

Jatropha multifida L stem sap gel versus *Aloe vera* gel to post-gingivectomy healing process



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ABSTRACT

Introduction: Gingivectomy is cutting the gingiva during a gingival enlargement condition that causes an open wound in the gingiva. *Jatropha multifida* L gel contains active ingredients of alkaloids, flavonoids, saponins and tannins, which are thought to accelerate the wound healing process, but its use in dentistry is limited. The objective of this research is to determine the effectiveness of the application of *Jatropha multifida* L stem sap gel in the wound healing process post-gingivectomy in Wistar rats (*Rattus norvegicus*) compare with *Aloe vera* gel (*Aloe Barbadensis* Miller) by using parameters the number of fibroblasts, blood vessels and the density of collagen fibers.

Methods: Rats were divided into 4 groups, namely group K (*Aloe vera* gel), P1 (*Jatropha multifida* L stem sap gel 2,5%), P2 (*Jatropha multifida* L stem sap gel 5%) and P3 (*Jatropha multifida* L stem sap gel 10%). Each group was given the gel twice a day in the wound area; then the wound was observed microscopically by Haematoxylin Eosin staining to count the number of fibroblasts and blood vessels also Masson Trichrome staining to observe the density of collagen fibers on day 3 and 7.

Results: The data obtained were statistically analyzed using the One Way Anova, Dunnet and Kruskal-Wallis test. One Way Anova test shows there is a significant difference ($p < 0.05$) in the number of fibroblasts, and the Dunnet test shows there is a significant difference ($p < 0.05$) in the number of fibroblasts in *Jatropha multifida* L stem sap gel group 2.5% and 5% on day 3. One Way Anova test shows no significant difference ($p > 0.05$) in the number of blood vessels. The Kruskal-Wallis test shows no significant difference ($p > 0.05$) in collagen fiber density.

Conclusion: *Jatropha multifida* L Stem Sap gel has the same potential as *Aloe vera* gel in accelerating wound healing after gingivectomy in Wistar rats.

Keywords: *Jatropha multifida* L, fibroblast, blood vessel, collagen, gingivectomy.

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INTRODUCTION

The prevalence of dental and mouth disease in Indonesia is still high, reaching 57.6%; caries and periodontal disease are the two most cases.¹ Gingival enlargement is a periodontal disease in which conditions change in the gingiva's size caused by a local factor or systemic conditions. The treatment for gingival enlargement is gingivectomy, which aims to restore physiological gingival contours.² Gingivectomy is the removal of enlarged gingiva tissue for pocket deletion, which raises an open wound in the gingiva and is usually closed by periodontal dressing in daily practice.³ In general, periodontal dressing protects open wounds, but it does not have healing factor properties. Furthermore, contact allergies also have been reported in several cases because of the use of this materia.⁴

Wound or injury is a state of anatomical structure and function tissue damage due to pathological processes. Wound healing is a complex process consisting of homeostasis, inflammation, proliferation and maturation phases. In the proliferation phase, angiogenesis, fibroblast proliferation and collagen formation play an important role in the wound healing process.^{5,6}

Currently, herbal medicine already has a place in society; the most popular and receiving much scientific attention is *Aloe vera* (*Aloe barbadensis* Miller), whose effectiveness is not inferior to chemical drugs and has minimal effect. Many studies have shown that *Aloe vera*, with its active ingredients such as saponin, tannin, flavonoid and acetylated mannan, can accelerate wound healing due to several mechanisms, including increasing collagen synthesis and rate of epithelization,

anti-inflammatory, antimicrobial and moisturizing effects. Several studies have proven the efficacy of *Aloe vera*; Tazkare et al. in Movaffagh (2022) confirm that aloe gel accelerated dermal wound healing and tissue creation in rats; another study stated that Aloe cream indicated accelerated wound healing in burned patients and had a better effect than silver sulfadiazine cream.^{7,8,9} Babae et al. report that aloe gel decreased the healing period of minor recurrent aphthous stomatitis.¹⁰ Hudwekar et al. inform that applying *Aloe vera* gel after a periodontal flap surgery in a chronic periodontitis patient improved the healing score significantly in the first post-operative week.¹¹ Although it has extraordinary potential, *Aloe vera* contraindications for a patient allergic to the *Liliaceae* family plant; therefore, there is a need for other candidates. *Jatropha multifida* L (Iodine plant) is one of the

