



Research Article

## Positive Effect of Konjac Glucomannan on Lowering Blood Pressure in Hypertensive Wistar Rats

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### ABSTRACT

Hypertension is a non-communicable disease that is currently a top priority for global health. Commonly offered anti-hypertensive pharmacological therapies such as ACE-inhibitors are known to have side effects in long-term use, unlike herbal glucomannan, which has been used as a treatment for patients with type 2 diabetes. The purpose of this study was to see what effect applying glucomannan supplements for 6 hours had on blood pressure parameters obtained from the wistar rat subjects who had hypertension. Twenty five male Wistar rats with normal systolic blood pressure (sBP)  $\pm$  110 mmHg were involved in the study; they received a 10% high salt diet for 14 days. They were divided into 4 groups: the positive control group G1 received captopril at 25 mg/kg of body weight and the treatment groups G2 50 mg KGM. Blood pressure measurement using sphygmonanometers with diastolic blood pressure (dBP) is the exclusion criterion of the study. Data analysis is done with a paired sample t-test. Blood pressure in each group decreased after 6 hours of intervention, but the most significant results were obtained in the G5 group that received glucomannan 100 mg/kg bb. In conclusion, Glucomannan can lower blood pressure; this potential is the same as that of red ginger, which modulates the production of angiotensin-converting enzymes.



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### INTRODUCTION

Hypertension, often known as high blood pressure, is characterized by an elevation in systolic blood pressure above 140 mmHg and diastolic blood pressure surpassing 90 mmHg. Hypertension, when left untreated, is a condition that lacks noticeable symptoms. However, it is regarded as one of the most severe conditions since it significantly increases the likelihood of experiencing stroke, myocardial infarction, heart failure, and renal failure (Iqbal & Jamal, 2023) (Keithley et al., 2013a). Hypertension, classified as a non-communicable disease (NCD), has emerged as a prominent concern in the field of global health. The prevalence of hypertension is particularly evident in developing nations like Indonesia (Mills, Stefanescu, & He, 2020). According to a study conducted by (Erni Astutik, Septa Indra Puspikawati, Desak Made Sintha Kurnia Dewi, Ayik Mirayanti Mandagi, & Susy Katikana Sebayang, 2020), the prevalence of hypertension in Indonesia in the year 2018 was found to be 34.1%. This indicates that a significant proportion of the Indonesian population, namely over 91 million individuals, were affected by hypertension. The rise in the prevalence of hypertension may be attributed to factors such as advancing age and unhealthy lifestyle choices, including excessive sodium intake, alcohol use, smoking, obesity, and inadequate physical exercise (Carey, Muntner, Bosworth, & Whelton, 2018). In addition, (Peltzer & Pengpid, 2018) discovered a notable scarcity of antihypertensive therapy in underdeveloped nations, which poses challenges to effectively mitigating hypertension. Conventional interventions, including the DASH diet, physical activity, salt restriction, and weight management, have been recognized as crucial components in the management of blood pressure (Ozemek, Tiwari, Sabbahi, Carbone,

& Lavie, 2020). However, their effectiveness in achieving significant reductions in blood pressure is limited without the concurrent use of commonly prescribed pharmacological therapies, such as diuretics, ACE inhibitors, calcium channel blockers, angiotensin receptor blockers, and beta-adrenergic blockers (Hong & Shan, 2021) (Khalil & Zeltser, 2023). It is important to note that these pharmacological interventions may have associated side effects when used over an extended period. It is important to note that captopril may cause dry cough, dizziness, fatigue, skin rash, taste disturbances, and hypotension when used over an extended period. Konjac glucomannan, a dietary fiber, is extensively used as a fundamental component in the production of noodles, flour, jelly, and tofu. Additionally, it has been utilized as a therapeutic intervention for individuals with type 2 diabetes mellitus, dysphagia, and related conditions (Devaraj, Reddy, & Xu, 2019) (Jiang, Li, Shi, & Xu, 2018). Despite its extensive use, there is little scientific evidence demonstrating the efficacy of glucomannan in improving several health indicators, particularly with blood pressure.

Glucomannan is a polysaccharide that is soluble in water. It is made up of D-glucose and D-mannose in a ratio of 1.6:1.0, with a  $\beta$ -1,4-backbone structure that is gently branched. The branches are formed by  $\beta$ -1,6-glycosyl bonds. The molecular formula of glucomannan is  $(C_6H_{10}O_5)_n$  (Sun et al., 2023a) (Takigami, 2021). Glucomannan is a kind of dietary fiber that is extracted from the roots of the konjac plant, scientifically known as *Amorphophallus konjac*. This plant is often found in the elephant foot yam (Behera & Ray, 2016; Xu et al., 2023). Glucomannan has a flavor profile that is considered neutral, along with notable characteristics such as a high capacity for water absorption as well as the ability to form gels and thicken substances. Consequently, it



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is recommended to eat glucomannan at lower doses compared to other fiber supplements, as suggested by (Keithley et al., 2013b) (Sun et al., 2023b). Long-term use of glucomannan doesn't seem to have any negative effects. However, using this substance too much could cause nutritional imbalances that cause bloating and other stomach problems (Jiang et al., 2018).

