# UTILIZATION OF WILD PLANT SURUHAN EXTRACTS (Peperomia pellucida l. kunth) AGAINST THE AMOUNT OF FIBROBLASTS IN THE HEALING PROCESS OF WOUNDS IN MICE (Mus musculus)

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# UTILIZATION OF WILD PLANT SURUHAN EXTRACTS (*Peperomia pellucida l. kunth*) AGAINST THE AMOUNT OF FIBROBLASTS IN THE HEALING PROCESS OF WOUNDS IN MICE (*Mus musculus*)

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**Abstract. Background:** The process of wound healing consists of three phases, namely inflammatory, proliferation and maturation. One of the plants that have the effect in accelerating the healing of wounds is suruhan (Peperomia pellucida) because the suruhan has a variety of active ingredients such as saponins, flavonoids, alkaloids, steroids and triterpenoids that are influential in the third phase of wound healing, especially the proliferative phase in stimulating the formation of fibroblasts. This study aims to prove the differences between the administration of the extract suruhan (Peperomia pellucida L. Kunth) and povidone-iodine 10% against the formation of the number fibroblasts in the wound healing process in mice (Mus musculus) days 3,5,7 and 14.
**Method:** This research is true experimental with a post-test control group design. The research sample was 32 mice (Mus musculus) male sex, healthy, 2-3 months old with a bodyweight of 20-40 g, which were divided into 2 groups, namely the treatment group (P) and the control group (K). Each group consists of 4 subgroups. The number of each mouse in the subgroup is 4 tails. The treatment group was the group given 10% suruhan extract topically once a day for 14 days. The control group was the group given 10% povidone-iodine once a day for 14 days. Skin tissue was taken and made preparations with hematoxylin-eosin staining to check the number of fibroblasts. An independent T-test analyzed the results of the study.
**Result:** The results of the independent t-test analysis showed p values on day 3 (p = 0.011), day 5 (p = 0.273), day 7 (p = 0.000) and day 14 (p = 0.000).
**Conclusion:** In conclusion, there was a significant difference in the number of fibroblasts between the control group and the treatment group.

Keywords**:** Fibroblasts, Povidone-iodine 10%, Suruhan (Peperomia pellucida), Wound

## Background

The wound is a state of tissue damage caused by trauma, chemicals, and animal bites. One of the most common are cuts caused by the lack of public awareness of sharp objects around them, such as knives, razor blades or sharp axes. Cuts have very distinctive characteristics; namely, the shape of the wound is elongated, and the edges of the wound angle are straight. Cuts are categorized as open wounds that can cause functional disturbances and damage to the epithelium of the skin. When these disturbances and damage occur, the body will respond to repair the skin, which is known as the wound healing process[2]. In general, the wound healing process is divided into three phases: the inflammatory phase, the proliferative phase, and the maturation phase. The inflammatory phase begins immediately after an injury occurs, where the body responds to stop bleeding by vasoconstriction of blood vessels to the wound area and activation of coagulation factors. The inflammatory phase is characterized by redness, heat, swelling, pain and impaired function[3]. The second phase is proliferation that begins on days 4 to 14 after the wound, where there is an increase in fibroblasts and extracellular matrix. There are three main processes in this phase, namely angiogenesis, fibroblasts and re-epithelization[4]. The third phase is the maturation (remodeling) takes place from day 21 to 2 years after the injury; this phase aims to maximize the integrity and strength of the

structure of the new organized tissue in the wound[5].

These three wound healing processes are a typical response from a person's body that causes the wound to heal on its own, although usually, the public will still use drugs, creams or ointments to help speed up wound healing. One that is often used is povidone-iodine 10%[6]. Povidone-iodine 10% is a local antibacterial substance that effectively kills bacteria and spores and is widely used for antiseptics on the skin. However, the development of treatment has been widely switched to using natural herbs to speed up wound healing because it is proven to be safer, does not cause side effects, and costs more economically. One of the natural herbs used is suruhan plant (*Peperomia pellucida L. Kunth*).

Plants in Indonesia are traditionally used in treating several diseases, such as abscesses, kidney disease and abdominal pain[7]. The plants are wild plants that belong to the Piperaceae tribe. The size ranges from 15 to 45 cm, with juicy and bright stems and dark green leaves, distinctive smells and flavours. This plant lives in groups in damp places, such as sewers, walls and shade.8 Based on the 2011 phytochemical screening of Majumder and Arum Kumar, many of the contents found in suruhan plants include saponins, flavonoids, alkaloids, steroids, triterpenoids, and carbohydrates, are influential in their pharmacological function[8].

