The Effect Of Giving Sambiloto Leaf Extract (*Andrographis Paniculata*) On Collagenization And Histopathological Picture Of Skin Tissue In The Healing Process Of Dermapen Wounds In White Wistar Male Rats

Ellen Aristika[1], Muhammad Arafat Muchtar[2], Linda Chiuman[3], Trishna[4], Suwarno[5*4,3,2,1]

Master of Biomedical Science Study Program, Faculty of medicine, dentistry and health sciences, Universitas Prima Indonesia, North Sumatra.

*E-mail : suwarnogustaf@unprimdn.ac.id

ABSTRACT

This study aims to analyze and test the administration of d extract*Andrographis paniculata* (*Andrographis paniculata*) affect growth collagen in the wound healing process of dermapen scars in male Wistar white rats (*Rattus norvegicus*) and assessing its histopathological features. This study is a true experimental study, using a post-test only control group design. The sample in this study was 24 animals. Preparation of test animals is to increase the weight of mice and make dermapen wounds. Dermapen action is carried out with a needle depth of 2 mm and a wound width of 2 cm. The wound healing process is observed every day for 14 days. This study showed that the group given *Andrographis paniculata* leaf extract cream with concentrations of 5%, 7%, and 10% had an effect on the healing process of wounds from dermapen in obese white rats (*Rattus norvegicus*) wistar strain. The treatment group experienced total healing, while the control group given base cream did not. The results of histopathological observations showed that the control group produced very thin collagen growth, while in the treatment given *Andrographis paniculata* leaf extract with concentrations of 5%, 7%, and 10% the collagen was fully filled and dense. The results of phytochemical tests showed that *Andrographis paniculata* leaf extract contained secondary metabolites in the form of flavonoids, saponins, tannins, and triterpenoids. These findings indicate that *Andrographis paniculata* extract increases collagenization and accelerates wound healing, making it a promising treatment for wounds caused by dermapen.

Keywords: *Sambiloto leaves, Collagen, Dermapen, Rattus norvegicus*

INTRODUCTION

Through its sensors, the skin plays a crucial part in our ability to communicate and comprehend our surroundings (Mirastschijski, 2020). It is also well recognized that the skin is crucial for a number of functions, such as hydration, defense against toxins and infections, the initiation of vitamin D production, secretion, communication, and temperature regulation. Consequently, any kind of skin injury needs to be taken into account (2020, Tottoli). Wounds are frequently caused by chemical or physical harm to the skin. A wound, often known as an ulcer, occurs when a bodily tissue is damaged or lost (Hidayati, 2019) damage to different bodily tissues is referred to as a wound (Abdulrahmat, 2014). Starting with the hemostasis stage, wound healing progresses through the inflammatory, proliferative, and tissue remodeling stages, culminating in the remodeling stage. In order to stop more bleeding, the hemostasis stage happens once the incision is open. Wounds often go through the inflammatory, proliferative, and remodeling stages in order to repair tissue damage. Whether in its soluble state in the wound environment or in its natural, fibrillar shape, collagen, a significant component of the extracellular matrix, is essential for controlling the stages of wound healing (Steiner and Mathew, 2021). Dermapen is a therapeutic motorized microneedle technology that may be customized to address specific skin issues. Using disposable needles and guides, the ergonomic Dermapen can change the needle length from 0.25 to 2.00 mm. Nine to twelve needles are positioned in a row at the tip. Using dermapen with sterilized needles and using them independently is crucial. As a result, one demapen may be used to treat small regions like the eyes, lips, and nose without causing harm to the surrounding skin (Purbosetyo,2020). Understanding the many forms of skin injury is crucial since the skin is a vital component of the human body. Skin dressings will aid in wound restoration even when the body's natural healing mechanism is already in place. Extract from *Andrographis paniculata*, or bitter leaf is one of the herbs that can be used to dress wounds. Sambiloto or *Andrographis paniculata* Nees, contains a variety of compounds, including as flavonoids, alkaloids, and saponins. Additionally, sambiloto includes flavonoids, such as 5-hydroxy-7,2',3'-trimethoxflavone and 5,7,2',3'-tetramethoxyflavanone, which are andrographolide and flavonoids, respectively. Sambiloto's active ingredients include health-promoting compounds including andrographolide, flavonoids, and essential oils that have anti-bacterial, anti-toxin, anti-cancer, and anti-infection properties. Researchers are interested in examining the plant's anti-inflammatory properties in light of this phenomena. Researchers are interested in the histopathology and if administering sambiloto leaf extract (*Andrographis paniculata*) has an impact on collagenization of the dermal wound healing process in male white Wistar rats (*Rattus norvegicus*).

