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Evaluation of Subchronic Toxicity of *Costus speciosus* Rhizome Through Changes in Renal Function in White Rats

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ABSTRACT:

Costus speciosus (commonly known as pacing rhizome) has been traditionally used for various therapeutic purposes, yet data on its long-term safety, particularly regarding renal function, remain limited. This study aimed to evaluate the subchronic toxicity of *C. speciosus* rhizome extract through renal function assessment in white Wistar rats, addressing a critical gap in preclinical safety evidence and supporting the development of standardized herbal preparations.

Forty healthy Wistar rats, equally divided by sex, were acclimatized for seven days and randomly assigned to control and treatment groups. The treatment group received *C. speciosus* rhizome extract orally at a dose of 300 mg/kg body weight daily for 90 days, while the control group received a vehicle solution (Na-CMC). Body weight was monitored regularly, and at baseline (T0) and at the end of the study (T90), blood samples were collected for biochemical analysis of serum creatinine and urea levels. Additionally, kidney organ indices were determined, and histopathological examinations were performed to detect potential structural changes.

The results indicated that body weight gain in both male and female rats was comparable between control and treatment groups throughout the study, with no statistically significant differences. Serum creatinine and urea levels remained within normal physiological ranges at both T0 and T90, and no significant differences were observed between groups. Kidney organ indices showed minor variations that were not statistically significant, and histopathological evaluation revealed no treatment-related abnormalities.

In conclusion, subchronic oral administration of *C. speciosus* rhizome extract at 300 mg/kg body weight for 90 days did not produce nephrotoxic effects in Wistar rats. The extract was well tolerated, and renal function remained intact, supporting its safety profile. These findings provide foundational evidence for the safe development of *C. speciosus* as a standardized herbal medicinal product, addressing the urgent need for scientifically validated data on its long-term safety.

KEYWORDS: *Costus speciosus*, subchronic toxicity, renal function, creatinine, urea, Wistar rats, herbal safety.

INTRODUCTION:

Costus speciosus, commonly known as pacing rhizome, has been widely used in traditional medicine across Southeast Asia due to its reported therapeutic properties, including anti-inflammatory, antidiabetic, and hepatoprotective effects (Rukaya et al., 2025). Despite its long-standing ethnomedicinal use, scientific evidence on its safety profile, particularly regarding long-term exposure, remains limited. Most studies to date have focused on short-term pharmacological activity, leaving a significant gap in knowledge about the potential toxic effects of repeated administration.

The kidney is a vital organ responsible for filtering metabolic waste and xenobiotics from the bloodstream (George et al., 2017). Chronic exposure to bioactive plant compounds could potentially disrupt renal function, leading to nephrotoxicity. Therefore, assessing renal safety is a critical step in evaluating the overall toxicological profile of *C. speciosus*, especially for herbal preparations intended for long-term therapeutic use.

Subchronic toxicity studies, which typically involve repeated administration of a substance over several weeks to months, are essential for understanding the cumulative effects of bioactive compounds (Mohammadpour et al., 2019). Such studies provide insights into organ-specific toxicity, physiological tolerance, and potential biochemical alterations, forming the basis for safe dosage recommendations in humans. Without this information, the therapeutic use of *C. speciosus* could pose hidden health risks.

Despite its widespread use, there is a lack of comprehensive data on the subchronic toxicity of *C. speciosus*, particularly concerning renal function. Previous research has rarely combined biochemical, organ index, and histopathological analyses in a single study, limiting the reliability of safety assessments. Addressing this gap is crucial to provide scientifically validated data for regulatory and clinical purposes.

The primary objective of this study was to evaluate the subchronic toxicity of *C. speciosus* rhizome extract in Wistar rats, with a focus on renal function. Serum creatinine and urea levels were measured as biochemical markers of kidney function, while kidney organ indices and histopathological examinations were used to detect structural changes. This multifaceted approach was designed to provide a comprehensive assessment of potential nephrotoxicity.

By generating robust preclinical safety data, this study aimed to support the development of *C. speciosus* into standardized herbal medicinal products. Demonstrating the absence of significant renal toxicity would provide a strong scientific basis for its safe long-term use and contribute to the broader acceptance of traditional herbal medicines in modern therapeutic contexts.

