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Wound Healing Efficacy of Dexpanthenol Versus Beta-Sitosterol: A Comparative Study in a Rat Model

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ABSTRACT

Numerous types of cells and biological pathways must work together to repair damaged tissue for wounds to heal. Traditional treatments often fail to heal acute wounds, which can lead to gangrene, chronic wounds, or even amputation. The healing process is complicated and depends on a lot of different factors working together. This is what made people look for new treatments that are safe and work.

MEBO and dexpanthenol have both been shown to play a role in the wound healing process by affecting different phases, such as inflammation, collagen deposition, angiogenesis, and re-epithelialization.

Aim: Compare the Effect of Dexpanthenol and Beta-sitosterol (MEBO) In Wound Healing In Rats

Methodology.

Fifteen albino rats took part in this study and were split into three groups. (N=5/group). A punch biopsy was used to obtain a full-thickness 1-cm wound on the back of each rat.

Group 1 Control: (animals without any treatment.)

Group 2 β-sitosterol group: (animals were treated with β-sitosterol only, every 12 hr. for 10 days)

Group 3 Dexpanthenol group: (animals were treated with Dexpanthenol only, every 12 hr. for 10 days)

Results. All treated groups compared to the induced wound control group, caused a very significant decrease in wound size.

($P \leq 0.001$).

Conclusion. 1-The topical application of MEBO cream accelerates wound healing through decreases in wound size, and promotion of angiogenesis, collagen deposition, re-epithelization, and modulation of inflammation.

2-The topical application of MEBO cream when used once a day for 10 days on an induced wound, seems to help the wound heal faster than Dexpanthenol so the use of beta-sitosterol is better than dexpanthenol in the treatment of wounds.

ARTICLE DETAILS

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INTRODUCTION

Process of wound healing

The process of healing a wound is a steady series of carefully planned steps. However, if any of these stages is prolonged, the entire healing process can be delayed .[1]

Optimal wound healing involves the following four stages:

Hemostasis: This is the initial stage of wound healing, in which bleeding is stopped through the contraction of blood vessels, the accumulation of platelets, and the formation of a blood clot.

Inflammation: This stage involves the infiltration, differentiation, and activation of white blood cells, which help to clear away debris and infection from the wound site.

Proliferation: This stage involves the re-epithelialization of the wound surface, the formation of new blood vessels, and the synthesis of collagen to provide strength to the healing tissue.

Remodeling or maturation: This stage involves the maturation of collagen and blood vessels, as well as the reorganization of the extracellular matrix. [2, 3].

WOUND TREATMENTS

The main goal of wound treatment is to promote rapid healing with better appearance and aesthetic results this can be achieved by providing an environment that is moist, free from infection, and protected from trauma [4].

A moist environment speeds up wound healing by keeping cells from drying out and encouraging collagen production and blood vessel growth. You can create a moist environment by using topical agents or occlusive dressings. (Singh *et al*., 2004). Occlusive dressings keep the wound moist and help it heal faster by encouraging epidermal migration, angiogenesis, and connective tissue synthesis. They also improve gas exchange, increase blood flow to the wound site, and keep bacteria from infecting it. [5].

Topical antibiotics' use in wound healing and the risk of bacterial resistance

Antimicrobial agents are used, such as iodine-based preparations and silver-releasing ointment or dressing to treat infected wounds with or without either alone or in combination with systemic or topical antibiotics [6]. Bacterial resistance to silver has been reported since 1975 [7].

Silver sulfadiazine and Topical bacitracin zinc are two examples of topical antibiotics used in wound management.[8, 9].

Silver sulfadiazine is a sulfa drug that is used topically to treat skin wounds due to its antiseptic effect it can be applied after emergency treatment of thermal injuries and does not require dressings. making it suitable for use in low-income settings [10].

THE AGENT ACTS ON WOUND HEALING

Beta sitosterol (MEBO):

MEBO is an oil-based ointment containing sesame oil, beta-sitosterol, and berberine**,** Beta-sitosterol (BS) is a plant sterol with a similar chemical structure to cholesterol, it is found naturally in plants and the blood and tissues of healthy people at levels much lower than that of endogenous cholesterol.[11]

Beta-sitosterol is generally considered to be a safe, natural, and effective natural supplement and has been shown to have many potential health benefits.[11]

Studies in rats have shown that Beta-sitosterol is not genotoxic or cytotoxic (does not damage cells or DNA). Beta-sitosterol also has antioxidant, antimicrobial, angiogenic, anti-inflammatory, and immunomodulatory properties, there are several nutraceutical products on the market that contain Beta-sitosterol under the trade name MEBO.[12]

