BIOMOLECULES (INTRODUCTION, STRUCTURE AND FUNCTIONS)

Porphyrin

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Porphyrin; Tetrapyrrole; Heme;, Haemoglobin; Myoglobin; Cytochrome; Catalase; Peroxidase; Chlorophyll; Bile pigments.

Porphyrin nucleus

Porphyrins are highly coloured cyclic tetrapyrrolic pigments formed by the linkage of four pyrrole rings through methene (–HC=) bridges (Fig. 1). The basic structure of a tetrapyrrole is four pyrrole rings surrounding a central metal atom. Porphyrins are 22*p* electron systems whose main conjugation pathway contains 18*p* electrons, which explains the aromatic nature from which the intense colour associated with them stems.

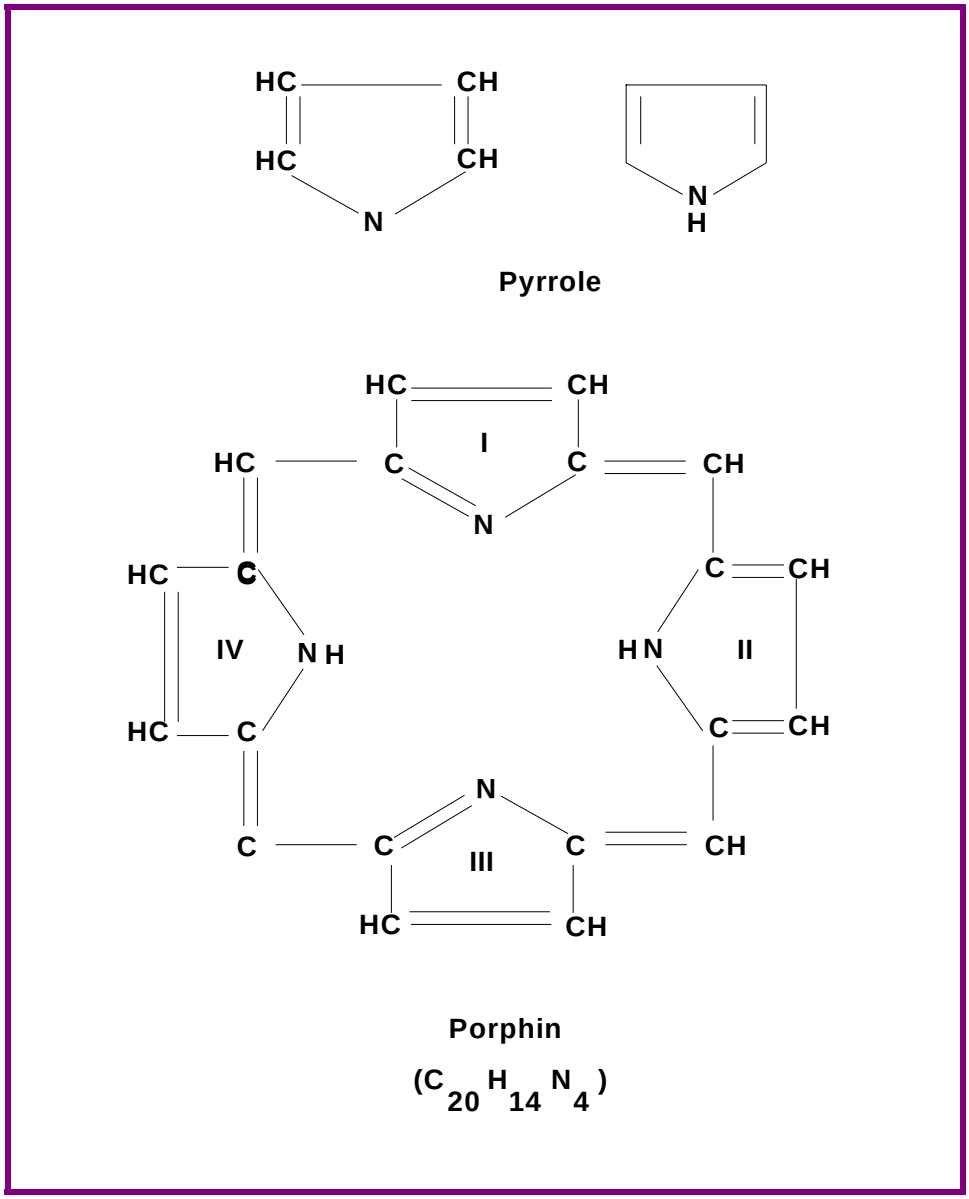


Fig. 1: Pyrrole and tetrapyrrole structure

The porphyrins represent the most widespread of all the prosthetic groups found in nature. They mediate a spectrum of critical functions in a variety of biological systems ranging from electron transfer, oxygen transport, photosynthetic energy transduction and conversion of carbon dioxide into fuel. In addition, porphyrins in which the macrocycle is oxidized, i.e. cation radicals, are important intermediates in the catalytic cycles of heme proteins and in photosynthetic processes. These are aptly termed as '**pigments of life**'. Common examples of important porphyrins include heme and cytochrome (with chelated iron), chlorophyll (with chelated magnesium), coenzyme B_{12} (with chelated nickel). Thus, the parent form of these tetrapyrrolic macrocycles has a common porphin nucleus shown in Fig. 2.

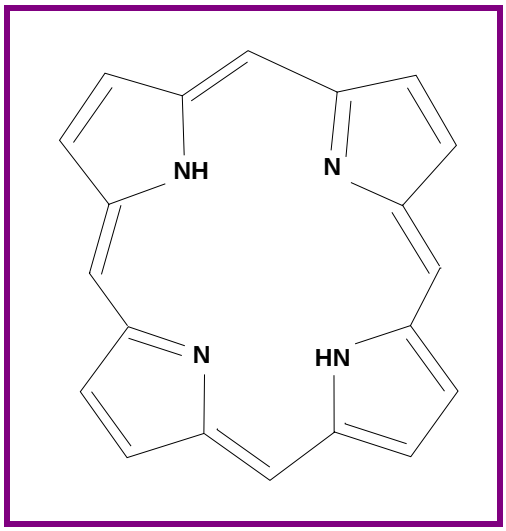


Fig. 2: Porphyrin nucleus

Classification of porphyrins

The porphyrins are named and classified on the basis of their side-chain substituent groups. In case of natural porphyrins, various side chains are substituted for the eight hydrogen atoms in the porphin nucleus. Thus, the naturally occurring porphyrins include:

- ☞ Type I
- ☞ Type III

A porphyrin with a completely symmetric arrangement of the acetate (A), propionate (P) and methylene (M) substituents is classified as a Type I porphyrin while the one with asymmetric arrangement of A, P and M substituents is classified as Type III. These types are shown as Fischer formulae in Fig. 3. Out of these two naturally occurring porphyrins, Type III is the most abundant.

