streptodomase, amylases and proteases etc. Immobilization of bacteria and plant cells.

PHAR 313 Lab Pharmaceutical Biotechnology Practical [30 hours]

1. Isolation of antibiotic producing microorganism from soil.
2. Enzyme immobilization by Ca-alginate method.
3. Determination of minimum inhibitory concentration of the given antibiotic. Antibiotic assay by cup plate method.
4. Collection, Processing, Storage and fractionation of blood.
5. Standardization of Cultures.
6. Microbiological assay of Antibiotics / Vitamins.
7. Production of alcohol by fermentation techniques.
8. Comparison of efficacy of immobilized cells.

9. Isolation of mutants by gradient plate technique.
10. Preparation of bacterial vaccine.
11. Extraction of DNA.
12. Separation techniques: Various types of Gel Electro Phoresis, Centrifugation.

Sample Experiments

Expt. 1: Immobilization by gel entrapment

1. Acrylamide,2. Bis-acrylamide, 3. TEMED (N,N,N,N'-tetramethylenediamine)
Expt. 2: Protein estimation by Lowry Method
Sodium carbonate, Sodium hydroxide, Sodium potassium tartrate, Copper sulphate,Folin-Phenol and
Bovine Serum Albumin
Expt. 3: Estimation of glucose by DNS method
1. 3, 5 dinitrosalicylic acid,2. Sodium hydroxide,3. Phenol,4. Rochelle salt (Sodium Potassium tartrate),5. Sodium meta bisulphate,6. Phenolphthalein,7. 0.5 M HCl and 8. Glucose
Other experiments related to the topics covered in theory.

Books & other resources recommended

1. Wulf Crueger and Anneliese Crueger, Biotechnology, 2nd Ed, Publ- Panima publication co-operation, New Delhi.
2. P. F. Stanbury & A. Whitaker, Principles of fermentation technology, Pergamon Press
3. B.P. Nagori & Roshan Issari, Foundations in Pharmaceutical Biotechnology
4. Sambamurthy. K, Text Book of Pharmaceutical Biotechnology.
5. S. S. Kori, Pharmaceutical biotechnology.
6. Prescott and Dunne, "Industrial Microbiology" MC Caraw Hill Bool Company
7. 8. K. Kielsliched "Biotechnology" Vol 6, Verlegchemic, Switzerland.
9. PF Standury & A. Whitaker, "Principles of fermentation Technology" Pergamon Press, Oxford
10. OP Ward" Fermentation Technology, Principles, Processes products" Open University press, Milton Keynes, UK.
11. A. M. Campbelli, Monoclinical antibody technology.
12. A. Wiseman, Handbook of enzyme biotechnology.
13. J. D. Watson, Recombinant DNA technology.
14. Smith and Hood, Molecular biology and biotechnology.
16. Brahamankar & Jaiswal– Biotechnology, SP Publication

PHAR 314 Pharmacology –II (45 hours)

Unit-1: Pharmacology of Cardiovascular System (15 hours)

1.1. MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of: Digitalis. Antihypertensive drugs (Hydrochlorothiazide, Calcium channel blockers as antihypertensive and
1.2. Antianginal: Nifedipine, Amlodipine, Verapamil, Diltiazem., Enalapril, Losartan, Telmesartan, Terazosin, Tamsulosin, Atenolol, Metoropolol, Hydralazine, Sodium Nitropruside, Antianginal- Nitroglycerine, Acebutolol, or non- cardioselectives beta blockers such as Sotalol.
1.3. Antiarrhythmic drugs **(**Quinidine, Procainamide, Propranolol, Amiodaron, Ibutilide, and Magnesium Sulphate).
1.4. Antihyperlipedemic drugs (Statins: Simvastatin, Atrovastatin, Rosuvastatin, Lovastatin.Fibrates: Clofibrate, Gemfibrozil Fenofibrate. Niacin, Bile acid sequestrants resins (chenodeoxycholic acid (CDCA) or ursodeoxycholic acid) and Orlistat.

Unit-2: Drugs used in Shock (2 hours)

Classifications of Shock, Signs and Symptoms, ABC management, Adrenaline, Dopamine, Dexamethasone and Sodium bicarbonate injection, Management of Septic Shock.

Unit-3: Drugs acting on the Hematopoietic System (8 hours)

- MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of following drugs: Erythropoietin, Iron Requirements and the Availability of Dietary Iron and Iron Salts, Folic acid and Vitamin B12, Therapy with Parenteral Iron.
- Hydroxyurea for sickle cell anemia. View of hematostasis: platelet function, blood coagulation and fibrinolysis. Heparin, Bivalirudin, Warfarin, Monitoring Anticoagulant Therapy: The INR (International Normalized Ratio). Phenprocoumon and Acenocoumarol. Aminocaproic Acid, Aprotinin, Abciximab, Aspirin, Dipyridamol, Ticlopedine, Clopidogrel, Etamsylate, Protamine sulphate, Traneximic acid and role of Vitamin K. Blood and plasma volume expanders (Albumin, Whole Blood,Dextran-70, Etherified starches, Polygeline).

Unit-4: Drugs acting on the urinary system (4 hours)

a. Fluid and electrolyte balance. .
b. Diuretics (Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of Acetazolamide, Hydrochlorothiazide, Frusemide, Spironolactone, Mannitol).

Unit-5: Autacoids and Autacoids Antagonists (6 hours)

1.1 Role of Histamine, Thromboxane and leukotrienes.

1.2 Therapeutic uses of prostaglandins, H1 antihistamins (Clssification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of Diphenhydramine, Pyrilamine, Pheniramine, Chlorpheniramine, Cetirizine, Promethazine, Cyproheptadine, Terfenadine, loratadine, and fexofenadine). Leukotriene inhibitor (Montelukast).

1.3 H2 receptor antagonists (MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of Cimetidine, Ranitidine and Famotidine).

