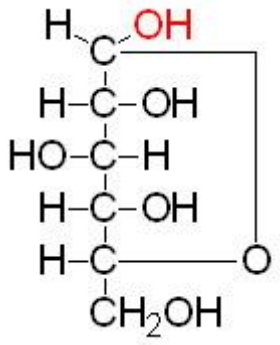
VBB201

CHEMISTRY AND BIOCHEMISTRY OF CARBOHYDRATES OF IMPORTANCE IN VETERINARY MEDICINE E.G OLIGOSACCHARIDES, ANTIBIOTICS, HEPARIN, AGAR, CHONDROITIN, DEXTRANS ETC

CHEMISTRY AND BIOCHEMISTRY OF CARBOHYDRATES

Carbohydrates are carbon compounds that have aldehyde (C-H=0) or ketone (C=O) moiety and comprises polyhyroxyl alcohol(polyhydroxyaldehyde or polyhyroxyketone); their polymers , which also contain an hemiacetal glycosidic linkage. Carbohydrates have the general molecular formula CH_2O.

For example:



A sugar is a Carbohydrate which is sweet to taste ,soluble in water an chars on heating.

Classification of carbohydrates

3 major classes of CHOs

- Monosaccharides-a single unit of polyhydroxylketone or aldehyde which cannot be broken down to simpler substances on acid hydrolysis.
- Oligosaccharides- two to ten monosaccharide units, linked by glycosidic bonds
- Polysaccharides- contain hundreds of monosaccharide units

Monosaccharides

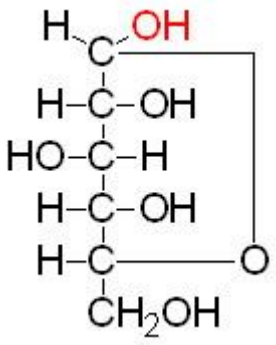
The monosaccharides commonly found in humans are classified according to the number of carbons they contain in their backbone structures. The major monosaccharides contain four to six carbon atoms.

Carbohydrate Classifications

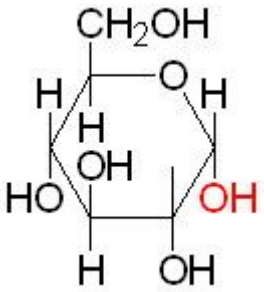
No of Carbon-atoms	Category Name	Relevant examples
3	Triose	Glyceraldehyde, Dihydroxyacetone
4	Tetrose	Erythrose
5	Pentose	Ribose, Ribulose, Xylulose
6	Hexose	Glucose, Galactose, Mannose, Fructose
7	Heptose	Sedoheptulose
9	Nanose	Neuraminic acid, also called sialic acid

The aldehyde and ketone moieties of the carbohydrates with five and six carbons will spontaneously react with alcohol groups present in neighboring carbons to produce intramolecular hemiacetals or hemiketals, respectively. This results in the formation of five- or six-membered rings. The five-membered ring structure are termed **furanoses**. Those with six-membered rings are termed **pyranoses.**

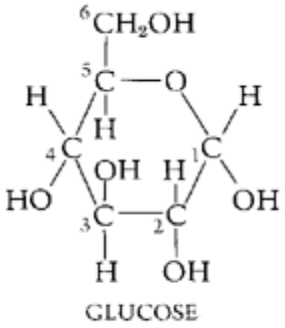
Such structures can be depicted by either **Fischer (linear)** or **Haworth (cyclic)** style diagrams. The numbering of the carbons in carbohydrates proceeds from the carbonyl carbon, for aldoses, or the carbon nearest the carbonyl, for ketoses.

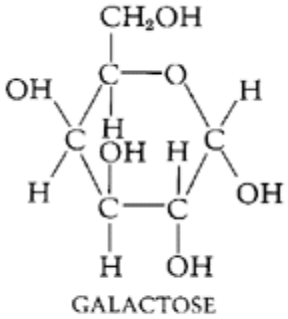


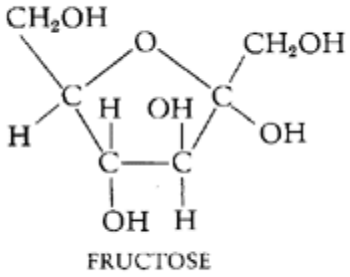
Cyclic Fischer Projection of α-D-Glucose



Haworth Projection of α-D-Glucose







The rings can open and re-close, allowing rotation to occur about the carbon bearing the reactive carbonyl yielding two distinct configurations (α and β) of the hemiacetals and hemiketals. The carbon about which this rotation occurs is the **anomeric carbon (that is carbonyl C-atom)** and the two forms are termed anomers. Carbohydrates can change spontaneously between the α and β configurations: a process known as **mutarotation**. When drawn in the Fischer projection, the α configuration places the hydroxyl attached to the anomeric carbon to the right, towards the ring. When drawn in the Haworth projection, the α-configuration places the hydroxyl downward.

