Yodium Plant (*Jatropha multifida Linn.*) Leaf Extract Reduces Bleeding Time

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ABSTRACT
Bleeding is a physiological response to vascular injury; however, prolonged bleeding time may indicate impaired hemostatic function. Various medicinal plants have been traditionally used to accelerate wound healing and control bleeding. One such plant is the yodium plant (*Jatropha multifida Linn.*), which is widely utilized in traditional medicine due to its potential hemostatic and anti-inflammatory properties. The bioactive compounds contained in its leaves are believed to contribute to the enhancement of blood coagulation and the reduction of bleeding duration. This study aimed to determine the effect of *Jatropha multifida Linn.* leaf extract on bleeding time. This study employed an experimental design to evaluate the effect of *Jatropha multifida Linn.* leaf extract on bleeding time. The subjects were divided into control and treatment groups. The treatment group received *Jatropha multifida* leaf extract, while the control group did not receive the extract. Bleeding time was measured after the intervention to assess the hemostatic effect of the extract. The collected data were analyzed to compare bleeding time between the groups. The results demonstrated that the administration of *Jatropha multifida Linn.* leaf extract was associated with a reduction in bleeding time compared with the control group. This finding suggests that the extract possesses hemostatic potential, which may be attributed to the presence of bioactive compounds that support the blood clotting process. *Jatropha multifida Linn.* leaf extract has the potential to reduce bleeding time, indicating its possible role as a natural hemostatic agent.
Keywords: *Jatropha multifida*; leaf extract; bleeding time; hemostatic effect; medicinal plants

INTRODUCTION
The development of the medicinal plant industry in Indonesia has shown considerable potential due to the country's rich biodiversity. Indonesia possesses a vast number of medicinal plant resources, with more than 9,609 species reported to have therapeutic properties and potential applications in traditional and modern medicine [1]. This abundance provides significant opportunities for the exploration and development of herbal medicines that can be utilized as alternative or complementary therapies. Furthermore, the recommendation of the Indonesian Minister of Health encouraging the public to utilize traditional medicine has strengthened the role of medicinal plants in supporting community health and promoting the integration of traditional remedies into healthcare systems [2]. Such policies have opened wider opportunities for scientific research aimed at validating the efficacy and safety of medicinal plants that have long been used by communities.

One plant that has attracted attention in traditional medicine is *Jatropha multifida Linn.*, commonly known as the yodium plant or Chinese physic nut. This plant is widely distributed in tropical regions and has long been utilized by local communities for various therapeutic purposes. In several areas, the sap and leaves of *Jatropha multifida* are traditionally used to treat infections on the tongues of infants as well as infected wounds on the skin. In addition, other parts of the plant, including the fruit, seeds, and seed oil, have been used for various medicinal purposes such as functioning as a laxative, treating bleeding wounds, and preventing or managing dental problems such as dental caries [3]. The widespread traditional use of this plant indicates that it may contain bioactive compounds with potential pharmacological effects, particularly in wound healing and bleeding control.

Previous scientific studies have provided evidence supporting the medicinal potential of *Jatropha multifida*. Research conducted by Septiardi in 2019 demonstrated that the sap of the Chinese physic nut was effective in promoting wound healing by accelerating scab formation on injured skin. The study also reported that the topical application of the sap on wounded skin facilitated faster recovery, enabling the skin surface to regenerate and return to its normal condition more rapidly [4]. These findings indicate that the plant may contain bioactive substances capable of stimulating tissue repair and supporting the body's natural healing mechanisms.

The findings of previous studies have encouraged further investigation into other parts of the plant, particularly its leaves. Compared with the sap, the leaves of *Jatropha multifida* are more easily obtained and can be processed more conveniently into herbal preparations such as extracts. Phytochemical studies have revealed that the leaves contain several bioactive compounds, including tannins and flavonoids [5]. These compounds are widely recognized for their pharmacological activities, particularly their roles in wound healing, anti-inflammatory effects, antimicrobial activity, and hemostatic mechanisms. Their presence suggests that the leaves of *Jatropha multifida* may also contribute to the control of bleeding and the acceleration of blood coagulation processes.

External bleeding is a common condition that often occurs in everyday environments, particularly within household settings. Such bleeding generally results from damage to the skin and underlying blood vessels caused by cuts, abrasions, or other types of trauma [6]. Under normal circumstances, the body possesses a natural hemostatic mechanism that functions to stop bleeding and prevent excessive blood loss. However, in certain conditions, bleeding may become difficult to control or may persist for a prolonged period, potentially interfering with the wound healing process. Excessive or prolonged bleeding may also hinder platelet aggregation, which is essential for forming an effective plug at the site of vascular injury.

