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MANAGEMENT OF CUTANEOUS WOUNDS WITH HERBAL ESSENTIAL OILS

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ABSTRACT
In order to improve the effectiveness of cutaneous wound healing, various efforts have been made. Multiresistant bacteria are one of the challenges of wound healing treatment. Herbal essential oil is one of the alternatives that can be used, because of its broad-spectrum antimicrobial effects. The purpose of this literature review is to discuss in more depth the role of herbal essential oils in wound healing. Articles were retrieved from several databases such as Google Scholar, Sciencedirect, Cochrane, and Pubmed. Articles were searched using predetermined keywords, which were then screened from 2014-2024, resulting in 11 articles that met the inclusion criteria. The herbal essential oils discussed, namely immortelle essential oil, lavender essential oil, tea tree essential oil, chamomile essential oil, calendula essential oil, and castor essential oil, have been shown to be significantly beneficial in wound healing in studies on mice. The herbal essential oils are expected to be an alternative treatment in wound healing, especially in humans.

Keywords: cutaneous; herbal essential oil; multiresistant bacteria; wound healing

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INTRODUCTION

In everyday life, we must have experienced cutaneous wounds. As a physical barrier from pathogens, the cutaneous is responsible for the occurrence of wounds (de Assis et al., 2020). Wounds are cellular or anatomical discontinuities that occur as a result of internal trauma or external trauma caused by mechanical, chemical, or physical agents. While wound healing is a natural reaction of the body that is formed as a tissue response to trauma. The effectiveness of wound healing is influenced by many factors. Factors such as diabetes, hypertension, aging, malnutrition, radiation, and drug use are associated with impaired cutaneous capacity, thereby delaying wound healing. Wound healing itself consists of several phases, including hemostasis, inflammation, proliferation, and maturation (Andjić et al., 2022; Valizadeh et al., 2020).

In improving the effectiveness of the wound healing process, various treatment methods are focused on such as increasing topical antimicrobial activity, preventing infection, encouraging tissue regeneration, and minimizing pain, discomfort, and scar formation. However, in recent decades, the presence of multiresistant bacteria has caused challenges in choosing the right treatment for patients with infections. Many other alternative treatments can be done, one of

which is with herbal essential oils (Mahboubi et al., 2018; Saporito et al., 2018). This herbal essential oils certainly contains several natural products such as triterpenes, alkaloids, and flavonoids that function to promote the wound healing process. Its content also has antimicrobial effects, especially against multiresistant bacteria, because of its broad spectrum of biological and antimicrobial activity (Saporito et al., 2018; Valizadeh et al., 2020). Several types of herbal essential oils have been widely studied regarding their effects on wound healing, such as immortelle essential oil, lavender essential oil, tea tree essential oil, chamomile essential oil, calendula essential oil, and castor essential oil. This literature review aims to discuss more deeply the role of these oils in wound healing.

METHOD

All articles were taken from various databases such as Google Scholar, Sciencedirect, Cochrane, and Pubmed. From these databases, the keywords used were ("herbal oil" OR "essential oil") AND ("cutaneous wound" OR "wound healing") AND ("management" OR "therapy"), which were then filtered with inclusion criteria, namely in English, publication period in the last 10 years (from 2014-2024), relevant to the topic, discuss about the herbal oil that has been determined (immortelle essential oil, or lavender essential oil, or tea tree essential oil, or chamomile essential oil, or calendula essential oil, or castor essential oil), and can be opened in full text. After filtering, 11 eligible articles were obtained, which were used as sources for this literature review, as in Figure 1.

