Water-soluble vitamins are associated with biochemical reactions that proceed in all organisms as they act as cofactors of many important enzymes involved in the metabolism of proteins, lipids, sugars, and many secondary products. Water-soluble vitamins of the B-group are principally synthesised by microorganisms (e.g. also by intestinal microflora) and plants, but animals must obtain these vitamins mostly through their diet. The mechanisms of the B-group vitamins formation have been investigated mainly in microorganisms. The biosynthetic pathways in organisms other than bacteria remain largely unknown. The biosynthesis of vitamin C occurs by different pathways in plants and animals. Microorganisms and higher fungi do not possess the ability to synthesise vitamin C.

1 THIAMIN

Vitamin $B_1$ (thiamin, formerly also known as aneurin) is a cofactor utilised in the reactions catalysed in branched-chain amino acid metabolism, the pentose phosphate pathway, and the citric acid cycle. In all cases, the mechanistic role of the active compound, thiamin diphosphate, which acts as a coenzyme, is the stabilisation of the intermediate acyl carbanions.

Many microorganisms form thiamin de novo, while others synthesise only the pyrimidine or only the thiazole part, and depend on the medium for the part they cannot synthesise. The biosynthesis of thiamin in eukaryotes is at a very early stage of understanding. Higher plants synthesise thiamin de novo. Animals can carry out only the
phosphorylation reactions on the pre-synthesised thiamin molecule.

The pyrimidine moiety (4-amino-5-hydroxymethyl-2-methylpyrimidine) and the thiazole moiety (5-hydroxyethyl-4-methylthiazole) of thiamin phosphate are synthesised in separate branches of the biosynthetic pathway and then coupled by a methylene group to yield thiamin phosphate, which is transformed to thiamin diphosphate. Several additional enzymes are involved in the salvage pathways of thiamin, its phosphates, and its pyrimidine and thiazole precursors.

1.1 Pyrimidine part of thiamin

The biosynthesis of the pyrimidine part of thiamin is still not well understood. In some bacteria (e.g. Escherichia coli), it starts with 1-(5-phospho-β-D-ribofuranosyl)-5-aminoimidazole (also known as 5- aminoimidazole ribonucleotide, AIR), an intermediate of purine metabolism (Friedrich 1988). The mechanism of the remarkable rearrangement involved in the conversion of AIR to pyrimidine has not yet been elucidated. It is supposed that the reaction begins with the cleavage of the bond between C-3' and C-4' of the ribose moiety; the C₂ fragment consisting of the C-4' and C'-5 of the ribose part of AIR is added across the C-4 and C-5 of the imidazole ring to form a three-membered ring (Figure 1). This is then opened to form the C-5 of the pyrimidine ring with the attached phosphorylated hydroxymethyl group in 4-amino-5-hydroxymethyl-2-methylpyrimidine phosphate (4-amino-2-methyl-5-phosphomethylpyrimidine). In addition, the rest of ribose is removed and a methyl group incorporated. The phosphate is finally transformed to 4-amino-5-hydroxymethyl-2-methylpyrimidine diphosphate under the action of phosphomethylpyrimidine kinase (EC 2.7.4.7).

d-Ribose is probably the source of the methyl group on the C-2 of the pyrimidine ring. Additionally, 4-amino-5-hydroxymethyl-2-methylpyrimidine phosphate can be formed by phosphorylation of 4-amino-5-hydroxymethyl-2-methylpyrimidine via a salvage pathway using hydroxymethylpyrimidine kinase (EC 2.7.1.49).

The biosynthesis of the pyrimidine moiety in eukaryotes is completely different from that in prokaryotes and is still poorly understood. It is

![Figure 1](attachment:image.png)

For example, the yeast Saccharomyces cerevisiae utilises external thiamin for the production of thiamin diphosphate or can synthesise the cofactor itself. Prior to the uptake into the cell, thiamin phosphates are first hydrolysed and thiamin is taken up as free vitamin, which is then transformed to the pyrophosphate. Synthesis of thiamin diphosphate starts with the production of hydroxyethylthiazole and hydroxymethylpyrimidine. These are linked to yield thiamin phosphate, which is hydrolysed to thiamin and subsequently diphosphorylated (Hohmann & Meacock 1998).
known that this part of the thiamin molecule is derived from L-histidine and pyridoxol (Settembre et al. 2003).

