mation on biochemistry books, visit our website www.jaypeebrothers.com, for detailed information on biochemistry books, visit our website www.jaypeebrothers.com

Essentials of Biochemistry

for BDS and Allied Life Sciences Students



Purvi Purohit

Foreword
Praveen Sharma

JAYPEE

Contents

Section 1

Chemistry of Biomolecules

Chapter 1 Chemistry of Carbohydrates **3**

Chemical Composition of Carbohydrates 3
Definition of Carbohydrate 3
Classification of Carbohydrates 3
Functions of Carbohydrates 4
Monosaccharides Structure 6
Disaccharides 12
Polysaccharides 15

Chapter 2 Chemistry of Lipids **22**

Distribution 22
Functions of Lipids 23
Classification of Lipids 23
Derived Lipids 23
Derivatives of Derived Lipids (Eicosanoids) 28
Simple Lipids/Neutral Fats 29
Compound Lipids 30
Glycolipids 32

Chapter 3 Chemistry of Amino Acids and Proteins **34**

Functions of Proteins 34
Chemistry of Proteins 35
Chemistry of Amino Acids 35
Classification of Amino Acids 35
Physical and Chemical Properties of Amino Acids 37
Classification of Protein 40
Structural Organization of Proteins 42

JAYPEE BROTHERS

Structural and Functional Relationship 46
Denaturation of Proteins 47
Separation of Proteins 48
Protein Sequencing 49

Chapter 4 Chemistry of Nucleic Acids **51**

Chemistry of Nucleic Acids 51
Purines 52
Pyrimidines 52
Some Biologically Important Nucleotides 53
Structure of DNA 55
Structure of RNA 56
Small Nuclear RNAs 58

Section 2

Biocatalysts, Vitamins, Minerals and Nutrition

Chapter 5 Biocatalysts: Enzymes, Enzyme Kinetics and Clinical Enzymology **63**

History of Enzymes 63
What are Enzymes? 64
Nomenclature and Classification of Enzymes 64
Coenzymes and Cofactors 65
Properties of Enzymes 66
Structure of Enzyme 67
Mechanism of Action of Enzyme 67
Enzyme-Substrates Interaction 67
Enzyme Kinetics 68
Michaelis-Menten Equation 70
Lineweaver-Burk Plot 71
Enzyme Activation 72
Allosteric Enzymes 72
Enzyme Inhibition 72
Noncompetitive Inhibition 73
Suicide Inhibition 74
Regulation of Enzyme Activity 74
Clinical Enzymology 75
Isoenzymes 76
Lactate Dehydrogenase 77
Creatine Phosphokinase 77

JAYPEE BROTHERS

Chapter 6 Vitamins 79

Classification 79
Water-soluble Vitamins 80
Fat-soluble Vitamins 100

Chapter 7 Mineral Metabolism 114

Macrominerals 114
Microminerals 126

Chapter 8 Nutrition 138

Proximate Principles 139
Calorific Value of Nutrients 145
Energy Requirements of a Person 145
Factors which have to be Considered while Calculating Energy Requirement 146
Nutritional Disorders 152

Section 3

Biological Oxidation and Energy Metabolism

Chapter 9 Biological Oxidation and Respiratory Chain 157

Biologic Systems Need Energy 157
Respiratory Chain 161
Chemiosmotic Theory—Mechanism of Oxidative Phosphorylation 164
Chemical Evidence for Chemiosmotic Theory 166
Inhibitors and Uncouplers of Oxidative Phosphorylation 166
Oxidation of Extramitochondrial NADH 167

Chapter 10 Carbohydrate Metabolism 169

Digestion and Absorption of Carbohydrates 169
Glycolysis (Embeden Meyerhof Pathway) 172
Energetics of Glycolysis 176
Tricarboxylic Acid Cycle (TCA)/Citric Acid Cycle (CAC)/Krebs Cycle 178
Glycogen Metabolism 182
Gluconeogenesis and Blood Sugar Level Regulation 189
Regulation of Gluconeogenesis 193
Hexose Monophosphate Shunt (HMP) and Minor Metabolic Pathways of Carbohydrate Metabolism 197

JAYPEE BROTHERS

Chapter 11 Lipid Metabolism 209

Digestion and Absorption of Lipids 209
Fatty Acid Synthesis 213
Oxidation of Fatty Acids 218
Lipid Transport and Storage 226
Cholesterol Metabolism 235

Chapter 12 Amino Acid Metabolism 244

Digestion and Absorption of Proteins 244

Dietary Proteins 244
Digestion of Proteins 245
Absorption of Amino Acids 247

Catabolism of Amino Acids—Fate of Amino Nitrogen: Ammonia Transport and Urea Cycle 248

Fate of the –NH_2 Group of Amino Acid 249
Fate of Ammonia 251
Transport of Ammonia 251
Synthesis of Urea 253
Significance of Urea Cycle 253
Regulation of Urea Cycle 254
Inborn Errors of Urea Cycle 254

Catabolism of Carbon Skeleton of Amino Acids: Aliphatic Amino Acids 255

Glycine 255
Catabolism of Glycine 256
Functions of Glycine 256
Inborn Errors of Glycine Metabolism 258
Sulfur-containing Amino Acids 258
Functions of Cysteine 260
Inborn Errors of Metabolism of S-containing Amino Acids 260
Serine (SER) and Threonine (THR) 262

Catabolism of Carbon Skeleton of Amino Acids: Aromatic Amino Acids 262

Phenylalanine 262
Inborn Errors of Phenylalanine Metabolism 262
Specialized Products of Tyrosine 265
Tryptophan 267
Specialized Products of Tryptophan 269
Inborn Errors of Tryptophan Metabolism 270

JAYPEE BROTHERS

Catabolism of Carbon Skeleton of Amino Acids: Branched Chain Amino Acids 271

Catabolism of Branched Chain Amino Acid's Carbon Skeleton 271
Inborn Errors of BCAA Metabolism 271

Biogenic Amines 273

Polyamines 275

Chapter 13 Purine and Pyrimidine Metabolism 277

Digestion and Absorption of Polynucleotides 278

Purine Metabolism 278

Purine Biosynthesis 278
Regulation of Purine Biosynthesis 282
Purine Catabolism 283
Disorders of Purine Metabolism 284

Pyrimidine Metabolism 286

De Novo Pyrimidine Synthesis 287
Salvage Pathway of Pyrimidine Nucleotide Biosynthesis 287
Regulation of Pyrimidine Biosynthesis 288
Coordinated Regulation of Purine and Pyrimidine Biosynthesis 288
Catabolism of Pyrimidine Nucleotides 289
Disorders of Pyrimidine Metabolism 289