plants that is easily found and thought to have the ability to accelerate the healing process. Phytochemical studies of various species of *Jatropha* reveal the presence of alkaloids, cardiac-glycoside, flobatannis, flavonoids, tannin and saponin. Various parts of the *Jatropha* plant, such as oil from seeds, sap, leaves, tree bark and roots, can be useful to cure skin diseases such as eczema, itching, boils, ulcer and swollen sores.^{12,13,14} Juniarti et al. state that the healing process of cuts using methanol extract of *Jatropha multifida* L leaves was better than the application of Bethasone-N, the number of pro-inflammatory PMN leukocytes was lower, the inflammatory phase was shorter, and the number of proliferative fibroblasts was higher.¹⁵ Another study by Sahrah et al. proved that 10% *Jatropha multifida* L extract can potentially epithelialize the healing process of traumatic ulcers of the oral mucosa.¹⁶

This research was conducted to determine the effectiveness of applying *Jatropha multifida* L stem sap gel in wound healing post-gingivectomy compared with *Aloe vera* gel (*Aloe barbadensis* Miller).

METHODS

Study Design

This research was experimental research. This study was conducted in a pharmaceutical laboratory, an anatomic pathology laboratory, and a Bioscience institute, Universitas Brawijaya. It is an in vivo true experimental study with a Randomized Group Post Test Control Only Design.

Sample Selection

This study used 32 male Wistar rats aged 2-3 months with a weight of 250-300 grams, consisting of 4 groups, namely group K (*Aloe vera* gel), P1 (*Jatropha multifida* L stem sap gel 2,5%), P2 (*Jatropha multifida* L stem sap gel 5%) and P3 (*Jatropha multifida* L stem sap gel 10%) and 2-time series (day 3 and 7).

Measurement of the Sample

Jatropha multifida L stem sap gel is obtained from tapping the stems of the iodine plant. The sap is dried by the freeze-drying method for 1 day and then formed into a gel preparation with a concentration

of 2.5%, 5% and 10%. The resulting gel is homogeneous with a semisolid shape, brown, with a distinctive odor from the sap of the iodine plant, and has a neutral pH. The *Aloe vera* gel used has been circulating in the market with the content of *Aloe vera*, hyaluronic acid, gliricetin acid and polyvinylpyrrolidone.

The gingivectomy procedure on rats was to make an open wound in the anterior region of the mandible using a fissure diamond bur with a diameter of 1.6 mm and depth of 1 mm on the attached gingiva, 2 mm from the gingival margin of the incisors. The gels were administered to the gingivectomy wound 2 times a day after eating as much as 0,4 grams using a tip applicator in each group. Tissue sampling was carried out on day 3 and day 7 after treatment by cervical dislocation. Hematoxylin Eosin staining was performed to observe fibroblast proliferation and the number of blood vessels. Masson Trichrome staining was performed to observe the density of collagen fiber.

Statistical Analysis

Statistical analysis using the One Way Anova test to evaluate the difference between each group on observation of proliferation fibroblast and the number of blood vessels, then continued with the Dunnett test to determine which groups were different. The Kruskal-Wallis test was carried out to see the difference in the result of collagen fiber scoring from each group.

RESULT

Fibroblast

Calculation of fibroblasts cell using 400x magnification for 5 fields of view using a light microscope (Olympus CX10) and OlyVia (Olympus Viewer for Imaging Application) software. Sample Preparations showed active fibroblasts had many irregular cytoplasmic branches, oval nuclei, large, pale on outward appearance and fine chromatin.¹⁷ The results of the observation can be seen in [figure 1](#). A comparison of the number of fibroblasts on day 3 and day 7 can be seen in [table 1](#).

The highest number of fibroblasts was found in the *Jatropha multifida* L stem sap gel, 5 % on days 3 and 7. Based on the

result of Anova shows a significance value of 0.000, it can be concluded that there is a significant difference in the number of fibroblasts between groups. Dunnett test results significantly different in group K1 with P13 and P23 on day 3.

Blood Vessel

Calculating blood vessels using 400x magnification for 5 fields of view using a light microscope (Olympus CX10 and OlyVia (Olympus Viewer for Imaging Application) software. Preparation showed that blood vessels had cavities surrounded by endothelial cells and filled with bright red erythrocytes.⁶ The results of the observation can be seen in [figure 2](#). A comparison of the number of blood vessels on day 3 and day 7 can be seen in [table 2](#).