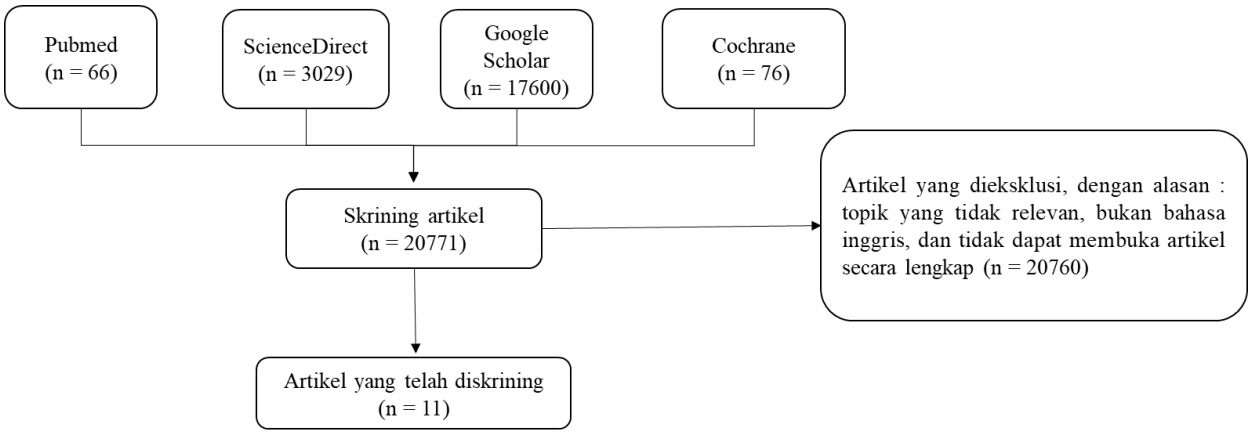

Figure 1. Article Screening Flow

RESULTS

Table 1.
The Characteristics of Herbal Oils in Wound Healing

No	Oil Name	Researcher Name	The Role of Wound Healing
1	Immortelle Essential Oil (Helichrysum italicum)	Andi *et al.* Serra *et al.*	Administration in the form of gel and ointment for 21 days in mice showed significant results on wound contraction or closure, which were 98.75% and 98.33%. This is because this oil increases collagen deposition, accelerates epithelialization and increases wound contraction by working on matrix deposition.
2	Lavender Essential Oil (Lavandula angustifolia)	Mori *et al.* Tepe *et al.*	The application of this essential oil to wounds in mice for 14 days showed a significant decrease in the wound area from day 4, this is because this oil significantly increased the synthesis of Type I and Type III collagen, TGF-β expression, and the number of myofibroblasts. In line with other studies in mice that showed significant results on days 4, 6, 8, and 10 after wound incision ($p < 0.01$ for untreated and control; on day 10: $p < 0.05$ for untreated and control).

No	Oil Name	Researcher Name	The Role of Wound Healing
3	Tea Tree Essential Oil (Melaleuca alternifolia)	by Assis *et al.* Nova *et al.*	The bicontinuous microemulsion formulation of 1% and 3.45% *M. alternifolia oil* on rat wounds showed complete healing after 11 days. This is in line with other studies using hydrogels containing 1% *M. alternifolia oil* that can reduce the growth of *Staphylococcus aureus* ATCC 6538 and accelerate wound healing in infected rats significantly ($p<0.05$).
4	Chamomile Essential Oil (Matricaria chamomila)	Niknam *et al.* Gad *et al* .	Topical ointment of chamomile flower extract with 10% concentration showed 96.27% healing of rat wounds on day 14. This is in line with other studies using solid lipid nanoparticles cream containing chamomile essential oil which has been shown to accelerate the percentage of wound healing activity in rats, reaching 96% on day 16.
5	Calendula Essential Oil (Calendula officinalis)	Okuma *et al.* Ashwlayan *et al.*	The administration of calendula essential oil with or without lamellar gel phase emulsion to wounds in mice experienced complete re-epithelialization on day 14. This is in line with other studies that showed a significant reduction in the total wound area of mice in the test (41.71%) when compared to the control (14.52%).
6	Castor Essential Oil (Ricinus communis)	Sharma *et al.*	Administration of a formulation containing 25% castor essential oil and a mixture of other ingredients to rat wounds showed a significant reduction in wound area with a p value <0.001 compared to the control group.

