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THE IMPACT OF KONJAC GLUCOMANNAN IN REDUCING BLOOD GLUCOSE LEVELS

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Abstract

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterised by dysregulation of many metabolic pathways. In recent years, there has been a significant emphasis on using dietary interventions to prevent the onset of type 2 diabetes. Konjac glucomannan (KGM) and its derivatives have gained significant popularity among the general population due to its natural and healthful characteristics. The objective of this research was to investigate the potential anti-diabetic effects of KGM in a diabetic animal model, namely Rattus norvegitus. The experimental design has five groups, each consisting of six individuals of the species Rattus norvegitus. Group 1 included Rattus norvegitus that were provided with a conventional diet, whereas group 2 comprised Rattus norvegitus that received an intragastric administration of 0.013 mg of Glibenklamid. Group 3 included of Rattus norvegicus with diabetes who were administered a dosage of 25 mg of KGM. Group 4 included of Rattus norvegitus with diabetes that were administered a dosage of 50 mg of KGM, while Group 5 comprised of Rattus norvegitus with diabetes that were also treated with a dosage of 100 mg of KGM. The findings of the study revealed that diabetic Rattus norvegitus treated with KGM saw a significant reduction in glucose levels. The use of the KGM therapy for the identification and regulation of changes in oxidative stress and inflammation has the potential to impede the advancement of diabetes. The existing research suggests that including dietary konjac glucomannan (KGM) may provide enhanced therapeutic advantages in managing type 2 diabetes mellitus (T2DM).

Keywords: Konjac Glucomannan, Type-2 Diabetes Mellitus, Rattus Norvegitus, Regulation of Oxidative Stress And Inflammation.

INTRODUCTION

Diabetes mellitus is a kind of metabolic illness that may affect people of any race, gender, or age anywhere in the globe. Life-threatening metabolic disease, type 2 diabetes mellitus (T2DM), caused by insulin resistance, insufficient insulin uptake by pancreatic -cells, and inadequate insulin production (Wu et al., 2014). Both the incidence and prevalence rates have risen dramatically during the last several decades. Research estimates that in 2017, there were over 400 million individuals with diabetes globally, and this number will climb dramatically to 629 million in 2045, placing a significant burden on public health professionals (Flannick et al., 2016; Kim et al., 2019). Reducing oxidative stress and inflammation are key to the management of type 2 diabetes. Traditional herbal weight increase and insulin resistance indicate diabetes Mellitus. In the diabetes Mellitus rat model, Traditional herbal inhibits TNF-a and IL-6 and improves blood lipid profiles, hepatoprotective the liver (Gunawan et al., 2023).

Patients may have side effects such as endocrine abnormalities if they have a long-term therapeutic remedy with synthetic pharmaceuticals such as metformin, despite the fact that the therapy for type 2 diabetes with existing drugs such as metformin exhibits a considerable result in glucose-lowering for persons with type 2 diabetes in a short amount of time (Jayachandran et al., 2019). Aside from this, synthetic anti-

diabetic medications may cause a variety of unpleasant side effects, such as headaches, dry mouth, rashes, dizziness, and coughing. Anxiety is also one of these negative effects. In light of this, it is of the utmost need to discover and develop more effective antihyperglycemic treatments. In today's world, dietary aspects are taken into consideration for essential positive measures on the treatment and prevention of a variety of disorders.

It has been shown that many dietary polysaccharides, such as those found in oats, mushrooms, tea, berries, and pumpkin, among other foods, may control blood glucose levels (Ganesan & Xu, 2019). Additionally, it has been shown that the viscous water-soluble fibers raise the viscosity of food that has been digested in the stomach while simultaneously lowering blood glucose levels (Chen et al., 2016). In relation to this, konjac glucomannan (KGM), which is a dietary polysaccharide that is water-soluble and extracted from the tuber of Amorphophallus konjac, may have the ability to lower blood glucose levels (Wang et al., 2018). The molecular weight is estimated to fall somewhere in the range of 500–2000 kDa, in accordance with the different processes and sources of extraction (Zhu, 2018). According to (Devaraj et al., 2019), the primary chain of KGM is composed of -1–4 connected D-glucosyl and D-mannosyl residues in a ratio of 1:1.6, and it has an approximately 8% degree of branching at the C-3 joint. Additionally, one acetyl substitution is connected to the C-6 position in the major chains for every 19 sugar residues (Wang et al., 2018). KGM has been shown to have a variety of positive effects on human health, including anticancer, antidiabetic, anti-inflammatory, and anti-obesity properties (Aoe et al., 2015; Zhang et al., 2019), which have been recorded in a large number of research. In addition, researchers (Vázquez-Velasco et al., 2015) found that glucomannan reduced hyperglycemia and increased adiponectin levels in the adipose tissue of fa/fa rats. These findings were published in the journal Diabetes. In addition, study conducted by (Luo et al., 2023) suggested that a low dose of KGM supplement (3.6 g/day) would give therapeutic advantages by altering the lipid profile in circulation by raising neutral sterol and bile acid in feces. These findings were based on the hypothesis that this would be the case. In diabetic patients who also had hyperlipidemia, KGM was able to reduce the elevated levels of glucose in their blood (Luo et al., 2023) (Bocanegra et al., 2021).

