Nucleic Acids

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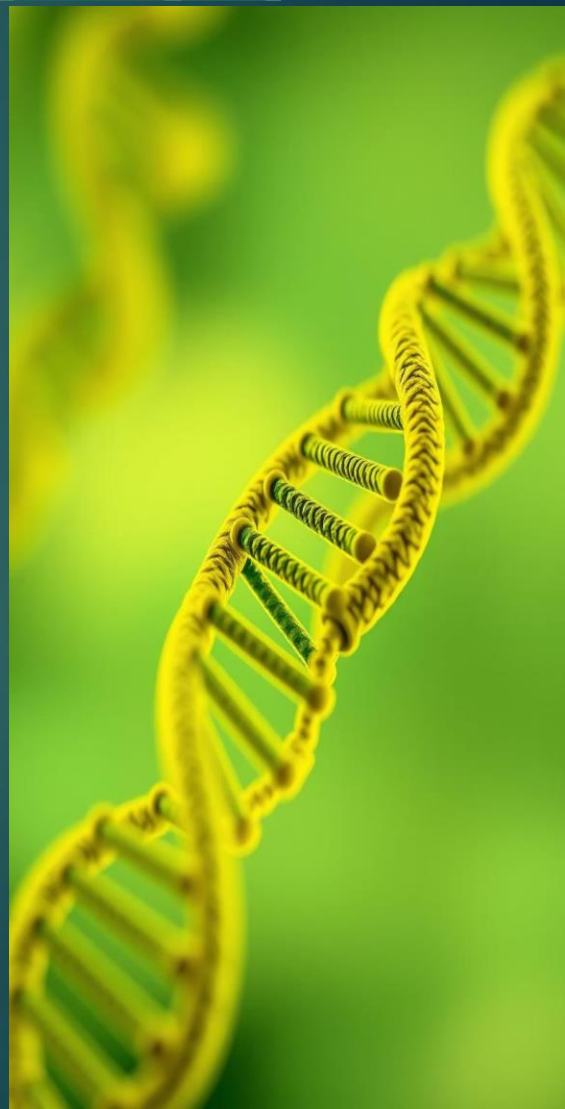
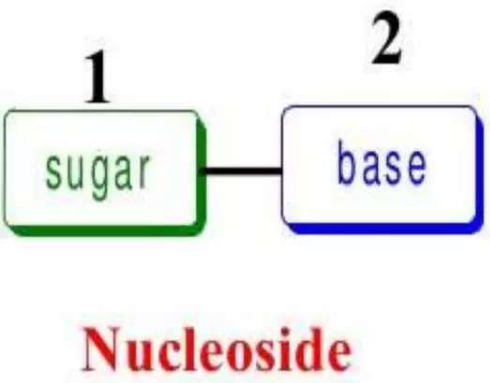


Historical Background

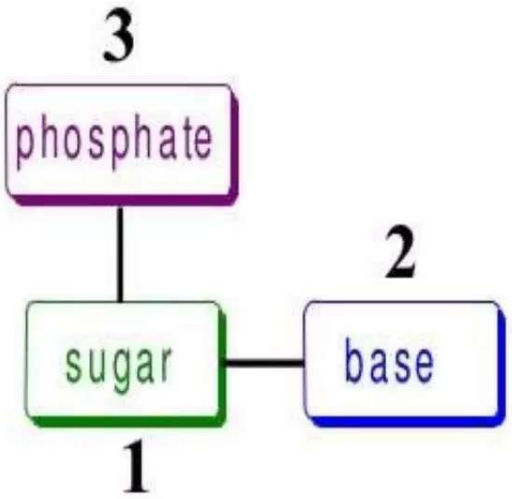
- - 1869: Friedrich Miescher discovered 'nuclein'
- - 1944: Avery, MacLeod, McCarty showed DNA as genetic material
- - 1953: Watson & Crick proposed DNA double helix

WHAT ARE NUCLEIC ACIDS?

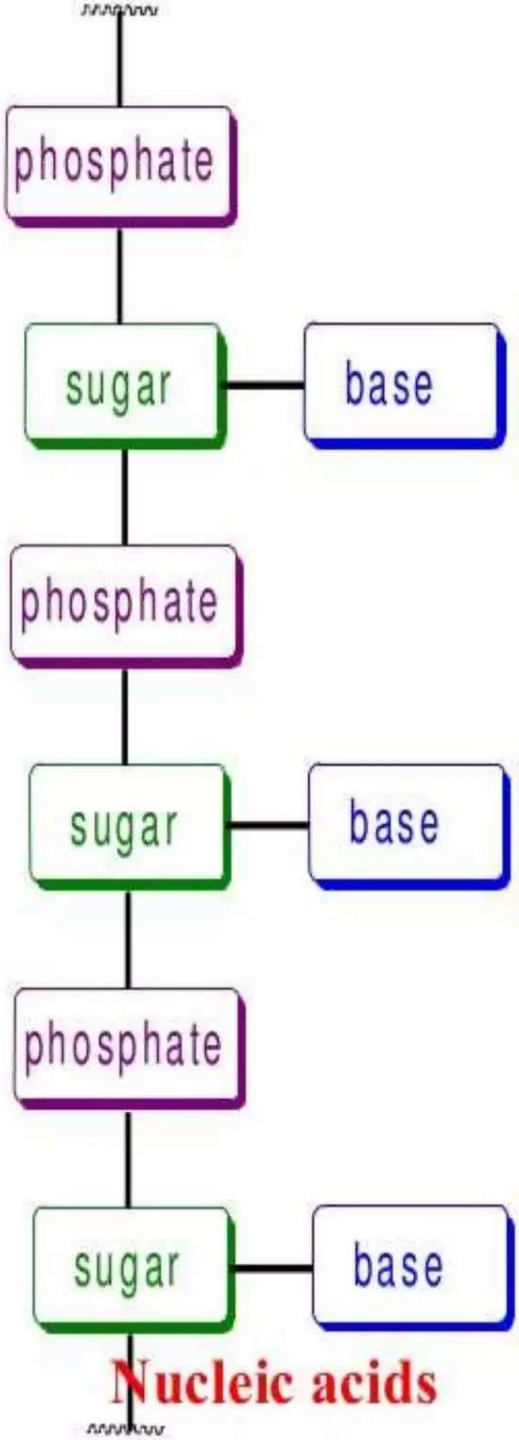
- Nucleic acids are polymers of a specific sequence of monomeric units called **nucleotides**, which are linked together through **3', 5' phosphodiester bonds.**



