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Toxicity and α-Glucosidase Inhibitory Activity of *Chromolaena odorata L.* for Antidiabetic Herbal Tea

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ABSTRACT

Background: Coppasanda (*Chromolaena odorata*) is a weed plant containing secondary metabolites with potential antidiabetic activity by lowering blood glucose levels. This plant has been developed into a tea bag formulation. Previous studies reported that Coppasanda tea significantly reduced blood glucose levels in alloxan-induced rats; however, higher concentrations caused unstable glucose levels. Therefore, toxicity testing and α-glucosidase inhibitory assays are required to evaluate its safety and enzyme-inhibiting potential.

Objectives: This study aimed to determine the toxicity profile and α-glucosidase inhibitory activity of Coppasanda tea bags.

Methods: Acute toxicity testing was conducted in vivo using 30 mice divided into five groups: control (0.5% CMC-Na), P1 (50 mg/kg BW), P2 (300 mg/kg BW), P3 (1000 mg/kg BW), and P4 (2000 mg/kg BW). The α-glucosidase inhibition assay was performed in vitro using p-nitrophenyl-α-D-glucopyranoside (pNPG) as the substrate and α-glucosidase enzyme. Absorbance was measured using a spectrophotometer at 405 nm.

Results: The toxicity test showed no toxic symptoms of Coppasanda tea bags, indicated by the absence of significant changes ($P > 0.05$) in body weight, mortality, clinical signs, and organ indices of the experimental animals. In vitro results demonstrated strong α-glucosidase inhibitory activity, with a maximum inhibition of 98% and an IC_{50} value of 29 μg/mL.

Conclusion: Coppasanda tea bags are non-toxic and exhibit strong α-glucosidase inhibitory activity, indicating potential as a safe antidiabetic herbal beverage.

Keywords : Antidiabetic; Chromolaena odorata L.; Inhibitory Activity; Toxicity; α-glucosidase

INTRODUCTION

Copasanda (*Chromolaena odorata* L.) is a weed plant that grows abundantly throughout Indonesia. Copasanda contains secondary metabolite compounds capable of suppressing blood glucose levels (Malita and Junaedi, 2025), antihyperuricemic (Lubis, A. A., Yunus, M., Naldi, J., Andry, M., Ginting, P., Safitri, F., & Nasution, 2023), accelerating blood clotting (Munawwarah M, Syamsul B, 2021), speeding up the epithelialization process (Sukmawati, Auliawati and Syasmari, 2023), possessing antibacterial properties (Wirawan, Kosman and Herwin, 2023), acting as a free radical scavenger (Maryam *et al.*, 2021), and demonstrating antidiabetic effects(Wiyati, Alfitroh and Hardini, 2025). Diabetes mellitus (DM) is a group of chronic metabolic diseases characterized by hyperglycemia. (Letsoin, Pinzon and Sugianto, 2020). Diabetes is one of the diseases widely suffered by the Indonesian population, spanning from children to the elderly. This is a long-term and life-threatening illness that requires vigilance. Approximately 1.5 million people die annually due to diabetes (World Health Organization, 2024). Various factors such as age, diet, family history, and physical activity influence the surge in diabetes prevalence (Irjayanti P, Zaenal and Suhartatik, 2022). Current diabetes management involves diverse methods, including inhibiting the rise in blood glucose levels with synthetic antidiabetic drugs. The use of these drugs often causes side effects. Therefore, the Indonesian public is now starting to shift towards alternative treatments using traditional medicines, as they offer lower side effects and are more affordable (Malita and Safitri, 2023). This research utilizes Indonesian natural resources as an alternative antidiabetic medicine, namely the herbal plant Copasanda, which has been studied for its ability to inhibit the rise in blood glucose levels (Malita and Junaedi, 2025).

Copasanda contains metabolite compounds such as flavonoids, tannins, alkaloids, steroids, and saponins, and is also high in antioxidants (Nurhanifah, Ratnah and Pakadang, 2022). Coumarins, quinones, steroids, and phenolics are also abundant in the Copasanda plant, which may enable it to act as an antidiabetic agent. Docking results have also shown the presence of the compounds 5,7-dihydroxy-6,4-dimethoxyflavanone and luteolin in Copasanda leaves. These compounds are suspected to reduce liver dysfunction caused by diabetes. Molecular docking studies also indicated that compounds from Copasanda leaves are capable of lowering the mRNA expression of GLUT-2, glucokinase, and Nrf2 (O. O. Elekofehinti and Iwaloye, 2021), as well as improving insulin sensitivity, protecting the insulin-producing β-pancreatic cells from damage, and inhibiting mucosal GLUT-2, which reduces the absorption of glucose and fructose in the intestines (Hasan *et al.*, 2024). However, at specific concentrations, flavonoid compounds can be toxic (Djohari *et al.*, 2023). Therefore, a toxicity test must be carried out on the Copasanda tea produc.

