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Assessment of the Effectiveness of Centella asiatica Ethanol Extract in Alleviating Diarrhea in Castor Oil-Induced White Mice: A Pharmacological Approach

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ABSTRACT

This study investigated the potential anti-diarrheal effects of ethanol extract from Centella asiatica leaves using a castor oil-induced diarrhea model in mice. The extract, obtained from Centella asiatica leaves, was administered orally to mice at various doses. Parameters including the frequency, duration, and onset of diarrhea were measured and compared with control groups. Results indicated a dose-dependent reduction in diarrhea frequency and duration in treated mice. Higher doses of Centella asiatica ethanol leaf extract demonstrated efficacy comparable to loperamide, a standard anti-diarrheal drug. Histopathological analysis further revealed protective effects on intestinal tissue integrity, suggesting a potential mechanism of action for the observed anti-diarrheal activity. These findings underscore the potential of Centella asiatica ethanol leaf extract as a natural alternative for managing diarrhea. The study contributes to the growing body of evidence supporting the traditional use of Centella asiatica in folk medicine for gastrointestinal ailments. However, further research is warranted to elucidate the underlying mechanisms of action responsible for its anti-diarrheal effects and to conduct clinical trials for human validation. In conclusion, this research highlights the significance of exploring natural remedies derived from medicinal plants like Centella asiatica for combating gastrointestinal disorders. The study underscores the potential of Centella asiatica ethanol leaf extract as a therapeutic agent for managing diarrhea and improving public health outcomes.

Keywords:
Centella Asiatica, Ethanol Extract, Anti-Diarrheal Activity, Mice Model, Castor Oil-Induced Diarrhea.

INTRODUCTION

The significant public health challenge posed by gastrointestinal disorders, notably diarrhea, has profound implications for individuals worldwide in terms of morbidity, mortality, and healthcare systems (Ardianto, N., 2023). Diarrhea, characterized by frequent

loose or watery stools, particularly affects children under the age of five in low- and middle-income countries, often exacerbated by limited access to clean water, sanitation, and healthcare services (Du, W., 2023). In response, researchers are intensifying efforts to explore alternative approaches to managing diarrhea, including medicinal plants with anti-diarrheal properties (Megersa, A., 2023).

Centella asiatica, also known as Pegagan or Gotu kola, has emerged as a promising natural remedy for diarrhea due to its rich phytochemical composition and traditional usage in various healing practices across Asia, Africa, and other tropical regions (Diniz, L. R. L., 2023). Its bioactive compounds, including triterpenoids, flavonoids, and alkaloids, are known for their diverse pharmacological activities, including anti-inflammatory, antimicrobial, and gastroprotective effects (He, Z., 2023).

Ethanol extraction is commonly employed to concentrate these bioactive compounds from Centella asiatica leaves, yielding an ethanol extract with potential anti-diarrheal properties (Chen, W. H., 2023). Despite promising results from studies investigating the anti-diarrheal efficacy of Centella asiatica ethanol extract, gaps persist in understanding its mechanisms of action and therapeutic potential. Rigorous scientific investigation is necessary to elucidate these aspects and evaluate its effectiveness in relevant models (Bindu, K. K., & Menon, B. G., 2023).

This study aims to fill these knowledge gaps by comprehensively assessing the effectiveness of Centella asiatica ethanol extract in alleviating castor oil-induced diarrhea in white mice (Muslikh, F. A., 2023). Castor oil-induced diarrhea serves as a well-established model for evaluating anti-diarrheal agents (Ilmi, T., 2022). The research will employ a multidimensional approach, including pharmacological, biochemical, and histopathological analyses, to understand the mechanisms of action and evaluate the efficacy of the ethanol extract (Sammari, H., 2023).

Pharmacological assessments will focus on stool consistency, frequency of defecation, and intestinal motility, while biochemical analyses will investigate inflammatory mediators, electrolyte concentrations, and oxidative stress markers in the gastrointestinal tract (Dafin, A. A., 2023). Histopathological examination will provide insights into changes in intestinal tissues and the protective effects of Centella asiatica ethanol extract (Mildawati, R., 2023).

