The Study and Challenge of Producing Sugar Substitutes via Microorganism Pathway

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Abstract. Nowadays, the ratio of obesity increases continually because of excessive sugar intake with the improvement of living standards, especially for children and teenagers. The obesity, caused by excessive sugar intake, is a main risk to induce cardiovascular disease both in adults and children because of abnormal glucose tolerance, such as hypertension, atherosclerosis and coronary heart disease. Consequently, it's important to find an effective method to limiting sugar intake, which are welcomed by sweet person, reducing onset of higher sugar intake associated diseases, contains optimistic business opportunities. Therefore, the research and development of sugar alternative products grew rapidly and soon occupied an important position in the market. In comparison with artificial sweeteners, erythritol, as a natural sugar substitutes (NSS), is widely used in good industry to add sweet tastes. But producing erythritol faces problems. One of the main problems is using erythritol is far more expensive by using traditional sugar, like sucrose and fructose. In order to solve this problem, scientists suggest to replace glucose by glycerol. At the same time, change the environment of bacterium or fungi greatly influence the efficiency. In this review, the author aims to summarize the production of erythritol, compare its advantages and limitations, and provide some references for its development as an important sugar substitute in future.

Keywords: Erythritol, Microorganism pathway, Glycerol, Environment factor.

1. Introduction

During these days, people are paying more and more attention to the risk of obesity. The data from the internet shows that about 13 percent of adults are suffered from obesity, which ratio is even higher in children. The number increases to 19.7% recently. More than 14.7 million of population are over-weighted in the worldwide. At the same time, the calculation data even includes developing countries' poor children. As an example, America is troubled by this puzzle. The percentage of overweight and obese children and adolescent is 30% and 15%, separately. It means that about half of young teenagers are unhealthy. One of the reasons is young children always taking in too much sugar from soft drinks and sweet foods. As so much useless sugar goes into human bodies, fat is produced. Parents cannot take the high risk of overweight for their children. The obesity, caused by excessive sugar intake, is a main risk to induce cardiovascular disease both in adults and children because of abnormal glucose tolerance, such as hypertension, atherosclerosis and coronary heart disease [1].

If the main factor of obesity, sugar, is replace by other sugar substitute products like polyols, the risk of getting heavier will decrease. Until now, there are two kinds of sugar substitute products in market, including artificial sweeteners and natural sugar substitutes (NSS). The main drawback of artificial sweeteners is that has risk to disruption of intestinal microflora. In contrast to artificial sweeteners, NSS received particular attention because it associated with a healthier lifestyle. One of the mature substitute goods of NSS is erythritol. These products have been produced through special progress that can be enjoyed by diabetics around the world, as the number of diabetics is 537 million. The number may be even higher in 2030, which the predicted number is 643 in 2030 and 783 million in 2045. Along with the sweetener sucralose, the sugar substitute, erythritol does not provide energy to the body because of excreting directly in the urine after metabolizing, which doesn't influence the levels of blood glucose, thus allowing to use population of diabetics or obesity by FDA [2]. The market size of erythritol is surprising and visible. The value is as much as 380.96 million dollars one year. In this review, the author aims to summarize the production of erythritol, compare its advantages

and limitations, and provide some references for its development as an important sugar substitute in future.

2. Advantages and Limitations of Erythritol as Sugar Substitute

First, the erythritol is equal to other polyols in sweeenting properties including lactitol, maltitol, mannitol, sorbitol, and xylitol. The sweetness and taste of erythritol are similar to sucrose, but without calories because it can't be metabolized and absorbed by the human body. Therefore, it has no effect on human blood sugar, lower risk of inducing cardiovascular diseases. In addition, its molecular weight is relatively small, making it easy to produce industrially [2]. But the disadvantage is that producing erythritol can be really expansive. For instance, the price per kilogram of erythritol was about 4.5 dollars in 2023. And the food companies can expect the price to be even higher than 2023, as people today care more and more about their own health, but the public do not wish to sacrifice the taste, sweet. The reason of the higher price of erythritol is its limited yields [3]. Erythritol can only be more competitive when its cost is close or even cheaper. If this vital problem has not been solved, erythritol will not be widely used. It is people's wish to make erythritol be a common ingredient in food production, instead of just keep advertising it as a healthy product.

3. Production of Erythritol

3.1. Two Pathway of Erythritol Production

During the period, the owners of the factories use fermentation to help produce the erythritol. They often use sucrose, pure glucose and corn starch to produce erythritol, which are expensive using these products as raw materials. The data in 2023 shows that the price of sucrose is $0.25/kg. In comparison of the price of erythritol ($4.5/kg), using sucrose and glucose may not be a good idea because they do not perform any advantage. To solve the problem, scientists have tried to use less expensive ingredients. One of the methods for scientists to reduce the cost is using different carbon sources. Things that are usually considered as waste may play as a carbon sources. For example, using other kinds of bacterial will cost less money. At the same time, the production can be more environmentally friendly, as the process only need the waste of other reactions. In Figure 1, the author compared the two pathways using for production of erythritol. The left half flow map is more traditional one using glucose as raw material. The first discovery of this process has passed more than 60 years, which great contribution was reported at 1961. The new process using glycerol as raw material on the right in Figure 1. There are some microorganisms that have been used to produced glycerol, thus it can become the raw materials of erythritol. For examples, Moniliella megachiliensis and Moniliella pollinis are often used to produce glycerol as ingredient of erythritol. In addition, the Yarrowia lipolytica are also capable of producing erythritol from glycerol as a recycle products discharging from biodiesel manufacture. In comparison with traditional pathways, this modern pathway of fermentation process using glycerol is low-cost carbon substrates original and recycle [4, 5].

