

Diuretic and Antihyperglycemic Potential of Screwpine (*Pandanus martellii* Elmer) in Female Albino Mice

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Abstract

This study evaluated the phytochemical constituents, acute oral toxicity, diuretic activity, and antihyperglycemic potential of the roots, fruits, and leaves of *Pandanus martellii* as a potential plant-based therapeutic agent for diabetes mellitus and hypertension. Anchored on the concept that phytochemicals possess biological activities that promote glucose regulation, antioxidant defense, and diuresis, the study employed a Completely Randomized Design using female Swiss albino mice assigned to treatment and control groups. Ethanolic extracts of *P. martellii* at doses of 100, 200, and 400 mg/kg were evaluated through qualitative phytochemical screening, acute oral toxicity testing, diuretic assays, and antihyperglycemic assessment using standard laboratory procedures. Data were analyzed using mean values, three-way Analysis of Variance (ANOVA), and Tukey's Honestly Significant Difference (HSD) test. The results confirmed the presence of alkaloids, flavonoids, saponins, glycosides, tannins, phenols, and other bioactive compounds. Acute oral toxicity testing demonstrated no mortality or severe toxic effects at 2000 mg/kg, indicating a favorable safety profile. The root extract exhibited the strongest diuretic activity, while the leaf extract at 100 mg/kg produced the greatest antihyperglycemic effect. Statistical analysis showed significant treatment effects on blood glucose levels, whereas diuretic responses among plant parts and dosage levels were generally comparable despite significant time-dependent changes. The findings demonstrate that *P. martellii* possesses promising diuretic and antihyperglycemic properties and may serve as a potential natural therapeutic alternative for managing diabetes and hypertension. Further studies are recommended to isolate the active compounds, investigate their mechanisms of action, evaluate chronic toxicity, optimize dosage, conduct clinical trials, and develop standardized pharmaceutical formulations. This study supports Sustainable Development Goal (SDG) 3: Good Health and Well-Being by exploring a potential plant-based therapeutic alternative for chronic diseases and SDG 9: Industry, Innovation and Infrastructure by providing scientific evidence that may contribute to the development of natural therapeutic products. The findings also promote public health and pharmaceutical sustainability by expanding scientific knowledge on indigenous medicinal plants and supporting future drug discovery and pharmacological research.

Keywords: Acute Oral Toxicity, Antihyperglycemic Activity, Diuretic Activity, *Pandanus Martellii*, Phytochemical Constituents, Swiss Albino Mice

1. Introduction

Diabetes mellitus and hypertension remain major global and national public health concerns due to their increasing prevalence, high mortality, and shared contribution to cardiovascular and metabolic complications. Conventional pharmacologic management often requires multiple medications, increasing the risk of adverse drug interactions and limiting treatment accessibility. Consequently, medicinal plants have gained attention as potential alternative therapeutic agents. Among these, *Pandanus martellii* has emerged as a promising but understudied species with potential antihyperglycemic and diuretic properties. This study evaluates the phytochemical constituents, acute oral toxicity, diuretic activity, and antihyperglycemic efficacy of the roots, fruits, and leaves of *P. martellii* to provide scientific evidence supporting its possible application in alternative medicine.

1.1 Background of the Study

Diabetes mellitus is a chronic metabolic disease characterized by impaired insulin production or action, resulting in persistent hyperglycemia and long-term organ damage (WHO, 2016; Tiwari et al., 2022). Diabetes and hypertension commonly coexist, increasing the risk of cardiovascular disease and other complications (Chukwuma et al., 2019). In the Philippines, both diseases remain among the leading causes of mortality (Philippine Statistics Authority, 2026). Diuretics are widely used as first-line antihypertensive drugs, but the concurrent use of antihypertensive and antidiabetic medications may increase adverse drug interactions. Consequently, medicinal plants are being explored as alternative sources of safer

therapeutic agents. *Pandanus martellii* is considered a promising candidate because of its potential antihyperglycemic and diuretic activities.