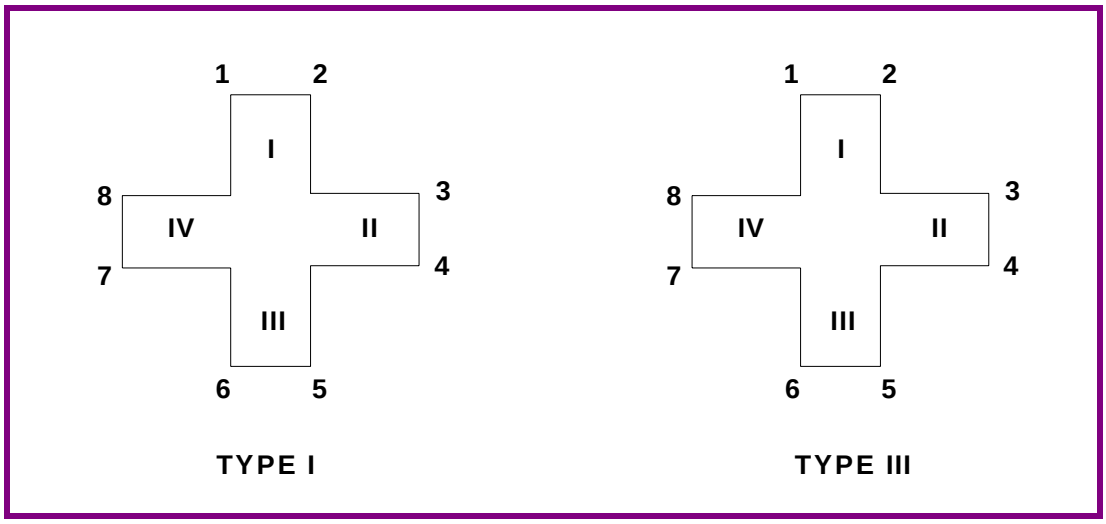


Fig. 3: Types I and III porphyrins

[In Type I: Positions 1, 3, 5 and 7 are occupied by acetyl / methyl groups; Positions 2, 4, 6, and 8 represent propionyl groups; In Type III: Positions 1, 3, 5 and 8 are occupied by acetyl / methyl groups; Positions 2, 4, 6, and 7 represent propionyl groups].

Some common examples of these porphyrin types are shown in Fig. 4. Similarly, there exist other isomeric forms with variation in the arrangement of substituent groups on the porphin nucleus.

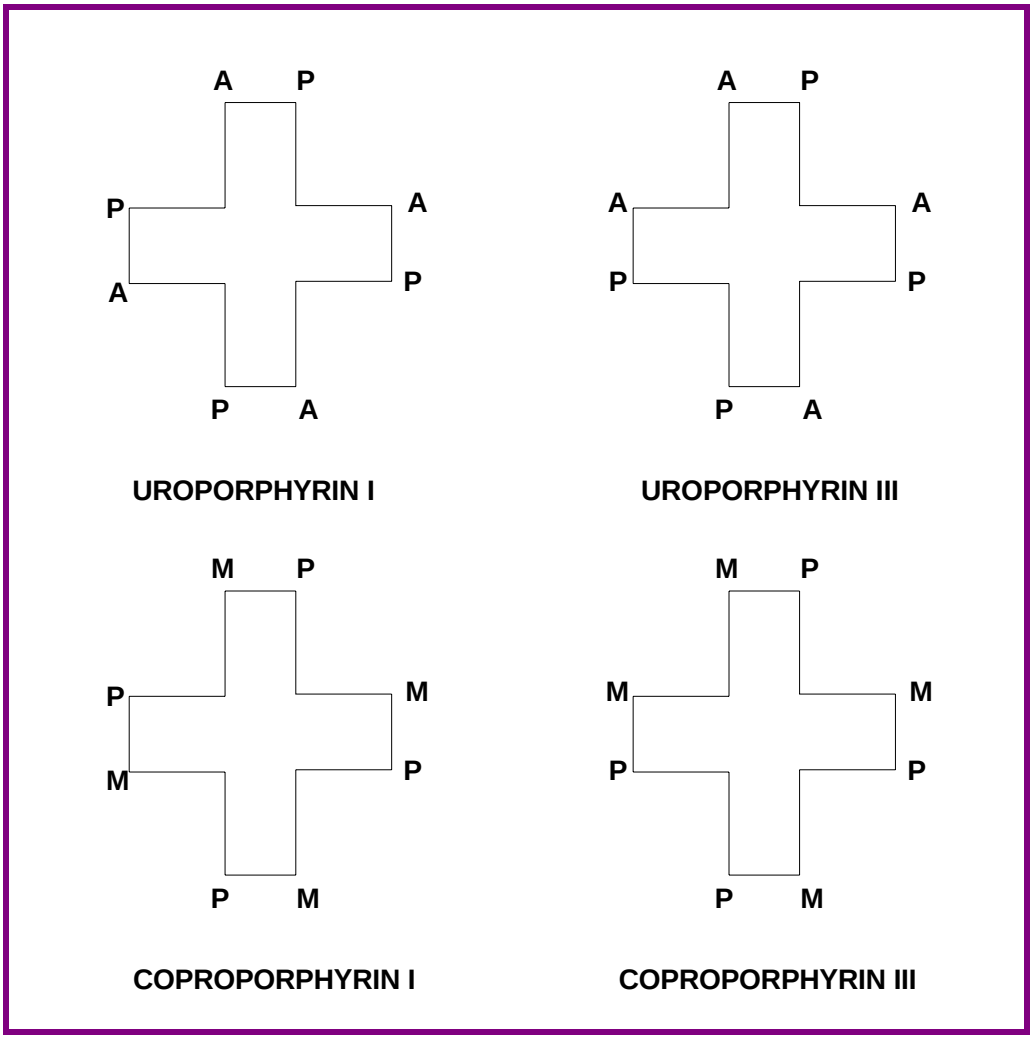


Fig. 4: Examples of Type I and Type III porphyrins
[A is acetyl group; M is methyl; P is propionyl group]

Biosynthesis of porphyrin

All the porphyrins are derived from a common monopyrrolic precursor, **δ-amino-levulinic acid (ALA)**. In mammals, the first step in the biosynthesis of porphyrins is the condensation of glycine and succinyl coenzyme A to form δ-amino-levulinate (ALA). This reaction is catalyzed by δ-amino-levulinate synthase (ALA synthase), a pyridoxal phosphate-requiring (PLP) enzyme present in mitochondria and is the rate-limiting step (Reaction 1).

δ-amino-levulinate synthase
(In mitochondria)
Succinyl-CoA + Glycine → δ-amino-levulinic acid (ALA) + $8H^+$ + 16 H_2O ….(1)

ALA is transported out of mitochondria and inside the cytoplasm two molecules of δ-

amino-levulinate condense to form porphobilinogen (PBA), the next intermediate. The reaction is catalyzed by δ-amino-levulinate dehydratase / dehydrogenase (ALA dehydratase / dehydrogenase) (Reaction 2).

$$2\ \text{ALA} \xrightarrow[\text{(In cytosol)}]{\text{ALA dehydratase}} \text{Porphobilinogen (PBA)} \quad \ldots\ldots(2)$$

Four molecules of porphobilinogen then condense head to tail to form a linear tetrapyrrole (hydroxymethyl bilane) in a reaction catalyzed by porphobilinogen deaminase (PBG deaminase). This enzyme-bound linear tetrapyrrole then cyclizes to form uroporphyrinogen III, which has an asymmetric arrangement of side chains. This reaction requires uroporphyrinogen cosynthase (Reaction 3). However, in the presence of synthase alone, uroporphyrinogen I, the nonphysiologic symmetric isomer, is produced.

$$4\ \text{PBA} \xrightarrow[\text{(In cytosol)}]{\text{PBG deaminase}} \text{Linear tetrapyrrole} \xrightarrow[\text{(In cytosol)}]{\text{Uroporphyrinogen cosynthase}} \text{Uroporphyrinogen III} \quad \ldots\ldots(3)$$

Up to this step, the porphyrin skeleton is formed. Subsequent reactions alter the side chains and the degree of saturation of the porphyrin ring. Thus, coproporphyrinogen III is formed by the decarboxylation of the acetate side chains. The reaction requires the catalysis by uroporphyrinogen decarboxylase (Reaction 4).

$$\text{Uroporphyrinogen III} \xrightarrow[\text{(In cytosol)}]{\text{Uroporphyrinogen decarboxylase}} \text{Coproporphyrinogen III} \quad \ldots\ldots(4)$$

In the next step, the desaturation of the porphyrin ring and the conversion of two of the propionate side chains into vinyl groups yield protoporphyrin IX. The reaction is catalyzed by coproporphyrinogen oxidase and protoporphyrinogen oxidase, with the intermediate formation of protoporphyrin III (Reactions 5 and 6).

$$\text{Coproporphyrinogen III} \xrightarrow[\text{(In mitochondria)}]{\text{Coproporphyrinogen oxidase}} \text{Protoporphyrinogen III} \xrightarrow[\text{(In mitochondria)}]{\text{Protoporphyrinogen oxidase}} \text{Protoporphrin IX} \quad \ldots\ldots(5, 6)$$

The outline of biosynthetic pathway for porphyrin occurring in mitochondria and cytoplasm is shown in Fig. 5.

