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Effect of *Rosa damascena* mill. extract on blood glucose levels in diabetes model rats (Rattus norvegicus)

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Abstract

Diabetes mellitus (DM) is a chronic metabolic disorder caused by a lack or resistance to insulin and is characterized by hyperglycemia in the postprandial and fasting states. Postprandial hyperglycemia can lead to non-enzymatic glycosylation of various proteins, leading to the development of chronic complications. Control of postprandial plasma glucose levels is very important in the initial treatment of DM to reduce chronic vascular complications. This study aims to determine the effect of Rosa damascena extract on blood glucose levels. RDM is obtained from Batu city. A total of 3 kg of rose petals was dried, mashed, soaked with 96% ethanol, filtered, then extracted from the filtration using a rotary evaporator. The study used male wistar rats (Rattus norvegicus) 8-10 weeks old and weighing 150-200 grams. Rats were randomly divided into 6 groups of negative control group (KN), positive control group (KP), metformin group (KM), treatment group 1 (P1) RDM 250 mg / kg body weight, treatment group 2 (P2) RDM 500 mg / kg body weight, treatment group 3 (P3) RDM 1000 mg / kg body weight. Examination of blood glucose using peripheral blood before euthanasia. The Kruskal Wallis test results showed a Sig (P-Value) of 0.030 (p <0.05), which means that there were significant differences in all treatment groups. The results of the Mann Whitney-U test showed that the KN group was significantly different from all groups (Sig P-Value <0, 05) while the KP, KM, P1, P2 and P3 groups had no significant differences with other groups (Sig P-Value > 0.05). The lowest blood glucose level was in the P1 group, the treatment group given STZ and Rosa damascena Mill extract at 250 mg/kg body wt. Meanwhile, the highest blood glucose level was in the KP group, the positive control group that was only given STZ. In conclusion, Rosa damascena Mill extract may have an antidiabetic effect by reducing postprandial blood sugar levels.

Keywords: Diabetes Mellitus, Rosa Damascena Mill, Blood Glucose

Background

Diabetes mellitus (DM) is a chronic metabolic disorder caused by a lack or resistance to insulin and is characterized by hyperglycemia in the postprandial and fasting states (1). Postprandial hyperglycemia can lead to non-enzymatic glycosylation of various proteins, leading to the development of chronic complications. Control of postprandial plasma glucose levels is very important in the initial treatment of DM to reduce chronic vascular complications (2). WHO data shows that the incidence rate of non-communicable diseases in 2004 which reached 48.30% was slightly higher than the incidence rate of infectious diseases, which was 47.50%. Even non-communicable diseases are the number one cause of death in the world (63.50%) (3). In Indonesia, the prevalence of DM based on a doctor's diagnosis in the population aged ≥ 15 years, the results of Riskesdas 2018 increased to 2% when compared to 2013. The lowest prevalence of DM based on doctor's diagnosis and age ≥ 15 years was found in NTT Province, which was 0.9% , while the highest prevalence of DM in DKI Jakarta Province was 3.4% (4).

Pharmacological management of DM is to administer blood sugar-lowering drugs. The pharmacological approach recommended by the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE) is with metformin, but the use of metformin often causes adverse drug reactions (ROM) in the form of side effects of gastrointestinal disorders such as diarrhea, nausea, vomiting, and flatulence (5).

Rosa damascene Mill. is one of the most famous ornamental plants that are cultivated around the world, especially for the fragrance industry. Rosa Damascene Mill has a lot of useful phytochemicals, such as polyphenols, flavonoids, glycosides, terpenes, and anthocyanin as well as various vitamins. Rosa damascene Mill has been researched for its medicinal benefits. Ibnu Sina (980-1037 AD) revealed that the medical benefits obtained from Rosa damascene Mill. include digestion, heart, helps in repairing skin and mucosal tissue, and has anti-inflammatory, antioxidant and antidiabetic effects (6).

In other research, Rosa damascene Mill. Significantly reduced the dose of postprandial glucose levels dependently in normal and diabetic rats with a single oral intake dose of 100-1000 mg / kg of methanol extract. The research shows that the extract of Rosa damascene Mill. demonstrated a noncompetitive intensive α-glucosidase inhibitory effect comparable to acarbose (7). With the increasing incidence of DM in Indonesia and the pharmacological effects of DM drugs, this study aims to determine the effect of Rosa damascene Mill extract on blood glucose levels.