Section 4

Endocrinology

Chapter 14 An Introduction to Endocrinology 293

Chapter 15 Hormone Action 296

Signal Transduction for Steroid Hormones 298
Mechanism of Action of Steroid Hormones 298
Signal Transduction in Peptide Hormones 299
G-Protein-Coupled Second Messengers 301
Second Messengers of GPCRs 303

Chapter 16 Hormones of Pituitary and Hypothalamus 307

Hormones of Posterior Pituitary 312

JAYPEE BROTHERS

Chapter 17 Hormones of Thyroid Gland 313

Biosynthesis and Secretion of Thyroid Hormones 313
Functions of Thyroid Hormones 315
Pathophysiology of Thyroid Disorders 317

Chapter 18 Hormones of Parathyroid Gland 319

Structure of Parathyroid Hormone 319
Secretion of PTH 320
Functions of PTH 320
Regulation of PTH Secretion 321
Calcitonin 321
Calcium Homeostasis 321
Hormonal Regulation of Calcium Homeostasis 322
Pathophysiology of Parathyroid Gland 324

Chapter 19 Hormones of Pancreas and Gut 326

Pancreatic Hormones 326
Insulin—Structure, Synthesis, Secretion and Metabolism 327
Diabetes Mellitus 330
Glucagon 334
Somatostatin 336
Pancreatic Polypeptide 337
Gut Hormones 337
Pathophysiology 337

Chapter 20 Hormones of Adrenal Gland 339

Hormones of Adrenal Cortex 339
Adrenal Androgens 341
Regulation of Secretion of Adrenal Cortex Hormones 341
Mechanism of Action of Adrenal Steroid Hormones 341
Transport, Functions and Catabolism of Adrenocorticoid 342
Hormones of Adrenal Medulla 344

Chapter 21 Hormones of Gonads 346

Male Sex Hormones Biosynthesis 346
Female Sex Hormones Biosynthesis 347

JAYPEE BROTHERS

Section 5

Genetics

Chapter 22 DNA Replication and Repair **353**

Cell Cycle 354
DNA Replication 355
DNA Repairs 359

Chapter 23 Transcription—RNA Synthesis **362**

Process of Transcription 363
Prokaryotic Transcription 363
Eukaryotic Transcription 365
Initiation of Transcription 365
RNA Processing in Eukaryotes 366

Chapter 24 Genetic Code, Mutations and Translation of mRNA **369**

Genetic Code 369
Mutations 371
Process of Translation 373
Post-translational Processing 375
Antibiotics 376
Protein Turnover/Degradation 376

Chapter 25 Regulation of Gene Expression **378**

Prokaryotic Gene Expression—Lac Operon Concept 379
Bacteriophage Lambda—Switch between Lysogenic and Lytic Phase 380
Eukaryotic Gene Expression Regulation 380

Chapter 26 Recombinant DNA Technology **385**

What is rDNA? 385
Restriction Endonucleases 386
Cloning Vectors 387
Plasmids 388
Cosmids 389
Steps for the Synthesis of rDNA 389
Polymerase Chain Reaction (PCR)—Artificial DNA Cloning Technique 391
DNA Libraries 392
Techniques for Identifying the DNA Sequences 392
Significance of rDNA Technology in Medicine 394

JAYPEE BROTHERS

Section 6

Miscellaneous

Chapter 27 Cancer and Oncogenes **399**

Occurrence 399
Etiology 400
Genetics of Cancer 402
Tumor Suppressor Genes 403
Telomeres and their Role in Cancer 403
Anticancer Drugs 404
Tumor Markers 404

Chapter 28 Immunology **406**

Antigens 406
Antibodies/Immunoglobulins 407
Innate Passive Immunity 408
Acquired/Adaptive Immunity 409
Disturbances of Immune System 410

Chapter 29 AIDS **412**

AIDS Virus 412
Immunology and Infection by AIDS Virus 413
Modes of Infection and Prevention 415
Diagnostic Tests for AIDS 415

Chapter 30 Xenobiotics Metabolism **417**

Phase – I 418

Hydroxylation of Xenobiotics Using CytP450 418
Oxidation 418
Reduction 419
Hydrolysis 419

Phase – II 420

Glucuronidation (Addition of Glucuronic Acid) 420
Sulfation 420
Glutathione 420
Acetylation 420

Chapter 31 Free Radicals and Antioxidants in Health and Disease **422**

What are Free Radicals? 422
Generation of Free Radicals 423
Free Radical in Diseases 423
Antioxidants 424

JAYPEE BROTHERS

Chapter 32 Regulation of Acid-Base Balance 427

What are Acids and Bases? 427
What are Buffers? 428
Important Physiological Buffer Systems (1st Line of Defense) 428
Respiratory Compensation (2nd Line of Defense) 430
Renal Compensation (3rd Line of Defense) 431
Imbalances of Acid–Base and their Compensatory Mechanisms 433

Chapter 33 Biochemistry of Saliva and Dental Caries 435

Saliva Composition and Functions 435
Saliva Analysis and its Clinical Significance (Biochemical Analysis of Saliva in Practical Biochemistry Section) 437
Dental Caries 437

Chapter 34 Biochemistry of Connective Tissue and Bones 439

Types and Functions of Connective Tissue 439
Components of Connective Tissue 440
Bones 443
Inherited Disorders of Connective Tissue 444

Chapter 35 Current Topics in Biochemistry 446

Human Genome Project (HGP) 446
Bioinformatics 448
Environmental Biochemistry 450

Section 7

Practical Biochemistry

Part A Introduction to Practical Biochemistry

Chapter 36 Practical Biochemistry in Dentistry and Allied Health Sciences 461

Chapter 37 A Peep into the Biochemistry Laboratory 462

Common Laboratory Equipment and Instruments 462

Chapter 38 Quality Control and Precision of Results 466

Importance of Quality Control in Clinical Practice 467

Chapter 39 How to Work in a Biochemistry Laboratory 468

Instructions for Working in a Biochemistry Laboratory 468

JAYPEE BROTHERS

Part B Qualitative Exercises

Chapter 40 Carbohydrate Analysis 473

Definition 473
Classification 473
Tests for Analysis of Carbohydrates 474
Tests for Polysaccharides 478
Identification of Unknown Carbohydrate 479
Viva Voce 480

Chapter 41 Lipid Analysis 481

Definition 481
Analysis of Lipids Based on Physical Properties 482
Analysis of Derived Lipids 483
Viva Voce 485

Chapter 42 Protein Analysis 486

Definition 486
Group-specific Test of Proteins 487
Color Reactions for Identification of Various Amino Acids 488
Precipitation of Proteins 490
Identification of Unknown Protein 493
Viva Voce 494

Part C Quantitative Exercises

Chapter 43 Gastric Juice Analysis 497

Analysis of Gastric Juice 497
Determination of Free and Total Acidity 499
Observation Table 499
Viva voce 500

