hysiotherapy books, visit our website www.ejaypee.com, for detailed information on physiotherapy books, visit our website www.ejaypee.com, for detailed information on physiotherapy books,

Medical Biochemistry

for Physiotherapy Students



2nd Edition

Harpreet Kaur
Jagmohan Singh

Forewords
Kamaljit Singh
MS Sohal

JAYPEE

Contents

1. Introduction 1
2. Water and Electrolytes 5
3. Chemistry of Carbohydrates 11
4. Chemistry of Lipids 19
5. Chemistry of Amino Acids and Proteins 26
6. Chemistry of Nucleotides and Nucleic Acids 34
7. Enzymes 40
8. Vitamins 49
9. Bioenergetics 63
10. Digestion and Absorption 68
11. Metabolism of Carbohydrates 75
12. Metabolism of Lipids 92
13. Metabolism of Proteins 101
14. Minerals 109
15. Fluid and Electrolytes Balance and Imbalance 116
16. Biophysics 120
17. Metabolism of Specialized Tissues 126
18. Hormones 133
19. Diet and Nutrition 146
20. Radioactivity and Radioisotopes 152
21. Normal and Abnormal Constituents of Urine 157

Index *163*

CHAPTER 6

Chemistry of Nucleotides and Nucleic Acids

NUCLEOTIDES

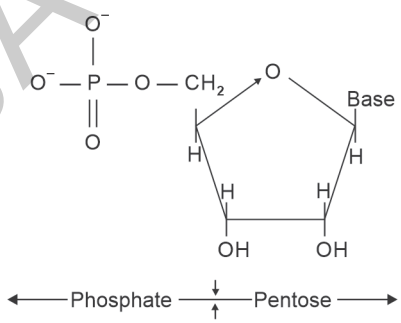
Nucleotides are energy rich compounds that drive metabolism (primarily biosynthesis) in all cells. They serve as chemical signals. They are structural components of a number of enzyme cofactors and metabolic intermediates.

Nucleic acids are biopolymers of high molecular weight with mononucleotide as their repeating units, just as amino acids are the repeating units of proteins. The nucleic acids are DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). DNA is found mainly on the chromatin of the cell nucleus whereas most of the RNA (90%) is present in the cell cytoplasm and a little (10%) in the nucleolus. The nucleic acids DNA and RNA are the molecular repositories for genetic information.

Components of Nucleotides

Nucleotides have three components:

a. A nitrogenous base
b. A pentose (sugar)
c. A phosphoric acid



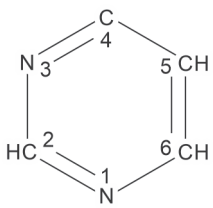
The General Structure of a Nucleotide

Nitrogenous Bases

The nitrogenous bases are derivatives of two parent compounds, pyrimidine and purine. Free purines and pyrimidines are weakly basic compounds and are thus called bases. The base is joined covalently (at N–1 of pyrimidines and N–9 of purines) in an N–glycosyl linkage to the 1 carbon of the pentose and the phosphate is esterified to the 5 carbon.

Pyrimidine bases

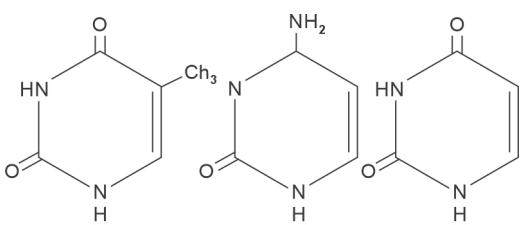
These are all derived from their parent heterocyclic compound pyrimidine.



Structure of a Pyrimidine Nucleus

Pyrimidine bases are three in number:

1. Cytosine (C)
2. Thymine (T)
3. Uracil (U)



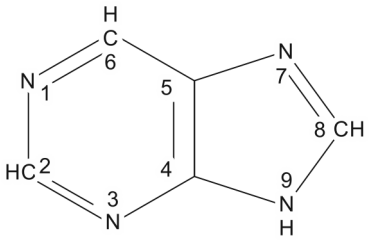
(a) Thymine (b) Cytosine (C) Uracil

Structure of Pyrimidine Bases

JAYPEE BROTHERS

Purine bases

Purine ring is more complex than the pyrimidine ring. It can be considered as the product of fusion of a pyrimidine ring with an imidazole ring.

