



FACULTY OF ENGINEERING & TECHNOLOGY

Unit-1

Topic -7th

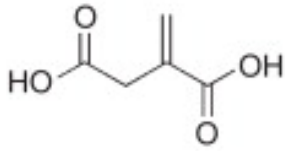
PRODUCTION OF ITACONIC ACID

Mrs. Vandana Yadav

Introduction

- Bentley and Thiessen (1957a) proposed a biosynthesis pathway of itaconic acid, Since the 1960s the production of itaconic acid is achieved by the fermentation with *Aspergillus terreus* on sugar containing media although also other microorganisms like *Ustilago zaeae*.
- Itaconic acid (2-methylidenebutanedioic acid) is an unsaturated dicarboxylic acid. Itaconic acid also known as 2-Methylenesuccinic acid, Methylenebutanedioic acid and methylenesuccinic acid.
- Itaconic acid is formed in fermentation of some sugars, it is also a metabolic product of *Aspergillus itaconicus*.
- Itaconic acid is also produced in cells of macrophage lineage.
- Itaconic acid was obtained by the distillation of citric acid, also produced by fermentation.

(Haskins et al., 1955)



- Itaconic acid is produced by the fermentation with *Aspergillus terreus* on sugar containing media, although also other microorganisms like *Ustilago zea*, *U. maydis*, *Candida* sp., and *Rhodotorula* sp. were found to produce itaconic acid.

(Haskins et al., 1955)

- Itaconic acid is an unsaturated di-carboxylic acid. Its application in industrial production of resins and is used as a building block for acrylic plastics, acrylate latexes, super-absorbents, and anti-scaling agents.
- The ideal temperature is 40°C, & pH must be reduced to 2 to start the production of Itaconic acid (methylene succinic acid)

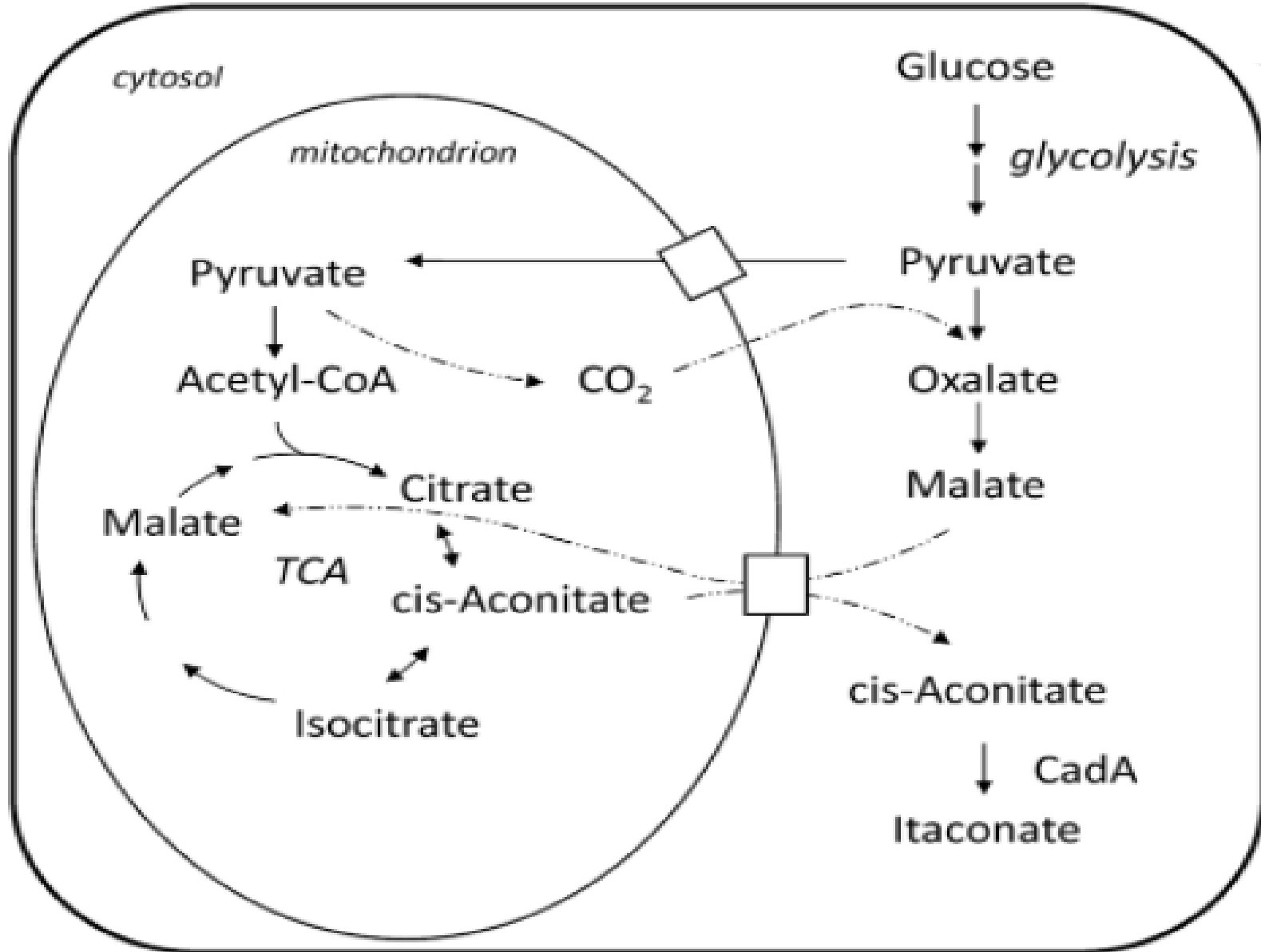
(Okabe et al., 2009)