Chapter 44 Colorimetry 501

Photometry 501
Viva voce 504
Estimation of Blood Glucose by Orthotoluidine Method of Dubowski 505

Chapter 45 Blood Sugar 505

Estimation of Blood Glucose by Glucose Oxidase or Peroxidase 506
Viva Voce 508

JAYPEE BROTHERS

Chapter 46 Total Protein and A:G Ratio **509**

Estimation of Total Protein by Biuret Method 509
Estimation of Albumin by BCG Method 510
Normal Value and its Significance 511
Viva Voce 511

Chapter 47 Serum Urea **513**

Estimation of Serum Urea by Berthelot Method 513
Viva Voce 514

Chapter 48 Serum Creatinine **515**

Estimation of Serum Creatinine (By Jaffe's Method) 515
Viva Voce 517

Chapter 49 Serum Lipid Profile **518**

Estimation of Serum Cholesterol (Enzymatic Method) 519
Estimation of HDLc 520
Estimation of Triglycerides 521
Very Low Density Lipoprotein Cholesterol 522
Low Density Lipoprotein Cholesterol 522
Viva Voce 523

Chapter 50 Estimation of Sugar in Urine (Benedict's Quantitative Method) **524**

Principle 524
Viva Voce 525

Part D Urine Analysis

Chapter 51 Analysis of Normal Urine **529**

General Characteristics 530
Test for Organic Constituents 532
Test for Inorganic Constituents 532
Viva Voce 533

Chapter 52 Analysis of Abnormal/Pathological Urine **534**

Proteins 534
Detection of Proteins in Urine 535
Detection of Sugar in Urine 535
Detection of Ketone Bodies 536
Detection of Bile Pigments and Bile Salts 537
Detection of Blood 537
Viva Voce 538

JAYPEE BROTHERS

Part E Applications of Clinical Biochemistry

Chapter 53 Liver Function Tests 541

Tests Based on Bilirubin Metabolism 542
Reagent 542
Tests Based upon Metabolic Function of Liver 542
Test Based on Synthesis of Plasma Proteins 543
Tests Based on Detoxication Action of Liver 543
Tests Based on Excretory Function of Liver 543
Tests Based on the Synthesis of Clotting Factors by Liver 544
Enzyme Assays 544
Alkaline Phosphatases 544
Viva Voce 544

Chapter 54 Renal Function Tests 545

Test for Assessment of Glomerular Function 546
Tests for Measuring Renal Plasma Flow 547
Tests for Tubular Function 548
Phenolsulfonphthalein Test 548
Kidney Imaging 549
Kidney Biopsy 549
Viva Voce 549

Chapter 55 Thyroid Function Tests 550

Hormone Concentration 550
Binding Proteins 551
Thyrotropin-releasing Hormone Response Test 551
Serum Cholesterol 551
Thyroid Autoantibodies 551
Thyroid Scan 552
Viva Voce 552

Chapter 56 Parathyroid Function Tests 553

PTH Level 553
Serum Calcium Level 554
Serum Phosphorus 554
Serum Vitamin D 554
Bone Scan 555
Viva Voce 555

JAYPEE BROTHERS

Part F Demonstrations

Chapter 57 Analysis of Saliva 559

Composition of Saliva 559
Analysis of Saliva 560
Tests for Organic Constituents 560
Tests for Inorganic Constituents 561
Viva Voce 561

Chapter 58 Analysis of Food-Stuffs 562

Milk 562
Composition 562
Analysis of Milk 563
Viva Voce 564

Chapter 59 Biochemical Techniques 565

Chromatography 565
Types of Chromatography 566
Electrophoresis 571
Viva Voce 575

Chapter 60 Titratable Acidity of Urine 576

Determination of Titratable Acidity 576
Viva Voce 577
Principle 578

Chapter 61 Nonprotein Nitrogen 578

Reagent 578
Viva Voce 579

Chapter 62 Recent Advances in Clinical Biochemistry 580

Spectroscopy 580
Gene Identification Techniques 583
Gene Multiplication Techniques 584
Gene Storage Techniques 586

Chapter 63 Preparation of Various Reagents 588

Reagents for Qualitative Analysis 588
Reagents for Quantitative Analysis 590

Chapter 64 Normal Reference Values of Various Biochemical Parameters 592

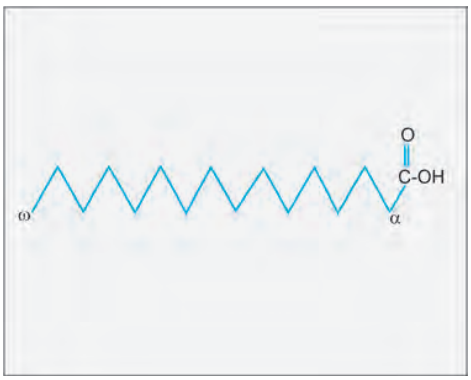
Glossary 595
Index 611

JAYPEE BROTHERS

CHAPTER

2

Chemistry of Lipids



Chapter Framework

- Introduction
- Definition
- Functions of Lipids
- Classification of Lipids
- Derived Lipids
- Physical and Chemical Properties of Lipids
- Simple Lipids
- Compound Lipids

Introduction

Lipids are a diverse group of organic compounds. They are grouped together primarily due to their insolubility in water. Functionally the lipids are as diverse as their chemical nature—ranging from storage form of energy to their role as structural component of biologic membranes and as coenzymes for enzymes.

Definition

Lipids are a heterogeneous group of organic compounds characterized by solubility in non – polar solvents and insolubility in polar solvents. Chemically lipids can be defined as esters of fatty acids with certain alcohols.

Distribution

- Lipids are distributed widely in the animal kingdom—from the stored fat in adipose tissue of mammals to the waxy secretion of preen glands of birds that helps to keep their feathers waterproof.
- In the plants, lipids are present as waxy coating on the leaves, preventing the loss of water by transpiration, as stored form in nuts and seeds that acts as a source of energy during germination.
- Humans have lipids as stored form of energy in the adipose tissue. This provides the necessary energy during period of dearth. The calorific value of fat is 9 kcal/g.
- Dietary lipids are found in vegetable seeds, nuts, fish liver oil and eggs.

JAYPEE BROTHERS

Functions of Lipids

- Dietary lipids are the cooking medium and give taste and palatability to food.
- Dietary lipids are the source of fat-soluble vitamins.
- Dietary lipids are the source of essential fatty acids.
- Lipids are present in the cell membrane as a phospholipid bilayer and are the provision for the structural integrity of the membrane.
- Excess calories are stored as triglycerides in adipose tissue.
- Lipid around the viscera protects them against shocks.
- Subcutaneous fat acts as an insulating layer against extremes of temperatures.
- Subcutaneous fat also gives shape and contour to body.
- Lipids present in the myelin sheath act as an insulating layer helping in saltatory conduction of nerve impulses.
- Amphipathic lipids like phospholipids help in emulsification of dietary fat during digestion.