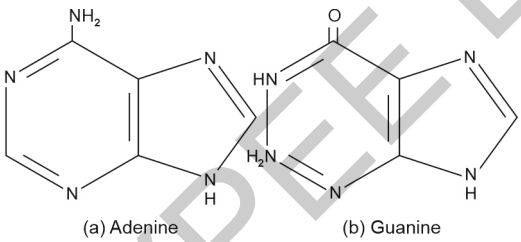


Structure of a Purine Nucleus

Purine bases are two in number:

1. Adenine (A)
2. Guanine (G)

Purine bases, i.e., adenine and guanine occur in both DNA and RNA. Pyrimidine bases, i.e., cytosine occurs in both DNA and RNA, thymine occurs in DNA only whereas uracil occurs in RNA only.



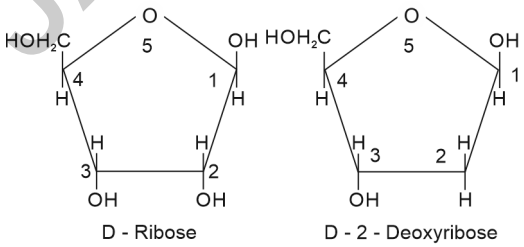
(a) Adenine (b) Guanine

Structure of a Purine Bases

Sugars (Pentoses)

Two kinds of pentoses are found in nucleic acids. The recurring deoxyribonucleotides units of DNA contain 2-deoxy-D-ribose and the ribonucleotide units of RNA contain D-ribose.

In nucleotides, both types of pentoses are in the form of their β-furanose structure (closed five membered ring structure).

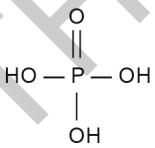


D - Ribose D - 2 - Deoxyribose

Structure of Pentoses

Phosphoric Acid

The molecular formula of phosphoric acid is H_3PO_4. It contains three monovalent hydroxyl groups and a divalent oxygen atom, all linked to the pentavalent phosphorous atom.



Structure of Phosphoric Acid

Nucleoside

A molecule composed of sugar (ribose or deoxyribose) and a base (purine or pyrimidine) without a phosphoric acid group. So, from this, nucleotides can be defined as phosphorylated nucleosides.

Example of nucleoside is adenosine present in RNA which contains purine base adenine and pentose sugar ribose. Another example is deoxyadenosine present in DNA which contains purine base adenine and pentose sugar deoxyribose. Similarly, other examples include guanosine, deoxyguanosine, etc.

Examples of nucleotides are AMP, dAMP, GMP, dGMP, CMP, dCMP, UMP and dTMP.

AMP (adenosine monophosphate) contains purine base adenine, pentose sugar ribose and one phosphate group. Nucleosides and nucleotides will be clearer from the table given **(Table 6.1)**.

So, it is clear from the above table that, DNA consists of adenine, guanine, cytosine, thymine, deoxy ribose sugar and phosphate and RNA consists of adenine, guanine, cytosine, uracil, ribose sugar and phosphate.

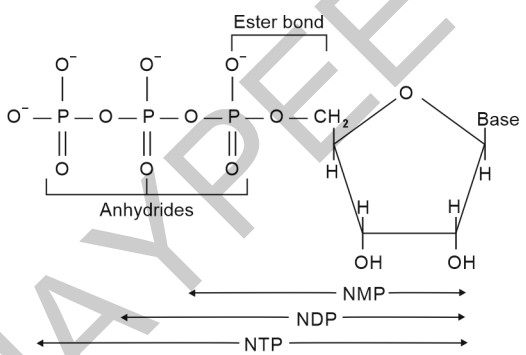
JAYPEE BROTHERS

Table 6.1: Nucleosides and nucleotides

Base	*Nucleoside*	*Nucleotide*	*Nucleic acid*
Adenine	Adenosine	AMP	RNA
	Deoxyadenosine	dAMP	DNA
Guanine	Guanosine	GMP	RNA
	Deoxyguanosine	dGMP	DNA
Cytosine	Cytidine	CMP	RNA
	Deoxycytidine	dCMP	DNA
Uracil	Uridine	UMP	RNA
Thymine	Deoxythymidine	dTMP	DNA