Copasanda tea bags have previously been evaluated for their preventive antidiabetic activity. However, at the end of the study, differences were observed in the spleen organs of the experimental animals treated with Copasanda tea bags. Therefore, further research is required to assess the toxicity of Copasanda tea bags and to determine an appropriate dosage that can be safely used for long-term

consumption by the community in efforts to inhibit diabetes. In addition, further studies are needed to evaluate the α-glucosidase inhibitory activity associated with diabetes inhibition, thereby ensuring safer consumption. The objective of this study aimed to determine the toxicity profile and α-glucosidase inhibitory activity of Coppasanda tea bags. The toxicity test on Copasanda tea aims to determine the harmful effects of consuming it. The test is conducted in vivo, involving 30 mice as experimental animals. The test parameters used include body weight progression, the number of mortalities during the treatment period, toxic symptoms, and organ indices to identify the safe dose for consumption that does not cause side effects on organs such as the liver, thymus, spleen, kidney, and heart. Accurate and precise dosage determination is essential for safe long-term consumption of Copasanda tea. Additionally, an α-glucosidase inhibition test on cottonwood tea is necessary to determine the enzyme's inhibitory activity in breaking down complex carbohydrates into simple glucose. Therefore, it can help stabilize blood glucose levels(Nurfajriah, Inggraini and Ilsan, 2021). The α-glucosidase inhibition assay for Copasanda tea is conducted in vitro using p-nitrophenyl-α-D-glucopyranoside (p-NPG) as the substrate and α-glucosidase. The test uses a spectrophotometer at 405 nm.

METHODS

Thi research is experemental with control group using test animals that have obtained ethical permission from the Health Research Ethics Commission of the Faculty of Medicine and Health, Mataram University with number 195/UN18.F8/ETIK/2025.

Tools and Materials

The tools used in this research included glassware, an analytical balance, a digital scale, an oven, micropipettes, a spectrophotometer, cuvettes, surgical instruments, mouse cages, and an oral sonde. The materials used were Copasanda tea, aquades, CMC-Na, the α-glucosidase enzyme, phosphate buffer (pH 7), Sodium Carbonate (Na_2CO_3) solution, CO_2-free water, acarbose, p-nitrophenyl-α-D-glucopyranoside (p-NPG) substrate, and HCl.

Preparation of Copasanda Tea Solution

Copasanda tea was infused in boiling water according to the designated doses (dose 1: 50 mg/kg BW, dose 2: 300 mg/kg BW, dose 3: 1000 mg/kg BW, and dose 4: 2000 mg/kg BW) in 10 mL of boiled water for each dose. After homogenization, each preparation was transferred into a sample bottle and labeled accordingly.

Preparation of Experimental Animals

The experimental animals were mice, divided into 5 groups of 6 individuals each. The animals were housed in cages lined with wood shavings and provided with standard feed. All animals were acclimatized for one week before treatment.

Toxicity Test

The experimental animals were divided into five groups, with each group consisting of six mice. The treatments included a normal control (distilled water), P1 (dose 1: 50 mg/kg BW), P2 (dose 2: 300 mg/kg BW), P3 (dose 3: 1000 mg/kg BW), and P4 (dose 4: 2000 mg/kg BW). Copasanda tea bags were administered as a single dose to the treatment groups orally each day. Observations were conducted over 21 days. The parameters observed included signs of toxicity, body weight, mortality, behavior, and organ indices. The toxicity signs assessed were tremors, diarrhea, lethargy, backward walking, hair loss, and hyperactivity[16]. Body weight was measured on days 0, 6, 9, 13, 16, and 21. Toxicity symptoms and mortality occurring in the mice were monitored daily throughout the observation period. All mice that died during the study, as well as those surviving until day 21, were euthanized and necropsied to weigh internal organs and observe any macroscopic changes. The organ indices evaluated included the weights of the liver, thymus, left kidney, right kidney, spleen, and heart, which were then compared with the organ indices of the normal control group (Ubang, Siregar and Herman, 2022).