Nucleoside



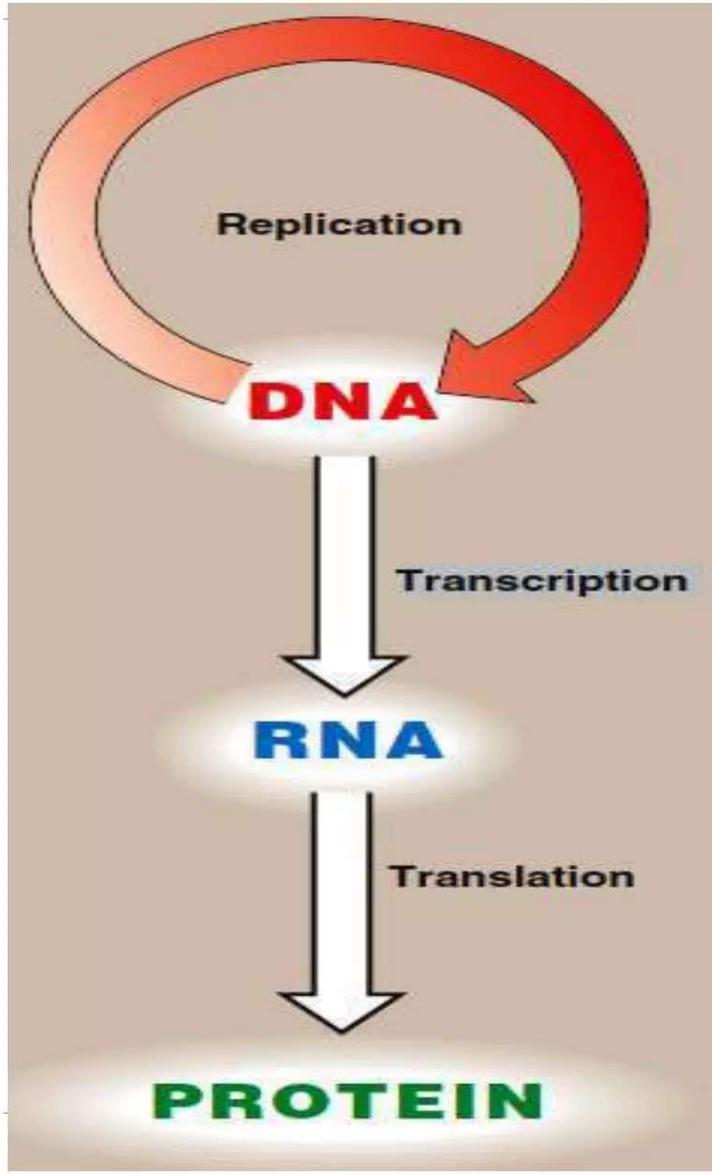
Nucleotides



Nucleic acids

- There are two type of nucleic acids:
- **Deoxyribonucleic acid (DNA)**
- **Ribonucleic acid (RNA)**

- Nucleic acids serve as **repositories** and **transmitters** of genetic information.



FUNCTIONS OF NUCLEIC ACIDS

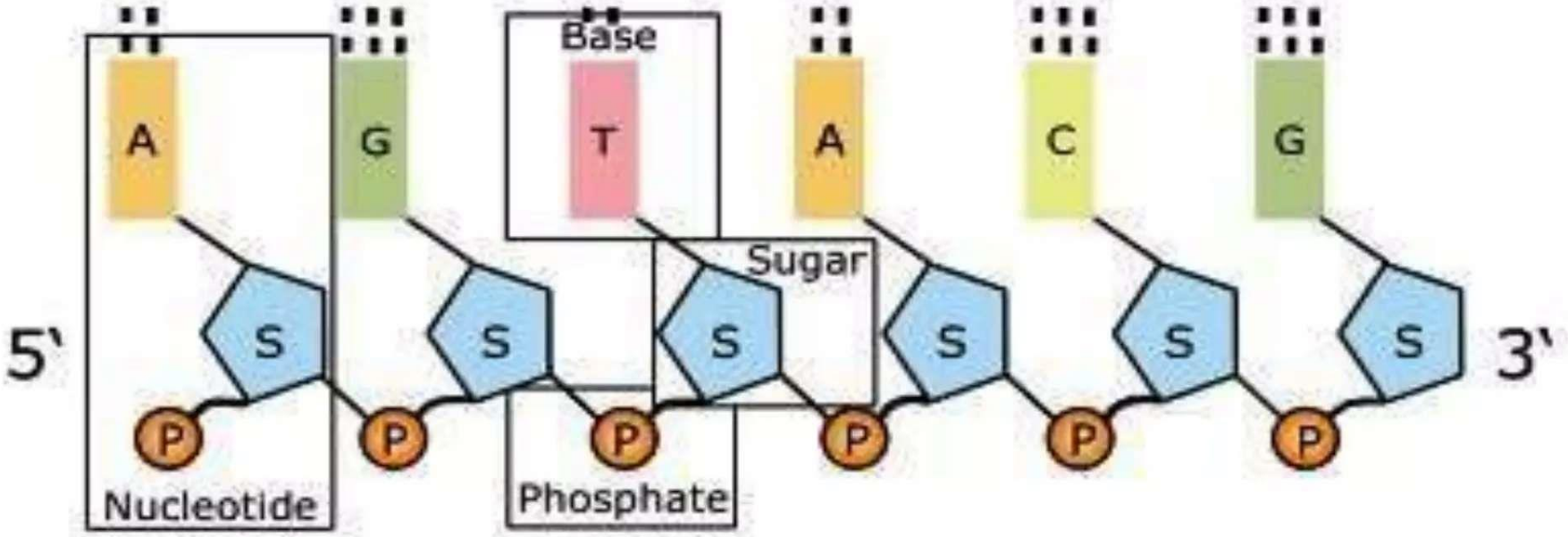
- DNA is the chemical **basis of heredity**.
- **Reserve bank** of genetic information.
- Responsible for **maintaining the identity of different species** of organisms over millions of years.
- **Cellular function** is under the control of DNA.
- The basic information pathway.
- DNA directs the **synthesis of RNA**, which in turn **directs protein synthesis**.