1.2 Thiazole part of thiamin

The thiazole part of thiamin has different precursors in bacteria and yeasts. In either case, the carbon atoms come from glycosuloses. The nitrogen atom and the neighbouring C-2 carbon atom are derived from an amino acid; in many bacteria and yeasts from glycine, and in some bacteria from L-tyrosine. The sulfur atom comes from L-cysteine (Begley et al. 1999, 2001a; Settembre et al. 2003; Dorrestein et al. 2004).

In Bacillus subtilis and most other bacteria, the thiazole moiety is biosynthesised from 1-deoxy-D-xylulose 5-phosphate (1-deoxy-D-threo-pent-2-ulose 5-phosphate), glycine, and cysteine in a complex oxidative condensation reaction (Dorrestein et al. 2004). Under the catalysis by deoxyxylulose phosphate synthase (EC 2.2.1.7), 1-deoxy-D-xylulose 5-phosphate forms from D-glyceraldehyde 3-phosphate (3-phospho-D-glyceraldehyde) and pyruvic acid that are obtained from the glycolysis (Begley et al. 2001b). Thiamin diphosphate mediated decarboxylation of pyruvic acid produces acetaldehyde bound in the form of enamine, which reacts as a nucleophile in the acyloin type condensation reaction with D-glyceraldehyde 3-phosphate (Velíšek & Cejpek 2005) (Figure 2).

The following reactions require four different proteins (glycine oxidase, EC 1.5.3.-; sulphur carrier protein adenylyl transferase, EC 2.7.7.-; cysteine desulfurase, EC 2.8.1.7, and thiazole synthase). Glycine oxidase (EC 1.5.3.-) catalyses the oxidation of glycine to the corresponding imine, sulphur-carrier protein adenylyl transferase catalyses the adenylation of the carboxy terminus of the sulfur-carrier protein, and cysteine desulfurase is responsible for the transfer of sulfur from cysteine to the sulfur-carrier protein-acyl adenylate to give the corresponding thiocarboxylic acid. Thiazole synthase catalyses the formation of the thiazole moiety of thiamin from dehydroglycine, 1-deoxy-D-xylulose 5-phosphate, and sulfur-carrier protein-carboxylic acid (Figure 3).

Thiazole biosynthesis is initiated by the formation of an imine (from 1-deoxy-D-xylulose 5-phosphate and an amino group of thiazole synthase), which tautomerises to an aminoketone. The addition of sulfur-carrier protein (thiocarboxylic acid) to the C-3 carbonyl group of the aminoketone, an S to O acyl shift, and the elimination of water then follows yielding an intermediate that covalently links both the thiazole synthase and the sulfur-carrier protein. Isomerisation of the intermediate, the elimination of the sulfur-carrier protein (carboxylic acid), the reaction of the intermediate thus formed with dehydroglycine, the elimination of the thiazole synthase followed by cyclisation, and decarboxylation finally yields 5-(2-hydroxyethyl)-4-methylthiazole phosphate.

The thiazole part of thiamin in eukaryotes is derived from L-cysteine, glycine, and an unidentified pentulose (Settembre et al. 2003).

Via a salvage pathway using hydroxyethylthiazole kinase (EC 2.7.1.50), 5-(2-hydroxyethyl)-4-methylthiazole phosphate can be formed by direct phosphorylation of 5-(2-hydroxyethyl)-4-methylthiazole.

