Biosynthesis of Aromatic Amino Acids & Porphyrins.

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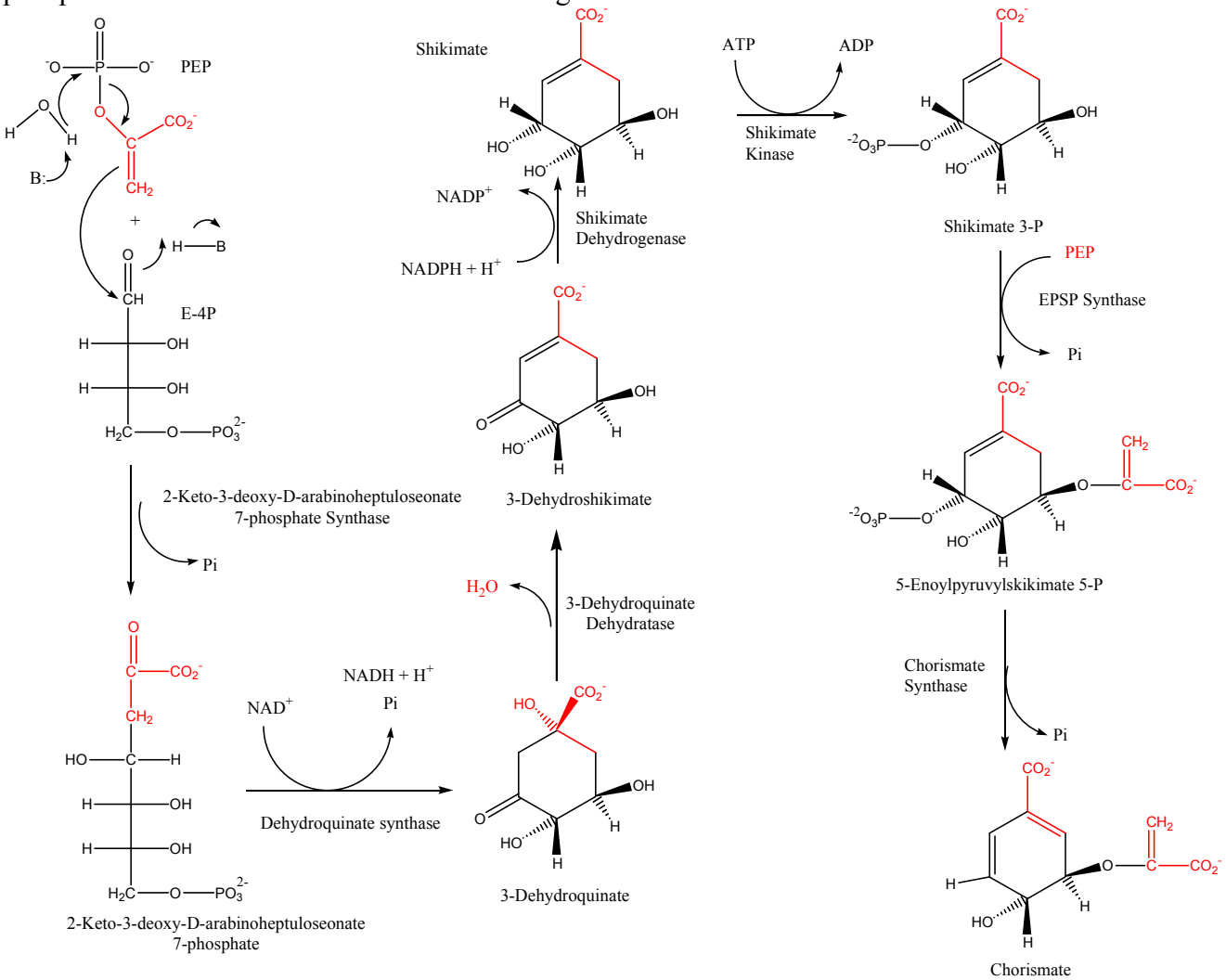
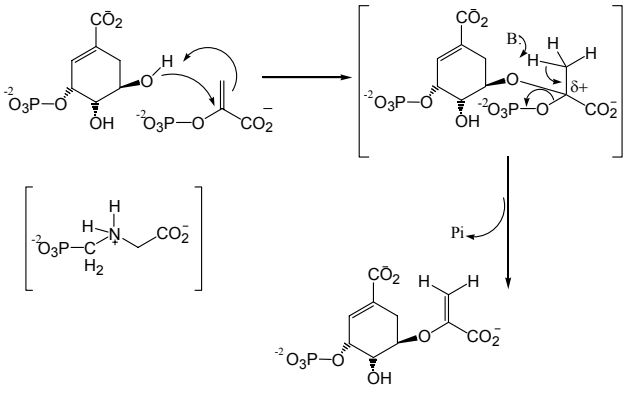
I. Biosynthesis of aromatic amino acids.

