α-oxidation fatty acid

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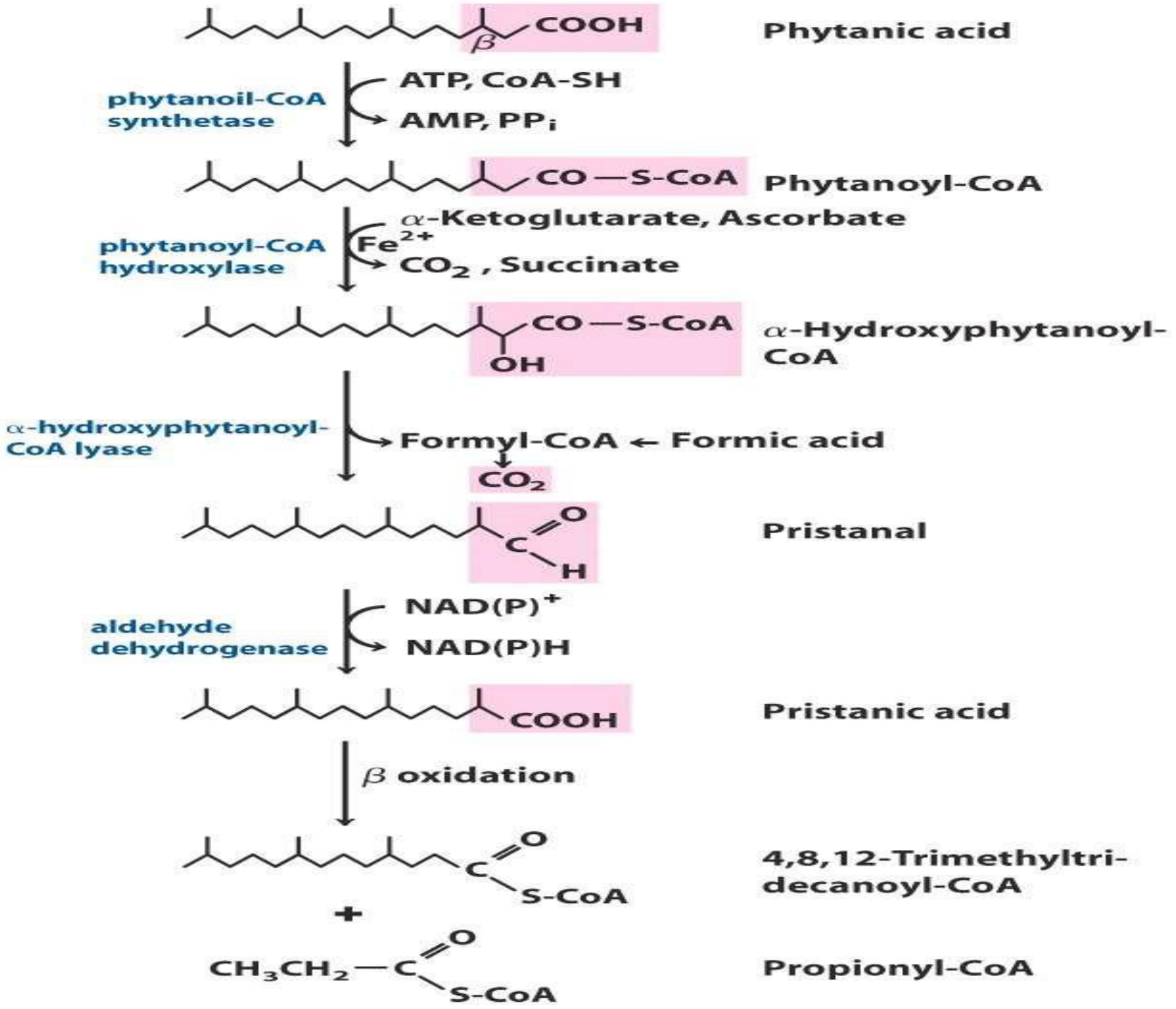
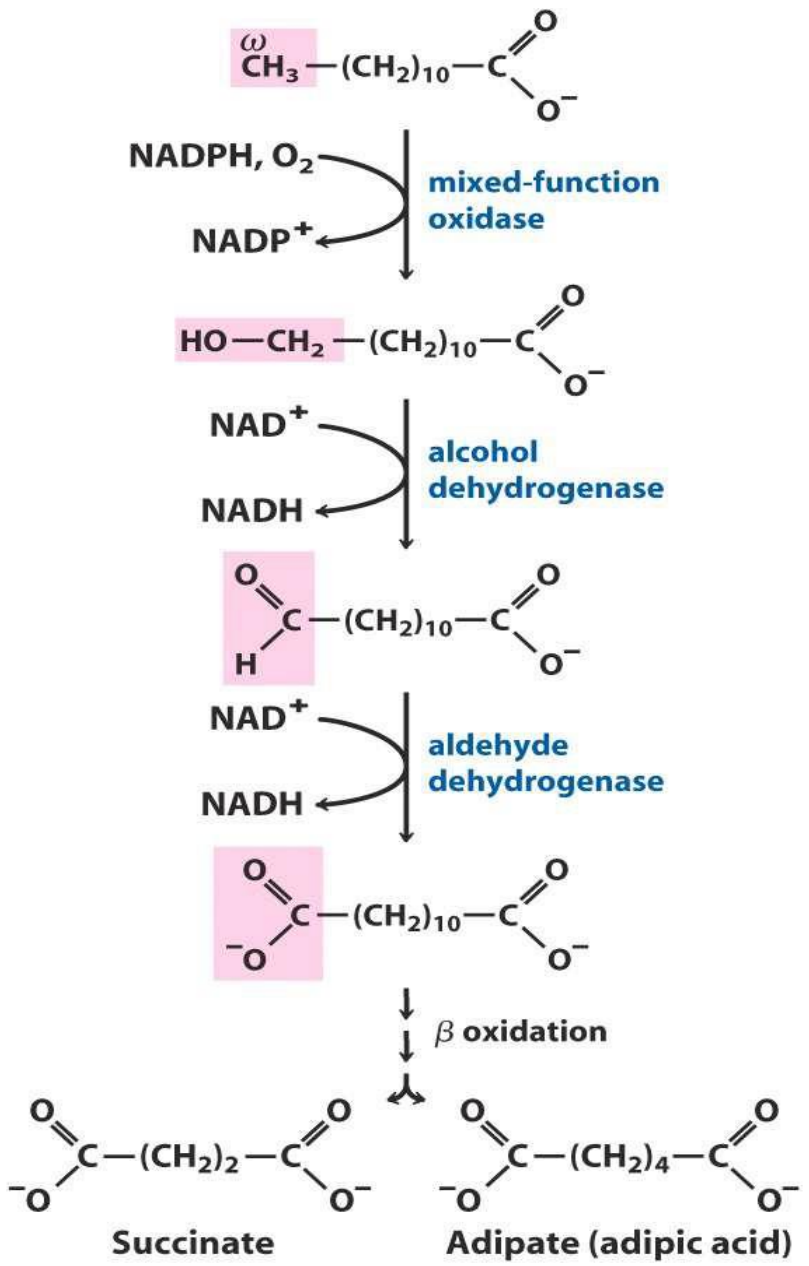
- α –oxidation of fatty acids are specialized pathways.
- α –oxidation i.e., removal of one carbon at a time from the carboxyl end of the molecule has been detected in brain tissue.
- It does not generate CoA intermediates and does not generate high-energy phosphates.
- It is mainly used for the fatty acids that have a methyl group at β–carbon, which block β–oxidation (Phytanic acid-a major dietary methylated fatty acid present in chlorophyll, milk, & animal fats).
- **The α -oxidation** of a branched-chain fatty acid (Phytanic acid).
- Phytanic acid cannot go β oxidation first. It undergoes a-**oxidation** to remove the α –carbon as CO2& this is followed by α –oxidation.


