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Free Fatty Acid Synthesis & Importance (Contd)
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Step-7 : Reduction of 3-Carbonyl-ACP

The trans-double bond between C-2 and C-3 of Crotonyl-ACP is reduced by the enzyme 2,3-transenoyl-ACP reductase, which utilizes reduced NADP as hydrogen donor. The reaction generates butyryl-ACP.

Step-8 :- Chain elongation by Repeated Addition of 2-Carbon Units.

From step 1 to step-7, a four-carbon unit as butyryl ACP has been synthesized from ~~two~~ 2-Carbon units (two acetyl Co-A). The process of condensation continues in the subsequent steps, where Butyryl-ACP condenses with another molecule of malonyl-ACP (step-4) and generates a 6-Carbon ACP (Acetyl butyryl CoA) that passes through next three steps (steps 5-7). Step 4 generates a 6-Carbon-ACP (acetyl butyryl CoA) that passes through next three steps (steps 5-7), step 4 generates a 6-Carbon acyl-ACP (Caproyl ACP). Likewise two Carbon units are added through each cycle of reactions of steps 5-7 increasing the lengths of Carbon chains of fatty acids by

two Carbons each time till a 16-Carbon (palmitic acid) chain of Palmitoyl-ACP is synthesized. The reactions fail to continue further as the enzyme acyl-ACP Synthase is unable to hold longer chain of Acyl-ACP.

Step-9 :- Release of Palmitic Acid

Palmitoyl-ACP, thus synthesized, is now hydrolyzed by the enzyme thioesterase, which cleaves ACP at the thiol end and sets palmitic acid free.

Chain Elongation of saturated Acids:-

Synthesis of fatty acids beyond 16-Carbon chain length (i.e. palmitic Acid or palmitoyl CoA) continues in the Endoplasmic reticulum (ER) by successive additions of 2-Carbon units utilizing malonyl CoA that provides energy by decarboxylation as in the first process. However, another pathway operates in mitochondria, which utilizes acetyl CoA and not malonyl CoA. This pathway brings about successive additions of 2-Carbon unit of acetyl CoA molecules to the chain length of palmitic acid (palmitoyl CoA) adopting

a process that is essentially a reversal of the last four enzymatic steps of β-oxidation of fatty acids. Obviously, first enzyme to act is thiolase bringing about transfer of acyl moiety of acyl coA to the methyl Carbon of acetyl coA generating thereby β-ketoacyl coA and a free coenzyme A. Next enzyme to act is L,β-hydroxyacyl coA dehydrogenase bringing about reduction of β-ketoacyl coA with the help of reduced NADP, generating L,β-hydroxyacyl coA and oxidized NADP. Next to act is hydratase that removes a molecule of H_2O from L,β-hydroxyacyl coA and, generates L,β trans-enoyl coA that is reduced finally by the enzyme enoyl coA dehydrogenase to acyl coA which is now longer by 2 Carbons than the initial acyl coA. Reduced NADP participates in the final reduction reaction and is released in oxidized form.

Synthesis of Unsaturated Fatty Acids:-

Unsaturated fatty acids are synthesized differently in prokaryotes and eukaryotes. In Prokaryotes, such as E. coli, unsaturated is eukaryotes (plants and animals) there is reactions don't require oxygen, whereas require reduced NADP, Cytochrome b, reductase. Cytochrome b_5 and O_2. Synthesis of Polyenoic acids require monoenoic or dienoic acid.

Prokaryotes, being devoid of polyenoic acids, possesses mainly palmitoleic acid (16-carbon) and cis-vaccenic acid (18-carbons) having a double bond at C-11 and C-13 positions, respectively. Once synthesis of saturated fatty acids has progressed to 10-carbon lengths (decanoyl-ACP), the enzyme β-hydroxy decanoyl-ACP dehydrase having preference for β-hydroxy carbon near the ACP terminus removes H_2O from β and γ-carbons. This dehydration creates a cis-double bond in between β and γ-carbons. The cis-decanoyl-ACP, thus formed, undergoes three successive additions of 2 carbons units from malonyl CoA molecules leading to the formation of palmitoyl-ACP. It is further elongated by one more addition of 2-carbons unit from malonyl-ACP forming, thereby, 11-cis-vaccenic acid. However this condensation is brought about by a specific enzyme, β-Ketoacyl-ACP Synthase II having preference for palmitoyl-ACP only.

However, in eukaryote introduction of single double bond is O_2 dependent and occurs only after the completion of saturated fatty acid synthesis. Palmitic acid, being the common saturated fatty acid, or stearic acid, is activated to palmitoyl CoA or stearyl CoA, respectively, by acyl CoA Synthase at the expense of coenzyme.