Classification of Lipids (Flowchart. 2.1)

Simple Lipids

These are esters of fatty acids with certain alcohols like glycerol or other high molecular weight alcohols, e.g. oils, fats and waxes.

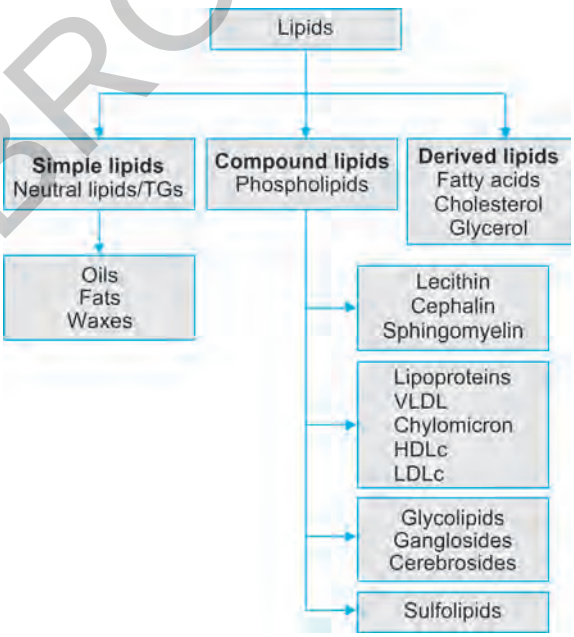
Compound Lipids

These are lipids which contain fatty acids, alcohol (Glycerol/ Sphingol) and other compounds like—phosphoric acid, N_2 base or protein in addition to fatty acids and alcohol, e.g. Phospholipids like—lecithin, sphingomyelin, lipoproteins like—LDLc, HDLc, VLDL, glycolipids like—cerebrosides, gangliosides.

Derived Lipids

These are compounds obtained on hydrolysis of simple and compound lipids but still possess the properties of lipids, e.g. fatty acids, glycerol, sterols like—cholesterol.

Flowchart 2.1 Classification of lipids



Derived Lipids

Fatty Acids

- Fatty acids are monocarboxylic acids ranging from C_4–C_{24}. These are aliphatic, unbranched and monocarboxylic acids.

JAYPEE BROTHERS

Nomenclature (Fig. 2.1)

- They generally contain an even number of carbon atoms because two carbon atoms are added at a time during their synthesis. Each fatty acid possesses a carboxy terminal end and a methyl terminal (ω) end.
- The carbon atoms are numbered from the carboxy terminal, the carboxyl atom being numbered 1. The second, third and fourth carbon atoms are also known as α, β and γ carbon atoms respectively. The position of double bond is shown by sign of Δ.

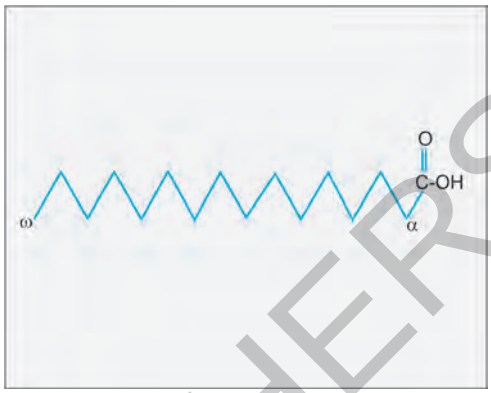


Fig. 2.1 Numbering of a saturated fatty acid

Isomerism

- The unsaturated fatty acids (FAs) show geometric isomerism, i.e. Cis-Trans due to presence of double bond. The naturally occurring fats contain cis-isomer predominately.

Types

– Fatty acids are of 2 types:

- *Saturated Fatty acids*: The saturated fatty acids have no double bonds and are saturated:
  e.g. C_4 – Butyric – Butter, ghee
  C_6—Caproic—Butter, ghee, vegetables
  C_8—Caprylic—Butter, vegetables
  C_{12}—Lauric—Coconut oil
  C_{14}—Myristic—Coconut oil
  C_{16}—Palmitic—Vegetable oil, animal fat
  C_{18}—Stearic—Vegetable oil, animal fat
  C_{20}—Arachidic—Peanut oil
- *Unsaturated fatty acids:* They have at least one double bond. Depending upon the number of double bonds unsaturated fatty acids are further of two types:
  MUFA—e.g. Oleic acid, palmitoleic acid (this occur in almost all natural fats and oils).
  PUFA—e.g. Linoleic, linolenic, arachidonic.

  The polyunsaturated fatty acids possess more than one double bond. They are termed as the ***essential fatty acids*** since they are essential for the normal growth and development and they cannot be synthesized in the body. Thus these fatty acids are nutritionally essential and have to be taken in diet.

Linoleic ω6	$C_{18}\Delta_{9,12}$	Soybean oil, peanut oil, cottonseed oil, corn oil
Linolenic ω3	$C_{18}\Delta_{9,12,15}$	Linseed oil, soybean oil, fish liver oil
Arachidonic ω6	$C_{20}\Delta_{5,8,11,14}$	Peanut oil

- Out of these three, linolenic acid is the most important one as the other two can be synthesized from linolenic acid in the body by introduction of a double bond.

JAYPEE BROTHERS

Functions/Importance of Essential Fatty Acids (EFAs)

- EFAs are present in the membrane phospholipids in cell membrane and other organelle membranes like mitochondrial membrane. Thus are responsible for the structural integrity of membrane.
- EFAs are present in the membranes of germinal epithelium of gonads.
- EFAs are present in the phospholipids of lipoprotein HDLc. HDLc helps in the transport of cholesterol from tissues to liver. The EFA present at C_2 of peripheral PLs of HDLc esterify the free cholesterol from LDLc and extra hepatic tissues to cholesterol esters (CES), which move to the center of nascent HDLc making it spherical. Now this HDLC transports the CES to liver, where they are oxidized to bile salts and excreted with feces. This is called **reverse cholesterol transport** (Fig. 2.2). This helps in reducing the serum cholesterol level.
- EFAs are needed for the synthesis of lipoprotein particles VLDL at the liver. VLDL transports the endogenously synthesized triglycerides. Thus in EFA deficiency there occurs fatty infiltration of liver—**Fatty liver** (Fig. 2.3).