1.4 5HT3 antagonist (Ondansetron)

Unit-6: Drugs acting on the Respiratory System (5 hours)

a. Anti-asthmatic drugs (Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of Salbutamol, Salmeterol, Formoterol, Theophylline, Etophylline, Streoids (Fluticasone, Budesonide),
b. Mast cell stabilizer (Chromoglycate). Anti-tussives and expectorants (Codeine, Noscapine. Dextromethorphan, Promethazine, Triprolidine, Terpine hydrate, Bromhexine, Ammonium Chloride, Ambroxol).
c. Respiratory stimulants (Doxapram, Caffeine citrate injection).

Unit- 7: Narcotic analgesics, NSAIDs and Anti-gout drugs: (5 hours)

a. Classification, Mechanism of action, Side-effects, Contraindications, Precautions and doses of commonly used drugs :
b. **Narcotic analgesics and antagonists:** Morphine, Methadone, codeine, Fentanyl, Pethidine, Naloxone
c. **NSAIDs and Anti-gout drugs:** Aspirin, Ibuprofen, Paracetamol, Indomethacin, Nimesulide, Diclofenac, Naproxen, Allopurinol, Colchicine and Febuxostat, Probenecid, Sulfinpyrazone.

Books & other resources recommended

1. Goodman & Gillman's: The Pharmacological basis of Therapeutics- 11th Edn. (2006)
2. Pharmacology by Rang and Dale
3. Pharmacology and Pharmacotherapeutic by Satoshkar and Bhandarkar.
4. Essentials of Pharmacotherapeutic by F.S.K.Barar.
5. Lewis Pharmacology by Crosslan.
6. Textbook of Pharmacology by Bowman and Rand.
7. Martindale: The Complete Drug Reference, 36th edition.
8. Basic & Clinical Pharmacology tenth edition, 2007 edited by Bertram G. Katzung, MD, PhD
9. Lippincott's Illustrated Reviews: Pharmacology, 4th Edition, Copyright Â©2009 Lippincott Williams & Wilkins

PHAR 316 Public Health Pharmacy (45 hours)

Unit-1: Introduction (2 hours)

Overview of Public Health & Pharmacy. Concept of health, disease, prevention and factors influence in health. Concepts of health and disease: Disease causing agents and prevention of disease.

Unit-2: Epidemiology and Pharmacoepidemiology (14 hours)

Definition, scope, concept and use of epidemiology disease transmission and control defense mechanism, immunity, immunization and occupational disease. Descriptive Studies (Case report, Case series and Ecological studies), Analytical Studies (Case control studies, Cohort studies), Experimental Studies (True experimental studies, Quasi experimental studies). Methods of quantifying drug interactions/ADR and adherence to drug therapy in pharmacoepidemiology. Spontaneous reporting, Global drug survillience and role of pharmacists. Discuss different methods of quantifying adherence to drug therapy. Methods of quantifying drug interaction using principles of epidemiology, more specifically the Rothman principle of causation and the Rothman Synergy index. Discuss different methods of quantifying adherence to drug therapy.

Unit-3: Pharmacoeconomic methodologies (8 hrs)

Describe the Nepalese health care system with respect to: public and private sectors, persons and organizations that provide health services. Describe how characteristics of the Nepalese health care system influence prescribing, dispensing, and use of prescription medications, non-prescription medications, and complementary/alternative medicines. Describe the effect of self medication to public health.
Cost Benefit Analysis (CBA), Cost Effectiveness Analysis (CEA), Cost Minimization Analysis (CMA), Cost Utility Analysis (CUA).

Unit-4: Health Promotion & Disease Prevention (8 hours)

.Principles, scope, planning and Method (induvidal, Group and Mass methods) of health education in Pharmacy. Describe stakeholders in and partnerships with public/private health professional and community groups that participate at the system, community, state, national and/or international levels to promote public health and safety. Planning of health education program (Rational use, Use of contraceptives, and health hazards of insecticides and pesticides).

Unit-4: Primary health care (10 hours)

Introduction, elements, Principles (explain 5 majors principles), Implementation of PHC (in terms of WHO and government of Nepal). History of health care delivery system in Nepal. Health care delivery system in Nepal and health care management models.

Promotion of pharmacy related issues of health maintenance and disease prevention and treatment to the lay public and to health professionals.

Describe population level strategies for disease prevention, detection, wellness, promotion and for resolving identified public health problems in the context of pharmacy practice.

Role of pharmacist in PHC, Theory that approach to the health (biological system, psychological system, spiritual system, socio-cultural system).First aid treatment of poisoning, shock, snake bite, burns, fracture and drowning. Diarrhea, vomiting and dehydration, fluid replacement therapy.

Unit-5: Environmental Pollution (3 hours)

A brief description on environment, pollution, pollutant, waste, type of waste and waste from pharmaceutical activities, Classification of pharmaceutical waste. Safe disposal method of pharmaceutical wastes, WHO guidelines for the disposal of pharmaceutical waste

PHAR 316 Public Health Pharmacy Field Work [30 hours]

Conduct educational diagnosis survey (in hospital or HP or community)
Select topic of interest, Prepare KAP questionnaire, Collect data from patients, Analyze and interpret data, Find out problem and Prioritize problems.

- Write a plan for the development of a health education action project based on results of the health education survey
- Observation visit of pharmaceutical industry to know their waste disposal methods and make a report for the better solution if any.
- List hazards due to food additives and food adulteration
- Organize and conduct a health education action project and assess the effectiveness of health education in relation to Pharmacy, action project (1 day field)

Books and Other Resources recommended

1. Levin BL, Hurd PD, Hanson A. *Introduction to Public Health in Pharmacy*. Sudbury, MA: Jones and Bartlett, 2008.
2. *The Future of the Public's Health in the 21st Century*. Washington, D.C: National Academies Press;2003: 97, 417.
3. Bush PJ, Johnson KW. Where is the public health pharmacist? *Am J of Pharm Edu*. 1979;43:249-253.
4. Berger ML, Bingefors K, Hedblom EC et. al. International society for pharmacoecomonics and outcomes research. Health Care Cost, Quality and Outcomes. 2003.
5. Pharmacoeconomics and Outcomes: Applications for Patient Care, American College of Clinical Pharmacy, Kansas City;1997.
6. Beaglehole R, bonita R, Kjellstrom T. Basic Epidemiology. World Health Organization, Geneva, 1993.
7. MacMahon B, Trichopoulos D. Epidemiology: Principles and Methods. 2nd Edition.
8. Boston: Little, Brown, 1996.
9. Rothman KJ. Epidemiology: an Introduction. Oxford University Press, 2002

PHAR 317 Pathophysiology (45 hours)

Unit – 1: Basic Concepts of Pathophysiology - Cell injury, death and adaptation. (6 hours)
Occurrence of Cellular adaptations occurring in atrophy, hypertrophy, hyperplasia, dysplasia, and metaplasia.
Mechanism of cellular injury from hypoxia, free radicals, chemicals, unintentional and intentional injuries, infectious agents, immunologic and inflammatory responses, and genetic factors. Cellular accumulations occurring in response to injury and the subsequent manifestations of cellular damage. Major types of cellular necrosis, cite examples of the tissues involved in each type and compare necrosis to apoptosis. Compare the different theories of aging. Characterize somatic death and its manifestations.