The biosynthesis of various porphyrins, such as chlorophyll, vitamin B_{12}, heme etc., branches from the two intermediates, uroporphyrinogen III (Fig. 6a) and protoporphrin IX (Fig. 6b) by insertion of either magnesium or iron into the central cavity and further modifications occur and finally specialized porphyrin prosthetic groups are attached to their respective apoproteins (the form of the protein consisting of just the polypeptide chain) to form the biologically functional holoprotein.

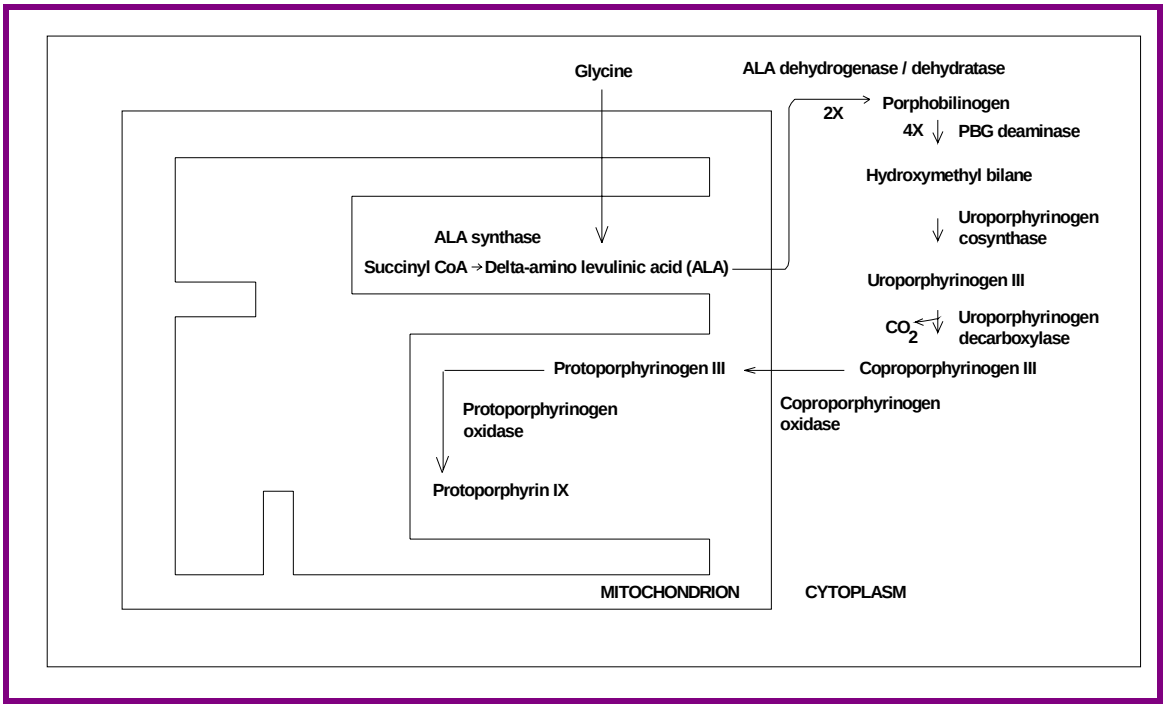
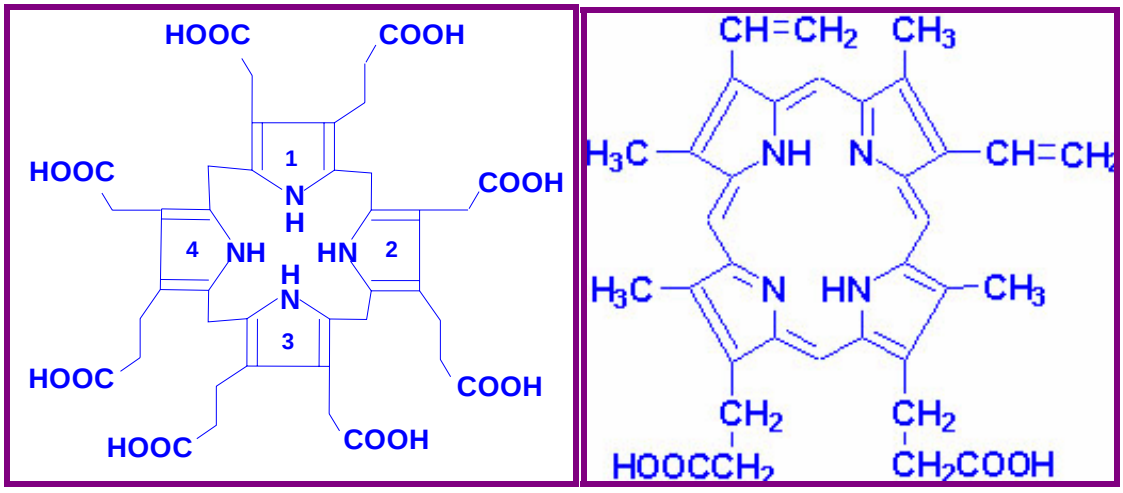


Fig. 5: Biosynthesis of porphyrin

Thus, uroporphyrinogen III is a key intermediate in the synthesis of vitamin B_{12} by bacteria and chlorophyll by bacteria and plants (described later). Protoporphyrin can form quadridentate (four teeth) chelate complexes with iron, magnesium, zinc, nickel, cobalt and copper ions, in which four coordination bonds hold the metal. Protoporphrin IX is the only isomeric form of protoporphyrin that exists in nature. It serves as precursor for the biosynthesis of haemoglobin (described later), myoglobin (Mb), most of the cytochromes (cyt), catalase and peroxidase.



(a) (b)

Fig. 6: Intermediates of porphyrin biosynthesis.

(a) Uroporphyrinogen; (b) Protoporphyrin IX

[Uroporphyrinogen III contains four propionic acid groups and four ethanoic acid groups, while protoporphyrin IX contains four methyl groups, two vinyl groups and two propionic acid groups substituted on eight available positions on the porphin nucleus].

Metalloporphyrins occurring in nature

The porphyrins containing the metal atom are called metalloproteins. The porphyrins have a characteristic property of formation of complexes with metal ions bound to the nitrogen atom of the pyrrole rings. Various examples of metalloproteins occurring in nature are:

- Iron containing porphyrins: Heme proteins (hemoglobin, myoglobin, cytochrome, enzymes catalase and peroxidase)
- Magnesium containing porphyrin: Chlorophyll
- Cobalt containing porphyrins: Vitamin B_{12}

Heme proteins

Hemes are a diverse group of tetrapyrrole pigments. Hemes are present as the prosthetic group of both Haemoglobin (Hb) and Myoglobin (Mb) along with other globin proteins. Heme is responsible for the characteristic red colour and is the site at which each globin monomer binds one molecule of O_2. Heme is also required by the cytochromes (including those involved in the respiratory and photosynthetic electron transport) and the cytochrome P450 that is used in detoxification reactions. Some enzymes, including catalase and peroxidase, also contain heme. In all these proteins, the function of the heme is either to bind and release a ligand to its central iron atom, or for the iron atom to undergo a change in oxidation state, releasing or accepting an electron for participation in a redox reaction.

