Potential of *Muntingia Calabura* L. Leaf Extract Cream on the Late Remodeling Phase of Wound Healing in Diabetic Rats *(Rattus Norvegicus)*

Muhammad Nur Salim[1*], Siti Aisyah[1], Dian Masyitha[2], Rumi Sahara Zamzami[3], Betrianis[4]

[1]Laboratory of Pathology; [2]Laboratory of Histology; [3]Laboratory of Clinical; [4]Veterinary Study Program,

Faculty of Veterinary Medicine, Syiah Kuala University, Banda Aceh, Indonesia

*** Corresponding Author**

DOI: https://doi.org/10.51584/IJRIAS.2025.100600144

Received: 19 June 2025; Accepted: 23 June 2025; Published: 24 July 2025

ABSTRACT

Wound healing is a complex biological mechanism of the body that repairs damaged tissue by involving various cellular activities. This study aimed to determine the effectiveness of *Muntingia calabura* L. leaf extract cream to accelerate incision wound healing on day 21 in white rats *(Rattus norvegicus)* with diabetes mellitus. This experiment used 12 male white rats weighing 150-200 g and 2-3 months old, induced by a single dose of streptozotocin. The incision was made on the paravertebral area along 2 cm and a depth of 2 mm. Wound therapy was given twice a day for 21 days, P1 was given cream base and distilled water , P2 was given 0.1% silver sulfadiazine cream and metformin 4, 5 mg/k g weight, P3 and P4 were given 5% and 15% *Muntingia calabura L*. leaf extract cream with oral extract 450 mg/k g body weight. ANOVA test results showed a significant effect ($P<0.05$) on the number of fibroblasts and density of collagen. Duncan test results on fibroblast, P1 were significantly different ($P<0.05$) from P2, P3, and P4, while the results on density of collagen, P3 were significantly different ($P<0.05$) from P1, P2, and P4. Based on the results, it can be concluded that 5% *Muntingia calabura* L . leaf extract cream can decrease the number of fibroblasts and increase the density of collagen, which is effective in accelerating incision wound healing on day 21 on white rats' skin with diabetes mellitus.

Keywords: Muntingia calabura cream; collagen fibers; fibroblast cells; wound healing; late remodeling phase

INTRODUCTION

Wound is a condition of damage to the continuity of the anatomical structure of the body tissue due to intentional although unintentional or disease (Velnar *et al* ., 2009). Wounds can be divided into several types of wounds, including acute and chronic wounds. Acute wounds are new and sudden wounds with fast healing time. Chronic wounds are wounds resulting from a failed wound healing process and risk of reappearing (Ardiansyah, 2021).

Wound healing is a complex biology of the body to restore injured tissue involved cellular, physical and chemical activity at ed (Fossum, 2012). Wound healing can take place in 3 main phases, namely the inflammatory phase, progressive phase and maturation phase (Wang *et al*., 2018). Of these three phases, the maturation phase is the longest wound healing phase, which is 3 weeks to 1 year. In this phase, the collagen remodeling phase occurs, so it needs to be tightly controlled so that wound healing is complete (Velnar *et al*., 2009).

Wound healing can take place quickly or slowly which is influenced by many interrelated factors (Antia, 2019). Factors that can accelerate the wound healing process are collagen. Collagen is the main component of extracellular matrix important in the wound healing process (Steiner *et al*., 2021). Collagen also has a role in tissue formation and regeneration (Imamah, 2015 and Fakhrurrazi *et al.*, 2020). Increasing the distribution of collagen in the incision wound area can accelerate the maturation phase of wound healing (Nanda *et al*., 2017 and Harris *et al*., 2019). Wound healing can also take place slowly due to several factors, including hyperglycemia which is an early symptom of diabetes mellitus (Kewuta *et al.*, 2021). Therefore, there is a need

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

for appropriate alternatives to speed up the process of wound healing in diabetes mellitus. One way is by giving medical plants (Leung, 2007).