DISCUSSION

The cutaneous is one of the largest organs in the body, one of its functions is to act as a physical barrier against pathogens. Any damage that occurs to the cutaneous due to physical, chemical, or thermal injury causes wound formation and can cause infection (de Assis et al., 2020). A wound itself is a cellular or anatomical discontinuity that occurs as a result of internal trauma or external trauma caused by mechanical, chemical, or physical agents. Wounds themselves are divided into 2 types, namely closed wounds and open wounds. In closed wounds, damaged tissue is not exposed to the outside environment. With open wounds, the body's surface barrier has been damaged, allowing foreign objects (such as contamination) to enter the tissue and cause further problems in the healing process (Andjić et al., 2022; Valizadeh et al., 2020).

Several phases occur in the wound healing process. Each phase of healing involves a series of cells and biochemical processes mediated by various growth factors, cytokines and enzymes. The hemostasis phase is the initial phase in wound healing that lasts only a few seconds to minutes and is very important to control bleeding after injury. The inflammation phase is the second phase, characterized by sequential infiltration of neutrophils, macrophages and lymphocytes. Prolonged inflammation can worsen scarring and delay wound healing. Interleukins (IL) are known to modulate the wound healing process, especially IL-6 in the early phase of inflammation and inflammatory response. An inflammatory cytokine called tumor necrosis factor-α (TNF-α), participates in the main stage of inflammation, while IL-1β calls neutrophils to the site of infection (Andjić et al., 2022; Khezri et al., 2019). Next, it enters the proliferation phase which is characterized by the development of granulation tissue, mainly driven by fibroblasts and the angiogenesis process. The final phase of wound healing, namely the maturation phase, begins 2-3 weeks after tissue injury and during this period, the formation of granulation tissue tips and collagen remodeling occurs (Andjić et al., 2022).

In the 1960s, wound care was performed by Dr. Jean Valnet using herbal essential oils such as lemon, clove, and chamomile essential oils (TEPE et al., 2024). Herbal essential oils have long been used for therapeutic purposes. Many studies have been conducted on various types of herbal essential oils and their chemical compounds. Most of them have antinociceptive, fungicidal, antioxidant, antitumor properties, and play a role in wound healing (Nadjib Boukhatem et al., 2021). The use of herbal medicines has long been used in traditional Chinese medicine, Ayurveda, Unani, Russian herbal medicine, and other medical systems to treat wounds and other skin conditions topically. The increased likelihood of unsuccessful treatment and recurrent infections is associated with persistent antimicrobial resistance. As a result, they play a significant role in increasing mortality rates, which increases health care costs (Shedoeva et al., 2019). Wounds have become a category in the National Institutes of Health Research Portfolio Online Reporting Tool, due to rising health care costs, an aging population, increasing awareness of the dangers of difficult-to-treat infections, and the worldwide prevalence of diabetes and obesity (Sen, 2019). Implementation of measures designed to reduce the development of antibiotic resistance and the spread of resistant bacteria must be enforced. Thus, for many years, plant-based medicines have been used to treat various medical disorders such as wounds and other skin disorders (Hoffmann et al., 2020; Thomford et al., 2018). In this literature review, several types of herbal essential oils that have been proven effective in wound healing have been described, as follows:

1. Immortelle Essential Oil (*Helichrysum italicum*)

This plant belongs to the Asteraceae family called immortelle, curry plant or perennial sandy plant because its flowers are bright yellow and do not fade. Various benefits of the plant with the Latin name *Helichrysum italicum* have been widely studied, such as antimicrobial, anti-inflammatory and antioxidant properties. In traditional medicine it has been widely used in the treatment of wounds, hematomas, or scars. Research conducted by Andjić *et al.* in mice showed that wound treatment with this oil in the form of gel and ointment for 21 days gave significant results on wound contraction or closure, which were 98.75% and 98.33%, as can be seen in Figure 2 (Andjić, Božin, Draginić, Kočović, Jeremić, Tomović, Milojević Šamanović, et al., 2021). This is in line with research conducted on skin stem cells (SSCs) and fibroblasts (HFF1) by Serra *et al.* which proved that this oil increases collagen deposition, accelerates epithelialization and increases wound contraction by working on matrix deposition (Serra et al., 2024). The effects of this oil cannot be separated from the content of its metabolite compounds. Neryl acetate and pinene have benefits in wound healing. Neryl acetate plays a role in the function of the cutaneous barrier by increasing the lipid and ceramide content in the stratum corneum by increasing the expression of enzymes related to ceramide synthesis in the glucosylceramide pathway. These two compounds will increase keratinocyte differentiation, cell cohesion and the formation of the cornified sheath, thus facilitating wound healing in the epidermis. While pinene plays a role in collagen deposition so as to produce scar tissue with effective tensile strength (Andjić, Božin, Draginić, Kočović, Jeremić, Tomović, Šamanović, et al., 2021; Lemaire et al., 2022). In addition, this oil can also control the function of macrophages which is one of the most challenging tasks during tissue repair and regeneration. Macrophages (Mφ) are dynamic cells that are in the first line of defense against invading pathogens, where they act as effectors of the immune response (Genčić et al., 2021).