The heterocyclic ring system of heme is a porphyrin derivative (protoporphyrin IX) and consists of four pyrrole rings linked by methene bridges. Besides, it forms a chelate complex with Fe (II), called protoheme or more simply heme prosthetic group. A similar complex with Fe (III) is called hemin or hematin. In heme, this Fe^{2+} bonds with four nitrogen atoms in the center of the protoporphyrin ring forming a square-planar complex, and the remaining fifth and sixth coordination positions of iron are perpendicular to the plane of the porphin ring on either side. When the fifth and sixth positions of iron are occupied, the resulting structure is a hemochrome or hemochromogen. The structure of heme prosthetic group (Fe-protoporphyrin IX) is shown in Fig. 7.

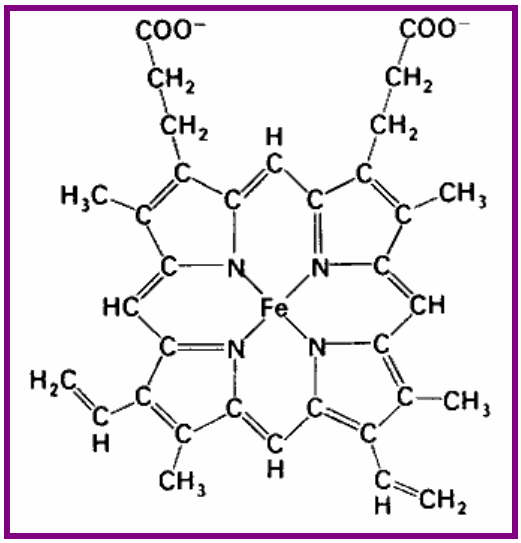


Fig. 7: Structure of heme (Fe-protoporphyrin IX)

In mammals, heme is synthesized primarily (85% of body's heme groups) in immature erythrocytes (erythroblasts) with the remainder occurring in the liver. Fig. 8 outlines the synthesis of heme from δ-amino-levulinic acid (ALA).

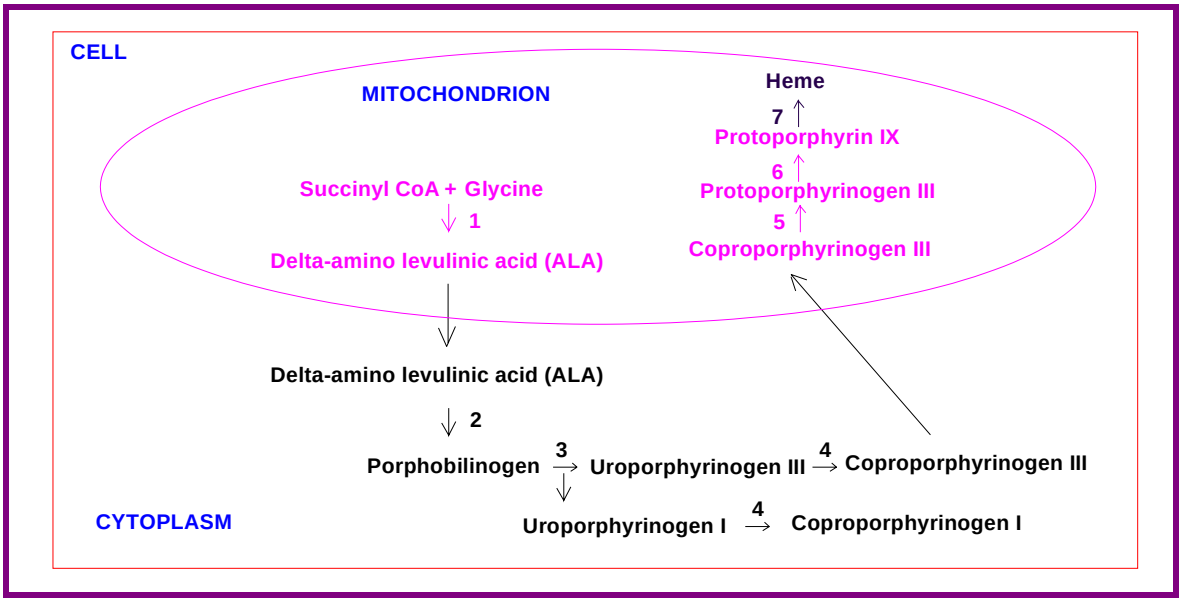


Fig. 8: Synthesis of heme

[The numbers 1 to 6 given in the figure represent the enzymes already mentioned in the section of biosynthesis of porphyrin, while 7 represents the chelation of protoporphyrin IX with iron to form heme].

Several inherited genetic defects in heme biosynthesis have been identified that give rise to disorders called porphyrias, which involve accumulation of porphyrins. Porphyrin is synthesized in both the erythroblasts and the liver, and either one may be the site of a disorder. Congenital erythropoietic porphyria, for example, prematurely destroys erythrocytes. This disease results from insufficient cosynthase. In this porphyria, the synthesis of the required amount of uroporphyrinogen III is accompanied by the formation of very large quantities of the symmetric isomer, uroporphyrinogen I. Uroporphyrin I, coproporphyrins I and other symmetric derivatives also accumulate. The urine of patients having this disease is red because of the excretion of large amounts of uroporphyrins I. Their teeth exhibit a strong red fluorescence under ultraviolet light because of the deposition of porphyrins. Furthermore, their skin is usually very sensitive to light because photoexcited porphyrins are quite reactive.

Acute intermittent porphyria is the most prevalent of the porphyrias affecting the liver. This porphyria is characterized by the overproduction of porphobilinogen and δ-aminolevulinate, which results in severe abdominal pain and neurological dysfunction. The 'madness' of George III, King of England during the American Revolution S, is believed to have been due to this porphyria.

In different molecular arrangements and combinations, heme serves as a prosthetic group of other important hemochromes or heme proteins such as haemoglobin and myoglobin, cytochrome, peroxidase, and catalase. Following section describes the structure and functions of various heme proteins.

❖ **Haemoglobin (Hb):** Hb is a member of the family of pigments called tetrapyrroles. It is a oxygen binding allosteric heme protein and the heme group is responsible for the deep red-brown colour of Hb. Hb is a heterotetramer, $\alpha_2\beta_2$ containing two types of subunits, α and β (Fig. 9). Each of the four subunits of haemoglobin (Hb) noncovalently binds a single heme group.

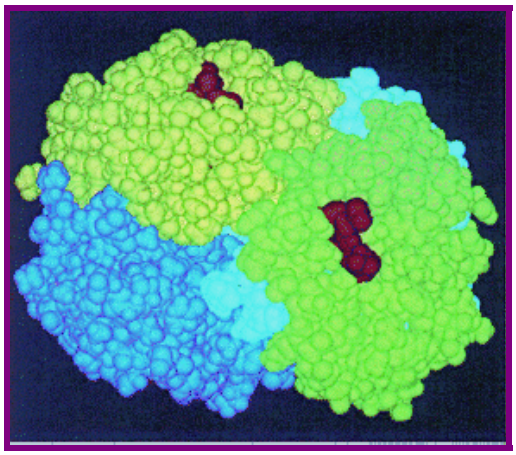


Fig. 9: Three-dimensional structure of haemoglobin

The α and β subunits are structurally and evolutionarily related to each other and to the Mb, the monomeric oxygen-binding protein of muscle. Close to where the O_2 binds to the heme group in Hb, is a histidine residue, the distal histidine (His E7). This serves two very important functions. First, it prevents heme groups on neighboring Hb molecules coming in contact with one another and oxidizing to the Fe^{3+} state in which they can no longer bind O_2. Second, it prevents carbon monoxide (CO) binding with the most favourable configuration to the Fe^{2+}, thereby lowering the affinity of heme for CO. This is important because once CO has bound irreversibly to the heme, the protein can no longer bind O_2. In the globins (Hb and Mb), four pyrrole nitrogens occupy the one to four positions of iron, the fifth position is occupied by an imidazole group of a histidine residue, the proximal histidine, which lies eighth residues along helix F of haemoglobin (HisF8). The sixth position is either unoccupied (deoxyHb and deoxyMb) or occupied by oxygen (oxyHb and oxyMb) or other ligands, such as carbon monoxide. In both Hb and Mb, the iron atom normally remains in the Fe (II) (ferrous) oxidation state whether or not the heme is oxygenated (binds O_2). Thus, although the oxygen-binding site in Hb and Mb is only a small part of whole protein, the polypeptide chain modulates the function of the heme prosthetic group.