Unit – 2: Acute and Chronic Inflammation. (3 hours)

Acute inflammation: vascular changes, leukocyte cellular events, chemical mediators of inflammation, outcomes of acute inflammation. Chronic inflammation. Role of lymphatics and lymph nodes in inflammation. Morphologic patterns in acute and chronic inflammation. Systemic effects of inflammation.

Unit – 3: Cell regeneration, fibrosis, and wound healing. (3 hours)
Regeneration. Control of cell growth and differentiation at sites of injury. Intracellular matrix and cell-matrix. Repair by connective tissue. Pathologic aspects of repair. Wound healing, Overview of the inflammatory-reparative response.

Unit – 4: Disorders of Immune System. (3 hours)
Cells of the immune system. Cytokines. Histocompatibility genes. Immune mechanisms of tissue injury. Autoimmune diseassess. Immunodeficiency diseases.

Unit – 5: Neoplasia. (4 hours)
Characteristics of benign and malignant neoplasms. Epidemiology of neoplasia. Carcinogenesis-the molecular basis of cancer. Biology of tumor growth. Etiology of cancer-carcinogenic agents. Host defense against tumors-tumor immunity. Clinical features of neoplasia.

Unit – 6: Hemodynamic disorders, thrombosis and shock. (3 hours)
Edema, hyperemia and congestion., Hemorrhage. Hemostasis and thrombosis. Embolism, infarction, shock. Congestive heart failure. Ischemic heart disease. Hypertensive heart disease and Shock.

Unit–7: Etiology, Pathophysiological features and symptoms of the following diseases. (27 hours)
Asthma, Chronic obstructive pulmonary diseases, Peptic ulcer. Chronic glomerulonephritis. Diarrheal diseases. Jaundice and cholestasis. Diabetes mellitus. Graves's disease. Diffuse nontoxic goiter and multinodular goiter. Osteomyelitis. Rheumatic and infectious arthritis. Myasthenia gravis. Epilepsy, Degenerative disorders (Alzheimer's disease, Parkinsonism disease), sexually transmitted diseases, tuberculosis, and anemias.

Books & Other Resources Recommended

1. Sue E. Huether and Kathryn L. McCance. Understanding Pathophysiology. Mosby. Latest Edition

2. Clayton, F. Parkinson. Study Guide and Workbook for Understanding Pathophysiology. Mosby. Latest Edition

3. Corwin E. Handbook of Pathophysiology 2nd edition, Lippincott, 2000 or most recent edition

4. Hogan, M & Hill, K Pathophysiology, Review & Rationales 2004 Prentice Hall publishing.

5. Muralitharan Nair and Ian Peate (2009) Fundamentals of Applied Pathophysiology: An Essential Guide for Nursing Students.
6. Kathryn L. McCance and Sue E. Huether (2009) - Pathophysiology: The Biologic Basis for Disease in Adults and Children.
7. Carol Mattson Porth and Glenn Matfin - Essentials of Pathophysiology: Concepts of Altered Health States (International Edition 2010).
8. Barbara E. Gould and Ruthanna Dyer (2010) - Pathophysiology for the Health Professions.
9. Robert A. Weinberg - The Biology of Cancer. Taylor & Francis -2006.

SIXTH SEMESTER

PHAR 321 Medicinal Chemistry II (60 hours)

Study of the following classes of compounds including their chemical classification, structure and nomenclature, physicochemical properties, mechanism of action, structure activity relationship (SAR), outline synthesis (of compounds with star)

Unit – 1: Drugs Acting on CNS (25 hours)

1.1. General anesthetics (3 hrs)
Classification of General anesthetics, Inhalation anesthetics: Ideal properties of volatile anesthetics, Nitrous oxide*, Halothane*, and Sevoflurane. Current intravenous anesthetic agents (non- opioid) Advantage, disadvantage and properties of Thiopental sodium*, Thiamylal, Propofol,Ketamine and Midazolam. Pre-anesthetic medication and Current intravenous reversal agents.

1.2. Local anesthetics: (3 hrs)

Procaine, Lignocaine* and Bupivacaine. Local anesthetics for eye surgery, eutectic mixture and its use, addition of vasoconstrictors in local anesthetic.

1.3. Sedative, Anxiolytics and Hypnotics: (4 hrs)
Barbiturates:, Alprazolam, Diazepam*, Nitrazepam and Lorazepam. Barbiturates verses Benzodiazepines as hypnotic and sedatives. Miscellaneous: Paraldehyde* Glutethimide, Chloral Hydrate*, Zolpidem and Zaleplon.

1.4.Neuroleptics (Antipsychotics): (2 hrs)

Haloperidol*, Chlorpromazine*, Olanzapine, Quetiapine and Aripiprazole.

1.5. Anticonvulsants: (2 hrs)
Phenobarbitone, Carbamazepine*, Phenytoin, Clonazepam.

1.6. Antidepressants: (2 hrs)

MAO inhibitors, Tricyclic Antidepressants and Selective Serotonin Reuptake ***Inhibitors*****.** Nortryptyline, Amoxepine, Fluoxetine, Citalopram,Sertraline, Amitryptiline, Imipramine, Doxepin, Bupropion,Lithium Carbonate.