Even if there are research that claim the therapeutic effects of KGM on T2DM, investigations that concentrate on the molecular mechanism of glucose metabolism that may be attributed to KGM have not yet been demonstrated. In light of this, we came up with the hypothesis that the KGM may alter T2DM via influencing metabolic pathways. The selection of KGM as an antidiabetic option for further validation by undertaking molecular investigations is based on the reasoning that it regulates adipose tissue, is effective against hyperglycemia, and lowers blood cholesterol levels. In order to provide an explanation for our hypothesis, we developed an experimental model of diabetes in rats by means of high-fat diet and streptozotocin. In addition, the diabetic rats were treated with KGM so that the target proteins and genes in the insulin signaling pathway could be identified. This was done in order to get a better understanding of the molecular mechanism that is responsible for the antidiabetic effectiveness of KGM through its control on metabolism glucose-insulin sensitivity. In the treatment of type 2 diabetes, rosiglitazone, often known as RSG, was considered the gold standard. We believe that to the best of our knowledge, we are the first people to report the antidiabetic benefits of KGM based on its control of metabolic pathways.

This research is also relevant in the treatment of type 2 diabetes that is mediated by food owing to the uniqueness of this medication having little or no adverse effects.

MATERIALS AND METHODS

Animal Conditions and Acclimatization

For the purpose of this investigation, a total of thirty male Wistar albino rats with bodyweights ranging from 180 to 220 g and normal glycemic circumstances were employed. The breeding environment was carried out in polypropylene cages at the animal care facility of AKAFARMA SUNAN GIRI in Ponorogo, which is located in East Java Province, Indonesia. The environment was pathogen-free. The approval to conduct the research according to ethical standards was granted by STRADA in Kediri, East Java Province, Indonesia (Animal Study Ethical Approval Number: 3849/KEPK/VI/2023. This allowed the research to be carried out in accordance with ethical standards. It was okay for the rats to drink and eat whenever they wanted. The National Institutes of Health gave its approval to both the research's protocol and its rules for the use of animals, and both were adhered to throughout the whole study. The rats were allowed to adjust to their environment for a period of two weeks prior to receiving therapy.

Type 2 Diabetes Mellitus Induction

It was shown that a combination of a high-fat diet and streptozotocin was the most effective strategy for inducing type 2 diabetes mellitus (T2DM) in rats (Kahksha et al., 2023; Magalhães et al., 2019). After the adaption period had passed, the remaining rats were fed a high-fat diet (with 60% of their total calories coming from fat, according to the AKAFARMA Sunan Giri in Ponorogo, Indonesia) for a period of 15 days. At the same time, a low dose of STZ (40 mg/kg b.w.) was administered through a single intraperitoneal injection. The control rats were not subjected to this treatment. Five days following the injection, the estimation of the glucose level in the fasting blood was performed. For the subsequent research, diabetes models were constructed using rats with blood glucose levels that were at least 300 mg/dl higher than the normal range. Throughout the whole of the trial, those diabetic rats were fed a diet heavy in fat.

Groups for the Experiment

As can be seen in the table below, the male Wistar rats were arbitrarily split up into five groups, each with a total of six rats. The KGM was then administered to the rats via intragastric tube feeding after it had been dissolved in water. After the diagnosis of type 2 diabetes was made, the patient started therapy with KGM and RSG, which lasted for a total of 28 days. Both our earlier work (Zhao, Jayachandran, & Xu, 2020) and a study that was quite similar to ours (Srinivasan, Viswanad, Asrat, Kaul, & Ramarao, 2005) were used as the basis for the design of the current investigation. The effective dosage of KGM was determined to be 80 mg/kg body weight.