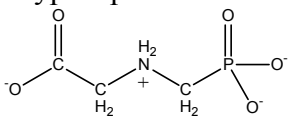
Aromatic rings are very stabile but hard to synthesize. Only plants and microorganisms are able to synthesize aromatic amino acids. The biosynthesis begins with Phosphoenolpyruvate and Erythrose-4-phosphate to form Shikimate. Shikimate then goes on to form chorismate.



ESPS Synthase



Glyphosphate is the herbicide found in RoundUp.

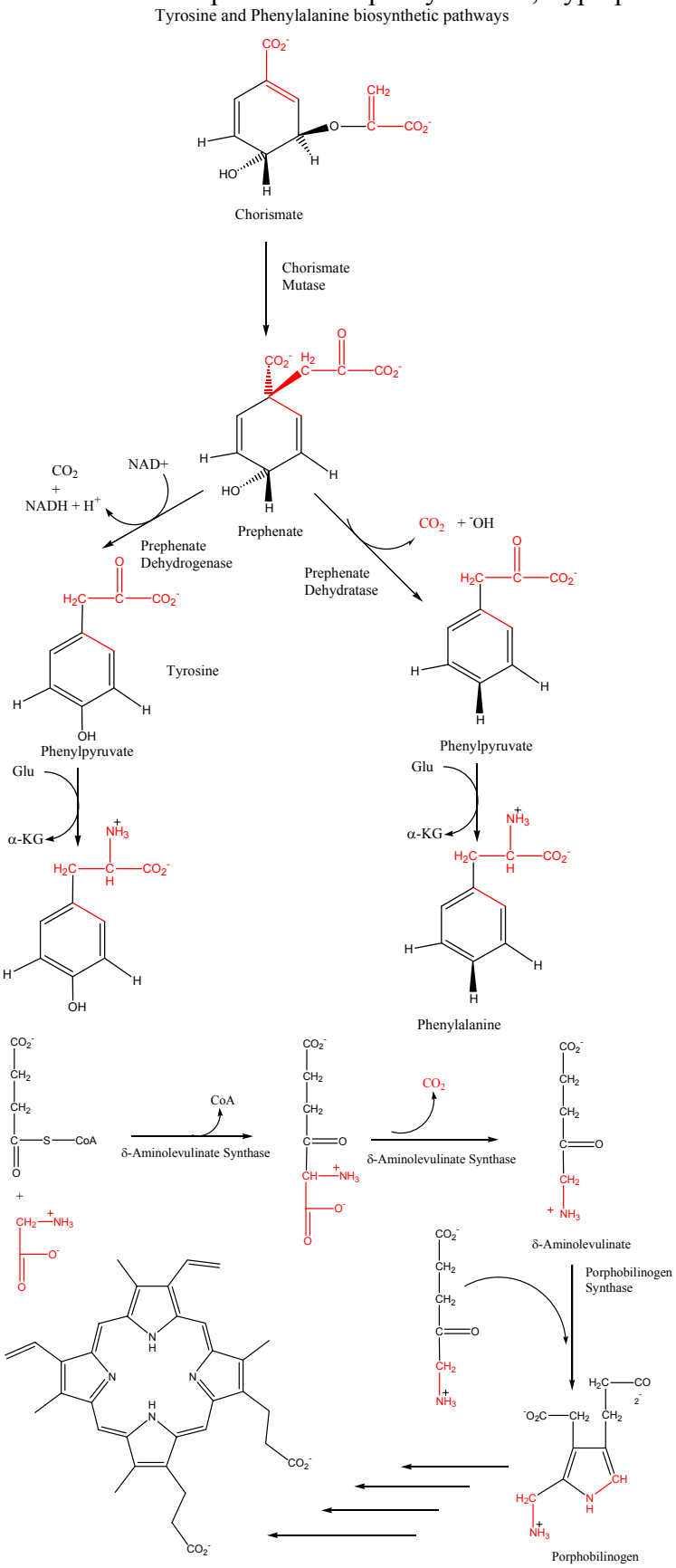


Glyphosphate

Glyphosphate is a potent inhibitor of ESPS synthase. The mechanism of ESPS is shown to the right. Glyphosphate resembles the tetrahedral intermediate in the catalytic pathway and is bound very tightly by this enzyme. The herbicide is nontoxic to animals because

animals lack this biosynthetic pathway. Aromatic amino acids are essential amino acids.

Chorismate is the precursor for phenylalanine, tryptophan and tyrosine.