One of the plants that has the potential as an anti-diabetic and anti-inflammatory traditional medicine is cherry *(Muntingia calabura L.)* (Ginting *et al.,* 2021). Andalia *et al*. (2021) reported that the *Muntingia calabura L.* decreases blood glucose levels in diabetic rats. Ariesti *et al*. (2014) explained that *Muntingia calabura L.* can accelerate wound healing comparable to Gentamicin 0.1% in non-hyperglycemic mice. Handayani and Sentat (2016), also reported that *Muntingia calabura L.* affects burn wound healing.

Based on the results of previous studies about the potential of *Muntingia calabura* L leaf in wound healing, the research ffectiveness of *Muntingia calabura* L leaf extract cream on incision wound healing day 21 on white rats *(Rattus norvegicus)* with diabetes mellitus is necessary.

MATERIALS AND METHODS

This research was an experimental study y us ing a completely randomized design divided into four treatments and each treatment consisted of three replications. Fresh green kersen leaves are collected and dried in the air. Then mashed , used a blender and weighed . The extract was prepared by maceration using 96% ethanol. 600 g of simplicia powder soaked in 3 L of 96% ethanol for 5 x 24 hours. Then let it stand until the macerate is obtainable in the form of a liquid extract. Then evaporated using a vacuum rotary evaporator to obtain a thick extract (Manarisip *et al* ., 2019). After that, *Muntingia calabura* L leaf extract was made into oral medication preparations and topical medications in the form of creams. Oral medication preparations were made by dissolving *Muntingia calabura* L leaf extract with 1% CMC-Na solvent and stirring until homogeneous.

Creams are made using the oil-in-water (O/W) type. Then stearic acid and cetyl alcohol were put into a porcelain cup and melted over a water bath at 70˚C. After that, the triethanolamine, distilled water, propylene glycol, and nipagin were evaporated over the water bath at 70˚C. Then the two ingredients were put together into a beaker, stirred with a homogenizer at a speed of 500 rpm, until a cream base was formed. Furthermore, the cream base is mixed with kersen leaf extract and made into a cream preparation with a concentration of 5% and 15%. After the cream preparation is well mixed, the cream is put into a container (Anief, 2010).

A hyperglycemic test was carried out three times, namely before STZ induction, three days before sample collection. The test was carried out by taking blood from the tail by the rail tail flick method, then dripping it into the Gluko DR strip test and reading the data in units of mg/dL. Twelve white rats were adapted for approximately two weeks. White rats were fasted for 12 hours before being induced by STZ. STZ induction was performed intraperitoneally with a single dose of 45 mg/kg BW (Zhang *et al*., 2008). Three days after STZ induction, blood glucose levels were measured using Gluko DR if blood glucose levels were ≥ 250 mg/dL, white rats were declared to have DM (Taher *et al*., 2016).

Incision wound begins with an anesthetic process using a combination of ketamine (40-100 mg/kg BW) and xylazine (5-10 mg/kg BW) intramuscular l y in the femur i s muscle (Fish *et al*., 2008) . After an e sthesia, the dorsal hair was shaved and cleaned with 70% alcohol. An incision wound is made with an incision length of 2 cm and a depth of 2 mm in the paravertebral area (Gunawan *et al.,* 2019). Wound care was carried out according to the treatment group. Tr e atment I was a negative control; the incision wound was smeared with cream base and given aqueous. Treatment II positive control, incision wound smeared with silver sulfadiazine cream and administration of metformin at a dose of 4.5 mg/kg BW (Tuljanah *et al*., 2020). Treatments III and IV were smeared with 5% and 15% kersen leaf extract cream, as well as giving kersen leaf extract orally at a dose of 450 mg/kg BW (Andalia *et al*, 2021).