Glucomannan, a kind of dietary fiber, undergoes limited or complete fermentation by colonic bacteria due to its indigestibility in the small intestine. Consequently, it can serve as a prebiotic (Guo, Yao, & Yang, 2022; Wan et al., 2022). Previous research has shown that the consumption of glucomannan promotes the proliferation of lactobacilli and bifidobacteria in the gastrointestinal tract (Wan et al., 2022). Based on empirical investigations, the ingestion of glucomannan has been shown to induce the formation of a viscous gel inside the gastrointestinal tract. This gel facilitates the process of gastric emptying and elicits a perception of satiety. Furthermore, it has been observed that glucomannan has the ability to impede the absorption of glucose derived from dietary sources (Yoshida et al., 2020) (Sun et al., 2023b). (Fang et al., 2023), the described intervention might improve insulin sensitivity and lower insulin resistance, which are both important ways to treat type 2 diabetes mellitus. In addition, it has been shown that glucomannan has the potential to enhance endothelial function inside blood vessels. Endothelin-1 (ET-1) is known to have vasoconstrictive effects, causing the narrowing of blood channel lumens. Conversely, nitric oxide (NO) molecules act as vasodilators, promoting the relaxing of blood vessel lumens. Both ET-1 and NO have significant roles in the regulation of blood vessel function, particularly with blood pressure (Genovesi et al., 2022). According to a study by (Weng et al., 2023), giving glucomannan to rabbits with atherosclerosis raised the levels

of nitric oxide (NO) and lowered the levels of endothelin (ET).

The relationship between glucomannan and various health outcomes has been examined in clinical and pre-clinical studies, with a particular focus on body weight, blood sugar, and cholesterol levels (Ho et al., 2017). Nevertheless, there is a lack of research that has specifically examined the beneficial impacts of glucomannan on reducing blood pressure. The purpose of this study was to find out what happened to hypertensive Wistar rats' blood pressure levels after they were given glucomannan supplements for 6 hours.

## MATERIALS AND METHODS

### Subject

This study was conducted under established protocols and received approval from the Health Study Ethics Committee (KEPK) STRADA Indonesia under the reference number 3849/KEPK/V1/2023. This research contained a sample of 10 male Wistar rats, all of whom were 3 months old and had normal blood pressure (systolic blood pressure  $\pm$  110 mmHg). The individuals were subjected to a period of quarantine inside the confines of the pharmacology laboratory, during which they were given one week to acclimate themselves to their novel living environment prior to being officially employed for research purposes. The rats were partitioned into two cohorts consisting of five Wistar rats each. They were provided with a diet and water that adhered to established criteria for their species.

### Study Design

The research design used in this study is classified as a true experimental design. The process of induction begins after the adaptation phase has been completed. Hypertension animal models were established with the administration of a 5% sodium chloride



solution dissolved in 100 ml of distilled water. Additionally, 1 cc of sodium chloride was orally administered and added to their daily consumed beverages for a duration of 14 days. Blood pressure measurements were taken on the seventh and fourteenth days, resulting in an average systolic blood pressure (sBP) of around 156 mmHg. This research consists of

two distinct groups. The study consists of two groups: the control group (K1) and the treatment group (K2). The blood pressure was measured before the induction of the rats, measured again after the induction, and measured one more time (6 hours post-intervention). There are eligibility criteria and exclusion criteria, as shown in Table 1.

**Table 1.** Eligibility criteria and Exclusion criteria

Eligibility Criteria	Exclusion Criteria
a. Systolic blood pressure (sBP) >140 mmHg b. No prior induction c. No prior medicine	a. Dyastolic blood pressure (dbp) data

**Table 2.** Treatment and dosages

Groups	Treatments	Dosages
Control (K1)	Captopril	NaCl 10% + (25 mg of Captopril) oral
Treatment (K2)	Glucomannan	NaCl 10% + (50 mg of glucomannan supplements) oral

**Treatments**

There are two groups; they are given the same food and drink and the same induction, but what differentiates them is their intervention.

Control group intervention (K1) using captopril. Captopril is a drug in the ACE-inhibitor class that acts by inhibiting the enzyme ACE that is responsible for converting angiotensin I to angiotensin II. It is a commonly used drug for treating hypertension. (Marte et al., 2023). The drug is obtained from an external clinic and used for comparison with glucomannan, which is the focus of research. Captopril 25 mg is diluted and dissolved in 25 ml of Aquadest, given orally once in the control group.