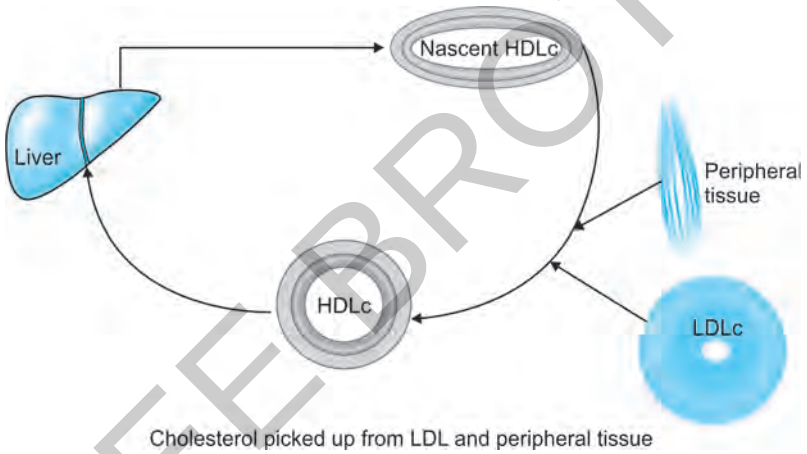


Fig. 2.2 Reverse cholesterol transport

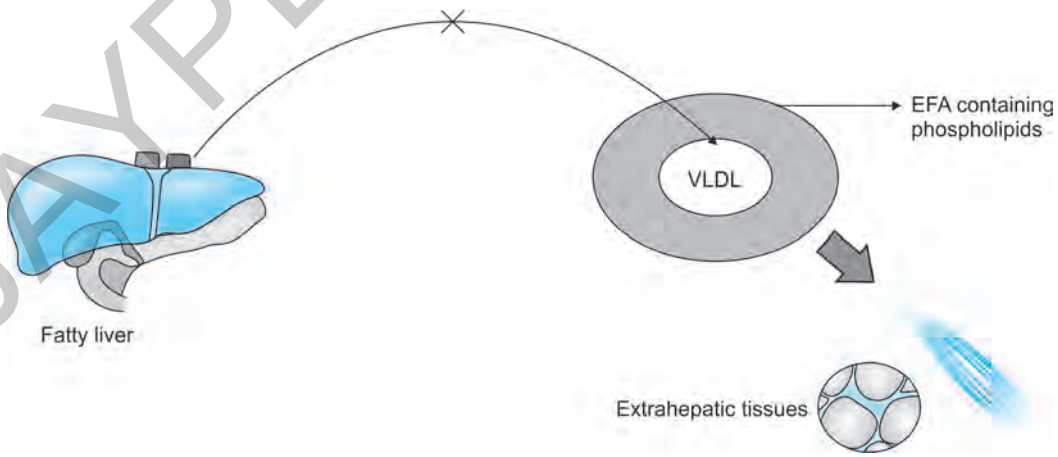


Fig. 2.3 Fatty liver due to EFA deficiency

JAYPEE BROTHERS

- EFAs arachidonic acid is the precursor of prostaglandin which acts as local hormone behaving as inflammatory mediators, vasodilators, smooth muscle constrictor, platelet aggregation inhibitors. Prostaglandins are formed by cyclooxygenase pathway and used as pharmacologic agent.
- EFAs arachidonic acid is also precursor of thromboxane. Thromboxanes are formed from prostaglandins. These are also potent physiologically active compounds. They are vasoconstrictor and platelet aggregators.
- Leukotrienes are synthesized from arachidonic acid by lipoxygenase pathway and are activators of leukocytes, vasoconstrictors, smooth muscle constrictors, increase vascular permeability, mediators of allergic reactions.
- Docosahexenoic acid (DHA) is synthesized from linolenic acid. It is present in the photoreceptor cells of eyes and increases their electrical response to illumination.
- DHA also helps in proper brain development in infants and children.

Deficiency of EFAs Leads to Impairment of Normal Health

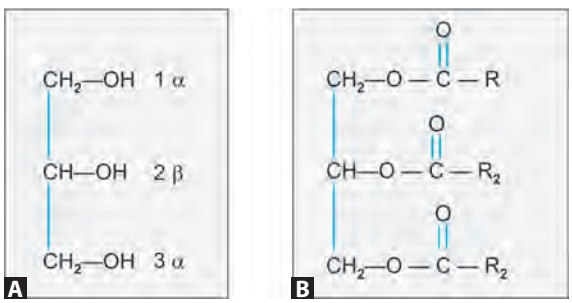
- Infertility in experimental animals but not seen in humans.
- In humans there are skin lesions like—dermatitis, eczema in skin.
- Degenerative changes in arterial wall.
- Fatty liver progressing to cirrhosis of liver.

Some Unique Fatty Acids

- Branched chain fatty acids found in sebum, and phytanic acid in butter
- Cyclic fatty acids—Chaulmoogric and hydnocarpic acid used for therapy in leprosy.
- Substituted fatty acids—Substituent group like –OH, or – CH_3 group, e.g. Cerebronic acid of glycolipids.

Glycerol (Figs 2.4A and B)

- It is a trihydric alcohol. It is obtained on hydrolysis of TGs in human body (lipolysis) and is converted to glucose at liver.
- Commercially, it is obtained as by product of soap manufacture.
- It is sweet in taste and is used in cosmetics.



Figs 2.4A and B Glycerol and triglyceride

- Clinically important preparation is nitroglycerin, which is used as vasodilator.

Cholesterol

Structure (Fig. 2.5)

- Cholesterol is an animal sterol. It has a sterol ring nucleus termed as the CPPP—Cyclo pentano per hydro phenanthrene nucleus. It has 3 cyclohexane rings, 1 cyclo pentane ring, a double bond between C_5 and C_6, an OH group at C_3 which participates in the esterification, a hydrocarbon chain at C_{17}, CH_3 groups at C_{10} and C_{13}.

JAYPEE BROTHERS

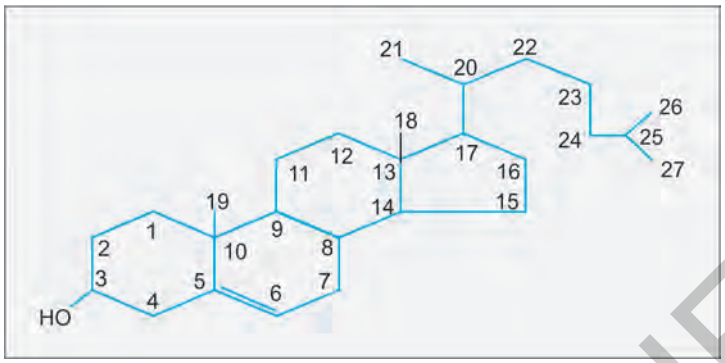


Fig. 2.5 Cholesterol

Occurrence

Cholesterol is abundantly present in brain nervous tissue, liver, adrenal cortex and other tissues. Serum cholesterol level is 150–220 mg/dL, 70% is esterified and 30% is free. Fifty percent of esterification is by linoleic acid. Rest is by oleic, palmitic and arachidonic acid.