Properties

- CHOs possess asymmetric carbon-atom that is C-atom that has 4 different atoms or functional groups attached to it.
- Isomers exists due to the presence of asymmetric C-atom, and number of isomers a compound has depends on the number of asymmetric C-atoms present and is given by 2^n where *n* indicates number of asymmetric C-atom in that compound.
- CHOs that differ in their configuration about a specific C-atom other than the carbonyl C-atom are called epimers. Example; glucose and galactose.
- If the hydroxyl group on the highest **asymmetric C-atom** or on the penultimate C-atom is on the right side then the compound will belong to the D-series while on the left side its L-series.
- CHOs that have amino group within their structure are called amino sugars common ones are glucosamine and galactosamine and they occur as N-acetyl compounds. These compounds are important components of the body; glucosamine is present in chitin shells

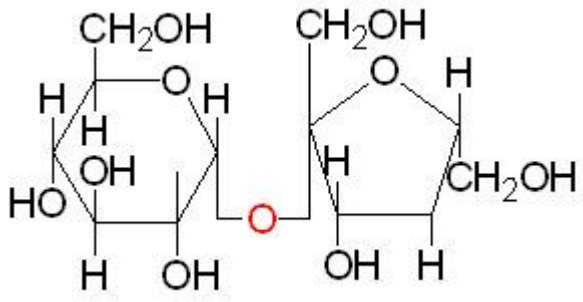
of insects and mammalian polysaccharides whereas galactosamine is present in polysaccharides of cartilage and chondrotin.

- Monosaccharides are able to:- undergo dehydration on treatment with strong acids to give furfural derivatives; mutarotation; reduce heavy metals metallic cations like Cu^{++} in alkaline solution and high temperature (hence termed reducing sugars); form osazones with phenylhydrazines; react with dilute alkali to have reducing action; aldoses can be oxidized to yield aldonic acids (first C-atom oxidized to carboxyl group), uronic acids (terminal C-atom oxidized to carboxyl group), and aldaric or saccharic acids (first and terminal C-atom are oxidized to carboxyl groups); undergoes reduction ,glucose to sorbitol and fructose to sorbitol and mannitol; form glycoside by the replacement of the H-atom of the hemiacetal/ketal group with an organic moiety with the loss of a molecule of water. When the organic moiety is not a carbohydrate it's called **Aglycone.** Examples are the cardiac glycosides digoxin, indicant (CHO + indoxyl), amygdalin (CHO+benzaldehyde) etc

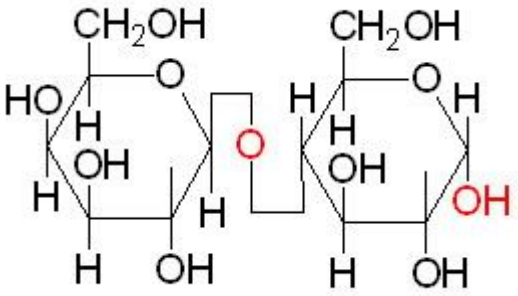
Disaccharides

Covalent bonds between the anomeric hydroxyl of a cyclic sugar and the hydroxyl of a second sugar (or another alcohol containing compound) are termed **glycosidic bonds**, and the resultant molecules are **glycosides**. The linkage of two monosaccharides to form disaccharides involves a glycosidic bond. Several physiogically important disaccharides are sucrose, lactose and maltose.

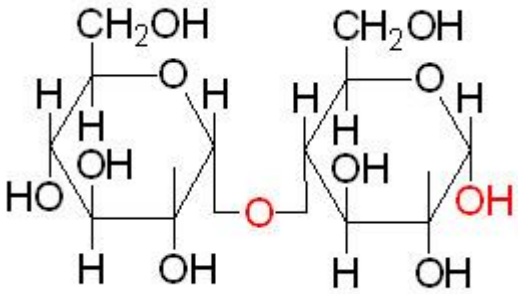
- **Sucrose**: prevalent in sugar cane and sugar beets, is composed of glucose and fructose through an α–(1,2)–β-glycosidic bond. On partial hydrolysis, sucrose, yields levorotatory (sucrose is dextrorotatory) equimolar amounts of glucose and fructose called invert sugar.



- **Lactose**: is found exclusively in the milk of mammals and consists of galactose and glucose in a β–(1,4) glycosidic bond.



- **Maltose**: the major degradation product of starch, is composed of 2 glucose monomers in an α–(1,4) glycosidic bond.



Maltose

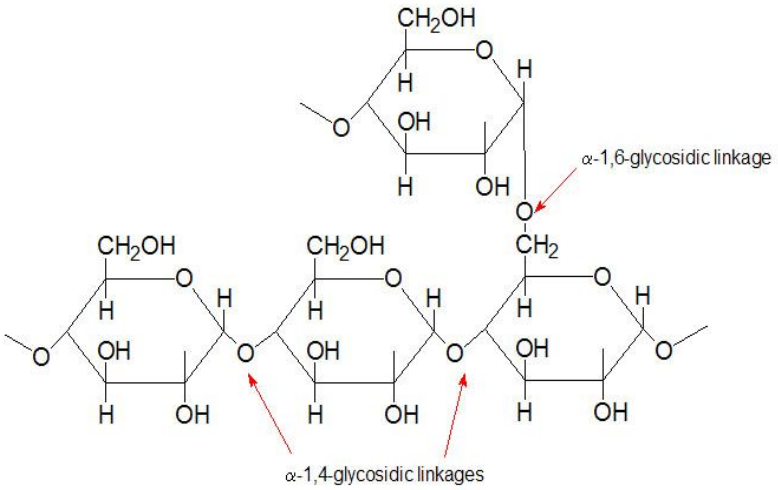
Polysaccharides

Most of the carbohydrates found in nature occur in the form of high molecular weight polymers called **polysaccharides**. The monomeric building blocks used to generate polysaccharides can be varied; in all cases, however, the predominant monosaccharide found in polysaccharides is D-glucose. When polysaccharides are composed of a single monosaccharide building block, they are termed **homopolysaccharides**. Polysaccharides composed of more than one type of monosaccharide are termed **heteropolysaccharides**.