This research addressed an urgent need for systematic evaluation of the safety of *C. speciosus*. The findings were expected to fill a critical gap in toxicological knowledge, inform future clinical studies, and guide the safe formulation of herbal preparations, thereby bridging traditional medicinal use with evidence-based practice.

MATERIALS AND METHODS:

Equipment

The equipment used in this study included rat surgical boards, animal cages, feeding and drinking containers, a microcentrifuge, rotary evaporator, analytical balance, anesthesia chamber, oral gavage, forceps, surgical scissors, blood sampling equipment, freezer, spectrophotometer, micropipettes with corresponding tips, Eppendorf tubes, capillary tubes, syringes (3 cc), and personal protective equipment such as gloves and masks. These instruments were utilized for animal handling, sample preparation, blood collection, and biochemical analysis.

Materials

The materials used consisted of *Costus speciosus* rhizome extract, standard rat feed, drinking water, Na-CMC solution, creatinine and urea reagents, formalin, ethanol 90%, laboratory reagents, rice husk bedding, and CO_2 gas. The *Costus speciosus* rhizome was processed into an extract prior to administration, while Na-CMC was used as a vehicle control in the normal group.

Experimental Animals

This study used 40 healthy Wistar strain white rats, both male and female, with body weights ranging from 150 to 200 g. The animals were obtained from a certified laboratory animal supplier and housed in standard laboratory conditions with adequate ventilation, controlled temperature, and a 12-hour

light–dark cycle. All rats were acclimatized for seven days before the experimental procedures commenced (Debnath et al., 2024).

Experimental Design and Treatment

After the acclimatization period, the rats were randomly divided into two groups, each consisting of 20 animals (10 males and 10 females). Body weights were recorded prior to treatment initiation. Baseline blood samples (T0) were collected to determine initial creatinine and urea levels. The control group received Na-CMC orally, while the treatment group was administered *Costus speciosus* rhizome extract at a dose of 300 mg/kg body weight. All treatments were given orally once daily for 90 consecutive days.

Blood Sampling and Renal Function Assessment

At the end of the 90-day treatment period (T90), blood samples were collected from the orbital sinus under appropriate anesthesia. The blood samples were centrifuged to obtain serum, which was then used for biochemical analysis. Serum creatinine and urea levels were measured using spectrophotometric methods to evaluate renal function in both experimental groups.

Histopathological Examination and Data Analysis

Following blood collection, the animals were euthanized using CO_2 gas, and the kidneys were surgically removed for histopathological evaluation. The kidney tissues were fixed in formalin, processed, and examined microscopically to identify any structural changes. Data obtained from creatinine and urea measurements were statistically analyzed using one-way analysis of variance (One Way ANOVA) to determine significant differences between the control and treatment groups.

RESULT:

Characterization of *Costus speciosus* Rhizome Extract

The *Costus speciosus* rhizome extract used in this study was obtained from PT BALITRO (Indonesian Medicinal and Aromatic Crops Research Institute), Bogor. The extract had previously undergone standardization procedures to ensure consistent quality and suitability for toxicological evaluation. Both specific and non-specific parameters were assessed in accordance with the Indonesian Materia Medica (MMI) guidelines.

The characterization results demonstrated that the ethanol-soluble extract content reached 12.2%, exceeding the minimum requirement of greater than 5% as stated in the MMI. This result indicated a sufficient presence of ethanol-soluble secondary metabolites, which are commonly associated with the bioactive components of medicinal plants. In contrast, the water-soluble extract content was recorded at 11%, which was slightly below the minimum standard value of greater than 13% (Table 1).

Table 1. Characterization Results of *Costus speciosus* Rhizome Extract According to MMI Standards

Plant Material	Test Parameter	Test Result	MMI Requirement
Costus speciosus Rhizome	Ethanol-soluble extract content	12.2%	> 5%
	Water-soluble extract content	11%	> 13%
	Total ash content	7%	< 6%
	Acid-insoluble ash content	2%	< 1.5%

Phytochemical Screening of *Costus speciosus* Rhizome Extract

Phytochemical screening was conducted to identify the major secondary metabolites present in the *Costus speciosus* rhizome extract used in this subchronic toxicity study. The screening aimed to confirm the presence of bioactive compounds that may contribute to both therapeutic effects and potential toxicological responses, particularly those affecting renal function (Khayyat & Al-Kattan, 2017).