Although many invertebrate species have haemoglobin-based oxygen transport systems, others produce one of two alternative types of O_2-binding proteins: (i) Haemocyanin, a copper containing protein that is blue in complex with oxygen and colorless otherwise; (ii) Haemerythrin, a non-heme Fe-containing protein that is burgundy coloured in complex with oxygen and colorless otherwise.

❖ **Myoglobin (Mb):** Mb molecule contains a single small polypeptide chain of 153 amino acids and a single prosthetic iron-porphyrin (or heme) group, identical with that of Hb. Like, haemoglobin, Mb is also an oxygen-binding heme protein and the heme group is responsible for the deep red-brown colour of Mb. Mb binds a single heme group. Fig. 8 depicts the 3D structure of Mb.

❖ **Cytochromes (Cyt):** In 1925, Keilin gave the name 'cytochrome' to a group of intracellular, electron-transferring hemoproteins containing iron-porphyrin groups. These are found only in aerobic cells. Some are located in the inner mitochondrial membrane, where they act sequentially to carry electrons originating from various dehydrogenase systems toward molecular oxygen. Cytochrome P450 is found in endoplasmic reticulum, where it plays a role in specialized hydroxylation reactions. All cytochromes undergo reversible Fe (II)-Fe (III) valence changes during their catalytic cycles.

Depending on the nature of the heme prosthetic groups, (*viz*. side chains of their porphyrins *etc*.), the cytochromes fall into different groups - *a, b, c* and *d*.
Cytochrome *a*: Heme group contains a formyl side chain.
Cytochrome *b*: Has protoheme prosthetic group, which is non-covalently bound to protein.
Cytochrome *c*: Has covalent linkages between the heme side chains and the protein.
Cytochrome *d*: Heme group contains a dihydro-porphyrin (chlorin).

In case of a cytochrome having two different heme groups attached to a specific protein, both hemes may be indicated, *e.g*., 'cytochrome *bc*'. The use of unprimed italic letters implies that not only are four of the coordinate places of the iron attached to the four nitrogen atoms of the porphyrin, but also positions five and six are attached to groups in the protein. For example, in cytochrome *c*, one of the places is occupied by a histidine and the other by a methionine residue in the protein. Where the heme is not in this type of structure, a prime is used, *e.g*., cytochrome *c'*. The well established cytochromes are identified by subscript numerals attached to the letter indicating the group, *e.g*., cytochrome c_3. The reduced forms of cytochromes show a marked absorption in the visible range. Hence, some cytochromes are given names based on the wavelength (in nm) of the α-band of the reduced form, *e.g.*, cytochrome *c*-554 *etc*. [The absorption spectrum of a typical single cytochrome in the reduced form shows three main bands in the visible region: these are called, in decreasing order of wavelength, the α-, β- and γ-bands].

The reduced forms cannot be oxidized by molecular oxygen, with the exception of the terminal cytochromes of mitochondrial respiration, namely, cytochrome a_3 or cytochromes *c* oxidase, which also contains tightly bound copper. In the mitochondria of higher animals, where the respiratory chain has been most thoroughly studied, at least five different cytochromes have been identified in the inner membrane: cytochromes *b*, c_1, *c*, *a* and a_3. At least one of these, cytochromes *b*, occurs in two or more forms. In addition to cytochromes found only in the inner membrane of mitochondria, another type, cytochromes b_5, occurs in the endoplasmic reticulum.

In nearly all the cytochromes, unlike globins, the fifth and sixth positions of the iron are occupied by the R groups of specific amino acid residues of proteins. These cytochromes therefore cannot bind with ligands like oxygen, carbon monoxide or cyanide; an important exception is cytochromes a_3, which normally binds oxygen in its biological function.

❖ **Heme containing enzymes (catalase and peroxidase):** Animal and plant cells also contain other heme enzymes, such as peroxidase and catalase.

☞ **Catalase (CAT):** Catalase catalyzes the decomposition of hydrogen peroxide to give water and oxygen.

$$2H_2O_2 \rightarrow 2H_2O + O_2$$

☞ **Peroxidase (POD):** Peroxidase catalyzes the dehydrogenation of a large

number of organic compounds such as phenols, aromatic amines, hydroquinones, etc. POD catalyzes the reaction:

Guaiacol + H_2O_2 → Oxidized Guaiacol + $2H_2O$

Chlorophyll

Chlorophylls are the essential components for photosynthesis and occur in chloroplasts as green pigments in all photosynthetic plant tissues. These are important in the energy producing mechanisms of photosynthesis. Like Hb, it is a member of the family of pigments called tetrapyrroles. Chemically, each chlorophyll molecule contains a porphyrin (tetrapyrrole) nucleus with a chelated magnesium atom at the center and a long chain hydrocarbon (phytyl) side chain attached through a carboxylic acid group. There are at least five types of chlorophylls in plants. Chlorophyll 'a' and 'b' occur in higher plants, ferns and mosses. Chlorophyll 'c', 'd' and 'e' are only found in algae and in certain bacteria. The structure of chlorophyll a and b is shown in Fig. 10.

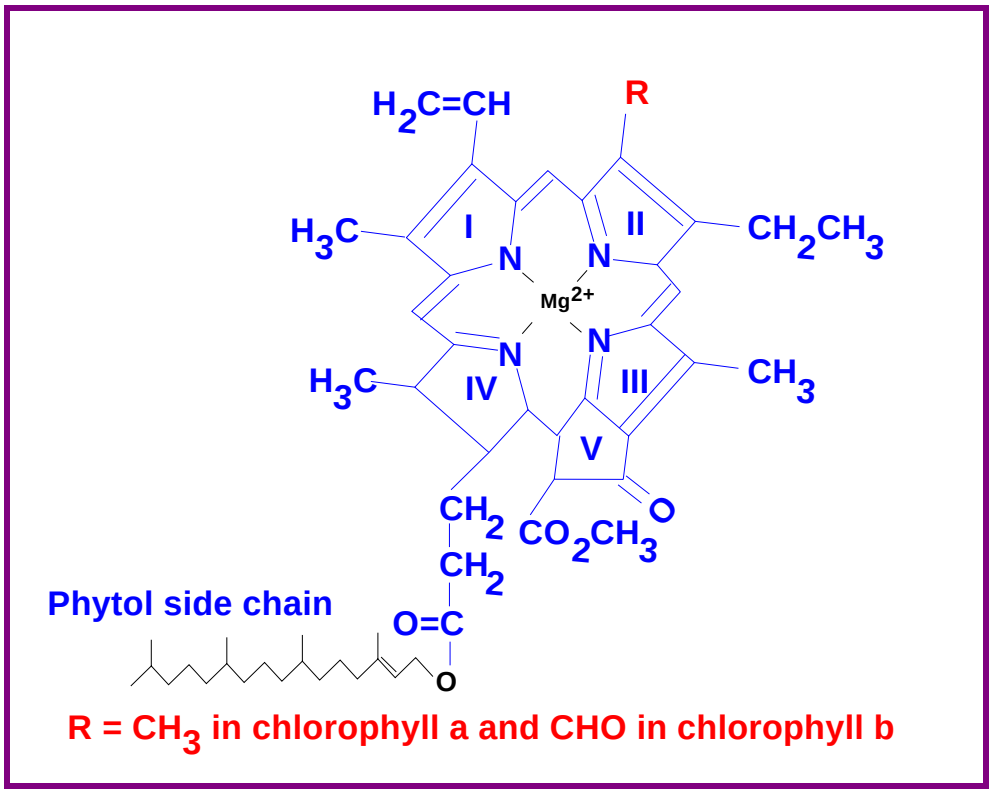


Fig. 10: Structure of chlorophyll

They share a common function in all of these organisms to act as light-harvesting and reaction center pigments in photosynthesis. This function is achieved by a number of modifications to the basic tetrapyrrole structure. These include:

- The insertion of magnesium as the central metal ion.
- The addition of a fifth ring to the tetrapyrrole structure.
- Loss of a double bond from one or more of the pyrrole rings.
- Binding of one specific side chain to a long fat-like molecule called phytol.