II. Metabolism of Hemes.

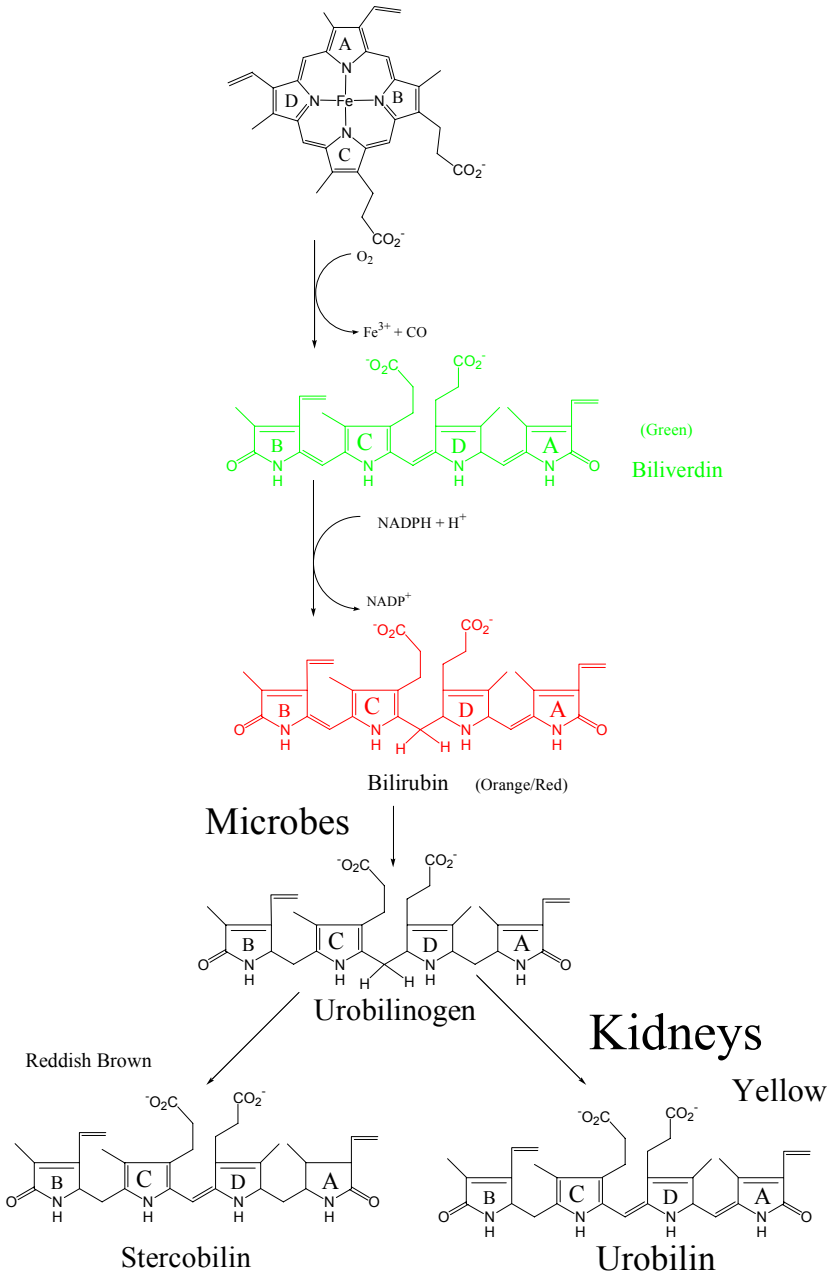
Biosynthesis

Glycine and succinyl-CoA are the precursors of porphyrins which are required for cytochromes and hemes. Glycine and succinyl CoA combine to form α-amino-β-ketoadipate which is a β-ketoacid that spontaneously decarboxylates to form δ-aminolevulonate. Two molecules of δ-aminolevulonate condense to form porphobilinogen. Four molecules of porphobilinogen react to ultimately form protoporphyrin.

Porphobilinogen synthase requires a Zn^{2+} cofactor. Lead poisoning, Pb^{2+} replaces the zinc resulting in an inactive enzyme. This is one of the major manifestations of lead poisoning. As you would expect, most heme biosynthesis occurs in the red blood cells. Red blood cells account for 85% of the heme production. The rest of the heme biosynthesis occurs in the liver.

Heme degradation.

Hemoglobin last as long as the erythrocyte lives. At the end of their lifetime red blood cells are degraded and the hemes catabolized. The first step is the oxidative break down of the porphyrin ring to form biliverdin which has a green color. The methylene bridge is then reduced to form bilirubin which is red-orange colored. The changing colors of a healing bruise are visible by the manifestation of heme degradation.



Bilirubin is not soluble in water. It is transported in the blood by serum albumin. Bilirubin are secreted in the bile and are digested in the large intestine tract by the microorganisms that dwell there. Microorganisms break down bilirubin into urobilinogen which is reabsorbed by the intestine and transported to the kidneys were it is converted into urobilin which is yellow and excreted in the urine giving urine its characteristic color.

The urobililogen that is not reabsorbed by the intestine is degraded into stercobilin which is reddish brown in color and the major pigment of feces.

When the blood contains excess amount of bilirubin, the water insoluble compound colors the skin and the whites of the eyes yellow. This condition is called jaundice. Jaundice signals abnormally high rates of red blood cell destruction or liver dysfunction or bile duct obstruction.

Premature infants are often jaundiced because the lack the enzyme to degrade bilirubin.