Glycogen

Glycogen is the major form of stored carbohydrate in animals. This crucial molecule is a homopolymer of glucose in α–(1,4) linkage; it is also highly branched, with α–(1,6) branch linkages occurring every 8-10 residues. Glycogen is a very compact structure that results from

the coiling of the polymer chains. This compactness allows large amounts of carbon energy to be stored in a small volume, with little effect on cellular osmolarity. The structure of glycogen is similar to that of amylopectin, although the branches in glycogen tend to be shorter and more frequent. The liver and skeletal muscles are major depots of glycogen. Glycogen is broken back down into glucose when energy is needed (a process called glycogenolysis).



Section of Glycogen Showing α–1,4– and α–1,6–Glycosidic Linkages

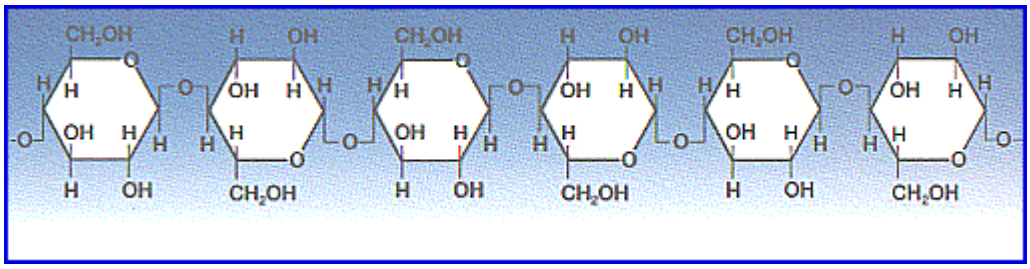
Starch

Starch is the major form of stored carbohydrate in plant cells. Its structure is identical to glycogen, except for a much lower degree of branching (about every 20–30 residues). Unbranched starch is called **amylose**; branched starch is called **amylopectin**. Starches are insoluble in water and thus can serve as storage depots of glucose. Plants convert excess glucose into starch for storage. Before starches can enter (or leave) cells, they must be digested. The hydrolysis of starch is done by amylases. With the aid of an **amylase** (such as pancreatic amylase), water molecules enter at the 1 -> 4 linkages, breaking the chain and eventually producing a mixture of **glucose** and **maltose**. A different amylase is needed to break the 1 -> 6 bonds of amylopectin.

Amylose consists of linear, unbranched chains of several hundred glucose residues (units). The glucose residues are linked by a glycosidic bond between their number 1 and 4 carbon atoms.

Amylopectin differs from amylose in being highly branched. At approximately every thirtieth residue along the chain, a short side chain is attached by a glycosidic bond to the #6 carbon atom (the carbon above the ring). The total number of glucose residues in a molecule of amylopectin is several thousands.

Cellulose



Cellulose is probably the single most abundant organic molecule in the biosphere. It is the major structural material of which plants are made. Wood is largely cellulose while cotton and paper are almost pure cellulose. Like starch, cellulose is a polysaccharide with glucose as its monomer. However, cellulose differs profoundly from starch in its properties.

- Because of the orientation of the glycosidic bonds linking the glucose residues, the rings of glucose are arranged in a flip-flop manner. This produces a long, straight, rigid molecule.
- There are no side chains in cellulose as there are in starch. The absence of side chains allows these linear molecules to lie close together.
- Because of the many -OH groups, as well as the oxygen atom in the ring, there are many opportunities for hydrogen bonds to form between adjacent chains.

It is the main constituent of supporting tissues of plants and therefore forms a considerable part of animal vegetable diet. Herbivores with the help of bacteria can utilize a considerable proportion of cellulose. it adds bulk to the intestinal contents (roughage) thereby stimulating peristalsis and elimination of indigetable food residues.

Dextrins

Partial hydrolytic products of starch by α-amylase, β-amylase or acids give what is called dextrins that have lower molecular weight but resemble starch in being precipitable by alcohol and have a free sugar group and can thus reduce alkaline copper sulphate solution.

Dextrin solutions are often used as mucilages (sticky gums) and are widely used in infant feeding. Limit dextrin is a well defined dextrin formed on total hydrolysis of starch by β-amylase.

Inulin

It is a polymer of D-fructose with low molecular weight of about 5000. It occurs in tubers of Dehlia,bulbs of onions and garlic etc. it can be hydrolysed by acid and inulinase to D-fructose.it is used in physiological investigation for determination of glomerular filtration rateand in estimation of total body water.

Dextrans

Synthesized by the action of *leuconostoc mesenteriodes* (a bacterium) in sucrose medium, it is a polymer of D-glucose. They are different from dextrins in structure but have D-glucose units joined by α1-4, α 1-6, α; 1-3 glycosidic linkages joined together to form a network. Dextran solutions have a mol. wt of about 75000 and are used as plasma expanders because they have the ability to increase blood volume because high viscosity, low osmotic pressured slow disintergration and utilization and slow elimination from the body they remain in the blood for many hours to exert its effect.

Agar

It is a homopolysaccharide made up of repeating units of galactose which is sulphated. It is present in sea weed. It is used as a laxative in constipation because like cellulose it is not digested hence adds bulk to feces and helps propulsion. In microbiology it is purified and dissolved in hot water and on cooling sets like gel and used in culture of bacteria.

Heteropolysaccharides/mucopolysaccharides

These are made up of mixed mixed disaccharide repeating units and on hydrolysis gives a mixture of more than one products of monosaccharides and their derivatives of amino sugars and uronic acids. The hexamine present is usually acetylated and these compounds are essentially components of tissues where they are generally present either in free form or in combination with proteins.

There are 2 major classes of MPS (mucopolysaccharides)

- Neutral MPS e.g. blood group substances
- Acidic MPS

Acid MPS are present in connective tissue and have hexamine as the repeating disaccharide units with alternating 1,4 and 1,3 linkages.