The hemostatic process involves a complex physiological mechanism consisting of several stages. The initial response is vascular vasoconstriction, which reduces blood flow to the injured area. This stage is followed by platelet adhesion and aggregation, forming a temporary platelet plug that helps block the damaged blood vessel. The final stage involves activation of the coagulation cascade, leading to the formation of fibrin strands that stabilize the platelet plug and form a stable blood clot [7]. The effectiveness and speed of these processes determine the duration of bleeding time, which is commonly used as an indicator of primary hemostasis.

Phytochemical investigations have further supported the medicinal potential of *Jatropha multifida*. A study conducted by Putri Kurnia Sari in 2022 identified several bioactive compounds present in the yodium plant, including alkaloids, flavonoids, tannins, and saponins [8]. Among these compounds, tannins and flavonoids are particularly important due to their role in the hemostatic process. These compounds function as procoagulants, which are substances capable of facilitating and accelerating the blood clotting process. Tannins and flavonoids have been reported to shorten platelet aggregation time and enhance blood coagulation by stimulating the synthesis of thromboxane A_2 and serotonin, both of which play essential roles in platelet activation and vasoconstriction [9].

Based on these findings, it can be assumed that the leaves of *Jatropha multifida Linn.* may possess hemostatic properties that could contribute to reducing bleeding time. However, despite the plant's widespread traditional use and the presence of bioactive compounds associated with coagulation

mechanisms, scientific studies specifically examining the effect of *Jatropha multifida* leaf extract on bleeding time remain limited. Therefore, further experimental research is required to provide scientific evidence regarding its effectiveness and potential application as a natural hemostatic agent.

This study aimed to evaluate the effect of *Jatropha multifida Linn.* leaf extract on bleeding time. Specifically, the study was conducted to investigate whether the administration of *Jatropha multifida* leaf extract could influence the duration of bleeding as an indicator of the hemostatic process. In addition, this research sought to provide scientific evidence regarding the potential hemostatic properties of the plant, particularly those associated with the presence of bioactive compounds such as tannins and flavonoids. Through this investigation, the study also intended to support the traditional use of *Jatropha multifida* in the management of bleeding and wound care, while contributing to the development of medicinal plant–based therapeutic alternatives.

METHODS

This study was conducted from October 2023 to January 2024 at the Pharmacology Laboratory, Faculty of Medicine, Universitas Muhammadiyah Surakarta. The research employed a laboratory experimental design aimed at determining the effect of a specific variable on another variable under strictly controlled conditions. The study used a post-test only with control group design, in which the outcomes of the treatment groups were compared with those of the control groups after the intervention was administered. The control groups served as a reference for evaluating the effects of the treatment.

The experimental subjects were male mice. Male mice were selected because they do not experience the estrous cycle, which helps maintain sample homogeneity and minimizes biological variability, thereby allowing better experimental control and improving the accuracy of the obtained data. A total of 25 mice were selected using purposive sampling. The inclusion criteria for the samples were male Swiss Webster strain mice aged approximately 2–3 months with body weights ranging from 20–30 grams. The total sample consisted of 25 mice divided into five groups. The number of experimental animals used in this study was determined using the Resource Equation Method (E value) with the following formula:

E = Total number of animals – Total number of groups = E = 25 – 5 = E = 20

An E value between 10 and 20 indicates an adequate sample size. If the E value is less than 10, additional experimental animals are required, whereas an E value greater than 20 indicates that the number of animals should be reduced [10]. In this study, the calculated E value was 20, indicating that the sample size was appropriate. Therefore, five experimental groups were formed, each consisting of five mice, resulting in a total of 25 experimental animals. All experimental animals met the inclusion criteria. The inclusion criteria were male Swiss Webster mice aged 2–3 months, in good health, displaying normal activity, and having body weights between 20–30 grams. The exclusion criteria included mice that became ill during the experiment or died during the research process.

Table 1. Mean body weight of mice

No	Group	Mean body weight of mice (grams) ± SD
1	Negative Control	25.12 ± 2.550
2	Positive Control	24.04 ± 2.677
3	Treatment 1	25.94 ± 2.205
4	Treatment 2	24.74 ± 1.328
5	Treatment 3	25.62 ± 0.996

The samples were divided into five groups: a negative control group treated with distilled water (aquadest), a positive control group treated with epinephrine, and three treatment groups receiving *Jatropha multifida* leaf extract at concentrations of 20%, 40%, and 80%. Each group consisted of five mice assigned through random allocation. Body weight measurements were performed at the beginning of the study to determine the average body weight of the mice used in the experiment. The average body weights of the mice are presented in Table 1.