Berberine is another natural compound found in MEBO. it has anti-microbial action and anti-inflammatory properties. [12]

Mechanism of Action

The exact way MEBO works is still not fully understood, but it is thought that oil-based ointment creates a moist environment that helps epithelial regeneration, with the added benefits of beta-anti-inflammatory sitosterol's properties and berberine's antimicrobial properties.[13]

Dexpanthenol

Dexpanthenol, an alcohol derivative of pantothenic acid, is a necessary component of a healthy epithelium. It is cleaved enzymatically to form pantothenic acid, which serves as a cofactor in many enzymatic reactions important for protein metabolism in the epithelium.[14]

Dexpanthenol's high local concentrations and good penetration make it ideal for topical use in dermatological ointments, creams, and lotions, It relieves itching, promotes healing, increases fibroblast proliferation, and speeds up wound healing, Dexpanthenol also functions as a topical protectant, moisturizer, and anti-inflammatory agent.[14]

Along with its dextrorotatory form (dexpanthenol) and levorotatory form (levopanthenol), panthenol is also offered as a racemic mixture. Although pantothenic acid has optical activity, its biological activity is limited to its dextrorotatory form or dexpanthenol.[15]

Mechanism of Action

Topical dexpanthenol has been shown to increase fibroblast proliferation and accelerate re-epithelization in wound healing, additionally, it acts as a topical protectant, moisturizer, and anti-inflammatory agent. [14]

Topical dexpanthenol has been shown to promote wound healing through a number of mechanisms, including, Increased fibroblast proliferation and collagen synthesis: Dexpanthenol is converted to pantothenic acid in the body, which is a cofactor for many enzymes involved in protein metabolism, including collagen synthesis. Fibroblasts are the cells that produce collagen, so dexpanthenol can help to speed up the wound healing process by increasing the number and activity of fibroblasts.[15]

Accelerated re-epithelialization: Dexpanthenol has been shown to increase the rate at which epithelial cells migrate and proliferate, which is essential for re-epithelialization, or the process of new skin forming over the wound, Anti-inflammatory effects Dexpanthenol has also been shown to have anti-inflammatory effects, which can help to reduce inflammation and promote wound healing.[16]

Some clinical studies have shown that dexpanthenol has been shown to promote wound healing: A study of patients with chronic venous leg ulcers found that treatment with dexpanthenol ointment significantly reduced the time to wound closure.[17]

Another study found that dexpanthenol cream was effective in reducing the healing time of superficial wounds, such as abrasions and lacerations.[18]

A third study found that dexpanthenol ointment was effective in reducing the healing time of post-operative wounds, such as cesarean section wounds.[19]

METHODS

β-sitosterol ointment was taken from already available ointment from the pharmacy (MEBO), from julphar Pharmaceutical Industries, and dexpanthenol (Bepanthen) from Bayer company for drug manufacturing.

Experimental Animals

Three groups of five Sprague Dawley rats each were created from fifteen 150–190 gm rats. For ten days, they were allowed unlimited access to food and water while being acclimated in our lab with equal amounts of light and darkness. They were kept in separate cages that were kept in good condition.

Experimental animal groups

Group 1 control: (animals without any treatment.)
Group 2 β-sitosterol group**:** (animals were treated with β-sitosterol only, every 12 hours for 10 days)
Group 3 Dexpanthenol group: (animals were treated with Dexpanthenol only, every 12 hr. for 10 days)

Creation of skin excisional wounds in rat

Excisional acute wound models:

The full-thickness excisional wound model was selected for this experiment, and various instruments, such as a biopsy punch, were employed to create this kind of wound (rats wound model) [20].

Rats wound model:

An intraperitoneal injection of "ketamine (100 mg/kg)/xylazine (10 mg/kg)" diluted with 0.4 ml of normal saline solution was used to anesthetize the rats. This procedure provided approximately 25 minutes of surgical anesthesia. Next, each rat had a full-thickness excisional wound made on its back using a sterile 10-mm biopsy punch after the back skin hair was manually shaved using a piece of sterile gauze and a 1-cm diameter shaving lotion. (figure 1) [20].