Functions of Nucleotides

1. They are the subunits of nucleic acids.
2. They carry chemical energy in cells. Nucleotides may have 1, 2 or 3 phosphate groups covalently linked at the 5'–OH of ribose. These are referred to as nucleoside monophosphate if they contain one phosphate group (NMP), nucleoside diphosphate if they contain two phosphate groups (NDP) and nucleoside triphosphate if they contain three phosphate groups (NTP).



Structure of Nucleotide Mono, Di and Triphosphates

3. Nucleoside triphosphates are used as a source of chemical energy to drive a wide variety of biochemical reactions.

   ATP is by far the most widely used, but UTP, GTP and CTP are used in specific reactions.

   The hydrolysis of ATP and the other nucleoside triphosphates is an energy yielding reaction because of the chemistry of triphosphate structure.

   The bond between the ribose and the phosphate is an ester linkage. The α–β and β–α linkages are phosphoric acid anhydrides. Hydrolysis of the ester linkage yields about 14 kJ/mol, whereas hydrolysis of each of the anhydride bonds yields about 30 kJ/mol.
4. Nucleotides are components of many enzyme cofactors. A variety of enzyme cofactors serving a wide range of chemical functions includes adenosine as a part of their structure. In these cofactors, the adenosine portion does not play part directly in the primary function, but removal of adenosine from these structures generally results in drastic reduction of their activities.
5. Some nucleotides are the intermediates in cellular communication. Cells respond to their environment by taking cues from hormones or other chemical signals in the surrounding medium. The interaction of these extra cellular chemical signals (first messengers) with receptors on the cell surface lead to the production of second messengers inside the cell, which in turn lead to adaptive changes in the cell interior. Second messenger is a nucleotide. One

JAYPEE BROTHERS

of the most common is the nucleotide 3', 5'-cyclic adenosine monophosphate (3', 5'-cAMP).

Structure of Nucleic Acid

1. **Primary structure:** The primary structure of a nucleic acid is its covalent structure and the nucleotide sequence.
2. **Secondary structure:** Any regular, stable structure taken up by some or all of the nucleotides in a nucleic acid can be referred to as secondary structure.
3. **Tertiary structure:** The complex folding of large chromosomes within the bacterial nucleoid and eukaryotic chromatin is considered as tertiary structure.

Chargaff's Rule

The base composition of DNA generally varies from one species to another.

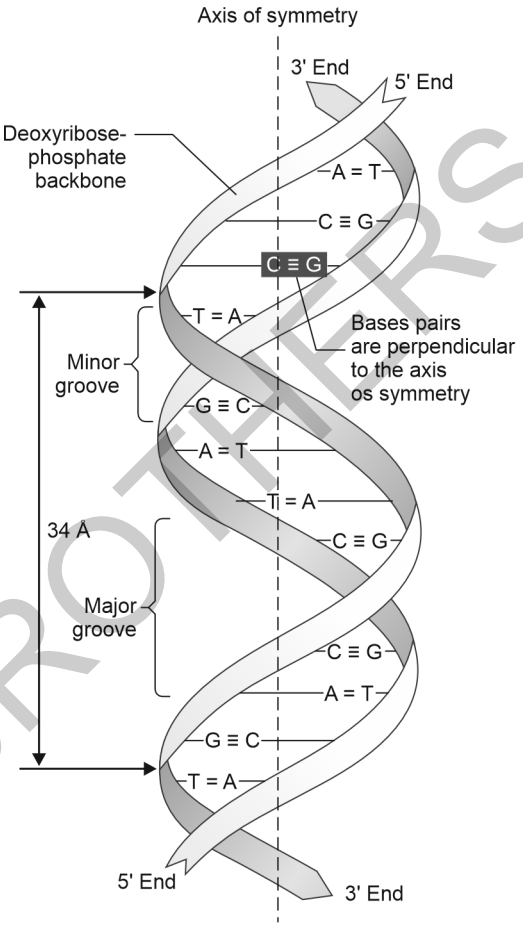
1. DNA isolated from different tissues of the same species has the same base composition.
2. The base composition of DNA in a given species does not change with the organism's age, nutritional state or change of environment.
3. Sum of purine residues equals the sum of pyrimidine residues.

$$A + G = T + C$$

Structure of DNA

DNA is a double helix. DNA contains recurring units of adenine, guanine, cytosine, thymine, deoxyribose sugar and phosphate. It is a polynucleotide.