Bleeding time was measured using the Duke method, which utilizes filter paper to determine the duration of bleeding [11]. Mice that met the inclusion criteria were subjected to a standardized tail incision procedure. The tail was first marked at a distance of 2 cm from the tip. The hair on the tail was shaved using a hair clipper and subsequently disinfected with 70% ethanol. After waiting for a short period, an incision approximately 3 mm in length was made precisely on the tail vein using a scalpel to induce bleeding.

Once bleeding occurred, the tail of each mouse was immediately immersed for five seconds into a container (evaporating dish) containing different solutions according to the group allocation. Group 1 (negative control) had the tail immersed in distilled water. Group 2 (positive control) had the tail immersed in epinephrine. Groups 3, 4, and 5 were treatment groups in which the tails were immersed in ethanol extract of *Jatropha multifida* leaves at concentrations of 20%, 40%, and 80%, respectively.

After the immersion procedure, the mice were placed in empty cages. The blood droplets were absorbed using filter paper every 15 seconds without touching the wound surface. The bleeding time measurement began when the first drop of blood appeared and was recorded using a stopwatch. The measurement ended when bleeding completely stopped, indicated by the absence of blood spots on the filter paper. The time interval between the first drop of blood and the cessation of bleeding was recorded as the bleeding time [12].

The study was conducted over a period of eight days, including seven days of acclimatization to allow the mice to adapt to the new environment and achieve optimal health conditions. During the acclimatization period, the mice were housed in cages according to their assigned groups and kept in a room with adequate lighting. Each group was given distinct identification markings. The mice were provided with pellet feed three times daily. Drinking water was supplied in 300 ml bottles equipped with small tubes and filled with mineral water.

The data obtained from this study were analyzed using statistical software. Initially, the Shapiro–Wilk test was performed to assess the normality of the data distribution. Subsequently, the Levene test was used to evaluate the homogeneity of variance. If the data were normally distributed and exhibited homogeneous variance, parametric statistical tests were applied. In this study, One-Way Analysis of Variance (ANOVA) was used to analyze differences in the mean bleeding time among the five experimental groups ($\alpha = 0.05$). If a statistically significant difference was identified, a Post Hoc comparative test using the Least Significant Difference (LSD) method was performed to determine differences between specific groups [13].

RESULTS

This study involved five experimental groups consisting of two control groups and three treatment groups. The negative control group / K(-) received distilled water (aquadest), while the positive control group / K(+) received epinephrine. The treatment groups received *Jatropha multifida Linn.* leaf extract at concentrations of 20% (P1), 40% (P2), and 80% (P3). The experimental and observational data regarding the effect of *Jatropha multifida* leaf extract on bleeding time are presented in Table 2.

Table 2. Bleeding time in mice

Sample	K(-) (seconds)	K(+) (seconds)	P1 (seconds)	P2 (seconds)	P3 (seconds)
1	231	79	166	168	116
2	170	83	209	153	119
3	195	85	172	156	126
4	178	77	189	170	124
5	185	69	176	162	131
Mean ± SD	191.80 ± 23.763	78.68 ± 6.229	182.40 ± 17.097	161.80 ± 7.362	123.20 ± 5.891

The positive control group / K(+), which received epinephrine, demonstrated the fastest bleeding cessation among all groups. In contrast, the negative control group / K(-) required the longest time to stop bleeding. Among the treatment groups, the group receiving *Jatropha multifida* leaf extract at a concentration of 80% (P3) showed a shorter bleeding time compared with the groups receiving 20% (P1) and 40% (P2) concentrations, indicating a possible dose-dependent effect of the extract on the reduction of bleeding time (Table 2).

To assess whether the data were normally distributed, the Shapiro–Wilk test was applied, as the number of samples in each group was fewer than 50. Data were considered normally distributed when the p-value was greater than 0.05. The results of the Shapiro–Wilk normality test are presented in Table 3. The results show that all groups had p-values greater than 0.05, indicating that the bleeding time data in each group were normally distributed. A Levene's Test of Variance was performed to evaluate the homogeneity of variance among the groups. The test produced a p-value of 0.064, indicating that the data had homogeneous variance because the value was greater than 0.05. The results of the homogeneity test are presented in Table 4. Since the data were normally distributed and demonstrated homogeneous variance, parametric statistical analysis was applied. Therefore, One-Way Analysis of Variance (ANOVA) was used to test the study hypothesis.