Group I - control rats fed standard pellet diet alone

Group II – T2DM + Glibenklamid (0.013 mg/kg b.w.)

Group III – T2DM + KGM (25 mg/kg b.w.)

Group IV – T2DM + KGM (50 mg/kg b.w.)

Group V – T2DM + KGM (100 mg/kg b.w.)

Animal dissection and storage of samples

At the conclusion of the trial, the animals were allowed to go without food for a full 24 hours. The rats were rendered unconscious by administering ketamine hydrochloride (24 mg/kg b.w.) intramuscularly, and they were afterwards put to death by having their heads severed at the cervical level. For the purpose of determining serum glucose levels and performing other analyses, blood samples were taken and stored in heparinized tubes. In order to test the carbohydrate metabolizing enzymes, the liver tissue was immediately removed and homogenized at a ratio of 1:10 in a buffer containing 0.1 M Tris–HCl with a pH of 7.4. After that, the homogenate was centrifuged at a speed of 10,000 g, and the supernatant that was produced was utilized for the tests.

Statistical Analysis

The full data sets were presented as the mean value together with the standard deviation (SD). The analysis of the data was carried out using SPSS (Version 15), using oneway analysis of variance (ANOVA) and Duncan's multiple range test (DMRT) for individual comparisons. A value of p 0.05 was used to indicate statistical significance.

RESULT

Effects of KGM on oral glucose tolerance (OGTT)

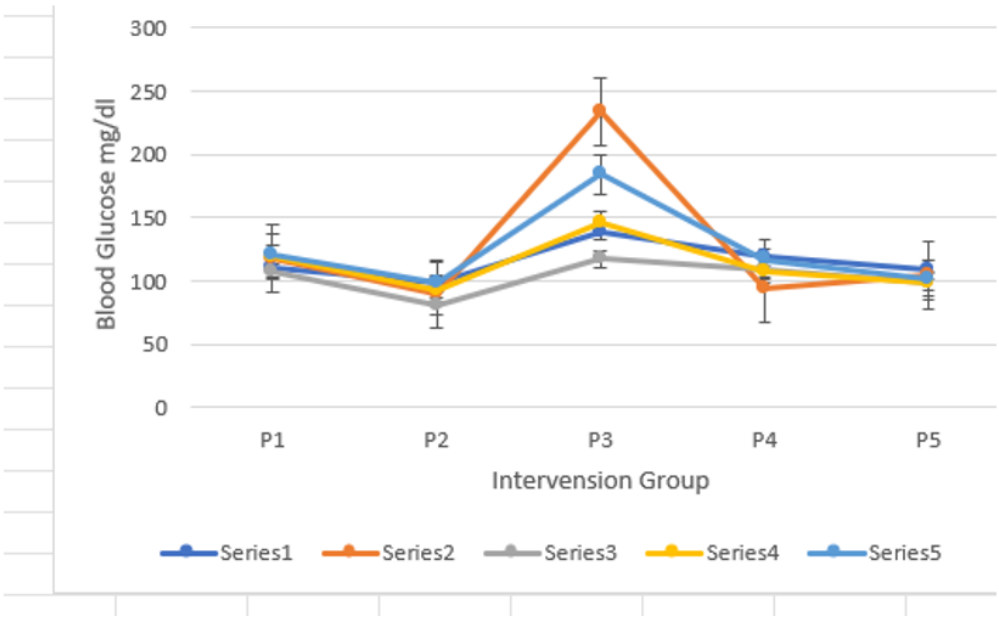

Figure 1: Effects of KGM on oral glucose tolerance. Series 1: Controle negatif, Series 2: Controle positif, Series 3: KGM 25 mg, Series 4: KGM 50 mg, Series 5: KGM 100 mg

The oral glucose tolerance test (OGTT) is used to evaluate how the body reacts to blood glucose. Because of this, it becomes an important consideration in determining the severity of diabetes mellitus. On display in Figure 1 are the concentrations of glucose found in the serum of rats used as both controls and subjects in an experiment. Rats with diabetes exhibit an elevation beginning at 30 minutes, which continued to increase and did not appreciably reduce even after 120 minutes.