α-Glucosidase Inhibition Assay

The α-glucosidase inhibition assay was performed using p-nitrophenyl-α-D-glucopyranoside (p-NPG) as the substrate and α-glucosidase as the enzyme. The enzyme substrate solution was obtained by diluting the α-glucosidase stock preparation in a pH 7 phosphate buffer. A blank solution was used to correct the absorbance measured in the control group (C); S0 served to correct the absorbance obtained from the Copasanda tea sample. The enzyme substrate reaction was halted by adding Na_2CO_3 to the mixture. The absorbance of each reaction sample was then recorded at 405 nm using a spectrophotometer. Acarbose tablets were used as the positive control at 1% (w/v) by dissolving them in phosphate buffer, and HCl 2N (ratio 1:1). The solution was centrifuged, and 1 µL of the supernatant was collected and added to the reaction mixture. α-glucosidase inhibitory activity was indicated by an inhibition percentage > 50%. The IC_{50} value was determined by substituting y=50 into the regression equation obtained from the inhibition activity measurements (Ritonga *et al.*, 2024).

Data Analysis

The toxicity data obtained from the Copasanda tea study were processed using IBM SPSS Statistics. A parametric analysis was performed through a One-Way ANOVA at a 95% confidence level, and further comparisons were carried out using the Least Significant Difference (LSD) post hoc test (Putra *et al.*, 2023). The results were considered statistically significant when $P < 0.05$ and not substantial when $P > 0.05$. The data analysis for the α-glucosidase inhibition assay was based on absorbance values used to calculate the percentage of Inhibition, as presented in Formula 1. The IC_{50} (Inhibitor Concentration 50%) value was determined by constructing a curve that relates the percentage of Inhibition to the concentrations of the Copasanda tea sample, from which a regression

equation was obtained. By applying the linear regression model expressed as y = a + bx, where *a* represents the intercept on the x-axis and *b* denotes the slope of the plot on the x and y axes, the IC_{50} value was calculated by substituting y = 50, as shown in Formula 2 (Rahmawati *et al.*, 2025).

$$\% \text{ Inhibition} = \frac{(B1 - B0) - (S1 - S0)}{(B1 - B0)} \text{ x } 100\% \text{ ..... (1)}$$

Notes:

B0 : Control Blank Absorbance

B1 : Blank Absorbance

S0 : Sample Control Absorbance

S1 : Sample Absorbance

$$IC_{50} = \frac{50 - Intersept\ plot\ x\ axix}{Slope\ plot\ \ x\ and\ y\ axis} \text{ .....(2)}$$

RESULTS AND DISCUSSION

Copasanda (Chromolaena odorata L.) tea bags have potential antidiabetic activity (Malita and Junaedi, 2025), because the plant contains various secondary metabolites, including flavonoids, tannins, alkaloids, steroids, and saponins, as well as high levels of antioxidants (Nurhanifah, Ratnah and Pakadang, 2022). Coumarins, quinones, steroids, and phenolics are also abundant in the Copasanda plant, which potentially allows its use as an antidiabetic agent. Docking results indicate the presence of the compounds 5,7-dihydroxy-6,4-dimethoxyflavanone and luteolin within the plant. Subsequent molecular docking evaluations indicated that these constituents have the potential to modulate mRNA expression associated with GLUT-2, glucokinase, and Nrf2 (O. Elekofehinti and Iwaloye, 2021). Furthermore, can enhance insulin sensitivity, protect β-pancreatic cells involved in insulin secretion, and downregulate mucosal GLUT-2 activity, thereby diminishing intestinal absorption of glucose and fructose(Hasan *et al.*, 2024). However, flavonoid compounds can exhibit toxic effects at certain concentrations (Djohari *et al.*, 2023). For this reason, a toxicity assessment of Copasanda tea bags was conducted to identify potential toxic effects and ensure their safety for consumption. The toxicity parameters observed included changes in body weight of the test animals, mortality rate, and clinical signs of toxicity such as tremors, diarrhea, lethargy, backward walking, fur loss, hyperactivity, and salivation, as well as organ indices of the liver, kidneys, heart, spleen, and thymus. The data analysis ANOVA results with LSD post-hoc testing are presented in Table 1 showed no significant difference in body weight between the animals treated with Copasanda tea and the control group (P> 0.05), as illustrated in Figure 1. The data in Table 1 show P > 0.05 for all groups, all weight-change percentages <20%. Thus, the body-weight variations observed in this study do not indicate any toxic symptoms such as discomfort or distress during administration of Copasanda tea bags.