LITERATURE REVIEW

The biggest organ in the human body, the skin is in charge of several bodily functions, including temperature regulation, vitamin D production, hydration, and defense against toxins and infections. Damage to the skin, mucous membranes, bones, or other organs is referred to as a wound. Wounds can be caused by a variety of disease processes and conditions that occur both within and outside the organ. Many individuals go about their regular lives unaware of the risks of wounds, particularly to the skin, which serves as the body's outermost barrier (Tottoli, 2020). Wound healing consists of three stages: inflammation, proliferation, and maturation. These stages can occur one after another or simultaneously (Townsend, 2016).

a. Inflammation

At this point, efforts are taken to minimize damage by halting the bleeding, covering the wound, and getting rid of germs, foreign objects, and necrotic tissue. Increased vascular permeability, chemotaxis that permits cell entry into the wound, cytokine and growth factor production into the wound, and migratory cell activation are characteristics of the inflammatory phase.

b. Proliferation

Granulation tissue made up of capillary beds, fibroblasts, macrophages, and loose configurations of collagen, fibronectin, and hyaluronic acid is indicative of this stage. Growth factors have been shown to alter granulation tissue, particularly fibroplasia, in a number of investigations. Through adenoviral transmission, topical application, and subcutaneous injection of PDFG, TGF-β, keratinocyte growth factor (KGF), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF), attempts have been made to promote the development of granulation tissue.

c. Remodeling

Collagen cross-linking was mostly responsible for the improvement in breaking strength after 21 days. In contrast to normal skin, collagen cross-linking contributes to the wound's increased fragility and decreased elasticity. Rete pegs, which are wavy epidermal projections that pierce the papillary dermis, are absent from the epidermodermal surface of healed wounds. The microneedle therapy system is a novel scar treatment technique. primarily to make the skin of the face appear younger by removing wrinkles, melasma, dyschromia, acne scars, and enlarged pores. The production of collagen and elastin, two essential building blocks of youthful skin, can be accelerated by microneedling. The fundamental idea is to inflict controlled damage so that the body reacts by increasing collagen production in the area that has been treated (Tottoli, 2020). The dermaroller and dermapen make up the microneedle treatment apparatus. A device with needles of various sizes and numbers is used in the mesotherapy process known as Dermapen. The benefits

of dermapen treatment, the most recent advancement in microneedling technology that takes the place of the dermaroller, include smoothing the skin and lessening acne scars or pockmarks. The nose, lips, and region around the eyes may be more easily reached with this ergonomic instrument. The issue of various pressure applications is also resolved by it (Singh A, 2016). Applying the instrument to the stretched scar in several directions (horizontal, vertical, and oblique) until a consistent bleeding point forms is the fundamental idea behind needling. Then, at various intervals, this process is repeated as needed (Hotimah, 2023). In different parts of Indonesia, Sambiloto is referred to by different names. People in Central Java and East Java refer to it as bidara, sambiroto, sandiloto, sadilata, takilo, paitan, and sambiloto. It is known as ki oray, takila, or ki peurat in West Java, and samiroto in Bali. The majority of Malay and Sumatran people refer to it as ampadu or pepaitan. The quantity of active chemicals found in medicinal plants is influenced not only by genetic factors but also by the plant's growing environment. The production of diterpene lactones in sambiloto plants is significantly influenced by these two factors. According to Yusron and Januwati (2004), sambiloto growth, yield, and quality are significantly influenced by agroecology. The location of sambiloto collection, the time of harvest, and the portion of the plant used are some of the aspects that affect its quality. variances in the time of sample, planting location, processing methods, and other variables might result in variances in the amount of active chemicals present in the same plant. The quality of medicinal plant simplicia is also influenced by the weather during cultivation, in addition to its geographic spread. Weather variations, harvest season, cultivation, post-harvest procedures, extraction, and the maufacturing of herbal medications are a few of these variables (Singh, 2020). Sambiloto is a herbaceous plant (shrub) that grows on the edge of rice fields, gardens, or forests. In addition to diterpenoid lactones (andrographolide), paniculides, and flavanoids, sambiloto leaves also contain saponins, flavonoids, alkaloids, and tannins. Sambiloto plants (*Andrographis paniculata* Nees) are classified as follows:

Kingdom	*: Plants*
Division	*: Spermatophyta*
Subdivision	*: Angiospermae*
Class	*: Dicotyledoneae*
Order	*: Solanaceae*
Family	*: Acanthaceae*
Genus	: *Andrographis*
Species	: *Andrographis paniculatan*

METHODS

The research design employed in this study is a post-test only control group design, which is a kind of study that only looks at the control and treatment groups after they have been given an activity. This study is a true experimental study. The Anatomical Pathology Laboratory and the Department of Pharmaceutical Pharmacology, Faculty of Medicine, University of North Sumatra, carried out this investigation. The study was carried out in 2024 between May and July. The procedure of obtaining ethical clearance is ongoing and will be submitted to Prima Indonesia University's Health Research Ethics Commission (KPEK). In order to address any ethical concerns pertaining to the treatment and care of animals, all methods adhere to animal welfare norms. Male white rats of the Wistar strain (*Rattus norvegicus*) aged 2 – 3 months and weighing between 200 and 300 grams. These rats were chosen as research subjects because they have physiology and characteristics that are almost the same as humans and are one of the most frequently used animals in biomedical research. In addition, white rats are very good at adapting to the laboratory environment. Male Wistar rats that have passed the acclimation period were then randomly divided into four groups. In this study, 24 obese male Wistar rats (*Rattus norvegicus*) were used as samples. Then they were divided into 4 groups, each with 6 rats, and given treatment for 14 days, which included, among others: 1) positive control group, rats were given bacitracin cream, 2) negative control group, rats were not given anything, 3) control group, rats were given base cream (0%), 4) treatment group-1, rats were smeared with sambiloto leaf extract cream with a concentration of 5%, 5) treatment group-2, ratssmeared with sambiloto leaf extract cream with a concentration of 7%, 6)treatment group-3, mice were smeared with sambiloto leaf extract cream with a concentration of 10%. Variables used in this studynamely the administration of sambiloto leaves (Andrographis paniculata) as the independent variable and collagenization of the wound healing process from dermapen and its histopathological picture as the dependent variable. Operational Definitions can be seen tablet 1.

Table 1 Operational Definitions

Variables	Operational Definition	Methods and Measuring Tools
Sambiloto Leaf Extract Cream	Sambiloto leaf extract cream is a cream base mixed with the results of sambiloto leaf extraction obtained through a maceration process with ethanol for 2x24 hours. Sambiloto	Apply with the help of cotton buds

	leaves are obtained from farmers in the city of Medan. Sambiloto leaf extract cream is given 1x a day for 14 days	
Dermapen wound healing collagenization and its histopathological features	Dermapen wound healing collagenization can be seen from the histopathological picture seen from the skin tissue.	Identified using a microscope with 400x magnification

A collection of maceration instruments, filters, rotary evaporators, evaporating cups, and water baths are among the equipment needed to make sambiloto leaf ethanol extract. Incubators, pH meters, cuvettes, centrifuges, beaker glasses, 1000 µL BioHit micropipettes, measuring pipettes, spatulas, vials, and 10 ml, 25 ml, and 100 ml measuring flasks are among the equipment used for in vitro studies. Simplexia sambiloto leaf extract (*Andrographis paniculata*) is one of the ingredients utilized. Aquades, ethanol PA (Brataco), and trichloroacetic acid (TCA) are among the compounds utilized. The manufacture of sambiloto leaves (*Andrographis paniculata*) refers to the research of Rahayu, (2020) which has been modified. The raw materials in the form of sambiloto leaves obtained from farmers in the city of Medan begin the wet sorting process to separate rotten leaves, then washed, and then dried using a temperature oven 50°C. The powdered simplicia is ground with a blender and sieved with a 40 mesh sieve. The manufacture of sambiloto leaf extract cream is carried out using the maceration method. The powder is weighed *Andrographis paniculata* as much as 100 grams using 96% ethanol ratio (1:10). After filtering the extract, the filtrate and dregs are separated. To create a thick extract, the filtered extract is then removed from the solvent using a rotary evaporator. A cream base is created by dissolving sambaloto leaf extract (*Andrographis paniculata*) in distilled water, adding it to the water phase, and stirring it until it is homogenous. The oil phase is then gradually added to the water phase, combined, and swirled continuously until it reaches room temperature. After that, the cream is placed in a jar. Every item used to make the product is weighed using the formula that is shown in table 2.