The highest number of blood vessels was found in the *Jatropha multifida* L stem sap gel, 5 % on day 3 and day 7. Based on the result of the Anova Test shows a p-value of 0.970, it can be concluded that there is no significant difference in the number of blood vessels between groups.

Collagen

Calculating collagen fibers formed using 400x magnification for 1 field of view using a light microscope (Olympus CX10). Collagen fibers will be stained blue, and the distribution of collagen is seen based on the criteria for assessing the density and distribution of collagen fibers which are converted into a score of 0 to 4.¹⁸ The histopathological scoring parameters according to Rizka et al. (2013) for collagen density are as follows : 0 = No collagen fibers were found, +1=Low density of collagen fibers (less than 10%), +2 = Medium density of collagen fibers (10%-50%), +3 = density of collagen fibers is tight (50%-90%), +4 = density of collagen fibers is very tight (100%).¹⁹ The results of the observation can be seen in [figure 3](#). Collagen scoring comparison on day 3 and day 7 can be seen in [table 3](#).

The highest scoring collagen fiber density was found in the *Jatropha multifida* L stem sap gel 5 % on day 3; on day 7, there was the same average score between *Aloe vera* gel and *Jatropha multifida* L stem sap gel 5%. Based on the result of the Kruskal-Wallis test shows a p-value of 0,055, it can

Table 1. Average data of the number of fibroblasts.

Group		Mean ± SD	p-value
Day 3	<i>Aloe vera</i> gel (K1)	47.00 ± 4.359	0.000*
	<i>Jatropha multifida</i> L stem sap gel 2,5% (P13)	63.67 ± 3.055	
	<i>Jatropha multifida</i> L stem sap gel 5% (P23)	90.00 ± 3.000	
	<i>Jatropha multifida</i> L stem sap gel 10% (P33)	51.33 ± 7.506	
Day 7	<i>Aloe vera</i> gel (K2)	86.00 ± 7.937	
	<i>Jatropha multifida</i> L stem sap gel 2,5% (P17)	73.33 ± 2.887	
	<i>Jatropha multifida</i> L stem sap gel 5% (P27)	91.00 ± 12.490	
	<i>Jatropha multifida</i> L stem sap gel 10% (P37)	71.71 ± 17.051	

Note: *significant at $p < 0.05$ by One Way Anova Test; SD = Standard of Deviation

Table 2. Average data on the number of blood vessels.

Group		Mean ± SD	p-value
Day 3	<i>Aloe vera</i> gel (K1)	3.27 ± 1.50	0.970
	<i>Jatropha multifida</i> L stem sap gel 2,5% (P13)	2.87 ± 1.50	
	<i>Jatropha multifida</i> L stem sap gel 5% (P23)	3.80 ± 1.04	
	<i>Jatropha multifida</i> L stem sap gel 10% (P33)	2.87 ± 0.70	
Day 7	<i>Aloe vera</i> gel (K2)	3.33 ± 1.60	
	<i>Jatropha multifida</i> L stem sap gel 2,5% (P17)	3.60 ± 0.92	
	<i>Jatropha multifida</i> L stem sap gel 5% (P27)	3.87 ± 1.70	
	<i>Jatropha multifida</i> L stem sap gel 10% (P37)	3.73 ± 1.96	

Note: SD = Standard of Deviation

Table 3. Average data of collagen fiber density scoring.

Group		Mean ± SD	p-value
Day 3	<i>Aloe vera</i> gel (K1)	1.33 ± 0.58	0.055
	<i>Jatropha multifida</i> L stem sap gel 2,5% (P13)	1.33 ± 0.58	
	<i>Jatropha multifida</i> L stem sap gel 5% (P23)	2.33 ± 0.58	
	<i>Jatropha multifida</i> L stem sap gel 10% (P33)	1.66 ± 0.58	
Day 7	<i>Aloe vera</i> gel (K2)	2.66 ± 0.58	
	<i>Jatropha multifida</i> L stem sap gel 2,5% (P17)	2 ± 0.58	
	<i>Jatropha multifida</i> L stem sap gel 5% (P27)	2.66 ± 0.58	
	<i>Jatropha multifida</i> L stem sap gel 10% (P37)	2 ± 0.00	

Note: SD = Standard of Deviation

be concluded that there is no significant difference in collagen fiber density scoring between groups.