These changes give chlorophylls and bacteriochlorophylls a number of useful properties. For example, chlorophylls are membrane bound, absorb light at longer wavelengths than

heme and are able to respond to excitation by light. In this way, chlorophylls can accept and release light energy and drive photosynthetic electron transport.

Biosynthesis of chlorophyll from the precursor uroporphyrinogen III is shown in Fig. 11.

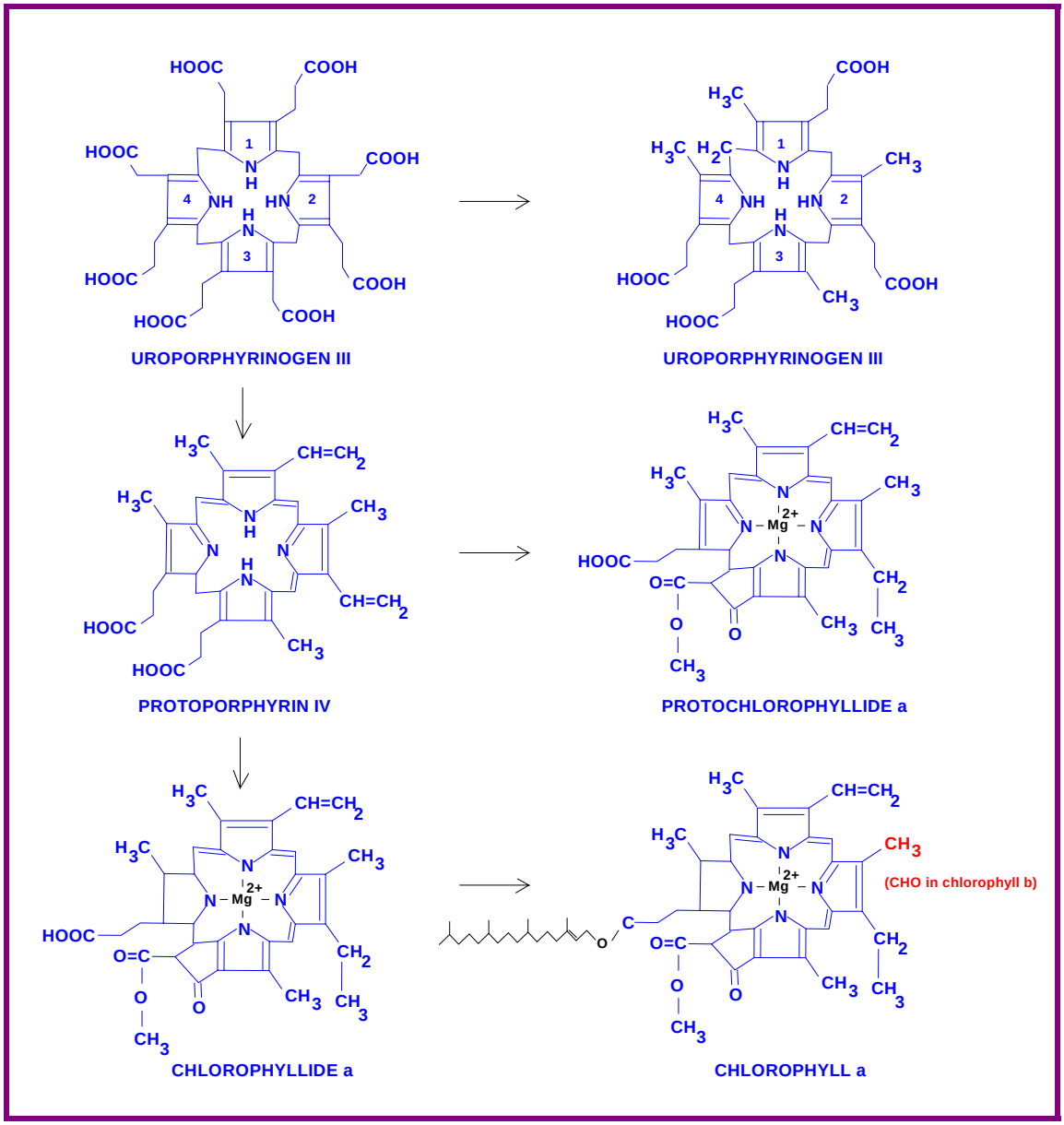


Fig. 11: Synthesis of chlorophyll

Vitamin B_{12}

Vitamin B_{12} is also called cyanocobalamin or anti-pernicious anemia factor. It has been found only in animals, chief source being liver. It is also found in milk, eggs, fish, oysters and clams. Under certain dietary conditions, In general, Cyanocobalamin is present in plant foods except in *Spirulina*, a blue-green algae. Animals and plants are unable to synthesize this vitamin. Cyanocobalamin is unique in that it appears to be synthesized only by microorganisms, especially anaerobic bacteria.

D. C. Hodgkin first established the structure of Vitamin B_{12} in 1957 (Fig. 12). The structure comprises of a centrally situated cobalt atom, surrounded by a macrocyclic structure of four reduced pyrrole rings (A, B, C and D) collectively called corrin. The six coordinate valencies of cobalt atom (Co^{2+}) are satisfied by the four nitrogens of the reduced tetrapyrrole, one nitrogen atom of 5,6-dimethylbenzimidazole and one cyanide ion. Corrin has lower degree of unsaturation with only six double bonds. Two of the pyrrole rings, namely A and D, are directly linked to each other. The other two pyrrole rings, namely B and C, are joined by a single methene carbon. Another distinctive feature of vitamin B_{12} molecule is the presence of a loop of the isopropanol, phosphate, ribose and 5,6-dimethylbenzimidazole in that order, the end of the loop attached to the central cobalt atom. It is deep red crystalline substance soluble in water, alcohol and acetone but not in chloroform. It is levorotatory. It is stable to heat in neutral solutions but is destroyed by heat in acidic or alkaline solutions.