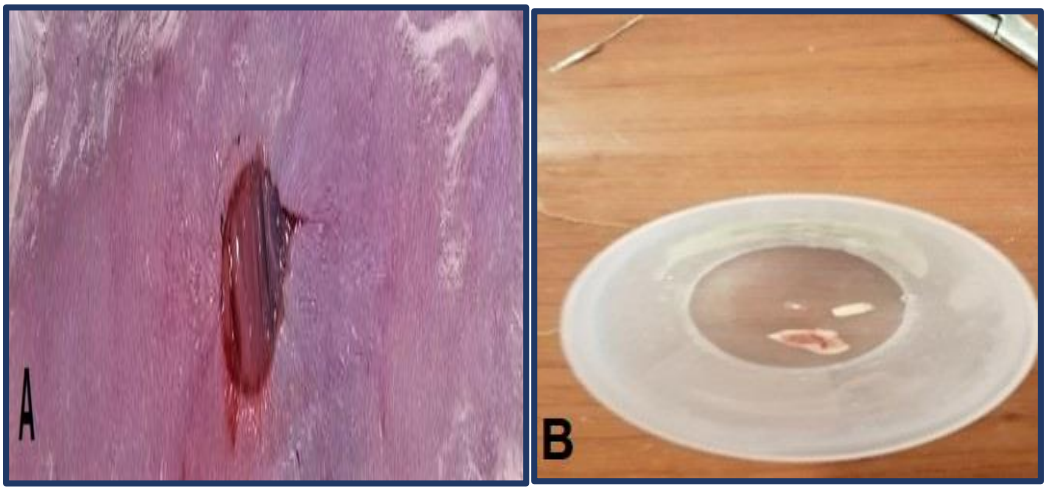

Figure 1: (A)Wound creation and (B) Wound excision after 10 days.

Wounds Size Measurement

Five rats from each group had their wounds randomly chosen, and on days zero, five, seven, and ten of the experiment, the size of the wounds was measured from edge to edge with a ruler. The following formula was used to compare the variations in wound size reduction among the experimental groups:

The following formula was used to get the wound closure percentage:

Primary wound area (in day 0) was defined as 1 cm. percent Wound closure = (primary wound area-end wound area)/primary wound area * 100 percent.[21].

Significance in wound healing of the test groups was derived by obtaining a faster reduction in the wound area on respective days of the study.

Results and discussion

Gross morphological wound healing (Wound size reduction)

Statistical analysis of wound size reduction in that study was expressed as Mean ± SE and p. values were significant when ($P \leq 0.05$) or highly significant when ($P \leq 0.001$).

Wound reduction which observed between the five to tenth days as shown below in Table (1), and Figure (3,4,5).

As indicated in Table (1) and Figure (2), zero-day data showed no significant differences in wound size reduction ($P > 0.05$) between each group.

On the other days, however, as indicated by Table (1) and Figure (3), there were no significant differences in comparisons between the treatment groups ($P > 0.05$), although the data obtained showed a highly significant reduction in the wound size of the treatment groups as compared with the induced control group ($P \leq 0.001$) (3, 4, 5).

Table 1, Figures 3, 4, 5, and Figure 6 illustrate the significant differences in wound size reduction between the β-sitosterol group and dexpanthenol in this study.

Table (1): Comparison of the millimeter-based wound size reduction between the induced control group and all other treatment groups using an unpaired t-test.

Day	Wound size	Control N=5	β –sitosterol N=5	dexpanthenol N=5
Day 0	Mean ± SE	0.0+0.0	0.0+0.0	0.0+0.0
	P-value		**1.000**	1.000
Day 3	Mean ± SE	12.08+1.0	27.17+0.87	20.67+1.67
	P-value		**<0.001**	<0.001
Day 5	Mean±SE	28.33+1.67	48.33+1.67	40.78+1.86
	P-value		**<0.001**	<0.001
Day 7	Mean±SE	49.17+1.54	78.5+1.28	64.67+1.67
	P-value		**<0.001**	<0.001
Day 10	Mean±SE	67.5+1.12	98.0+1.0	85.0+1.83
	P-value	**<0.001**		

- **The data is shown as Mean± Standard error (SE).**
- **N the total number of animals examined daily from each group.**