DNA consists of two helical DNA chains coiled around the same axis to form a right-handed double helix. The two helices are wound in such a way so as to produce two interchain spacings or grooves, a major (or wide) groove and a minor groove (or narrow) groove.



DNA double helix, illustrating some of its major structural features

The two chains/strands of the helix are antiparallel, i.e., one strand runs in the 5'–3' direction and the other in the 3'–5' direction.

The diameter of the helix is 20 Å. The bases are 3.4 Å apart along the helix axis and are related by a rotation of 36°. Therefore, the helical structure repeats after 10 residues on each chain, i.e., at intervals of 34 Å. In other words, each turn of the helix contains 10 nucleotide sequences.

The backbones of alternating deoxyribose and negatively charged phosphate groups are on the outside of the double helix and

JAYPEE BROTHERS

the bases (purines and pyrimidines) of both strands are stacked inside the double helix. The planes of the bases are perpendicular to the helix axis. The planes of the sugars are almost at right angles to those of the bases.

The two chains are held together by hydrogen bonds between pairs of bases. Adenine always pairs with thymine by two hydrogen bonds and guanine with cytosine with three hydrogen bonds. This specific positioning of the bases is called base complementarity.

The DNA double helix or duplex is held together by two sets of forces:

1. Hydrogen bonding between complementary base pairs.
2. Base-stacking interactions.

Different structural forms of DNA

Many significant deviations from the Watson–Crick structure of DNA are found in cellular DNA and these may play important roles in DNA metabolism. These structural variations do not affect the key properties of DNA as defined by Watson and Crick. Different forms are:

1. B—DNA
2. A—DNA
3. Z—DNA

The Watson–Crick structure is also referred to as B–form of DNA. The B–form is the most stable structure. A–DNA is right handed helix. Z–DNA is left-handed helix.

In A–DNA, rise per base pair is 0.23 nm and number of base pair per helical turn is 11. In Z–DNA, rise per base pair is 0.38 nm and number of base pair per helical turn is 12.

Denaturation of DNA

Solutions of carefully, isolated native DNA are highly viscous at pH 7.0 and room temperature (20–25°C). When such a solution is subjected to extremes of pH or to temperatures above 80–90°C, its viscosity decreases sharply, indicating that DNA has undergone a physical change. This involves disruption of hydrogen bonds between the paired bases and the interactions between the stacked bases. As a result, double helix unwinds to form to single strands. No covalent bonds in the DNA are broken.

Renaturation of DNA is a rapid one step process. When the temperature or pH is returned to the biological range, the unwound segments of the two strands spontaneously rewind or anneal to yield the intact duplex. However, if the two strands are completely separated, renaturation occurs in two steps. The first step is relatively slow, because the two strands must first find each other by random collisions and form a short segment of complementary double helix. The second step is much faster: the remaining unpaired bases successively come into register as base pairs, and the two strands zipper themselves together to form the double helix.

Each species of DNA has a characteristic denaturation temperature or melting point: the higher its content of G≡C base pairs, the higher the melting point of the DNA. This is because G≡C base pairs, with three hydrogen bonds are more stable and require more heat energy to dissociate than A=T base pairs.

Circular DNA

In certain microorganisms, such as bacteria and bacteriophages, the DNA molecule does not possess free 3' and 5' ends but the two ends of the molecule are joined together forming a circular DNA.

Cellular functions of DNA

DNA controls every aspect of cellular function.

1. It makes copies of itself as a cell divides and thus transfers genetic information from one generation to the next known as replication.
2. DNA also determines the properties of a living cell and regulates biological information by control of protein synthesis. This flow of biological information from one class of nucleic acid to another, i.e., from DNA to RNA is known as transcription and from there to protein is called translation.