BASIC NUCLEIC ACID STRUCTURE

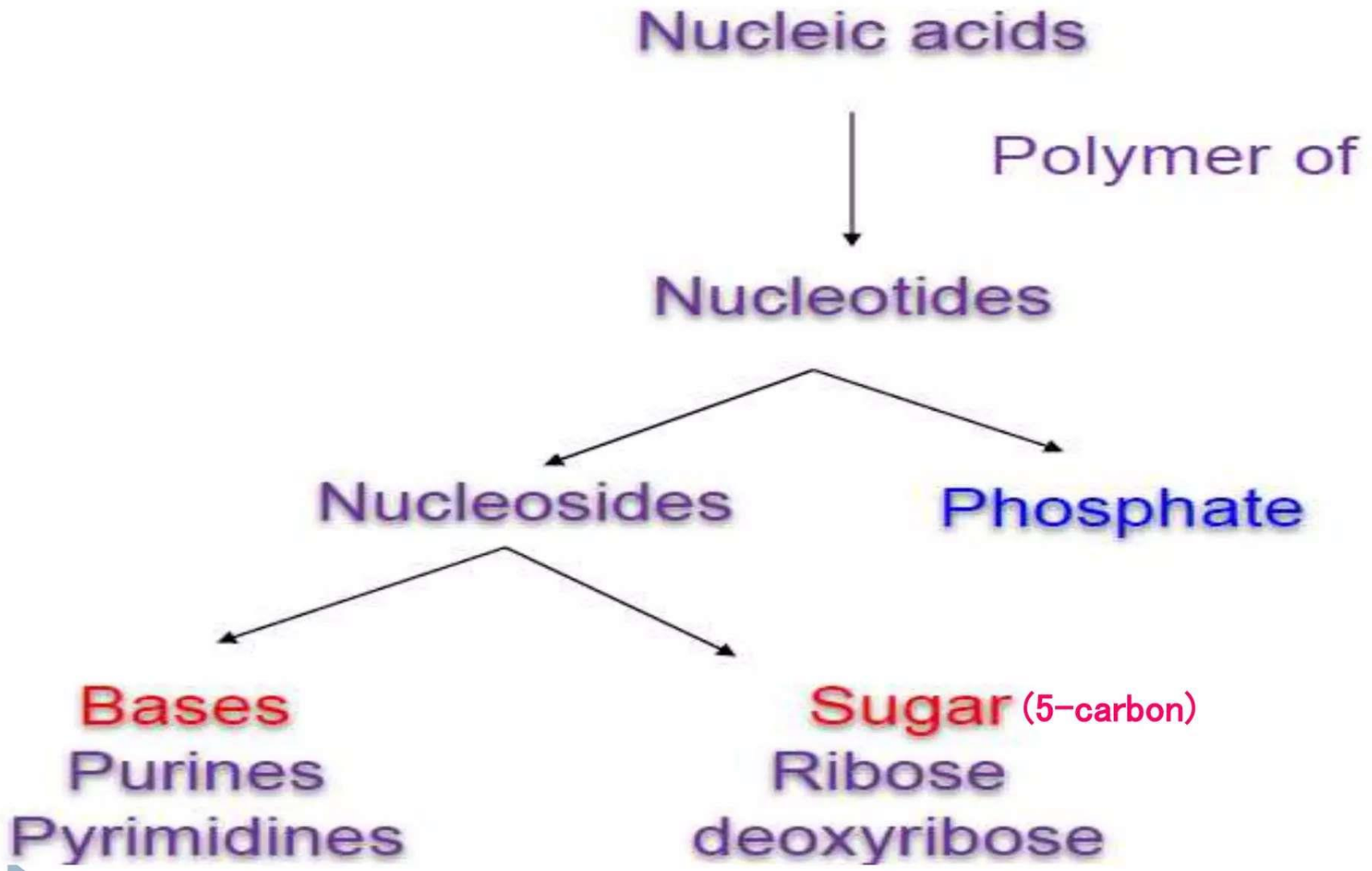
POLYMERS of NUCLEOTIDES

↓ Held by

5' and 3' SUGAR PHOSPHATE BRIDGES



COMPOSITION OF NUCLEIC ACIDS



NUCLEOTIDES

- Nucleotides are the **building blocks of nucleic acid.**
- A nucleotide consists of three parts:

1. Heterocyclic base

2. Sugar

3. Phosphate

NUCLEOSIDE

- The molecules **without phosphate group** is called **nucleoside.**

- The nitrogenous bases of nucleic acids are derivatives of two parents compounds **Purines and Pyrimidines**.

- The nitrogenous base of nucleotide is linked covantly to pentose sugar by β-N-glycosidic bond, almost always to N-1 of a pyrimidine or to N-9 of a purine.