Physical Characteristics

It is yellowish white crystalline solid, soluble in nonpolar solvent.

Biomedical Importance of Cholesterol

- Cholesterol is the component of all the biological membrane.
- Cholesterol is precursor of sex hormones of male and female.
- Cholesterol is the precursor of adrenocorticoid hormones, e.g. Glucocorticoids, mineralocorticoids.
- Cholesterol is the precursor of bile acids in liver. The bile acids are needed for the emulsification of dietary lipids.
- Cholesterol is present as 7-dehydrocholesterol in the malphigian layer of skin and it is this 7-dehydrocholesterol that an exposure to sunlight is activated to vitamin-D.
- Cholesterol is the component of myelin sheath of nerves and acts as an insulator thus helps in nerve impulse conduction and prevents leakage of charge.

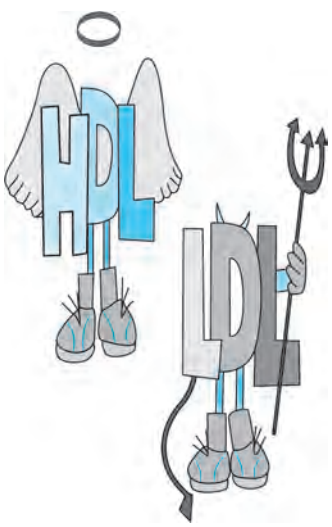


Fig. 2.6 Good and bad cholesterol

Serum Cholesterol and Hypercholesterolemia

- The normal serum cholesterol level is 150–220 mg/dL. This level should be maintained levels higher than 250 mg/dL are harmful and the condition is termed as *hypercholesterolemia*.
  - Dietary and endogenously synthesized cholesterol is transported via the plasma lipoproteins HDLc, LDLc (mainly endogenous), chylomicron (dietary) and chylomicron remnants.

JAYPEE BROTHERS

- HDLc is termed as good cholesterol and LDLc as bad cholesterol (Fig. 2.6). HDLc scavenges the free cholesterol (harmful) in the LDLc and carries it to the liver to be oxidized to bile acids which are ultimately excreted out via bile in feces.
- When the serum cholesterol level exceeds the normal value, the cholesterol particularly LDL cholesterol tends to deposit in the intima of blood vessels.
- Oxidized LDLc has a greater tendency to deposit in the intima of medium and large sized arteries, narrowing them leading to formation of atherosclerotic plaques. This phenomenon is called atherosclerosis, which leads to cardiovascular diseases like myocardial infarction and hypertension.
- Primary hypercholesterolemia is seen in some inherited disorders of cholesterol metabolism.
- Secondary hypercholesterolemia occurs secondary to diseases like—diabetes mellitus, nephrotic syndrome, obstructive jaundice, hypothyroidism, etc.
- Management of hypercholesterolemia is discussed with cholesterol metabolism in chapter 11.

Derivatives of Derived Lipids (Eicosanoids)

Prostaglandins

- They are named after the prostate tissue where they were first extracted from.
- These are derived from arachidonic acid of membrane phospholipids.
- Phospholipids in membranes of various tissues like—blood vessel wall, lungs are acted upon by enzymes phospholipases, which hydrolyze and release arachidonic acid.
- Arachidonic acid is then acted upon by cyclooxygenase pathway enzymes—prostaglandin synthase, peroxidase to give prostaglandins.
- Structurally all prostaglandins have a saturated cyclopentane ring and unsaturated hydrocarbon chain.
- They are named as *PG1, PG3* etc. depending upon their position of double bonds.
- Functionally, they act like local hormones, since they affect the local tissue where they are produced and are not transported by blood to different tissues.
- Their important functions are:
  - They are smooth muscle constrictors/relaxation.
  - They are vasodilators.
  - They cause inhibition of platelet aggregation.
  - They act as mediators of inflammation.

  (Aspirin—antiinflammatory—inhibits PG synthesis by blocking enzyme cyclooxygenase)
  - Bronchodilator prostaglandin is PGE, and is used in asthma pumps.

Thromboxanes (TXAs)

- They are derived from PGs.
- They are secreted by platelets, hence the name thromboxanes.
- They cause *platelet aggregation* and *vasoconstriction.*
- Aspirin inhibition of cyclooxygenase completely blocks synthesis of TXA2 as the platelets cannot regenerate cyclooxygenase. Thus it is *helpful in heart attacks.*

JAYPEE BROTHERS

Leukotrienes (LTs)

- They are synthesized from arachidonic acid by *lipoxygenase* pathway.
- These are:
  - *Activators of leukocytes*
  - *Vasoconstrictors*
  - *Smooth muscle constrictors*
  - *Bronchoconstrictors*
  - *Increases capillary permeability.*
  - Mediators of *allergic reactions* (hypersensitivity).

Simple Lipids/Neutral Fats

- They are esters of Fatty acid with glycerol. They are present in the adipose tissue as TGs.
- Naturally occurring TGs are mostly mixed TGs, i.e. there are more than one type of fatty acids esterifying the – 3OH groups.
- C1 and C3 are mostly esterified with C16 and C18 Palmitic and Stearic acids respectively.
- C2 is mostly PUFA.
- Oils are neutral lipids that are liquid with one or more fatty acids residues unsaturated at room temperature whereas fats are neutral lipids that are solid or semi-solid at room temperature.

Physical Properties of Simple Lipids

- *Solubility*—The lipids, by definition, are insoluble in water and soluble in organic solvents.
- *Melting point*—Some of them are liquid at room temperature while others are solid. Melting temperature is dependent upon the hydrocarbon chain length of the FAs. If the FAs are unsaturated, the TG will be liquid at room temperature as in vegetable oils. Conversely if it is saturated the TGs will be solid (long chain) or semi-solid (shorter chain) at room temperature as in ghee, butter, or other animal fat.
- *Odor and taste*—They have characteristic odors and tastes.
- *Specific gravity* is less than water.
- *Emulsification*—Lipids get emulsified in presence of surfactants like—detergents and bile salts. Emulsification is the breakdown of a large lipid globule into smaller droplets due to physical agents (vigorous shaking) or chemical agents (bile salts, soap solution) as they reduce the surface tension of water *(also see practical section lipid analysis)*.

Chemical Properties of Simple Lipids

- *Hydrolysis*—The ester bonds of lipids can be hydrolyzed by specific enzymes.
- *Saponification*—Hydrolysis of triglycerides by alkalis is known as saponification, and results in the formation of alkali salts of fatty acids (soaps).
- Saponification number is the number of mgs of KOH required to completely saponify 1 g of fat.
- *Hydrogenation*—Double bonds of unsaturated fatty acids can be hydrogenated in the presence of catalysts, e.g. nickel. This process of hydrogenation is used for the commercial preparation of vegetable ghee from vegetable oils.
- *Iodination*—Iodine can also reduce the double bonds of unsaturated fatty acids. Thus can be used to find out adulteration of vegetable oils as oils have a specific number of double bonds to be saturated by iodine.

