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Prospects for Gamma Aminobutyric Acid-Enriched Dadih as a Diabetic Functional Food

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ABSTRACT
Around 415 million people worldwide suffer from diabetes mellitus (DM). DM is associated with changes in the endocrine pancreas. This condition is regulated by several neuropeptides and neurotransmitters in the pancreas, one of which is gamma aminobutyric acid (GABA). In fermented milk products, GABA can be added to provide a functional food. The potential of GABA-enriched dadih (fermented buffalo milk) as a functional food for diabetic patients is discussed in this paper. Journals, books, societies, and diabetes federations have been used to gather information. Based on the discussion, this could be concluded that GABA has a good chance of being developed into a functional food for diabetics due to the availability of raw ingredients, high added value, and a feasible process and can support the government's import substitution program. Furthermore, its development as a functional food may improve people's desire to consume dadih.

Keywords: diabetes mellitus, gamma aminobutyric acid, dadih, functional food, lactic acid bacteria

I. INTRODUCTION

Diabetes mellitus affects around 415 million people globally. The global death rate from DM is estimated to be over 5.0 million individuals per year. The number of individuals living with DM is expected to rise to 642 million by 2040.The number of DM sufferers in Indonesia is ranked 7th after China, India, the United States, Brazil, Russia and Mexico [1]. DM is a group of chronic metabolic diseases due to abnormalities in insulin secretion and/or action [2]. DM is associated with changes in the endocrine pancreas. These changes include a significant decrease in the number of pancreatic beta cells, the cells that produce and secrete insulin. The decrease in the number of pancreatic beta cells occurred along with the increase in the number of glucagon, somatostatin and pancreatic polypeptide cells. Improvement of these decreased and increased conditions is regulated by several neuropeptides and neurotransmitters in the pancreas [3].

Neuropeptides and neurotransmitters are present in the endocrine pancreas and play a role in insulin metabolism. The content of these neuropeptides and neurotransmitters decreases significantly in DM, reducing or even stopping their ability to regulate insulin metabolism. Improved insulin metabolism can be achieved by increasing the number of neuropeptides and neurotransmitters in the endocrine pancreas, allowing insulin to be re-secreted to maintain normal blood glucose levels. Neuropeptide Y (NPY), calcitonin gene-related peptide (CGRP), and gamma aminobutyric (GABA) acid are types of neuropeptides and neurotransmitters. GABA is a non-essential amino acid with a primary role in the central nervous system as a neurotransmitter. GABA calms neuronal activity by inhibiting nerve transmission in the brain [4]. GABA is produced by the enzyme glutamate decarboxylase (GAD) catalyzing glutamate decarboxylation [5]. GABA is a neurotransmitter that also serves as a blood pressure regulator, cell regulator, cancer cell growth inhibitor, anti-inflammatory, anti-depressant, and other functions [6]. According to previous studies, GABA was found to improve insulin secretors in both its pure form (GABA without any other substances) and GABA-enriched products.

Fermented milk is one example of a GABA-enriched product that can be manufactured, as GABA can be produced by lactic acid bacteria (LAB) as a fermentation starter. Dadih is a traditional Indonesian fermented milk product that has been used as a food source by the locals. This product is a well-known traditional food in West Sumatra, Jambi and Riau. Dadih is still manufactured traditionally in Indonesia, which involves milking buffalo and placing it in a bamboo tube with or without a banana leaf covering, then tying it with a rubber band and leaving it to ferment at room temperature for 1-2 days [8].

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The results of bacterial isolation in dadih showed that 36 LAB strains were dominating. The metabolites produced by LAB are known to inhibit pathogenic bacteria, lower cholesterol, improve the immune system, prevent constipation, and produce B vitamins and bacteriocins [8]. They are also antimutagenic, anticarcinogenic, and anti vaginitis. GABA could be produced by LAB since its cells contain the GAD enzyme, which acts as a catalyst for GABA synthesis. This demonstrates that, by using LAB strains with high GABA content as a fermentation starter, dadih has the potential to be turned into a functional diet for diabetics.

This study discusses the potential of dadih as a functional food product for diabetics, as well as the potential for its development in Indonesia.

II. COLLECTING INFORMATION

The information in this paper was gathered from a variety of journals, books, associations, and diabetes federations, and then it was discussed how functional foods, such as GABA-enriched dadih could be used to treat diabetes.

III. DADIH'S PROSPECTS AS A DIABETIC FUNCTIONAL FOOD

Functional food is food that contains live microbes which when consumed will have a therapeutic effect on the body by improving the balance of microflora in the digestive tract [9]. Dadih is a fermented milk product that is efficacious as a functional food, because it has 36 dominant LAB strains. This buffalo milk product found in West Sumatra has long been known and favored by the local community [10, 11]. Dadih is a white tofu-like substance that may be chopped and eaten with a spoon. Dadih is used as a side dish, a compliment to traditional ceremonies, and as traditional medicine in general [11]. Dadih can be eaten straight after fermentation (as is customary) or flavored in a number of ways (as shown in Figure 1).