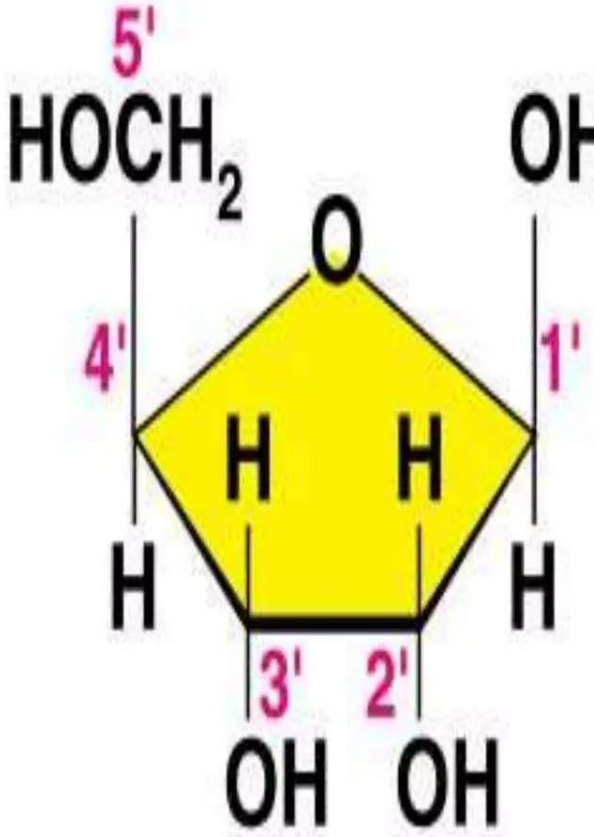
FUNCTIONS OF NUCLEOTIDES

- **Activated precursors** of DNA & RNA.
- ATP – Universal **currency of energy**.
- GTP-involved in **protein biosynthesis** as source of energy.
- **Activation of metabolic intermediates** in many biosynthetic pathway-e.g.UDP-glucose & CDP-diacylglycerol.
- **Carrier of methyl group:** e.g., SAM (S-adenosylmethionine).
- **Components of coenzymes**: NAD, FAD & CoA.
- **Metabolic regulators & chemical messengers** e.g. cAMP, cGMP.

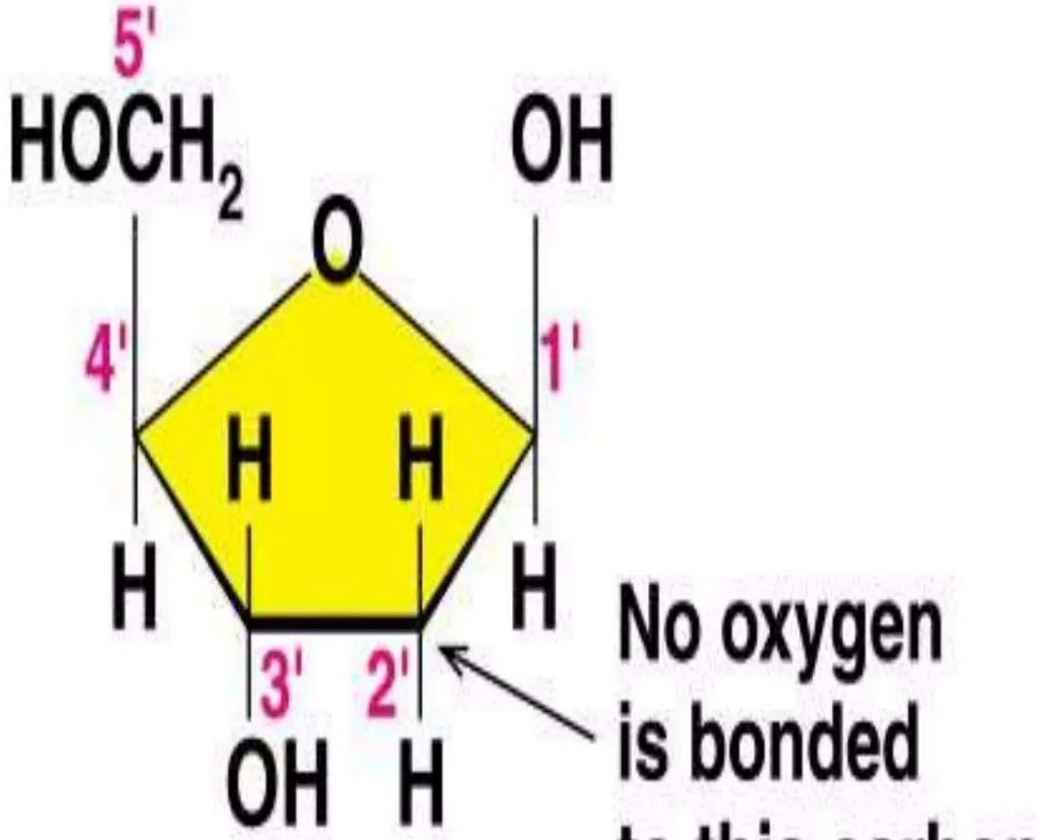
SUGAR in nucleotide

- Nucleic acid have two kinds of **PENTOSES.**
- Ribonucleotides of RNA contain **β-D-ribose.**
- Deoxyribonucleotides of DNA contain **β-2'-deoxy-D-ribose.**
- The prefix ***deoxy - means "without oxygen"*** . Nucleotides can be hydrolyzed to yield nucleosides and phosphoric acid.