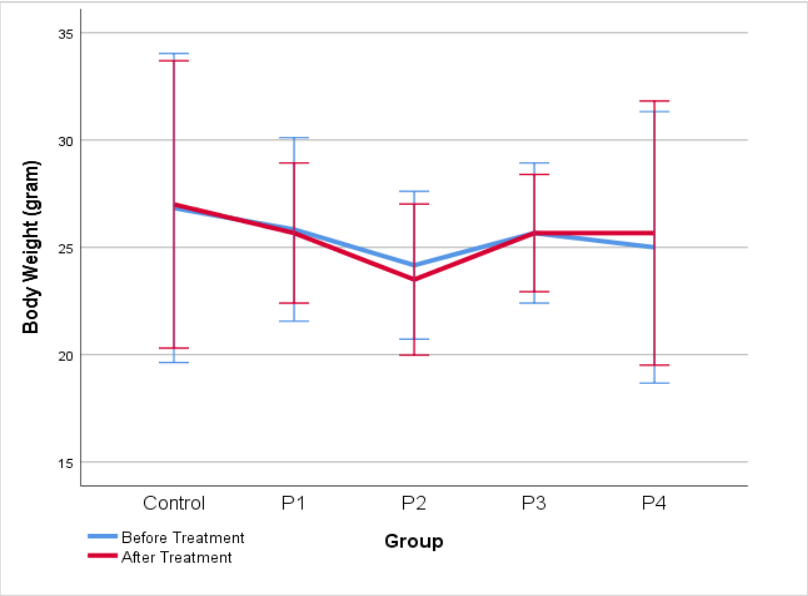

Figure 1. Average Body Weight of Test Animals Before and After Treatment

Table 1. ANOVA Test of the Mean Body Weight Difference of Test Animals

Group	Mean Body Weight (g) ± SD Observed on Day–				Body Weight
	0	9	16	21	Change (%) ± Sig.
Control	26.83 ± 3.60	27.67 ± 3.33	27.00 ± 3.35	27.33 ± 3.78	1.863 ± 0.000
P1	25.83 ± 2.14	26.17 ± 1.72	25.67 ± 1.63	25.67 ± 1.63	0.645± 0.040
P2	24.17 ± 1.72	23.67 ± 1.75	23.50 ± 1.76	23.50 ± 2.43	2.759± 0.000
P3	25.67 ± 1.63	26.50 ± 1.52	25.67 ± 1.37	25.67 ± 1.37	0.000± 0.045
P4	25.00 ± 3.16	25.17 ± 3.06	25.67 ± 3.08	25.17 ± 3.06	0.667± 0.001

The data in Table 1 show P > 0.05 for all groups, indicating that the mean body weight of the test animals did not differ significantly from baseline (day 0) to the end of the treatment period (day 21). These findings also demonstrate that the body weights of animals receiving Copasanda tea bag treatment did not differ notably from those in the control group. The percentage changes in body weight during the treatment period were 1.863% in the normal group, 0.645% in doses 50 mg/kg BW group (P1), 2.759% in doses 300 mg/kg BW group (P2), 0% in doses 1000 mg/kg BW group (P3), and 0.667% in doses 2000 mg/kg BW group (P4). All weight-change percentages <20%. Animals are considered to experience pain or distress when body weight fluctuates by >20% during treatment (Tedjasulaksana et al., 2023). Thus, the body-weight variations observed in this study do not indicate any toxic symptoms such as discomfort or distress during administration of Copasanda tea bags.

Table 2. Number of Animal Deaths During Treatment

Groups	Doses	Number of Mice	Number of Deaths	Number of Survivors	PI
Control	CMC-Na 0.5%	6	0	6	0
P1	50 mg/Kg BW	6	0	6	0
P2	300 mg/Kg BW	6	0	6	0
P3	1000 mg/Kg BW	6	0	6	0
P4	2000 mg/Kg BW	6	0	6	0

Table 2 showed that none of the study animals perished throughout the duration of the Copasanda tea bag administration, neither in the control group nor in the treatment groups across all tested concentrations. This evidence strongly suggests that Copasanda tea bags are non-toxic within the tested range of 50 to 2000 mg/Kg BW. Although a minor hyperactivity symptom was observed in the highest dose group (2000 mg/Kg BW), as referenced in Table 3.

