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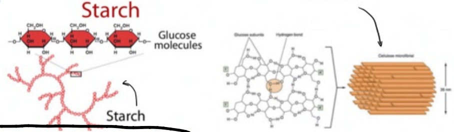
carbohydrates

The name «carbohydrates» means «hydrates of carbons» as many of them have the formula $C_n(H_2O)_m$.

Glucose: $C_6H_{12}O_6$ $C_6(H_2O)_6$

They can form polymers and are used to store energy in living beings (starch, glycogen), as support structures in plants (cellulose), and are essential components of nucleic acids (DNA and RNA).



Carbohydrates can form polymers. Depending on their lenght, they can be classified as:

carbohydrates
- Monosaccharides (1 unit)
- disaccharides (2)
- Oligosaccharides (few units) (2-10)
- Polysaccharides (many units)

Monosaccharides

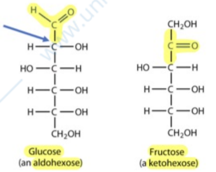
Simple sugars

Cannot be further hydrolyzed into simple carbohydrates

Building blocks of oligo and polysaccharides

At the molecular level, they are polyhydroxyaldehydes or polyhydroxyketones.

Stereochemistry is indicated by Fischer notation.



! The chemical behaviour of carbohydrates is complicated by the presence of multilpe chiral centers.

Monosaccarides:
Series of natural aldoses

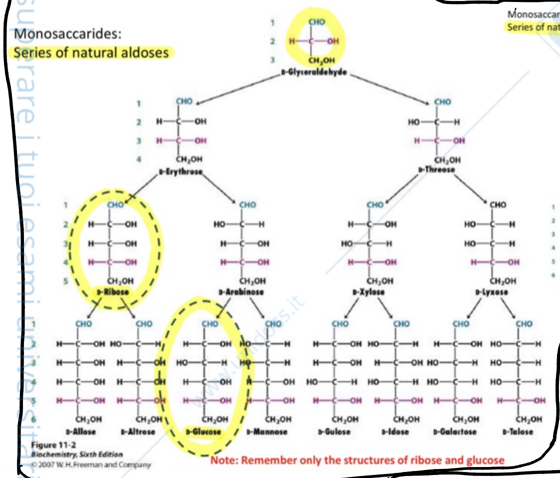


Figure 11-2
Biochemistry, Sixth Edition
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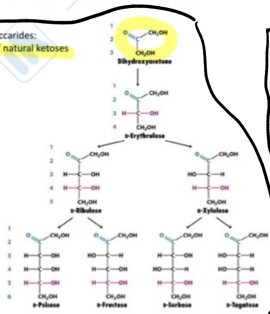
Note: Remember only the structures of ribose and glucose

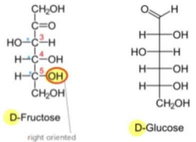
Monosaccarides:
Series of natural ketoses



D and L monosaccharides

D – L notation describes the configuration of the chiral carbons of a monosaccharide. It uses as reference the penultimate carbon.

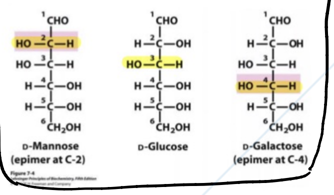
If written in the Fisher projection, with the oxidized part «up», D monosaccharides have the OH group of the penultimate carbon on the right, L have it on the left.



Most common monosaccharides are D.

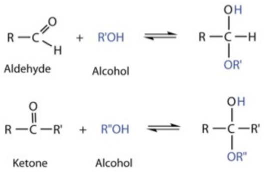
Epimers

Two isomers differing in configuration at only one chiral center (i.e. two diastereoisomers).

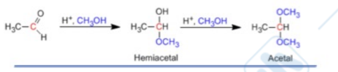


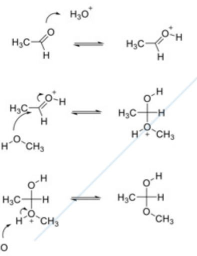
The cyclic structure of monosaccharides

So far we have represented monosaccharides as linear molecules, but many of them also adopt cyclic structures. This conversion occurs because of the ability of aldehydes and ketones to react with alcohols.



Addition of 1 or 2 alcohols to a carbonyl group forms an hemiacetal or an acetal, respectively.



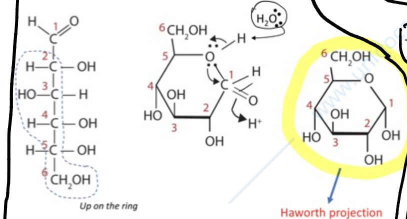


1) Protonation of the carbonyl oxygen

2) Nucleophylic attack of alcohol

3) Deprotonation

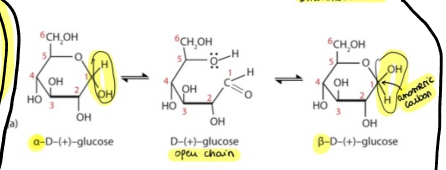
Formation of the cyclic structure of glucose



Formation of a hemiacetal. This reaction is catalyzed by acids.

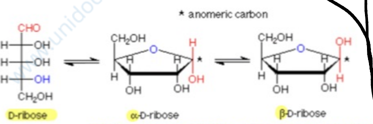
The reaction involves the OH on C5, to form a 6-membered ring.

The cyclization reaction produces two anomers: α and β. DIASTEREOISOMERS



In water, at equilibrium, the mixture consists of about 36% α-D-glucose, 64% β-D-glucose, and less than 0.02% of the open-chain aldehyde form.

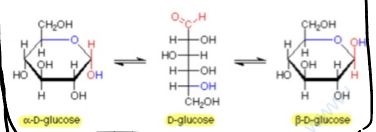
Ribose forms 5-membered rings

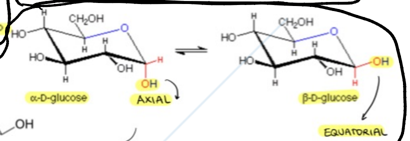


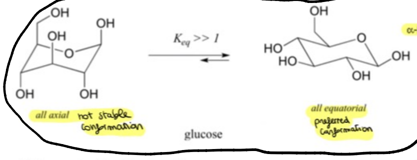
OH at anomeric carbon down

OH at anomeric carbon up

Chair conformation of 6-membered rings, α and β anomers

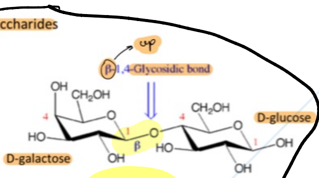




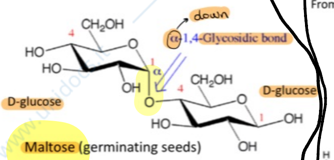


22-carbohydrates2

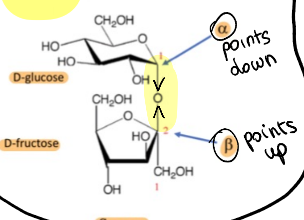
Disaccharides



Lactose (milk sugar)



Maltose (germinating seeds)



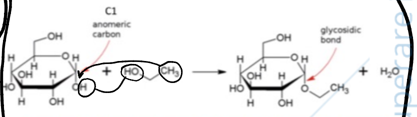
Sucrose

The glycosidic bond

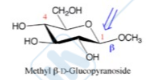
The glycosidic bond is formed between the C1 of a monosaccharide (in the cyclic form) with the OH group of another molecule.

From a chemical point of view, it is an acetal.

Glycosidic bond between D-glucose and ethanol



The glycosidic bond can be α or β depending if it points «down» or «up», respectively.

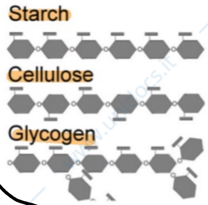


Polysaccharides

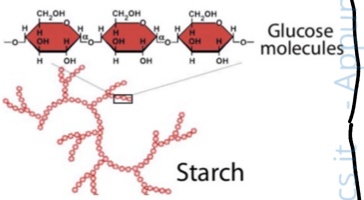
Large number of monosaccharide units bound together by glycosidic bonds.