JAYPEE BROTHERS

DNA molecule thus serves as a template, both for the transcription of information from RNA as well as for the replication of information into daughter DNA.

Genetic code

The genetic code is dictionary that gives the correspondence between a sequence of nucleotide bases and a sequence of amino acids. Each individual word in the code is composed of three nucleotide bases. These genetic words are called codons.

The four nucleotide bases are used to produce the three base codons. There are therefore, 64 different combinations of bases taken three at a time (4^3).

Characteristics of genetic code

1. **Specificity:** The genetic code is specific—that is, a specific codon always code for the same amino acid.
2. **Universality:** The genetic code is universal (with a few minor exceptions)—that is, the specificity of the genetic code has been conserved from very early stages of evolution, with only slight differences in the manner the code is translated.
3. **Redundancy:** The genetic code is redundant (sometimes called degenerate). Although each codon corresponds to a single amino acid, a given amino acid may have more than one triplet coding for it. For example, arginine is specified by six different codons.
4. **Nonoverlapping and commaless:** The genetic code is nonoverlapping and commaless, i.e., the code is read from a fixed starting point as a continuous sequence of bases, taken three at a time. For example, ABCDEFGHIJKL….is read as ABC/DEF/GHI/JKL….without any punctuation between the codons.

JAYPEE BROTHERS

for detailed information on physiotherapy books, visit our website www.ejaypee.com, for detailed information on physiotherapy books, visit our website www.ejaypee.com, for detailed inform

Medical Biochemistry
for Physiotherapy Students

Salient Features

- The book is very simple in language.
- It covers all the necessary aspects for Bachelor of Physiotherapy students.
- Painstaking presentation of the text is provided.
- There is lucid presentation of diagrams and pictures.
- It covers the syllabi of all the important universities.
- It is the first and only of its kind in India.

Harpreet Kaur MSc (Medical Biochemistry) PhD is graduated and postgraduated from Government Medical College, Amritsar, Punjab, India, in the subject of Medical Biochemistry. She completed her PhD under the Faculty of Medicine at Punjabi University, Patiala, Punjab. She has several years of experience in teaching and training Physiotherapy, Nursing, and Paramedical students.

Jagmohan Singh Postdoctoral Fellow PhD has acquired international experience by successfully completing a Postdoctoral Fellowship from the Department of Physical Therapy, Faculty of Medicine, University of Toronto and Toronto Rehabilitation Institute, Canada. He has worked as Dean, Faculty of Physiotherapy and Chairman, Board of Studies in Physiotherapy at Baba Farid University of Health Sciences, Faridkot, Punjab, India. He has also worked as a Professor and Principal at Gian Sagar College of Physiotherapy and Adesh University, Punjab. He is a fellow member of The Indian Association of Physiotherapists and a life member of the Indian Association of Sports Medicine. He has been awarded the Significant Contribution Award and IAP Oration Award by The Indian Association of Physiotherapists. He is on the panel of several national and international universities for various graduate, postgraduate, and doctoral-level courses. He has supervised several doctoral and master-level students. He has worked as Editor-in-Chief of the official journal of The Indian Association of Physiotherapy and Editor-in-Chief of Baba Farid University Physiotherapy Journal. He is a member of the International Society of Medical Journal Editors. He has achieved a very high academic record at a very young age. He has a good command of the subject and has achieved distinction in the subject of Electrotherapy from the National Institute of Rehabilitation Training and Research, Olatpur, Cuttack, Odisha, India. He completed his postgraduation from Guru Nanak Dev University, Punjab, and topped the University Postgraduation Entrance Examination. He earned his Doctor of Philosophy Degree from the Faculty of Medicine, Punjabi University, Patiala, Punjab, and completed a Postdoctoral Fellowship from the Department of Physical Therapy, Faculty of Medicine, University of Toronto and Toronto Rehabilitation Institute, Ontario, Canada.

Buy from ejaypee

JAYPEE BROTHERS

Shelving Recommendation
PHYSIOTHERAPY

ISBN 978-93-6616-569-1

9 789366 165691