Figure 1. (left to right) Traditionally and flavored dadih.

Dadih is traditionally made from buffalo milk that has been cured in a bamboo tube and covered with withered banana leaves over a fire, then incubated for two days at room temperature (about 27-33^{o}C) [11]. Various types of microorganisms interact with one other in traditional dadih fermentation. Microorganisms that play a role in this fermentation process are thought to come from the bamboo tube's inner surface, the leaf cover's surface, and the buffalo milk used. The microorganisms consist of bacteria and yeast with a bacterial count of about 10^{6}-10^{7}cfu/ml and yeasts about 10^{5}cfu/ml [12].

Improving the quality of the resulting dadih can help to transform it from a traditional dish to a commercial product. Producing dadih as a diabetic-friendly food is one of them. Indonesia was ranked seventh in the world for diabetics, according to data released by the International Diabetes Federation in 2015. (Table 1). Indonesia is predicted to be the sixth largest country in the world by 2040 [1]. As a result, food products with a therapeutic effect on diabetics must be produced, as food products will be more in demand by diabetics than medications in tablet or injection form.

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Dadih can be modified into a diabetic-friendly functional food by using LAB, which can produce high levels of GABA. GABA is a neurotransmitter that promotes pancreatic beta cells secrete more insulin. GABA-enriched dadih is expected to be able to regenerate damage to diabetic pancreatic beta cells, allowing insulin to be re-secreted.

The availability of raw materials, high added value, a technique that is feasible, and import substitution are all factors that contribute to the potential of dadih as a functional food product for diabetics, as mentioned below.

3.1 Availability of raw materials

Traditionally, the raw material for making dadih is buffalo milk (Figure 2). In order to develop dadih as a functional food for diabetics, high quantities of GABA-producing LAB strains must be used as a starter for fermentation. This high concentration of GABA-producing LAB strain can be isolated from traditionally prepared dadih. The ability to produce GABA was examined in all of the LAB isolates obtained. To achieve GABA-enriched dadih, the LAB with the highest GABA production was utilized as a starter for dadih fermentation. The use of a high-quality starter is also intended to provide a consistent-tasting result [13].

Table 1. Top 10 countries of most people living with diabetes (aged 20-75 years) 2015 and 2040

Rank	Country/territory	2015 Number of people with diabetes
1	China	109.6 million (99.6-133.4)
2	India	69.2 million (56.2-84.8)
3	United States of America	29.3 million (27.6-30.9)
4	Brazil	14.3 million (12.9-15.8)
5	Russian Federation	12.1 million (6.2-17.0)
6	Mexico	11.5 million (6.2-13.7)
7	Indonesia	10.0 million (8.7-10.9)
8	Egypt	7.8 million (3.8-9.0)
9	Japan	7.2 million (6.1-9.6)
10	Bangladesh	7.1 million (5.3-12.0)

Rank	Country/territory	2040 Number of people with diabetes
1	China	150.7 million (138.0-179.4)
2	India	123.5 million (99.1-150.3)
3	United States of America	35.1 million (33.0-37.2)
4	Brazil	23.3 million (21.0-25.9)
5	Mexico	20.6 million (11.4-24.7)
6	Indonesia	16.2 million (14.3-17.7)
7	Egypt	15.1 million (7.3-17.3)
8	Pakistan	14.4 million (10.6-20.4)
9	Bangladesh	13.6 million (10.7-24.6)
10	Russian Federation	12.4 million (6.4-17.1)

Source: International Diabetes Federation, 2015.

Figure 2. Buffalo milk (dadih raw material) fermented in bamboo

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The quality of the dadih obtained in each manufacturer varies due to traditional fermented dadih [14]. Meanwhile, buffalo milk, which is used to make dadih, is in short supply. This can be solved by substituting cow's milk for buffalo milk. Cow's milk is widely consumed and is reasonably easy to obtain in large quantities. Buffalo milk, on the other hand, has a higher nutritional content and solids than cow's milk, implying a higher quality. As a result, modifications are required to obtain dadih from cow's milk, such as: 1) Cow's milk has a lower dry matter content than buffalo milk, hence it must be **evaporated**. This approach should raise the dry matter of cow's milk to a level comparable to buffalo milk. Evaporation of milk can improve protein and fat content by up to 50%, but it is still lower than buffalo milk without evaporation. 2) **Toning** can also be accomplished by adding 3-4% full powdered milk or skim milk powder [13]. 3) Replacement of traditional bamboo containers with plastic **containers** or stainless steel fermenters, which are more sanitary and hygienic.

As a result, in terms of raw material availability, dadih has a strong chance of becoming a functional food for diabetics.

2. High added value

When compared to traditional processed dadih, GABA enriched-dadih offers a high added value. This is due to the fact that the dadih used can be used not only as a food source, but also as a functional food for diabetics. As a result, the high added value of this dadih product is due to the study's originality, which is the usage of GABA as an amino acid to increase insulin secretors. GABA's ability to repair insulin secretors has only been investigated by a few researchers. GABA has been extensively researched in the past for its potential as a neurotransmitter, blood pressure regulator, and other applications.

