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Effect of Iles-Iles (Amorphophallus oncophyllus) Synbiotic Effervescent Tablet to Decrease in Blood Sugar Levels in Hyperglycemic White Rat (Rattus norvegicus)

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Effect of Iles-Iles (*Amorphophallus oncophyllus*) Synbiotic Effervescent Tablet to Decrease in Blood Sugar Levels in Hyperglycemic White Rat (*Rattus norvegicus*)

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Abstract

This study aims to determine the effect of giving Iles-iles synbiotic effervescent tablets to decrease blood sugar levels of hyperglycemic white rats and find out the lowest dose of effervescent tablets in decreasing blood sugar levels. This study used the Completely Randomized Design (CRD) with single factor (dose of Iles-iles synbiotic effervescent tablet) with 4 levels (dose 0.045 gram/day (½ normal dose), dose 0.09 gram/day (normal dose), dose 0.18 gram/day (2X normal dose) and Control (without treatment dose). The analysis carried out was blood sugar levels and rat body weight. The administration of Iles-iles synbiotic effervescent tablets can reduce blood sugar levels in white mice but does not affect changes in the weight of white mice. The biggest decrease in blood sugar levels in white rats for synbiotic month was obtained from the administration of a dose of 0.18 grams/day (normal 2X dose) which was as much as 49.16% The administration of effervescent tablets in the fourth week with a normal dose of 0.09 grams/200 grams of weight has been able to reduce blood sugar levels in white rats to normal levels.

Keywords

iles-iles, synbiotic, hyperglycemic

1 Introduction

Diabetes mellitus is a chronic disease caused by the inability of the body to produce insulin or the ineffective use of insulin production, which is characterized by high levels of sugar in the blood. Diabetes mellitus Type 2 (DM2) is the world's fastest-growing metabolic disorder that mostly concerns with obese adult patients. An increase in blood glucose which exceeds the normal level often follows within Diabetes Mellitus patients [1].

The factors that affect blood glucose levels are various such as the lack of exercise, stress, obesity, poor treatment of medication, and shortage of fiber. The increase in the amount of food consumed one of them tends to consume fast food which is usually high in carbohydrates and low in fiber. Fiber can reduce the efficiency of carbohydrate absorption which will cause a decrease in insulin response. The work of the pancreas will be easier and it will improve the function of the pancreas in producing insulin. Dietary fiber that can provide this function is soluble fiber, such as pectin, guar gum, and glucomannan that can be abundantly found in vegetables, fruits, and tubers [2].

Many oral antidiabetic drugs are available for the treatment and control of symptoms of Type 2 DM, such as sulfonylurea agents, biguanides (metformin), thiazolidinedione (TZD), α-glucosidase inhibitors, and glucagon-like peptide-1 (GLP-1) inhibitors. However, these drugs can cause serious side effects, including hypoglycemia, liver toxicity, weight gain, physconia (enlarged stomach), and lactic acidosis [3]. It is necessary to develop another alternative medicine to prevent diabetes. One of them is through synbiotic products. Synbiotics are combinations between probiotic and prebiotic. The use of probiotics on a regular basis before a meal may increase the population of microbes which may use glucose only as a sole source of energy. The microbes as probiotics may oxidize glucose through anaerobic glycolysis into lactic acid which can be absorbed in the blood [1]. Probiotics can affect gut bacteria to produce insulin-tropic polypeptides and GLP-1 (glucagon-like peptide-l), thus increasing glucose uptake by muscle and stimulating the liver absorption of blood glucose [4]. Many clinical studies have proven the effectiveness of probiotics for the treatment of diseases such as obesity, insulin resistance syndrome, type 2 diabetes, and non-alcoholic fatty liver disease [5]. The gut microbiota is related to type 2 diabetes mellitus with numerous

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molecular mechanisms. Supplementation of *L. casei* affected SIRT1 and fetuin-A level in a way that improved glycemic response in subjects with type 2 diabetes mellitus [6]. *L. casei* Shirota has been reported to reduce blood glucose levels by reducing lipopolysaccharide-binding protein [7]. Hyperglycemia was favorably suppressed by *L. casei* Zhang treatment. Moreover, hyperglycemia is related to type 1 immune response, high plasma bile acids and urine chloride ion loss. This chloride ion loss was significantly prevented by *L. casei* by upregulating of chloride ion-dependent genes (ClC1-7, GlyRa1, SLC26A3, SLC26A6, GABAAa1, Bestrophin-3 and CFTR [8].