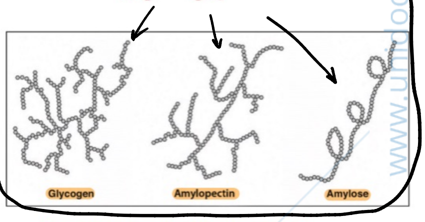
Starch and glycogen are used as energy storage in plants and animals, respectively.

Cellulose has structural functions in plants.

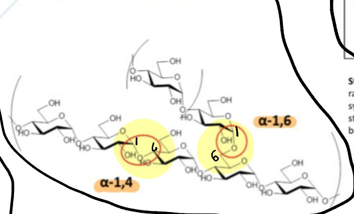


Starch and glycogen are formed by glucose units linked together mainly by α-1,4-glycosidic bonds.



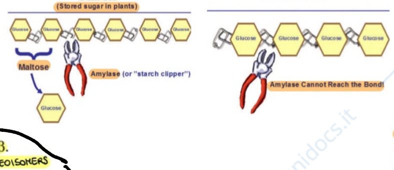


Ramifications are due to α-1,6 glycosidic bonds.

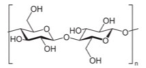


Starch. Amylose is the most abundant form of starch present in plants. Eating raw foods containing starches provides very little energy as the digestive system has a hard time breaking them down. Cooking breaks down the crystal structure of starches, making them much easier to break down in the human body.

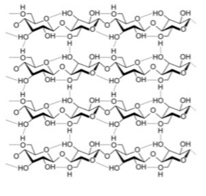
Humans and animals store glucose energy from starches in the form of the very large molecule, **glycogen**. It has many branches that allow it to break down quickly when energy is needed by cells in the body. It is predominantly found in liver and muscle tissue in animals.



Cellulose is formed by glucose units linked together by β-1,4-glycosidic bonds



This kind of linkage allows a ordered structure with the presence of many hydrogen bonds, holding the chains firmly together side-by-side and forming *microfibrils* with high strength.



The enzyme present in animals α-amylase only breaks α-1,4 glycosidic bonds, so cellulose is not digested.

Only herbivores host microbes that can digest cellulose.

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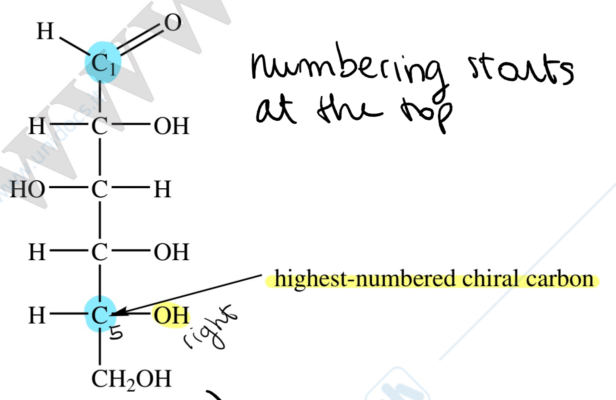


Figure 7-2: Structure of D-glucose.

cyclization

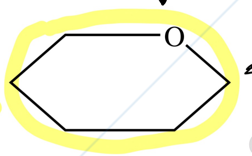
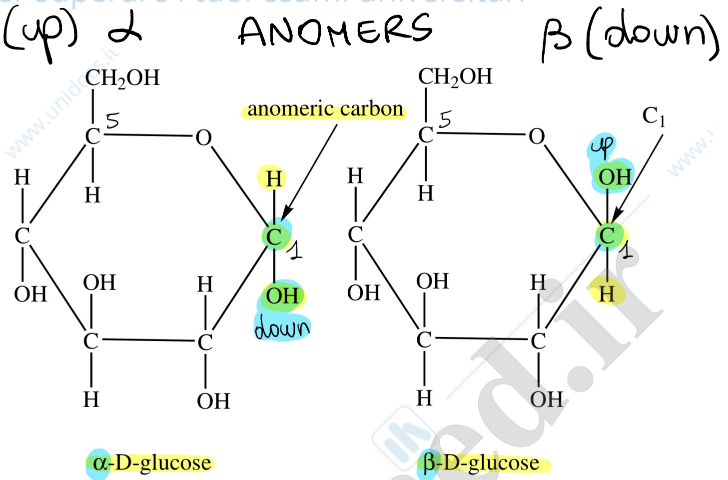


Figure 7-5: A pyranose ring.



α-D-glucose

β-D-glucose

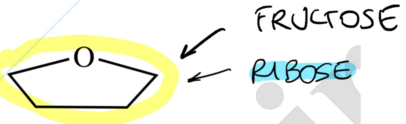
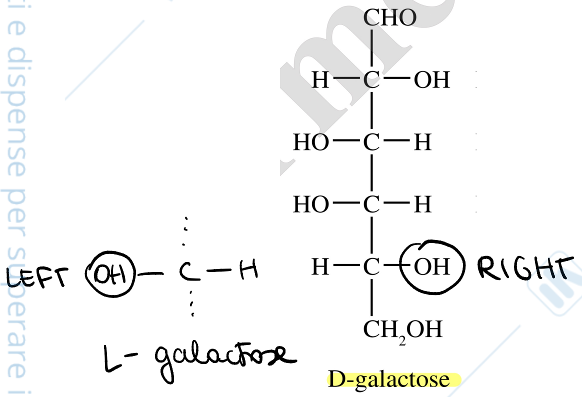


Figure 7-7: A furanose ring.

if the –OH on this carbon atom appears on the right, it's the D form of the monosaccharide; if it is on the left, it's the L form.



D-galactose

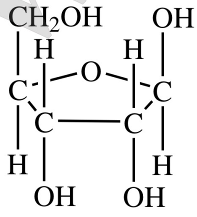
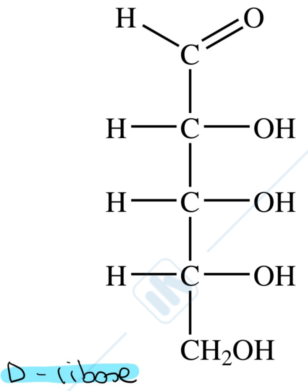
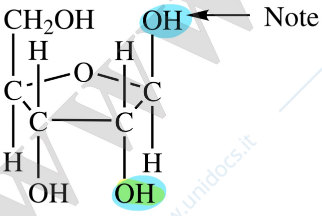
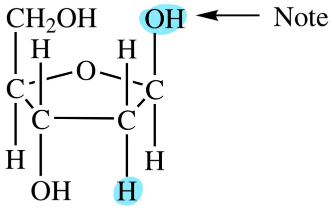


Figure 7-9: Two representations of the structure of D-ribose.

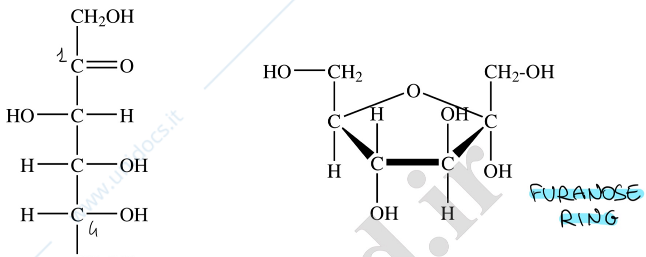




ribose



deoxyribose



D-fructose

α-D-fructose

Figure 7-8: Two forms of D-fructose.

The reaction of a monosaccharide with methanol, CH_3OH, in the presence of hydrochloric acid, HCl, replaces the hydrogen atom of the hydroxyl group on C_1 with a methyl group, forming a *glycosidic bond*.