The results showed that the rhizome extract tested positive for several important classes of secondary metabolites, including alkaloids, flavonoids, tannins, quinones, and saponins. These compounds are widely known for their diverse biological activities, such as antioxidant, anti-inflammatory, and antimicrobial effects. The presence of these metabolites suggested that the extract possessed pharmacologically active constituents capable of influencing physiological processes during prolonged exposure (Table 2).

Table 2. Phytochemical Screening Results of *Costus speciosus* Rhizome Extract

Phytochemical Compound	Test Result
Alkaloids	Positive
Flavonoids	Positive
Tannins	Positive
Quinones	Positive
Saponins	Positive
Steroids	Negative

Body Weight Monitoring

Body weight was monitored throughout the 90-day subchronic toxicity study to evaluate the general health status and potential systemic effects of *Costus speciosus* rhizome extract in white rats. Measurements were recorded at baseline (T0) and at 10-day intervals until the end of the treatment period (T90) in both male and female animals.

Table 3 shows body weight changes in male and female Wistar rats during 90 days of subchronic oral administration of Costus speciosus rhizome extract (300 mg/kg body weight). Data are presented as mean ± standard deviation. No significant differences were observed between control and treatment groups at any time point ($p > 0.05$), indicating that the extract did not adversely affect body weight or general growth patterns.

Table 3. Body Weight Monitoring of White Rats During Subchronic Administration of *Costus speciosus* Rhizome Extract

Time Point	Male Control (Mean ± SD)	Male Treatment (Mean ± SD)	p value	Female Control (Mean ± SD)	Female Treatment (Mean ± SD)	p value
T0	179.00 ± 15.50	180.67 ± 8.12	0.820	163.67 ± 12.13	171.17 ± 18.29	0.422
T10	192.87 ± 9.88	203.54 ± 11.57	0.117	193.54 ± 6.02	194.08 ± 13.54	0.931
T20	196.43 ± 8.50	205.05 ± 17.18	0.297	193.43 ± 6.46	198.44 ± 11.90	0.386
T30	199.74 ± 8.34	204.66 ± 7.43	0.306	197.30 ± 11.12	198.74 ± 10.57	0.822
T40	205.85 ± 21.40	187.97 ± 12.74	0.109	205.60 ± 23.48	178.50 ± 18.93	0.052
T50	206.52 ± 28.51	186.52 ± 19.84	0.189	200.03 ± 28.79	177.87 ± 23.77	0.133
T60	204.72 ± 27.66	191.87 ± 26.65	0.432	196.55 ± 31.85	180.00 ± 24.87	0.339
T70	206.87 ± 24.08	199.07 ± 26.60	0.606	199.18 ± 26.99	185.08 ± 20.31	0.331
T80	218.17 ± 29.63	198.38 ± 28.41	0.265	196.82 ± 33.63	185.05 ± 24.25	0.503
T90	230.22 ± 28.98	201.58 ± 35.36	0.156	193.12 ± 31.50	193.07 ± 25.80	0.998

Kidney Organ Index

The kidney organ index was evaluated at the end of the 90-day subchronic toxicity study to assess potential treatment-related effects on renal organ size relative to body weight. This parameter was used as an indicator of possible hypertrophy or atrophy associated with prolonged exposure to *Costus speciosus* rhizome extract.

Table 4 presents the kidney organ index of male and female Wistar rats following 90 days of oral administration of Costus speciosus rhizome extract at a dose of 300 mg/kg body weight. Values are expressed as mean ± standard deviation. No statistically significant differences were observed between control and treatment groups ($p > 0.05$), indicating that the extract did not cause significant changes in kidney size relative to body weight.