COOH
β
Phytanic acid
phytanoil-CoA synthetase
ATP, CoA-SH
AMP, PPi
CO—S-CoA
Phytanoyl-CoA
α-Ketoglutarate, Ascorbate
phytanoyl-CoA hydroxylase
Fe2+
CO2 , Succinate
CO—S-CoA
OH
α-Hydroxyphytanoyl-CoA
α-hydroxyphytanoyl-CoA lyase
Formyl-CoA ← Formic acid
CO2
O
C
H
Pristanal
aldehyde dehydrogenase
NAD(P)+
NAD(P)H
COOH
Pristanic acid
β oxidation
O
C
S-CoA
4,8,12-Trimethyltri-decanoyl-CoA
+
CH3CH2
O
C
S-CoA
Propionyl-CoA

Omega oxidation of fatty acid

- Occurs in the endoplasmic reticulum (liver and kidney).
- ω-oxidation is a minor pathway and is brought about by cytochrome P450in the endoplasmic reticulum.
- In this, the fatty acids is oxidized at the w-carbon of the chain by series of enzymes
- CH3group (e.g.Lauric acid) is converted to a -CH2OH group that subsequently is oxidized to -COOH, thus forming a dicarboxylic acid. They subsequently undergo ß-oxidation and are excreted in the urine.
- The omega oxidation becomes important when beta oxidation is defective.
- Short chain dicarboxylic acid such as **pimelic acid,**a precursor of **biotin** formed by omega oxidation.



Refsum's disease

- Refsum disease was first recognized as a distinct disease entity by Sigvald Refsum in the 1940s.
- Also known as **Phytanate storage disease**.
- Rare neurologic inborn error of lipid metabolism.
- Occurs due to inherited defect in **α-oxidation**.
- Caused due to genetic deficiency in the enzyme **phytanoyl CoA hydroxylase (phytanic acid α-oxidase).**
- Inability to metabolize phytanic acid (a branched chain fatty acid)
- Accumulation of large quantities of phytanic acid occurs.

Symptoms:

- Clinical symptoms include **retinitis pigmentosa** (progressive degeneration of retina), **peripheral neuropathy** and **ataxia.**

- **Treated** with a diet low in phytol and phytanic acid (no green leafy vegetables, animal fats, or milk products).