1.7. Opiod Analgesics: (3 hrs)

Morphine, Codeine, Diacetyl morphine, Buprenorphine, Meperidine, Fentanyl, Pentazocine, Tramadol (structure and properties) and narcotic antagonists: Naloxone. Antitussive agents: Noscapine, Dextromethorphan, Terpin Hydrate.

1.8. Antiparkinsonics: (3 hrs)
Levdopa, Carbidopa and Amantidine only), Antichlonergics: Benzhexol* (Trihexyphenidyl), Catechol–O-methyl transferase inhibitors – Entacapone. Cholinesterase inhibitors – Rivastigmine. Dopa decarboxylase inhibitors – Carbidopa. Dopamine precursor – Levdopa*, Dopamine agonist – Amantadine

1.9. CNS stimulants: (2 hrs)

Xanthine Derivatives: caffeine* theophylline, aminophylline and etofylline., Analeptics: Nikethamide, Doxapram and Bemegride. Miscellaneous Central Nervous System Stilmulants. Mazindol

Unit-2: Antimicrobials (36 Hours)

2.1. Penicillin (4 hours)

β-Lactam antibiotics: Classification, Structure and nomenclature of penicillin's, MOA, classification and sources, General preparation of semi synthetic penicillin, SAR, Penicillin G* and its properties, Acid resistance (Penicillin v and ampicillin)β-Lactamase resistance (oxacillin, cloxacillin and flucloxacillin), Broad spectrum(ampicillin, amoxicillin* and carbenicillin). Combination with Prodrugs (pivampicillin)β-Lactamase inhibitors (sulbactam, clavulanic acid and imipenem) and MOA, Latent penicillin (penicillin G procaine and benzathine penicillin).

2.2: Cephalosporin & carbamapenams (3 Hours)

Cephalosporin structure and nomenclature, Cephalosporin C. 1st Generation (cephalexin and cephadroxil),2nd Generation (cefaclor), 3rd Generation (Cepodoxime, cefotaxime and cefixime),4th Generation (cefepime), Cephamycin (cefoxitin).

Carbamapenams: Imipenam & Meropenam

2.3. Tetracycline and Chloramphenicol (2 Hours)

Tétracycline, Demeclocycline, Oxytetracycline, Doxycycline, Minocycline.Structure, property and SAR of the Tetracycline. Structure, property, synthesis and SAR Chloramphenicol.

2.4. Aminoglycosides, macrolides & lincomycins (2 Hours)

Aminoglycosides: Members, Mode of Action and uses of Aminoglycoside. SAR of Streptomycin.
Macrolides- Members, Structure, Mode of action and uses.
Lincomycins: Lincomycin.

2.5.Quinolones: (3 Hours)

Classification, Structure, SAR and MOA of Fluoroquinolones. Structure and uses of Nalidixic acid, Norfloxacin, Ciprofloxacin* and Ofloxacin*

2.6. Antituberculars and Antileprotics: (4 Hours)

Tuberculosis and classification of anti T.B. drugs, INH* and its SAR, Ethambutol* and its SAR, Rifampin. Ethionamide, Pyrezinamide* aminosaicylic acid, cycloserine and other 2nd line antitubercular drugs; Dapsone* and Clofazimine

2.7. Chemotherapy of Malaria (3hours)

Classification of antimalarial drugs in relation to plasmodium life cycle, properties and SAR of chloroquine, Mefloquine, Primaquine and Quinacrine. Artemisinin and derivatives.

2.8. Antifungal agents: (2 Hours)

Miconazole, Ketoconazole, Amphotericin B, Nystatin, Griseofulvin.

2.9. Antiprotozoal agents: (2 Hours)

Metronidazole, Tinidazole, Secnidazole. Diloxanide furoate,

2.10. Anthelmintics: (2 Hours)

Classification, Piperazine, Diethyl carbamazine, Pyrantel pamoate, Mebendazole, Niclosamide, Praziquantel, Albendazole*

2.11: Antiviral agents: (3 Hours)

Amantidine hydrochloride, Idoxuridine, Acyclovir, Lamivudine, Zidovidine and other Anti-HIV drugs.

2.13. Antineoplastic agents (6 Hours)

Alkylating agents: cyclophosphamide, chlorambucil, busulphan, uracil, mustard; Antimetabolites: mercaptopurine, flurouracil, methotrexate, azothioprine; Antibiotics: Doxorubicin, Mitomycin; Tubulin Inhibitors: Etoposide, Vincristine, Vinblastine, Taxol and Docitaxel. Miscellaneous: Cisplatin. Hormones: Mitotane, Tamoxifen.Immunotherapy: Interferon.

PHAR 321 Lab Medicinal Chemistry II Practical [30 hours]

(Minimum 8 experiments)

Synthesis & pharmacopoeial analysis of some medicinal compounds:

- Benzyl from benjoin
- Benzanilide from aniline
- Salicylic acid from methyl salicylate
- Methyl salicylate from Salicylic acid
- Phenytion from Benzoin or Benzil
- Paracetomol from para- nitro phenol or para- aminophenol
- 1,4- di hydro pyridine from ethyl aceto acetate
- Quinazolinone from anthranilic acid via benzoxazinone
- Sulfanilamide from acetanilide
- Isoniazid from γ -picoline

- Benzocaine from para- nitro benzoic acid
- Methyl orange and methyl red
- Benzoic acid from toluene
- Acetophenone from Benzene

Books and other resources Recommended

1. Block JH, Beale JM, editor. Wilson and gisvold's textbook of organic medicinal and pharmaceutical chemistry. 11th ed. Baltimore: Lippincott Williams & Wilkins; 2004.
2. Lemke TL, Williams DA, editor. Foye's principles of medicinal chemistry. 6th ed. New Delhi: Wolters Kluwer and Lippincott Williams & Wilkins; 2008.
3. Kadam Dr. SS et al. – Principles of Medicinal Chemistry Vol. I and II.Nirali Prakashan, India.
4. Abraham DJ, editor. Burger's Medicinal Chemistry and Drug Discovery, 6th ed. Vol 1-6. New Jersey: John Wiley & Sons; 2007.
5. Hansch C, editor. Hansch's comprehensive medicinal chemistry, Delhi: Rajkamal Electronic Press; 2005.
6. Ariens EJ, editor. Drug design vol. I-X. Noida: Academic Press; 2009.
7. Roth HJ, Kleemann A. Pharmaceutical Chemistry. Vol-I. Drug synthesis. New
8. . Lednicer D, Mitscher LA, The organic chemistry of drug synthesis, Volume-1-6. New York: A wiley-interscience publication; 2005.
9. Remington: The science and practice of pharmacy. 21st ed., vol. I & II, Lippincatt Willams & Wilkings, New Delhi, 2005.
10. Smith & Williams. Introduction to principles of drug design-Harwood academic press.