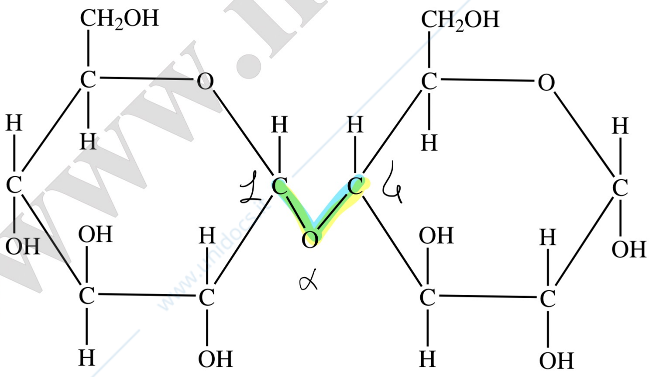


Figure 7-16: The structure of maltose with a α(1-4) linkage present.

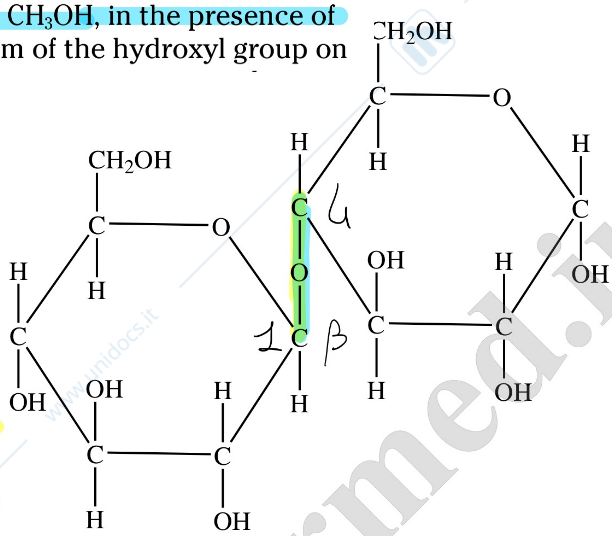


Figure 7-17: Lactose showing its β(1-4) linkage.

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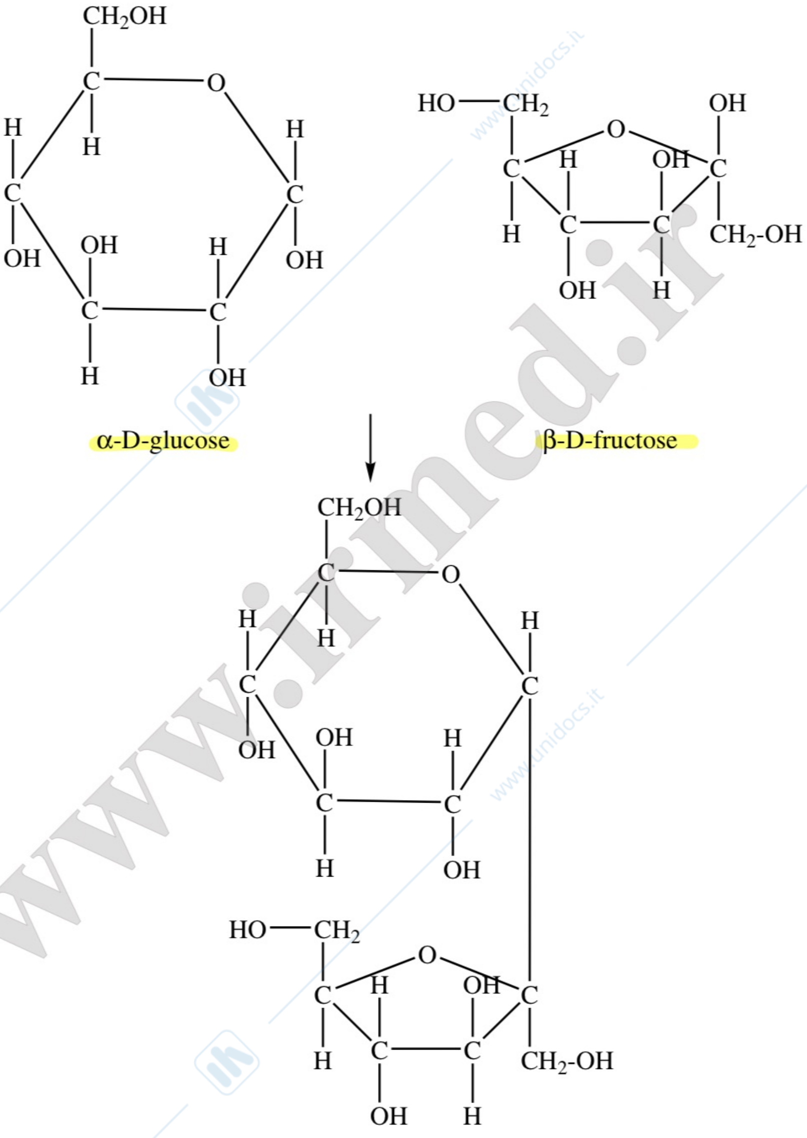

α-D-glucose

β-D-fructose

Sucrose

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Starch is a polymer of α-D-glucose. There are three common types of starch: amylase, amylopectin, and glycogen. Amylase is the combination of α(1-4) glucose groups. Amylopectin, like amylase, has α((1-4) glucose linkages, but, in addition, it has α((1-6) branches.

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26-lipids

Lipids are a heterogeneous group of naturally occurring compounds, classified together on the basis of their common solubility properties.

Insoluble in water

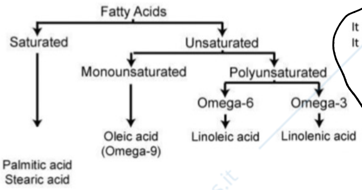
Soluble in aprotic organic solvents (ether, acetone, hexane)

Divided in:
- Fats = solid
- Oils = liquid

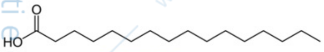
Fatty acids

Fatty acids consist of a long carbon chain ending with a carboxylic group. They can be classified on the basis of:
1. Number of C-atoms
2. Degree of unsaturation

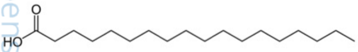
This is indicated by two numbers separated by a column. A 18:2 fatty acid has a chain of 18 carbons and two double bonds.



Saturated fatty acids



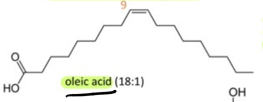
Palmitic acid (16:0)



Stearic acid (18:0)

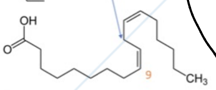
Unsaturated fatty acids

The double bonds are always «cis»

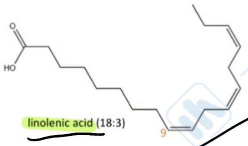


oleic acid (18:1)

In polyunsaturated fatty acids doublebonds are always separated by one CH_2



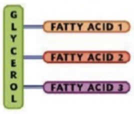
linoleic acid (18:2)



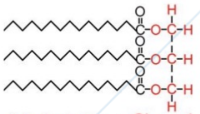
linolenic acid (18:3)

Triglycerides

The most abundant natural lipids, found in animal fats and vegetable oils. They are used as energy reserve.

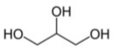


Triacylglycerols: tri-esters of glycerol and fatty acids.



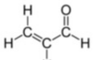
3 Fatty Acids + Glycerol

Glycerol (or glycerine)



It is a colorless, odorless, viscous liquid that is sweet-tasting and non-toxic. It is widely used in the cosmetic and food industries.

When heated at high temperature (280 °C), glycerol decomposes to acrolein, that is toxic (causes lung cancer) and bad smelling.

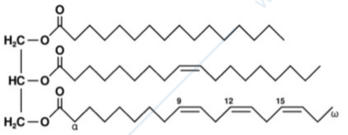


Physical properties of fatty acids

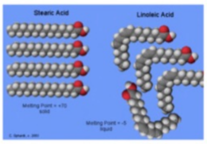
The melting point increases with the chain length and decreases with the number of double bonds.