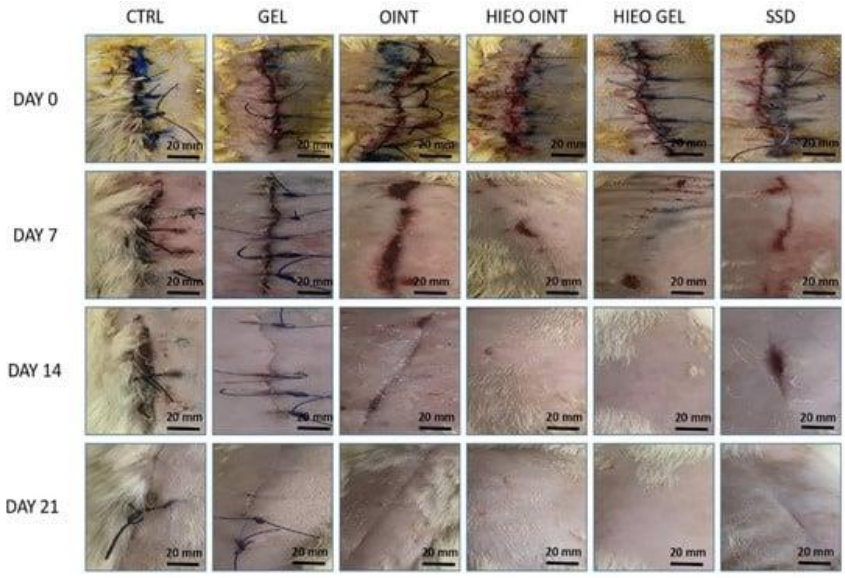

Figure 2. Wound healing process in six treatment groups from day 0-21 (Andjić, Božin, Draginić, Kočović, Jeremić, Tomović, Milojević Šamanović, et al., 2021)

Information :

CTRL = negative control group,

GEL = gel base group,

OINT = ointment base group,

HIEO OINT = *H. italicum* essential oil ointment group,

HIEO GEL = *H. italicum* essential oil gel group,

SSD = 1% silver sulfadiazine group.

2. Lavender Essential Oil (*Lavandula angustifolia*)

Lavender is a flowering plant consisting of more than 20 unique species. The herbal oil of the plant with the Latin name *Lavandula angustifolia* is produced by a secretion structure on the surface of the plant. In 1910, a French chemist applied lavender essential oil to his burned hand after a laboratory accident and reported a rapid healing process. This oil was later used by military doctors in World War II to disinfect and wounds treatment (Samuelson et al., 2020). In a study conducted on mice, by making a full-thickness circular cutaneous wound, *Lavandula angustifolia* essential oil was applied to the wound for 14 days. Approximately 4 days after application, a significant decrease in the wound area was seen. This oil is known to significantly increase Type I and Type III collagen synthesis, TGF-β expression, and the number of myofibroblasts (Mori et al., 2016; TEPE et al., 2024). This is in line with research conducted by Mori *et al.* by making wounds on mice and treating them with lavender essential oil. Wound healing occurred significantly compared to untreated mice (only wound incision was performed) and control mice (wound incision was performed and given control solution containing 0.1% DMSO and Tween 20) on days 4, 6, 8, and 10 after wound incision (on days 4, 6, 8: $p < 0.01$ for untreated and control mice; on day 10: $p < 0.05$ for untreated and control mice) as seen in Figure 3 (Mori et al., 2016). The wound healing effect of this oil cannot be separated from the compounds contained in it, namely biologically active terpenoids, linalool and linalyl acetate (Samuelson et al., 2020). The compound content varies widely, as ecological conditions such as latitude, altitude, temperature, and rainfall can affect the relative amounts of chemicals in the oil depending on