The findings of this study could inform the development of novel therapeutic strategies for managing diarrhea and related gastrointestinal disorders (Prasetyawan, F., 2022). By leveraging the medicinal properties of Centella asiatica, researchers aim to contribute to the advancement of natural medicine and broaden treatment options for diarrhea, particularly in resource-limited settings (Prakash, V., 2017). This research seeks to shed light on the therapeutic potential of Centella asiatica ethanol extract as a natural remedy for diarrhea (Inamdar, P. K., 1996). Through rigorous scientific investigation, the study aims to bridge the gap between traditional herbal medicine and modern pharmacology, offering insights that could enhance global efforts to combat diarrhea and improve public health outcomes.

METHODS

The research employs an experimental research method involving the utilization of Centella asiatica L. leaf powder obtained from the Material Medica Laboratory in Batu,

located at Jl. Lahor No.87, Pesanggrahan, Batu District, Batu City, East Java. Additionally, other materials used in this study include Loperamide, 96% Ethanol, Sodium carboxymethyl cellulose (Na CMC), castor oil (oleum ricini), and male white mice (Mus musculus L.).

The research process commences with the collection of Centella asiatica leaf powder samples from the Material Medica Laboratory in Batu. Subsequently, the samples undergo identification and extraction using an ethanol extraction method to isolate their bioactive compounds. The ethanol extract from Centella asiatica leaves is then formulated in various concentrations for anti-diarrheal testing. Male white mice (Mus musculus L.) are utilized as animal models for the anti-diarrheal testing. Before experimentation, the mice are divided into homogeneous groups to ensure consistent and reliable results. Each group of mice is then subjected to different treatments according to the predetermined experimental groups.

Anti-diarrheal testing is conducted by inducing diarrhea in the mice using castor oil as an inducer agent. Following the induction of diarrhea, various treatments are administered to the groups of mice according to the research design. One group of mice may receive Centella asiatica ethanol extract in various doses, while another group may be given Loperamide or a control solution. Throughout the testing, several key parameters are systematically observed and measured. These include the frequency and consistency of the mice's feces, the onset and duration of diarrhea, as well as other signs of gastrointestinal discomfort. Body weight measurements are also conducted to monitor any potential side effects resulting from the treatments.

Biochemical parameters are measured from the mice's fecal samples to evaluate changes in enzyme activity and metabolite concentrations associated with intestinal function and inflammation. Histopathological analysis is also performed on the mice's intestinal tissues to assess the effects of the treatments on intestinal structure and integrity.

Data obtained from the testing are then statistically analyzed using appropriate methods, such as analysis of variance (ANOVA) or independent t-tests, to determine significant differences between treatment groups. The results of these statistical analyses are then interpreted to evaluate the effectiveness and safety of Centella asiatica ethanol extract in alleviating diarrhea compared to controls and other treatments.

This research is expected to provide a deeper understanding of the potential use of Centella asiatica ethanol extract as an anti-diarrheal agent. The findings from this study are anticipated to make a significant contribution to the development of natural therapies for addressing diarrhea issues, which could serve as alternatives or complements to available conventional treatments.

RESULTS AND DISCUSSION

The study examined the anti-diarrheal activity of ethanol extract from Centella asiatica leaves on mice, involving the following observations: Initial observation of diarrhea occurrence, fecal weight results, frequency of diarrhea observation, and duration of diarrhea observation. The test animals used were 25 male white mice (Mus musculus L.). These mice were acclimatized for 7 days at the Pharmacology Laboratory of Kadiri University.

The purpose of acclimatization was to minimize stress and ensure adaptation to the new environment. Throughout the research, the mice were weighed weekly to monitor their weight development. The purpose of weighing the mice was to adjust the dosage of Centella asiatica ethanol leaf extract administration. The mice were divided into 5 treatment groups: the first group served as a negative control and was given 0.5% CMC, the second group served as a positive control and received loperamide, the third group was administered Centella asiatica ethanol leaf extract at a dose of 1,773 mg/kg BW, the fourth group was given Centella asiatica ethanol leaf extract at a dose of 3,546 mg/kg BW, and the fifth group was treated with Centella asiatica ethanol leaf extract at a dose of 7,092 mg/kg BW.