PHAR 322 Pharmaceutical Technology II (45 hours)

Unit -1 – Capsules (6 hours)

Advantages and disadvantages of capsule dosage form, material for production of hard gelatin capsules, Manufacture of hard gelatin capsule, size of capsules, method of capsule filling (manual & semiautomatic), basic formulation(excipients), soft gelatin, Advantages and disadvantages of soft gel, capsule shell formulation and capsule content: Bloom strength, Viscosity & iron content, base absorption and minim per gm, Manufacturing of soft gels: Plate process & Rotary die process, factors in soft capsules, quality control, stability testing and storage of capsule dosage forms.

Unit 2 – Microencapsulation (6 hours)

Advantages and disadvantages, Pharmaceutical Application, Fundamental consideration: Nature of core & coating materials, Stability & release characteristic of coated materials, Microencapsulation method; Examples illustrating improved stabilization: Stabilization of Vitamin A Palmitate Oil; Stabilization of incompatible aspirin mixture; Microencapsulation Techniques: Pan Coating, Air suspension, Microorifice-Centrifugal Process, Solvent evaporation, Spray drying and spray congealing, Coacervation Phase separation; General mechanism of drug release from microencapsulated product Polymerization.

Unit -3 – Tablets (15 hours)

General Concept, Advantages & disadvantages, Types of Tablets, Formulation of Tablets: Excipients: Diluents with common examples, Binders with common examples , Disintegrants with common examples: mechanism of tablet disintegration, Factors affecting disintegration, superdisintegrants, Antifrictional Agents with common examples, Miscellaneous Excipients, **Operations involved in tablet manufacturing:** Dispensing, sieving, blending, granulation, drying, Lubrication, compression, coating, **Tablets Manufacturing methods:** Wet Granulation : Objective of granulation, Mechanism of wet granulation (Pendular State, Funicular State, Capillary State, Droplet or Suspension State), Dry Granulation (slugging & roll compaction), Direct compression : ideal DC excipients requirements,

Compression Machines or tablet press: List of Components or parts of tablet compression machines, General information of parts & MOC of punches & dies, Brief knowledge of Standard tooling of compression machines (D, DB, B, BB toolings), General Tablet press cycle (Filling zone, compression zone, Ejection Zone), general concept of Single station & multistation rotary compression machine, knowledge of shape & dimension of tablets & punches (concavity, breakline, embossing), Tablet processing problems & remedies: capping, lamination, cracking, chipping, sticking, picking, binding, mottling, double impression;

Tablet Coating: Objectives, components of coating, Tablet properties, Coating Process: Coating Distribution: spray application system High pressure airless system, Low pressure air atomized system, Coating equipments, Parameters of coating process, Facility and ancillary equipments; Types of tablet coating: Sugar coating ; Film Coating : process variables, Pan variables. Process air variables, Spray variables, General Coating suspension Composition; Enteric coating : objectives, common enteric polymers;, Film defects: causes & remedies; Quality Control test for coated tablets (General Appearance, Size & shape, Organoleptic Properties, Assay, Content Uniformity test, Mechanical strength, Friability, Hardness or crushing strength, Disintegration, Dissolution).

Unit -4 - Parenteral Products (8 hours)

Preformulation factors, routes of administration, water for injection, pyrogenicity, non-aqueous vehicles, isotonicity and methods of its adjustment. Formulation details, containers and closures and selection. Prefilling treatment, washing of containers and closures, preparation of solution and suspensions, filling and closing of ampoules, vials, infusion fluids, lyophilization & preparation of sterile powders, equipment for large scale manufacture and evaluation of parenteral products. Aseptic Techniques:- source of contamination and methods of prevention, design of aseptic area, laminar flow bench services and maintenance. Sterility testing of Pharmaceuticals.

Unit-5: Pharmaceutical Packaging: (10 hours)

Classification of Packaging; **Glass containers**: props, advantages & disadvantage, composition & manufacturing of glass, Types of glass, **Plastic Containers**: properties, advantages & disadvantages, list of plastic polymers, Drug Plastic interaction (Permeation, Leaching, Sorption, Chemical reaction, Modification of the materials properties),Environmental issues, resin identification codes; **Collapsible Tubes**: Metal, Foils (PVC, PVdC, Aluminum)**; Closures:** Threaded screw cap, Crown cap, Pilfer proof closure, Lug cap, Roll On Closure (ROPP); **Liners:** Closure Liner, Homogenous liner, Heteroge nous liner, Torque testing of caps, Rubber stoppers, **Tamper resistant packaging**: Blister package, Strip package, Alu-Alu pack, bubble pack, shrink pack, Foil, paper or plastic pouch, Bottle seals, Breakable caps, Sealed tubes (Collapsible Tubes), Sealed Box (Printed carton duplex), Induction seal.

Brief concept **of Packaging equipments** (Blister packing machines, Strip packing machine, Alu-ALu packing machine, Shrink Packing machine, Induction Sealing Machine, Strapping Machine)

PHAR 322 Lab Pharmaceutical Technology II Practical [30 hours]

1. Experiments to illustrate preparation, stabilization, physical and biological evaluation of pharmaceutical products like powders, capsules, tablets, parenterals, micro-capsules (Sterile water for injection, Calcium gluconate injection, Sodium chloride injection, Formulation, isotonicity, packaging and quality control of the following LVPs as per British pharmacopoeia. Also explain industrial scale manufacturing processes, Contact lens solution, Sodium chloride and Dextrose infusion

2. Micro encapsulation (using one solid and one liquid drug) by coacervation and polymer incompatibility, evaluation of microcapsules.

