



## Effect of Garlic (*Allium sativum*) and Turmeric (*Curcuma domestica* Val.) Extract Combination in Type 2 Diabetic Rats.

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### Abstract

Type 2 diabetes mellitus (T2DM) often leads to kidney damage due to chronic hyperglycemia and oxidative stress. Garlic (*Allium sativum*) and turmeric (*Curcuma domestica* Val.) are traditional medicinal plants with known antioxidant and anti-inflammatory properties. This study evaluated the nephroprotective effect of their combined extracts in streptozotocin (STZ)-induced diabetic rats. Twenty-five male rats were divided into five groups: negative control, positive control (metformin 500 mg/kg BW), and three treatment groups receiving extract combinations at doses of 100, 200, and 300 mg/kg BW. Blood glucose, urea, and creatinine levels were measured, followed by histopathological examination. Phytochemical analysis confirmed the presence of alkaloids, flavonoids, and other secondary metabolites. Although statistical analysis showed no significant difference in glucose, urea, and creatinine levels among groups ( $p > 0.05$ ), the 200 mg/kg BW group exhibited the most favorable trends in reduced blood glucose ( $226.70 \pm 89.70$  mg/dL) and kidney biomarkers. These results suggest the combination extract may offer protective effects on kidney function in diabetic conditions, warranting further investigation.

**Keywords:** Type 2 diabetes mellitus, *Allium sativum*, *Curcuma domestica* Val., kidney function, nephroprotection.

### Abstrak

Diabetes melitus tipe 2 (DMT2) sering menyebabkan kerusakan ginjal akibat hiperglikemia kronis dan stres oksidatif. Bawang putih (*Allium sativum*) dan kunyit (*Curcuma domestica* Val.) merupakan tanaman obat tradisional yang memiliki sifat antioksidan dan antiinflamasi. Penelitian ini bertujuan mengevaluasi efek nefroprotektif kombinasi ekstrak keduanya pada tikus jantan yang diinduksi streptozotocin (STZ). Sebanyak 25 ekor tikus dibagi dalam lima kelompok: kontrol negatif, kontrol positif (metformin 500 mg/kgBB), serta tiga kelompok uji dengan kombinasi ekstrak dosis 100, 200, dan 300 mg/kgBB. Pemeriksaan dilakukan terhadap kadar glukosa darah, urea, kreatinin, serta gambaran histopatologi ginjal. Hasil skrining fitokimia menunjukkan kandungan alkaloid, flavonoid, dan metabolit sekunder lainnya. Meskipun analisis statistik tidak menunjukkan perbedaan signifikan antar kelompok ( $p > 0,05$ ), kelompok dosis 200 mg/kgBB menunjukkan tren penurunan glukosa darah ( $226,70 \pm 89,70$  mg/dL) dan biomarker ginjal yang paling baik. Temuan ini mengindikasikan potensi kombinasi ekstrak bawang putih dan kunyit dalam menjaga fungsi ginjal pada kondisi diabetes, meskipun diperlukan penelitian lanjutan dengan sampel lebih besar.

**Kata kunci:** Diabetes melitus tipe 2, *Allium sativum*, *Curcuma domestica*, fungsi ginjal, nefroproteksi

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## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and hyperglycemia, often leading to long-term complications affecting vital organs, including the kidneys<sup>1</sup>. Diabetic nephropathy is one of the most serious microvascular complications of T2DM, contributing significantly to morbidity and mortality<sup>2</sup>. Prolonged hyperglycemia results in oxidative stress, inflammation, and structural damage in renal tissues, leading

to progressive deterioration in kidney function. Early detection and intervention are crucial to prevent irreversible renal damage in diabetic patients<sup>3</sup>.

Current pharmacological therapies for T2DM and its complications may pose undesirable side effects and are often costly, prompting a growing interest in alternative therapies using natural products<sup>4</sup>. Medicinal plants rich in bioactive compounds offer promising protective effects due to their antioxidant, anti-inflammatory, and hypoglycemic



properties. Among them, garlic (*Allium sativum*) and turmeric (*Curcuma domestica* Val.) are well-known traditional remedies used for centuries in various cultures. Both have been extensively studied for their beneficial roles in metabolic disorders<sup>5-7</sup>.