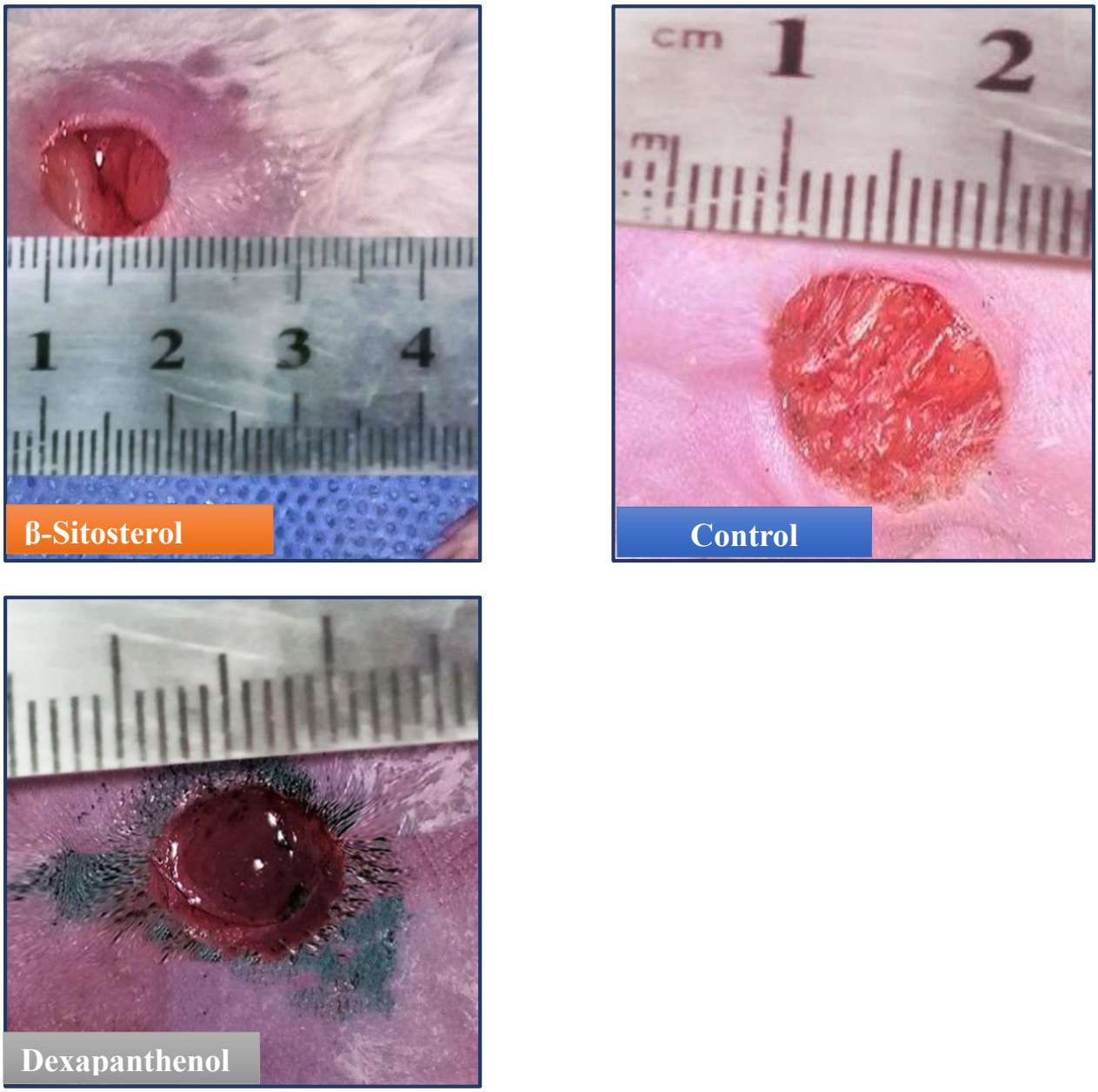

Figure (2): Wound pictures in all groups on the day-zero, showed approximately the same size when measured.