3. Evaluation of materials used in pharmaceutical packaging.

Books and Other Resources recommended

1. Lachman, L. Lieberman, H.A. Kanig, J.L. The Theory & Practice of industrial Pharmacy. Lea & Febiger, Phialdelphia.
2. Turco, S & King, R.E. Sterile Dosage Forms. Lea & Febiger, Philadelphia
3. Remington's the science and practice of Pharmacy mack Publishing Co. Easton, PA.
4. Lieberman, H.A. Lachman, L. Sachwartz, J.B. Pharmaceutical Dosage Forms: Tablets Vols 1-3 Marcel Dekker, N.Y.
5. Lieberman, H.A. Rieger, M.M. & Banker, G.S. Pharmaceutical Dosage Forms: Disperse Systems. Vol 1-2 Marcel Dekker, N.Y.
6. Ridgway, K. Hard Capsules The Pharmaceutical Press, London.

7. Ansel, H.C. Introduction to Pharmaceutical Dosage Forms KM Verghese.
2. J. Swarbrick, J. Boylan; Encyclopedia of Pharmaceutical technology, 2nd ed, Marcel Dekker,2002.
3. Aulton, M.E. Pharmaceutics- The Science of Dosage form Design ELBS.
4. Avis, K.E. Lachman, L. & Lieberman, H.A. "Pharmaceutical Dosage Forms: Parenteral Medications" Vols. I & II Marcel Decker.
5. I. R. Berry; R.A. Nash; Pharmaceutical Process Validation; 2nd ed, Marcel Dekker, 1993.

PHAR 323 Pharmacology –III (45 hrs)

Unit-1: Drugs Acting on GIT (5 hours)

1.1 Anti-ulcer drugs (Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions-

1.2 H1 receptor Antagonists, Proton Pump Inhibitors, Ulcer healers, Antacids and treatment of H pylori ulcer).

1.3 Laxative (Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions),

1.4 Emetics and anti-emetics (Ipecac syrup, Apomorphine, prokinetics, Promethazine, Ondansetron, Ginger, Peppermint and Ajwain.).

1.5 Antispasmodics (Dicyclomine, Drotaverine, and Hyoscine Butylbromide)

1.6 Antidiarrhoeal drugs (ORS, causal treatment, Role of Zinc in diarrhea, Loperamide, treatment of traveler's diarrhea).

1.7 Appetite Stimulants and Suppressants.

1.8 Digestive Enzymes.

Unit-2: Pharmacology of Endocrine System (4 hours)

a. Hypothalamic and pituitary hormones, Thyroid hormones and anti thyroid drugs, parathormone, calcitonin and Vitamin D.

b. Insulin, oral hypoglycaemic agents & glucagon.

c. ACTH and corticosteroids.

d. Androgens and anabolic steroids. Estrogens, progesterone and oral contraceptives.

e. Drugs acting on the uterus.

Unit-3: Antimicrobials (25 hours)

3.1 Selection and use of Antibacterial agents (Empirical therapy and definitive Therapy)

3.2 Rational of combination of antimicrobials (Antibacterial, antiviral, antiprotozoal).

3.3 Resistance of antimicrobials in example of β-lactamase and Mycobacterium).

3.4 **Sulfonamides** - Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (Sulfacetamide, Silver sulfadiazine, sulfadimethoxin and Cotrimoxazole).

3.5 **Penicillin** - Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (Benzyl penicillin, Procaine penicillin, Benzathine penicillin, Ampicillin + Cloxacillin, Ampicillin, Amoxycillin, Flucloxacillin, Methicillin, Azocillin).

3.6 **Beta-lactamase inhibitors:** Clavulanic acid, Sulbactam, Tazobactam.

3.7 **Cephalosporin** - Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (Cephalexin, Cefadroxil, Cefaclor, Ceftriaxone, Cefotoxime, Cefixime, Cepodoxime, Cefepime, Cefpirome, cephalosporin combination with β-lactamase inhibitors).

3.8 **Monobactams :** (Aztreonam)

3.9 **Carbapenems :** (Imipenem, Meropenem, Faropenem)

3.10 **Tetracycline** - Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (Tetracycline HCl, Doxycycline, Demeclocycline, Minocycline).

3.11 **Chloramphenicol-** MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions.

3.12 **Macrolides-** MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (Erythromycin, Azithromycin, Roxithromycin and Clarithromycin).

3.12.1 **Aminoglycosides**- MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (Streptomycin, Gentamicin, Kanamycin, Tobramicin, Amikacin, Netilmicin and Neomicin)

3.12.2 **Antitubercular and Antileprotics**- Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (INH, Rifampicin, Pyrizenamide, Ethambutol, PAS, Cycloserine). WHO regimen for pulmonary and extrapulmunary tuberculosis, DOTS. Dapsone and Clofazemine.

3.12.3 Classification, MOA of **Fluoroquinolones**. Structure and uses of Nalidixic acid, Norfloxacin, Ciprofloxacin Levofloxin, Ofloxacin, Gatifloxacin and other member.

3.13 **Miscellaneous Antibiotics drugs:** Vancomycin, Clindamycin, Colistin Sulphate.

3.13.1 **Anthelmintics:** Classification, Piperazine, Diethyl carbamazine, Pyrantel pamoate, Mebendazole, Niclosamide, Praziquantel, Albendazole.

3.14 **Antiamoebic:** Metronidazole, Tinidazole, Secnidazole, Diloxanide furoate.

3.14.1 **Antifungal:** Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (Nystatin, Natamycin, Amphotericin B, Miconazole, Ketoconazole, Clotrimazole, Fluconazole, Flucytosine, Griseofulvin. Topical Antifungal (Terbinafine, Caspofungin, Benzoic Acid, Ciclopirox, Tolnaftate).

3.14.2 **Antiviral:** Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of (Acyclovir,Amantadine). Zidovudine and other anti HIV drugs.