Pentose sugars in RNA and DNA



Ribose in RNA

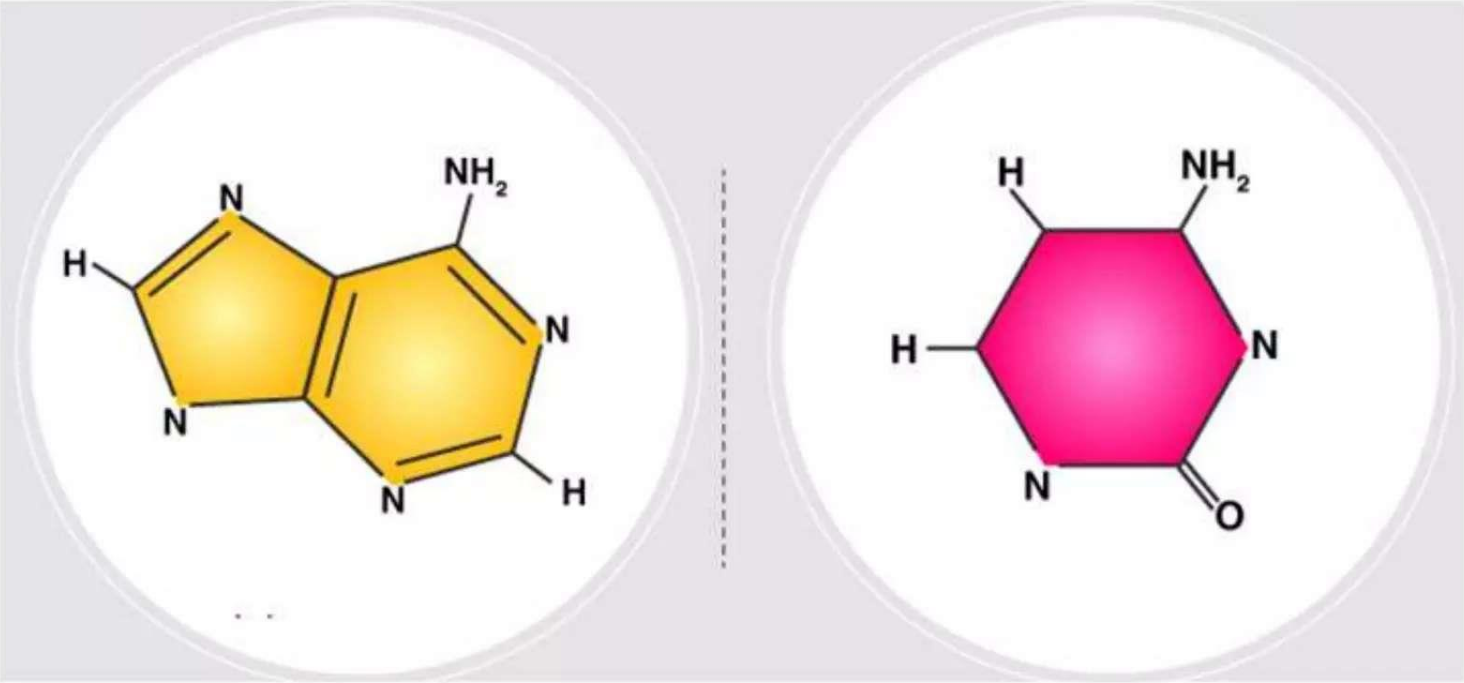


Deoxyribose in DNA

HETEROCYCLIC BASES

- **Nitrogenous Bases** present in nucleic acids are divided into two types-

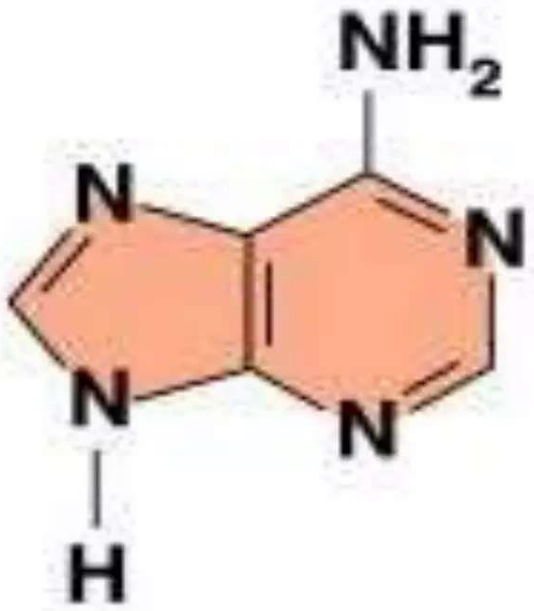
1. **PURINES** 2. **PYRIMIDINES**



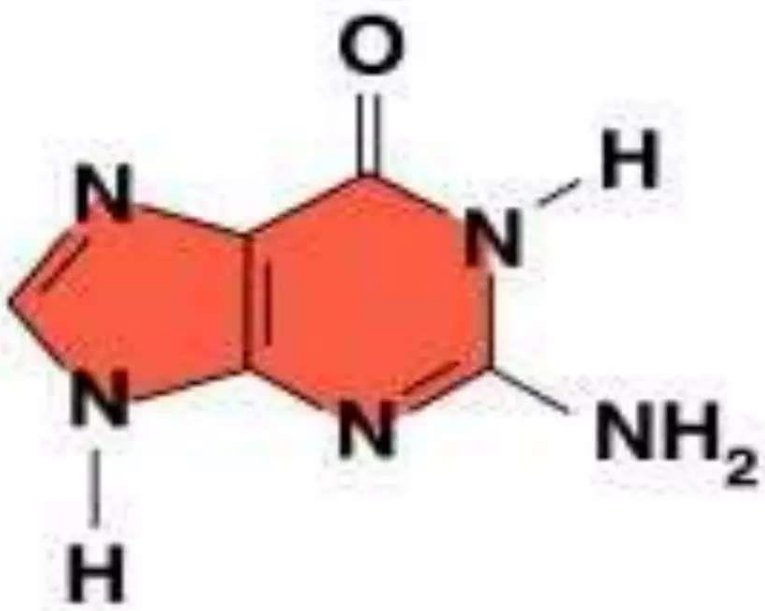
PURINE BASES

- Two principle purines bases are present in both DNA and RNA-

1. **ADENINE (A)**
2. **GUANINE (G)**



Adenine (A)
(DNA and RNA)