Table 3. Toxicological Symptoms Observed During the Treatment

Toxic Symptoms	Groups				
	Control	P1 (50 mg/Kg BW)	P2 (300 mg/Kg BW)	P3 (1000 mg/Kg BW)	P4 (2000 mg/Kg BW)
Tremor	−	−	−	−	−
Diarrhea	−	−	−	−	−
Weakness	−	−	−	−	−
Backward Walking	−	−	−	−	−
Hair Loss	−	−	−	−	−
Hyperactivity	−	−	−	−	+
Salivaton	−	−	−	−	−

Table 2 showed that none of the study animals perished throughout the duration of the Copasanda tea bag administration, neither in the control group nor in the treatment groups across all tested concentrations. Crucially, major toxic signs such as tremor, diarrhea, muscle weakness (lemas), backward movement, and salivation were completely absent in every experimental cohort. The mice maintained a normal gait without backward movement, and no hair loss was observed. Although a minor hyperactivity symptom was observed in the highest dose group (2000 mg/Kg BW), as referenced in Table 3. Hyperactivity may indicate a condition in which the test animals become more active than usual. This response suggests a possible alteration in the nervous system. However, doses of 50–1000 mg/kg BW did not cause any toxic effects (Putra *et al.*, 2023). Organ index measurements

were performed on day 21 at the end of the experiment. All animals in both the control group and the Copasanda tea treatment groups were euthanized by cervical dislocation, after which internal organs including the liver, spleen, thymus, left kidney, right kidney, and heart were collected. Each organ was carefully weighed, and the organ index was calculated as the organ weight divided by the animal's body weight (Chen *et al.*, 2022). The mean organ indices for each group are presented in Table 4. In comparison, the results of the post hoc LSD statistical analysis are shown in Table 5 to determine differences in organ indices between the Copasanda tea treatment bag groups and the control group.

Table 4. Organ Index of the Toxicity Test

Organ/Groups	Mean Organ Weight (g) ± SD				
	Control	P1	P2	P3	P4
Liver	4.89 ± 1.06	5.34 ± 0.62	4.58 ± 0.96	4.81 ± 0.67	3.84 ± 0.41
Spleen	0.55 ± 0.21	0.86 ± 0.25	0.51 ± 0.21	0.72 ± 0.28	0.48 ± 0.09
Thymus	0.22 ± 0.06	0.25 ±0.06	0.32 ± 0.15	0.27 ± 0.08	0.44 ± 0.16
Left Kidney	0.64 ± 0.06	0.64 ±0.13	0.63 ± 0.07	0.61 ± 0.07	0.52 ± 0.07
Right Kidney	0.55 ± 0.04	0.61 ± 0.09	0.60 ± 0.06	0.59 ± 0.09	0.59 ± 0.06
Heart	0.46 ± 0.08	0.47 ± 0.11	0.43 ± 0.11	0.47 ± 0.13	0.47 ± 0.07

Table 4 reveals that the average organ indices across the Copasanda tea bag groups and the control cohort were largely comparable. Nevertheless, the liver index for the highest-dose group, P4 (2000 mg/Kg BW), measured 3.84 grams, representing a decrease of 1.05 grams compared to the control. In addition to the liver, the 2000 mg/Kg BW concentration also resulted in a thymus index that was twice that of the control group, and the left kidney index was also statistically different from the control. Conversely, data from Table 5 confirmed that all organs within the 50 to 1000 mg/Kg BW range were statistically similar to the control group (P>0.05), except for the spleen index at the 50 mg/Kg BW concentration.

Table 5. Results of the Post Hoc LSD Test between the Treatment Group and the Control

Group	Liver	Spleen	Thymus	Left Kidney	Right Kidney	Heart
P1	0.331	0.024*	0.661	0.918	0.164	0.890
P2	0.483	0.755	0.107	0.863	0.202	0.620
P3	0.849	0.191	0.441	0.537	0.297	0.868
P4	0.028*	0.585	0.002*	0.024*	0.279	0.912