Prebiotics as a nonviable food component that confers a health benefit on the host associated with modulation of the microbiota [9]. One of prebiotic is glucomannan. One source of glucomannan is from Iles-iles. The Iles-iles tuber (*Amorphophallus oncophylus*) has a chemical composition in the form of 79.7% water content, 20.3% dry matter, 2.0% starch, Glucomannan 55%, other polyoses 14%, crude fiber 8% and free sugar 0% [10]. The Iles-iles tuber has a high potential for prebiotic sources because it contains undigested carbohydrates, namely glucomannan, starch, and crude fiber. The glucomannan supplementation increased the concentration of beneficial probiotics in the gut, including specific strains like bifidobacteria and *Lactobacilli* [11]. Glucomannan is able to decrease the absorption of cholesterol in the gut by sponging up water in the digestive tract, which reduces the absorption cholesterol by the body [12].

The glucomannan flour will be developed as an encapsulating agent for probiotics such as *L. casei*, thus it will form synbiotic microcapsules. Microcapsules symbiotic can be developed into effervescent tablets. Synbiotic effervescent tablets role as carriers of glucomannan compounds and probiotics. Glucomannan also provides a prebiotic source for probiotic bacteria in the large intestine.

One of the probiotic bacteria is *L. casei* which is a lactic acid bacterium, this bacterium is able to survive the influence of stomach acid and in bile salt so that it can survive to the small intestine. Almost LABs obtain energy from sugar metabolism so that their growth habitat is limited to an environment that provides enough sugar or can be called a nutrient-rich environment [13].

To get the function value of glucomannan and *L. casei*, a carrier product is needed to reach the body. One of these carrier products is the effervescent tablets. The effervescent tablet innovations need to be developed in order to add more selling points and functions. The advantage of this effervescent tablet is that the way it is presented is more attractive when compared to conventional tablets, it can be given to people who have difficulty in swallowing medicine tablets or capsules, easy to carry and has a long shelf life than other drug preparations.

To find out the effectiveness of this synbiotic effervescent tablet, it is necessary to do an in vivo trial of living things, one of which is by treating animals to the effect of giving effervescent tablets in reducing blood sugar levels. Rats and mice are more often used, especially Wistar strain rats because of their easy maintenance, large numbers, and relatively inexpensive than rabbits, cats or monkeys. The other main reason is when a medical experiment using rats was carried out in a laboratory, it turns out that rats have genes that are biologically similar in characteristics to genes possessed by humans that many symptoms of disease in humans could be "created" in rats thus researcher can find out the cures for the disease.

The problem, in this case, is that there are no trials conducted on synbiotic effervescent tablets that contain Iles-iles and *L. casei* to decrease blood sugar levels. Therefore, through this research, it is necessary to know the lowest dosage that can reduce blood sugar levels which can later be applied to humans. Therefore, with the increasing number of diabetics, through this research, it is expected to find new breakthroughs to overcome diabetes.

The research purposes were: (1) To determine the effect of administration of effervescent synbiotic tablets from Iles-iles on the decrease in blood sugar of hyperglycemic white rats, (2) To obtain the right dose in the treatment of diabetes mellitus using effervescent synbiotic tablets from Iles-iles.

2 Methods

2.1 Material

The material used in this study was white rat, synbiotic effervescent tablets made from the mixture of synbiotic microcapsules (made from biomass *Lactobacillus casei* FNCC 0090 cell, glucomannan Iles-iles and Arabic gum), and effervescent tablet ingredients such as citric acid, tartaric acid, sodium bicarbonate, PEG 6000, and stevia obtained from Biotechnology Laboratories, Faculty of Pharmacy Universitas Gadjah Mada. The formula and method in making the synbiotic effervescent tablets refer to Ngatirah's method which was published in patent news [14]. Iles-iles tubers were obtained from the Kulonprogo area (Sentolo Market),

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protective material (Arabic gum) and Comfeed AD-2 obtained from Tekun Jaya store. The rats obtained were from Food and Nutrition Laboratories UGM and injected with alloxan monohydrate with dosage 20 mg/200 g rat weight to make the diabetes rat (blood sugar level over than 135 mg/dL).

2.2 Method

24 white rats weighing ± 200 grams were randomly divided into 4 groups (3 treatments and 1 as a control). The three treatments are the number of effervescent tablet doses (half of normal dosage 0,0045g/200g of rat weight (A), normal dosage 0,09g/200g of rat weight (B) and twice of normal dosage 0,18g/200g of rat weight (C). The calculation of the normal dose of effervescent tablets to rats is the dosage of effervescent tablets for humans (5 gram) x 0,018 (conversion factor) = 0,09g/200g weight of rat.