Nur Fitri's research in 2015 said saponins in suruhan plants could minimize the necrosis zone of wounds. Triterpenoids have an astringent effect that speeds up the drying process of the wound. Tannins and flavonoids are antiseptic and antibacterial to inhibit and kill bacteria that infect wounds. Saponin content can increase collagen formation in wound healing, and steroids as an anti-inflammatory can reduce pain in wounds[9]. The research of Suciyati et al. in 2018 proved that the compounds found in suruhan plants were able to prevent infection and accelerate the wound healing process in mice (*Mus musculus*)[10]. Based on the description above, researchers are interested in examining the use of wild plant suruhan extracts (*Peperomia pellucida*) on the number of fibroblasts in the process of wound healing in mice (*Mus musculus*).

## Method

This research was carried out at the Pharmacology Laboratory, Andalas University Padang and Pathology and Anatomy Laboratory, Faculty of Medicine, Andalas University, Padang, from August to October 2021. The sample of this study was mice (Mus musculus) aged 2-3 months, male sex with bodyweight 20-40 gr. A total of 32 mice (*Mus musculus*) were grouped into 2 groups, namely the treatment group (P) and the control group (K), where each group consisted of 4 subgroups. The number of each mouse in the subgroup is 4 tails.

This type of research is true experimental with a post-test only control group design. The treatment group was the group that was given 10% suruhan extract, and the control group was the group that was given 10% povidone-iodine topically once a day for 14 days. Skin tissue was taken and made preparations with hematoxylin-eosin staining to check the number of fibroblast cells.

Order extract was obtained by the maceration method. A total of 5 kg of orders were dried and then crushed to form a powder. The simplicia powder was then extracted using the maceration method with 70% ethanol as a solvent. The results obtained were 43,371 g of suruhan extract. The ethanol extract of the suruhan plant was made to a concentration of 10% with distilled water as the solvent.

## Result

Based on the research that has been done, the results of the calculation of the number of fibroblast cells are as follows:

**Table 1.** The difference between the administration of suruhan extract with povidone iodine on the number of fibroblasts in the wound healing process in mice on day 3

| Kelompok | N | Mean±Std.Dev | Pvalue |
|---|---|---|---|
| Control D3 | 4 | 50,95±9,178 | 0,011 |
| Treatment D3 | 4 | 74,57±9,304 | |

In table 1 obtained independent t test results a P-value of 0.011 (P<0.05), meaning that there was a significant difference between the administration of suruhan extract with povidone iodine on the number of fibroblasts in the wound healing process in mice on day 3.

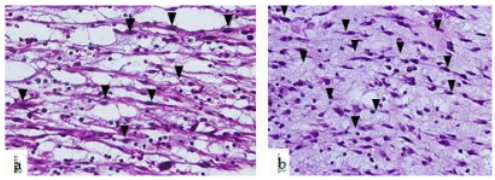

**Figure 1.** Histology of animal skin tissue at an objective enlargement of 40x, showing granulation tissue containing fibroblast cells under the scar. Control group (a) and treatment group (b) day 3. (Hematoxilin eosin scale h; 100 µm)

**Table 2.** The difference between the administration of suruhan extract with povidone iodine on the number of fibroblasts in the wound healing process in mice on day 5

| Group | N | Mean±Std.Dev | P value |
|---|---|---|---|
| Control D5 | 4 | 74,35±6,915 | 0,273 |
| Treatment D5 | 4 | 83,42±12,854 | |

In table 2 obtained independent t test results a P-value of 0.273 (P<0.05), meaning that there was no significant difference between the administration of suruhan extract with povidone iodine on the number of fibroblasts in the wound healing process in mice on day 5.

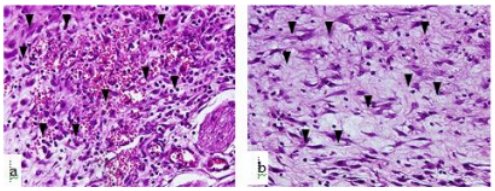

**Figure 2.** Histology of animal skin tissue at an objective enlargement of 40x, showing granulation tissue containing fibroblast cells under the scar. Control group (a) and treatment group (b) day 5. (Hematoxilin eosin scale h; 100 µm)

**Table 3.** The difference between the administration of suruhan extract with povidone iodine on the number of fibroblasts in the wound healing process in mice on day 7

| Group | N | Mean±Std.Dev | P value |
|---|---|---|---|
| Control D7 | 4 | 172,15±4,728 | 0,000 |
| Treatment D7 | 4 | 125,27±3,990 | |

In table 3 obtained independent t test results a P-value of 0.000 (P<0.05), meaning that there was a significant difference between the administration of suruhan extract with povidone iodine on the number of fibroblasts in the wound healing process in mice on day 7.