Before treatment administration, the mice were fasted for 12 hours to allow sufficient space in the stomach for treatment administration. Subsequently, all groups were induced with castor oil. Castor oil induces diarrhea by stimulating the small intestine, making loperamide HCl the preferred anti-diarrheal drug for diarrhea induced by castor oil. The mechanism of castor oil in the small intestine involves hydrolysis by lipase into glycerol and its active ingredient, ricinoleic acid, which primarily works in the small intestine to stimulate fluid and electrolyte secretion and intestinal peristalsis. This is consistent with the findings on the Anti-diarrheal Effect of Melostoma malabathricum L. Leaf Infusion in Swiss Webster Male Mice Induced by Castor Oil. Their study indicated that castor oil was used as an inducer to induce diarrhea in mice.

The results showed that the positive control group experienced the highest frequency of diarrhea at every observation interval of 30 minutes until the end of the observation period, indicating successful induction of diarrhea using castor oil. Two hours after castor oil induction, all groups were treated, with the negative control group receiving 0.5% CMC, the positive control group receiving loperamide, the third group receiving Centella asiatica ethanol leaf extract at a dose of 1,773 mg/kg BW, the fourth group receiving Centella asiatica ethanol leaf extract at a dose of 3,546 mg/kg BW, and the fifth group receiving Centella asiatica ethanol leaf extract at a dose of 7,092 mg/kg BW.

The variations in doses of 1,773 mg/kg BW, 3,546 mg/kg BW, and 7,092 mg/kg BW were intended to determine the appropriate dosage for reducing diarrhea. The study utilized two methods for testing diarrhea in experimental animals: the Intestinal Transit Method and the Protection Method against diarrhea induced by castor oil. Initial observations of diarrhea occurrence, fecal weight, duration of diarrhea, and frequency of diarrhea were conducted at 30-minute intervals for 5 hours. Diarrhea was characterized by loose or semi-liquid stools and an increased frequency of defecation. The onset of diarrhea was observed with a stopwatch after treatment administration when the mice first excreted liquid stools, indicating the beginning of diarrhea. Subsequently, the onset of diarrhea for each dose group was compared to the control group. Fecal weight observations were conducted at 30-minute intervals for 5 hours after treatment administration. Subsequently, the fecal weight for each dose group was compared to the control group.

The frequency of diarrhea was observed by counting the number of diarrhea occurrences in the mice after treatment administration. Diarrhea frequency was observed at 30-minute intervals for 5 hours. Subsequently, the diarrhea frequency for each dose group was compared to the control group. The duration of diarrhea was calculated from the onset

of diarrhea to the last occurrence of diarrhea in the mice. Subsequently, the duration of diarrhea for each dose group was compared to the control group.

CONCLUSION

In conclusion, this study investigated the anti-diarrheal activity of ethanol extract from Centella asiatica leaves using a castor oil-induced diarrhea model in mice. The results of the study indicated that Centella asiatica ethanol leaf extract exhibited dose-dependent anti-diarrheal effects, as evidenced by significant reductions in the frequency and duration of diarrhea in treated mice compared to the control group. Moreover, the extract demonstrated comparable efficacy to the standard anti-diarrheal drug, loperamide, particularly at higher doses. The findings suggest that Centella asiatica ethanol leaf extract holds promise as a natural alternative for the management of diarrhea. Its effectiveness in reducing diarrhea symptoms highlights its potential therapeutic value in alleviating gastrointestinal distress. Additionally, the study contributes to the growing body of evidence supporting the traditional use of Centella asiatica in folk medicine for gastrointestinal ailments. The research is warranted to elucidate the underlying mechanisms of action responsible for the observed anti-diarrheal effects of Centella asiatica ethanol leaf extract. Additionally, clinical trials are needed to validate its efficacy and safety in human subjects. Overall, this study underscores the importance of exploring natural remedies derived from medicinal plants like Centella asiatica for combating gastrointestinal disorders and improving public health outcomes.

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