- Hyaluronic acid; it is sulphate free and found in vitreous humour, synovial fluid, skin, umbilicalcord and rheumatic nodule. it occurs as both free and in salt like combination with proteins hence called the ground substance of mesenchyme and intergral part of the gel-like ground substance of C.T and other tissues. Composed of repeating units of N-acetylglucosamine and D-glucuronic acid.
- Heparin

It is an anticoagulant present in liver and is produced mainly by mast cells of liver. It can also be found in lungs, thymus, spleen, walls of large vessels, skin etc. both the hydroxyl and the amino groups are combined with sulphuric acid. Repeating disaccharide units are D-glucosamine and either D-glucuronic acid or L-iduronic acid. There is a α;1-4 linkage from the anomeric C-atom of the glucuronic acid to the C4 hydroxyl group of the glucosamine.

- Chondroitin sulphates

They are present in connective tissue and serve as structural material such as cartilage, tendons and bones. It differs from hyaluronic acid in that it has N-acetyl galactosamine instead of N-acetyl glucosamine. there are 4 different types of chondroitin SO4s named as Chondroitin Sulphate-A,B,C and D. these differ at points of C-atom linkages, positions and /or number of sulphate groups etc

- Heparin sulphate

It has been isolated from amyloid liver (a diseased state) and certain normal tissue such as human and cattle aorta. It has negligible anticoagulant activity and though structurally similar to heparin has a lower mol. wt. unlike heparin its predominant uronic acid is D-glucurononic acid

- Sialic acids

These are N-acetyl derivatives of neuraminic acid and are widely distributed in tissues and are present in blood group substances. Neuraminic acid is a condensation product of pyruvic acid and mannosamine.

Proteoglycans

These are conjugated proteins. Core proteins are covalently linked to glycosaminoglycans (GAGS). The amount of carbohydrates in proteoglycans is up to 95%, higher than that in glycoproteins. These compounds are constituents of extracellular matrix or ground substance;

they interact with collagen and elastin. They also act as polyanions, barriers in tissues, lubricants, in release of hormones etc

METABOLISM OF CARBOHYDRATES

- This begins in the mouth where on contact with salivary amylase and maltase starch and glycogen is split into constituent monosaccharides.
- In the stomach acid hydrolysis may occur sparingly whilst the action of saliva enzymes is arrested by the acid pH.
- Carbohydrate splitting enzymes contained in pancreatic juice is released into small intestine where they rapidly break polysaccharides to Monosaccharides.
- Monosaccharides (predominantly glucose, fructose and galactose) are absorbed into the mucosa cells of the intestine through Na^+ dependent-active-transport mechanism using a glucose co-transporter; leave the cells into the portal circulation via facilitated diffusion in the presence of glucose-transporters.
- In the liver two major mechanisms operate, glucose(carbohydrate is either withdrawn from blood into the cells, to further undergo breakdown for ultimate release of energy to power cellular processes or it is converted to storage forms to be drawn upon when the body later needs energy (including conversion to fatty acids and storage as triglycerides).
- For energy production, glucose is oxidized in a series of steps and pathways that leads to its complete catabolism to yield ATPs, carbon dioxide and water. The initial pathway involved in this energy production step is the pathway known as GLYCOLYSIS or the EMBDEN-MEYERHOF pathway.
- Glucose also provide the carbon skeleton backbone for synthesis of non-essential amino acids and as well other biologically useful carbohydrates such as mucoploysaccharides, glycoproteins etc.

- Fructose and galactose are absorbed into the liver where they are intergrated into the metabolic pathway of glucose (converted to glucose) through a number of steps starting with phosphorylation. They may also be used for specific functions in some special cells e.g fructose is required for metabolism of spermatozoa in the seminferous tubules and fructose can also be formed from glucose through the Sorbitol (polyol) pathway in the seminiferous tubular epithelia cells. Galactose is used in the synthesis of lactose in the mammary gland for milk production.

- Uronic acid pathway is another alternative pathway of glucose metabolism that utilizes glucose for the production of glucuronic acids which can be further used for synthesis of mucopolysaccharides

- Through the hexose monophosphate shunt/pentose phosphate pathway,another alternative pathway of glucose metabolism, glucose is used in the formation of 5-carbon atom monosaccharides e.g. ribose, ribulose, deoxyribose which is required in the synthesis of nucleic acids.

Glycolysis/Embden –Meyerhof Pathway.

This pathway cleaves the six carbon glucose molecule ($C_6H_{12}O_6$) into two molecules of the three carbon compound pyruvate ($C_3H_3O_3^-$). This oxidation is coupled to the net production of two molecules of ATP/glucose. The pathway was described by Embden, Meyerhof and Parnas.

Gylcolysis can be broken down into 2 steps Glycolysis I which is endothermic activation that uses ATP) and the second is glycolysis II which is an Exothermic reaction that creates ATP and pyruvate. Glycolysis does not need oxygen for any of its chemical reactions and takes place in the cytoplasm of cells. Glycolysis is the one metabolic pathway found in all living organisms, and in virtually all cells of the body. Particularly in the erythrocytes and nervous tissue , energy is derived mainly from glycolysis**.** This pathway may utilize oxygen or occur in the absence of oxygen.