DISCUSSION

This study aims to compare the effectiveness of *Jatropha multifida* L stem sap gel with *Aloe vera* gel (*Aloe barbadensis* Miller) in the wound healing process post-gingivectomy. Based on the calculation of the average number of fibroblasts and blood vessels also collagen fiber density scoring, the treatment group applying *Jatropha multifida* L stem sap gel 5% had the highest average. Broadly stated that there were no significant differences in all parameters on day 3 and day 7. The significant difference was only found in the number of fibroblasts in the *Jatropha*

multifida L stem sap gel group of 2,5% and 5 % on day 3. These results indicate that the *Jatropha multifida* L stem sap gel group has the equivalent ability to the *Aloe vera* gel group, which has been widely used as a medicine to heal wounds.

Aloe vera contains active substances such as saponins, tannins, and flavonoids. Tannin functions as an antioxidant that can increase macrophage migration, and acetylated mannan in *Aloe vera* extract is also useful as an anti-inflammatory that plays a role in activating macrophages. Macrophages will stimulate the secretion of growth factors that can increase fibroblast proliferation. Fibroblasts will produce collagen, which can close the wound. In addition to the *Aloe vera* gel used in this study, there are also sodium

hyaluronate, glycyrrhithnic acid, and polyvinylpyrrolidone (PVP), which affect healing, PVP can form a layer over the ulcer so that can protect wound nerve endings and prevent irritation. *Aloe vera* is effective as an anti-inflammatory agent with analgesic properties by inhibiting the arachidonic acid pathway via cyclooxygenase, inhibiting inflammation. *Aloe vera* is proven to have benefits for treating skin problems by increasing the activity of fibroblasts. Fibroblasts can produce collagen and elastic fiber to give the skin its structure. Many studies showed that *Aloe vera* has healing properties. It can improve healing by increasing the blood supply, which increases oxygenation.²⁰ One of the ingredients of *Aloe vera* is saponin; saponin can activate the function of TGF-b. Saponin will increase TGF-b expression at fibroblast receptor. TGF-b will stimulate migration and proliferation of fibroblasts. Vitamin C and vitamin E in *Aloe vera* can neutralize free radicals resulting from neutrophil phagocytosis against a bacterium and debris in the process of wound healing. That antioxidant will reduce lipid peroxidation, which will slow down cell necrosis and increase vascularity. According to a study conducted by Fatmawati (2020), *Aloe vera* has the same ability as silver sulfadiazine 1%, which is the golden standard of treatment in the wound-healing process of burns.²¹

The results of this study show that, in general, there is no significant difference between *Jatropha multifida* L stem sap gel when compared with *Aloe vera* gel on the healing process after gingivectomy seen from the number of fibroblasts, blood vessels and collagen density. *Jatropha multifida* L stem sap gel contains various active substances such as saponins, flavonoids, alkaloids and tannins. Saponins in the *Jatropha multifida* L stem sap gel can stimulate the formation of VEGF and activate fibroblasts in wound tissue by increasing the production of cytokines. It can stimulate TGF-b which affects the proliferation, differentiation and migration of fibroblast cells so that it can trigger collagen formation.²² Tannins can cause tissue contraction by binding to these tissue proteins and have antimicrobial and anti-inflammatory properties.

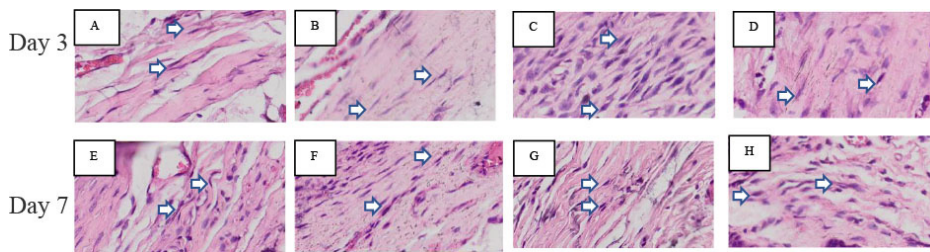


Figure 1. Microscopic image of Fibroblasts in the group. (A) K1 Group : (B) P13 Group : (C) P23 Group : (D) P33 Group : (E) K2 Group : (F) P27 Group : (G) P27 Group : (H) P37 Group.