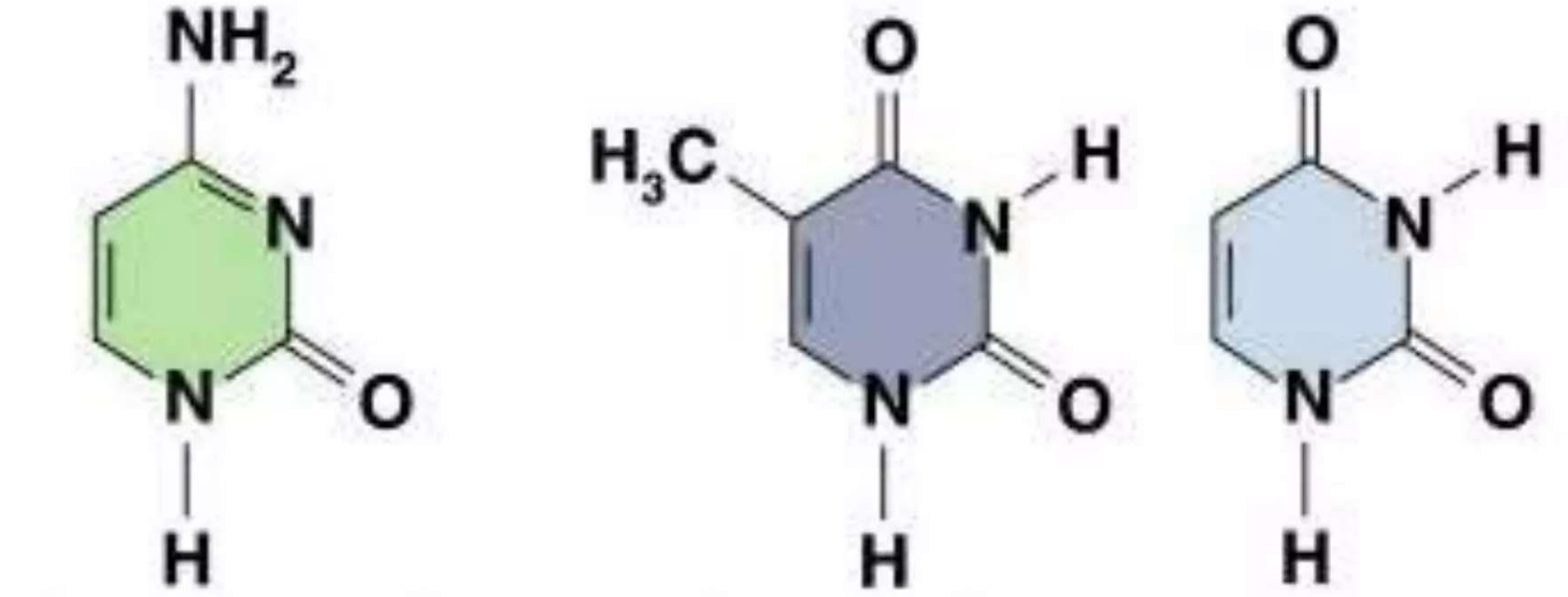


Guanine (G)
(DNA and RNA)

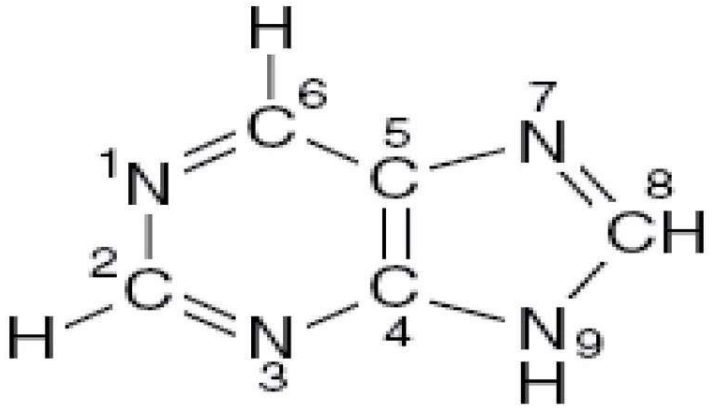
PYRIMIDINE BASES

- The major pyrimidine bases are-

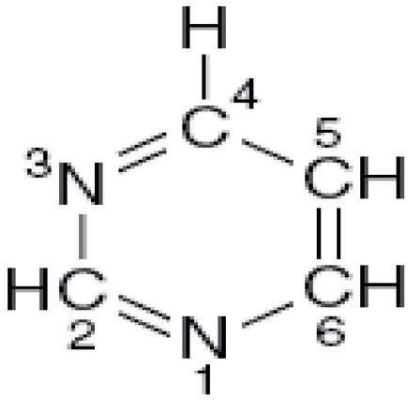
1. **Cytosine (C)**
2. **Uracil (U)**
3. **Thymine (T)**



PURINES AND PYRIMIDINES



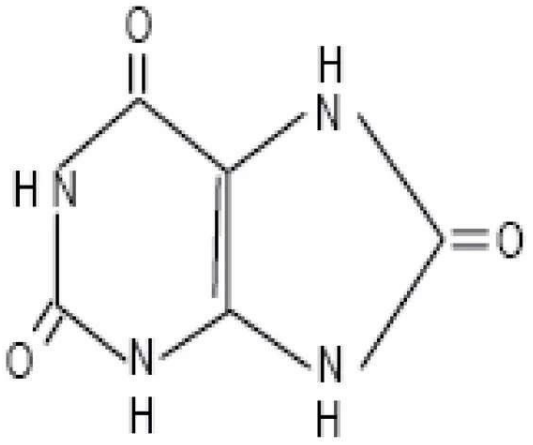
Purine



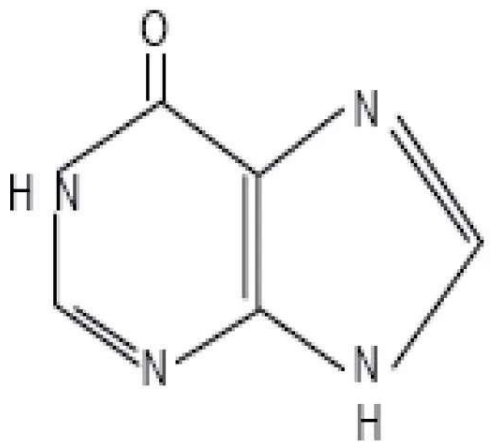
Pyrimidine

- Purines and pyrimidines are **AROMATIC HETEROCYCLIC COMPOUNDS** contain both carbon and other elements (hetero atoms).

