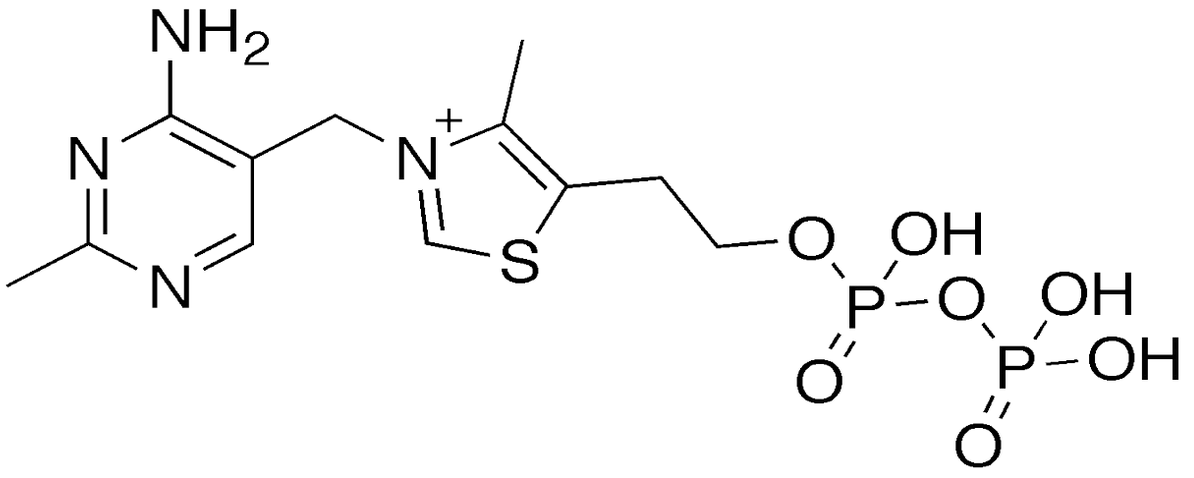
Co-enzyme :Thiamine pyrophosphate (TPP)

Thiamine pyrophosphate (TPP), the biologically active form of vitamin B1 (thiamine), is a crucial coenzyme composed of a **pyrimidine ring, a thiazole ring, and a pyrophosphate group**. It plays a central role in energy metabolism and nerve function by acting as an essential cofactor for several key enzymes involved in the breakdown of carbohydrates and amino acids.

Structure of Thiamine Pyrophosphate

The TPP molecule consists of three main parts:

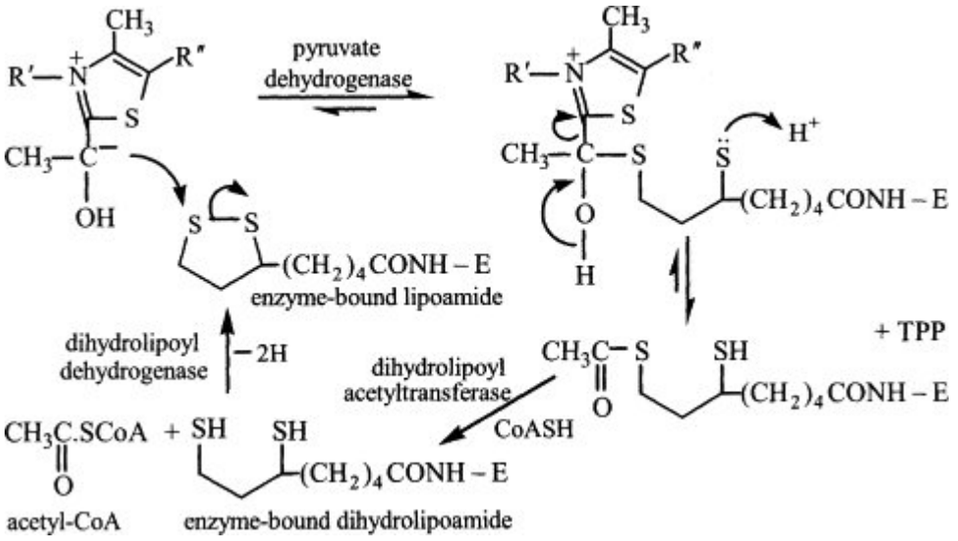
- **A pyrimidine ring** (specifically, a 4-amino-2-methylpyrimidine ring).
- **A thiazole ring** (a 4-methyl-5-hydroxyethylthiazole ring), which contains a positively charged nitrogen atom (a thiazolium core).
- **A pyrophosphate (diphosphate) functional group** attached to the hydroxyethyl side chain of the thiazole ring.



The key reactive portion of the molecule is the C2 carbon of the thiazole ring. This carbon can easily lose a proton, forming a nucleophilic carbanion (also known as the "ylide form"), which is stabilized by the adjacent positively charged nitrogen atom. This unique chemical property allows TPP to participate in reactions involving the attack on carbonyl groups, facilitating the transfer of two-carbon units and the cleavage of carbon-carbon bonds.

Biological Function

TPP functions as a coenzyme in a variety of enzymatic reactions, primarily those involving decarboxylation and transketolation. These reactions are vital for energy production and general cellular function. Thiamine pyrophosphate is the biologically active derivative of B_1 and is required for the oxidative decarboxylation of pyruvate to form acetyl-coenzyme A, initiating the Krebs cycle. It also functions as a coenzyme for transketolase in the pentose phosphate pathway, an alternative pathway for glucose oxidation.



Key TPP-dependent enzymes and their functions include:

- **Pyruvate dehydrogenase complex:** This mitochondrial enzyme complex uses TPP to convert pyruvate (from glycolysis) into acetyl-CoA, which then enters the Krebs (citric acid) cycle for further energy production.
- **Alpha-ketoglutarate dehydrogenase complex:** Another key enzyme in the Krebs cycle that requires TPP to convert alpha-ketoglutarate to succinyl-CoA.
- **Pyruvate decarboxylase:** In organisms like yeast, this enzyme uses TPP for the decarboxylation of pyruvate to acetaldehyde during ethanol fermentation.
- **Transketolase:** This enzyme, active in the pentose phosphate pathway (an important pathway for producing NADPH and five-carbon sugars for nucleotide synthesis), uses TPP to transfer two-carbon units between sugar molecules.
- **Branched-chain alpha-keto acid dehydrogenase complex:** Involved in the metabolism of branched-chain amino acids (leucine, isoleucine, and valine).

Overall, TPP is essential for carbohydrate and amino acid metabolism, ATP production, nerve signal transmission, and maintaining normal heart function. Deficiency in thiamine and, consequently, TPP can lead to severe conditions like beriberi and Wernicke-Korsakoff syndrome, which affect the nervous system and heart.