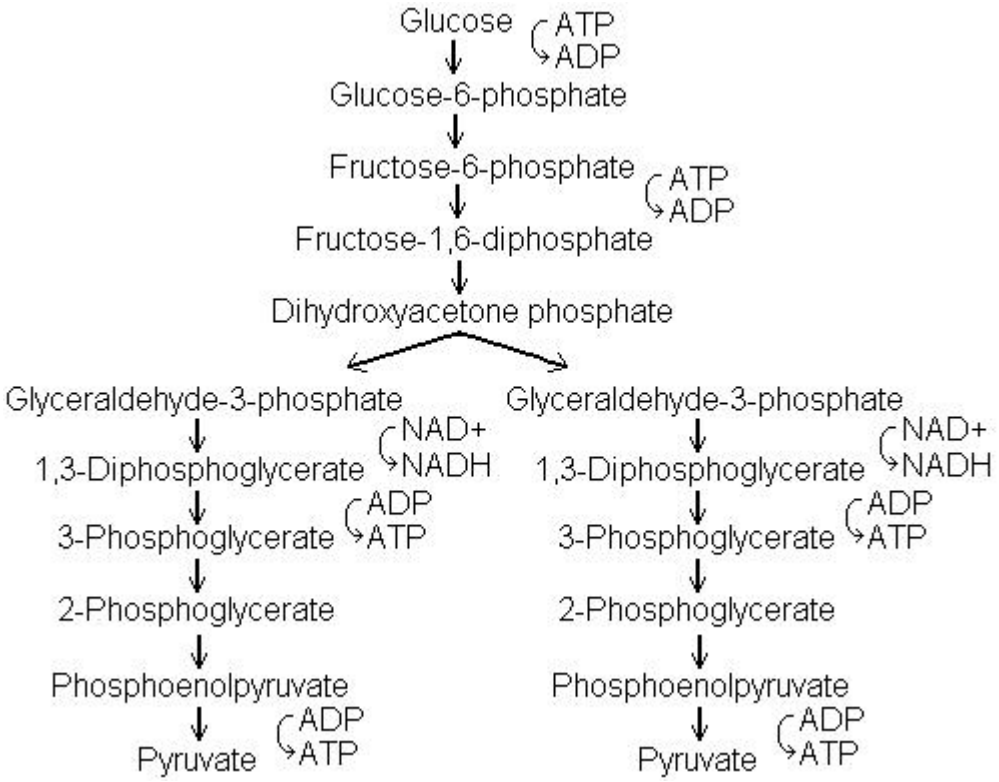
- In the presence of oxygen , oxidation is carried out with the production of reducing equivalents NADH (nicotinamide dinucleotide hydrogen) from NAD^+ which is further reoxidized in the electron transport chain (ETC) to yield ATP (adenosine triphosphate)
- In the anerobic phase the NADH cannot be oxidized in the (ETC) but is oxidized by the conversion of pyruvate to lactate without the production of ATP.
- The above phase is important in skeletal muscle for the provision of energy even in the absence of oxygen, with the accumulation of lactate which can then be transported to the liver for reconversion to glucose in a series of steps known as the CORI cycle.

GLYCOLYSIS

- The first reaction of Glycolysis; During this reaction an enzyme transfers a Pi from one substrate to another (An ATP molecule is used to add a phosphate to glucose to form glucose 6 phosphate). The negative charge of the phosphate group does not permit the glucose to flow out of the cell. Catalysed by enzyme Glucokinase in the liver or Hexokinase in other cells with Mg^{2+} as a coenzyme. The G-6-P can undergo one of atleast five different reactions depending on particular cellular needs at the time, which are;
  I. reconverted back to free glucose that can enter sysytemic circulation,
  II. glycogenesis(synthesis of glycogen)
  III. glycolysis

IV. hexomonophophate shunt
V. glucuronate pathway

- G-6-P is then converted to Rfructose -6-p under the influence of the enzyme phosphohexose isomerase as indicated from the enzyme name it is an isomerisation reaction.
- With the addition of Another phosphate group from ATP, by the enzyme phosphofructokinase and coenzyme Mg^{2+}, F-6-P converted to F-1,6- bisphosphate. This is the rate limiting step of glycolysis and is stimulated by F-6-P, AMP (adenosine monophophate) and ADP(adenosine diphosphate) and inhibited by ATP i.e AMP, ADP, AND F-6-P are activators of the enzyme Phsophofructokinsae while ATP is and inhibitor.this step is ireeversible just as hexokinase.
- Aldolase catalyses the splitting of F-1,6-bisphohate to two 3-carbon atom compounds namelyglyceraldehyde -3-phophate (GA-3-P) and dihydroxyacetone phosphate (DHAP). Dihyroxyactone phosphate is then converted back to glyceraldehydes -3-phophate by triose isomerase.