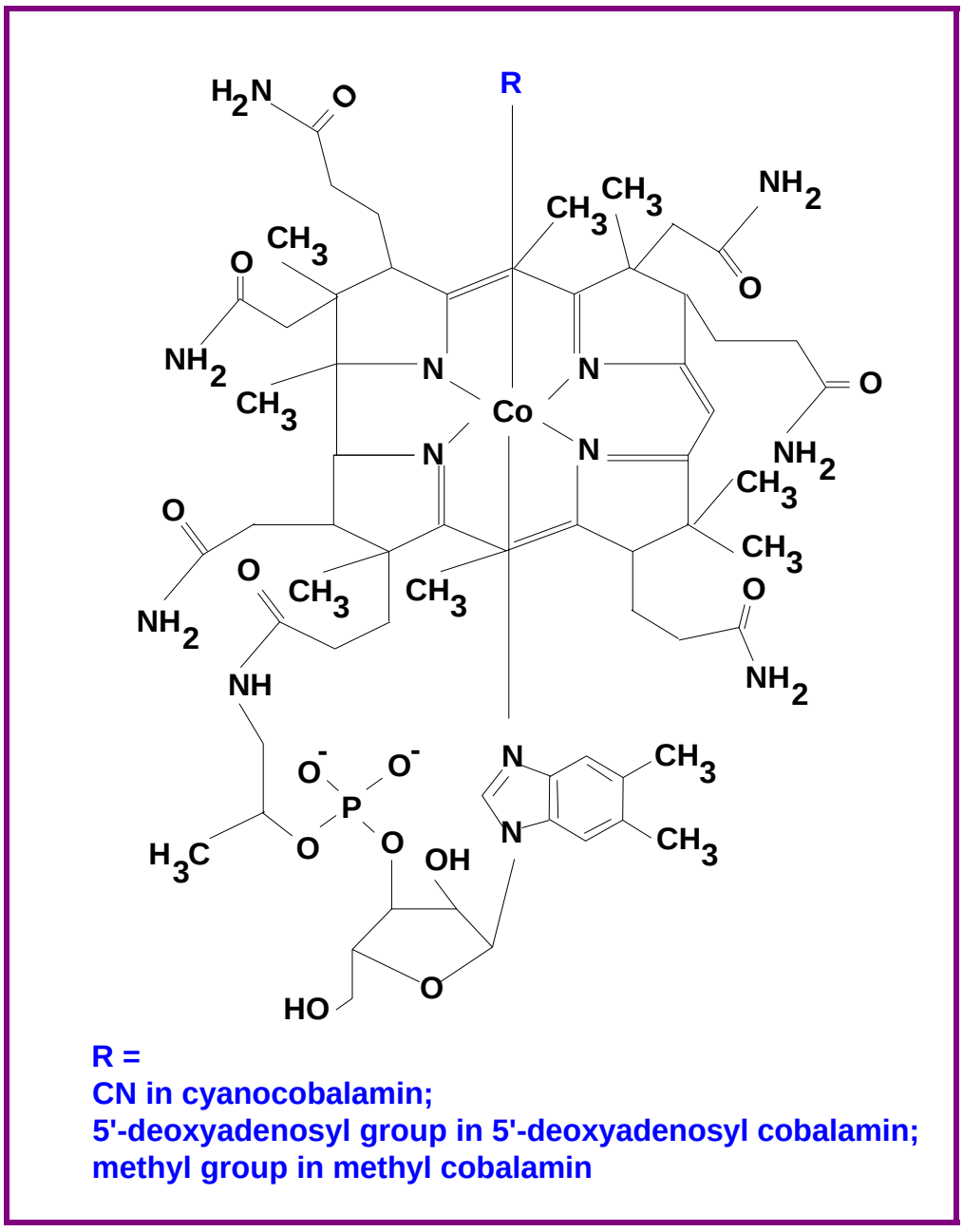


Fig. 12: Structure of Vitamin B_{12} and its coenzymes

Vitamin B_{12} is converted to coenzyme B_{12} by microorganisms in presence of ATP. Coenzyme B_{12} is also called 5'-deoxyadenosyl cobalamin. Its structure is similar to that of cyanocobalamin except that the cyanide group is replaced by adenosine and the linking with cobalt atom takes place at 5' carbon atom of the ribose of adenosine (Fig. 12). Another example of coenzyme B_{12} is methyl cobalamin, where methyl group occupies the sixth coordination position. Coenzyme B_{12} is the only known example of a carbon-metal bond in a biomolecule.

Detection of porphyrins

Porphyrins can be detected both spectrophotometrically as well as by fluorescence. The porphyrins and their derivatives exhibit a characteristic spectrum in both visible and U.V. regions. Thus, a solution of porphyrin in 5% HCl exhibits a sharp band near 400 nm, owing to the presence of porphin ring. This characteristic absorption is shown by all porphyrins regardless of the side chains present. This band is termed the Soret band after its discoverer, Charles Soret.

When porphyrins dissolved in strong mineral acids or in organic solvents are illuminated by U.V. light, they emit a strong red fluorescence. This fluorescence is so characteristic that it is often used to detect small amounts of free porphyrins. The double bonds joining the pyrrole rings in the porphyrins are responsible for the characteristic absorption and fluorescence of these compounds; these double bonds are absent in the porphyrinogens thereby making them colourless.
Coproporphyrins and uroporphyrins, which are excreted in increased amounts in the porphyrias, are quantified in urine and feces after extraction with appropriate solvent mixtures. ALA and porphobilinogen are also estimated in urine by appropriate colorimetric tests.

Estimation of chlorophyll is done by extracting the pigment in organic solvents such as 80% acetone or ether. Then the absorption is measured at 663 and 645 nm by a spectrophotometer to determine chlorophyll 'a' and 'b' using the following formulae:

$$\text{mg chlorophyll 'a' / g tissue} = \frac{12.7\,(A_{663}) - 2.69\,(A_{645})\ X\ V}{1000\ X\ W}$$

$$\text{mg chlorophyll 'b' / g tissue} = \frac{22.9\,(A645) - 4.68\,(A663)\ X\ V}{1000\ X\ W}$$

$$\text{mg total chlorophyll / g tissue} = \frac{20.2\,(A645) + 8.02\,(A663)\ X\ V}{1000\ X\ W}$$

where, A is absorbance at specific wavelengths; V is final volume of chlorophyll extract in 80% acetone; W is fresh weight of tissue extracted.

The enzyme activity of catalase can be assayed by measuring the decrease in absorbance (due to decomposition of hydrogen peroxide) at 220 nm. Catalase can also be observed spectrophotometrically by measuring the release of O_2.

The peroxidase enzyme activity can be determined using guaiacol as substrate. The resulting oxidized (dehydrogenated) guaiacol is probably more than one compound and depends on the reaction conditions. The rate of formation of guaiacol dehydrogenation product is a measure of the peroxidase activity and can be assayed spectrophotometrically at 470 nm.

Bile pigments – Chemical structure and physiological significance

Bile pigments are the products of breakdown of the cyclic tetrapyrrole structure of heme in both animals and plants. In animals, this pathway is an excretory system by which the heme from the Hb of aging RBCs and other hemoproteins is removed from the blood. At the end of their lifetime, RBCs are removed from the circulation and their components degraded to biliverdin and / or bilirubin (Fig. 13).