1.2 Themes and Insights from Related Literature

Studies show that species of the Pandanaceae family contain bioactive compounds such as flavonoids, phenolics, alkaloids, saponins, tannins, terpenoids, and steroids that exhibit antioxidant, anti-inflammatory, antihyperglycemic, and diuretic properties (Brink & Jansen, 2003; PROSEA – Plant Resources of Southeast Asia, 2025; Pelser, 2023; Quyen et al., 2020; Chiabchalard & Nooron, 2015). Several *Pandanus* species, particularly *P. tectorius*, have demonstrated diuretic, antihyperglycemic, anti-inflammatory, antibacterial, and antihyperlipidemic activities, supporting their traditional medicinal use (Quisumbing (1978), as cited by Tan et al. (2014); Matondang and Rahayu (2022); del Mundo et al. (2020); Chingming et al., 2018; Wang et al., 2011; Wu et al. (2013); Baba et al., 2016; Tan et al. (2014); Adriana et al. (2015); Meharie & Tunata (2020)). Likewise, several *Pandanus* species have shown significant glucose-lowering effects through improved insulin sensitivity and antioxidant activity (Suvannaporn et al., 2014; Wu et al., 2014; Patel et al., 2012; Vijayakumar et al., 2013). However, *Pandanus martellii* remains poorly studied, warranting investigation of its phytochemical composition and therapeutic potential.

1.3 Local, National, and Global Context

Globally, diabetes and hypertension continue to increase and remain leading contributors to morbidity and mortality (Chukwuma et al., 2019). In the Philippines, Diabetes mellitus and heart diseases are among the top causes of death, emphasizing the need for effective and accessible treatment alternatives (Philippine Statistics Authority, 2026). Traditional medicinal plants, including species of the *Pandanus* genus, have long been utilized in Southeast Asia and the Philippines for various therapeutic purposes, highlighting their potential as complementary sources of antihyperglycemic and diuretic agents (Quisumbing, 1951; Quisumbing (1978), as cited by Tan et al. (2014); Pelser et al., 2011).

1.4 Theoretical or Conceptual Basis

The study is anchored on the concept that phytochemicals such as flavonoids, phenolics, saponins, tannins, and caffeoylquinic acids possess biological activities that promote glucose regulation, antioxidant defense, and diuresis. Previous studies demonstrated that these compounds improve insulin sensitivity, inhibit carbohydrate digestion, reduce oxidative stress, and enhance urine production, supporting the therapeutic potential of *Pandanus* species (Quyen et al., 2020; Chiabchalard & Nooron, 2015; Wu et al., 2014; Vijayakumar et al., 2013; Meharie & Tunata, 2020).

1.5 Research Gaps and Rationale

Although several *Pandanus* species have been reported to possess antihyperglycemic and diuretic properties, *Pandanus martellii* remains poorly investigated. Existing studies largely focus on other species, while information regarding the phytochemical composition, biological characteristics, and pharmacological potential of *P. martellii* is lacking. This study addresses these gaps by evaluating the phytochemical constituents, toxicity, diuretic activity, and antihyperglycemic efficacy of the roots, fruits, and leaves of *P. martellii*.

1.6 Alignment with Relevant Sustainable Development Goals (SDGs)

This study supports SDG 3 – Good Health and Well-Being by exploring a potential plant-based alternative for managing diabetes and hypertension. It also aligns with SDG 9 – Industry, Innovation and Infrastructure by providing scientific evidence that may contribute to the development of natural therapeutic products derived from indigenous plant resources.

1.7 Importance of the Study to Multidisciplinary Sustainability

The study contributes to public health sustainability by investigating affordable alternative therapies for chronic diseases. It also promotes scientific and pharmaceutical sustainability by expanding knowledge on indigenous medicinal plants that may support future drug discovery and encourage further pharmacological research on *Pandanus martellii*.

2. Material and methods

2.1 Research Design

The study employed a Completely Randomized Design (CRD) using ten mice per treatment group. Experimental doses were based on the LD₅₀ obtained from the acute oral toxicity test, with the median dose set at one-tenth of the LD₅₀ and supplemented by lower and higher doses. The experiment consisted of a negative control, a positive control (Furosemide for diuretic activity and Metformin for antihyperglycemic activity), and treatment groups receiving 100, 200, and 400 mg/kg ethanolic extracts of the fruits, roots, and leaves of *P. martellii*. The conceptual framework illustrates that the independent variable, *P. martellii* ethanolic extracts, exerts physiological effects through its phytochemical constituents, resulting in reduced blood glucose levels and increased urine output. Experimental animal characteristics, environmental conditions, and treatment duration were maintained as control variables to minimize confounding factors and ensure that observed effects were attributable to the plant extracts.