Table 2 Cream Preparation FormulaSambiloto leaves (*Andrographis paniculata*)

Material Name	**Cream Formula (grams)**			
	F0	**F1**	**F2**	**F3**
Sambiloto leaf extract	**0**	**5**	**7**	**10**
Cetyl alcohol	4	4	4	4
Glycerin	15	15	15	15

TEA (triethanolamine)	3	3	3	3
Stearic acid	12	12	12	12
Methyl paraben	0.2	0.2	0.2	0.2
Propyl paraben	0.02	0.02	0.02	0.02
Aquades until..	100	100	100	100

The process of adjusting to a new environment is where the research process starts. Ad libitum food and water were provided to mice based on their normal requirements. Test animal preparation, included giving mice more weight and creating dermapen wounds. First, dermapen activity is used to inflict wounds on white wistar rats. The first thing to do is to shave the mouse's back fur or hair. The mice employ a combination of xylasin (5 ml/kg BW) and ketamine (80 ml/kg BW) after shaving in order to reduce discomfort and stop excessive movement brought on by dermapen action. After completing the acclimatization phase, male wistar rats are randomized into four groups. This study employed 24 male wistar rats (*Rattus norvegicus*) that had been given dermapen action once after acclimatization. Prior to this, the mice were cleaned with 10% povidone iodine, and their backs were then shaved. The needle depth may be adjusted between 0.25 and 2 mm using the dermapen action (Purbosetyo, 2020). The needle depth and wound diameter in this investigation were 2 mm and 2 cm, respectively. Over the course of 14 days, the wound healing process was monitored daily. From the first day of production to day 14, the average length of the wound is measured daily in white mice to assess the healing process of Dermapen wounds.

$$P = \frac{do - dx}{do} \times 100\%$$ (Calsum, et. al., 2018).

Information: P : Wound healing percentage
do : Initial wound length
dx : Length of wound on a given day

As the typical wound healing process progresses to the proliferation phase, which happens between the third and fourteenth days after the wound forms, observations were performed for a maximum of fourteen days. All of the mice were put to death after 14 days by inhaling too much technical chloroform. The control group and the treatment group were compared in order to undertake a histopathological analysis of the skin tissue. The alterations will be fatty degeneration, hydropic degeneration, and necrosis. Quantitative data is obtained by grading each change. The distribution of collagen tissue produced during wound healing was one of

the study's parameters. Collagen tissue distribution density histopathology scoring criteria were calculated using a 400x magnification object and one field of view.

0= No collagen fibers were found in the wound area.

+1= Collagen fiber density in the wound area is low (less than 10%)

+2= Collagen fiber density in the wound area is moderate (10-50%)

+3= Collagen fiber density in the wound area is tight (50-90%)

+4= The density of collagen fibers in the wound area is very dense (90-100%)

(Rizka and Vicky, 2013).

The information gathered from microscopic analysis of histopathological findings was then used to assign scores. The study's data were tallied, examined for any alterations, and then given in a descriptive manner. Additionally, the Statistical Package for the Social Sciences (SPSS) 25.0 for Windows was used to analyze the research data. The Kolmogorov-Smirnov test was employed to determine whether the data was normal ($p>0.05$). Additionally, a one-way analysis of variance (ANOVA) at a 95% confidence level was used to evaluate for significance between the test groups. The Post Hoc Test and LSD methods were used for additional testing or analysis.