Skin retrieval was carried out one day after the last treatment by euthanizing white rats using the cervical dislocation method. After being euthanized, the skin was cleaned of hair and cut into an area of 1-1.5 cm^2 and a thickness of ± 3 mm. Then cleaned with 0.9% NaCl and fixed with 10% Buffer Neutral Formalin (BNF) for 18-25 hours. Each sample was labeled and then continued with a stopping point with a 70% alcohol solution ± 6-12 hours. Specimens were dehydrated with graded alcohol 80%, 90%, 95%, absolute I and II ± 2 hours, followed by clearing with xylol solution three times. After that, infiltrate in liquid paraffin 1, II, and III at 60 ˚C ± 1 hour.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

Next is embedding in liquid paraffin to become a block of tissue (blocking). Then sectioning was used on a microtome with a thickness of 4-5 micro meters, the slices were placed in a water bath, and viewed with an objective glass. Specimens were incubated in an incubator at 56-58° °C and continued with Hematoxylin Eosin (HE) staining.

HE staining was initiated by deparaffinization using xylol three times, for 2 minutes. Then rehydrated with a decreasing concentration of alcohol solution (absolute, 95%, 90%, and 80%) for ± 5 minutes and rinsed with running water. After that, stained with hematoxylin for ± 5 minutes and rinsed again with water. Then stained with eosin ± 2 minutes, followed by dehydration, clearing, and ending with the mounting process using entellan ® adhesive and covered with a slide (Kiernan, 1990).

Histopathological observations were made with an Olympus light microscope connected to a computer and followed by taking micrographs. Parameters observed were fibroblasts and the density of collagen fibers formed on the 21st day of wound healing on the skin of white rats, based on the calculation of three visual fields with 400x magnification. Scoring of collagen fiber density is based on Rizka *et al*. (2013), with the score converted to a standardized score.

0 = No collagen fibers found

+1 = Low density of collagen fibers (less than 10% of view)

+2 = Moderate density of collagen fibers (10%-50% of view)

+3 = Density of dense collagen fibers (50% - 90% of view)

+4 = Very dense collagen fiber density (90% - 100% of views)

Data Analysis

The result data were analyzed by *analysis of variance* (ANOVA) and continued with Duncan's test at a significance level of 5 %.

RESULTS AND DISCUSSION

Fibroblast cells

The results of the ANOVA test showed that administration of cream base (P1), 0.1% silver sulfadiazine cream (P2), 5% cherry leaf extract cream (P3) 15 % cherry leaf extract cream (P4) had signi fi cant effect ($P<0.05$) on the total fibroblast cells incised wound healing on day 21 of the skin of white rats. The results of Duncan's further test, in groups P1, P2, P3, and P4, showed a significant difference ($P<0.05$) in the number of fibroblast cells between treatments. Group P1 was significantly different from groups P2, P3, and P4, but the differences between groups P2, P3, and P4 were not significantly different. Group P1 showed an average number of fibroblast cells of 65.11±8.56, group P2 35.67±3.84, group P3 30.00±7.57, and group P4 34.00±9.02. The average number of fibroblast cells can be seen in Table 1 .

Wound healing on the 21st day shows the stage of maturation or remodeling. The maturation phase begins with fibroblasts leaving the wound area along with a fully formed re-epithelialization process, and collagen activation occurs (Putri and Tasminatun, 2012). Fibroblasts are the predominant cells in the first week of the healing phase, with their numbers reaching a peak about one week after trauma (Falanga, 2004). The number of fibroblasts that decreased on day 21 indicated that the activity of the proliferative phase was finished and starting to enter the maturation stage to accelerate wound healing (Fitri and Wael, 2015).

An overview of the results of histopathological observations of fibroblast cells in incised wound healing on day 21 of the skin of post-treated white rats can be seen in Figure 1. The cream base (P1) group showed many fibroblast cells with an average of 65.11 ± 8 , 56. This indicates that the wound healing process is still in the proliferation phase. This situation was caused by the P1 group being only given a cream base that did not contain

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume X Issue VI June 2025

active compounds to accelerate the wound healing of white rats, causing the proliferation phase to last longer (Islami *et al*, 2018).