Regulation of Fatty Acid Synthesis -

Fatty acid biosynthesis is regulated by fatty acid oxidation & vice versa. The concentration of acetyl co-A, a central metabolite in energy metabolism, affects the oxidation and biosynthesis of fatty acid. Acetyl co-A, when in excess, due to either β-oxidation of fatty acid or aerobic glycolysis, is converted to citrate that comes out of mitochondrion and activates acetyl CoA carboxylase that promotes synthesis of malonyl coA. Malonyl CoA now participates in fatty acid synthesis leading to the synthesis of long chain fatty acid (palmitoyl coA). However, high concentration of palmitoyl coA inhibits acetyl CoA carboxylase inhibiting further conversion of acetyl CoA into malonyl coA leading to the inhibition of fatty acid synthesis. Activity of acetyl coA carboxylase is regulated by hormone epinephrine and glucagon; fatty acid synthesis is also hormone regulated.

Thus, Synthesis of Fatty Acid is somewhere related to oxidation of Fatty acids, however, both the process are related to addition or deletion of 2-carbon residues.

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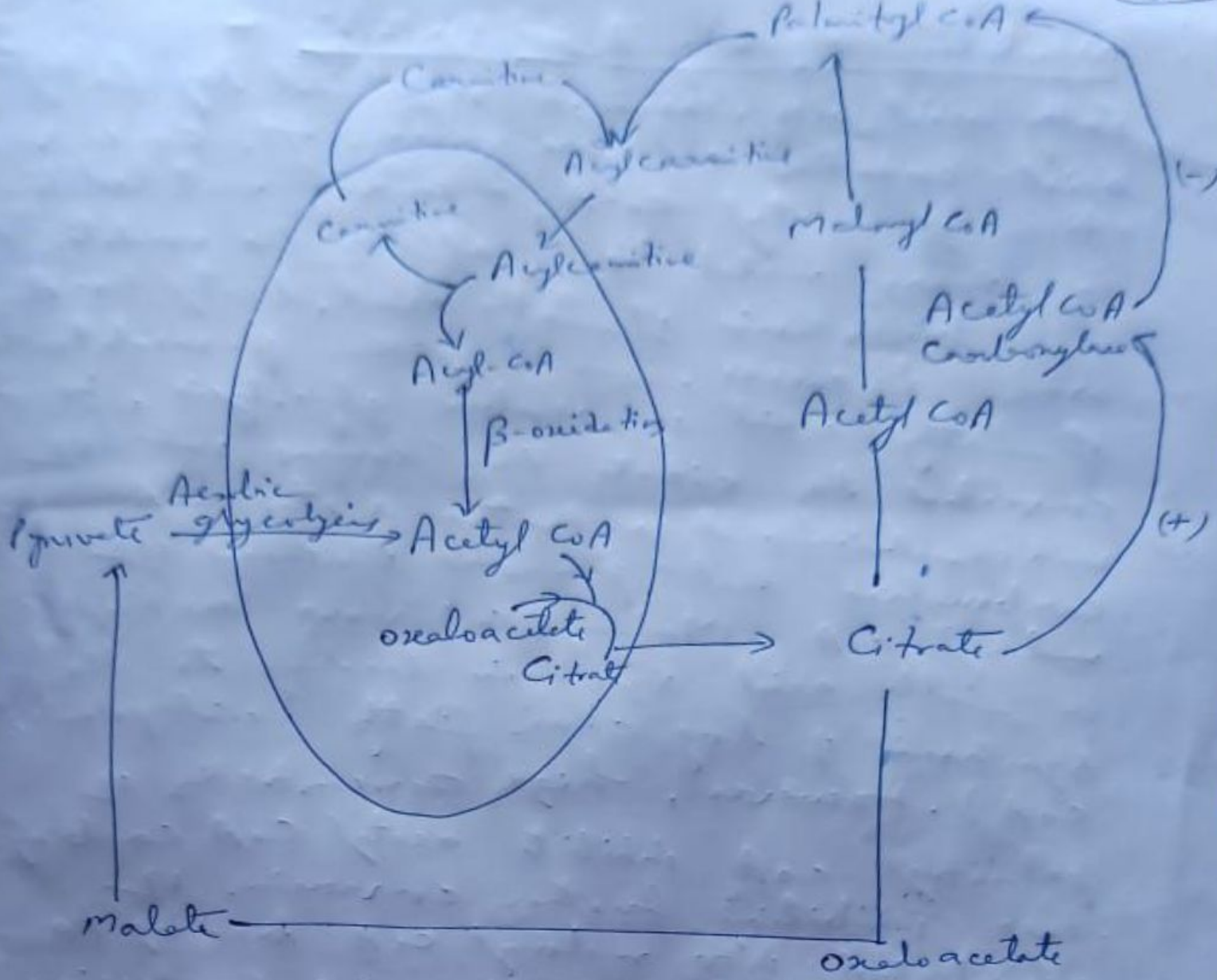
contd.



Synthesis of fatty acids and oxidation of fatty acids are inversely regulated.