Table 3. Results of the data normality test

No	Group	p-value	Description
1	Negative control	0.321	Normally distributed
2	Positive control	0.670	Normally distributed
3	Treatment 1	0.489	Normally distributed
4	Treatment 2	0.593	Normally distributed
5	Treatment 3	0.931	Normally distributed

Table 4. Results of the homogeneity test

Variable	Levene statistic	p-value	Description
Bleeding time	2.649	0.064	Homogeneous variance

The One-Way ANOVA test was performed to determine whether there were statistically significant differences in bleeding time among the five experimental groups. The results are presented in Table 5. The ANOVA analysis produced a p-value of less than 0.001. In statistical decision-making, a p-value less than 0.05 indicates a statistically significant difference. Therefore, the results demonstrate a significant difference in bleeding time among the experimental groups receiving distilled water, epinephrine, and *Jatropha multifida* leaf extract.

Table 5. Results of the One-Way ANOVA test

Variable	F	p-value	Description
Bleeding time	55.364	<0.001	Significant difference between aquadest, epinephrine, and Jatropha multifida leaf extract

A Post Hoc analysis was conducted to determine which groups differed significantly after the One-Way ANOVA test. The Least Significant Difference (LSD) test was used for pairwise comparisons. A p-value less than 0.05 indicates a significant difference, while a p-value greater than 0.05 indicates no significant difference. The results are presented in Table 6. The results of the Least Significant Difference (LSD) analysis revealed significant differences in bleeding time among several experimental groups. Significant differences were observed between the negative control group and the positive control group, as well as between the negative control group and treatment groups P2 and P3. However, no significant difference was found between the negative control group and treatment group P1.

Table 6. Results of the Post Hoc (LSD) test

Groups Compared	p-value	Description
K(-) – K(+)	<0.001	Significant difference
K(-) – P1	0.302	No significant difference
K(-) – P2	0.003	Significant difference
K(-) – P3	<0.001	Significant difference
K(+) – P1	<0.001	Significant difference
K(+) – P2	<0.001	Significant difference
K(+) – P3	<0.001	Significant difference
P1 – P2	0.031	Significant difference
P1 – P3	<0.001	Significant difference
P2 – P3	<0.001	Significant difference

Furthermore, significant differences were observed between the positive control group and all treatment groups (P1, P2, and P3). Significant differences were also found between treatment group P1 and treatment groups P2 and P3, as well as between treatment groups P2 and P3. These findings indicate that *Jatropha multifida* leaf extract significantly affects bleeding time in the treatment groups, supporting the potential of this plant as a hemostatic agent capable of accelerating the cessation of bleeding.

DISCUSSION

This study was conducted at the Pharmacology Laboratory, Faculty of Medicine, Universitas Muhammadiyah Surakarta, with the aim of evaluating the effect of yodium leaf extract (*Jatropha multifida Linn.*) on bleeding time. The experimental subjects consisted of 25 male mice selected through purposive sampling while adhering to predetermined inclusion and exclusion criteria. The use of male mice was intended to minimize biological variability associated with hormonal fluctuations that occur in female animals, thereby ensuring more homogeneous experimental conditions. The sample animals were divided into five groups: a negative control group receiving distilled water (aquadest), a positive control group receiving epinephrine at a dilution of 1:1000, and three treatment groups receiving *Jatropha multifida* leaf extract at concentrations of 20% (P1), 40% (P2), and 80% (P3). The Duke method was used to measure bleeding time, which is a commonly used technique to evaluate primary hemostasis through the observation of the duration required for bleeding to cease after a standardized incision.

Distilled water was used as the negative control because of its neutral characteristics. As a neutral substance, distilled water does not contain active compounds that could influence the physiological mechanisms involved in the hemostatic process. Consequently, it is not expected to affect the natural bleeding cessation process in experimental animals. In contrast, epinephrine was used as the positive control due to its well-known pharmacological effects in promoting hemostasis. Epinephrine induces vasoconstriction of blood vessels and facilitates faster formation of blood clots, thereby accelerating the cessation of bleeding. These physiological effects directly influence the speed of bleeding time and make epinephrine a suitable reference agent for evaluating the hemostatic activity of other substances [14].

According to Gumawan, bleeding time can be defined as the time interval between the onset of bleeding and the point at which bleeding stops due to the formation of a temporary platelet plug [15]. In the present study, bleeding time was determined by observing the absence of blood spots on filter paper, which indicated that bleeding had ceased. The duration from the first appearance of blood until the complete cessation of bleeding was recorded using a stopwatch. The collected data were subsequently analyzed using statistical software to determine whether the administration of *Jatropha multifida* leaf extract had a significant effect on bleeding time.