The group receiving 0.1 % silver sulfadiazine cream (P2) showed a lower number of fibroblast cells than P1, with an average of 35.67±3.84. This was caused by the administration of 0.1% silver sulfadiazine 0.1% cream, which is a standard topical medicine in the sulfonamide class that has antibacterial properties. 0.1% Silver sulfadiazine can accelerate wound healing by stimulating an increase in macrophages to produce growth factors and cytokines, thereby increasing fibroblast proliferation (Eshafani *et al*, 2012 and Mohan *et al*., 2019).

Groups P3 and P4 showed that administration of 5% and 15% *Muntingia calabura* L leaf extract cream affected the number of fibroblast cells on the 21st day of incision wound healing in the skin of white rats. Kewuta *et al*. (2021) reported that giving *Muntingia calabura* L leaf extract to hyperglycemic mice accelerated wound healing because it contains a flavonoid, namely quercetin, which plays a role in lowering blood glucose levels. Flavonoids are antioxidants and antibacterial, so they can improve the wound healing process (Handayani and Sentat, 2016). Laut *et al*. (2019) reported that flavonoids can accelerate the wound healing process, which is marked by the number of fibroblasts increasing on day 7, so that the proliferation phase is accelerated and decreases the next day because it begins to enter the maturation phase.

Table 1. The average number of post-treatment fibroblast cells

Treatment Group	Average Number of Fibroblast t Cells
P1 (Control -)	65.11±8 , 56 [b]
P2 (Control +)	35.67±3.84 [a]
P3 (5% cream extract)	30.00±7.57 [a]
P4 (15% cream extract)	34.00±9.02 [a]

Note : [a,b] Different superscript letters in the same column indicate a significant difference (P<0.05). P1: group given base cream, P2: group given 0.1% silver sulfadiazine cream, P3: group given 5% *Muntingia calabura* leaf extract cream, and P4: group given 1 5% *Muntingia calabura* leaf extract cream.

Collagen Fiber Density

The results of the ANOVA test showed that the administration of cream base (P1), 0.1% silver sulfadiazine cream (P2), 5% cherry leaf extract (P3) and 15% cherry leaf extract (P4) had a significant effect (P<0.05) on the density of collagen fibers in incision wound healing day on 21 of the skin of DM white rats . The results of Duncan's further test, in the P1, P2, P3, and P4 groups, were a significant difference (P<0.05) in the density of collagen fibers between treatments. Group P3 was significantly different from groups P1, P2, and P4, but groups P1 , P2, and P4 were not significant. The average density of collagen fibers can be seen in Table 2.

The results showed that the P1 group had a low collagen fiber density with an average of 49.30 ± 3.21. this was because the P1 group was only given a cream base, so the wound healing process was slow, which was still in the proliferation phase, characterized by many fibroblast cells . This situation is caused by the cream base not containing active compounds to increase the density of collagen fibers. P2 group has moderate collagen fiber density with an average of 52.10±2.10, which is caused by silver sulfadiazine 0.1% which has antibacterial properties, thus preventing infections caused by disease agents. Silver sulfadiazine can also increase the number of fibroblasts, which play an important role in collagen synthesis.

Groups P3 and P4 showed that administration of *Muntingia calabura L* leaf extract cream affected the density of collagen fibers in wound healing on day 21 of the skin of white rats. This is because of the content of saponin and tannin compounds in *Muntingia calabura L* leaf extract cream can increase the density of collagen fibers, speeding up the wound healing process in diabetic conditions. Sembiring *et al* (2021) reported that administration

of *Muntingia calabura L* leaf extract can increase the density of collagen fibers in incised wounds of hyperglycemic rats because it contains saponins and tannins. Saponin can stimulate the formation of fibroblasts and increase the ability of the growth factor needed by fibroblasts by synthesizing collagen, namely TGF-β, to bind the TGF-β receptor on fibroblasts (Rupina *et al* ., 2016). Saponin plays an important role in the wound closure process by stimulating the formation of type I collagen (Miladiyah and Prabowo, 2012). The tannin content in *Muntingia calabura* Leaf extract cream also speeds up the wound healing process, because tannin can increase collagen, epithelium, and new blood vessels for wound closure (Palumpuan *et al*., 2017). An overview of the results of histopathological observations of collagen in incised wound healing on day 21 of the skin of post-treated white rats can be seen in Figure 1.