where and when the plant was grown and harvested.

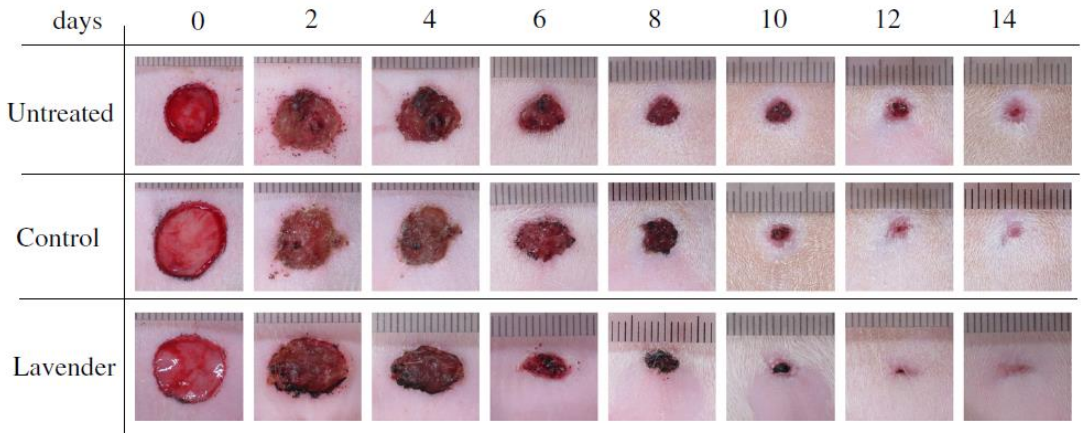

Figure 3. Wound healing process in three treatment groups from day 0-14 (Mori et al., 2016)

3. Tea Tree Essential Oil (*Melaleuca alternifolia*)

Tea tree essential oil, also known by the Latin name *Melaleuca alternifolia* , has been shown to have antimicrobial, antifungal, antioxidant, anti-inflammatory, immunomodulatory properties, and helps in wound healing. It is known that the main active components are terpinen-4-ol, γ-terpinene, and α-terpinene (Han & Parker, 2017). In an in vivo study, it was found that the bicontinuous microemulsion formulation containing *M. alternifolia* essential oil applied to the wound experienced complete healing after 11 days observed in the formulation containing 1% and 3.45% *M. alternifolia* essential oil as in Figure 4 (de Assis et al., 2020). While in another study conducted by Nova *et al.* using a hydrogel containing 1% *M. alternifolia* essential oil was found to reduce the growth of *Staphylococcus aureus* ATCC 6538 both in vitro and in an ex vivo wound model using pig skin. In addition, the evolution of wound size showed that uninfected mice treated with this hydrogel showed a progressive and significant reduction in wound area (67.67 ± 25.47%) when compared to the infected + PBS (Phosphate Buffer Saline) group (86.38 ± 23.38%) with $p<0.05$. Similarly, mice with wounds infected by *S. aureus* treated with this hydrogel (80.03 ± 15.33%), showed a significant reduction in wound area when compared to the infected + PBS group (128.3 ± 17.49%) with $p<0.05$. The average wound area treated with the hydrogel was 96.14 ± 5.79% (Vila Nova et al., 2024).