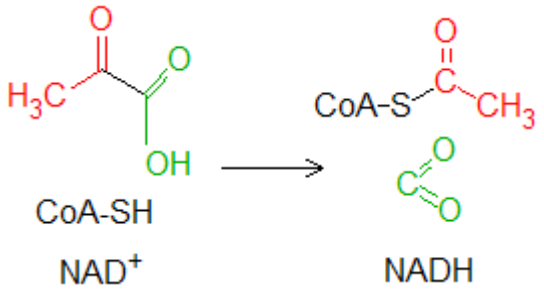


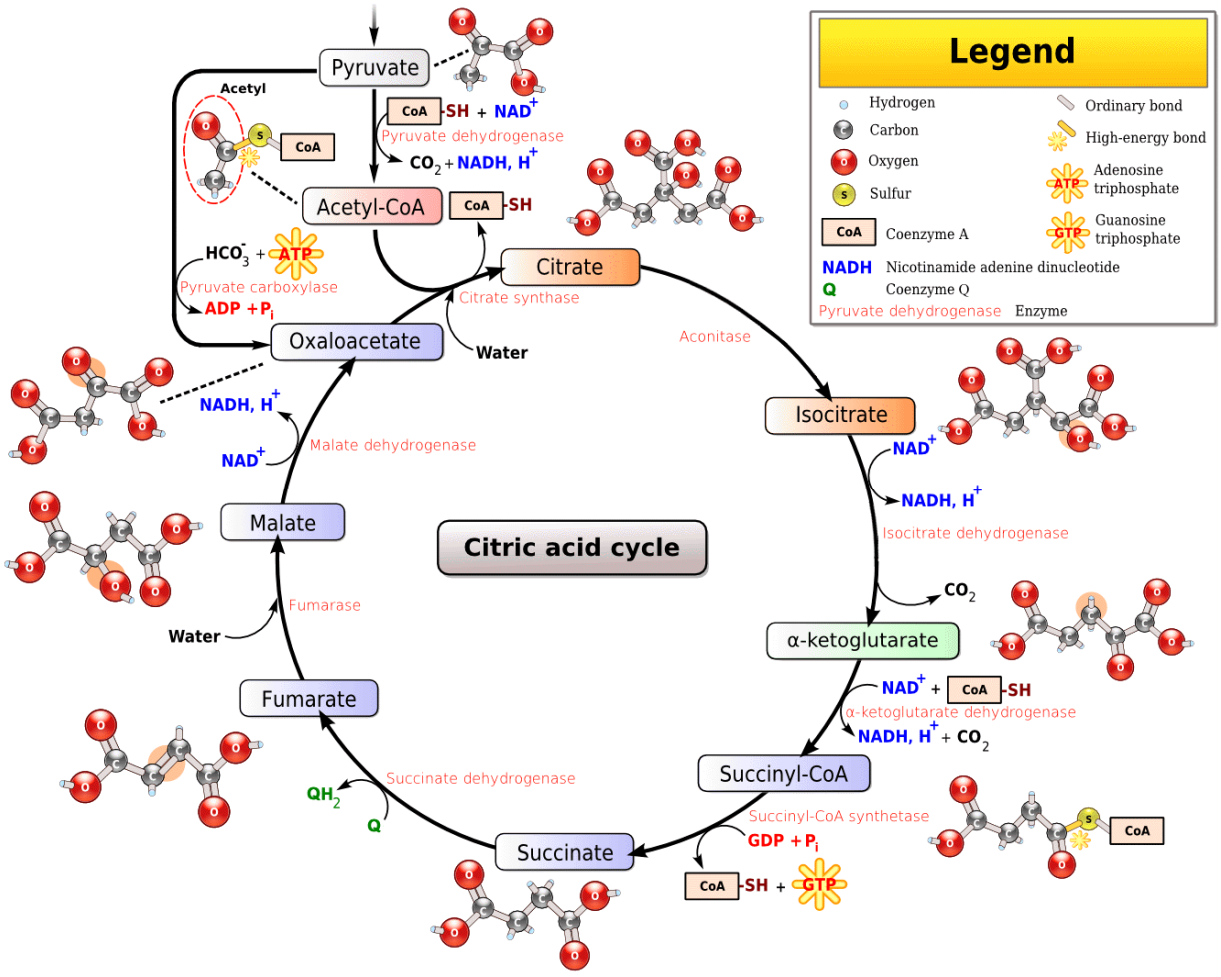
A total of 4 ATPS are produced directly however during oxidation of GA-3-P two NADHs are produced (from both sides) and on oxidation in the ETC 6 molecules of ATP results, hence a total of 10 ATP results from aerobic oxidation, while a net of 8

ATPs remains. In anaerobic condition lactate is formed, oxidizing the NADH back to NAD^+ by the enzyme lactate dehydrogenase.

TRICARBOXYLIC ACID CYCLE, CITRIC ACID CYCLE OR KREBS CYCLE

Following the production of pyruvate from glycolysis in the cytosol of cell, a next cycle of events necessary for further energy production must take place within the mitochondrial correctly delineated powerhouse of the cell. Hence there is transport of pyruvate from the cytosol into the matrix of the mitochondria via special carriers, where it is then oxidatively decarboxylated in a series of steps to yield acetyl CoA, reaction catalysed by the multi enzyme complex called pyruvate dehydrogenase which is made up of pyruvate dehydrogenase(E1), dihyrolipoate transactylase (E2) and dihyrolipoate dehydrogenase (E3). Co factors involved in this reaction are Mg^{2+}, thiamine pyrophosphate. Lipoic acid, coenzyme A (CoA-SH).