2.2 Locale of the Study

The study was conducted at the Science Building Laboratory of Isabela State University–Echague. Fresh and mature roots, fruits, and leaves of *P. martellii* were collected from a riverbank in Echague, Isabela. Plant samples were cleaned, air-dried, and taxonomically verified by the Museum of Natural History, University of the Philippines Los Baños, Laguna before extraction.

2.3 Respondents of the Study

The experimental subjects were female Swiss albino mice aged 8–10 weeks and weighing 20–30 g. Female mice were selected because of their greater sensitivity in toxicity studies. Before experimentation, the animals underwent a seven-day acclimatization period under controlled laboratory conditions ($25 \pm 2^\circ\text{C}$, $60 \pm 4\%$ relative humidity, and a 12-hour light-dark cycle) with unrestricted access to food and water (OECD, 2001).

2.4 Sample and Sampling Procedure

Fresh plant materials were extracted through ethanol maceration using a 1:10 (g/v) ratio of plant powder to 95% ethanol for 48 hours. The filtrate was concentrated using a rotary evaporator at a maximum temperature of 50°C and stored until use (Mahi et al., 2022). Qualitative phytochemical screening of the ethanolic extracts was conducted following the procedures of Sofowora (1993) to detect flavonoids, alkaloids, steroids, glycosides, saponins, tannins, and phenolic compounds based on characteristic color changes or precipitate formation. Acute oral toxicity was evaluated following OECD (2001) guidelines. Mice received a single oral dose of 2000 mg/kg extract after overnight fasting and were monitored for mortality, behavioral changes, physical abnormalities, and body weight over a 14-day observation period. For the diuretic assay, Furosemide was prepared as the positive control, and urine samples were collected hourly for five hours using the Modified Multiple Animal Method described by Kurien and Scofield (2024). Hyperglycemia was induced through intraperitoneal dexamethasone administration (5 mg/kg) for ten consecutive days, after which fasting blood glucose levels were measured using a glucometer to identify hyperglycemic mice. Metformin served as the positive control for antihyperglycemic evaluation. Blood glucose measurements were obtained at baseline and on Days 7 and 14 using tail vein blood samples collected under appropriate restraint techniques.

2.5 Research Instrument

The study utilized laboratory instruments and standard experimental procedures for plant extraction, phytochemical analysis, toxicity testing, diuretic assessment, and blood glucose determination. Plant extracts were prepared through ethanol maceration and rotary evaporation, while qualitative phytochemical tests followed Sofowora (1993). Blood glucose levels were measured using a glucometer, urine output was collected through the Modified Multiple Animal Method, and Furosemide and Metformin served as standard reference drugs for diuretic and antihyperglycemic evaluation, respectively (Sofowora, 1993; Mahi et al., 2022; OECD, 2001; Kurien and Scofield, 2024).

2.6 Data Gathering Procedure

All experimental procedures were conducted in a controlled laboratory environment following the approved IACUC ethical guidelines. Experimental mice were acclimatized for one week under standard laboratory conditions before treatment. Throughout the study, animals were handled carefully to minimize stress and discomfort while ensuring proper ventilation, food, and water. Plant extracts, Furosemide, and Metformin were administered according to the experimental design, and all observations and measurements were recorded systematically to maintain consistency and accuracy. Blood glucose levels were measured using tail vein blood samples obtained through the tube-restraint technique, while dexamethasone was administered using the scruffing technique. Urine samples were collected at designated intervals to evaluate diuretic activity, and all physiological responses were documented throughout the experimental period.

2.7 Data Analysis Techniques

The collected data were summarized using mean values. Differences in blood glucose levels among treatment groups and across different time intervals were analyzed using a three-way Analysis of Variance (ANOVA) through R software. When significant differences were detected, Tukey's Post Hoc Honestly Significant Difference (HSD) test was performed to identify which treatment groups differed significantly, thereby supporting reliable interpretation of the experimental findings.