The findings of this study indicate that the bleeding time in mice was influenced by the administration of *Jatropha multifida Linn.* leaf extract. The results demonstrated that bleeding cessation occurred more rapidly as the concentration of the extract increased from 20% to 40% and 80%, suggesting the presence of a dose–response relationship. In other words, higher concentrations of the extract were associated with shorter bleeding times. Nevertheless, although the extract showed a hemostatic effect, its effectiveness remained lower than that of epinephrine, which is widely used as a pharmacological hemostatic agent.

The hemostatic effect observed in this study is assumed to be associated with the presence of bioactive compounds contained in *Jatropha multifida* leaves, particularly tannins and flavonoids. Tannins are known to possess astringent properties that contribute to the hemostatic process. These compounds promote protein precipitation, enhance tissue contraction, and cause constriction of damaged blood vessels, thereby helping

to stop bleeding more rapidly [16]. Through these mechanisms, tannins may facilitate the stabilization of the wound site and support the formation of a temporary hemostatic barrier.

Flavonoids also play an important role in the hemostatic process by promoting platelet aggregation. These compounds stimulate the synthesis of serotonin and thromboxane A_2, both of which are involved in platelet activation and aggregation. Thromboxane A_2 acts as a vasoconstrictor and enhances platelet adhesion and aggregation, thereby accelerating the formation of a platelet plug that is essential in primary hemostasis [17]. In addition, flavonoids may inhibit the activity of prostacyclin (prostaglandin I_2), a compound that normally acts as a vasodilator. By suppressing prostacyclin activity, flavonoids promote vasoconstriction at the site of vascular injury, which further contributes to faster bleeding cessation [18]. These mechanisms collectively explain how the bioactive compounds present in *Jatropha multifida* leaves may contribute to the reduction of bleeding time observed in the experimental animals.

The results of this study are consistent with previous findings reported by Hidayati & Bahri in 2023, which demonstrated that the extract of yodium leaves—having phytochemical components similar to those found in the plant's sap—exhibited positive effects in accelerating the healing of incision wounds in mice without causing signs of infection [19]. These findings support the hypothesis that the bioactive compounds present in *Jatropha multifida* contribute to wound healing and hemostatic mechanisms [20]. However, another study conducted by Zaetun in 2014 reported that the direct application of the sap of the yodium plant was less effective and potentially unsafe when applied to fresh wounds. Therefore, proper extraction processes are required to optimize the pharmacological properties and ensure safer therapeutic use [21].

Despite the significant findings obtained in this study, several limitations should be acknowledged. First, the standardization of wound length and depth in the mice could not be perfectly controlled due to the movement of the animals during the incision procedure. This factor may have influenced the bleeding time measurements and introduced variability in the results. Second, the present study only evaluated the effect of *Jatropha multifida* leaf extract on bleeding time as a clinical indicator of primary hemostasis without examining the underlying molecular or biochemical mechanisms in greater detail. As a result, the precise biological pathways responsible for the observed effects remain unclear.

Therefore, further research is necessary to confirm and elucidate the mechanisms of action of *Jatropha multifida* leaf extract. Future studies may include histopathological examinations or biomolecular analyses related to platelet activity, coagulation factors, and vascular responses in order to better understand the pharmacological effects of this plant extract.

In addition, future investigations are recommended to compare the effectiveness of *Jatropha multifida* leaf extract with other natural hemostatic agents. Research exploring more suitable pharmaceutical formulations—such as gels, ointments, or topical preparations—would also be valuable in improving the practical applicability of this plant extract in clinical settings. Through such studies, the findings of the present research may serve as an important foundation for the development of plant-based natural therapies aimed at supporting the hemostatic process and improving wound management.

CONCLUSION

The administration of *Jatropha multifida Linn.* leaf extract at concentrations of 40% and 80% demonstrated a significant effect in reducing bleeding time. These findings indicate that yodium leaf extract possesses potential hemostatic properties and may influence the physiological mechanisms involved in hemostasis in mice. The observed reduction in bleeding time suggests that the bioactive compounds present in the extract may contribute to accelerating the formation of a platelet plug and enhancing the early stages of the blood clotting process.

Ethical consideration, competing interest and source of funding

-This study received ethical approval from the Health Research Ethics Committee of Dr. Moewardi Regional General Hospital with approval number 2.038/XI/HREC/2023.
-There is no conflict of interest related to this publication.
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