JAYPEE BROTHERS

– Iodine number is the number of gram of iodine taken up by 100 g of the lipid. It gives the degree of unsaturation in oil.
  - *Oxidation*—Unsaturated fatty acids can spontaneously react with atmospheric oxygen to form fatty acid peroxides, fatty acids epoxides and fatty acid aldehydes. Fat which undergoes this type of oxidation becomes rancid.
  - Oxidized fat becomes rancid, i.e. it develops a bad taste, color, odor and is not suitable for use. This process is termed as rancidity. Rancidity can be oxidative and hydrolytic.
  - *Hydrolytic rancidity* is observed in case of vegetable oils kept for a long time in high temperatures, where the naturally occurring lipases of the oils hydrolyze them into free fatty acids which are then oxidized by the atmospheric oxygen in the presence of catalyst like metal containers of Cu.
  - *Oxidative rancidity*—This is seen in vegetable oils exposed to atmospheric oxygen in presence of metallic catalyst like copper. Under such conditions the fatty acids of oil are oxidized to their respective peroxides, epoxides and aldehydes giving characteristic taste and odor to it.
  - Vegetable oils contain vitamin – E which is an antioxidant and prevents the oxidation, increasing shelf life of these oils.

Compound Lipids

These contain some groups in addition to fatty acids and alcohols like—phosphoric acid, protein, or a carbohydrate moiety. They are further classified into:

Phospholipids

- These can be defined as esters of fatty acids with alcohol like glycerol or sphingol and contain an additional group like phosphoric acid and nitrogenous base.
- The former are known as *glycerophospholipids* and the latter are known as *sphingophospholipids*.
- Glycerophospholipids may be considered to be the derivatives of *phosphatidic acid (Fig. 2.7)*.
- C_2 is always a PUFA in glycerophospholipid.
  – The phosphate group of phosphatidic acid gets linked with a nitrogenous base by an ester linkage at C_3 phosphoric acid OH group, to form phospholipids, e.g. choline in phosphatidyl choline *(lecithin),* ethanolamine in phosphatidyl ethanolamine *(cephalin),* serine in phosphatidyl serine.

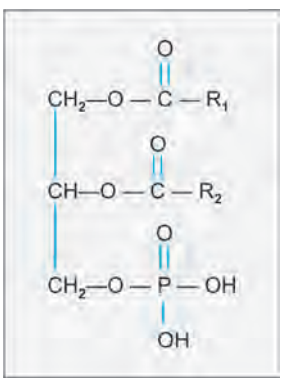


Fig. 2.7 Phosphatidic acid

  – Plasmalogens—They are similar to cephalin except that at C_1 instead of a fatty acid in ester linkage, it is an unsaturated aldehyde in ether linkage.
  – Sphingolipids—In sphingolipids, the alcohol is a long chain amino alcohol sphingol instead of glycerol of glycerophospholipids (Fig. 2.8).
  – The most important sphingophospholipid in our body is sphingomyelin which is a constituent of nervous tissue (Fig. 2.9).
  – It is made up of sphingosine, a fatty acid, phosphoric acid and choline.
  – It is present in the myelin sheath.

JAYPEE BROTHERS

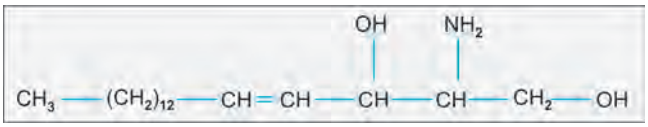


Fig. 2.8 Sphingol

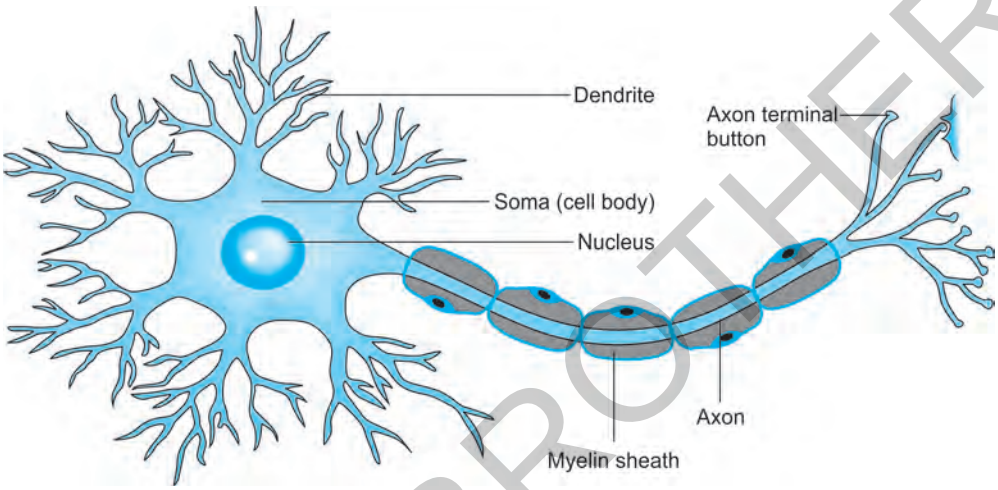


Fig. 2.9 Neuron with myelin sheath

JAYPEE BROTHERS

Functions of Phospholipids

- Phospholipids are present in the cell membrane as lipid bilayer and are responsible for the *semipermeability* of cell membrane.
- As component of *mitochondrial membrane,* phospholipids give the structural integrity to mitochondrial membrane and thus a proper site of oxidative phosphorylation.
- Phospholipids are *amphipathic,* thus required for *micellization* during lipids digestion.
- Dipalmitoyl lecithin *(DPL)* is present in alveoli as a surfactant and prevents the collapse of alveoli when they deflate. Its deficiency is seen in an inherited disorder—*Respiratory distress syndrome.*
- Phospholipids are components of *lipoprotein complexes,* therefore necessary for the synthesis of lipoproteins.
- Phospholipids of lipoproteins act like *coenzyme* for enzyme lipoprotein lipase (LPL) during metabolism of lipoproteins.
- Phospholipids like—lecithin, cephalin, plasmalogens are important components of *brain and nervous tissue.*
- *Cardiolipin* is a component of *mitochondrial membrane.*
- *Sphingomyelin* is necessary for the formation of *myelin sheath.*
- *Phospholipids of platelets* help in the process of blood coagulation.