Table 2. The average number of post-treatment collagen fibers

Treatment Group	Average Collagen Fiber Density
P1 (Control -)	49.30±3.21 [a]
P2 (Control +)	52.10±2.10 [a]
P3 (5% cream extract)	60.54±2.11 [b]
P4 (15% cream extract)	53.51±3.21 [a]

Note : [a,b] Different superscript letters in the same column indicate a signi fi cant difference (P<0.05). P1: group given base cream , P2: group given 0.1% silver sulfadiazine cream , P3: group given 5% *Muntingia calabura* leaf extract cream, and P4: group given 1 5% *Muntingia calabura* leaf extract cream .

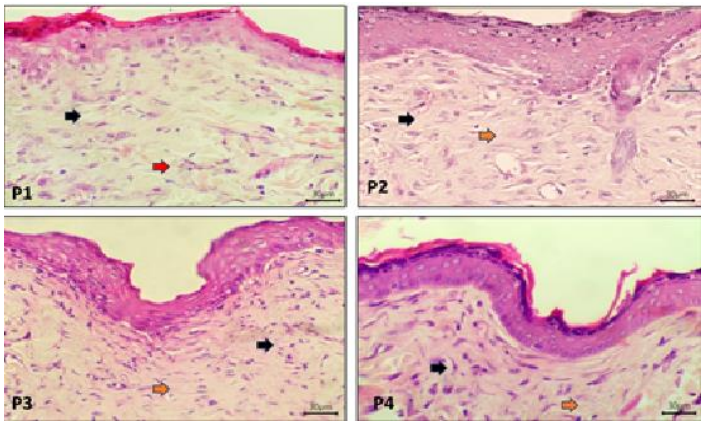

Figure 1 . Histopathological picture of fibroblast cells (black arrows) and collagen fibers (red arrows) in the wound area of the late remodeling phase: negative control group (P1) given cream base: fibroblast cells are very abundant and solid collagen fibers; positive control group (P2) received silver sulfadiazine cream: very few fibroblasts and very dense collagen fibers; given *Muntingia calabura* L. leaf extract cream 5% (P3): few fibroblast cells and moderate density collagen fiber; given *Muntingia calabura* L. leaf extract cream 15% (P4): few fibroblast cells and non-solid collagen fibers. HE staining, 400x magnification.

CONCLUSION

Based on the research results, it can be concluded that administering 5% *Muntingia calabura* L. leaf extract cream can decrease the number of fibroblasts and increase the density of collagen, which is effective in accelerating incision wound healing on day 21 (late remodeling phase) on white rats' skin with diabetes mellitus.

Further research is needed to examine the mechanisms and explore the bioactive compounds of *Muntingia calabura* that modulate the diabetic wound healing pathway in the late remodeling phase.