RESULTS

General Objective Description Results

Based on the general characteristics of the test animals, in general the mice were in a healthy condition during this study, namely before and after treatment. A total of 24 test animals were able to follow this study until the end without any drop outs. Weighing was carried out on the 24 test animals. The average body weight of each group before and after treatment for 14 days can be seen in Table 2.

Table 2 Characteristics of test animals

Component	Group					
	K	**K-**	**K+**	**P1**	**P2**	**P3**
Types of Rats	*Rattus norvegicus*white wistar strain					
Gender	Male					
General Condition	White fur color, healthy and active					
Average Initial Body Weight	242gr	242 gr	246gr	240gr	245gr	243gr
Average Final Weight	325 gr	310gr	315 gr	312 gr	320 gr	321 gr

Specific Objective Description Results

The results of phytochemical screening tests on sambiloto leaf extract (*Andrographis paniculata*) to see the content of secondary metabolite compounds in the extract, which can be used to heal wounds from dermapen and increase collagen density in white rats (*Rattus norvegicus*) Wistar strain. The results of testing secondary metabolites of sambiloto leaves can be seen in table 3.

Table 3 Phytochemical Tests

Secondary Metabolites	Results	Color
Flavonoid	+	Red
Saponins	+	Yellow and foamy
Tannin	+	turquoise
Alkaloid	+	Yellow
Steroid	+	Green

Description:

(+) = Contains the tested compound group

(-) = Does not contain the tested compound

The results of phytochemical tests contained in sambiloto leaf extract *(Andrographis paniculata*) contain metabolite compounds including flavonoids, saponins, tannins, alkaloids, and steroids/triterpenes. Researchers conducted macroscopic observations of wound healing in mice by measuring the length of the wound using a caliper. The wound healing process produces scars that can be seen without the aid of a microscope, making it possible to observe through macroscopic observation or with the naked eye. This observation was carried out with the aim of comparing wound healing between the group given the base cream and the group given the sambiloto leaf extract cream (*Andrographis paniculata*) with 3 different concentrations, namely 5%, 7%, and 10%. This observation was carried out every day for 14 days. The results of observations of dermapen scars on the backs of mice are presented in the following table 4:

Table 4 Average Percentage of Wound Healing (%)

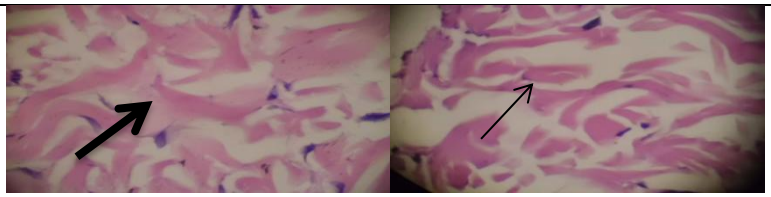
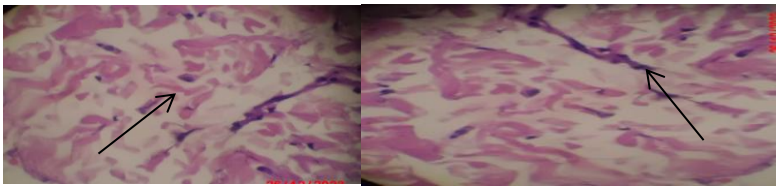
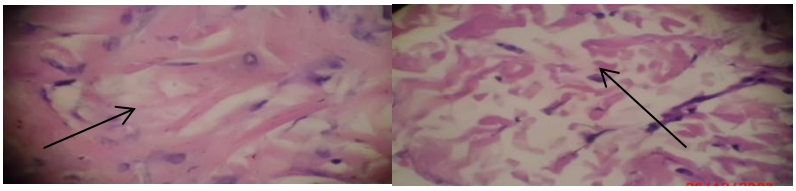
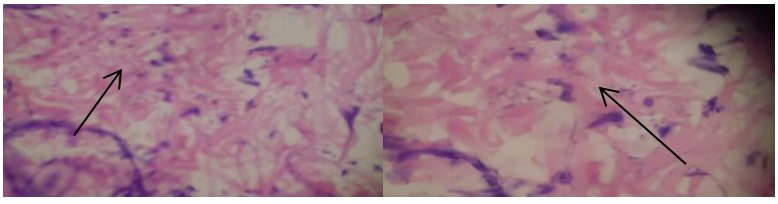
Day	Control	Negative Control	Control Positive	P1	P2	P3