Description:*statistically significant difference

The level of toxicity can affect vital organs involved in metabolism and detoxification, including the heart, lungs, spleen, liver, kidneys, thymus, and other visceral organs. Therefore, all test animals both those that survived and those that died must undergo necropsy to evaluate organ conditions through macroscopic observation. Organ damage resulting from exposure to toxic substances is generally identifiable through changes in organ size, either enlargement or shrinkage (Ifana, Andriyanto and Pristihadi, 2024). Copasanda tea bag solution at the highest dose (2000 mg/kg BW) showed a significant difference in organ indices of the liver, thymus, and left kidney compared with the control group ($P < 0.05$; Table 5). At this dose, the left kidney of the test animals showed a size reduction (Table 4). This condition is presumed to be associated with the presence of saponin compounds in Copasanda (Amalia, Pratiwi, Ryn and Erwin, 2022) , the potential to exert toxic effects on the kidneys, liver, and thymus.

Saponins are known to disrupt cell membranes, leading to erythrocyte lysis. The hemolytic process releases hemoglobin and iron (Fe). The released iron is subsequently transported to the reticuloendothelial system or hepatic macrophages and reutilized in erythropoiesis. Iron accumulation in liver tissue may enhance the formation of free radicals. These free radicals can damage lipid and protein structures in cellular membranes and organelles, ultimately triggering necrosis or membrane leakage (Lesmana, Setiawan and Pranitasari, 2022). This mechanism is presumed to underlie the observed liver shrinkage at the highest dose of the Copasanda tea bags.

α-Glucosidase Inhibition Assay

The alpha-glucosidase enzyme plays a pivotal role in regulating postprandial blood glucose levels by hydrolyzing complex carbohydrates (starch, disaccharides) into absorbable monosaccharides (glucose) within the small intestine brush border. Excessive alpha-glucosidase activity leads to rapid glucose absorption, resulting in postprandial hyperglycemia, a primary pathological feature of diabetes. Consequently, the alpha-glucosidase inhibition assay is a crucial in vitro experiment method used to evaluate the potential of Copasanda plant extracts or isolated compounds to act as effective antidiabetic agents (Sun, Li and Wang, 2023). The purpose of this test is to quantify the ability of a test substance to reduce the catalytic rate of the alpha-glucosidase enzyme, mimicking the action of established pharmaceutical inhibitors like acarbose (Dewi, Handayani and Handayani, 2024).

The principle of the alpha-glucosidase inhibition assay relies on spectrophotometric quantification of the Copasanda tea bags released by the enzyme during its catalytic reaction. The standard substrate used is p-nitrophenyl-alpha-D-glucopyranoside (p-NPG), a chromogenic molecule. Enzyme Reaction: In the absence of an inhibitor, alpha-glucosidase hydrolyzes p-NPG into glucose and p-nitrophenol (p-NP). Chromophore Detection: The product, p-NP, is a yellowish compound that absorbs light strongly at 405 nm. Inhibition Measurement: When a potential inhibitor, Copasanda tea bags, is present, the rate of p-NP production decreases. By measuring the absorbance difference between the control reaction (no inhibitor) and the inhibited reaction (with Copasanda

tea), the percentage of inhibition can be calculated. Inhibitory strength is often expressed as the IC_{50} value, the concentration required to inhibit 50% of enzyme activity (Swargiary, Roy and Mahmud, 2022). Based on the α-glucosidase inhibitory activity data in Table 6, Copasanda tea shows good inhibitory activity comparable to that of acarbose. Therefore, Copasanda tea can be utilized as an antidiabetic agent. The α-glucosidase enzyme inhibitor activity data for Copasanda tea and acarbose, used as a comparative standard, are presented in Table 6. Based on the α-glucosidase inhibitory activity data in Table 6, the percentage inhibition of Copasanda tea bags at low concentrations is 43.4%, and the highest inhibition (98%) is observed at a dose of 2000 mg/Kg BW. The inhibition percentages at concentrations of 300–1000 mg/Kg BW are also above 50%. Based on these inhibition values, Copasanda tea shows good inhibitory activity comparable to that of acarbose.