Unit-4: Antineoplastic agents ***(4 hours)***

Classification, MOA, Indication, Dosage, ADRs, Contraindication and Drug interactions of:

4.1 Alkylating agents: (cyclophosphamide, chlorambucil, busulphan, uracil mustard).

4.2 Antimetabolites: (mercaptopurine, flurouracil, methotrexate, azothioprine).

4.3 Antibiotics: (Doxorubicin, Mitomycin).

4.4 Plant products : (Vincristine, Vinblastine, Taxol).Cisplatin, Mitotane, Tamoxifen, Interferon alpha.

Unit-5: Immunosuppressant and Immunostimulants (3 hours)

a. Glucocorticoids, calcineurin inhibitors (cyclosporine and tacrolimus).
b. Antiproliferative and Antimetabolic Drugs (Sirolimus, Azathioprine), *Mycophenolate mofetil,* other cytotoxic and antimetabolic agents. Anti-CD3 Monoclonal Antibodies.
c. Interferons, Interleukin-2, Levamisole. Thalidomide. Bacillus Calmette-Guerin (BCG).

Unit-6. Principles of Toxicology (4 hours)

a. Definition of poison, general principles of management of poisoning with particular reference to barbiturates, opioids, organophosphates, Heavy metals and heavy metal antagonists.

PHAR 323 Lab Pharmacology –III Practical [30 hours]

1. Stages of chloroform and ether anesthesia with and without premedication.
2. Study of phenobarbitone induced hypnosis (Demonstration).
3. Determination of analgesic activity (codeine/aspirin).
4. Study of anticonvulsant activity.

5. Study of local anesthetic activity.

i) Surface anesthesia activity on rabbits.

ii) Infiltration anesthesia using guinea pigs.

6. Identification of unknown drugs using rat ileum.

7. Seminars on the drugs studied in theory.

For Practical

1. Pharmacological experiments on isolated preparations by Edinburgh University Pharmacology Staff, 1968.
2. Robert A.Turner and Peter Hebbom: Screening methods in Pharmacology, Vol.1 edited
3. S.K.Kulkarni: Handbook of experimental Pharmacology
4. M.N.Ghosh: Fundamentals of experimental pharmacology
5. lan Kitchen: Text book of invitro Pharmacology
6. U.K.Sheth, N.K.Dadkar, Usha G.Kamat: Selected topics in Experimental Pharmacology
7. K. K. Pillai: Experimental Pharmacology, CBS, Delhi.

Books and Other Resources Recommended

1. C.R.Craig and R.E.Stitzel: Modem Pharmacology
2. Theodore W.Rall, Alan S.Nies and Palmer Taylor: Goodman Gilman's : The Pharmacological Basis of Therapeutics by Alfred Goodman Gilman.
3. D.R.Laurence and P.N.Bennett: Clinical Pharmacology.
4. K.D.Tripathi: Essentials of Medical Pharmacology.
5. R.S.Satoskar and S.D.Bhandarkar: Pharmacology and Pharmacotherapeutics.
6. F.S.K. Barar: Essentials of Pharmacotherapeuties.
7. H.P.Rang and M.M.Dale: Pharmacology.
8. James Crossland: Lewis's Pharmacology, revised.
9. Pharmacology by Lippincott.

PHAR 324 Biopharmaceutics & Pharmacokinetics (45 hours)

Unit-1: Concept, definition and Introduction: (3 hours)
Biopharmaceutics and Pharmacokinetics and their role in formulation development and clinical setting. Pharamacokinetics Pharmacodynamics and clinical Pharmacokinetics with respect to design of dosage regimens. Plasma drug concentration Profile.

Unit-2: Review of Pharamacokinetics: (10 hours)
Absorption of Drug (Physicochemical. Physiological. Pharmaceutical. pH partition hypothesis, Pharmacokinetics of drug absorption-Zero order and first order absorption rate constant using Wagner – Nelson and Loo-Reigelman method).**Drug distribution(**Protein binding (intravascular and extravascular). Significance of drug-protein binding and drug displacement interactions. Kinetics of protein binding).**Drug metabolism. (**Study of factors affecting metabolism. Bioactivation and first pass effect).**Excretion:** (Introduction, types of drug excretion, Clearance concept, Mechanism of renal clearance, clearance ratio, determination of renal clearance. Extraction ratio, hepatic clearance, biliary excretion, Extrahepatic circulation).

Unit-3: Bioavailability and Bioequivalence (8 hours)
Definition and concept of absolute & relative bioavailability. Methods of assessing bioavailability. Measures of bioavailability (Cmax, tmax. AUC etc.) Bioequivalence study and introduction to various study designs. Single dose bioequivalence study and relevant statistics, Review of regulatory requirements for conducting bioequivalence study in Nepal and international prespective. Methods for
enhancement of bioavailability. Clinical significance of bioavailability and bioequivalence.

Unit-4: Dissolution studies. (5 hours)
Introduction to Biopharmaceutical classification system, Mechanism of dissolution, In-vitro studies, and all latest models: Zero order, Matrix, First order, Higuchi. In-vitro in-vivo correlation: Definition, objectives & methods. Introduction to pharmacokinetic models. Physiologic versus compartment approach.

Unit-5: Compartment models (4 hours)
Concepts and their importance in the study of pharmacokinetics. One compartment open model. Assessment of pharmacokinetic parameters from plasma and urine data after i. v. bolus, i.v. infusion, i. v. injection with loading dose and oral administration. Percent absorbed time plot and determination of absorption rates based on one compartment model. Introduction to 'Two compartment model.'

Unit-6: Non-Linear Pharmacokinetics (4 hours)
Causes of nonlinearity, Detection of non-linearity (saturation mechanism).Michaeles Menten equation. Definition of Vmax and Km. Determination of Vmax and Km. Significance of Non-Linear Pharmacokinetics: Case studies.

Unit-7: Clinical Pharmacokinetics (4 hours)

Definition and scope, Therapeutic drug monitoring. Case study of Digoxin and theophyline. Individualization of Dosage. Dose adjustment in patients with and without renal and hepatic

failure. Design of single dose bio-equivalence study and relevant statistics. Pharmacokinetic drug interactions and their significance in combination therapy.

Unit-8: Numerical (7 hours)
Based on AUC, Elimination half life (t1/2), Volume of distribution (Vd), Clearance (Cl), elimination rate constant (ke) and amount of drug (X). Dose adjustment in Renal Failure.