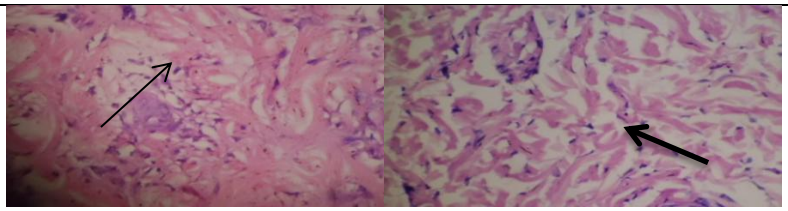
1	0	0	0	0	0	0
2	1	1.5	2	2	2.5	3.5
3	4	5	7.5	10	14.5	14
4	8.5	10	10.5	14	25	27
5	12.5	13.5	15	19.5	36	40
6	19.5	15.5	27.5	31.5	47	50
7	27	28	33.5	43.5	57.5	62.5
8	32.5	33.5	36	48	68.5	72
9	38.5	39	38	59.5	76	79
10	44.5	50	45	71	83.5	88.5
11	53.5	56	61	78.5	94	99
12	56.5	58	67.5	89	100	100
13	62.5	61	75	92.5	100	100
14	71.5	73	85	100	100	100

Based on the results of observations made on all groups, it shows that there is a healing process of wounds from dermapen in white rats (*Rattus norvegicus*) Wistar strain. There is a difference in the average percentage of healing from the control group, negative control, positive control and treatment. The average percentage of healing of wounds from dermapen on the last day of the control group was 71.5%, 73% and 85%. In the control group, there was no perfect wound healing because the control group (K-0), the rats were given base cream (0%), in the positive control group (K^+), the rats were given bacitracin cream. While in the negative control group (K^-), the rats were not given anything. Treatment group 1 got a wound healing percentage of 100% on the 14th day, while treatment groups 2 and 3 on the 12th day. The researcher concluded that the control group, negative control and positive control did not experience total healing and treatment groups 2 and 3 required the fastest time to experience total healing than treatment 1. Dermapen wound healing consists of several phases, namely the inflammation, proliferation and maturation phases. In the proliferation phase, fibroblasts play an important role in producing proteins for wound healing, one of which is collagen. The results of histopathological examination using a 400x magnification light microscope on wound healing showed the following differences in collagen density:

Table 6 Histopathological Description of Skin Tissue

No	Group	Histopathological Image of Skin Tissue

1	Control (0%)	 KThe rim base produces very thin collagen growth, so it gets a score of 1 (less than 10%). This is because the skin tissue is still in an inflammatory condition so that collagen is not yet widely visible.
2	Negative Control	 No collagen fibers were found in the wound area because in this negative control group no treatment was given to heal the dermapen wound so it entered the score category 0.
3	Positive Control	 The density of collagen fibers in the wound area is moderate (10-50%) so it falls into the score category 2. In the control groupgiven bacitracin cream
4	Treatment 1 (5%)	 The density of collagen fibers in the wound area is dense (50-90%) so that it enters the score category 3. In treatment group 1, 5% sambiloto leaf extract was given.
5	Treatment 2 (7%)	 The density of collagen fibers in the wound area is dense (50-90%) so that it enters the score category 3. In treatment group 2, 7% sambiloto leaf extract was given.

6	Treatment 3 (10%)		Treatment Group 3 experienced rapid and dense collagen growth, so it entered the score category 4 (90-100%), treatment group 3 was given 10% sambiloto leaf extract.