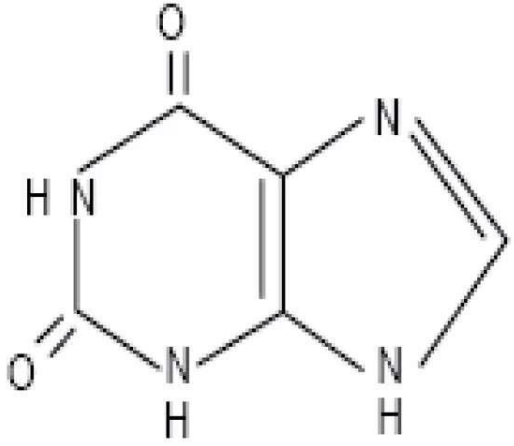
BIOLOGICALLY IMPORTANT BASES



Uric acid (2, 6, 8 trioxy purine)



Hypoxanthine (6–oxy purine)



Xanthine (2, 6–dioxy purine)

URIC ACID is another purine base. It is the end product of purine nucleotide catabolism.

Other Purine bases are HYPOXANTHINE & XANTHINE. They are intermediates in the formation of ADENINE & GUANINE nucleotides.

Base + sugar are nucleosides

Ribonucleosides

Adenine	**+**	**Ribose**	**→**	**Adenosine**
Guanine	**+**	**Ribose**	**→**	**Guanosine**
Uracil	**+**	**Ribose**	**→**	**Uridine**
Cytosine	**+**	**Ribose**	**→**	**Cytidine**

Deoxy ribonucleosides

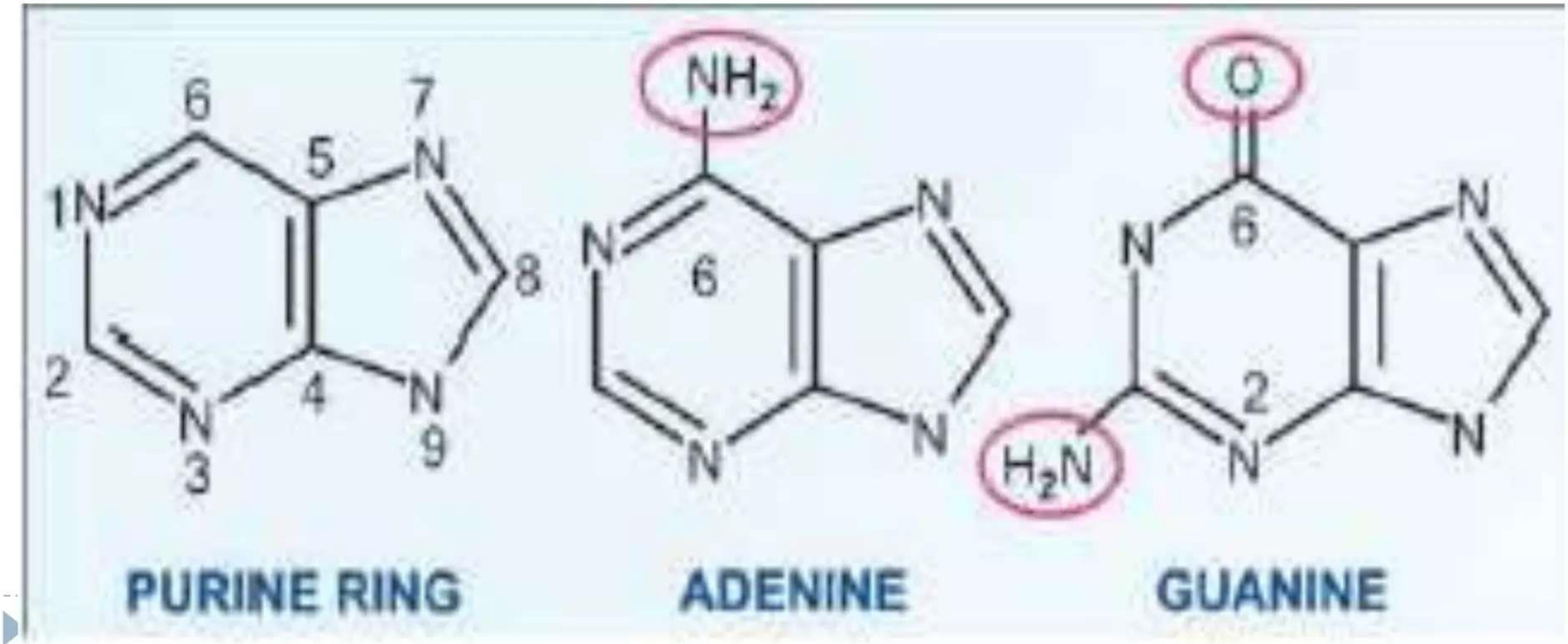
Adenine	+	Deoxy ribose	→	Deoxy adenosine (d-adenosine)
Guanine	+	Deoxy ribose	→	d-guanosine
Cytosine	+	Deoxy ribose	→	d-cytidine
Thymine	+	Deoxy ribose	→	d-thymidine

PURINES

- Purine bases are nine membered ring structures consisting of **pyrimidine ring fused to imidazole ring.**
- The atoms of purine ring are numbered in the *anticlockwise manner.*

- **Adenine** has an amino group (-NH2) on the C6 position of the ring.