The rats were kept in individual cages with a temperature of ± 25 ° C. Before being treated, the rats were first habituated to a standard diet for 7 days. At the end of the adaptation period, the rats fasted for 24 hours but were still given a drink on an ad libitum basis. After fasting, they were weighed, and their blood glucose levels were measured.

Furthermore, the three groups of rats treated with intraperitoneal injections of alloxan monohydrate at a dose of 100 mg/kg body weight or means ± 20 mg / 200 grams of body weight to make the diabetes rat. The normal level of rat blood sugar is 50-135 mg / dL. The blood sugar level of the hyperglycemic rat must exceed 135 mg / dL. The administration of synbiotic effervescent tablets is given daily (once a day) and observed for 1 month. The administration of symbiotic effervescent tablets dissolved in water and taken to rats. During the treatment, the rats were fed (comfeed AD-2) as much as 10% of body weight and were given ± 200 ml drink per group. The testing was done once a week in order to find out the blood sugar and body weight.

3 Result and Discussion

3.1 The rat blood sugar levels

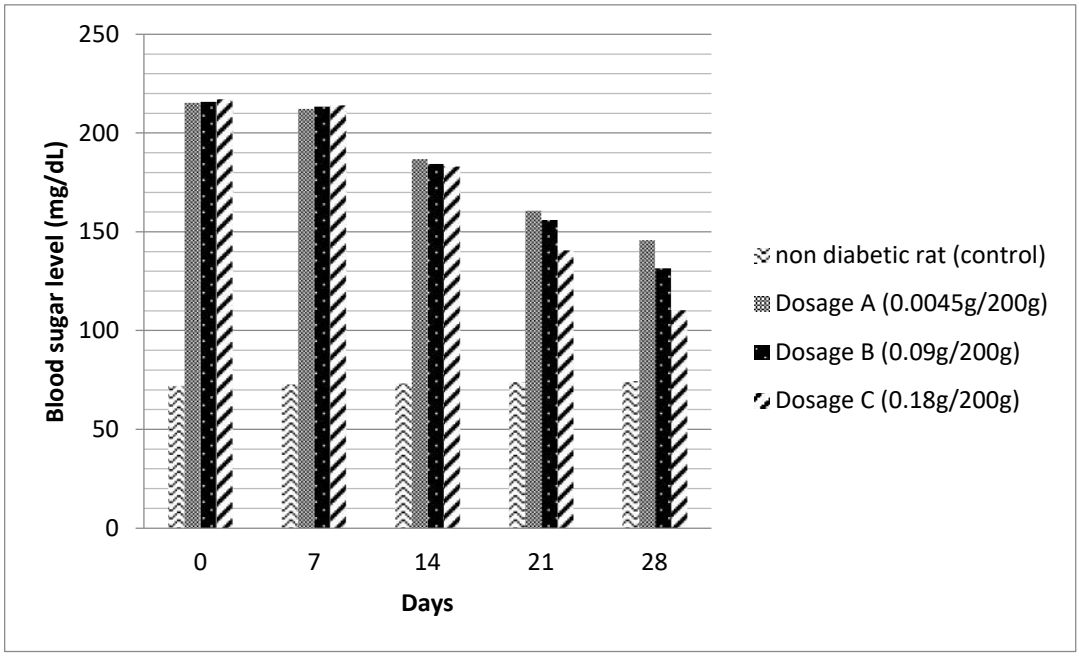

Fig. 1 The Rat blood sugar levels

Dosage A, Dosage B, and Dosage C decreased blood sugar levels after the treatment of effervescent tablets given daily for 4 weeks **Fig. 1** According to the prescribed dose, a decrease in blood sugar levels showed a different percentage decrease due to the treatment of the number of different doses of concentration. The most significant decrease was in the C dose, which was equal to 49.16%, while the B dose and dose A were smaller at 39.08% and 32.28%. The control treatment group did not experience a decrease because it contained the nondiabetic rats (not injected with alloxan monohydrate) and did not administer the

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effervescent tablets. According to the data above from the first week to the fourth week, the blood sugar levels of control rats experienced an increase to 3.15%.

Based on the chart above, the decrease in blood sugar levels is influenced by the administration of effervescent tablets which contain glucomannan, which is a soluble fiber. This is in accordance with previous related research, which states that glucomannan modulates the absorption rate of nutrients in the small intestine. As a result, glucomannan increases insulin sensitivity. Other results suggest that improvements in hyperlipoproteinemia and hyperglycemia caused by dietary fiber supplements can help inhibit or prevent the atheromatous formation in cholesterol in rats fed diabetic [5]. Meanwhile, the glycemic level decreases gradually after breakfast with glucomannan biscuits. A decrease in insulin secretion and a reduction in insulin requirements can maintain longer functional reserves of cells [1].

