STUDY MATERIALS

PHARMACEUTICAL CHEMISTRY
PART-1
SEC-I, SEMESTER I

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FERMENTATION

Fermentation is the enzymatic decomposition and utililization of foodstuffs, particularly carbohydrates, by microbes. It is also an energy yielding process in which organic molecules serve as both electron donors and acceptors. In microbial fermentation NADH is oxidised to NAD+ and the electron acceptor is either pyruvate or a pyruvate derivative. There are different types of fermentation. First a type of fermentation known as alcoholic fermentation involves the conversion of sugars to ethanol and carbon dioxide. In this type of fermentation, pyruvate is decarboxylated to acetyldehyde which is then reduced to ethanol by alcohol dehydrogenase with NADH as the electron donor. Further, lactic acid fermentation involves the reduction of pyruvate to lactate. Here, lactic acid fermenters can be classified into two –

1. Homolactic fermenters 2. Heterolactic fermenters

Homolactic fermenters used the glycolytic pathway and directly reduced almost all the pyruvate to lactate with the enzyme lactate dehydrogenase. While heterolactic fermenters forms substantial amounts of product other than lactate. Another fermentation type is the formic acid fermentation. In this type of fermentation, bacteria metabolized pyruvate to formic acid and other products. Further formic acid may be converted to H_2 and CO_2 by formic hydrogenylase.

There are two types of formic acid fermentation – 1. Mixed acid fermentation and 2. Butanediol fermentation Mixed acid fermentation results in the excertion of ethanol and a complex mixture of acids such as acetic, lactic, succinic and formic acids. While in butanediol fermentation, pyruvate is converted to acetoin which is then reduced to 2,3-butanediol with NADH. A large amount of ethanol is also produced together with smaller amounts of acids found in the mixed acid fermentation. Formic acid fermentation is very useful in identification of the members of the Enterobacteriaceae family. Formic acid fermenters sometimes generate ATP while re-oxidizing NADH. They use acetyl CoA to synthesized acetyl phosphate which then further donates its phosphate to ADP.

Conclusion Microbes employed different metabolic strategies and they can be differentiated from each other based on their metabolic characteristics. All forms of metabolism involve

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chemical exchange of electrons through oxidation and reduction. The transport of electrons between the donor and acceptor molecules through membrane embedded complexes generates ion gradients across the membrane. This transport of electrons is fundamental to respiration, the oxidative completion of catabolism to CO_2.

Fermentation is the chemical transformation of organic substances into simpler compounds by the action of enzymes and complex organic catalysts, which are produced by microorganisms such as yeasts, bacteria or molds. Enzymes act by a process called hydrolysis, which breaks down or predigests complex organic molecules to form smaller compounds and nutrients. Some of the products of fermentation are wine, beer, vinegar, yogurt, cheese, sauerkraut, kimchi, pepperoni, pickled cucumbers, etc. Based upon the respiration, fermentation is of 2 types namely aerobic and anaerobic.

Aerobic fermentation

Aerobic fermentation occurs in presence of oxygen. Wine, beer and acetic acid vinegar needs oxygen in the primary or first stage of fermentation. For example, preparation of acetic acid vinegar is done by exposing the surface of the vinegar to oxygen as much as possible, which helps in creating healthy, flavorful vinegar with the correct pH.

Anaerobic fermentation

Anaerobic fermentation is a method in which cells are used to extract energy from carbohydrates when oxygen is not available in the surrounding environment. This process can follow glycolysis as the next step in the breakdown of glucose and other sugars to produce molecules of Adenosine Tri Phosphate (ATP) that create an energy source for the cell. Anaerobic fermentation is of 2 types namely ethanol fermentation and lactic acid fermentation.

Ethanol fermentation:

It converts two pyruvate molecules, which are the products of glycolysis, into two molecules of ethanol and two molecules of carbon dioxide. This reaction is a two-step process in which pyruvate is converted to acetaldehyde and carbon dioxide by the enzyme pyruvate decarboxylase. Yeast and certain bacteria perform this type of fermentation. It is used in the production of wine, beer and bread.

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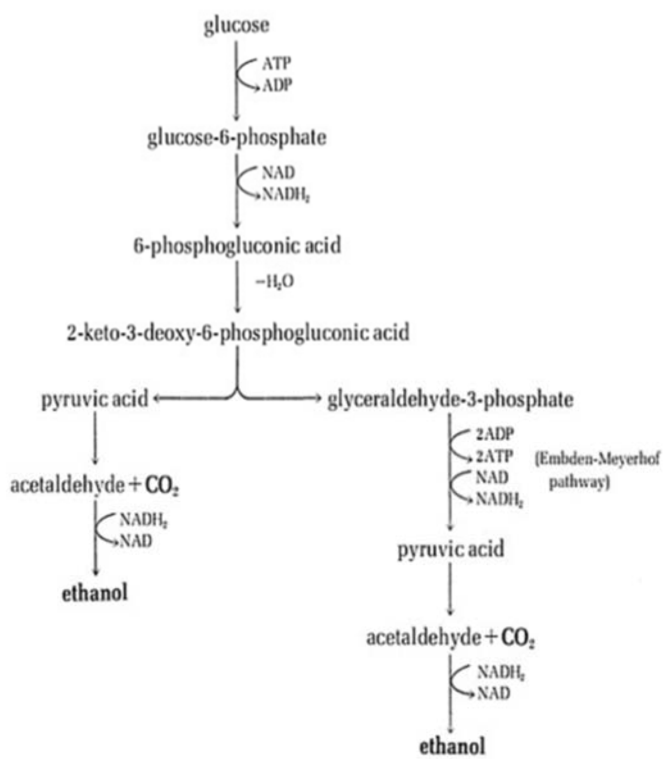
Lactic acid fermentation:



