***Original article:***

# The Potential Hypoglycemic Activities of Red Onion Extracts in Alloxan-Induced Hyperglycemic Mice

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**Abstract:**

***Objective:*** The present study aimed to determine the potential effect of red onion extracts on ameliorating the blood glucose levels in alloxan-induced hyperglycemic mice. ***Material and Methods:***Hyperglicemia was induced by single intramuscular injection of 70 mg/kg body weight of alloxan monohydrate. 24 mice were randomly assigned to four groups of 6 each including alloxan control (group AC), and three alloxan groups treated with doses 25 mg/kg body weight (group AR25), 50 mg/kg body weight (group AR50), and 100 mg/kg body weight (group AR100) of red onion extracts. The latter three groups were treated with red onion extract for two weeks. The blood glucose levels were measured using a glucometer. ***Results and Discussion:*** The different doses of red onion extracts induced the different responses of blood glucose levels in hyperglycemia mice. The main finding of the present study revealed the significant capacity to ameliorate the blood glucose levels were shown in mice treated with 100 mg/kg body weight of red onion extracts ($p<0.05$). ***Conclusion:*** The red onion extracts at 100 mg/kg body weight significantly ameliorated the blood glucose in alloxan-induced hyperglycemic mice.

**Keywords:** Red onion extracts; hyperglycemia; blood glucose

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## Introduction

Diabetes mellitus is a group of metabolic disorder characterized by hyperglycemia either due to the abnormalities of insulin secretion or action of insulin.[1] Prevalence of diabetes mellitus has been rising rapidly worldwide.[2] Lifestyle changes in modern era plays an enormous role in contributing to increase the prevalence of diabetes mellitus. The complication resulted from diabetes mellitus leads to high mortality in this population. Therefore, various treatment approaches have been investigated and used to overcome this condition. The main target of the treatment approaches is controlling blood glucose levels in people with diabetes mellitus. Oral hypoglycemia drugs/antihyperglicemia agent drugs or insulin injection have been used as medical treatment to combat the diabetes mellitus. However, the limited efficacy and adverse side effects of those treatments encourages the needs for the exploration of other substances. Plants are natural resources which have tremendous properties in terms of medicinal values.[3]Red onions are widely consumed vegetables as well as the traditional/alternative medicine.Red onions (*allium ascalonicum*) are reported containing high levels of quercetin. Quercetin, one of flavonoid compounds,is part of polyphenol groupswhich represents many potential properties in terms of health benefit. The study revealed the role of quercetin as hypoglycemia agent.[4] *Quercetin* is α-amilase inhibitor which functions in carbohydrate breakdown. Among flavonol classes, *quercetin*has the strongest potential in enzyme inhibition.The inhibition of the enzymes results in the inhibition of carbohydrate breakdown and

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absorption, leads to lowering blood glucose levels in hyperglycemia condition.[2,5,6]To the best of our knowledge, the study on antihyperglycemic effect of red onion extracts has not been explored yet. Therefore, this study was aimed to investigate the antihyperglycemic potential of red onion (*alliumascalonicum*)extracts and determining the optimal dose of the extracts needed to overcome the hyperglycemia condition.

**Material and Methods**

*Preparation of Red Onion Extracts*

Red onions **(***allium ascalonecum)* were obtained from the plantations in Sidrap, South Sulawesi. The red onions were extracted with 70% acidic ethanol.

*Experimental Animals*

All experiments in this study were approved by the Ethical Committee of Faculty of Medicine, Universitas Muslim Indonesia. Twenty-four mice (2-3 months of age) weighing 20-30 g were purchased from Pharmacy Laboratory in Airlangga University. The mice were housed in cages for a one week period of acclimatization. The animals were fed with standard diet. Sample size was determined using Federer's formula, thus the total number of animals used in this study were 24 animals.

*Hyperglicemia Induction*

The animals were kept out of food for 12-24 hours before alloxan injection. Alloxan monohydrate firstly were dissolved in 0.9% NaCl. The mice were intramuscular injected with alloxan solution at a single dose of 70 mg/kg body weight in group AR25, group AR50, and group AR100. Three days after alloxan administration, blood glucose levels were measured using a glucometer. The alloxan injection were repeatedly given in mice until the hyperglycemia conditions were developed.

*Experimental Design*

In this experimental study, 24 mice were randomly assigned to four groups of 6 each including alloxan control (group AC), and three alloxan groups treated with doses 25 mg/kgbody weight (group AR25), 50 mg/kgbody weight (group AR50), and 100 mg/body weight (group AR100) of red onion extracts. The latter three groups were treated with red onion extract for two weeks.After two weeks, all mice were terminated.

*Determination of Blood Glucose Level*

Blood samples of the animals were collected by cutting ±0.2 cm tail tip of the mice. Blood glucose levels were measured before and after alloxan induction, as well as after administering the red onion extracts. Blood glucose levels were determined using glucometer.