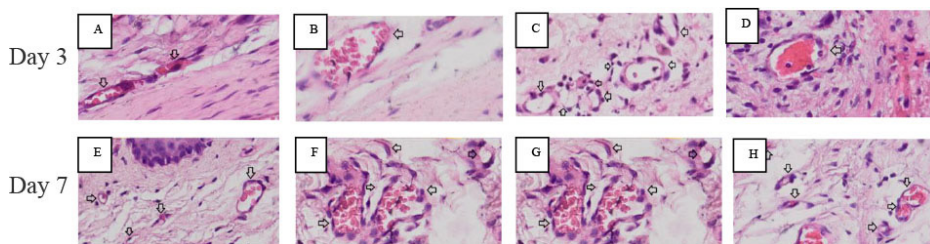


Figure 2. Microscopic image of Blood vessels in the group. (A) K1 Group : (B) P13 Group : (C) P23 Group : (D) P33 Group : (E) K2 Group : (F) P27 Group : (G) P27 Group : (H) P37 Group.

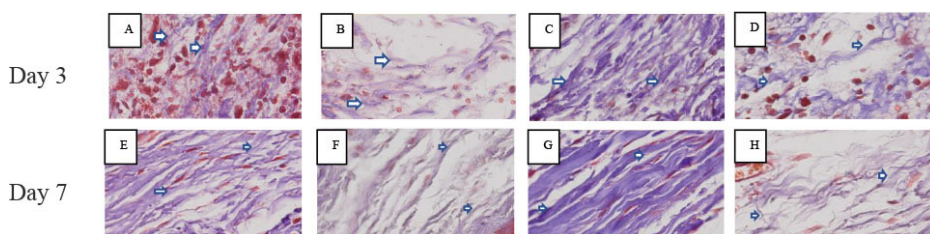


Figure 3. Microscopic image of collagens in the group. (A) K1 Group : (B) P13 Group: (C) P23 Group : (D) P33 Group : (E) K2 Group : (F) P27 Group : (G) P27 Group : (H) P37 Group.

Flavonoids have been known to function as vasodilators which can facilitate blood flow. Flavonoids can also function as an antibacterial by forming complex compounds to disrupt the integrity of bacterial cell membranes. This bacterial death can reduce phagocytosis by PMN so that the inflammatory phase takes place quickly and the proliferative phase begins earlier. Alkaloids are responsible for the wound-healing process by responding to cell proliferation and being able to increase collagen production. *Jatropha multifida L* stem sap gel also contains terpenoids. It has antimicrobial and antioxidant effects, which are thought to be responsible for increasing wound contraction and the speed of epithelialization.^{15,23,24}

CONCLUSION

Jatropha multifida L gel has the same potential as *Aloe vera* gel (*Aloe barbadensis Miller*) in accelerating the wound healing process after gingivectomy. *Jatropha multifida L* 5% has better abilities in wound healing post gingivectomy on the number of fibroblast and blood vessels also collagen fiber density. Therefore, further research regarding the toxicity and safe dosage of *Jatropha multifida L* for use in the wider community is needed.

CONFLICT OF INTEREST

The authors have no conflict of interest regarding all aspects of this study.

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This research did not receive any specific grant.

ETHICAL CONSIDERATION

This study was approved by the health research ethics commission medical school of Universitas Brawijaya (certificate number: 281/EC/KEPK-S1-FKG/11/2018)

AUTHOR CONTRIBUTION

All Authors contribute equally in conducting research and writing manuscripts

REFERENCES

1. Badan Penelitian dan Pengembangan Kesehatan. Laporan Nasional Risesdas 2018. Riset Kesehatan Dasar 2018. 2019. p. 674.
2. Andriani I. Perawatan Pembesaran Gingiva dengan Gingivektomi. *J Mutiara Med.* 2009;9(Januari):70–3.
3. Cohen ES. Atlas Of Cosmetic And Reconstructive Periodontal Surgery. third Edit. Hamilton, Ontario: BC Decker Inc; 2007. 39 p.
4. Newman M, Takei, Klokkevold, Carranza. Clinical Periodontology. Thirteenth. Carranza F, editor. Philadelphia: Elsevier; 2019. 602 p.
5. Sumbayak EM. Tinjauan Pustaka Fibroblas : Struktur dan Perannya dalam Penyembuhan Luka. *J Kedokt Meditek.* 2015;21(6):1–6.
6. Yuhernita, Juniarti A. Pengaruh Pemberian Gel Dari Ekstrak Metanol Daun Jarak Tintir (*Jatropha Multifida L*) Terhadap Kepadatan Serabut Kolagen Dan Jumlah Angiogenesis Dalam Proses Penyembuhan Luka. In Prosiding Seminar Nasional dan Workshop “Perkembangan Terkini Sains Farmasi dan Klinik IV” tahun 2014; 2014. p. 47.
7. Sajjad A, Subhani Sajjad S. *Aloe vera* : An Ancient Herb for Modern Dentistry—A Literature Review. *J Dent Surg.* 2014;2014:1–6.
8. Thomas D, Nath MS, Mathew N, R R, Philip E, Latha MS. Alginate film modified with aloe vera gel and cellulose nanocrystals for wound dressing application: Preparation, characterization and in vitro evaluation. *J Drug Deliv Sci Technol.* 2020;59(June):101894.
9. Movaffagh J, Fazli S, Taherzadeh Z. Evaluation of wound-healing efficiency of a functional Chitosan / *Aloe vera* hydrogel on the improvement of re-epithelialization in full thickness wound model of rat. *J Tissue Viability.* 2022;(July).
10. Babae N, Zabihi E, Mohseni S, Moghadamnia AA. Evaluation of the therapeutic effects of *Aloe vera* gel on minor recurrent aphthous stomatitis. *Dent Res J (Isfahan).* 2012;9(4):381–5.