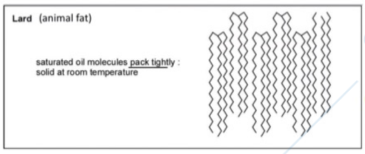
name		Melting point (°C)
Palmitic acid	16:0	63
Stearic acid	18:0	70
Oleic acid	18:1	16
Linoleic acid	18:2	-5
Linolenic acid	18:3	-11

In a typical triglyceride, the OH groups of glycerol are esterified by different fatty acids.
The fatty acid composition defines the physical properties.



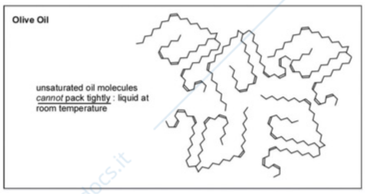
Unsaturated fatty acids do not pack well together. Dispersion forces are weaker.





Lard (animal fat)

saturated oil molecules pack tightly : solid at room temperature

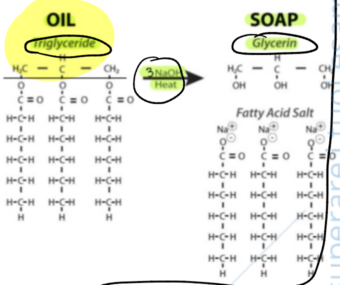


Olive Oil

unsaturated oil molecules *cannot* pack tightly : liquid at room temperature

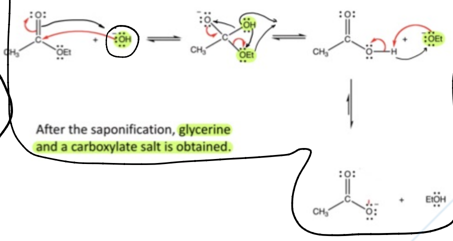
Breaking triglicerides: saponification

Natural soaps are produced by boiling triglycerides in NaOH.



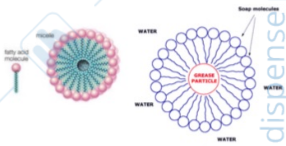
Saponification: reaction mechanism

The reaction is an ester hydrolysis in presence of a strong base.



After the saponification, glycerine and a carboxylate salt is obtained.

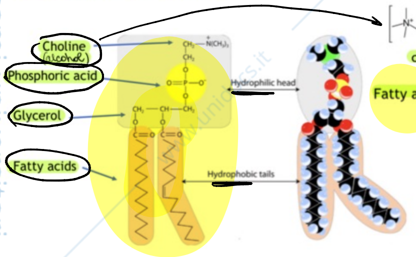
How soap works

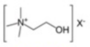


Phospholipids

Phospholipids are found in plant and animal cell membranes.

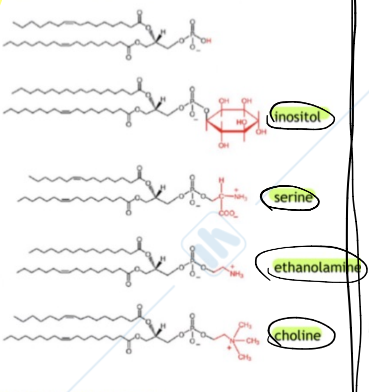
They are composed of glycerol esterified by two fatty acids and a phosphoric acid molecule, which is further esterified by different alcohols (such as choline).



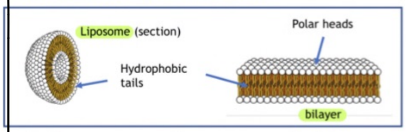


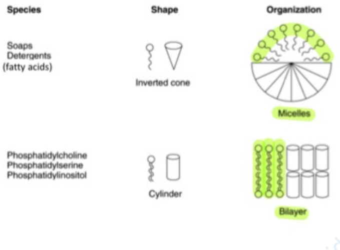
choline

Fatty acid composition is variable and depend on the species.



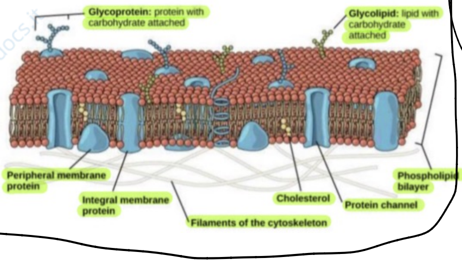
Phospholipids form bilayers and liposomes





Phospholipids form cellular membranes

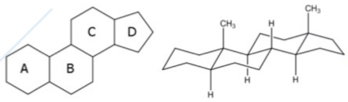
A cellular membrane is composed of phospholipids and proteins. Unsaturation degree of phospholipids tails modulates the membrane fluidity.



Steroids

Steroids have structures totally different from the other classes of lipids.
The main feature of steroids is the ring system of three cyclohexanes and one cyclopentane in a fused ring system as shown below. There are a variety of functional groups that may be attached. The main feature, as in all lipids, is the large number of carbon-hydrogens which make steroids non-polar.

Steroids include such well known compounds as cholesterol, sex hormones, and cortisone.

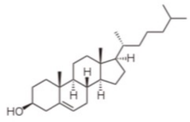


The «trans» junction between the cyclohexane rings blocks the conformation.

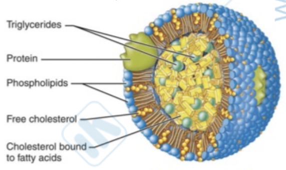
Cholesterol

most abundant

Cholesterol is found in all membranes and helps in mantaining their fluidity. It is the starting point for the synthesis of steroid hormones.



As cholesterol is insoluble in water, it is transported in the blood by lipoproteins.

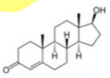


LDL lipoprotein

Low-density lipoproteins (LDL) transport cholesterol to the various tissues. When blood vessels become damaged, LDL accumulates along the walls, forming deposits (or plaques).

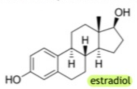
High-density lipoproteins (HDL) transport cholesterol back to the liver to be eliminated.

Steroid hormones



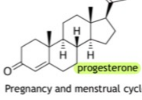
testosterone

Male secondary sex characteristics.



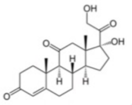
estradiol

Female secondary sex characteristics, menstrual cycle.



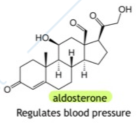
progesterone

Pregnancy and menstrual cycle.



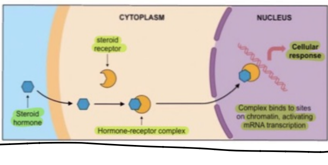
cortisone

Decrease inflammation, regulates metabolism of carbohydrates



aldosterone

Regulates blood pressure



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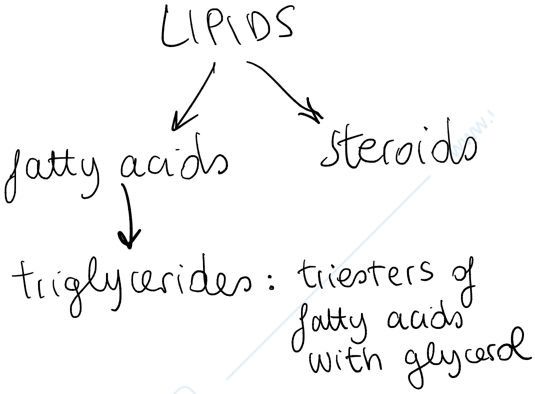
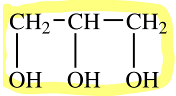
Palmitic acid	$CH_3(CH_2)_{14}COOH$
Stearic acid	$CH_3(CH_2)_{16}COOH$
Oleic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$
Linoleic acid	$CH_3(CH_2)_3(CH_2CH{=}CH)_2(CH_2)_7COOH$
Linolinic acid	$CH_3(CH_2CH{=}CH)_3(CH_2)_7COOH$



A *saturated* fat consists of fatty acids with no carbon-carbon double bonds. An *unsaturated* fat has a double bond while a *polyunsaturated* fat has multiple double bonds.