It is a biological process in which glucose and other 6-carbon sugars are converted into cellular energy and the metabolite lactate. The pyruvate molecules from glucose metabolism may be fermented into lactic acid. It is used to convert lactose into lactic acid in yogurt production. It is of 2 types namely homo lactic acid fermentation and hetero lactic acid fermentation. Homo lactic acid fermentation is a process in which only lactic acid is produced with absence of byproducts whereas hetero lactic acid fermentation is a process in which lactic acid is produced along with some of the byproducts like gases.

Advantages of fermentation

1. Preserves and enriches food, improves digestibility and enhances the taste and flavor of foods. 2. Potential of enhancing food safety by controlling the growth and multiplication of pathogens in food. 3. Low energy consumption. 4. Detoxification of food.

Disadvantages of fermentation

1. Hazardous microbial contamination always exists in fermented food. 2. The uneven distribution of salt in lactic acid fermented fish products and contamination of Aspergillus flavus in traditional starter cultures for rice wine and soybean sauce result in severe food poisoning incidences. 3. Obesity and cancer issues. Applications 1. Used in the production

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of antibiotics and ethyl alcohol. 2. To produce alcoholic beverages like beer from barley or wheat and wine from grapes. 3. Used to store vegetables in the form of pickling. 4. Aerobic bacteria are used to ferment organic material in waste water.

Citric Acid Production Fermentation Process

Citric acid fermentation was first observed as a fungal product by Wehmer in 1893 by a culture of Penicillium glaucum on sugar medium. After a few years, he isolated two new fungal strains with the ability to accumulate citric acid, which were designated *Citromyces* (*Penicillium*). However, industrial trials did not succeed due to contamination problems and long duration of fermentation. It was the work of Currie which opened up the way for successful industrial production of citric acid. In 1916, he found that numerous strains of *Aspergillus niger* produced significant amounts of citric acid. The most important finding was that *Aspergillus niger* grew well at pH values around 2.5–3.5 and high concentrations of sugars favour citric acid production.

The first citric acid fermentations were carried out in surface cultures. In the 1930s, some units were implanted in England, in Soviet Union, and in Germany for the commercial production. In general, citric acid is commercially produced by submerged microbial fermentation of molasses; the fermentation process using *Aspergillus niger* is still the main source of citric acid worldwide. Although methods were well developed to synthesise citric acid using chemical means, better successes were achieved using microbial fermentations, and over the period of time, this technique has become the method of ultimate choice for its commercial production over chemical synthesis. Despite that, the introduction of submerged fermentation presented several problems, including the choice of productive strains with low sensitivity to trace elements. It was necessary to consider raw material much more carefully. Several works were dedicated to the optimization of the conditions for the utilization of cheap material like sugar cane molasses, beet molasses, starch and hydrolysate starch. Various processes for treating and purifying molasses were developed, especially for the removal of trace metals. Moreover, it was found that a small excess of copper ions was beneficial to achieve high yields of citric acid.

There are annual growths of 3.5–4.0 % in demand/ consumption of citric acid. In the last years, a considerable interest has been shown in using agricultural products as alternative sources of

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carbon and their wastes such as maize, apple and grape pomace, pineapple, mandarin orange and brewery wastes, citrus and kiwi fruit peel for citric acid production by *Aspergillus niger.* The industry is seeking newer cheap and economic process technology.

Citric acid is mainly used in food industry because of its pleasant acid taste and its high solubility in water. It is worldwide accepted as "GRAS" (generally recognized as safe), approved by the Joint FAO/WHO Expert Committee on Food Additives. The pharmaceutical and cosmetic industries retain 10% of its utilization and the remainder is used for various other purposes. Table 1 presents main applications of citric acid.

Industry	Applications
Beverages	Provides tartness and complements fruits and berries flavours. Increases the effectiveness of antimicrobial preservatives. Used in pH adjustment to provide uniform acidity.
Jellies, Jams and Preserves	Provides tartness. pH adjustment.
Candy	Provides tartness. Minimizes sucrose inversion. Produces dark colour in hard candies. Acts as acidulant.
Frozen fruit	Lowers pH to inactivate oxidative enzymes. Protects ascorbic acid by inactivating trace metals
Dairy products	As emulsifier in ice creams and processed cheese; acidifying agent in many cheese products and as an antioxidant.
Fats and oils	Synergist for other antioxidants, as sequestrate.
Pharmaceuticals	As effervescent in powders and tablets in combination with bicarbonates. Provides rapid dissolution of active ingredients. Acidulant in mild astringent formulation. Anticoagulant.
Cosmetics and toiletries	pH adjustment, antioxidant as a metallic ion chelator, buffering agent.
Industrial applications	Sequestrant of metal ions, neutralizing, buffer agent
Metal cleaning	Removes metal oxides from surface of ferrous and nonferrous metals, for preparational and operational cleaning of iron and copper oxides

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