1.3 Phosphate esters of thiamin

The diphosphate ester of the pyrimidine moiety of thiamin and the phosphate ester of its thiazole part condense to thiamin phosphate under the action of thiamin phosphate pyrophosphorylase (EC 2.5.1.3) (Figure 4). Thiamin phosphate is then converted to thiamin diphosphate by direct phosphorylation in the presence of thiamin phosphate kinase (EC 2.7.4.16). In yeasts, thiamin phosphate is first dephosphorylated (phosphatase) and then

Figure 2
diphosphorylated by thiamin pyrophosphokinase (EC 2.7.6.2). In the salvage pathway, thiamin yields either thiamin phosphate in a reaction catalysed by thiamin kinase (2.7.1.89) or thiamin diphosphate under the catalysis by thiamin kinase (EC 2.7.6.2).

The synthesis of thiamin triphosphate is achieved by thiamin diphosphate kinase (phosphoryltransferase, EC 2.7.4.15) which catalyses the transfer of the phosphoryl group from ATP to protein-bound thiamin diphosphate to yield protein-bound thiamin triphosphate2.

2 Riboflavin

Vitamin B2, better known as riboflavin, i.e. 7,8-dimethyl-10-(1-deoxy-D-ribitol-1-yl)isoalloxazine

2There are indications that thiamin triphosphate has a role in the function of nerves. The level of thiamin triphosphate in the brain positively correlates with the genetic disease necrotising encephalomyelopathy (Leigh syndrome).
Riboflavin is synthesised in various microorganisms and plants, often in large amounts in the former. Within the mammalian cells, most of the dietary riboflavin is converted to FAD and FMN.

The biosynthesis of riboflavin starts from guanosine 5'-triphosphate (GTP) (HERZ et al. 2000; BACHER et al. 2001) (Figure 5). GTP cyclohydrolase II (EC 3.5.4.25) catalyses the hydrolytic cleavage of the C-8 and its removal from the purine ring as formic acid (analogously to the folic acid biosynthesis), which is accompanied by the loss of diphosphate from the triphosphoribosyl side-chain yielding 2,5-diamino-6-(5-phospho-β-D-ri-

\[ \text{AMP} \rightarrow \text{ADP} \rightarrow \text{ATP} \]

Riboflavin also plays a role in the biosynthesis of vitamin B\textsubscript{12}. The 5,6-dimethylbenzimidazole moiety of vitamin B\textsubscript{12} is formed from riboflavin in aerobic and some aerotolerant bacteria.

\[ \text{PP} \rightarrow \text{ADP} \rightarrow \text{ATP} \]

Certain bacteria and plants possess bifunctional enzymes with GTP cyclohydrolase II and 3,4-dihydroxybutan-2-one 4-phosphate synthase activities.

\[ \text{AMP} \rightarrow \text{ADP} \rightarrow \text{ATP} \]

3 The terms flavin mononucleotide and flavin adenine dinucleotide are formally incorrect, because FMN is no nucleotide and FAD is no dinucleotide. However, these terms are still accepted.

4 As they can participate both in two- and one-electron processes, flavins can act as a redox switch between two-electron donors (e.g. NADH) and one-electrone acceptors (e.g. heme proteins and iron-sulfur proteins). In addition, flavins can react with molecular oxygen. As a consequence, flavoproteins catalyse a large number of different chemical reactions, e.g. dehydrogenation, oxygen activation (hydroxylation, monooxygenation), and electron transfer.

5 Certain bacteria and plants possess bifunctional enzymes with GTP cyclohydrolase II and 3,4-dihydroxybutan-2-one 4-phosphate synthase activities.
bofuranosylamino)-(3H)-pyrimidin-4-one. This intermediate is converted to 5-amino-6-(1-deoxy-\(\beta\)-ribofuranosyl-1-yl)amino-(1H,3H)-pyrimidin-2,4-dione by a sequence of hydrolytic deamination, side-chain reduction and dephosphorylation reactions. Condensation of the dephosphorylated product, 5-amino-6-(1-deoxy-\(\beta\)-ribofuranosyl-1-yl)amino-(1H,3H)-pyrimidin-2,4-dione, with (3\(S\))-3,4-dihydroxybutan-2-one 4-phosphate (1-deoxy-\(l\)-erythulose 4-phosphate), catalysed by lumazine synthase, yields 6,7-dimethyl-8-(1-deoxy-\(\beta\)-ribofuranosyl-1-yl)lumazine. (3\(S\))-3,4-Dihydroxybutan-2-one 4-phosphate is obtained from \(d\)-ribulose 5-phosphate under the catalysis by 3,4-Dihydroxybutan-2-one 4-phosphate synthase.