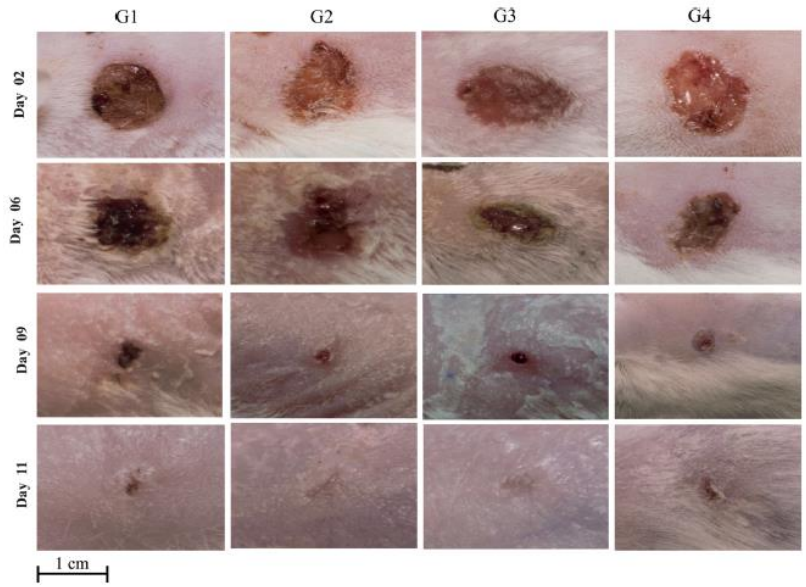

Figure 4. Wound healing process in four treatment groups on days 2, 6, 9 and 11(de Assis et al., 2020)

Information :

G1 = given 200 μg of bicontinuous microemulsion without *M. alternifolia* essential oil,

G2 = given 200 μg of bicontinuous microemulsion with 3.45% *M. alternifolia* essential oil,

G3 = given 200 μg of bicontinuous microemulsion with 1% *M. alternifolia* essential oil,

G4 (positive control) = 200 μg of betamethasone dipropionate cream (0.5 mg/g) and gentamicin sulfate (1.0 mg/g).

4. Chamomile Essential Oil (*Matricaria chamomila*)

Chamomile is a herbal plant that has extensive benefits, especially in skin care. Topical application of plant extract with the Latin name Matricaria *chamomila* has a significant effect in treating various cutaneous diseases (Anis et al., 2021). In a study conducted by Niknam *et al. on mice* , it was shown that the group given topical ointment treatment containing methanol fractions of chamomile flower extract with different concentrations (2.5%, 5% and 10%) showed significant wound healing compared to the control group as seen in Figure 5. Seen on the 14th day, wound healing was 96.27% at a 10% concentrate. This is known because chamomile can stimulate the formation of skin epithelium, fibroblast function and the formation of collagen fibers (Niknam et al., 2021). Its flavonoid content has benefits as an antioxidant and anti-inflammatory by inhibiting the COX-2 pathway (Liu et al., 2022).

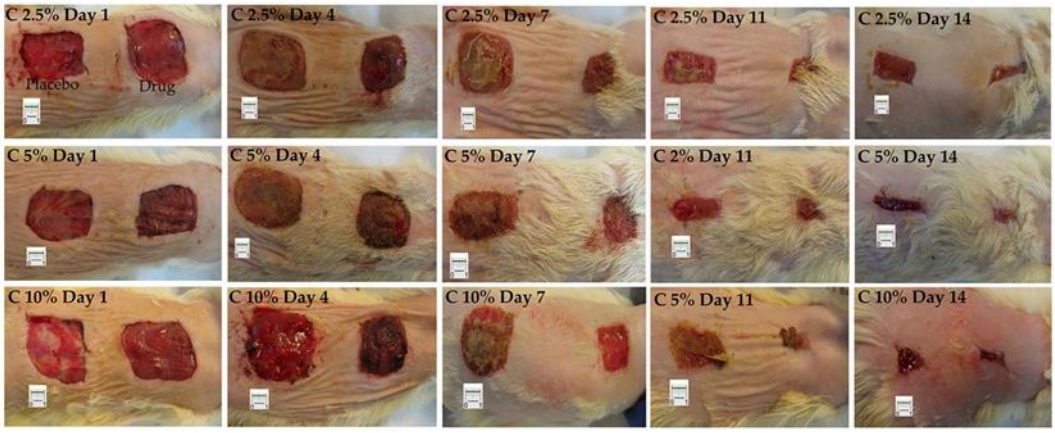

Figure 5. Wound healing process in three treatment groups on days 1, 4, 7, 11 and 14 (Liu et al., 2022)