Table 6. alpha-Glucosidase Inhibitory Activity of Copasanda Tea Bags Compared with Acarbose

Sample	Consentration (ppm)	Absorbance					
		Blank	Control Blank	Control Sample (S0)	Sample (S1)	%inhibisi	IC_{50} (µg/mL)
Acarbose	0,05	0,453	0,354	0,018	0,176	36,0	0,24
	0,3			0,023	0,137	53,8	
	0,5			0,017	0,115	60,3	
	0,8			0,012	0,085	70,4	
	1			0,016	0,076	75,7	
	2			0,013	0,019	97,6	
Copasanda Tea Bags	50	0,601	0,354	0,028	0,084	43,4	29,00
	300			0,038	0,080	57,6	
	500			0,041	0,077	63,6	
	800			0,049	0,074	74,7	
	1000			0,055	0,071	83,8	
	2000			0,063	0,065	98,0	

The mechanism of enzyme inhibition by the bioactive compounds in Copasanda tea, particularly flavonoids, phenolic acids, and alkaloids, demonstrates an α-glucosidase inhibitory effect. These compounds generally follow a mechanism similar to synthetic drugs: secondary metabolites, especially polyhydroxy flavonoids (such as quercetin and luteolin), possess molecular structures that enable them to bind effectively to the active site of the α-glucosidase enzyme (Lam *et al.*, 2024). Docking results of flavonoid compounds from the Copasanda plant also show their ability to interact with the PDB ID 2HV5 receptor, which forms a complex with the inhibitor zopolrestat. This indicates that the flavonoids present in Copasanda have strong potential as antidiabetic agents (Wiyati, Alfitroh and Hardini, 2025) The obtained percentage inhibition values were used to calculate

the IC_{50} (the concentration required to inhibit 50% of enzyme activity) for Copasanda tea and acarbose as a comparator. The IC_{50} value is used to determine the inhibitory strength of Copasanda tea against the α-glucosidase enzyme. The lower the IC_{50} value, the greater the inhibitory activity against α-glucosidase, and vice versa (Maryam, Sehaenah and Amrullah, 2020).

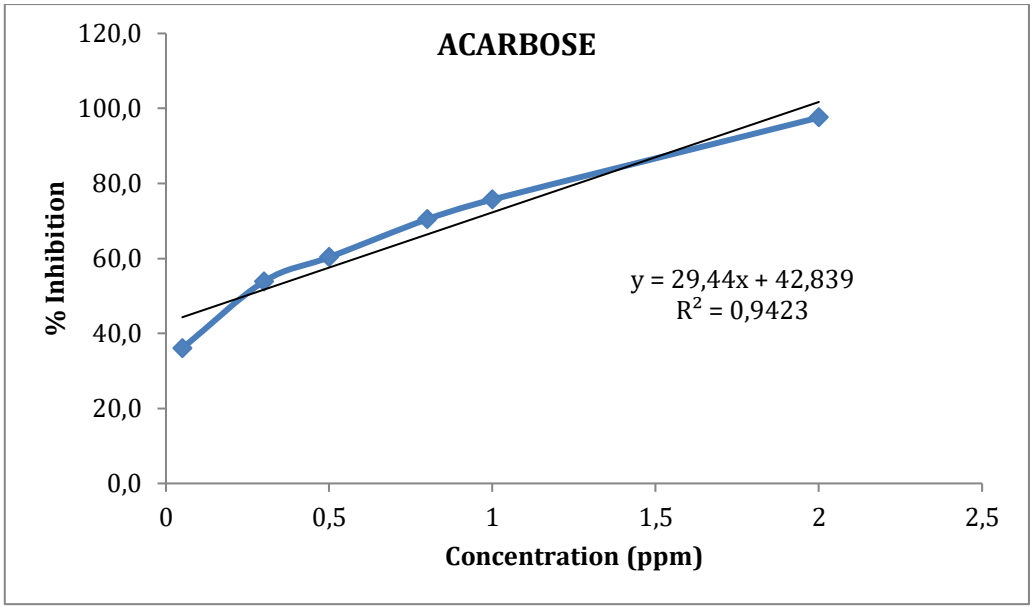

Figure 2. α-Glucosidase Enzyme Inhibition Activity of Standard Acarbose

The measurement of α-glucosidase inhibition percentage at various concentrations is presented in Figure 2 (acarbose) and Figure 3 (Copasanda tea bag). Linear regression in Figure 2 yields the equation y = 29.44x + 42.839 with R^2 = 0.9423, while in Figure 3 the regression equation is y = 0.0271x + 49.214 with R^2 = 0.9195. Based on these regression equations, the IC50 values obtained for acarbose and the Copasanda tea bag extract are 0.24 ppm and 29.1 ppm, respectively.