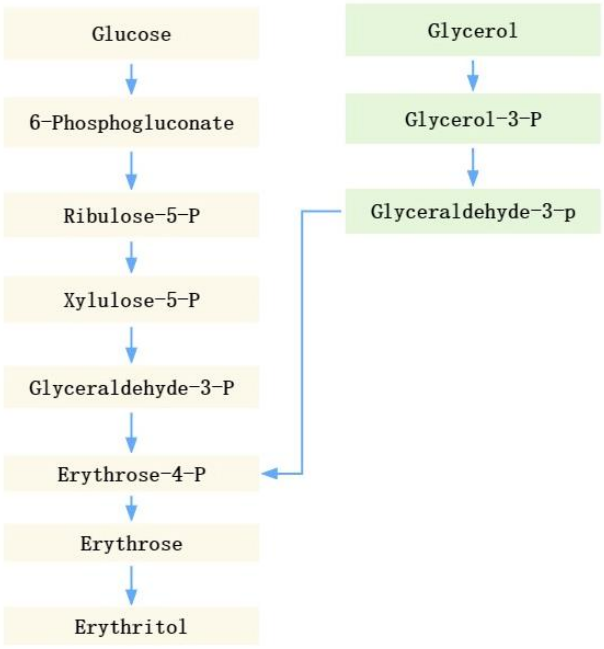


Figure 1. Two pathways of erythritol production

3.2. Limitations using Glucose

There are still some problems with conventional glucose production. This type of production has a slight advantage in terms of efficiency. In fact, performance can even be very low. There are usually two ways to make lichen glycol. One way is to use a chemical solution. However, this approach ultimately proved ineffective, although using nickel as catalyst produced starch diformaldehyde at high temperatures. Another approach is to replace the use of biotechnology by developing production processes. For example, some researchers claim that controlling glucose during this process is more effective. Glucose control by Torula Sp., can increase butter alcohol production. The maximum volume yield of cracked acid was achieved by controlling the glucose concentration to 225 g/l and the basic acid supply of fission acid. Applying 400 g/l glucose are capable of gaining 192 g/l of solar alcohol after 88 hours, that means the volume yield of 48% (2.26 g/l) [6].

At the same time, other factors are also considered. For example, the synthesis of erythritol maybe induced hyperosmotic stress of cells through regulation of high osmolarity glycerol (HOG) pathway, influencing downstream of the MAPK pathway. The Hog1 MAP kinase plays a key function, when activation leads glycerol accumulation and production in short time, or regulate gene transcription and translation in long time. The knockout of Hog1 gene resulted mutants to impair growth and reduce production both solid and liquid medium, separately. For example, the production of erythritol increased 1.4 folds during 20% glucose liquid culture. The synthesis of protein was associated with erythritol production and high osmolality in Yarrowia lipolytica. Research data showed that the osmotic pressure increased from 3.17 osmol/kg to 4.15 osmol/kg with the addition 30g/l Nacl in glycerol medium, thus increment expression of 26 kinds of protein [6, 7]. Thus, providing yeasts with certain amount of glucose or change of gene of can greatly improve the producing effieciency. Although scientists made some improvement in technologies, using glucose to produce this method is still very costly to industrialize.

3.3. Key Technologies to Increase the Yield of Erythritol using Glycerol

There are some key technologies to increase the yield at the same time to decrease the cost of raw materials. First, it’s very important to using optimal fermentation conditions, such as PH. The Y. lipolytica Wratislavia K1 mutation showed the optimal PH 5.5 produced higher erythritol in glycerol medium. In addition, the yield enhanced 56% after cultured 7days when PH decreased to 3. Secondly, various kinds of improvement to increase the purity are used. As an example, the standard

fermentation culture is to infuse 5 ml of sperm culture-medium with 50 ml containing 12% hydroxyl and 0.5% yeast extract for 6 days at 30°C with 180 AD shaking/min. The result shows there is a close relationship between reed and yeast extract synthesis. In addition, lower efficiency index indicated that the production of erythritol was influenced by yeast extract and Korpo 4. furthermore, culture using shake-flasks are capable of producing more erythritol (58.8 ± 1.68 g/L) in comparison with using batch growth. Furthermore, the efficiency increased by 250%, demonstrating that improving culture conditions with glycerol medium was help produce more erythritol [8].

The upregulation of associated genes with metabolism in cells have important relationship with the yield of erythritol, thus changing these conditions of genes expression or modifying them through genetic engineering resulting in further increasing the yield. The glycerol catabolic pathway associated genes upregulated expression with increment of osmotic stress. For example, the erythritol yield incresed with upregulation of heterologous overexpression in sugar alcohol phosphatase, eventually further increasing the production of erythritol through increment glycerol kinase (GK), and transketolase (TKL) production [9], demonstrating that it's benefit to produce cheaper erythritol using new types of microorganism.

4. Summary

By those experiment mentioned above, the improvement of productivity of erythritol has shown great progress recently. By using glycerol, the production of erythritol can be provided with cheaper ingredient, by still maintaining a high efficiency, as row glycerol is the byproduct of many chemical reaction and often treated as waste. In this case, the cost of making erythritol by microorganism can be greatly reduced, which will be helpful in exploring the market of seasoning. If the owners of the firms tend use more traditional method to lower the risk, they can try to control the concentration of glucose. Until now, the two methods to produce erythritol still face many challenges, needing improvement the production progress with the development of biological technologies and associated theory. Since the human living standards become more higher, the demand for sugar substitutes is gradually increasing. Finding suitable and cheap methods to produce sugar substitutes is an interesting research direction and urgent issue to be resolved in the next decade.

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