Production

- Itaconic acid is produced in batch fermentation in a process, *A. niger* are able to excrete different type of organic acids such as oxalic, citric, and itaconic acids and are thus used in their industrial production.
- At the industrial scale the most explored organism for the fermentative production of itaconic acid is *Aspergillus terreus*.
- The biosynthetic pathway of itaconic acid is like citrate biosynthesis, where the catalytic conversion of *cis*-aconitate into itaconic acid. Thus citrate is synthesized from oxaloacetate and acetyl CoA, while oxaloacetate is synthesized from pyruvate by anaplerosis, which starts from the pyruvate that is the end product of glycolysis.



Biosynthesis Pathway of Itaconate





- Bentley and Thiessen 1957 proposed a pathway for the biosynthesis of itaconic acid, which Starting from a sugar substrate like glucose the carbon molecules are processed via glycolysis to pyruvate.
- Then the pathway is split and part of the carbon is metabolized to Acetyl-CoA releasing a carbon dioxide molecule. The other part is converted to oxaloacetate so that the previously released carbon dioxide molecule is again incorporated.
- In the first steps of the citric acid cycle, citrate and *cis*-aconitate are formed. In the last step, the only itaconic acid pathway dedicated step, *cis*-aconitate decarboxylase (CadA) forms itaconic acid releasing carbon dioxide.
- The formation of carboxylic acids, like citric and itaconic acid, involves the shuttling of intermediate metabolites between different intracellular compartments and utilizes the different enzymatic capabilities of the respective compartment. In case of itaconic acid the compartmentalization of the pathway was analyzed by fractionized cell extracts distinguishing the enzymatic activity of a mitochondrial from a cytosolic enzyme.

(Bonnarme et al., 1995)

(Jaklitsch et al., 1991)

Properties and Application of Itaconic Acid

- Its melting point is 167–168 °C
 - boiling point is 268 °C.
 - pH of 2.0, Water Soluble
-
- ✓ It is a white colorless crystalline, hygroscopic powder soluble in water, ethanol, and acetone.
 - ✓ It is an unsaturated diprotic acid, which derives its unique chemical properties from the conjugation of one of its two carboxylic acid groups with its methylene group.
 - ✓ Itaconic acid are used as building blocks for large numbers of compounds, such as resins, paints, plastics, and synthetic fibers (acrylic plastic, super absorbants, and antiscaling agents).
 - ✓ These diverse properties have led to a variety of applications in the pharmaceutical, architectural, paper, paint, and medical industries such as plastics, resins, paints, synthetic fibers, plasticizers, and detergents.
 - ✓ Itaconic acid applications have penetrated the dental, ophthalmic and drug delivery fields (Hajian and Yusoff, 2015).
 - ✓ Itaconic acid also induces a transcription factor which is essential for protection against oxidative and xenobiotic stresses, and to reduce inflammation.
 - ✓ Itaconic acid is an unsaturated dicarbonic acid, and can readily be incorporated into polymers so its mainly used in the plastic and paint industry.