PHAR 324 Lab Biopharmaceutics & Pharmacokinetics Practical [30 hours]

Experiments designed for the estimation of various pharmacokinetic parameters with given data.
In *vitro* evaluation of different dosage forms for drug release.
Absorption studies – in vitro.
Statistical treatment of pharmaceutical data.

Suggested Practical

1. In-vitro drug release study of the given powder dosage form using various dissolution media.
2. In-vitro drug release study of the given uncoated tablet dosage form using different dissolution media.
3. In-vitro drug release study of the given capsule dosage form using various dissolution media.
4. In-vitro drug release study of the given film coated dosage form using various dissolution media.
5. In-vitro dissolution study of the given sustained release dosage form.
6. In-vitro dissolution study of the given fast release (M.D, Dispersible etc.) dosage form.
7. To study the effect of hardness of tablet on dissolution rate.
8. To study the effect of various diluents on dissolution rate of dosage form (Tablets, Capsules, Ointment etc.).
9. To study the effect of formulation on drug release (powder, suspension etc.).
10. To determine the % protein binding of the given drugs.
11. To determine the effect of protein binding on drug bioavailability.
12. To calculate various Pharmacokinetic parameters from the given zero order drug release data.
13. To calculate various Pharmacokinetic parameters from the given first order drug release data.
14. To calculate the various Pharmacokinetic parameters from the given blood data of I.V bolus injection(one compartment model).
15. To calculate various Pharmacokinetic parameters from the given urinary excretion data of I.V bolus.injection using both methods (Rate of elimination & sigma minus method one compartment model).
16. To study the in- vitro drug- drug interaction.
17. To study the passive diffusion of the given drug using cellophane membrane.
18. To study the passive diffusion of the given drug using egg or goat membrane.
19. To determine the various Pharmacokinetic parameters from the given blood data of oral administration of dosge form.
20. DEMONSTRATION EXPERIMENTS

a) Dissolution Apparatus.
b) Preparation of Buffers & membranes.
c) Use of semilog paper.

d) Operation of colorimeter & U.V spectrophotometer.

Books and Other Resources Recommended

1. Brahmankar and Jaiswal; Biopharmaceutics and Pharmacokinetics: A treatise; 2nd Edition; CBS Publication;2009
2. Leon Shargel and Andrew B. C.Yu: Applied Biopharmaceutics and Pharmacokinetics 5th Edition; McGraw Hill; 2005.

3. Rowland and Tozer Text book of Clinical Pharmacokinetics 2nd edition, Lippincott Williams & Wilkins; 1995
4. Robert E. Notari, Biopharmaceutics and Clinical Pharmacokinetics: An Introduction Fourth Edition, Revised and Expanded. Marcel Dekker, New York.2005
5. Remington: The Science and Practice of Pharmacy, 21st Edition. Philadelphia, PA: Lippincott Williams & Wilkins, 2005
6. J Swarbrick, Current Concepts in the Pharmaceutical Sciences: Biopharmaceutics, Lea & Febiger, Philadelphia (1970)
7. Javed Ali, Roop.K.Khar and Alka Ahuja: Textbook of Biopharmaceutics and Pharmacokinetics: 1st edition; Birla Publication, 2001-2002
8. Robinson, J.R.Lee, V.H.L. Controlled Drug Delivery: Fundamentals and Applications2nd edition, Macel Dekker, New York, 1987
9. H.F.Lodish and J.E.Rothman "The assembly of cell membranes Sci. Am. 240: 48-63,1979
10. R.I.Oberle, G.L.Amidon; J. Pharmacokinetics and Biopharmaceutics, 15:529-544,1987
11. A.Rubinstein, V.H.K.Li and J.R. Robinson In oral sustained release formulation, Design and Evaluation, New York, Pergamon, 1988 cap. 6
12. Notari, R.E, Biopharmaceutics and Pharmacokinetics – An introduction Marcel Dekker Inc. N.Y.
13. Wagner J.G. Fundamentals of Clinical Pharmacokinetics, Drugs Intelligence Publishers, Hamilton.
14. Wagner J.G. Pharmacokinetics for the Pharmaceutical Scientist, Technomic Publishing A.G. Basel, Switzerland.

PHAR 325 Biostatistics (45 hours)

Unit-1: Basic concepts of Statistics (10 hours)

Data, Data Graphic, frequency distribution measures of central tendency (Mean, Median, Mode, Harmonic mean, Geometric mean and scattering of data, range, Mean, Deviation, Standard deviation, SEM Applications in Pharmaceutical Validation)

Unit-2: Introduction to probabilities (10 hours)

Binomial and Normal Probabilities distribution.

Unit-3: Sample and sampling method (5 hours)

Sample size and its significance. Sampling techniques and their application in pharmacy.

Unit-4: Hypothesis testing (5 hours)

[T-statistics (Application in dissolution testing of solid dosage forms) chi-square test]

Unit-5: Correlation and Regression (10 hours)

Correlation analysis, Correlation coefficient, Spearman's rank correlation coefficient. Linear regression analysis (applications in Beer's Lamberts Curve, stability study), Introduction to curve fitting techniques. Analysis of variance: Introduction and application of the test in the pharmacokinetic study.

Unit-6: Introduction to Software (5 hours)

SPSS and EPI info.

Books and Other Resources recommended

1. Health Research Methodology- A guide for Training in Research methods. WHO.
2. Green, J. 2004. Qualitative methods for health research. 2nd ed. London: Sage.
3. Methodology and Techniques of Social Research by Bhandarkar and Wilkinson. Himalyan Publishing House
4. Research methodology- Methods and Techniques By CR Kothari- Wiley Eastren limited.
5. Polagar, S. 1995. Introduction to research in the health sciences. 3rd ed. Edinburgh: Churchill Livingstone.
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PHAR 326 Engineering Drawing

1. Isometric and orthographic projections
2. Basic Engineering Drawing Practice - Bolts, nuts, rivetted fronts, screws, worn screws as per specification.
3. Drawing of simple pharmaceutical machinery parts.
4. Layout designing of pharmaceutical production units, retail shops and wholesale