Dismutation of two molecules of 6,7-dimethyl-8-(1-deoxy-\(d\)-ribofuranosyl-1-yl)lumazine is catalysed by riboflavin synthase (EC 2.5.1.9) and yields riboflavin and 5-amino-6-(1-deoxy-\(d\)-ribofuranosyl-1-yl)amino-(1H,3H)-pyrimidin-2,4-dione, which is then recycled in the biosynthetic pathway.

It is supposed that the 1-deoxy-\(d\)-ribofuranosyl-1-ylamino group formation in 2,5-diamino-6-(1-deoxy-5-phospho-\(d\)-ribofuranosyl-1-yl)amino-(3\(H\))-pyrimidin-4-one from the \(\beta\)-\(d\)-ribofuranosylamino group in 2,5-diamino-6-(5-phospho-\(\beta\)-\(d\)-ribofuranosylamino)-(3\(H\))-pyrimidin-4-one proceeds via a Schiff base. The enzyme-catalysed reaction is stereospecific and the reducing agent is incorporated into the pro-(\(S\)) position (Figure 6).
The enzyme catalysing the hydrolytic deamination of 2,5-diamino-6-(1-deoxy-5-phospho-D-ribitol-1-yl)amino-(3H)-pyrimidin-4-one to 5-amino-6-(1-deoxy-5-phospho-D-ribitol-1-yl)-amino-(1H,3H)-pyrimidin-2,4-dione is a bifunctional enzyme with deaminase and reductase activities. The enzyme responsible for the dephosphorylation of 5-amino-6-(1-deoxy-5-phospho-D-ribitol-1-yl)-amino-(1H,3H)-pyrimidin-2,4-dione is unknown.

The hypothetical mechanism of the (3S)-3,4-dihydroxybutan-2-one 4-phosphate formation from D-ribulose 5-phosphate involves an unusual skeletal rearrangement. It is initiated by the formation of a 2,3-enediol; the elimination of water yields enol, which is converted to methyldiketone by tautomerisation. A sigmatropic migration of the terminal phosphoryl carbinol group is assumed to yield a branched sugar. The elimination of formic acid and keto-enol tautomerisation of the resulting enediol, under the incorporation of a solvent proton, forms (3S)-3,4-dihydroxybutan-2-one 4-phosphate (Figure 7).

The formation of 6,7-dimethyl-8-(1-deoxy-D-ribitol-1-yl)lumazine is initiated by the formation of a Schiff base from 5-amino-6-ribitylamino-(1H,3H)-pyrimidine-2,4-dione and (3S)-3,4-dihydroxybutan-2-one 4-phosphate. The hydrogen atom at the position C-3 of the imine intermediate is activated by the imine bond, which is conjugated to the pyrimidine ring. The elimination of phosphoric acid then yields an enol type intermediate which is supposed to cyclise by intramolecular addition of the ribityl-substituted amino group in the posi-
tation C-6 of the pyrimidine (tautomerisation of the enol type structure may precede the ring closure, but the details are unknown) (Figure 8).

2.1 Cofactors of riboflavin

Flavokinase (riboflavin kinase, EC 2.7.1.26) converts riboflavin to FMN, and FAD synthetase (FAD diphosphorylase, EC 2.7.7.2) converts FMN to FAD (Figure 9).

3 NICOTINIC ACID AND NICOTINAMIDE

Nicotinic acid (pyridine-3-carboxylic acid) is also known as vitamin PP and its amide, nicotinamide (nicotinic acid amide, pyridine-3-carboxamide), as vitamin B₃. In the form of nicotinamide adenine dinucleotides (NAD⁺, NADH, NADP⁺, and NADPH), nicotinamide plays, as a coenzyme, a vital role in biochemical redox reactions. In addition, nicotinamide adenine dinucleotides play a non-redox role in the posttranslational modifications of some proteins, in the biosynthesis of cyclic ADP-ribose, and as dehydrating agents for DNA ligase (EC 6.5.1.2) (Begley et al. 2001a).

