Gluconeogenesis

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The synthesis of glucose from non-carbohydrate precursors is known as gluconeogenesis. The mechanism involved in gluconeogenesis is reversal of Citric acid cycle and glycolysis. Hence any substances which can form any one of the derivatives of citric acid cycle or glycolysis can therefore give rise to glucose. The most important of those are glucogenic amino acids, lactic acid, propionic acid and glycerol.

The major site of gluconeogenesis is liver. It also occurs in the cortex of the kidney but it is only about one tenth of that formed in the liver

Gluconeogenesis generally occurs when the carbohydrates in the diet is insufficient to meet the glucose demand in the body.

Reactions involved in Gluconeogenesis

1) Pyruvate + CO_2 + ATP + H_2O $\rightleftharpoons$ Oxaloacetate + ADP + P_i + $2H^+$

Oxaloacetate + GTP $\rightleftharpoons$ phosphoenolpyruvate + GDP + CO_2

2) Fructo 1-6 di phosphatase + H_2O $\longrightarrow$ Fructose 6- phosphate + P_i

3) Glucose 6-phosphate + H_2O $\longrightarrow$ Glucose + P_i

The stoichiochemistry of gluconeogenesis is

2 Pyruvic acid + 4ATP + 2GTP + 2NDH + $2H_2O$ $\longrightarrow$ Glucose + 4ADP + 2GDP

Here six high energy bonds (4ATP + 2GTP) are used to synthesized Glucose from pyruvic acid where as only two ATP are generated in glycolysis in the conversion of glucose to pyruvic acid. The Stoichiometry of glycolysis is

Glucose + 2ADP + 2P_i + 2NAD$^+$ $\longrightarrow$ 2 Pyruvic acid + 2ATP + 2NADH + $2H_2O$

Thus the extra price of gluconeogenesis is four high energy phosphate bonds per glucose synthesized from pyruvic acid.

Gluconeogenesis of Amino acids :-

Amino acids which could be converted to glucose are called gluconeogenic amino acids. Most of the glucogenic amino acids are converted to the intermediates of citric acid cycle either by transamination or deamination. Thus about 20 amino acids enter the TCA cycle of which some enter the cycle by producing only one intermediate eg. Alanine and glutamine acid while some other enters two intermediates eg. phenyl alanine and tyrosine. Thus the amino acids are metabolically routed through oxalo acetic acid and phosphoenol pyruvic acid resulting in the formation of glucose.

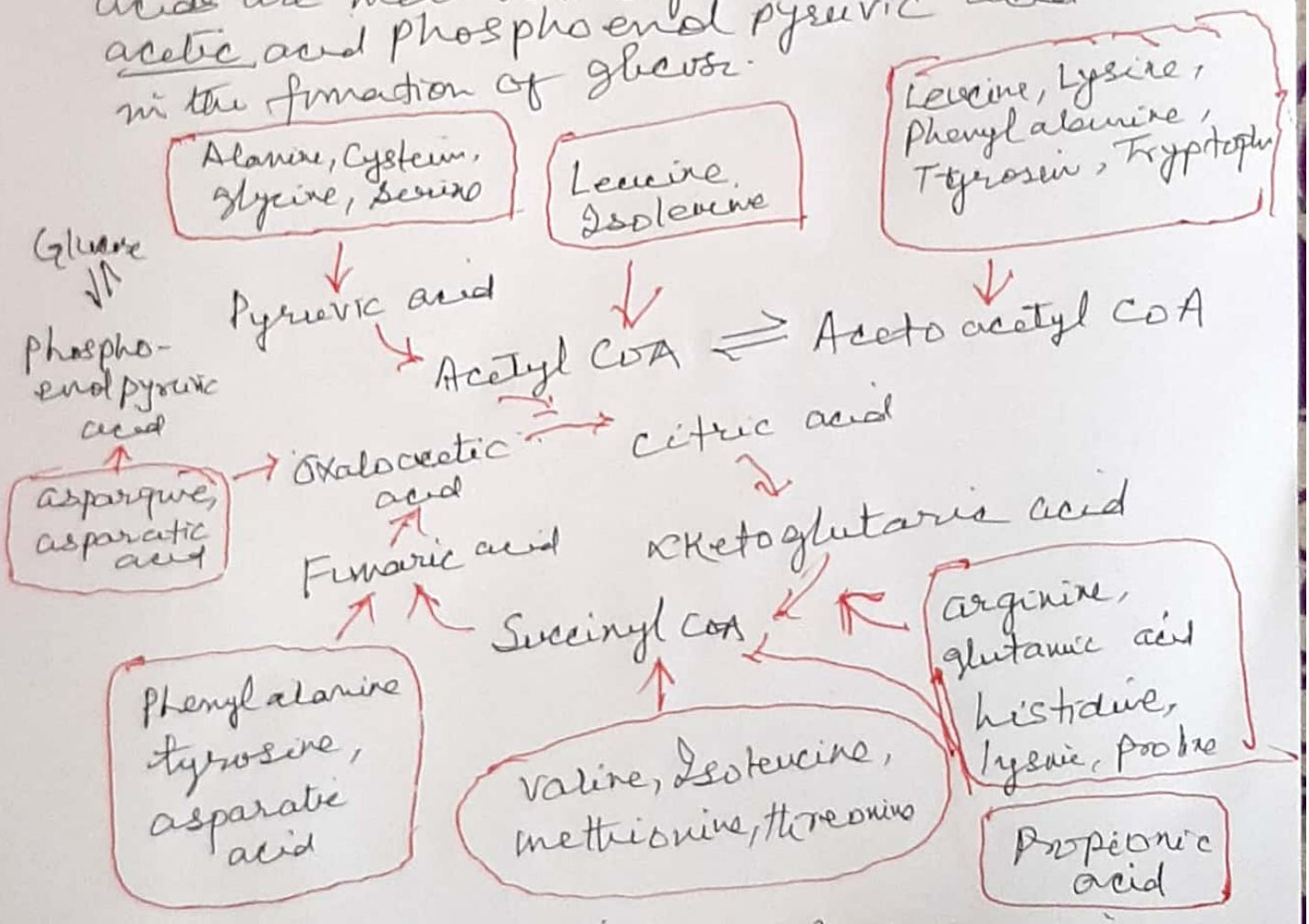

Fig - Entry of amino acids and Propionic acid in citric acid cycle.