2.8 Ethical Considerations

Prior to the conduct of the study, ethical approval was obtained from the Institutional Animal Care and Use Committee (IACUC) of Isabela State University–Echague. All experimental procedures complied with IACUC guidelines to ensure the humane treatment of laboratory animals by minimizing stress, discomfort, and unnecessary suffering throughout the experiment. Animal health and welfare were continuously monitored during the study. Artificial intelligence (AI) tools were used solely for grammar checking and citation formatting, while all interpretations, analyses, and conclusions remained the original work of the researchers. Laboratory waste disposal was carried out responsibly, and any indigenous knowledge associated with *Pandanus martellii* was appropriately acknowledged and respected.

3. Results and Discussion

3.1 Phytochemical Composition and Safety Evaluation

3.1.1 Phytochemical Constituents of *P. martellii*

The phytochemical screening revealed that the roots, leaves, and fruits of *P. martellii* contained several bioactive compounds. Alkaloids, flavonoids, and saponins were detected in all plant parts. Tannins and phenols were present in the roots and leaves but absent in the fruits, while glycosides were detected in the roots and fruits but not in the leaves. Overall, the roots and fruits exhibited a greater diversity of phytochemical constituents than the leaves, suggesting higher pharmacological potential. The presence of these phytochemicals supports the medicinal value of *P. martellii*. Similar findings were reported by Vo et al. (2022), Dumaoal et al. (2010), and Navera et al. (2013), who identified comparable bioactive compounds in Pandanus species. Alkaloids possess therapeutic and antimicrobial properties (Roy, 2017; Kaur and Arora, 2015), while saponins exhibit diverse pharmacological applications (Nguyen et al., 2020; Cheok et al., 2014; Singh and Chaudhuri, 2018; Aziz et al., 2019; Sochacki and Vogt, 2022; Amraei and Ahmadi, 2022). Tannins contribute antioxidant and pharmaceutical benefits (Farha et al., 2020; Okuda and Ito, 2011; Bachran et al., 2008; Bang et al., 2005; Catalan et al., 2010), glycosides possess therapeutic potential (Deshpande et al., 2017; Aboul-enein et al., 2014), and flavonoids are recognized for their antioxidant, anti-inflammatory, and antihyperglycemic activities (Gorniak et al., 2019; Narendra, 2024; Hossain et al., 2012; LeJeube et al., 2015; Panche et al., 2016).

3.1.2 Acute Oral Toxicity of *P. martellii* Extract

Acute oral toxicity testing demonstrated that mice administered 2000 mg/kg of *P. martellii* extract showed no mortality or significant toxic manifestations during the 14-day observation period. No abnormalities were observed in fur, skin, eyes, salivation, respiration, urination, fecal consistency, mucous membranes, or convulsions. Mild itching and increased activity were observed only during the first 30 minutes after administration. Overall, the extract exhibited an approximate lethal dose greater than 2000 mg/kg, indicating a favorable safety profile. The absence of mortality and toxic signs indicates that *P. martellii* extract is relatively safe for acute administration. These findings agree with previous studies reporting no mortality or significant behavioral abnormalities following administration of similar plant extracts at 2000 mg/kg (Shukor et al. (2018); Sireeratawog et al. (2016); Castillo et al. (2023)). The lack of observable toxicity also supports the findings of Saleem et al. (2017), who emphasized that metabolic toxicity primarily affects major organs such as the liver, kidneys, heart, and lungs. Collectively, these results suggest that *P. martellii* possesses low acute toxicity and may be considered safe for further pharmacological evaluation.

3.2 Diuretic Potential of *P. martellii* Extracts

3.2.1 Diuretic Activity of Fruit Extract

The fruit extracts of *P. martellii* increased urine output in experimental mice, with the 400 mg/kg dose producing the highest diuretic response, followed by the 200 mg/kg and 100 mg/kg doses. Urine output was greatest during the first hour of treatment and gradually declined over the succeeding hours. During the fourth and fifth hours, urine output among treatment groups became similar, indicating a reduction in the diuretic effect over time. The highest fruit dose showed urine output comparable to the positive control (Furosemide) during the early observation period, suggesting a dose-related response. The observed increase in urine production indicates that *P. martellii* fruit extract possesses diuretic activity. The gradual decline in urine output over time suggests that the extract's pharmacological effect diminishes as its active compounds are metabolized and eliminated. These findings support the potential of the fruit extract as a natural diuretic, particularly at higher doses.