REFERENCES

1. Andalia, N., Salim, MN, Nurdin, and Balqis, U. (2021). Decreasing blood glucose levels using Muntingia calabura L. leaf extract in rats with diabetes mellitus. Advances in Biological Sciences Research, 12: 179-183.
2. Anief, M. (2010). The Science of Compounding Medicine: Theory and Practice. Gadjah Mada University Press, Yogyakarta.
3. Antia. (2019). Classification of characteristics patient and the time healing wound is treated. road. Indonesian Journal of Nursing Health Science, 4(1): 1-6.
4. Ardiansyah, AO (2021). Surgical Competence for General Practitioners Airlangga University Press, Surabaya.
5. Ariesti, ND, Sunnah, I., and Widiantara, IGR (2014). Effectiveness test ointment extract leaf of cherry (Muntingia calabura L.) on the duration of healing wound incision in mice infected with white bacteria, Staphylococcus aureus. Journal of Pharmacy and Natural Medicine, 2(2): 16-23.
6. Eshafani, S.A., Imanieh, M.H, Khoshneviszadeh, M, Meshksar, A, Noorafshan, A., Geramizadeh, B., Ebrahimi, S., Handjani, F., and Tanideh,, N. (2012). The healing effect of Arnebia Euchroma in second-degree burn wounds in rats as an animal model. Iranian Red Crescent Medical Journal, 14(2): 70-74.
7. Fakhrurrazi, Hakim, RF, and Chairunnisa, A. (2020). Effects of the extract leaf cherry blossom leaf (Phyllanthus acidus (L.) Skeels) against the healing wound mucosa mouse wistar (Rattus norvegicus). Cakradonya Dental Journal, 12(2): 119-125.
8. Falanga, V. (2004). The chronic wound: impaired healing and solutions in the context of wound bed preparation. Blood Cells, Molecules and Diseases, 32(1): 88-94.
9. Fish, R.E, Brown, M.J., Danneman, P.J. and Karas, A.Z. (2008). Anesthesia and Analgesia in Laboratory Animals . 2 Edition. Academic Press, United States.
10. Fitri, N. and Wael, S. (2015). Use of cream extract stem and leaves order (Peperomia pellucida LHBK) in the healing process wound burn on rats white (Rattus norvegicus). Molluca Medica , 8(1): 82-97.
11. Fossum, T. W. (2012). Small Animal Surgery Fourth Edition. Elsavier Health Sciences, USA.
12. Ginting, GIN, Jayawardhana. AAG and Dharmawan, NS (2021). Ointment extract leaf cherry leaves lowers blood sugar levels and migration of cell polymorphonucleases in mice with hyperglycemia. Indonesia Medicus Veterinus, 10(2): 211-222.
13. Gunawan, SA, Berata , IK and Wirata, IW (2019). Histopathology skin on healing wound incision mouse white post administration of extracellular matrix (ECM) derived from the vesica urinary pig . Indonesian Medicus Veterinus, 8(3): 313-324.
14. Handayani, F. and Sentat, T. (2016). Activity test extract ethanol leaf cherry (Muntingia calabura L.) against healing wound burn on skin mouse male white (Mus musculus) . Journal Ibn Sina's Science , 1(2): 131-142.
15. Harris, A. Amran, CMF, Salim, MN, Balqis, U., Armansyah, T., Karmil, T. F. and Riady, G. (2019). Efficacy of Jatropha cream (Jatropha curcas L.) on the maturation phase of cutaneous healing process in mice (Mus musculus). Journal of Veterinary Medicine , 13(2): 274-280.
16. Imamah, IN (2015). The Influence giving fish collagen on the process healing wound incision (study experiments on mice white Rattus norvegicus). Journal Mahakam Health, 4(1): 53-62.
17. Islami, SI, Munawir , A. and Astuti, ISW (2018). Effect administration of the Bakiko membrane (spinach-chitosan-collagen) to amount fibroblasts in wounds burn degree II. Hang Tuah Medical Journal, 15(2): 93-111.
18. Kewuta, NNN, Dada, IKA, and Jayawardhita, AAG (2021). Based on the sign inflammation and scabs, ointment extract of cherry leaf speeds up the healing wound incision in mice hyperglycemia . Indonesia Medicus Veterinus , 10(1): 30-40.
19. Kiernan, J. A. (1990). Histological and Histochemical Methods: Theory and Practice. 2nd Edition. Pergamon Press, Oxford.
20. Laut, M., Ndaong, N., Utami, T., Junersi, M., and Seran, YB (2019). Effectiveness of giving ointment extract ethanol earring leaves (Acalypha indica Linn.) against healing wound incision in mice (Mus musculus). Journal of Veterinary Studies, 7(1): 1-11.
21. Leung, P. C. (2007). Diabetic foot ulcers a comprehensive review. The Surgeon, 5(4): 219-231.