This processed dadih has added value because it not only uses raw ingredients from buffalo milk, but also raw materials from cow's milk. The two dadih were then compared organoleptically in order to determine which dadih with the raw components the community preferred. Thereafter, the dadih with the most desirable raw material is mass-produced.

3.3 Feasibility process

Using the lactic acid fermentation process, GABA-enriched dadih can be developed as an useful food for diabetics. This fermentation process can be started on a small scale in the lab to discover the best conditions for fermentation (pH, temperature, and number of LAB), and then scaled up to a pilot plan and production scale. Thus, understanding the fermentation process might make it easier to process dadih and obtain the desired ideal conditions.

3.4 Import substitution

GABA-enriched dadih has the advantage of supporting the government's import substitution program due to its functional qualities, which are comparable to other imported fermented milks such as yakult, yogurt, and kefir. This import substitution will undoubtedly have a positive impact, including: 1) reducing the country's reliance on imported fermented milk products like yakult, yogurt, and kefir; 2) strengthening the industrial sector; 3) expanding employment opportunities; and 4) saving foreign exchange due to a reduction in the trade balance deficit [15]. Because its properties are not confined to food goods, but also capable of serving as a diabetic functional food, the resulting dadih product has the potential to be marketed for export.

IV. THE PRODUCTION OF DADIH

To produce GABA-enriched dadih as a functional food for diabetics, a relatively long initial stage is required. The resulting product must really prove its ability to improve the quality of pancreatic beta cells as insulin secretors. For this reason, the resulting product must be tested both in vitro and in vivo. After obtaining the optimum conditions for the product's ability as functional food for diabetics, the product can be developed on a production scale.

The development of dadih took place in 2 stages of research. Stage 1 was the isolation of LAB from traditional dadih using Gram staining, catalase test, motility test and endospore staining on bacterial colonies. The LAB isolates were then analyzed for their ability to produce GABA qualitatively (thin layer chromatography) and quantitatively (RPHPLC, Reverse-Phase High Performance Liquid Chromatography) [16]. LAB isolates producing the highest GABA were characterized molecularly by 16S rRNA and analyzed for their ability as probiotics through tolerance testing for bile acids and salts, hydrophobicity tests and antibacterial tests.

The LAB isolate with the highest GABA producer was applied to ferment dadih from cow's milk and buffalo's milk (stage 2). The fermentation conditions (pH, temperature and number of LAB) were tested to determine the optimum state of

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GABA produced by LAB during fermentation. The GABA-enriched dadih were analyzed in vivo (oral glucose tolerance test, insulin resistance test, intestinal villi and pancreatic histology analysis) and in vitro (alpha amylase and alpha glucosidase inhibition tests). Dadih with the highest antidiabetic ability was tested organoleptically (taste, smell, color and texture) to determine public acceptance of the resulting product. The next step is to commercialize dadih by developing it on an industrial scale with a range of tastes to enhance the flavor and make it more marketable like other fermented milk products.

V. PROSPECTS OF GABA-ENRICHED DADIH TO BE DEVELOPED IN INDONESIA

In Indonesia, GABA-enriched dadih as a diabetic functional food has a good chance of being developed. Because of the following reasons:

1) Dadih is a functional food made from fermented milk that is well-known and consumed by the general people, allowing for national production. This means that dadih will be commercially produced not just for people in West Sumatra, but for people all around Indonesia.
2) The production of dadih with beneficial properties (in this example, diabetes) will raise public interest in consuming it, particularly in diabetics. Diabetics prefer to be treated with functional foods rather than medicines like pills and fluids injected into their bodies. Furthermore, the production of dadih in a variety of tastes will undoubtedly increase the taste. As a result, the public will be more interested in dadih.
3) The availability of equipment, major raw materials, and other components in Indonesia allows for large-scale production of GABA-enriched dadih. It will be feasible to develop a fermenter for increasing the dadih scale from a laboratory scale to a production scale by examining the optimum conditions of fermentation.
4) The prospect of dadih in supporting the government's import substitution policy will certainly facilitate the process of funding dadih production from the government.
5) Since products that are beneficial to health and use traditional food ingredients that are well-known and consumed by the general population have not been widely produced, this GABA-enriched dadih has a bright future in terms of novelty.
6) Fermented items like yakult, yogurt and kefir are still being exported by the country because they are in high demand. Dadih can grow quickly and be in high demand as a processed product with a procedure that is similar to other fermented milk processing, especially if its flavor and capabilities as a functional meal for diabetics are continually improved.

VI. CONCLUSIONS

Dadih can be developed as a functional food for diabetics by using high GABA producing LAB as a fermentation starter. The development of dadih as a functional food for diabetics has good prospects in terms of the availability of raw materials, high added value, easy process and can help government policies, namely import substitution, or even export promotion. On a laboratory scale, the optimum conditions for fermentation must be obtained before doubling the dadih fermentation scale to the production quantity. Before it to be considered a functional diet for diabetics, GABA-enriched dadih must undergo extensive testing (in this study it was tested on diabetic mice first).

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