Methods

Rosa Damascena Mill flowers obtained from Gunungsari village, Bumi Aji District, Batu City. A total of 3 kg of dried rose petals. Then mashed until it becomes a powder. Rosa damascena Mill powder. then soaked in 96% ethanol for 3 days. After that it was filtered using Whatmann paper no. 41. The results of the filtration were extracted with a rotary evaporator at 40 C and dried in an oven at 40 C. Rosa damascena Mill extract. stored at -20 C. This research is an experimental study with a research design using a posttest control group design. The *Posttest Only Control Design* is a design with the experimental group and the control group not chosen randomly. In this design

both the experimental group and the control group are compared. The experimental group received treatment while the control group received no treatment (8). This study used male wistar rats (Rattus norvegicus) aged 8-10 weeks and weighing 150-200 grams. The mice were acclimatized for 7 days with room temperature (22 ± 30C) and lighting for 12 hours. Furthermore, the rats were randomly divided into 6 groups, namely the negative control group (KN) which was only given standard feed without intervention, the positive control (KP) was given STZ without Rosa damascena Mill, the metformin group (KM) was given STZ and Metformin 150 mg/kg body wt, treatment group 1 (P1) given STZ and Rosa damascena Mill extract. 250 mg/kg body wt, treatment group 2 (P2) given STZ and Rosa damascena Mill extract. 500 mg/kg body wt, treatment group 3 (P3) were given STZ and Rosa damascena Mill extract. 1000 mg/kg body wt. The treatment was carried out for 28 days, then euthanized. Before euthanasia, the rats were tested for blood sugar levels. Sugar levels were checked by taking blood from the rats and using a glucometer. The results of blood sugar levels were analyzed statistically.

Results

The independent variable in this study was the Rosa damascena Mill extract, while the dependent variable was the blood sugar level before euthanasia. The results of the normality test of Saphiro Wilk show Sig (P-Value)> 0.05, which means the data is normally distributed. However, the results of the Levene homogeneity test showed a Sig (P-Value) of 0.003 which means that the data was not homogeneous (Sig (P-Value)> 0.05). therefore, the kruskal wallis statistical analysis was used in this study.

The results of the *Kruskal Wallis* statistical test showed a Sig (P-Value) of 0.030 (p <0.05) which indicated that there were significant differences in all treatment groups. Furthermore, to determine the differences between groups, the *Mann Whitney-U* test was used (Table 1).

The results of the *Mann Whitney-U* test showed that the KN group had significant differences with all groups (Sig P-Value <0.05), while the KP, KM, P1, P2 and P3 groups had no significant differences with other groups (Sig P-Value > 0.05). Figure 1 show that the lowest blood glucose level was in the P1 group, the treatment group given STZ and Rosa damascena Mill extract at 250 mg/kg body wt. Meanwhile, the highest blood glucose level was in the KP group, the positive control group that was only given STZ.

Discussion

This study aims to determine the effect of Rosa damascena Mill extract on blood glucose levels in diabetic rats. These results are the same as the results of research conducted by Gholamhoseinian *et al.* that Rosa Damascena Mill. has a significant effect on blood glucose levels (7). Diabetes Mellitus (DM) is a chronic disease characterized by hyperglycemia and glucose intolerance that occurs because the pancreas gland is unable to produce insulin adequately or because the body cannot use the insulin produced effectively or both (9). Chronic hyperglycemia conditions in diabetes mellitus patients can cause several complications through various mechanisms, namely the formation of superoxide, advanced glycation, polyol pathways, increased PKC (Protein Kinase C) and the hexosamine pathway (10).

Diabetes can cause complications, a lot of protein glycation and free radicals (ROS) are formed in body tissues. An imbalance between the formation of ROS and antioxidants contributes to tissue damage. Giving antioxidants is an attempt to inhibit the production of intracellular free radicals or increase the ability of defense enzymes against free radicals in order to prevent the emergence of oxidative stress and vascular complications related to diabetes. Various kinds of supplements that contain antioxidants and/ or factors that can increase the production of nitric oxide (NO) have the potential to improve endothelial dysfunction and mitochondrial function in cells, and reduce the activity of the enzyme NAD (P) H oxidase. (11).