3.2.2 Diuretic Activity of Root Extract

Root extracts also demonstrated positive diuretic activity. During the first hour, the 100 mg/kg dose produced the highest urine output, followed by the positive control, 400 mg/kg, 200 mg/kg, and the negative control. Unlike the fruit extract, the 200 mg/kg dose exhibited a delayed increase in urine output during the second hour before declining steadily. Overall, all root treatments showed decreasing urine output throughout the observation period, with 100 mg/kg producing the greatest overall diuretic response. These findings indicate that the root extract effectively promotes diuresis; however, increasing the dose did not necessarily enhance its effect. The delayed response observed at 200 mg/kg suggests that different doses may vary in their onset of action rather than their overall efficacy.

3.2.3 Comparative Diuretic Effects of Plant Parts

Across all plant parts, urine output generally declined over the five-hour observation period after an initial increase. The root extract produced relatively greater urine output during the early hours compared with the leaf and fruit extracts, indicating a stronger initial diuretic response. Overall, the findings suggest that *P. martellii*, particularly its root extract, possesses compounds capable of increasing urine production. The stronger early response of the root extract may be attributed to its phytochemical composition. The presence of flavonoids, alkaloids, saponins, and tannins may enhance renal blood flow, increase glomerular filtration, and reduce electrolyte reabsorption, thereby promoting urine production.

The decline in urine output over time likely reflects reduced pharmacological activity as the bioactive compounds are metabolized.

3.2.4 Statistical Analysis of Diuretic Activity

Statistical analysis showed no significant differences in urine output among the root, leaf, and fruit extracts, indicating that the three plant parts produced comparable diuretic effects. Likewise, comparisons among the 100, 200, and 400 mg/kg doses revealed no significant differences. However, urine output differed significantly across observation times, with significant changes occurring during the earlier hours and a plateau observed between the third and fifth hours. Despite the absence of statistically significant differences among plant parts and doses, the observed biological responses may be explained by the shared phytochemical constituents of *P. martellii*. Flavonoids, saponins, alkaloids, and glycosides have been reported to enhance renal blood flow, increase glomerular filtration, and promote electrolyte excretion (Dearing et al., 2018; Aneja et al., 2013; Evans, 2009). The similar responses among treatments may also result from synergistic interactions among phytochemicals, producing comparable pharmacological effects despite differences in composition (Wagner & Ulrich-Merzenich, 2009). These findings are consistent with previous reports demonstrating that plants containing multiple bioactive compounds often exhibit similar physiological responses (Vo et al., 2022). Furthermore, the significant time-dependent response agrees with studies showing that diuretics produce rapid increases in urine output followed by stabilization as peak activity is reached (Goodman & Gilman, 2018; Rang & Dale, 2019; Khan et al., 2014; Afsar et al., 2012). Collectively, these findings support the potential of *P. martellii* as a natural diuretic.

3.3 Antihyperglycemic Potential of *P. martellii* Extracts

3.3.1 Antihyperglycemic Activity of Fruit Extract

All fruit extract treatments reduced blood glucose levels from Day 0 to Day 14. The 100 mg/kg dose produced the greatest reduction, decreasing from 146 mg/dL to 123 mg/dL, while the 400 mg/kg dose also showed a steady decline. The 200 mg/kg dose exhibited the least reduction. Although all treatments lowered blood glucose, their effects were less pronounced than the positive control. These findings indicate that the fruit extract possesses antihyperglycemic activity but does not exhibit a dose-dependent response. The reduction in blood glucose suggests that the fruit extract contains bioactive compounds capable of improving glucose regulation. However, the lack of a dose-dependent effect indicates that increasing the concentration does not necessarily enhance antihyperglycemic activity, suggesting that optimal efficacy may occur at lower doses.

3.3.2 Antihyperglycemic Activity of Root Extract

Root extracts also demonstrated consistent reductions in blood glucose levels throughout the treatment period. Among the doses tested, 200 mg/kg produced the greatest reduction, lowering blood glucose from 139 mg/dL at baseline to 104 mg/dL by Day 14, making its effect comparable to Metformin. The 100 mg/kg and 400 mg/kg doses also reduced glucose levels but were less effective than the 200 mg/kg treatment. These findings indicate that the root extract possesses significant antihyperglycemic activity, with 200 mg/kg representing the most effective dose. The results suggest that the therapeutic response depends on an optimal concentration rather than increasing dosage alone.