3.1 Nicotinamide adenine dinucleotides

Bacteria synthesise NAD(P)⁺ de novo from L-aspartic acid and 1,3-dihydroxyacetone phosphate (glyceron phosphate) (Begley et al. 2001b; KEGG). The enzyme L-aspartate oxidase (EC 1.4.3.16) catalyses the oxidation of aspartic acid to iminosuccinic acid⁶ (Figure 10). The complex of quinolinate synthase then catalyses the isomerisation of glycerol phosphate to d-glyceraldehyde 3-phosphate and furthers the condensation of iminosuccinic acid with d-glyceraldehyde 3-phosphate, which yields imine (Figure 11). The condensation reaction is followed by the loss of phosphoric acid. Electrocyclic ring closure of the intermediate formed, followed by tautomerisation and dehydration,

⁶The enzyme utilises FAD as a cofactor and can use oxygen (yielding hydrogen peroxide) or fumaric acid (yielding succinic acid) as cosubstrates. This cosubstrate tolerance allows to participate in NAD⁺ biosynthesis under both aerobic and anaerobic conditions.
yields quinolinic acid (pyridine-2,3-dicarboxylic acid). Phosphoribosylation using 5-phospho-α-D-ribose 1-diphosphate and decarboxylation of quinolinic acid catalysed by quinolinate phosphoribosyltransferase (EC 2.4.2.19) give nicotinic acid mononucleotide. Adenylation of nicotinic acid mononucleotide using ATP (nicotinic acid mononucleotide adenylyltransferase, EC 2.7.2.18) yields nicotinic acid dinucleotide (deamido NAD⁺). This reaction followed by amide formation (NAD synthetase, EC 6.3.5.1) completes the biosynthesis of NAD⁺. Finally, NAD⁺ kinase (EC 2.7.1.23) catalyses the phosphorylation of NAD⁺ to give NADP⁺ (Figure 10).

In animals and some microorganisms, and in at least some plants, L-tryptophan is the quinolinic acid precursor (Begley et al. 2001b; KEGG). The eucaryotic pathway (Figure 12) begins with the oxidative opening of the tryptophan ring by the action of a protohemoprotein tryptophan 2,3-dioxygenase (EC 1.13.11.11) to yield N-formyl-L-kynurenine. This reaction is followed by deamorylization catalysed by kynurenine formidase (EC 3.5.1.9) to give L-kynurenine. Hydroxylation of L-kynurenine carried out by a flavoprotein (FAD) kynurenine 3-hydroxylase (EC 1.14.13.9) yields 3-hydroxy-L-kynurenine. The side-chain of 3-hydroxy-L-kynurenine is then cleaved by kynureninase (pyridoxal phosphate as a cofactor, EC 3.7.1.3) to give 3-hydroxyanthranilic acid. An oxidative opening of 3-hydroxyanthranilic acid ring by 3-hydroxyanthranilate 3,4-dioxogenase (requires Fe³⁺, EC 1.13.11.6) followed by a spontaneous ring closure yields quinolinic acid, which is converted to NAD(P)⁺ using the same reaction pathway as that in bacteria.

In addition to the de novo biosynthesis, the pyridine moiety of NAD⁺ undergoes extensive recycling and salvage pathways. Most of the enzymes on these pathways have not yet been characterised (Begley et al. 2001b). NAD(P)⁺ from the diet is first hydrolysed to a mixture of nicotinic acid and nicotinamide by NAD⁺ nucleotidase (EC 3.2.2.5) or NAD(P)⁺ nucleosidase (EC 3.2.2.6) in the intestine. For example, nicotinic acid can be converted to nicotinamide by the action of nicotinamidase (EC 3.5.1.19), then to nicotinic acid mononucleotide (nicotinic acid phosphoribosyltransferase, EC 2.4.2.11) and further to NAD(P)⁺ (KEGG).