Garlic contains sulfur compounds such as allicin, which exhibit potent antioxidant and antihyperglycemic activities. These compounds help reduce oxidative stress and improve insulin sensitivity, potentially protecting renal tissue from damage caused by diabetes<sup>5</sup>. Similarly, turmeric contains curcumin, a polyphenolic compound with strong anti-inflammatory and antioxidant effects<sup>8</sup> that may mitigate diabetic complications, including renal inflammation and fibrosis<sup>9</sup>. Previous studies have shown that both herbs individually can exert nephroprotective effects in diabetic models.

However, the synergistic potential of combining garlic and turmeric extracts in the context of diabetic nephropathy remains underexplored. Investigating their combined effect may offer a more potent therapeutic approach by targeting multiple pathological pathways simultaneously<sup>9</sup>. Therefore, this study aims to evaluate the histopathological changes in kidney tissues of type 2 diabetic rats following administration of a combination of *Allium sativum* and *Curcuma domestica* Val. extracts, in order to determine their potential role in renal protection and diabetes management.

## METHODOLOGY

### *Tools and Materials*

The tools used in this study were measuring cups (Pyrex), dropper pipettes, spatulas, analytical scales (Mettler Toledo), maceration vessels, stirring rods, rotary

evaporators, jars. The materials used in this study were garlic (*Allium sativum*) and turmeric rhizome (*Curcuma domestica* Val.), 96% ethanol, 1% Na CMC, streptozotocin (STZ), Metformin, white male rats, rice husks for rat cages, rat feed, rat drinking water.

### *Preparation of Test Animals*

In this study, 2- to 3-month-old male white rats weighing between 150–180 grams were used. Prior to the experiment, the animals were acclimatized to the laboratory environment for seven days. Throughout the study period, the rats were housed in cages, and their body weight was monitored daily. They were fed twice a day with standard feed and had access to water *ad libitum*. The experimental design consisted of five treatment groups, each containing five rats housed together in a single cage. The cages, often made of plastic with wire tops, were lined with rice husks to help maintain appropriate humidity levels and provide bedding comfort for the animals.

### *Process of Making Extracts from Garlic (*Allium Sativum*) and Turmeric Rhizome (*Curcuma Domestica* Val.)*

Garlic and turmeric rhizomes are first washed clean, then dried using an oven at a temperature of 40°C until completely dry. After the garlic and turmeric rhizomes are dry, cut them into small pieces to make them easier to process. Furthermore, the garlic and turmeric rhizomes are pureed using a blender and sieved to produce a simple medicine to separate the coarse or unwanted parts. The simple medicine weighed 800 grams is dissolved in 8 L of 96% ethanol for 7x24 hours by stirring the



mixture every 24 hours. After the maceration is complete, filter the mixture using a filter to separate the filtrate from the simple medicine dregs. Additional maceration is carried out by stirring 12 times for 15 minutes, then filtered again using a funnel and filter paper to ensure the separation of the filtrate from the remaining dregs. The filtered filtrate is evaporated using a Vacuum Rotavapor tool, until a thick extract is obtained that is free of solvents<sup>10,11</sup>.

### Phytochemical Screening

Phytochemical screening of simple drugs is carried out to identify the content of flavonoid, alkaloid, tannin, saponin, glycoside, steroid and triterpenoid compounds<sup>12</sup>.

### Calculation of Na-CMC 1% dosage

Na-CMC 1% was made by dissolving 1 gram of Na-CMC in 100 mL of hot distilled water, then ground until homogeneous. Na-CMC 1% as a negative control was given to rats with a volume of 0.2 mL/20grBW of rats.

### Animal Test Treatment Procedures

Animals in 1 group were placed together in 1 cage. In groups 3 to 5 were given a combination of garlic extract (*Allium sativum*) and turmeric rhizome (*Curcuma Domestica* Val.) orally according to the dose level, while the negative control group was given 1% Na CMC solution and the positive control was given metformin 500 mg/KgBW.

*Group I:* the group not induced by streptozotocin was given 1% Na-CMC orally (negative control).

*Group II:* the group induced by streptozotocin 45mg/KgBW was given Metformin 500mg/KgBW orally (positive control).

*Group III:* the group induced by streptozotocin 45mg/KgBW in test animals given a combination of garlic extract (*Allium sativum*) and turmeric rhizome (*Curcuma Domestica* Val.) 100mg/KgBW.

