MODULE 14

AIM

The aim of this module is to provide students with an introduction to Citric Acid Cycle.

CONTENTS AND OBJECTIVES

- Introduction
- Reactions involved in citric acid cycle
- Significance of citric acid cycle

Citric Acid Cycle

INTRODUCTION

- The citric acid cycle is known by 3 different names- Krebs cycle, citric acid cycle and Tricarboxylic acid cycle.
- This cycle is named Krebs cycle because most of the reactions were discovered by the scientist **Hans Krebs**.
- The citric acid cycle extracts the energy of sugar by breaking the acetic acid molecule all the way down to **Carbon Dioxide (CO_2).**
- Besides forming CO_2, it also results in the formation of **NADH** and **$FADH_2$**.
- At the end of this cycle a high energy compound is produced.
- The NADH and $FADH_2$ formed in the TCA cycle move on to enter the electron transport chain where energy is derived from them for oxidative phosphorylation.
- The citric acid cycle is central to all the respiratory oxidation reactions, oxidizing acetyl-CoA from glucose, lipid and protein catabolism in aerobic respiration to maximize energy gain.
- In addition, the intermediates from the TCA cycle are often utilized for the biosynthesis of many compounds inside the cells.
- All the enzymatic reactions associated with TCA cycle take place in the mitochondrial matrix or inner mitochondrial membrane.

REACTIONS INVOLVED IN CITRIC ACID CYCLE

1) Production of Acetyl-CoA

The pyruvate generated in glycolysis gets converted into Acetyl CoA. The reaction is irreversible. CO2 is released and thus it is called oxidative decarboxylation. The reaction also reduces NAD^+ into NADH. The entire reaction is catalyzed by Pyruvate Dehydrogenase Complex.

Note- Acetyl CoA cannot be converted back to pyruvate and that is why fat cannot be converted to carbohydrate.

After being produced Acetyl-CoA enters in the Krebs cycle and produces energy.

2) Formation of Citric Acid Cycle

Citric acid is formed as a result of condensation of oxaloacetate and Acetyl-CoA. Thi reaction is catalyzed by **Citrate Synthase.**

3) Formation of Isocitrate

The conversion of citrate to isocitrate is a reversible reaction with cis-aconitase as an intermediate. This reaction is catalyzed by **aconitase**.

4) Conversion of Isocitrate to α-Ketoglutarate

This reaction is an oxidative phosphorylation reaction i.e., CO_2 is released in this reaction. It is catalyzed by **isocitrate dehydrogenase**. Along with CO_2, one molecule of NADH is also produced.

5) Formation of Succinyl-CoA

Conversion of α- ketoglutarate to succinyl-CoA is an oxidation reaction. It results in the release of CO2 and one molecule of NADH.

6) Formation of Succinate

A high energy product having a thioester linkage is converted into a low energy product. Enzyme involved is **succinyl CoA synthase**. The energy so released is used to form GTP by the condensation of GDP and $P_{i.}$

7) Formation of Succinate to Fumarate

The oxidation of succinate to fumarate is catalyzed by **succinate dehydrogenase**. One molecule of FADH is generated in this reaction.

8) Formation of Fumarate to Malate

It is a dehydration reaction. This reaction is catalyzed by **fumarase.**

9) Conversion of Malate to Oxaloacetate

It is an oxidation reaction catalyzed by **malate dehydrogenase**. One molecule of NADH is generated.

Oxaloacetate again combines with a new molecule of Acetyl-CoA to start a new cycle.

SIGNIFICANCE OF KREB CYCLE

1) **Provides carbohydrate intermediates for lipid, protein and carbohydrate metabolism-** A few of the TCA cycle intermediates are of central importance. They are directly extracted from the TCA cycle for the metabolism of lipids and proteins. Therefore, Kreb cycle can regulate other metabolic pathways through product inhibition.
2) **Role in evolution**- Kreb cycle is directly associated with running of Electron Transport Chain and hence, depends on availability of oxygen. Kreb cycle has let the organism evolve and adapt to high Oxygen environment.