The treatment group intervention (K2) uses glucomannan supplements (KGMs) extracted from shrub plants. PT. Raja Porang Indonesia is the supplier of this supplement. The supplement has a glucomannan purity of 40% and is free of calcium oxalate, so it is safe to use. 50 mg of glucomannan supplement is dissolved in 100 ml of aquadest and administered orally once in the treatment group.

**Statistical analysis**

The results of the study are shown in the form of average ± standard deviation values (SD). The differences in blood pressure before intervention (0 hours) and after intervention (6





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hours) of both treatment groups were analyzed with a t-test paired sample using SPSS version 29, and the significance value was determined when ( $\alpha < 0.01$ ).

## RESULT

### Characteristics of the Subjects

Induction treatment begins one day after the environmental adaptation period is completed. They got 5% of sodium chloride orally and 5% of chlorine sodium indirectly mixed into their beverages. Standard meals and drinks that have been mixed with sodium chloride are replaced once a day at the same time intervals. Table 3 shows descriptive data on blood pressure before and after induction (hari ke-14). It can be observed that the average systolic blood pressure (sBP) before induction in each group was 108 mmHg (K1) and 112 mmHg (K2). The systolic pressure of mice increased to 164 mmHg at K1 and 148 mmHg at K2 after inducing hypertension with a total NaCl of 10% for 14 days. This condition indicates that they

are ready for intervention, as they have met the eligibility criteria mentioned in Table 2.

### Study Outcome

Significant decreases ( $\alpha < 0.01$ ) were shown in both groups. A significant decrease in blood pressure occurred in the control group (K1) after captopril was administered, with a 14.63% decline in the presence of an initial value of 164 mmHg (0 hours) to the final value of 140 mmHg (6 hours). This result showed a statistically significant value with a p-value of 0.0006 ( $p$ -values  $< \alpha$ ). However, a significant reduction of blood pressure was also observed in the treatment group (K2) given glucomannan supplementation, with a starting value of 148 mmHg (0 hours) up to 130 mmHg (6 hours), with a decline of 12.16%. Although both have statistically significant values, p values are obtained in different groups. As observed in Table 4, the treatment group had a slightly larger p-value than the control group, indicating that the blood pressure decrease in the glucomannan group had a somewhat lower effect than the captopril group.

**Table 3.** Before and after induction

Groups	n	Mean	SD	Min.	Med.	Max.
K1	Before	108	13.03	90	110	120
	After	164	15.16	140	170	180
K2	Before	112	17.88	90	110	130
	After	148	13.03	130	150	160

**Table 4.** Treatment effect on Systolic Blood Pressure (sBP)

Groups	Baseline	Endpoint	Change (%)	$\alpha$	p-value
K1	164 ± 15.16	140 ± 14.14*	-14.63	0.01	0.0006*
K2	148 ± 13.03	130 ± 10*	-12.16	0.01	0.0008*

\*Significant value ( $\alpha < 0,01$ ).



## DISCUSSION

KGM as a new therapeutic innovation in hypertension management. Hypertension is associated with persistently high systolic and diastolic blood pressure, contributing to the onset of cardiovascular disease (CVD), including coronary heart disease, heart failure, stroke, myocardial infarction, atrial fibrillation, and peripheral artery disease, as well as chronic kidney disease (CRD) (Oparil et al., 2018). The risk factors that are difficult to modify are age and genetic factors, but poor lifestyles, an irregular diet, and a low public understanding of the disease also contribute directly to the prevalence of hypertension, which is difficult to reduce (Mills et al., 2020; Zhou et al., 2021). For this reason, it becomes vital to develop an herbal-based anti-hypertensive medicine as an alternative intervention for the treatment of existing hypertension. As is known, long-term use of an ace-inhibitor-class medication that is not pure or natural from herbal plants can cause hyperkalemia and arterial hypertrophy. (Hong & Shan, 2021; Watanabe et al., 2021).

Glucomannan is a potentially promising solution due to the properties of glucomannan itself, making it often used as an additional raw material in food as well as as a treatment for those suffering from diabetes mellitus 2. There are many benefits but no side effects from long-term use (Devaraj et al., 2019; Fang et al., 2023; Jiang et al., 2018).