11. Hudwekar AD, Beldar A, Supriya M, Lendhey S, MT. *Aloe vera* on wound healing after periodontal flap surgery in chronic periodontitis patient: A randomized control trial. *J Oral Res Rev.* 2019;11:72–6.
12. Destri C, Sudiana IK, Nugraha J. POTENSI EKSTRAK *Jatropha multifida* TERHADAP EKSPRESI VEGF APHTHOUS ULCER Rat norvegicus. *J SainHealth.* 2017;1(2):5–12.
13. Hirota BCK, Miyazaki CMS, Mercali CA, Verdan MC, Kalegari M, Gemin C, et al. C-glycosyl flavones and a comparative study of the antioxidant, hemolytic and toxic potential of *Jatropha Multifida* Leaves and bark. *Int J Phytomedicine.* 2012;4(1):1–5.
14. Sabandar CW, Ahmat N, Jaafar FM, Sahidin I. Medicinal property, phytochemistry and pharmacology of several *Jatropha* species (Euphorbiaceae): A review. *Phytochemistry.* 2013;85:7–29.
15. Juniarti, Aryenti, Yuhernita, Poerwaningsih E.H, Jusuf A.A, Freisleben J S. Effects of Methanolic *Jatropha Multifida* L. Extract in Wound Healing Assessed by the Total Number of PMN Leukocytes and Fibroblasts. *MAKARA Sci Ser.* 2013;16(3):178–82.
16. Sahrah, Sudiana I, Nugraha J. Epitelisasi Pada Ulkus Traumatikus Oral. 2015;17(3):110–4.
17. Mescher AL. No Title. 14th ed. EGC, editor. Jakarta; 2017. 626 p.
18. Permatasari N, Handayani MP, Diah. Efek Jus Belimbing (*Averrhoa carambola* Linn.) dalam Meningkatkan Pembentukan Kolagen pada Soket Pasca Pencabutan Gigi Tikus Wistar. *Prodentia J Dent.* 2013;1:7–14.
19. Rizka A, Budipramana VS, Fauziah D. Kepadatan Kolagen tipe 1 pada luka operasi tikus Wistar yang mengalami anemia karena perdarahan akut. *Media J Emerg.* 2013;2(1):1.
20. Sujatha G, Senthil Kumar G, Muruganandan J, Srinivasa Prasad T. *Aloe vera* in dentistry. *J Clin Diagnostic Res.* 2014;8(10):ZI01–2.
21. Fatmawati CN, Retnanin E, Wahyuni TD. The Effect of *Aloe vera* Toward the Number of Fibroblasts on the Wound Incision of Wistar Rat'S (Ratus Norvegicus). *J Vocat Nurs.* 2020;1(1):30.
22. Kimura Y, Sumiyoshi M, Kawahira K, Sakanaka M. Effects of ginseng saponins isolated from Red Ginseng roots on burn wound healing in mice. *Br J Pharmacol.* 2006;148(6):860–70.
23. Ivan I, Sudigdoadi S, Kartamihardja AHS. Antibacterial Effect of *Jatropha Multifida* L. Leaf Infusion towards *Staphylococcus aureus* and *Pseudomonas aeruginosa*. *Althea Med J.* 2019;6(2):95–9.
24. Syarfati, Eriani K, Damhoeri A. The Potential of Jarak Cina (*Jatropha Multifida* L.) Secretion in Healing New-Wounded Mice. *J Nat.* 2011;11(1):39–44.



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