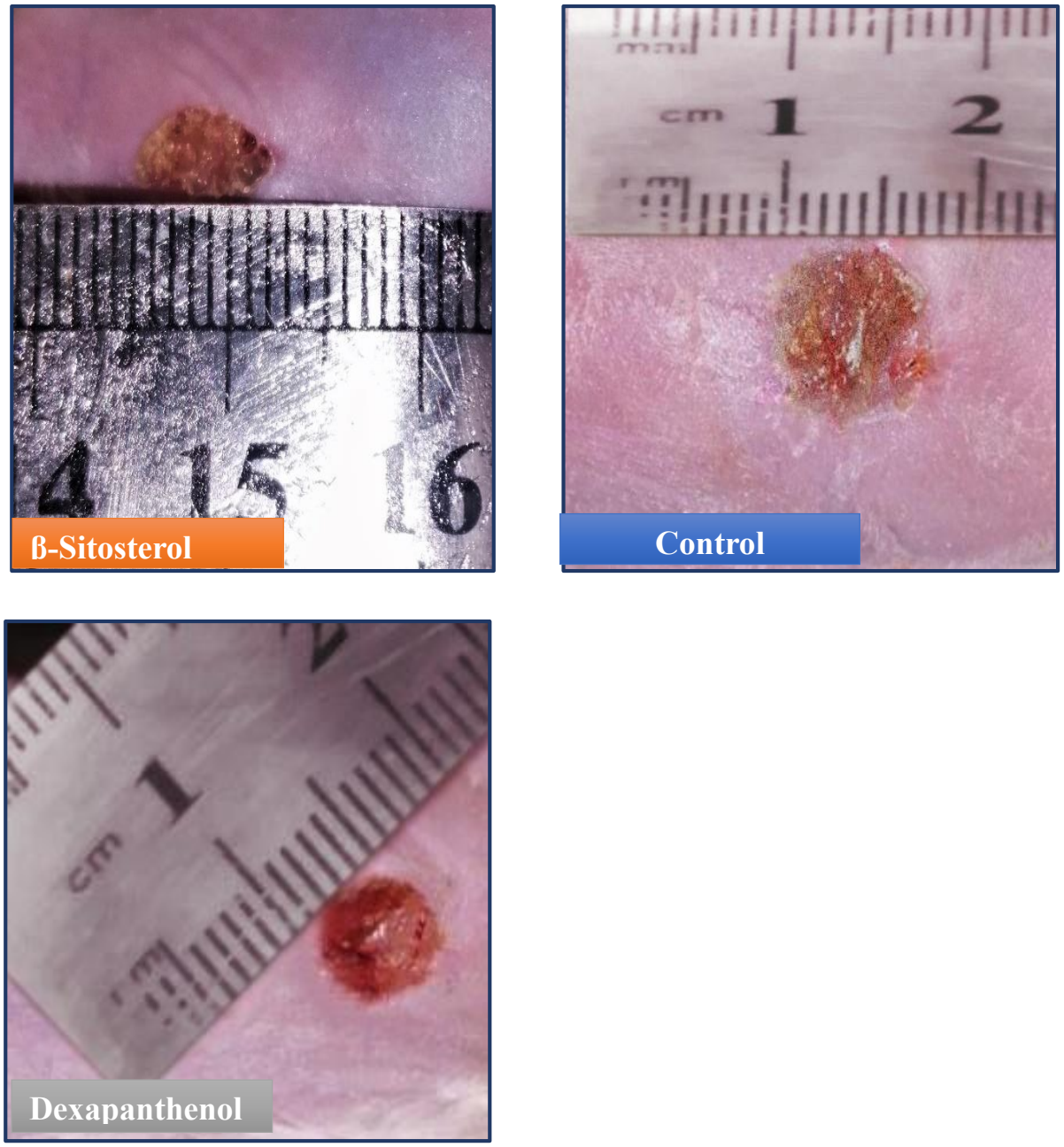

Figure (3): The size and appearance of wound pictures on the fifth day, showed a great difference in treatment groups in comparison with the control group.