Rosa Damascena Mill contains polyphenols, flavonoids, glycosides, terpenes and anthocyanins as well as various vitamins such as vitamins C, A, B1, B2, B3 and K. The other ingredients are citric acid, malic acid, pectin, tannins and carotenoids. Rosa Damascene Mill. also contains active phenolic compounds, such as kaempferol, cyanidine 3,5 d-glycosides, quercetin, and gallic acid. The main chemical constituent structures are β Citronellol, nonadecane, geraniol and henicosane (6).

The content of Rosa Damascena Mill is thought to be able to prevent these complications through inhibition of the formation of free radicals which is characterized by a decrease in blood glucose levels. As in Anjani's study, anthocyanin substances can be used as an option for non-pharmacological diet therapy because their content can control blood glucose levels so that they can prevent insulin resistance in people with diabetes, especially type 2 diabetes (12). Cyanidine and glycosides are included in anthocyanins, both of which have anti-diabetic functions. In in vitro studies, it was stated that cyanidine and glycosides inhibited the pancreatic α-glucosidase and α-amylase enzymes. Anthocyanins inhibit the release of glucose in the blood by inhibiting enzymes that digest carbohydrates (13).

The results showed that the blood sugar levels in the treatment group (P1, P2, P3) decreased insignificantly. This interpreted that the blood sugar levels in the treatment group (P1, P2, P3) were not much different from those in the positive control group (KP) and the metformin group (KM). The first reason is probably due to the quality of the ethanol used to make the RDM extract. The ethanol used is not food grade ethanol so this may affect the quality of the RDM extract produced. The second reason is probably because the body weight of Rattus norvegicus varies so that it may affect the effectiveness of the RDM extract. Blood sugar levels in the positive control group (KP) and the metformin group (KM) were still higher than the treatment group (P1, P2, P3). Although not significantly, however in this case it appears that RDM is better for lowering postprandial blood sugar levels.

Conclusion

Rosa damascena Mill extract may have an antidiabetic effect by reducing postprandial blood sugar levels.

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Table 1. *Mann Whitney-U* Test Result

	KN	KP	KM	P1	P2	P3
KN		0,021*	0,021*	0,021*	0,021*	0,021*
KP	0,021*		0,564	0,149	0,248	0,248
KM	0,021*	0,564		0,386	0,248	0,149
P1	0,021*	0,149	0,386		0,564	0,773
P2	0,021*	0,248	0,248	0,564		0,564
P3	0,021*	0,248	0,149	0,773	0,564	

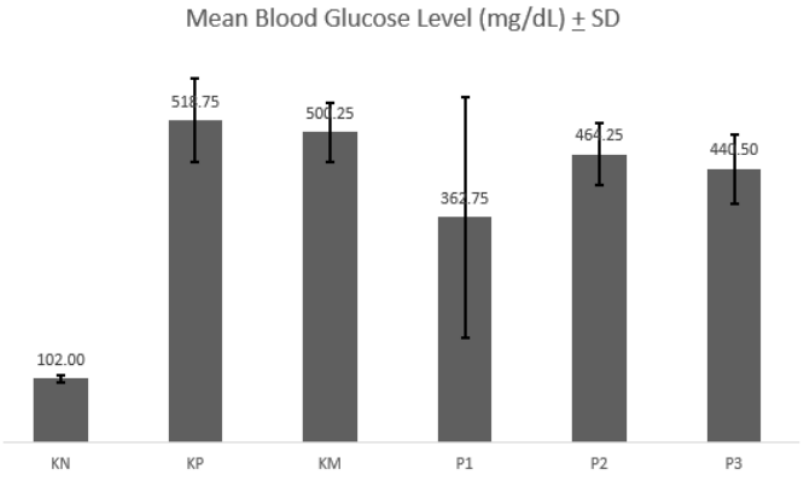

Figure 1. Mean ± SD Blood Glucose Level (mg/dL)

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