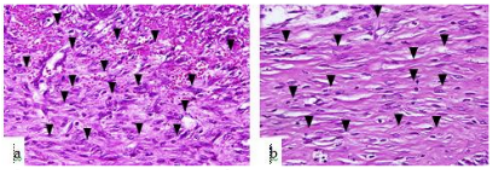

**Figure 3.** Histology of animal skin tissue at an objective enlargement of 40x, showing granulation tissue containing fibroblast cells under the scar. Control group (a) and treatment group (b) day 7. (Hematoxilin eosin scale h; 100 µm)

**Table 4.** The difference between the administration of suruhan extract with povidone iodine on the number of fibroblasts in the wound healing process in mice on day 14

| Group | N | Mean±Std.Dev | P value |
|---|---|---|---|
| Control D14 | 4 | 234,67±2,036 | 0,000 |
| Treatment D14 | 4 | 120,50±14,653 | |

In table 4 obtained independent t test results a P-value of 0.000 (P<0.05), meaning that there was a significant difference between the administration of suruhan extract with povidone iodine on the number of fibroblasts in the wound healing process in mice on day 14.

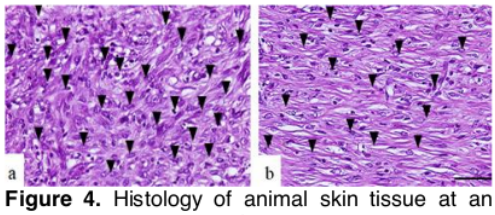

**Figure 4.** Histology of animal skin tissue at an objective enlargement of 40x, showing granulation tissue containing fibroblast cells under the scar. Control group (a) and treatment group (b) day 14. (Hematoxilin eosin scale h; 100 µm)

The study was conducted by obtaining data from the calculation of the number of fibroblasts on day 3, 5, 7 and 14 under a microscope. The reason for seeing it from the third day is because it is adjusted to the theory of wound healing fibroplasia that on the third day a number of young fibroblasts migrate to the wound area and proliferate actively, indicating that the wound has entered the proliferative phase.[11] Fibroblast Proliferation can be stimulated by the presence of epidermal growth factor (EGF) and fibroblasts. Growth factor (FGF).12 Fibroblasts will function to synthesize extracellular matrix such as type III collagen fibers and can change into their phenotype, namely myofibroblasts that play a role in wound contraction.12 Fibroblasts also stimulate macrophages to produce growth factors which then synthesize vasculature. The presence of new vascular will accelerate the formation of granulation tissue.12

Based on the research conducted, it was found that on day 3, there was a significant difference between the control group and, therefore, the treatment group. The difference in the number of fibroblasts between the control and treatment groups showed that the suruhan extract treatment group (*Peperomia pellucida*) could accelerate wound healing compared to the povidone-iodine control group. The results of this study are supported by the research of Suciyati et al. in 2018, which showed that the formulation and

gel suruhan extract could accelerate the healing process of burns in rabbits (Oryctolagus cuniculus) because the plant contains various active ingredients like saponins which will trigger the formation of collagen within the wound healing process. Saponins will stimulate vascular endothelial growth factor (VEGF) and increase the number of macrophages that migrate to the wound area. Flavonoids as antioxidants can counteract free radicals during the wound healing process. Together with triterpenoids, they have an astringent effect that can shrink skin tissue and stop exudate and light bleeding so that wounds dry quickly.10 Tannins and flavonoids have an antiseptic and antibacterial activity that can inhibit and even kill bacteria that infects the wound. The content of steroids is an anti-inflammatory pain reliever in the wound area.13

On day 5, the number of fibroblasts between the control and treatment groups did not show a significant difference ($p = 0.273$). The indicates that the wound healing process in the treatment group entered a faster stage than the control group; as a result, the control group will continue to increase the number of fibroblasts so that it can reach its peak in the proliferative phase and the wound healed. Still, it was different from the treatment group. From the beginning, on day 3, it has shown the process of accelerating wound healing to the proliferative stage earlier than the control group.

On days 7 and 14, there were significant differences between the control and treatment groups, but the number of fibroblast cells in the treatment group was less than in the control group. The decrease in the number of fibroblasts in the treatment group indicates that the proliferative phase of wound healing will soon end and enter the final stage, the remodeling phase, because fibroblast cells have been replaced by collagen matrix that fills the area of the wound.14 It showed that the suruhan extract treatment group experienced faster-wound healing than the povidone-iodine control group.

## Conclusion

Based on the results of the research that has been carried out, it is concluded that there are differences in the number of fibroblast cells formed between the control group and the treatment group on days 3, 5, 7 and 14 in the process of wound healing in mice (*Mus musculus*). The density of fibroblasts in the control group showed an increase from day 3 to day 14 and did not show a decrease, while the treatment group found an increase in the number of fibroblasts from day 3 to its peak 7 and began to decrease on day 14.

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