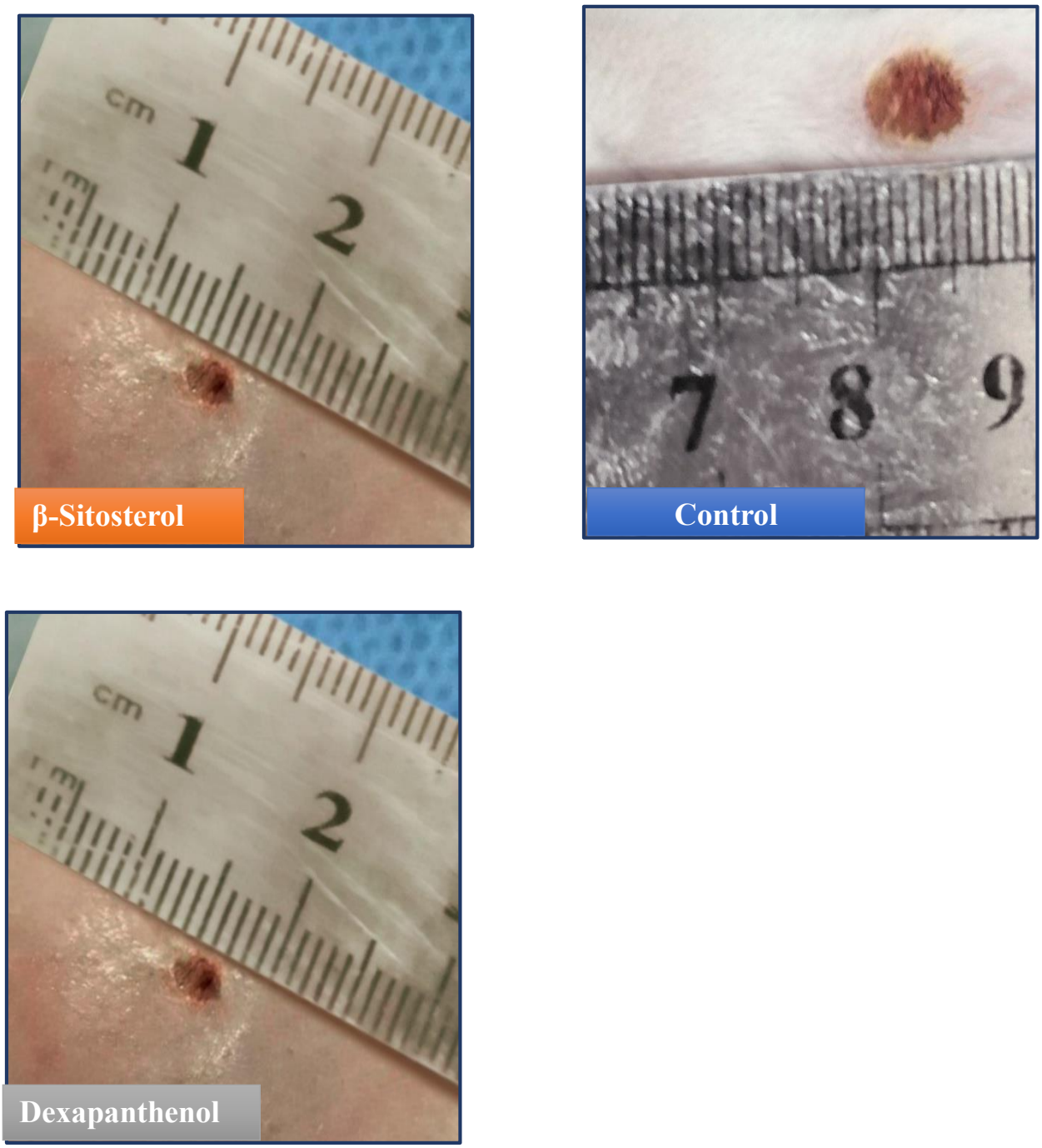

Figure (4): Wound images on the seventh day, showed an apparent and statistically high significant decrease in wound size of β-sitosterol and Dexpanthenol groups in comparison with the control group.