$$\underset{OH}{CH_2}-\underset{OH}{CH}-\underset{OH}{CH_2}$$

Glycerol

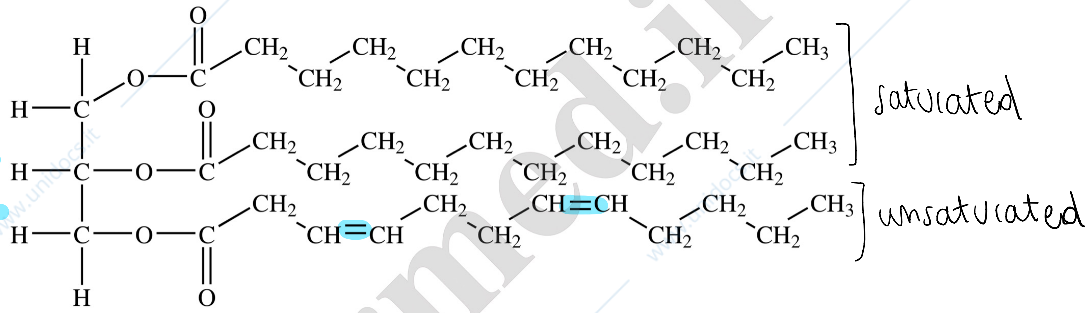


Figure 8-4: Structure of a typical fat: Upper chains are saturated, bottom chain is unsaturated.

saponification reaction, hydrolysis of the ester groups in the presence of a base yields glycerol and the carboxylate ions of the three fatty acids.

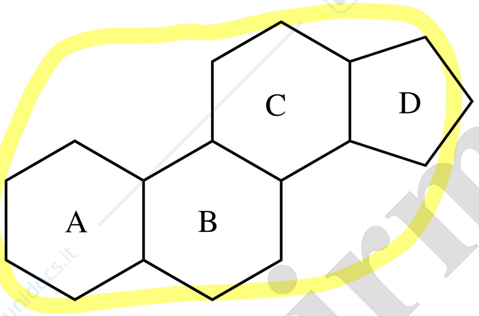


Figure 8-11: Basic structure of a steriod.

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27-nucleic acids

Nucleic acids

Nucleic acids contain information for organization and regulation of cellular functions.

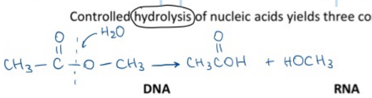
DNA = deoxyribonucleic acid

RNA = ribonucleic acid

DNA is the repository of genetic information.
RNA is the responsable for the transcription and for the synthesis of proteins.

DNA → RNA → proteins

Controlled hydrolysis of nucleic acids yields three components.



$CH_3-\overset{O}{\overset{\|}{C}}-O-CH_3 \xrightarrow{H_2O} CH_3\overset{O}{\overset{\|}{C}}OH + HOCH_3$

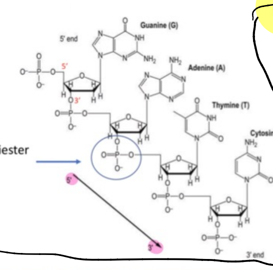
DNA	RNA
Heterocyclic amines	Heterocyclic amines
2-deoxy-D-ribose	D-ribose
Phosphate ion (PO_4^{3-})	Phosphate ion (PO_4^{3-})

Structure of DNA

DNA is a polynucleotide, that is a biopolymer composed by several **nucleotides**.

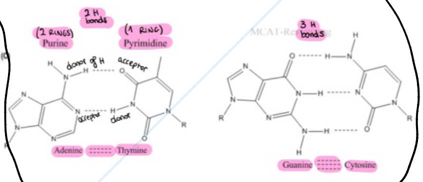
Nucleotides are linked by an ester bond between the phosphate of a nucleotide and the 3' OH group of another nucleotide.
A sequence of polynucleotides is indicated by starting from the 5' end.

Phosphodiester bond



Base pairing

Adenine is able to pair with thymine, guanine with cytosine. As a general rule, a purine binds to a pyrimidine.

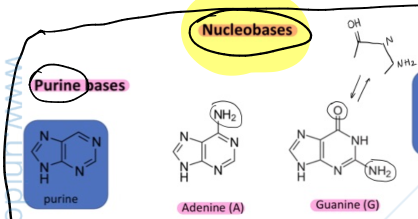


2 hydrogen bonds

3 hydrogen bonds

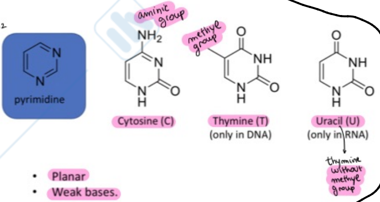
Nucleobases

Purine bases



- Planar
- Weak bases.

Pyrimidine bases

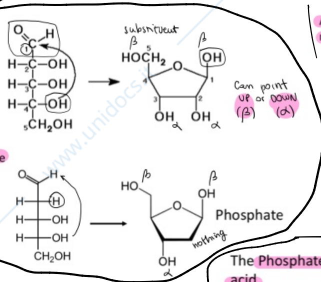


- Planar
- Weak bases.

At physiological pH, all nucleobases are neutral and are neither protonated nor deprotonated.

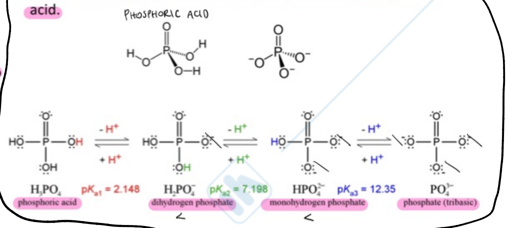
D-Ribose (in RNA)

2-Deoxy-D-ribose (in DNA)

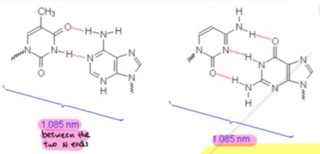


Numbering starts from the aldehyde group

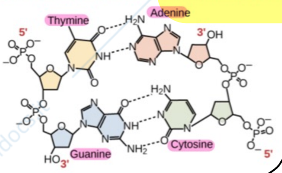
The Phosphate group derives from phosphoric acid, a triprotic acid.



The dimensions of the A-T and G-C base pairs are identical



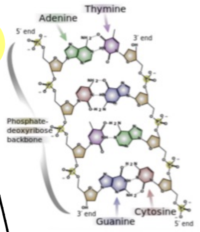
Two DNA single strands can bind if they have complementary bases.



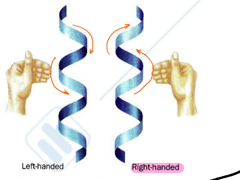
Double helix of DNA

A single polynucleotide strand is associated with another complementary strand forming a double strand.

The two strands are **antiparallel** (one is 5'→ 3'; the other is 3'→ 5'), and are joined by hydrogen bonds between the nucleobases.



DNA helix is usually right-handed



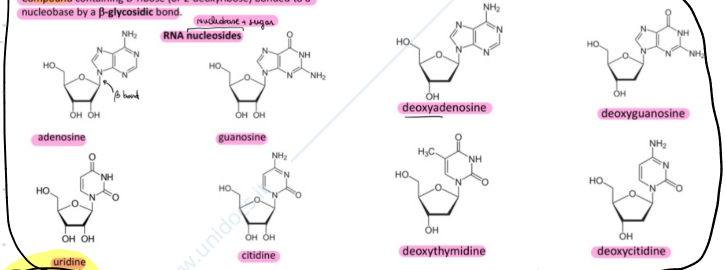
Note that the handness is retained when the helices are turned upside down.

Nucleoside

Compound containing D-ribose (or 2-deoxyribose) bonded to a nucleobase by a **β-glycosidic** bond.

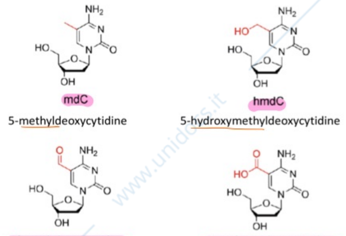
RNA nucleosides

DNA nucleosides



Non-canonical bases in the genome

Probable regulatory elements of the transcription of genes.