22. Manarisip, T, Yamlean, PVY and Lolo, WA (2019). Formulation and test effectiveness of antibacterial extract gel preparation ethanol leaf cherry (Muntingia calabura L.) as an antiseptic for hand. Pharmacon, 8(3): 580-590.
23. Miladiyah, I. and Prabowo, BR (2012). Ethanolic extract of Anredera cordifolia (Ten.) Steenis leaves improved wound healing in guinea pigs. Universa Medicina , 31(1): 4-11.
24. Mohan, Jailani, M. and Amirsyah, M. (2019). Comparison of the effectiveness of silver sulfadiazine and gentamicin on abrasion wound healing. Journal of Plastics and Reconstruction, 4(1): 20-23.
25. Nanda, Y., Salim, MN and Iskandar, CD (2017). Histopathology skin mouse (Mus musculus) remodeling phase of healing wound It with ointment sap distance hedge (Jatropha curcas Linn). Journal Scientific Student Veterinary, 1(4): 780-787.
26. Palumpuan , EF, Wiraguna , AAGP and Pangkahila, W. (2017). Provision of extract leaf betel (Piper betle) topically increase thickness of epidermis, the number of fibroblasts, and the number collagen in the healing process of wound on rat male Wistar strain rats (Rattus norvegicus). Journal of e-Biomedic, 5(1): 1-7.
27. Putri, FR and Tasminatun, S. (2012). The effectiveness of chitosan ointment in healing wound burn chemistry in Rattus norvegicus. Mutiara Medika, 12(1): 24-30.
28. Rizka, A., Budipramana , V. and Fauziah, D. (2013). The density of collagen type 1 in the wound operation in Wistar rats that experience anemia due to acute bleeding. Media Journal of Emergency, 2(1): 1-12.
29. Rupina, W, Trianto , HF, Fitrianingrum, I. (2016). Effects of extracting 70% leaf ethanol the karamunting on the reepithelialization of wound incision skin in Wistar mice. eJournal Indonesian Medicine , 4(1): 26-30.
30. Sembiring, ICB, Jayawardhita, AAG and Adi, AAAM (2021). Ointment extract of cherry leaf increases the density of collagen and accelerates wound cut in mice with hyperglycemia. Indonesia Medicus Veterinus, 10(2):189-199.
31. Steiner, S.S.M., Roy, S. and Sen, C.K. (2021). Collagen in wound healing. Bioengineering, 8(5): 1-15.
32. Taher, M., Zakaria, TMFST, Susanti, D. and Zakaria, ZA (2016). Hypoglycaemic activity of ethanolic extract of Gircinia mangostana Linn. in normoglycaemic and streptozotocin induced diabetic rats. BMC Complimentary and Alternative Medicine, 16(135): 1-12.
33. Tuljanah , M., Wirawan, W. and Setiawati, NP (2020). Testing the effects of extract ethanol leaf Africa (Gymnanthemum amygdalium (dellie) Sch. Beep. Ex Walp) against the level of glucose blood mouse white mice (Rattus norvegicus). Journal of Science and Health, 2(4): 340-346.
34. Velnar, T., Bailey, T. and Smrkolj, V. (2009). The wound healing: an overview of the cellular and molecular mechanisms. The Journal of International Medical Research , 37(5): 1528-1542.
35. Wang, PH, Huang, BS, Horng, HC, Yeh, CC and Chen, YJ (2018). Wound Healing. Journal of the Chinese Medical Association , 81(2): 94-101.
36. Widyaningrum, N., Murrukmihadi , M. and Ekawati, SK (2012). The Influence of concentration extract ethanol leaf tea green (Camellia sinesis L.) in stock cream to characteristic physical and activity antibacterial. Medical Science, 4(2): 147-156.
37. Yunitasari, D., Alfifar, I. and Priatna, M. (2016). Activity test extract ethanol leaf jengkol (Pithecellobium lobatum Benth) against healing wound incision in mice white male Wistar strain. Journal of Pharmaceutical Science and Practice, 2(1): 30-35.
38. Zhang, M., Lv, XY, Li, J., Xu, Z.G. and Chen, L. (2008). The characterization of high-fat diet and multiple low-dose streptozotocin induced type 2 diabetes rat model. Experimental Diabetes research , 6(9): 1-9.