4 PANTOTHENIC ACID

Pantothenic acid (formerly also known as vitamin B₅) occurs in nature only as the D- or (R)-enantiomer (Friedrich 1988). Pantothenic acid is an essential nutrient for many strains of yeast, for lactic acid and propionic acid bacteria, and for many other kinds of bacteria. Some bacteria and plants synthesise pantothenic acid de novo. Animals do not synthesise pantothenic acid. However, animals (as well as microorganisms) convert the exogenous vitamin derived from the diet to coenzyme A (HS-CoA) and acyl-carrier protein (ACP, enzyme-bound 4'-phosphopantetheine), the two metabolically active forms of pantothenic acid. The ingested HS-CoA is first hydrolysed to pantothenic acid and pantetheine via 4'-phosphopantetheine.

The biosynthesis of pantothenic acid in plants and microorganisms branches off from the biosynthesis of L-valine (Velišek & Cejpek 2006a, b) and starts from 3-methyl-2-oxobutanoic acid (2-oxoisovaleric acid), a precursor of valine (Friedrich 1988; Begley et al. 2001c) (Figure 13). The enzyme 3-methyl-2-oxobutanoate hydroxymethyl-transferase (dehydropantoate hydroxymethyl-transferase, EC 2.1.2.11) uses 5,10-methylene-tetrahydrofolic
acid (5,10-methylene-\(\text{H}_4\)PteGlu) as a donor of the hydroxymethyl group for 3-methyl-2-oxobutanoic acid and the formation of 2-oxo-3,3-dimethyl-4-hydroxybutanoic acid (2-oxopantoic acid) (Figure 14, \(R = \text{benzoylglutamic acid residue}\)). In this mechanism that resembles the formylation reaction, the ring opening of 5,10-methylene-\(\text{H}_4\)PteGlu followed by the addition of water to the resulting iminium ion gives the corresponding hydroxymethyl compound. The elimination of formaldehyde followed by its trapping by the enol of 3-methyl-2-oxobutanoic acid gives 2-oxopantoic acid. The reaction is reversible and proceeds with the inversion of the configuration at C-3 of the 3-methyl-2-oxobutanoic acid.

2-Oxopantoic acid is then reduced to (\(R\))-pantoic acid by the enzyme oxopantoate reductase (EC 1.1.1.169). The biosynthesis of (\(R\))-pantothenic acid from \(\beta\)-alanine (3-aminopropanoic acid) and pantoic acid is catalysed by pantothenate synthetase (EC 6.3.2.1). \(\beta\)-Alanine involved in the biosynthesis of pantothenic acid forms by decarboxylation of L-aspartic acid catalysed by the pyridoxal 5'-phosphate enzyme aspartate-1-decarboxylase (EC 4.1.1.11) (Velíšek et al. 2006).

The natural higher homologue of pantothenic acid called homopantothenic acid or hopanteic acid occurs in biological fluids of animals (Umeno et al. 1981). Homopantothenic acid is derived from pantoic acid and 4-aminobutanoic acid (GABA). 4-Aminobutanoic acid is predominantly formed by decarboxylation of L-glutamic acid catalysed by the pyridoxal 5'-phosphate enzyme, glutamate decarboxylase (EC 4.1.1.15) (Velíšek et al. 2006).
4.1 Coenzyme A and ACP

The biosynthesis of coenzyme A from pantothenic acid requires five enzymes (FRIEDRICH 1988; BEGLEY et al. 2001c; KEGG). The reaction pathway starts by phosphorylation of pantothenic acid which yields 4'-phosphopantothenic acid (pantothenate kinase, EC 2.7.1.33). The condensation of 4'-phosphopantothenic acid with l-cysteine (4'-phosphopantothenoylcysteine synthetase, EC 6.3.2.5) creates 4'-phosphopantothenoylcysteine which yields, under the elimination of carbon dioxide, 4'-phosphopantetheine (4'-phosphopantothenoylcysteine decarboxylase, EC 4.1.1.36). Subsequent reactions with two molecules of ATP lead to dephospho coenzyme A (4'-phosphopantetheine adenylyltransferase, EC 2.7.7.3) and then (dephospho coenzyme A kinase, EC 2.7.1.24) to coenzyme A (Figure 15).