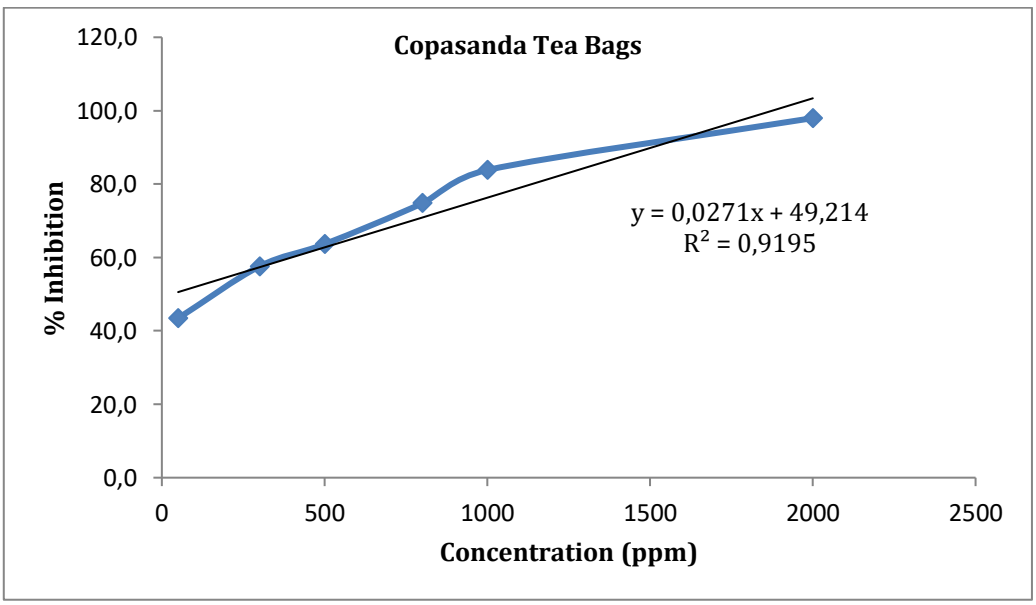

Figure 3. α-Glucosidase Enzyme Inhibition Activity of Copasanda Tea Bags

These findings are consistent with reports that acarbose has a high affinity for the active site of α-glucosidase in in vitro assays and generally exhibits a relatively low IC_{50} (Akmal, Patel and Wadhwa, 2024), indicating that acarbose has a much stronger inhibitory potential (lower IC_{50}) than Copasanda tea bags. However, Copasanda tea bags still show increasing inhibitory activity with increasing concentration and achieve high inhibition percentages at 500–2000 ppm (Figures 2–3). Although the IC_{50} of the Copasanda tea bag is higher than that of acarbose, it still exhibits very strong antidiabetic potential because the IC_{50} value is < 50 μg/mL (Rahmawati *et al.*, 2025), namely 29.1 μg/mL. The inhibitory strength is strongly presumed to originate from the secondary metabolites contained in Copasanda leaves, such as flavonoids, phenolics, and quinones (Lesmana, Suryani and Wijaya, 2023). The inhibitory activity of Copasanda extract can inhibit α-glucosidase through non-covalent interactions (hydrogen bonding, intermolecular interactions, and hydrophobic interactions) with the enzyme's active-site residues or allosteric sites. These compounds bind to the active site of the α-glucosidase enzyme, alter its conformation, and effectively inhibit the breakdown of complex carbohydrates (Putra, Sari and Kholid, 2024). Therefore, phytochemically, Copasanda (a complex mixture of polyphenolics) may explain why its inhibitory activity is strong, although not as strong as acarbose.

CONCLUSION

The toxicity test results for Copasanda tea bags (Chromolaena odorata L.) showed no mortality at any administered dose. However, at a dose of 2000 mg/Kg BW, toxic symptoms were observed in the form of hyperactive behavior and a reduction in the organ index of the liver, thymus, and left kidney. The α-glucosidase inhibition assay showed an inhibitory activity (IC50) of 29 μg/mL, which falls into the category of very strong inhibition. Copasanda tea bags are effective as an antidiabetic agent and safe for long-term use at doses of 50–1000 mg/Kg BW, whereas higher doses may cause toxic symptoms. Future research is recommended to further evaluate the chronic toxicity and long-term safety profile of Copasanda tea bags, as well as to investigate their pharmacological mechanisms and efficacy through in vivo antidiabetic studies and clinical trials in humans. Additionally, studies on the standardization of active compounds and optimization of dosage in herbal tea formulations are needed to ensure product safety, effectiveness, and quality for wider community use.

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