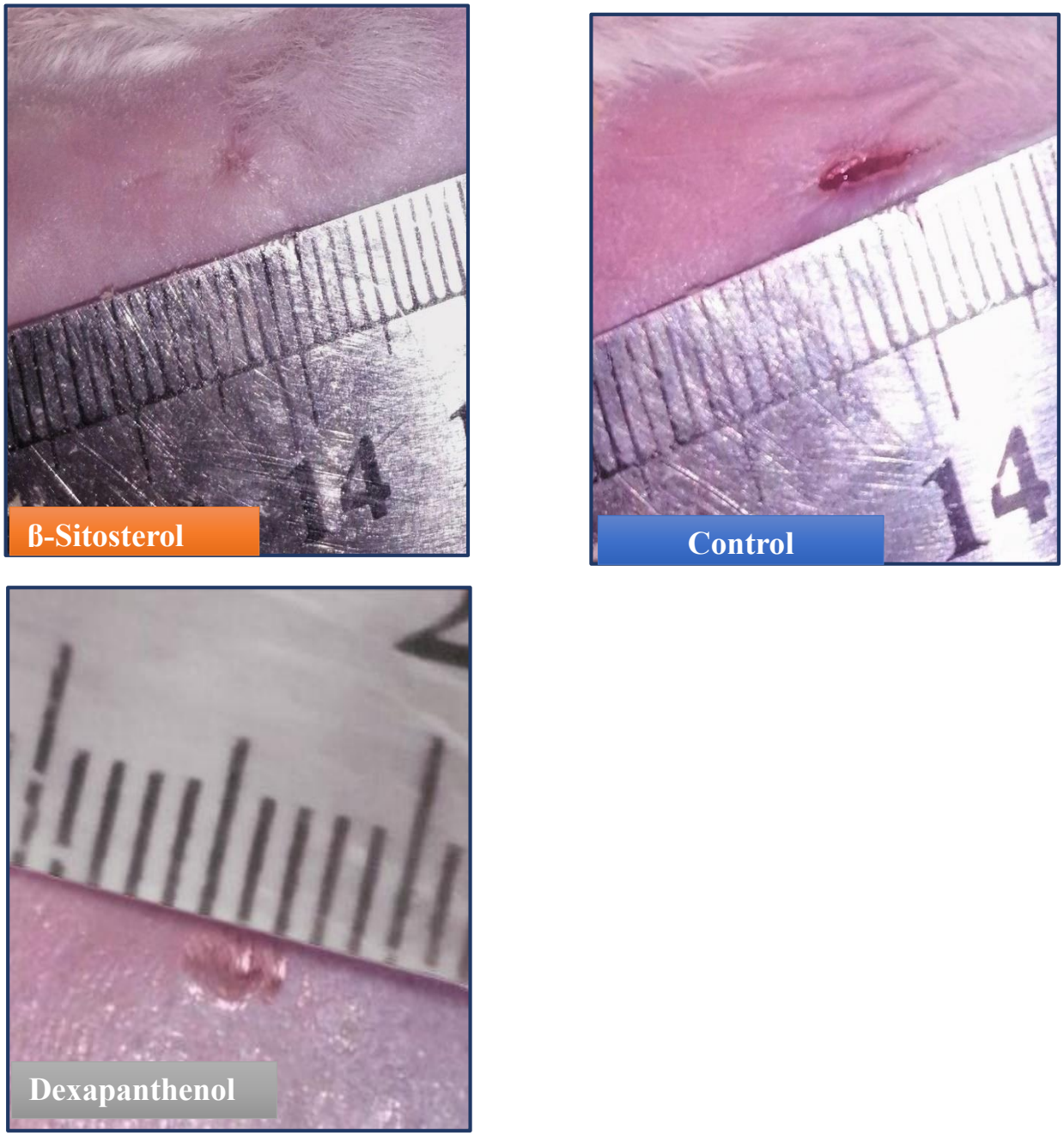

Figure (5): On the tenth day, the wound images displayed full wound closure in the treatment groups and partial wound closure in the petrolatum base group.

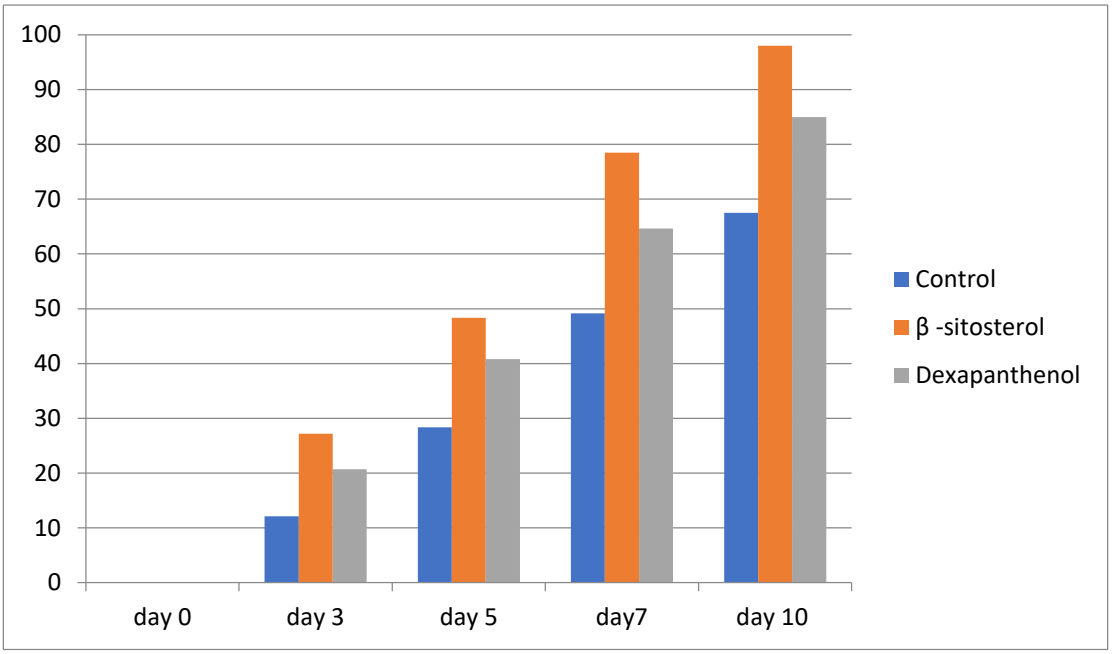

Figure (6): variation in wound size reduction in comparison between the control group with β-sitosterol and dexpanthenol groups

DISCUSSION

Wound healing is a multi-phases and precisely controlled process that includes interaction between epidermal and dermal cells, which is influenced by local factors such as wound size and location, and systemic factors such as diabetes mellitus [22].

Successful healing depends upon precisely controlling inflammation, re-epithelialization, granular tissue formation, collagen maturation, tissue remodeling, and wound contraction [23].

Shortening the time of wound healing by accelerating the necessary elements like angiogenesis and re-epithelization, also reducing the impact of harmful elements like excessive inflammations are of major importance in research [23].