- **Guanine** has an amino group at the C2 position and carbonyl group at the C6 position.



Minor Purines Present Nucleic Acids

- Several minor & unusual bases are often found in DNA & RNA.
- These include

  5-methylcytosine,

  N4-acetylcytosine,

  N6 methyladenine,

  N6 dimethyl adenine

  N7 methylguanine.

Importance:

- The unusual bases in nucleic acids help in the recognition of specific enzymes.

Purine Bases Of Plants

- Plants contain certain methylated purines.

Caffeine in **coffee**.

It acts as a **stimulant**.

Theophylline in **tea leaves**.

It acts as a **bronchial smooth muscle relaxant**.

Theobromine in **cocoa**

It acts as **vasodilator ,lower blood pressure**

PURINE ANALOG

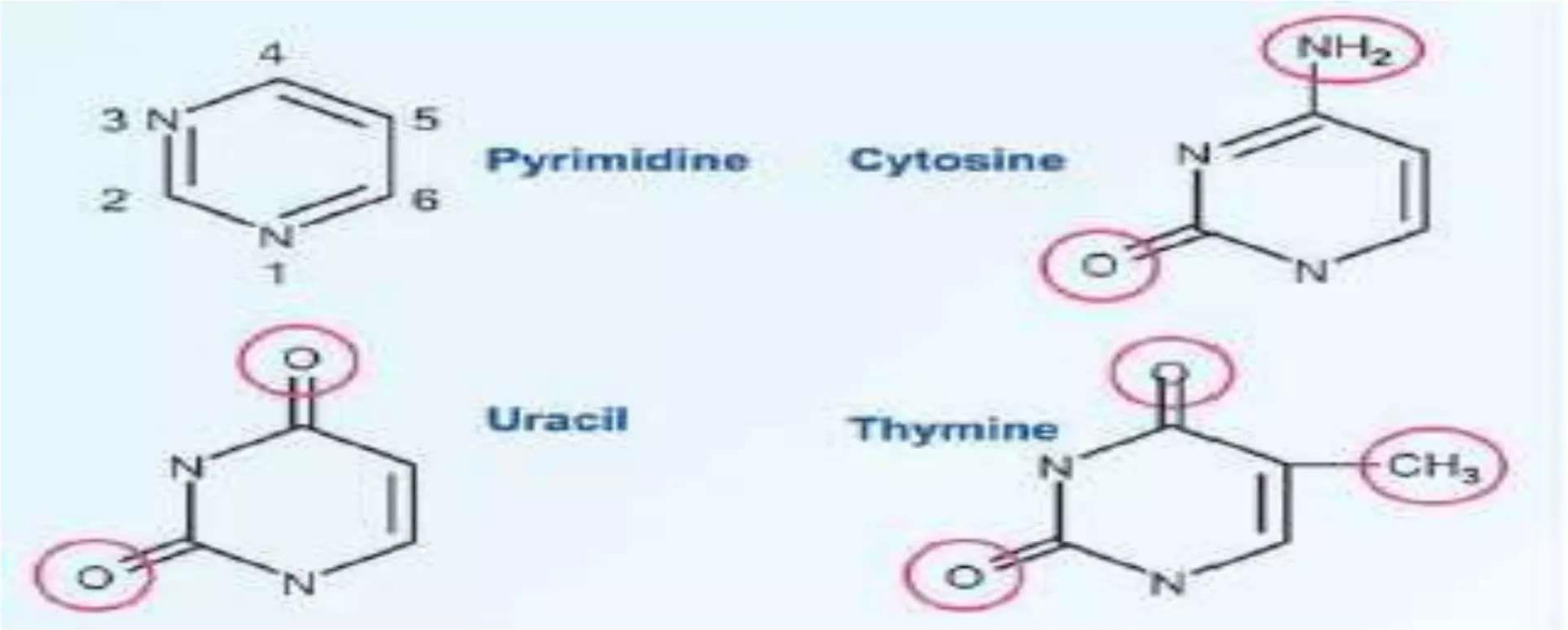
- They have structural similarities but inhibit the enzymes involved in the metabolism of purine nucleotides.

1. **ALLOPURINOL:**
   - Inhibits xanthine oxidase & used in the treatment of hyperuricemia (gout).
2. **6-MERCAPTOPURINE:**
   - It inhibits purine nucleotide synthesis & used as an anticancer drug.
3. **METABOLIC INTERMEDIATES**:
   - These are formed during metabolism of nucleotides
   - E.g. hypoxanthine, xanthine & uric acid.

PYRIMIDINE BASES

- Pyrimidines contain six membered nitrogenous ring.
- The atoms in pyrimidine ring are numbered in clockwise direction.

- **Thymine** contains a methyl group at C5 position with carbonyl groups at C4 and C2 positions.
- **Cytosine** contains a carbonyl group at C2 position an amino group at C4.



Minor (Unusual) Pyrimidines

- Methylcytosine present in DNA
- Dihydrouracil present in tRNA.

PYRIMIDINE ANALOGS:

- They have structural similarities but act as inhibitors of enzymes or interact with nucleic acids.

1. **5-fluorouracil:**

- It inhibits the enzyme thymidylate synthase.
- It is used in the treatment of cancer.

Minor/Unusual Bases

- Specific DNA and RNA contains small quantities of Minor/modified bases also.
- These modifications includes-

- Methylation
- Hydroxymethylation
- Glycosylation
- Alteration of atoms

Minor/Unusual base

- Modification of Adenine:
  - N-methyladenine,
  - N6N6- dimethyladenine
- Modification of Guanine:
  - 7-methylguanine
- Modification of Cytosine:
  - 5-methylcytosine
  - 5-hydroxymethylcytosine
- Modification of Uracil:
  - Dihydroxyuracil