3.3.3 Antihyperglycemic Activity of Leaf Extract

The leaf extracts exhibited progressive reductions in blood glucose levels across all treatment groups. The 100 mg/kg dose produced the greatest decrease, from 149.5 mg/dL to 82.33 mg/dL by Day 14, outperforming both the higher doses and the positive control. The 200 mg/kg dose also demonstrated substantial glucose reduction, while the 400 mg/kg dose showed a slight increase between Day 0 and Day 7 before declining sharply by Day 14, suggesting a delayed response. Overall, the leaf extract at 100 mg/kg showed the strongest antihyperglycemic effect among all treatments. The marked reduction in blood glucose indicates that the leaf extract possesses potent antihyperglycemic properties. The delayed response observed at the highest dose suggests that higher concentrations may alter the onset of pharmacological activity without improving overall efficacy. These findings highlight the effectiveness of lower-dose leaf extracts in glucose regulation.

3.3.4 Statistical Analysis and Therapeutic Significance

Baseline measurements confirmed that all mice were hyperglycemic before treatment. Significant reductions in blood glucose were observed across treatment groups over time, with the 100 mg/kg leaf extract producing the greatest decrease, followed by the 200 mg/kg root extract. Post-hoc analysis showed that only selected pairwise comparisons, primarily involving the 100 mg/kg leaf extract, were statistically significant. Effect size analysis further demonstrated that treatment type and the interaction between treatment and time had large biological effects, whereas body weight and time alone had relatively small effects. The antihyperglycemic activity of *P. martellii* is supported by its phytochemical constituents, particularly flavonoids, alkaloids, tannins, and saponins, which have been associated with antioxidant activity, improved insulin sensitivity, enhanced glucose uptake, and inhibition of carbohydrate-digesting enzymes. These findings are consistent with previous reports by Vo, T. S. et al. (2022), E. O. Oboh (2007), and S. B. Patil et al. (2012), which demonstrated that phytochemical-rich medicinal plants produce gradual but sustained glucose-lowering effects. The large

treatment and treatment-by-time effect sizes further emphasize the biological significance of *P. martellii*, particularly the 100 mg/kg leaf extract, as a promising natural antihyperglycemic agent.

4. Conclusion & Recommendations

The findings demonstrate that *Pandanus martellii* possesses significant diuretic and antihyperglycemic properties, supported by the presence of bioactive phytochemicals such as flavonoids, alkaloids, saponins, glycosides, and tannins. The extracts were found to be relatively safe at a dose of 2000 mg/kg, with no mortality or severe toxicity observed. Among the plant parts evaluated, the root extract exhibited the strongest diuretic activity, while the leaf extract at 100 mg/kg showed the greatest antihyperglycemic effect. These results indicate that the pharmacological activity of *P. martellii* varies according to plant part and dosage, highlighting its potential as a natural therapeutic alternative for managing diabetes and hypertension.

Further studies should isolate and identify the specific bioactive compounds responsible for the observed pharmacological activities and investigate their mechanisms of action. Additional research on chronic toxicity, dose optimization, and long-term safety is recommended to establish the appropriate therapeutic dosage and evaluate potential adverse effects. Clinical trials involving human participants should also be conducted to validate the efficacy and safety of *P. martellii*, while pharmaceutical studies may focus on developing standardized dosage forms suitable for safe and practical therapeutic use.

This study was limited to evaluating the phytochemical constituents, acute oral toxicity, diuretic activity, and antihyperglycemic effects of the roots, leaves, and fruits of *P. martellii* using female albino mice under controlled laboratory conditions. The investigation focused only on acute toxicity and did not assess chronic toxicity, isolate the specific active compounds, determine their mechanisms of action, or evaluate the efficacy and safety of the extracts in human subjects. These limitations restrict the direct generalization of the findings to long-term clinical applications.

Compliance with ethical standards

The authors declares no conflict of interest. This study received no external funding and was conducted with the voluntary participation of all involved, with informed consent obtained prior to data collection. The study was carried out in the designated research institution using non-invasive experimental procedures, and all collected data were treated confidentially to ensure that no identifying information was disclosed.

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