This study investigated the effects of 6-hour glucomannan supplementation on blood pressure profiles in rats induced by hypertension for 14 days. We have observed a significant decrease in blood pressure after 6 hours of taking 50 mg of glucomannan supplement. The p-value was lower than the specified alpha value ( $p\text{-value } 0.0008 < \alpha 0.01$ ). This is a little boastful, as the significance value obtained is not much different from that of the group of mice treated with captopril ( $0.0006 < \alpha 0.01$ ), which means its effect in lowering blood pressure is almost the same as that of captopril, a conventional drug that has been used for centuries to lower hypertension. A rather promising alternative, but not immediately, can be used without prejudice to the public because,

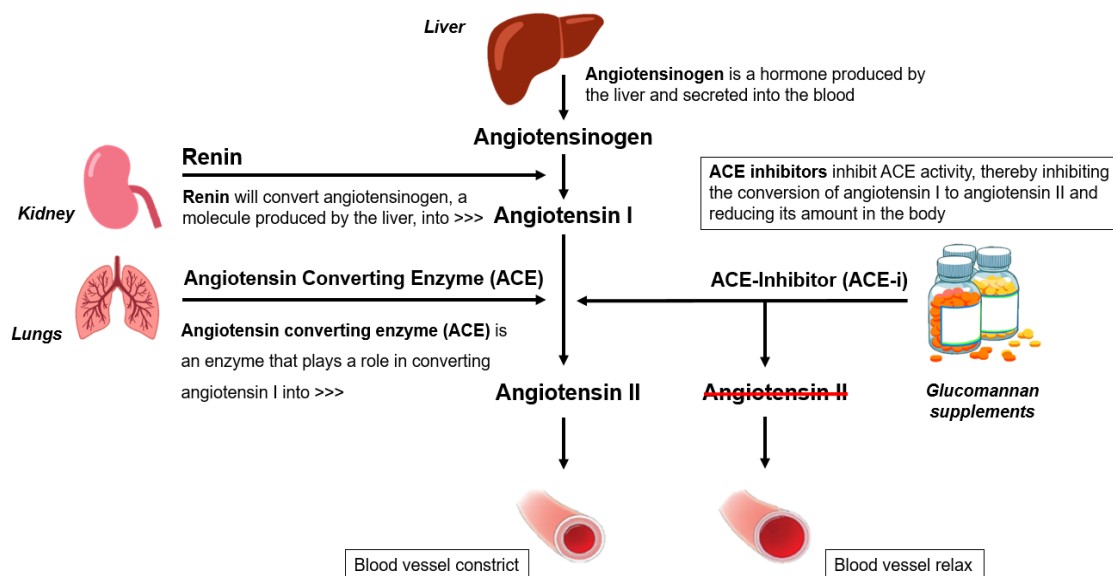


Figure 1. Blood pressure reduction by ACE-i mechanism (Carey, et.al, 2019)



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in addition to glucomannan in shell plants, there are compounds of calcium oxalate that can irritate the mouth and esophagus if not properly managed before ingestion (Pillay et al., 2020). In this study, the glucomannan used was free of calcium oxalate, so it's safe to use.

We assume that glucomannan can lower blood pressure through the mechanism of the Angiotensin Converting Enzyme Inhibitor (ACE-i), just like red ginger (Hanifah et al., 2021). Blood pressure is controlled by the renin-angiotensin system, which consists of several major components, including renin, angiotensinogen, and angiotensin-converting enzymes (ACE). Angiotensins are protein precursor that is synthesized and secreted constitutively by the liver and released into the bloodstream, whereas renin is an enzyme manufactured by the kidneys that interacts with angiotensinogen and turns it into angiotensin I. Angiotensin I is an inactive compound that has no biological activity and must be converted to angiotensin II by the angiotensin-converting enzyme (ACE) to produce physiological effects (Fountain et al., 2023; Herman et al., 2023; Yan et al., 2019).

This study uses male Wistar rats as the subject of research. The weakness of this study is that the results found in rats cannot be used as a reference when applied to humans. Consideration of dosage for humans can be considered again by future researchers because the biological responses between animals and humans may differ. Sample sizes in limited studies can also be used as study material, as the results displayed are likely to be less representative. In addition, the design of a short study can be a weakness, as it is difficult to determine whether the blood pressure reduction effects given glucomannan can give long-term results or only temporary effects. Finally, some speculations may be relevantly related to the mechanisms of

glucomannan in lowering blood pressure, such as the article (Weng et al., 2023) that represents that glucomannan can stimulate the production of a nitric oxide compound (NO) known as a powerful vasodilator in vascular endothelial function. The article (Miyamoto et al. 2016) also represents glucomannan as a dietary fiber that has a prebiotic function that can promote the formation of short-chain fatty fiber (SCFA), which is known to be a new pathway involved in blood pressure regulation. However, both are not reviewed in this article.

### CONCLUSION

Glucomannan may reduce blood pressure by inhibiting the Angiotensin-Converting Enzyme (ACE) similar to red ginger. This study, using male Wistar rats, suggests potential human application is limited due to differing biological responses and the temporary nature of effects, with glucomannan possibly enhancing nitric oxide production and promoting prebiotic functions that regulate blood pressure.

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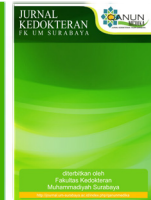
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