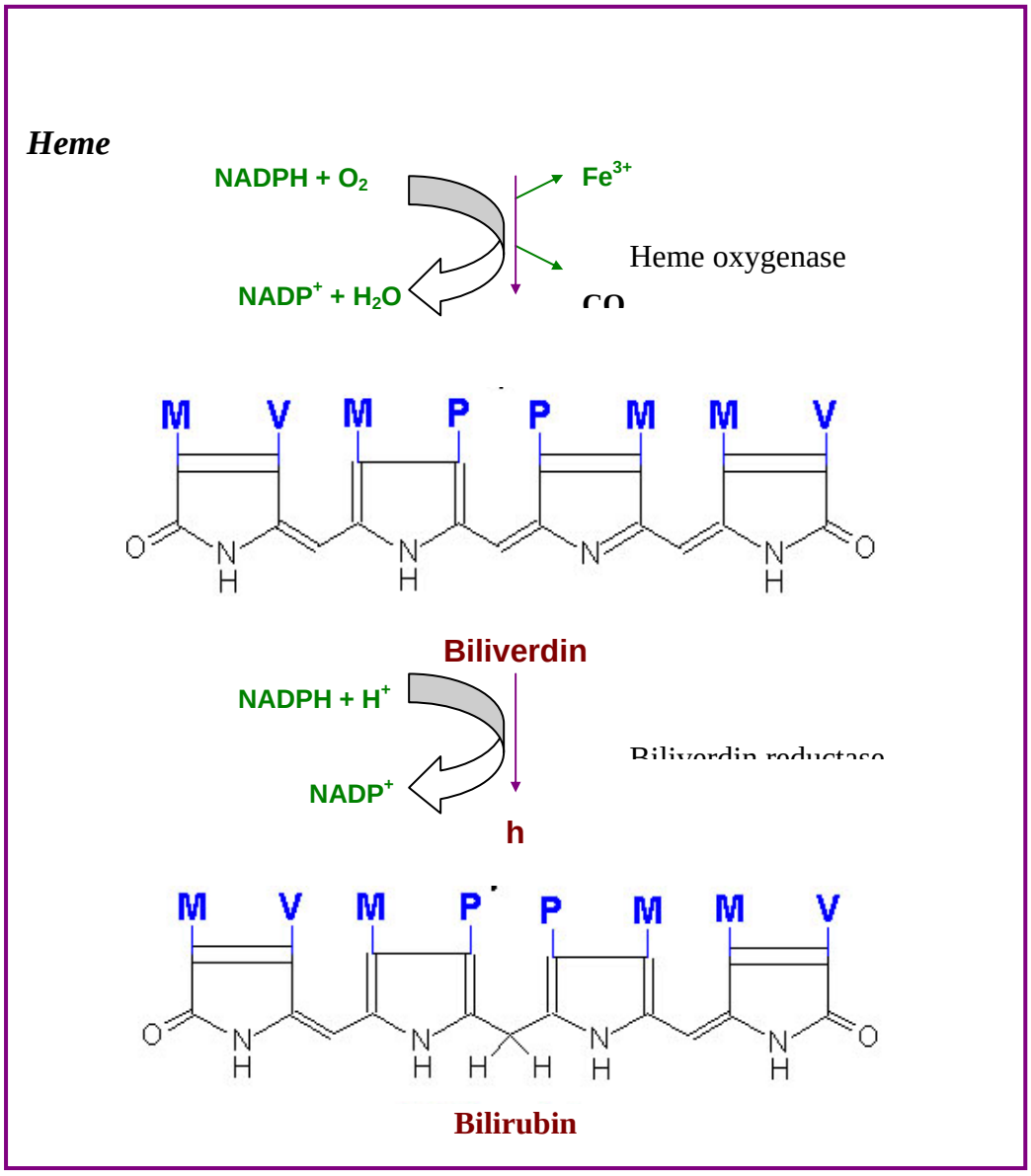


Fig. 13: Degradation of heme to bile pigments biliverdin and bilirubin
[M is methyl (-CH_3), P is propionyl ($CH_2CH_2CH_2OH$) and V is vinyl ($CH=CH_2$)].

Heme catabolism begins with oxidative cleavage of the porphyrin between rings A and B by heme oxygenase to form biliverdin, a green linear tetrapyrrole. Heme oxygenase is a member of the cytochrome P450 family of enzymes and is present mainly in the spleen and liver of vertebrates. This enzyme requires NADPH and O_2. In birds, reptiles and amphibians this water soluble pigment, biliverdin, is the final product of heme degradation and is excreted directly. In mammals, the central methenyl bridge (between rings C and D) of biliverdin is then reduced by biliverdin reductase to form the red-orange bilirubin.

The highly lipophilic bilirubin is insoluble in aqueous solutions. Like other lipophilic metabolites, such as free fatty acids, it is transported in the blood in complex with serum albumin. In the liver, its aqueous solubility is increased by esterification of its two propionate side groups with glucuronic acid, yielding bilirubin diglucuronide (Fig. 14a), which is secreted into the bile and then into the intestine. Bacterial enzymes in the large intestine hydrolyze the glucuronic acid groups and in a multistep process, convert bilirubin to several products, most notably urobilinogen (Fig. 14b). Some urobilinogen is reabsorbed and transported via the bloodstream to the kidney, where it is converted to the yellow urobilin (Fig. 14c) and excreted, thus giving urine its characteristic colour. Most of the urobilinogen, however, is microbially converted to the deeply red-brown stercobilin (Fig. 14d), the major pigment of feces. When the blood contains excessive amounts of bilirubin, the deposition of this highly insoluble substance colours the skin and the whites of the eyes yellow. This condition is called jaundice.

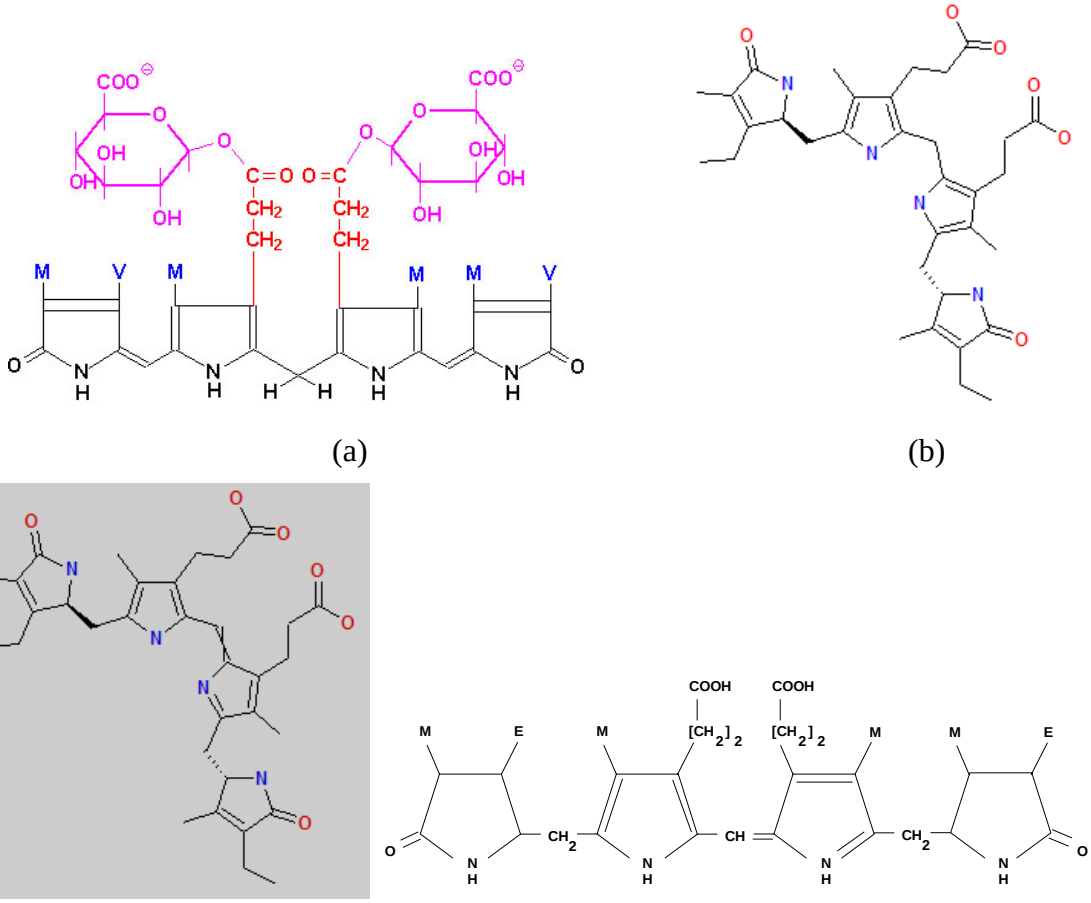


Fig. 14: Heme degradation products
(a) Bilirubin diglucuronide; (b) Urobilinogen; (c) Urobilin; (d) Stercobilin
[M is methyl group; V is vinyl group; E is ethyl group].

In the plant kingdom, heme is broken down to form bile pigments, which play major roles in coordinating light responses and in light-harvesting. In higher plants heme is broken down to the phycobiliprotein phytochrome, which is involved in coordinating light responses, while in algae it is metabolized to the light-harvesting pigments phycocyanin and phycoerythrin.

Suggested Reading

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