STUDY DESIGN

rats were chosen here for wound healing studies because of their local availability and ease of control [24].

The advantages of the rat wound model are that wound healing occurs from the edges of the wound, so it permits a clear evaluation of the mechanisms implicated in wound healing, and also the easy removal of wound areas with blades and scissors to be examined later by microscopy, in addition to this model permits treatments to be applied directly on the wound bed that allows valuation of a new drug formulation.

On the other hand using an individual metal cage for each rat to prevent rats from harming each other [20, 25].

The results of the current study showed on the fifth day that there were statistically significant differences between the control group and the other groups, which means the success of this model.

Effects of β-sitosterol cream on the wound healing process

This study has shown that MEBO has significantly reduced the wound size in comparison with the control group and dexapanthenol group due to MEBO has anti-infection and analgesic effects MEBO stimulates fibroblasts and neovascularization in granulation tissue, which aids in the development of granulation tissue and wound healing. to ascertain the mechanisms that underlie MEBO's effects.

MEBO can increase the level of interleukin-1 produced by local skin tissue cells and promote cell division in the basal layer of rat skin, which is closely related to promoting wound healing and reducing scar formation [26, 27]

After ten days, the wound images in the treatment groups showed full wound closure, while the petrolatum base group's wounds were still partially closed. [20]

B-sitosterol, a member of the plant steroid family found in many plants, particularly soya, is thought to help with this. MEBO limits tissue damage and promotes better healing results, even though it may also change healing times.. [5].

When compared to the model group using dexpanthenol and the control group, the MEBO group's wound healing time was shorter.

A popular natural oil-based preparation in Asia and the Middle East is called MEB0 ®. Oils keep moisture in the skin, ease pain, and soothe wounds. Epithelialization is aided by beta-sitosterol. Even though MEBO has been the subject of numerous studies on wound healing, the literature review only included a small number of controlled animal trials.[28].

According to studies by Smahel (1993), β-sitosterol ointment lowers exposure to burn surfaces, limits tissue damage, and promotes faster healing. When used in a clinical setting, β-

sitosterol inhibits the growth of pathogenic bacteria, potentially preventing wound infections. [29]

4.3 Effects of Dexpanthenol cream on the wound healing process

Creams with dexpanthenol have been used for a long time to treat sores and cuts on the skin and mucous membranes. Tissues change dexpanthenol into pantothenic acid, which is a part of coenzyme A. Coenzyme A speeds up the first steps in making fatty acids and sphingolipids, which are very important for maintaining the integrity of the cell membrane and the stratum corneum lipid bilayers.[4]

After using a cream containing dexpanthenol, the stratum corneum's hydration and skin barrier repair were markedly improved, and the skin's roughness and inflammation were decreased, Skin roughness and inflammation were reduced, and skin barrier repair and stratum corneum hydration were markedly improved after application of a cream containing dexpanthenol.[17]

Investigations were conducted on topical dexpanthenol which promotes wound healing and epidermal regeneration. Objective, non-invasive methods were used to assess the epidermal response to injury and therapy. The results show that topical dexpanthenol has wound-healing properties that support wound closure, restore the function of the epidermal barrier, and act as an anti-inflammatory. [30]

GROSS MORPHOLOGICAL WOUND HEALING

The present study showed complete wound closure in both beta sitosterol groups and dexapanthenol on day ten in comparison to the control group which presented complete wound healing. This demonstrates how well these medications work to reduce wound size and speed up wound closure. [31] also used an excisional wound model and measured wound size reduction to assess wound healing and found that wound closure was significantly faster in the MEBO-treated group than in the group treated with dexpanthenol.

Furthermore, MEBO speeds up wound healing in the wild but not in knockout rats, according to Victor-Vega et al. (2002) and Montesinos et al. (2002), which is consistent with the results of the current study.[32]

According to Sardari et al. (2007), the central gravitational motion of the dermis and epidermis causes a contraction that reduces the size of the wound, In addition, they found that both MEBO and dexpanthenol contribute to increased fibroblast and endothelial cell migration, and wound fibroblasts achieve a contracting type, famous as myofibroblasts, which is accountable for wound contraction, it is the most essential event in a full-thickness wound. [33]

CONCLUSIONS

1-The topical application of MEBO cream accelerates wound healing through decreases in wound size, and promotion of angiogenesis, collagen deposition, re-epithelization, and modulation of inflammation.

2-The use of beta-sitosterol is superior to dexpanthenol in the treatment of wounds because the topical application of MEBO cream twice daily for ten days on wounds that are induced appears to be more effective in accelerating wound healing.

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