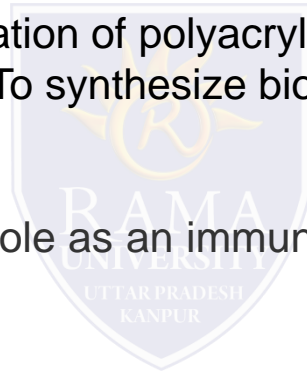
Cont...

- ✓ Itaconic acid is a biochemical building block, because it can be used as a monomer for the production of a plethora of products including resins, plastics, paints, and synthetic fibers.
- ✓ Some *Aspergillus* species, like *A. itaconicus* and *A. terreus*, show the ability to synthesize this organic acid and *A. terreus* can secrete significant amounts to the media, itaconic acid possess anti-inflammatory or analgesic activities.
- ✓ Itaconic acid is used exclusively in nonfood applications, especially in the polymer industry. Itaconic acid derivatives are used in medicine, cosmetics, lubricants, thickeners, and herbicides (e.g., substituted itaconic acid anilides).
- ✓ speculate on the role of itaconic acid as an inhibitor of metabolic pathways, because it is described as an enzymatic inhibitor.
- ✓ can act as an antibacterial agent although itaconic acid can inhibit fructose-6-phosphate 2-kinase and thus have a direct influence on the central carbon metabolism.
- ✓ The presence of the conjugated double bond of the methylene group allows polymerization both by addition and condensation.

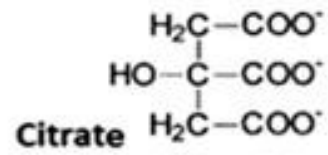
(Sakai et al., 2004)

Application

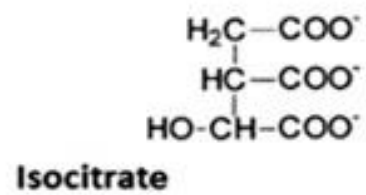
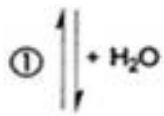
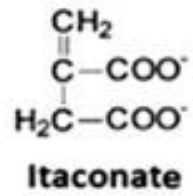
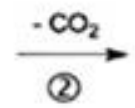
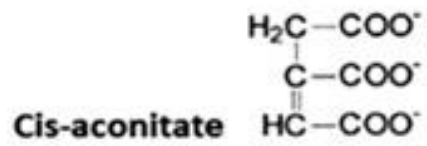
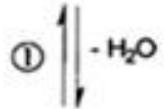
- ✓ The polymerized methyl, ethyl, or vinyl esters of itaconic acid are used as plastics, adhesives elastomers, and coatings.
- ✓ As a comonomer in the polymerization of polyacrylonitrile (PAN) to promote the thermo-oxidative stabilization of polymer. To synthesize biodegradable polyester composite in fabric industry.
- ✓ itaconic acid was found to play a role as an immune-supportive metabolite in mammalian immune cells.



from glycolysis



- ① Aconitase
- ② Aconitate-decarboxylase



Catabolization of Itaconic Acid

- ❑ In mammalian cells (guinea pig and rat liver) it was found that itaconate is converted to itaconyl-CoA and is further processed via pyruvate and acetyl-CoA.
- ❑ it was found that malonate has an inhibitory effect and an addition prevents the degradation of itaconic acid
(Adler et al., 1957)
- ❑ The first step of this degradation pathway can be catalyzed by the ubiquitous succinyl-CoA synthetase.
(Schürmann et al., 2011)
- ❑ Itaconic acid is a dicarboxylic acid that is methacrylic acid in which one of the methyl hydrogens is substituted by a carboxylic acid group. It has a role as a fungal and a human metabolite. It is a dicarboxylic acid, derives from a succinic acid and conjugate acid of an itaconate.

(Kawamura et al., 1981)

THANK YOU