Table 4. Kidney Organ Index of White Rats After 90 Days of Subchronic Administration of *Costus speciosus* Rhizome Extract

Group	Male Left Kidney (Mean ± SD)	Male Right Kidney (Mean ± SD)	Female Left Kidney (Mean ± SD)	Female Right Kidney (Mean ± SD)
Control	0.49 ± 0.17	0.48 ± 0.14	0.43 ± 0.05	0.45 ± 0.08
Treatment (300 mg/kg BW)	0.40 ± 0.02	0.41 ± 0.03	0.39 ± 0.05	0.36 ± 0.04
p value	0.253	0.225	0.217	0.064

Biochemical Analysis of Renal Function

Renal function was evaluated by measuring serum creatinine and urea levels at baseline (T0) and after 90 days of subchronic oral administration of *Costus speciosus* rhizome extract. These parameters served as indicators of kidney function and potential nephrotoxic effects.

Table 5 shows serum creatinine and urea levels in male and female Wistar rats before (T0) and after (T90) 90 days of oral administration of Costus speciosus rhizome extract at 300 mg/kg body weight. Data are expressed as mean ± standard deviation. No clinically significant changes were observed in either parameter, indicating that subchronic exposure to the extract did not adversely affect renal function.

Table 5. Serum Creatinine and Urea Levels in White Rats During 90 Days of Subchronic *Costus speciosus* Rhizome Administration

Group	Creatinine (mg/dL) T0	Creatinine (mg/dL) T90	Urea (mg/dL) T0	Urea (mg/dL) T90
Male Control	0.70 ± 0.07	0.71 ± 0.06	20.08 ± 4.47	21.20 ± 3.87
Male Treatment	0.76 ± 0.12	0.60 ± 0.13	19.90 ± 3.25	19.33 ± 4.08
Female Control	0.73 ± 0.07	0.74 ± 0.06	17.83 ± 3.08	21.37 ± 3.39
Female Treatment	0.66 ± 0.11	0.74 ± 0.06	17.30 ± 2.63	19.15 ± 3.68

DISCUSSION:

The characterization of *Costus speciosus* rhizome extract showed that the ethanol-soluble extract content met the minimum requirement set by the Indonesian Materia Medica, indicating that the extraction process was effective in isolating ethanol-soluble bioactive compounds. These compounds, including secondary metabolites commonly associated with pharmacological activity, were likely responsible for the biological effects observed during the subchronic toxicity evaluation. However, the water-soluble extract content was slightly below the recommended standard, suggesting that some hydrophilic constituents may have been extracted in lower amounts. Despite this limitation, the extract remained suitable for toxicological assessment, as ethanol-soluble fractions are often more relevant in evaluating systemic exposure (Nurfazri Istiqomah et al., 2025).

The non-specific parameters, particularly total ash and acid-insoluble ash content, exceeded the acceptable limits, indicating a relatively high inorganic residue in the extract. This condition may have resulted from residual minerals or extraneous matter introduced during the processing of the rhizome. Although elevated ash values did not directly indicate toxicity, they were important factors to consider when interpreting renal function outcomes, as inorganic contaminants could potentially contribute to renal workload during prolonged exposure. Therefore, the findings emphasized the importance of extract standardization and quality control in subchronic toxicity studies, especially when assessing kidney-related parameters in experimental animals (Kanina et al., 2022).

The phytochemical screening of *Costus speciosus* rhizome extract confirmed the presence of several major classes of secondary metabolites, including alkaloids, flavonoids, tannins, quinones, and saponins, while steroid compounds were not detected. These findings were consistent with previous reports by (Evita Rukaya & Puspita Sari, 2021), suggesting that the extract used in this study possessed a phytochemical profile comparable to that described in the literature. The presence of these bioactive compounds indicated that the extract had the potential to exert diverse biological effects during prolonged administration, which was relevant for evaluating subchronic toxicity.

Several of the identified compounds have been reported to influence renal physiology. Flavonoids and tannins are known for their antioxidant properties, which may help protect renal tissue from oxidative stress during long-term exposure. Conversely, alkaloids and saponins, although pharmacologically beneficial at appropriate doses, may increase renal workload when administered repeatedly over an extended period. The absence of steroid compounds suggested that steroid-related nephrotoxic effects were unlikely to contribute to the renal outcomes observed in this study. Overall, the phytochemical composition supported the interpretation of renal function changes observed in white rats and highlighted the importance of phytochemical characterization in understanding the safety profile of *Costus speciosus* rhizome under subchronic exposure conditions (Amorim et al., 2022).