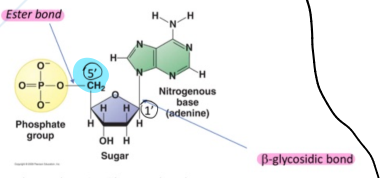
Ribonucleic acid (RNA)

It is a polynucleotide that transfer the information contained in DNA and performs the proteic synthesis.

1. Messenger RNA (mRNA) is the RNA that carries information from DNA to the ribosome (organelle that performs the proteic synthesis)
2. Transfer RNA (tRNA) recognizes and transports a specific aminoacid
3. Ribosomial RNA (rRNA) is the functional core of ribosomes.

Nucleotide

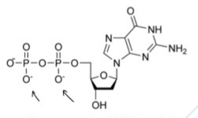
A nucleotide is a nucleoside bound to at least one phosphoric acid



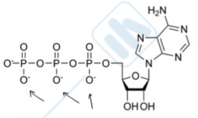
deoxyadenosine 5'-monophosphate

The name of a nucleotide is that of the corresponding nucleoside followed by «monophosphate» and the position of the ester.
The numbering of ribose is 1', 2', 3', 4', 5' to differentiate it from the numbering of the base.

Nucleotides can be further phosphorylated



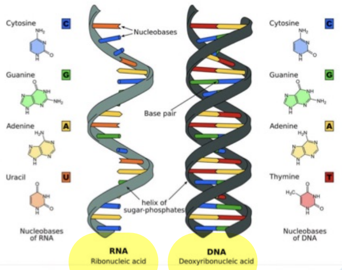
deoxyguanosine 5'-diphosphate



adenosine 5'-triphosphate

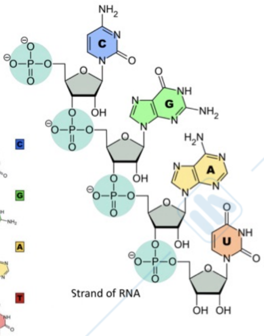
Differences between DNA and RNA

- Ribose instead of 2'-deoxyribose
- RNA is single stranded
- Thymine is replaced with uracil

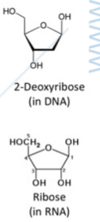


Nucleobase

Nucleoside



Strand of RNA

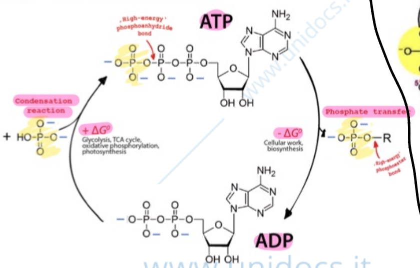


ATP – ADP system

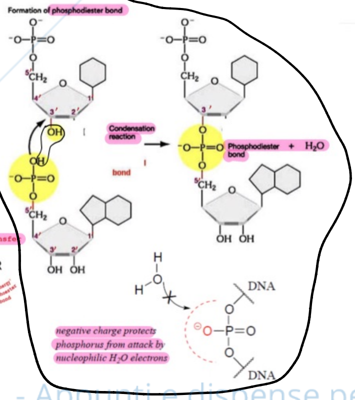
ATP = adenosine triphosphate
ADP = adenosine diphosphate

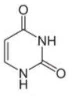
Adenosine triphosphate (ATP) stores energy inside the cell and makes it available where eneregy is needed.

$ATP + H_2O \longrightarrow ADP + P + 7\ kcal/mol$

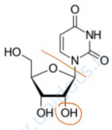


Polynucleotides



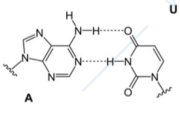


uracil



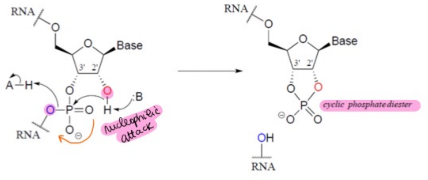
uridin

U



Pairing with adenine

RNA nucleotides, unlike the deoxynucleotides of DNA, have a hydroxyl group at the neighboring 2' carbon. The 2' hydroxyl group is right next to the electrophilic phosphorus atom, poised in a good position to make a nucleophilic attack, breaking the RNA chain and forming a cyclic phosphate diester intermediate.



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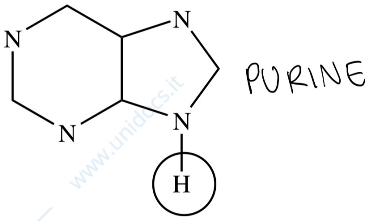
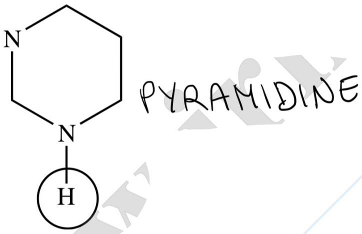
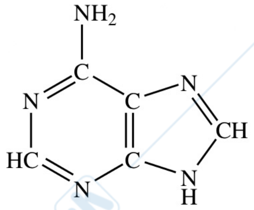


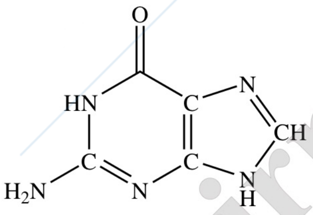
- The purines (adenine and guanine), composed of two fused rings incorporating two nitrogen atoms in each ring and
- The pyramidines (cytosine, thymine, and uracil), composed of a single ring with two nitrogen atoms in the ring structure



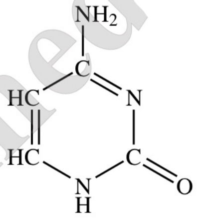


Adenine (A)

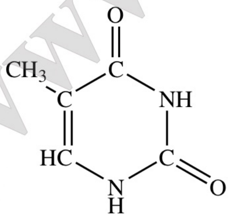
Adenine (A), guanine (G), and cytosine (C) occur in both DNA and RNA. Thymine (T) is only found in DNA, whereas uracil (U) only occurs in RNA.



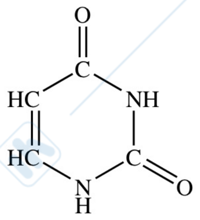
Guanine (G)



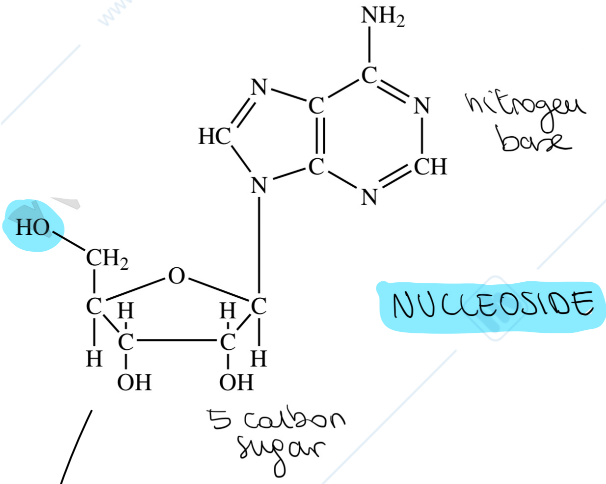
Cytosine (C)

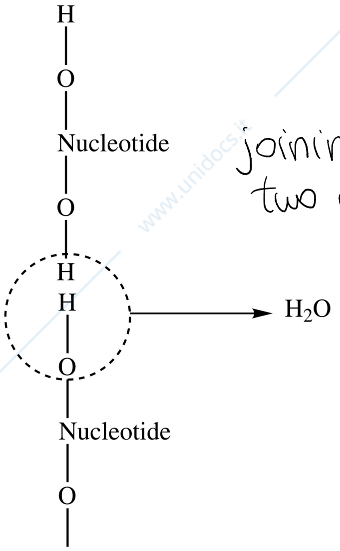


Thymine (T)