The cleavage of coenzyme A yields 3',5'-ADP (adenosine 3',5'-bisphosphate) and 4'-phosphopantetheine (phosphopantetheinyl transferase, EC 2.7.8.7); the latter is bound to serine hydroxyl group in apo-ACP to form acyl-carrier protein (holo-ACP).
5 VITAMIN B₆

The generic term vitamin B₆ refers to three 3-hydroxy-2-methylpyridine derivatives, pyridoxol or 3-hydroxy-4,5-bis(hydroxymethyl)-2-methylpyridine, pyridoxal (4-formyl-3-hydroxy-5-hydroxymethyl-2-methylpyridine), and pyridoxamine (4-aminomethyl-3-hydroxy-5-hydroxymethyl-2-methylpyridine), and also to their 5'-phosphates (IUPAC). Pyridoxal-5'-phosphate and pyridoxamine-5'-phosphate are the catalytically active forms of vitamin B₆. Pyridoxal-5’-phosphate and pyridoxamine-5'-phosphate are the catalytically active forms of vitamin B₆. Pyridoxal-5’-phosphate is involved in many reactions, e.g. in the decarboxylation, deamination, racemisation, transamination, and transsulfuration of amino acids, and in lipid and sugar metabolism. In nature, pyridoxal-5’-phosphate and the non-phosphorylated forms (pyridoxal, pyridoxamine, and pyridoxol) accompany pyridoxal-5'-phosphate and pyridoxamine-5'-phosphate. Pyridoxal and its phosphate are the predominating forms in plant materials, while pyridoxal, pyridoxamine, and their phosphates are the main forms in animal tissues.

The initial form of vitamin B₆ synthesised de novo in prokaryotes is pyridoxol-5’-phosphate (DREWKE & LEISTNER 2001). It is supposed that pyridoxol-5’-phosphate is synthesised from one molecule of the deoxypentulose 1-deoxy-d-xylulose 5-phosphate (1-deoxy-d-threo-pent-2-ulose 5-phosphate)⁷ and one molecule of the aminosugar 2-amino-2-deoxy-d-threo-tetronic acid (2-amino-2-deoxy-d-threonic acid) better known as

Figure 13

![Diagram of vitamin B₆ metabolism]

Figure 14

\[ \text{3-methyl-2-oxobutanoic acid} \]

\[ \text{2-oxopantoic acid} \]

\[ \text{5,10-methylene-}\text{H₄PteGlu} \]

\[ \text{H₄PteGlu} \]

\[ \text{AMP + PP} \]

\[ \text{ATP + H₂N} \]

\[ \text{EC 6.3.2.1} \]

\[ \text{NADPH + H⁺} \]

\[ \text{EC 1.1.1.169} \]

\[ \beta\text{-alanine} \]

\[ \text{(R)-pantothenic acid} \]

\[ \text{(R)-pantoic acid} \]

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⁷1-Deoxy-d-xylulose 5-phosphate plays a pivotal role also in the biosynthesis of the thiazole moiety of thiamin (Figure 2).
4-(phosphohydroxy)-L-threonine or 4-hydroxy-L-threonine 4-phosphate (Figure 16). It is postulated that 4-(phosphohydroxy)-L-threonine is first oxidised to (S)-2-amino-3-oxo-4-(phosphohydroxy)butanoic acid, after which its decarboxylation yields 1-amino-3-(phosphohydroxy)propan-2-one. The reaction of 1-deoxy-d-xylulose 5-phosphate with 1-amino-3-(phosphohydroxy)propan-2-one leads to a Schiff base, which, in a series of elimination, hydration, and isomerisation reactions, finally yields pyridoxol-5'-phosphate.