The results of the histopathology conclusions in this study showed that administering *Andrographis paniculata* leaf extract cream can affect collagen density in wound healing from dermapen in male white rats (Rattus norvegicus) of the Wistar strain that were given dermapen treatment

DISCUSSION

According to the explanation of the first phenomena, the skin plays a crucial role in a number of functions, including communication, excretion, hydration, defense against chemicals and infections, the start of vitamin D production, and temperature control. As a result, it is crucial to pay attention to any type of skin injury (Tottoli et al., 2020). Wounds are one type of skin injury. A pathological condition brought on by illness, trauma, or physiochemical damage is called a skin wound. Wounds are categorized as either acute or chronic depending on where the damage occurred and how long it took to heal. Acute wounds are caused by traumatic physical or chemical damage or surgical treatments, but chronic wounds, also known as difficult-to-heal wounds, are caused by illnesses including cancer, diabetes, and vascular disease (Shafiee and Farahani, 2021). The wound healing process starts as soon as the wound is created. In response to tissue damage, normal wound healing goes through the proliferative, remodeling, and inflammatory stages. Either in its natural fibrillar state or as a soluble substance in the wound environment, collagen, a crucial part of the extracellular matrix, regulates the wound healing phase (Mathew-Steiner et al., 2021). One method is to apply a lotion containing *Andrographis paniculata* leaf extract to the wound to hasten its healing process. Proteins, rutin, alkaloids, anthraquinones, anthocyanins, tannins, phlobates, carbohydrates, saponins, triterpenoids, flavonoid phenols, flavanol glycosides, essential oils, and steroids are among the phytochemicals found in sambiloto (*Andrographis paniculata*) leaves. Linoleic, stearic, palmitic, and linoleic oleic acids are all part of the fatty acid makeup. Phenolics, flavonoids, anthocyanins, flavonol glycosides, kaempferol glycosides, quercetin

glycosides, myristetin glycosides, terpenoids, flavonoids, tannins, and steroids are among the antioxidants found in sambiloto leaves (*Andrographis paniculata*) (Valentine et al., 2021). Researchers believe that using a lotion containing *Andrographis paniculata* leaf extract has an impact on the healing of dermapen wounds in obese male Wistar strain white rats (Rattus norvegicus). To confirm this idea, researchers experimented on male Wistar strain white rats (Rattus norvegicus). The study's findings demonstrate that giving *Andrographis paniculata* leaf extract cream can alter the amount of collagen in wound healing from dermapen in male Wistar strain white rats (Rattus norvegicus) treated with dermapen. The difference in collagen density between the treatment group and the control group serves as evidence for this. The table displays the microscopic appearance of the skin tissue's histopathology after therapy. In comparison to the control group, treatment 1 and treatment 2, the histopathology of treatment groups 2 and 3 that were smeared with 10% pagoda flower extract cream had the densest collagen structure. The study's findings demonstrate that giving *Andrographis paniculata* leaf extract cream can alter the amount of collagen in wound healing from dermapen in male Wistar strain white rats (Rattus norvegicus) treated with dermapen. The difference in collagen density between the treatment group and the control group serves as evidence for this. The table displays the microscopic appearance of the skin tissue's histopathology after therapy. In comparison to the control group, treatment 1 and treatment 2, the histopathology of treatment groups 2 and 3 that were smeared with 10% pagoda flower extract cream had the densest collagen structure. Secondary metabolites found in Andrographis paniculata leaf extract, such as saponins, tannins, triterpenoids, and flavonoids, which function as free radical transporters and are produced by dermal and adipose wounds, speed up the healing of wounds. The findings of this investigation are consistent with those of a study by Hotimah et al. (2023). The purpose of the study was to determine how well Andrographis paniculata leaf extract ointment healed injuries on white rabbits' backs. The findings demonstrated the effectiveness of Andrographis paniculata leaf extract cream in curing mice's dermapen sores on their backs.

CONCLUSION

1. Administration of *Andrographis paniculata* (*Andrographis paniculata*) leaf extract cream with concentrations of 5%, 7%, and 10% affected the healing process of dermapen wounds in obese white rats (*Rattus norvegicus*) Wistar strain. The treatment group experienced total healing, while the control group given the base cream did not.
2. The results of histopathological observations showed that the control group produced very thin collagen growth, while in the treatment given sambiloto leaf extract (*Andrographis paniculata*) with concentrations of 5%, 7%, and 10% the collagen was fully filled and dense.

3. Phytochemical test results show that sambiloto leaf extract (*Andrographis paniculata*) contains secondary metabolites in the form of flavonoids, saponins, tannins, and triterpenoids. These compounds help heal wounds from dermapen and the growth of collagen cells.

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