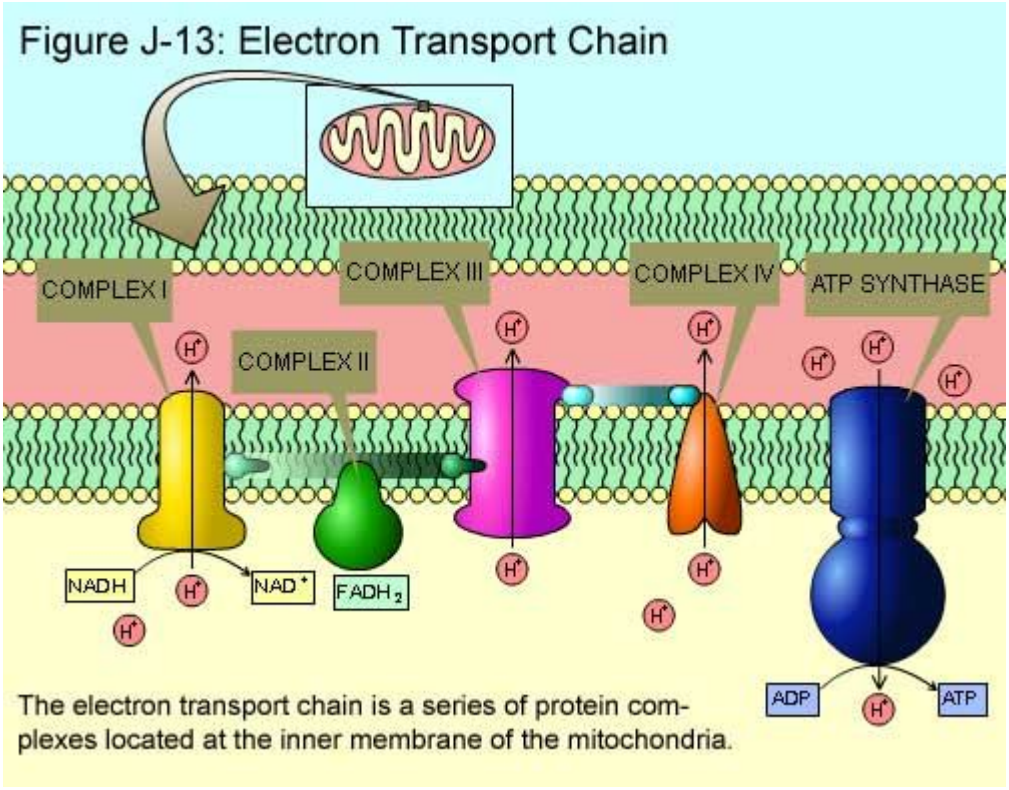




The citric acid cycle.

The CAC has dual roles catabolic and anabolic.

The catabolic role involves oxidation of acetyl coA produced from carbohydratye, lipid and protein metabolism to produce ATP. While for the synthetic role involves the production of intermediates for synthesis of various compounds for example synthesis of non-essential amino acids from transamination of alanine, aspartate and glutamate to produce pyruvic acid, oxaloacetate and ketoglutarate respectively.; formation of glucose in the gluconeogenesis pathway via pyruvate., fatty acid,cholesterol and steroid synthesis through acetyl coA, heme synthesis form succinyl coA ,



The electron transport chain is a series of electron transfer from NADH and $FADH_2$ to oxygen occurring in the inner mitochondrial membrane and coupled to the generation of proton motive force., the energy stored in the electrochemical proton gradient is then used for ATP synthesis by the F_0F_1 ATPase complex or ATP synthetase. The reactions in the glycolytic pathway and citric acid cycle result in the conversion of one glucose molecule to 6 CO_2 molecules and the concomitant reduction of 10 NAD^+ to 10 NADH molecules and 2 FAD to $FADH_2$ molecules. These reduced co-enzymes are the reoxidized in the ETC. components of the ETC are located on the inner mitochondrial membrane and are 4 distinct multiprotein complexes; complex I (NADH-Co Q reductase or NADH dehydrogenase),complex II (succinate-Q-reductase), complex III (cytochrome reductase , cytochrome b-c-1 complex) and complex IV (cytochrome oxidase)

as well as two mobile elements coenzyme Q and cytochrome C. terminally there is the ATP synthase complex sometimes called complex V.

Complex I; it contains about 25 different proteins and contains a flavoprotein consisting of FMN and an iron sulphur protein (Fe-S). NADH donates 2 electrons to the FMN moiety which gets reduced to $FMNH_2$. The 2 electrons are then transferred from the $FMNH_2$ to Fe-S from where the e^-s are transferred to coenzyme Q (ubiquinone), in this process protons are driven out of the mitochondria matrix into the intermembrane space.

Complex II; here electrons from $FADH_2$ enter the ETC ($FADH_2$ by passes the complex I, hence less ATP is generated from this, 2 instead of 3). It also receives the 2 electrons carried by coenzyme Q,

Coenzyme Q is reduced to semiquinone (QH) and then to quinol (QH_2), these coenzymes can diffuse through the lipid layer, accepts electrons from complex I and complex II and transfers them to complex III

Complex III; it is a multiprotein complex having a cyt b and cyt c 1 componrent, electrons are transferred from the quinol compound to the cyt b and cyt C1 respectively with shuttle of the iron in heme between Fe^{2+} and Fe^{3+} forms and the emlectrons are finally transferred to cytochrome C (the second mobile constituent).Protons are pumped out of the matrix too.

Cytochrome C is a single electron carrier and collects electrons from complex III and delivers it to complex IV . it has only one heme prosthetic group.

Complex IV it contains cytochrome a and cytochrome a3. It accepts 4 electrons from cyt c and passes it to molecular oxygen to yield 2 molecules of water. It contains 2 heme groups and 2 copper ions. Protons are pumped out of matrix.

$4H^+ + O_2 + 4cytC\text{-}Fe^{2+}$ _____ $2H_2O + 4cytC\ Fe^{3+}$

ATP synthase complex/F_0F_1 ATPase; it is sometimes referred to as the fifith complex, it has two units F_0 and F_1. The F_0 unit serves as a proton channel that chamnels the H^+ back into the matrix of the mitochondria. The F_1 unit catalyses the synthesis of ATP from ADP and Pi. Ithas several chains that have binding sites for ATP, ADP and Pi and also catalytic sites.