Probiotic administration (containing several strains of *Bifidobacterium* and *Lactobacillus*) in rats induced a high fructose diet (HFD) improved the composition of intestinal microbiota and increased SCFA metabolites (butyrate) produced. This increase in the amount of butyrate is correlated with an increase in the amount of the hormone GLP-1. Butyrate increases the secretion of GLP-1 secretion from L-intestinal cells and increases insulin sensitivity. Giving probiotics is known to reduce inflammation which is correlated with obesity and diabetes. Reduced inflammation can increase insulin sensitivity [9].

3.2 Rat Weight

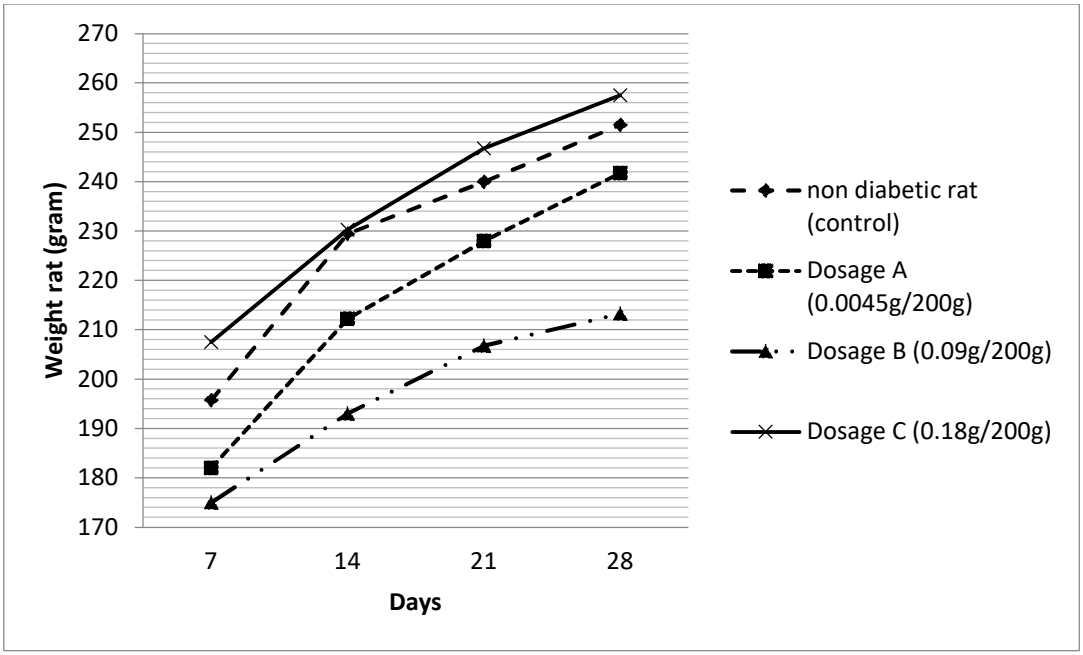

Fig. 2 Changes in body weight of rats for 28 days after alloxan induction and given effervescent tablets

Based on the results from **Fig. 2**, there is no relation between body weight and blood sugar levels. This is due to the administration of effervescent synbiotic tablets from these Iles-iles containing glucomannan which has high enough fiber content and no cholesterol besides glucomannan is one of the oligosaccharides that cannot be digested in the digestive tract and function as a prebiotic. In this effervescent synbiotic tablet, there are also probiotics in the form of lactic acid bacteria that can digest glucomannan thus it is beneficial for the growth of microorganisms in the intestine, especially *Bifidobacteria*, that decreases the intensity of pathogenic enteric bacteria, regulates immunoreactions, and increases mucosal integrity in the intestine. Thus, the white rat's body weight can be maintained and even increased.

In addition, irrelevancy between body weight and blood sugar levels can also be caused by feeding a high enough protein content, so that the nutritional needs of the white mouse are met with the help of effervescent synbiotic tablets that can improve the digestive tract.

4 Conclusions

Giving effervescent synbiotic tablets that contain glucomannan Iles-iles and *L. casei* can reduce the blood sugar levels of white rats but do not affect changes in the weight of white rats. The biggest decrease in blood glucose level in white mice for 1 month was obtained from a dose of 0.18 grams/head/day (twice the normal dose), which was 49.16%. Giving effervescent tablets in the fourth week with a normal dose of 0.09 gram/200-gram weight has been able to reduce the blood sugar levels of white rats to normal levels.

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