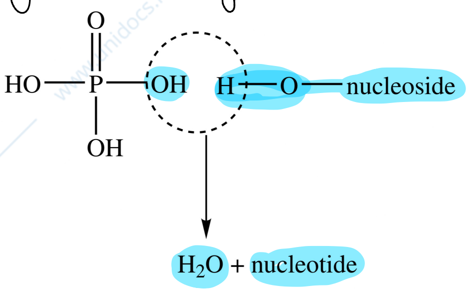
Uracil (U)

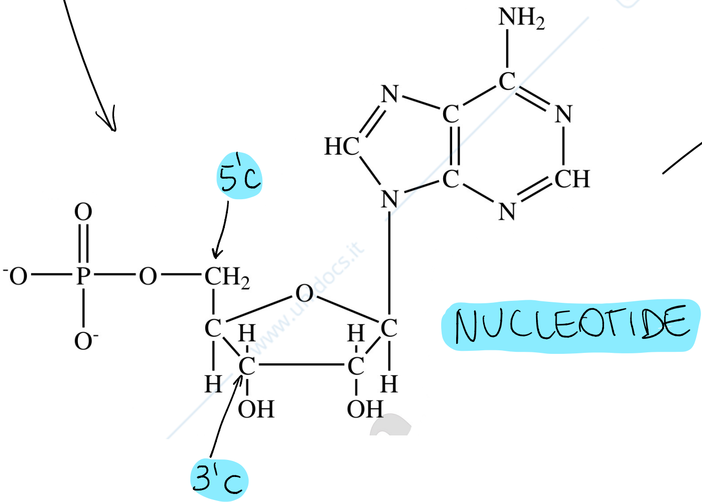


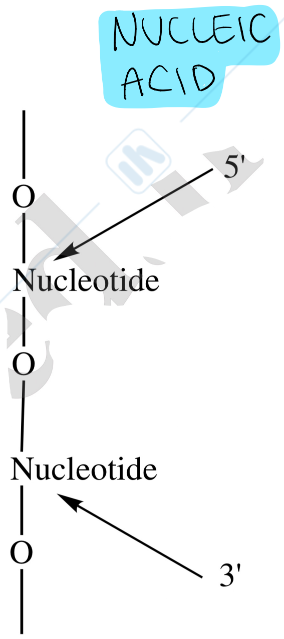


joining of two nucleotides

formation of a nucleotide







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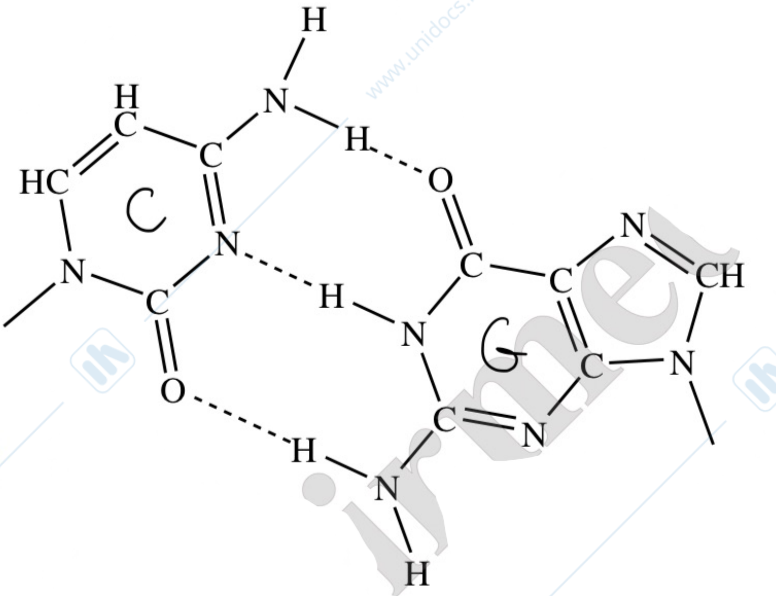


Figure 9-12: Hydrogen bonds (dotted lines) form between guanine (right) and cytosine (left).

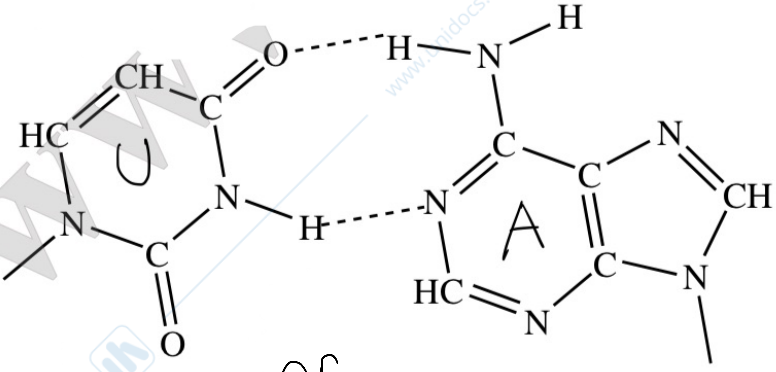
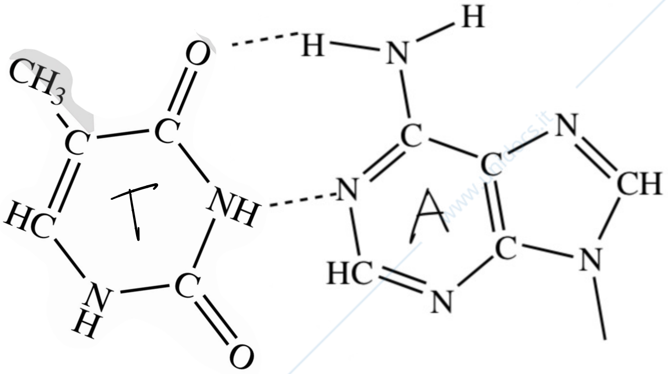


Figure 9-13: Hydrogen bonds (dotted lines) form between adenine (right) and uracil (left).

or



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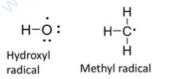
Free radicals

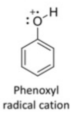
What are free radicals

Free radicals (or, more simply, radicals) are molecule or ions having unpaired electrons in the valence shell.

Neutral radicals
(no charge)



Radical ions
(positive or negative charge)



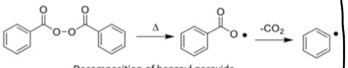
$O_2^{\bullet -}$
superoxide

- Radical formation
- Reactions of radicals
  - recombination
  - Addition (polymerization)
  - H-atom transfer
- Stability and persistency
- Reactive oxygen species
- Lipid peroxidation
- Antioxidants

Radical formation

1) Homolytic cleavage of a bond, due to: heat and radiations

$A{-}B \longrightarrow A^\bullet + B^\bullet$



Decomposition of benzoyl peroxide

2) Capture or loss of one electron:

$O_2 + e^- \rightarrow O_2^{\bullet -}$

Formation of superoxide in mitochondria

3) Bond cleavage coupled to an electron transfer:

Formation of HO• in the presence of iron II and hydroperoxides (Fenton reaction)

$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + HO^\circ + OH^-$

Reaction of radicals

Radicals are very reactive and have a short life in solution, because they lack the octet. Radicals undergo to two kinds of reactions:

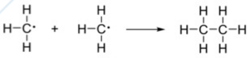
1. With themselves (radical-radical or decay reactions)
2. With closed-shell molecules

Radical-radical reactions

These reactions are extremely fast and cause the disappearance of radicals.

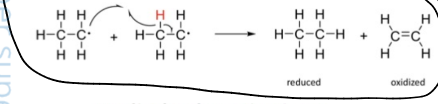
1) recombination

Two radicals bind together



2) disproportionation

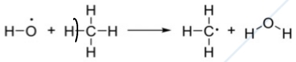
One radical is reduced while another one is oxidized.