However, when the rats were given KGM as a supplement, there was a significant drop in activity after 120 minutes, after a strong surge in activity at the 60-minute mark. Rats given RSG had the same successful outcomes as the control group.

Effect of KGM on Adipocytokines

Adiponectin and leptin were measured in the blood as well as in the adipose tissues in order to evaluate the involvement of adipocytokines in the control of IR and inflammation. These measurements were made in both of these locations. As can be seen in Figures 1B and 1C, Rattus norvegitus who were given the HFHF diet had greater levels of leptin in both their blood and their adipose tissue in comparison to rats that were given the ND diet. On the other hand, the blood and adipose levels of adiponectin were lower in rats that were given the HFHF diet compared to rats that were fed the ND diet (Fig. 1D and E). It is interesting to note that the treatment of 6-gingerol in HFHF Rattus norvegitus dose-dependently lowered the levels of leptin in the blood and adipose tissue when compared to similar levels in HFHF rats that were treated with a vehicle. However, despite the fact that 6-gingerol was capable of increasing blood and adipose adiponectin levels, there was not a statistically significant difference between the 6-gingerol-treated HFHF rats and the vehicle-treated rats.

DISCUSSION

Fruits, vegetables, and dietary fibers are examples of functional foods. These foods help prevent type 2 diabetes by lowering insulin resistance and improving blood glucose homeostasis and insulin levels (Jayachandran et al., 2018). One of these potential dietary fibers that has been shown to provide a variety of health benefits is called konjac glucomannan (KGM). As a result, the purpose of this research was to determine whether or not KGM may effectively treat type 2 diabetes by modulating the insulin signaling system. The amount of KGM that would be administered was predetermined by the results of our earlier studies. In our earlier dose-dependent research on KGM (25, 50, and 100), we found that One of these potential dietary fibers that has been shown to provide a variety of health benefits is called konjac glucomannan (KGM). As a result, the purpose of this research was to determine whether or not KGM may effectively treat type 2 diabetes by modulating the insulin signaling system. The amount of KGM that would be administered was predetermined by the results of our earlier studies. In a prior dose-dependent research on KGM (25, 50, and 100), we concluded that 80 mg/k body weight would be the most effective dosage, after considering a number of fundamental characteristics. Both the RSG dosage and the whole time of the trial were predetermined based on prior research.

The oral glucose tolerance test, often known as the OGTT, is a first and preliminary test that is used to screen for type 2 diabetes. According to the findings of our research, diabetic rats have a fast increase in the levels of glucose in their blood at 30 minutes, reach a peak at 60 minutes, and then stay in the 90 and 120 minute range. On the other hand, the rats that were injected with KGM exhibited a gradual rise in glucose levels after 60 minutes, which then decreased after 90 and 120 minutes. In addition to this, when contrasted with the diabetic rats, the fluctuating range of blood glucose concentration seen in the rats treated with KGM implies that KGM helps to normalize insulin production, which in turn encourages glucose consumption. Diabetes mellitus, if not treated, can cause metabolic disorders, including heart problems, therefore,

apart from herbal therapy, heart health can be maintained by consuming vitamin D (Moin, Qasim, & Ashraf, 2023).

CONCLUSIONS

Our hypothesis has successfully established the T2DM rat model using the HFD/STZ method, and the Rattus norvegitus with diabetes have been adequately treated with KGM. Based on the results obtained from our study, it is suggested that KGM might potentially serve as a viable dietary option for the management of type 2 diabetes. In summary, the administration of KGM treatment resulted in enhanced cellular glucose tolerance, regulation of glycolytic and gluconeogenic enzymes, reduction in hepatic glycogen storage, and restoration of liver enzyme levels. Significantly, the administration of KGM has been seen to enhance insulin sensitivity via the regulation of insulin receptors, resulting in the upregulation of genes and proteins associated with the insulin signalling pathway. After careful analysis of the aforementioned findings, it may be inferred that KGM has the potential to mitigate diabetes through modulating oxidative stress and inflammation. Further investigation on the impact of KGM's antidiabetic properties on interconnected pathways might delve into mechanistic principles with more depth.

Recommendatıon

This Research is recommended as a complementer therapy that should be applied to skizophrenia with high level glucose level.

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Conflıcts Of Interest

The authors declare they have no conflicts of interest

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