*Statistical Analysis*

All measurement data are expressed as mean ± standard error mean (SEM) and analyzed using paired T-test. P values less than 0.05 ($p<0.05$) were considered significant. All statistical analysis were performed using the statistical software SPSS version 23.0.

**Results**

In the present study, firstly we developed the hyperglycemia condition in mice by injecting them with alloxan. As we expected, single dose (70 mg /kg body weight) injection of alloxan resulted in hyperglycemia condition, characterized by blood glucose >175 mg/dl in all mice. Three days after alloxan injection, the mice exhibited the hyperglycemia condition (Table 1).

After developing the hyperglycemia condition in all mice, we were trying to identify the potential effect of red onion extracts on hyperglycemia condition. The findings of this study revealed that the red onion extracts resulted in dose-dependent reduction in blood glucose levels of alloxan-induced hyperglycemic mice. We observed the highest dose (100 mg/kg body weight) of red onion extracts significantly induced the highest reduction (72%) of blood glucose levels ($p<0.05$). The AR25 group were shown not sufficient to ameliorate the hyperglycemic condition. On the other hand, the slight reduction of blood glucose levels was observed in AR50 group, although it is not statistically significant (Table 1).

**Table 1.** Blood Glucose Levels of Mice Pre, Post Alloxan Induction, and after treatment with Red Onion Extracts

| Groups | Blood Glucose Levels | | |
|---|---|---|---|
| | Pre Alloxan Induction (mg/dl) | Post Alloxan Induction (mg/dl) | Post Red Onion Extract Treatment (mg/dl) |
| AC | 81.5±0.76 | 480±29.74 | 497.6±21.22 |
| AR25 | 114.5±1.40 | 440.5±45.58 | 477.8±29.31 |
| AR50 | 123±0.96 | 320.1±47.33 | 274.3±68.76 |
| AR100 | 112.8±4.72 | 402.1±44.36 | 115.6±22.75* |

AC, alloxan control; AR25, alloxan induced and treated with red onion 25 mg/kg body weight; AR50, alloxan induced and treated with red onion 50 mg/kgbody weight; AR100, alloxan induced and treated with red onion 100 mg/kgbody weight. Values are mean±SEM (n=6)

*statistica.which results in other complications and leads to the higher mortality worldwide. It

is characterized by hyperglycemia condition. In the present study, we induced the hyperglycemic animal model by injections with alloxan. The mice injected with alloxan developed the hyperglycemic conditions on day 4 post injection. Alloxan permanently induce the diabetes, characterized by hyperglycemia. It plays as diabetogenic agent because its capability in rapidly inducing hyperglycemia.[7]Alloxan is one of urea derivatives which can result in selective necrosis in β-cells of pancreas, and leads to the disruption of insulin metabolism.

The main finding of the present study revealed the antihyperglycemia effect of red onion extracts. However, its potential effects were reported to be dose dependent. It is proven that 100 mg/kg body weight of red onion extracts significantly ameliorated the hyperglycemia condition in alloxan-induced mice. Red onions are widely consumed vegetables as well as the traditional/ alternative medicine.[4]Various scientific evidence reported the functional properties of the red onions as hypoglycemic agents. High levels of quercetin and flavonoid contributes to its role as hypoglycemic agent. Quercetin functions as inhibitor agent of α-amylase enzyme, which acts in carbohydrate metabolism. Inhibiting the enzyme activity leads to disruption of carbohydrate breakdown and absorption, thus it may lower the blood glucose levels. Moreover, flavonoid has been reported to have similar functions to acarbose, which is frequently used as drugs to treat the diabetes mellitus. Its function is mediated by interaction of flavonoid with the ligands of the α-amylase enzyme and by hydrogen and hydrophobic bindings. Flavonoid also has the inhibition effect on α-glucosidase by constructing hydroxylation bonds and substitution in β-rings. Its mechanism of inhibition is similar to acarbose, by delaying the carbohydrate and disaccharide hydrolysis, and leads to the inhibition of glucose absorption and sucrose metabolism.[2,8,9]Therefore, we assumed the flavonoid and quercetin contained in the red onion extracts which contributes to its role as antihyperglycemic agents.

**Conclusion**

Based on our findings, we concluded that 100 mg/ kg body weight of red onion extracts were required to significantly induce blood glucose reduction in alloxan-induced hyperglycemic mice. However, the comprehensive underlying mechanisms of this finding were not elucidated yet. We suggest to assess the phytochemical composition of the red onion extracts which were obtained from plantation in Sidrap, South Sulawesi, Indonesia. In addition further studies are needed to assess other biochemical parameters related to regulation of blood glucose, thus the mechanisms underlying the role of red onion extracts can be explored.

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Conflict of interest : The authors declare that there is no conflict of interest.

**Authors's contribution:**

Data gathering and idea owner of this study: Armanto Makmun.

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Editing and approval of final draft: All Authors

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