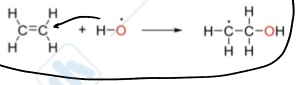
Reaction with closed-shell molecules

These reactions may be fast or slow, and trasform one radical into another one.

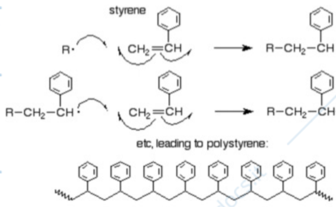
1) H atom abstraction



2) Addition to double bonds

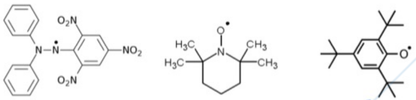


Radical polymerization



Persistent radicals

In very specific and limited cases, radicals can survive for long time, because recombination or disproportionation are not occurring. This happens in the case of radicals having bulky substituents.



Bulky tert-butyl groups

Radical stability

Radical stability describes how easily a radical can be formed starting from a closed-shell molecule.
Also, this parameter is (roughly) inversely proportional to the tendency of a radical to react with closed-shell molecules.

Stability of **neutral radicals** is inversely proportional to the Bond Dissociation Energy (BDE), that is the energy required to break a bond (usually, the bond with H).

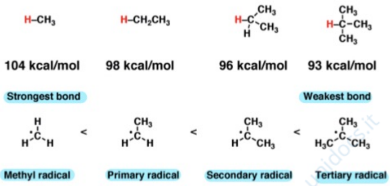
Bond dissociation energy:

$H{-}OH \longrightarrow H^\bullet \quad {}^\bullet\ddot{O}H$ 119 kcal/mol

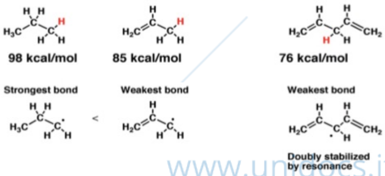
$H{-}CH_3 \longrightarrow H^\bullet \quad {}^\bullet CH_3$ 104 kcal/mol

The methyl radical is more stable than the hydroxyl radical.

Radical stability increases in the order methyl < primary < secondary < tertiary

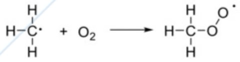


Radical stability increases if stabilized by resonance



Peroxyl radicals

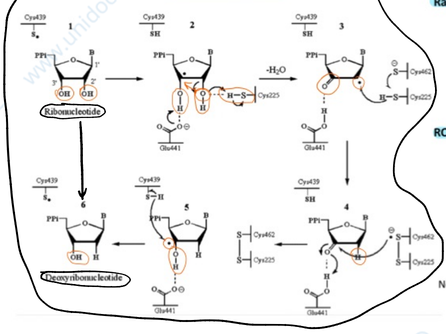
Carbon-centered radicals quickly react with oxygen to form peroxyl radicals.



With this reaction, O_2 is incorporated into organic molecules. This is the reason why radicals mediate oxidation reaction.

Radical enzymes: Ribonucleotide reductase

Ribose → deoxyribose



Radical damage to biomolecules

Oxidation of membranes (lipid peroxidation)
Is mediated by peroxyl radicals (ROO•).

Damage to DNA:
Is mediated by HO•

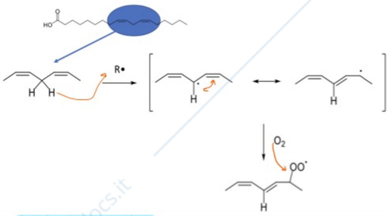
ROS: «Reactive Oxygen Species»

ROS is a term used in biochemistry that includes all species (radical or not) containing oxygen that are associated with radical damage.

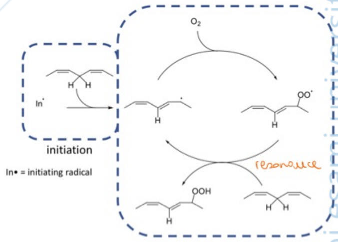
radical	Hydroxyl radical: HO• Superoxide radical: HOO• / $OO^{\bullet -}$ Alkylperoxyl radical: AlkOO•
Non-radical	Hydrogen peroxide: H_2O_2

Lipid peroxidation

Cellular membranes contains polyunsaturated lipids. The bis-allylic moiety is very reactive toward radicals, because it can form a radical that is stabilized by resonance on both double bonds. Further reaction with oxygen yields peroxyl radicals.



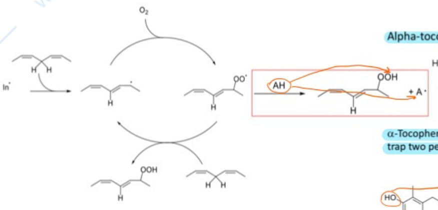
Lipid peroxidation radical cycle



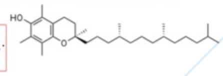
Radical oxidation of lipids is a chain reaction. One initiation event destroys many lipid molecules.

Chain-breaking antioxidants

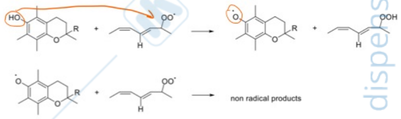
Lipid peroxidation is blocked by molecules able to intecept peroxyl radicals – the chain-breaking antioxidants (AH).



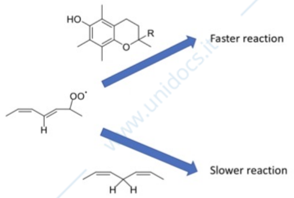
Alpha-tocopherol is a typical antioxidant



α-Tocopherol is the main component of Vitamin E. It is able to trap two peroxyl radicals by the following reactions.

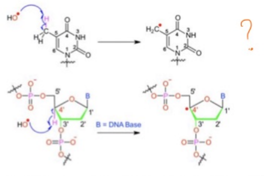


The antioxidant ability of α-tocopherol is due to the fact that it reacts with peroxyl radical much faster than unsaturated lipids do.



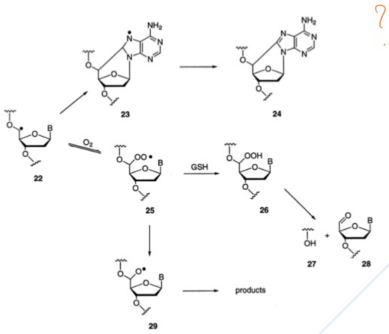
Radical damage to DNA

DNA is more resistant to radical attack than unsaturated lipids. Only the very unstable (i.e. very reactive) hydroxyl radical is able to attack it.

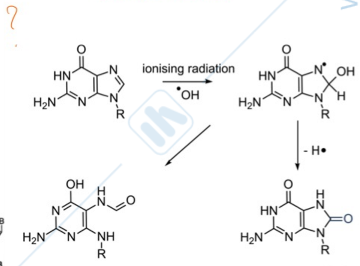


Scheme of the different possible oxidative attacks by OH· on DNA nucleobase (T) or backbone sugar moiety.

Damage to the sugar

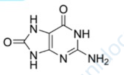


Damage to the bases

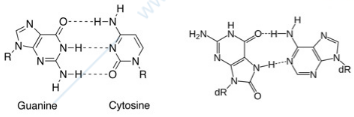


8-oxoguanine (O8G)

The most common oxidative lesion is 8-oxoguanine. It causes pairing mismatch



8-oxoG



Normal pairing

mismatch

Being so reactive, hydroxyl radicals (HO•) must be formed in proximity of DNA. These radicals are formed by the Fenton reaction between H_2O_2 produced by mitochondria and Fe^{2+} or Cu^+ present in the nucleus, or by radiations.

Hydroxyl radicals are not efficiently blocked by antioxidants, because HO• reacts with DNA and with antioxidants at similar rates.

The best defence against DNA radical damage is the <u>prevention</u> of HO• radicals formation:

- Limit H_2O_2 / ROOH build up inside cells.
- Remove excess Fe^{2+} and Cu^+ ions.
- Avoid ionizing radiations.

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