Figure 15

4-(Phosphohydroxy)-L-threonine yielding N-1, C-6, C-5, and C-5' atoms in pyridoxol-5'-phosphate forms from d-erythrose 4-phosphate (Drewke & Leistner 2001) which is the decomposition product of d-fructose 6-phosphate (Veříšek & Čejpek 2005). The conversion of d-erythrose 4-phosphate to 4-(phosphohydroxy)-L-threonine proceeds via d-erythrulose 4-phosphate (the reaction is catalysed by erythrose 4-phosphate dehydrogenase) and d-erythrulose 4-phosphate, which yields 4-(phosphohydroxy)-L-threonine in a transami-
nation reaction (catalysed e.g. by glutamate dehydrogenase, EC 1.4.1.2) curiously using pyridoxal-5'-phosphate as a cofactor (Figure 17).

The salvage pathways carried out by all organisms comprise phosphorylation of either pyridoxol or pyridoxamine (pyridoxal kinase or vitamin B₆ kinase, EC 2.7.1.35) to yield the corresponding 5'-phosphorylated products, which are then oxidised to pyridoxal-5'-phosphate (Figure 18) (KEGG). These reactions are catalysed by pyridoxamine phosphate oxidase (EC 1.4.3.5, an FMN-dependent enzyme which requires molecular oxygen as an electron acceptor). As a control mechanism to maintain the equilibrium in the biosynthetic pathway, the phosphorylated forms of vitamin B₆ can be reverted to free non-phosphorylated forms by catalysis with a phosphatase (EC 3.1.3.-). Yeasts and fungi can also utilise all three non-phosphorylated forms of the vitamin. Animals are not able to synthesise vitamin B₆ de novo, but they can interconvert all six forms of the vitamin. Generally, the non-phosphorylated forms can be interconverted using various oxidoreductases and transaminases. For example, human beings as well as yeasts Saccharomyces cerevisiae use pyridoxamine phosphate oxidase (EC 1.4.3.5) for this purpose.

5.1 Structurally related compounds

The formation of vitamin B₆ vitamers in organisms other than bacteria Escherichia coli, for example in fungi and in higher plants, remains unclear, but it may resemble that described for E. coli (Drewke & Leistner 2001). In higher plants, glycosylated forms of pyridoxol are commonly found. The major glycosidic form (5–80%) is 5'-O-(β-d-glucopyranosyl)pyridoxol (Velíšek 2002). Ginkgotoxin (4'-O-methylpyridoxol) is a minor constituent of Ginkgo biloba (Drewke & Leistner 2001) that acts as the B₆ antivitamin (Figure 19).
EC (Enzyme Commission) Numbers and Some Common Abbreviations

EC (Enzyme Commission) numbers, assigned by IUPAC-IUBMB, were taken from KEGG. In many structures, the unionised forms are depicted to simplify the structures, to eliminate the need for counter-ions, and to avoid the mechanistic confusion.

ACP – acyl-carrier protein
AH2 – hydrogen donor
AIR – 5-aminoimidazole ribonucleotide
ADP – adenosine 5’-diphosphate
AMP – adenosine 5’-monophosphate
ATP – adenosine 5’-triphosphate
CMP – cytidine 5’-monophosphate
CTP – cytidine 5’-triphosphate
CoA – coenzyme A as a part of a thioester
DNA – deoxyribonucleic acid
FAD – flavine adenine dinucleotide
FMN – flavin mononucleotide
GABA – α-amino-γ-butyrolactone acid
GTP – guanosine 5’-triphosphate
H4PteGlu – (6S)-5,6,7,8-tetrahydropteroylglutamic acid
NADH – nicotinamide adenine dinucleotide
NADPH – nicotinamide adenine dinucleotide phosphate
P – phosphoric acid
PP – diphosphoric acid
PPP – triphosphoric acid
SAH – S-adenosyl-1-homocysteine (AdoHcy)
SAM – S-adenosyl-1-methionine (AdoMet)

References


Velišek J., Cejpek K. (2006a): Biosynthesis of food constituents: amino acids. 1. The glutamic acid and


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