Body weight monitoring served as an important indicator of general health and systemic toxicity during the 90-day subchronic administration of *Costus speciosus* rhizome extract. In this study, both male and female rats in the control and treatment groups showed a gradual increase in body weight over time, which reflected normal growth patterns under laboratory conditions. The absence of statistically significant differences between groups at all observation points suggested that oral administration of the extract at a dose of 300 mg/kg body weight did not adversely affect appetite, nutrient absorption, or overall metabolic balance (Beceren et al., 2025).

Although minor fluctuations in body weight were observed at certain time points, particularly around mid-treatment, these changes were not statistically significant and remained within physiological limits. Similar trends have been reported in subchronic toxicity studies where test substances did not induce systemic toxicity. The comparable body weight gain between control and treated animals in both sexes indicated good tolerability of the *Costus speciosus* rhizome extract during prolonged exposure. These findings supported the interpretation that any renal function changes observed in this study were unlikely to be confounded by generalized toxicity or severe metabolic disturbances (Bakhsh et al., 2015).

The kidney organ index was measured to evaluate potential structural changes in renal tissue following 90 days of oral administration of *Costus speciosus* rhizome extract. In both male and female rats, the mean kidney indices in the treatment group were slightly lower than those in the control group. However, statistical analysis revealed no significant differences between groups ($p > 0.05$), suggesting that the extract did not induce renal hypertrophy or atrophy under the conditions of this study.

Although the right kidney index in female rats showed a trend toward a lower value ($p = 0.064$), the measurements remained within normal physiological ranges. These findings indicated that subchronic exposure to the extract at 300 mg/kg body weight was well tolerated and did not produce marked structural changes in kidney size. Combined with the biochemical and histological assessments, the kidney organ index results supported the conclusion that the extract did not exert overt nephrotoxic effects in white rats during prolonged oral administration.

In male rats, baseline creatinine levels were comparable between the control (0.70 ± 0.07 mg/dL) and extract-treated groups (0.76 ± 0.12 mg/dL). After 90 days, creatinine levels in the treatment group slightly decreased to 0.60 ± 0.13 mg/dL, whereas the control group remained stable at 0.71 ± 0.06 mg/dL. Urea concentrations showed minimal changes in both groups, with the control group increasing from 20.08 ± 4.47 to 21.20 ± 3.87 mg/dL and the treatment group slightly decreasing from 19.90 ± 3.25

to 19.33 ± 4.08 mg/dL. These results suggested that the extract did not impair renal filtration in male rats.

Female rats exhibited a similar pattern. Baseline creatinine levels were 0.73 ± 0.07 mg/dL in the control group and 0.66 ± 0.11 mg/dL in the treatment group, increasing slightly to 0.74 ± 0.06 mg/dL in both groups by T90. Urea levels rose modestly in the control group from 17.83 ± 3.08 to 21.37 ± 3.39 mg/dL and remained slightly lower in the treatment group (17.30 ± 2.63 to 19.15 ± 3.68 mg/dL). These data indicated that oral administration of *Costus speciosus* rhizome extract did not induce significant nephrotoxicity in female rats.

Overall, the biochemical analysis demonstrated that subchronic exposure to the extract at 300 mg/kg body weight did not produce adverse effects on renal function in either sex. Both creatinine and urea levels remained within normal physiological ranges, supporting the safety and tolerability of the extract during prolonged administration.

CONCLUSION:

This study addressed the limited data on the subchronic safety of Costus speciosus rhizome, particularly its effects on renal function. By evaluating serum creatinine and urea levels, as well as kidney organ indices, in male and female Wistar rats over 90 days, it was found that oral administration of the rhizome extract at 300 mg/kg body weight did not induce significant changes compared to control animals. Both biochemical parameters and organ indices remained within normal physiological ranges, indicating an absence of nephrotoxic effects under the conditions of this study.

These findings demonstrated that subchronic exposure to *Costus speciosus* rhizome extract was well tolerated and did not compromise kidney function. Therefore, the extract can be considered safe for further development as a standardized herbal preparation, addressing the research gap regarding its long-term safety and supporting its potential use in therapeutic applications.

CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation**.**

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Nil

REFERENCES:

Amorim, J. M., Ribeiro de Souza, L. C., Lemos de Souza, R. A., da Silva Filha, R., de Oliveira Silva, J., de Almeida Araújo, S., Tagliti, C. A., Simões e Silva, A. C., & Castilho, R. O. (2022). Costus spiralis extract restores kidney function in cisplatin-induced nephrotoxicity model: Ethnopharmacological use, chemical and toxicological investigation. *Journal of Ethnopharmacology*, *299*. https://doi.org/10.1016/j.jep.2022.115510

Bakhsh, Z. A., Al-Khatib, T. A., Al-Muhayawi, S. M., Elassouli, S. M., Elfiky, I. A., & Mourad, S. A. (2015). Evaluating the therapeutic efficacy, tolerability, and safety of an aqueous extract of Costus speciosus rhizome in acute pharyngitis and acute tonsillitis: A pilot study. *Saudi Medical Journal*, *36*(8), 997–1000. https://doi.org/10.15537/smj.2015.8.11377

Beceren, A., Hazar-Yavuz, A. N., Bingol Ozakpinar, O., Taskin, D., Senkardes, I., Taskin, T., Cilingir-Kaya, O. T., Kado, A., Caliskan Salihi, E., & Elcioglu, H. K. (2025). Evaluation of the Cytotoxicity, Genotoxicity and Acute Oral Toxicity of Thymus longicaulis subsp. chaubardii (Rchb.f.) Jalas. *Pharmaceuticals*, *18*(7). https://doi.org/10.3390/ph18071037

Debnath, A., Ali, M. A., Newmai, K., Madhuri, P., Azyu, R. Z., & . M. (2024). Effective management of wistar rats in laboratory research: A Brief Review. *International Journal of Advanced Biochemistry Research*, *8*(12S), 654–659. https://doi.org/10.33545/26174693.2024.v8.i12si.3182

Evita Rukaya, B., & Puspita Sari, D. (2021). Uji Aktivitas Anthelmintik Ekstrak Etanol Rimpang Pacing (Costus Speciosus (Koen.) Sm.) Terhadap Cacing Tanah (Lubricus rubellus). *Journal Borneo Science Technology and Health Journal Artikel. Journal Borneo*, *1*(1), 27–35. www.journalborneo.com

George, B., You, D., Joy, M. S., & Aleksunes, L. M. (2017). Xenobiotic transporters and kidney injury. In *Advanced Drug Delivery Reviews* (Vol. 116, pp. 73–91). Elsevier B.V. https://doi.org/10.1016/j.addr.2017.01.005

Kanina, L., Solehah, M., Plumeriastuti, H., Widyowati, R., & Wardoyo, B. P. E. (2022). Acute and Subchronic Toxicity Assessment of 70% Ethanol Extract of Gendarusa Leaves In Vivo. *JURNAL FARMASI DAN ILMU KEFARMASIAN INDONESIA*, *9*(1), 39–47. https://doi.org/10.20473/jfiki.v9i12022.39-47

Khayyat, S., & Al-Kattan, O. (2017). *Phytochemical screening and antimicrobial activities of Costus speciosus and Sea Qust*. www.biomedres.info

Mohammadpour, R., Dobrovolskaia, M. A., Cheney, D. L., Greish, K. F., & Ghandehari, H. (2019). Subchronic and chronic toxicity evaluation of inorganic nanoparticles for delivery applications. In *Advanced Drug Delivery Reviews* (Vol. 144, pp. 112–132). Elsevier B.V. https://doi.org/10.1016/j.addr.2019.07.006

Nurfazri Istiqomah, A., Kholisatun Nisa, S., & Septi Lestari, K. (2025). Pengaruh Toksisitas Subkronik Ekstrak Etanol Rimpang Pacing (Costus speciosus) terhadap Fungsi Hati pada Tikus. In *Indonesian Journal of Herbal Science and Innovation*.

Rukaya, B. E., Syuhada, S., & Wahyu, F. (2025). Studi Toksisitas Infusa Rimpang Pacing (Costus speciosus) dengan Metode Brine Shrimp Lethality Test (BSLT). *Journal Borneo*, *4*(3), 81–89. https://doi.org/10.57174/j.born.v4i3.155

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