*Group IV:* the group induced by streptozotocin 45mg/KgBW in test animals given a combination of garlic extract (*Allium sativum*) and turmeric rhizome (*Curcuma Domestica* Val.) with the previous group, with a different extract dose of 200mg/KgBW.

*Group V:* group induced by streptozotocin 45mg/KgBW in test animals given a combination of garlic extract (*Allium sativum*) and turmeric rhizome (*Curcuma Domestica* Val.) with different doses of 300mg/KgBW.

Initial blood glucose level examination was performed on day 0. After normal blood sugar levels were identified, the mice were fasted for 8 hours. Before being induced with streptozotocin intraperitoneally with a dose of 45 mg/KgBW on day 1, blood glucose levels were checked again on day 3. Rats were declared hyperglycemic when blood glucose levels were  $\geq 135$  mg/dL<sup>13</sup>. Rats identified as having diabetes mellitus were then monitored for their glucose levels, once every 3 days until day 28<sup>14</sup>. Examination of urea, creatinine, SGOT and SGPT levels was examined on day 28. After that, kidney and liver organ samples were taken for histopathological examination<sup>15,16</sup>.



## RESULT AND DISCUSSION

### *Results of Turmeric and Garlic Rhizome Extract Tests*

Results of Turmeric and Garlic Rhizome Extract Tests can be seen in Table 1.

The phytochemical screening results of garlic (*Allium sativum*) and turmeric rhizome (*Curcuma domestica* Val.) extracts revealed differences in their secondary metabolite profiles. As shown in Table 1, both extracts contained alkaloids and

steroids/triterpenoids. However, only the turmeric extract tested positive for flavonoids, saponins, and tannins. Neither extract showed the presence of quinones. The presence of these bioactive compounds—particularly flavonoids and tannins known for their antioxidant and anti-inflammatory properties—may contribute to the observed nephroprotective and antidiabetic effects in the *in vivo* studies.

**Table 1.** Results of Turmeric and Garlic Rhizome Extract Tests

Secondary Metabolites	Garlic extract ( <i>Allium Sativum</i> )	Turmeric rhizome ( <i>Curcuma Domestica</i> Val.)
Alkaloids	Positive	Positive
Steroids/Triterpenoids	Positive	Positive
Saponins	Negative	Positive
Flavonoids	Negative	Positive
Tannins	Negative	Positive
Quinones	Negative	Negative

### *Blood Sugar Level Measurement*

The results of blood sugar level measurements in the experiment can be seen in Table 2 below. The present study evaluated the effect of combined *Allium sativum* (garlic) and *Curcuma domestica* Val. (turmeric) extracts on blood glucose levels (BGL) in male rats with streptozotocin-induced type 2 diabetes mellitus<sup>17</sup>. Prior to comparative analysis between treatment groups, statistical assumptions were tested to ensure data reliability. The Shapiro-Wilk normality test revealed that BGL data from all groups followed a normal distribution ( $p > 0.05$ ), indicating that the data met the assumption of normality required for parametric testing<sup>18</sup>.

Subsequently, Levene's test for homogeneity of variances demonstrated a

p-value of 0.279, suggesting that variance among the treatment groups was statistically homogeneous. This confirmed that the data were appropriate for further analysis using One-way ANOVA.

The One-way ANOVA test yielded a p-value of 0.151, indicating no statistically significant differences in mean BGL among the five groups: negative control, positive control (metformin), and three treatment groups receiving combined extract doses of 100 mg/kg, 200 mg/kg, and 300 mg/kg body weight, respectively. Although not statistically significant, a reduction in mean glucose levels was observed in all treatment groups compared to the negative control. Notably, the F2 group (200 mg/kg BW) showed the lowest mean BGL ( $226.70 \pm$





89.70 mg/dL), suggesting a potential hypoglycemic effect at this dose.