Glycolipids

They contain carbohydrate moiety (glucose/galactose/NANA) in addition to Fatty acid and alcohol sphingosine. They are of 2 types:

Cerebrosides

They contain galactose as carbohydrate moiety

For example,
- Nervon – Nervonic acid
- Kerasin – Lignoceric acid
- Oxy nervon – Oxynervonic acid
- Cerebron – Cerebronic acid

– They are present in white matter of brain. They accumulate in the RE cells of spleen, liver, CNS in Gaucher's disease—an inherited disorder (Lipid storage disease) (Table 2.1).

Gangliosides

- They contain n-acetyl neuraminic acid, sphingosine, fatty acid and 3 carbohydrate moieties glucose/galactose. They are present in gray matter. Accumulate of gangliosides is seen in inherited disease Niemannpick's disease.

Lipoproteins

- Lipids are insoluble in water therefore for the transport of dietary lipids and lipids of endogenous origin lipids complex with proteins to form lipoprotein complexes. These lipoprotein complexes are HDLc, LDLc, VLDL and Chylomicron.
- The protein part is called apo protein. These apo protein have specific roles to play—
  – They help in recognition of the specific lipoprotein by its tissue receptor, i.e. act as ligand.
  – Some of the apo proteins act as a coenzyme and activate certain enzymes of lipid metabolism.
  – Structurally lipoproteins are made up of a central core of hydrophobic nonpolar lipids cholesterol esters and TGs and a peripheral coat of amphipathic lipids like—cholesterol, phospholipids with apo proteins attached either peripherally or integrally (Fig. 2.10).

Table 2.1 Important lipid storage diseases

Gaucher's	Glucosidase	Glucocerebroside	Hepatosplenomegaly, moderate anemia, bone deformities
Niemann Pick	Sphingomyelinase	Sphingomyelin	Mental retardation, hepatosplenomegaly, cherry red spot in macula and fatal in early life
Tay Sach's	Hexoseaminidase	Ganglioside GM2	Mental retardation, blindness, muscle weakness

JAYPEE BROTHERS

Types of Lipoproteins

- Lipoproteins are classified based upon their relative densities. Greater the lipid content as compared to apo protein, lesser the density and vice versa.
  - Chylomicron—Transports all dietary lipids to different body tissues and liver.
  - VLDL—Very low density lipoprotein—Transports endogenously synthesized TGs from liver to extra hepatic tissues.
  - IDL—Intermediate density lipoprotein—Formed as an intermediate of metabolism from VLDL to LDL.
  - LDL—Low density lipoprotein—Transports cholesterol from liver to extra hepatic tissues
  - HDL—High density lipoprotein—Transports cholesterol from extra hepatic tissues to liver as cholesterol esters.

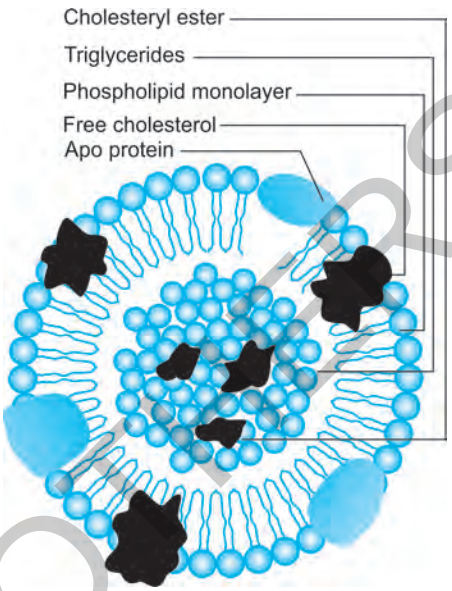


Fig. 2.10 Lipoprotein structure

Sulfolipids

- Sulfated derivatives of glycolipids are sulfolipids. They are abundantly found in the white matter of brain, e.g. Sulfogalactoceremide of myelin sheath.

A Quick Look at the Lipids

- ❖ Lipids are esters of fatty acids with alcohols.
- ❖ Lipids are classified into Simple, compound and derived lipids.
- ❖ Simple lipids are neutral lipids/ triglycerides—esters of fatty acids with glycerol.
- ❖ Compound lipids are esters of fatty acids with alcohol that may be glycerol or sphingol with some additional group.
- ❖ Derived lipids are derived by hydrolysis of simple and compound lipids and still retain properties of lipids.
- ❖ Important derived lipids are—essential fatty acids, cholesterol and glycerol.
- ❖ Essential fatty acids are important for normal growth and development and are essential in diet as they cannot be synthesized by the body.
- ❖ Deficiency of EFAs causes fatty liver owing to the blockage of VLDL synthesis by liver.
- ❖ Cholesterol plays important roles in steroid hormones synthesis, vitamin D synthesis, bile acid synthesis.
- ❖ Hypercholestrolemia causes atherosclerosis which is the prime cause of CVDs.
- ❖ Compound lipids like phospholipids and glycolipids are important in normal development of nervous system.
- ❖ Defects in metabolism of phospho and glycolipids cause lipid storage diseases.
- ❖ Oxidation of neutral lipids like oils causes their rancidity.

JAYPEE BROTHERS

for detailed information on biochemistry books, visit our website **www.jaypeebrothers.com,** for detailed information on biochemistry books, visit our website **www**

Essentials of Biochemistry

for BDS and Allied Life Sciences Students

Salient Features

- The book is written in a lucid manner and presents both theory as well as practical exercises
- It is highly illustrated to facilitate easy understanding of the subject
- It shall aid the readers, faculties and students alike to understand the various domains of biochemistry and its application in clinical side
- It meets the national standards for the understanding of biochemistry in dentistry and allied health sciences like nursing, physiotherapy, pharmacy, etc.
- It is a perfect blend of basic and advanced clinical biochemistry
- It shall serve as a lifelong companion for students pursuing career in biochemistry
- The practical section is summed up with selected viva-voce questions
- There is an elaborate glossary and reagent preparation guide included at the end of the book as a tabletop assistance during practical exercises.



Purvi Purohit MSc (Med) Biochemistry PhD (Med) Biochemistry is Assistant Professor, Department of Biochemistry, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India. She was awarded PhD (Med) Biochemistry by the Rajasthan University of Health Sciences, Jaipur, Rajasthan. She has more than 10 years of teaching and research experience. She has pursued her research in cardiovascular risk of thyroid disorders, diabetes mellitus and opium–dependent patients. She has published in several indexed peer-reviewed journals of national and international repute. Her research has been recognized at various national and international conferences namely—at 13th WCIRDC, Los Angeles 2012; 13th APFCB Bali, Indonesia, 2013; AACC 2014, Chicago, and AACC 2015, Atlanta.

Available at all medical bookstores or buy online at www.jaypeebrothers.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
BIOCHEMISTRY

ISBN 978-93-5250-146-5