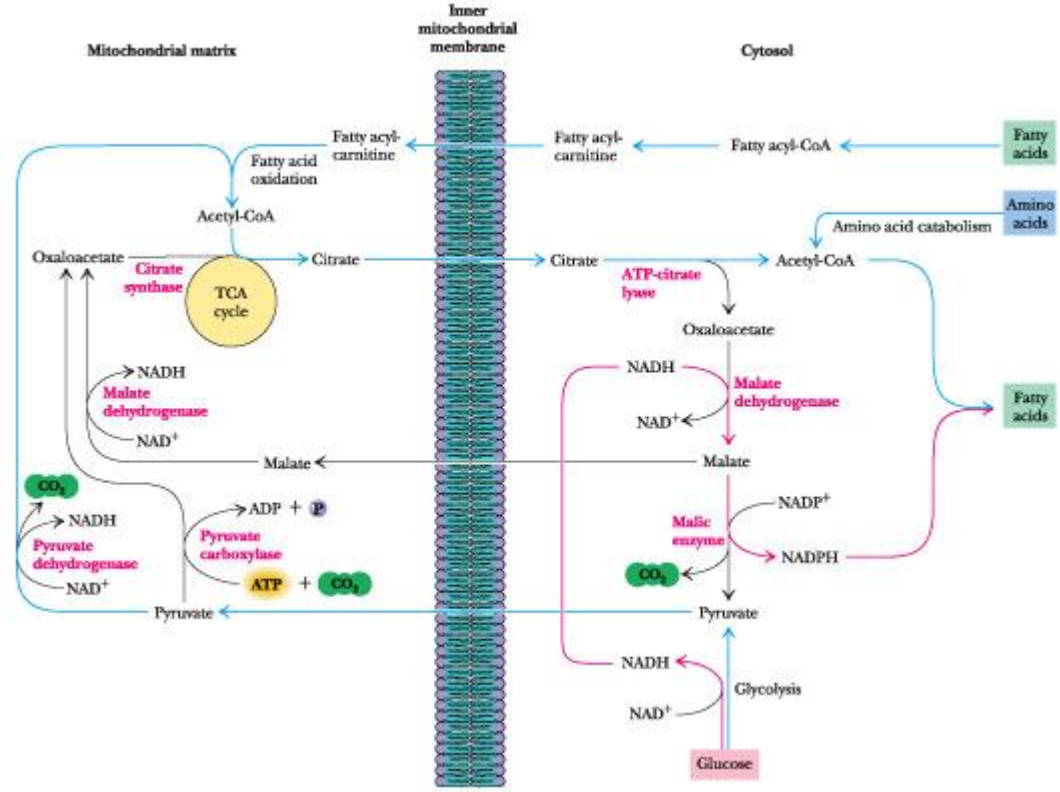
The accumulated protons in the intermembrane space produce a gradient and an electrochemical potential difference, this proton motive force drives the synthesis of ATP when the protons are channeled back into the matrix through the ATP synthase.

Hence the oxidation of coenzymes or electrons in the chains is coupled to phosphorylation of ADP to yield ATP hence the term oxidative phosphorylation.

Defects in coupling of oxidation /phosphorylation may occur and this uncoupling causes a yield of heat.

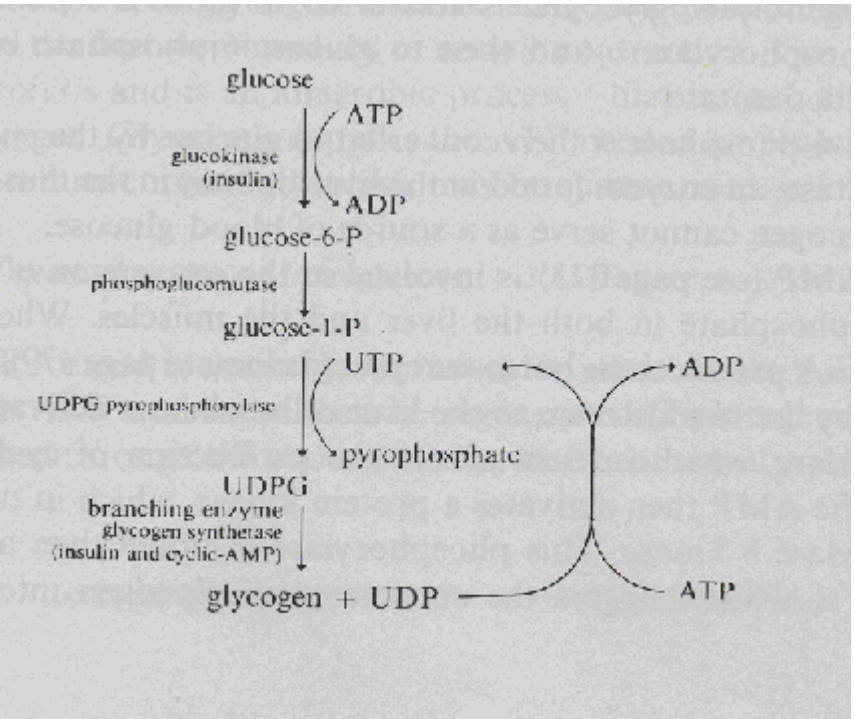
A total of 38 ATPS are produced from the complete oxidation of one molecule of glucose as well as 2 molecules of water and 6 CO_2. Generation of ATP along the glycolytic pathway is called substrate level phosphorylation. While from the ETChain is oxidative phosphorylation

The malate-aspartate shuttle.



Malate-aspartate shuttle.

GLYCOGENESIS



Glycogenesis: this is the formation of glycogen from glucose. It occurs majorly in liver and skeletal muscles but can also occur in some tissues to some extent (see pathway above)

- Glycogen is the storage form of carbohydrate in the animal body especially in the liver and muscles from where it is mobilized as glucose whenever tissue requires.
- Glycogen is insoluble and exerts no osmotic pressure and does not diffuse from its storage sites. It is also readily broken down under the influence of hormones and enzymes to either glucose (in the liver) and lower intermediates in skeletal muscles and other tissues for energy.
- Liver glycogen is the only immediately available source of glucose to the blood, glycogen is broken down to glucose -1-phophate and then glucose for maintenance of blood glucose levels, and also serves as protection of liver from toxic substances in high concentration.
- Certain detoxification reactions e.g conjugation of compound s with glucuronic acids are influenced by liver glycogen levels.