**Table 2.** Analysis of blood sugar level

Type of statistical Test	Treatment Group	Mean $\pm$ SD (mg/mL)	P – Value	Interpretation
Normality Group	Positive control	241.10 $\pm$ 127.48	0.113	Normally distributed
	Negative control	320.90 $\pm$ 84.37	0.912	Normally distributed
	F1 (100 mg/kg BW)	246.00 $\pm$ 101.36	0.322	Normally distributed
	F2 (200 mg/kg BW)	226.70 $\pm$ 89.7	0.684	Normally distributed
	F3 (300 mg/kg BW)	267.10 $\pm$ 100.89	0.299	Normally distributed
Homogeneity Test			0.279	Homogeneous
One-way ANOVA			0.151	No statistically significant difference observed ( $p > 0.05$ )

These findings suggest that the combination of garlic and turmeric extracts may exert a glucose-lowering effect, although the current study did not demonstrate a significant difference between groups, likely due to the limited sample size and variability in response. Nevertheless, the downward trend in glucose levels observed across all treatment groups supports the potential antidiabetic effect of the extract combination. Further

studies with larger sample sizes, longer treatment durations, and additional biomarkers are warranted to confirm these findings and elucidate the underlying mechanisms

#### *Urea and Creatinine Level Examination*

Testing of blood urea and creatinine levels in experimental mice can be seen in table 3 below.

**Tabel 3.** Urea and Creatinine Levels in Each Group

Group	Urea ( $\mu$ /L) $\pm$ SD	Creatinine ( $\mu$ /L) $\pm$ SD
Positive control	32.67 $\pm$ 2.51	1.00 $\pm$ 0.10
Negative control	23.33 $\pm$ 5.50	0.88 $\pm$ 0.07
F1 (100 mg/kg BW)	30.67 $\pm$ 4.72	0.90 $\pm$ 0.10
F2 (200 mg/kg BW)	27.33 $\pm$ 9.60	0.80 $\pm$ 0.10
F3 (300 mg/kg BW)	27.00 $\pm$ 4.58	1.00 $\pm$ 0.10

The evaluation of renal function in this study was conducted by measuring serum urea and creatinine levels in streptozotocin (STZ)-induced diabetic male

rats<sup>19</sup>. These biomarkers serve as reliable indicators of glomerular filtration rate (GFR) and are commonly elevated in the presence of renal impairment.



Based on the results, the highest mean urea level was observed in the positive control group ( $32.67 \pm 2.51 \mu\text{L}$ ), while the lowest was in the negative control group ( $23.33 \pm 5.50 \mu\text{L}$ ). The treatment groups F1, F2, and F3 showed intermediate values ( $30.67$ ,  $27.33$ , and  $27.00 \mu\text{L}$ , respectively), suggesting a potential reduction in urea levels following administration of the combined extracts. For creatinine, the values were relatively consistent across all groups, ranging from  $0.80$  to  $1.00 \mu\text{L}$ , with F2 ( $200 \text{ mg/kg BW}$ ) showing the lowest mean value ( $0.80 \pm 0.10 \mu\text{L}$ ).

To assess statistical significance, a One-way ANOVA was performed using SPSS software. The analysis returned a p-value of  $0.39$  for urea and  $0.12$  for creatinine. Both values are greater than  $0.05$ , indicating that the differences in mean urea and creatinine levels among the five groups were not statistically significant. These findings imply that while trends in biomarker changes were observed, they were not strong enough to reject the null hypothesis within the scope of this study<sup>20</sup>.

The lack of statistical significance may be attributed to biological variability, sample size limitations, or the relatively short treatment duration. However, the observed decrease in urea and creatinine levels in the treatment groups, particularly F2 and F3, may reflect a potential nephroprotective effect of the combined *Allium sativum* and *Curcuma domestica* Val. extracts. Both herbs contain bioactive compounds known for their antioxidant and anti-inflammatory properties, which may mitigate renal injury associated with hyperglycemia and oxidative stress.

Overall, while the One-way ANOVA did not detect significant differences between groups, the numerical trends support the potential role of herbal extracts in preserving kidney function in diabetic conditions. Future research with larger sample sizes, histological correlation, and extended intervention periods is recommended to validate these preliminary findings.

## CONCLUSION

The combination of garlic (*Allium sativum*) and turmeric (*Curcuma domestica*) extracts showed potential nephroprotective effects in streptozotocin-induced type 2 diabetic rats, as indicated by favorable trends in blood glucose, urea, and creatinine levels—particularly at the  $200 \text{ mg/kg BW}$  dose—along with improved kidney histopathology. Although the results were not statistically significant, the findings suggest that this herbal combination may support kidney function in diabetic conditions and warrants further investigation with larger sample sizes and extended study duration.

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