Information :

Group 1 was given a topical ointment containing 2.5% methanol fraction of chamomile flower extract,

Group 2 was given a topical ointment containing methanol fraction and 5% chamomile flower extract,

Group 3 was given a topical ointment containing methanol fraction and 10% chamomile flower extract.

Similar to its flower extract, chamomile essential oil also has anti-inflammatory, antibacterial, antioxidant, and anti-irritation activities, in addition to its occlusive effect as a protective skin barrier, promoting the rate of re-epithelialization and stimulating collagen deposition. In a study conducted by Gad *et al* . on mice, it was found that administration of solid lipid nanoparticles (SLN) cream and regular chamomile essential oil showed a significant reduction in wound area on days 8 and 16, compared to those not treated, as can be seen in Figure 6. SLN cream containing chamomile essential oil was shown to accelerate the percentage of healing activity, reaching 96% on day 16. This formulation produced the lowest percentage of wound area ($p < 0.001$), compared to its control (Gad et al., 2019).

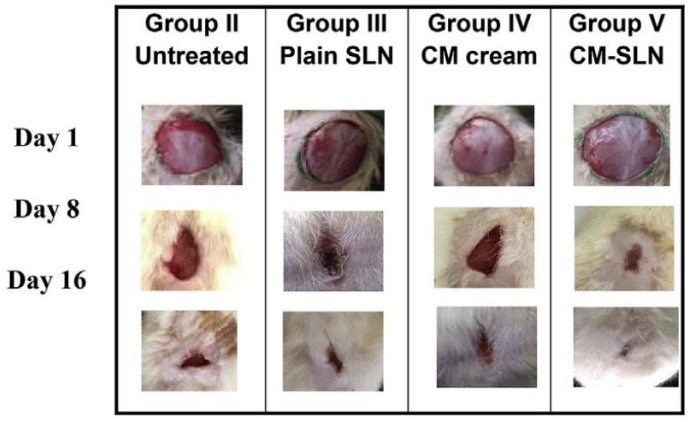

Figure 6. Wound healing process in four treatment groups on days 1, 8 and 16 (Gad et al., 2019)

Information:

Group I: uninjured mice (not in the picture),

Group II: injured and untreated mice,

Group III : mice that were injured and given plain SLN topically,

Group IV: mice that were injured and given chamomile oil cream topically,

Group V: mice that were injured and given SLN containing chamomile oil topically.

5. Calendula Essential Oil (*Calendula officinalis*)

Tis plant is a plant from the Asteraceae family with the Latin name *Calendula officinalis* which is commonly used as medicine in Europe, China, the United States, and India. This plant, also known as "English Marigold" or "Pot Marigold", is known to have many secondary metabolites, especially triterpenoids, flavonoids, coumarins, quinones and carotenoids. In particular, triterpenoids are reported as anti-inflammatory and anti-edema compounds as well as fibroblast stimulation effects (Ashwlayan et al., 2018; Givol et al., 2019). In a study using lamellar gel phase emulsion with calendula essential oil, which was divided into 4 groups, it was seen that the calendula essential oil group with and without lamellar gel phase emulsion experienced complete re-epithelialization on the 14th day, unlike the group without calendula essential oil, as can be seen in Figure 7. This is also supported by the histological picture which shows a significant increase in collagenesis ($p < 0.05$) on the 14th day in the group containing calendula essential oil compared to the group without (Okuma et al., 2015). This is in line with other studies that reported a significant reduction in total wound area in the test compared to the control ($p<0.05$), which was 41.71% in the test group and 14.52% in the control group (Ashwlayan et al., 2018).

Figure 7. Wound healing process on days 0, 2, 7, 14 and 21 (Okuma et al., 2015)

Information:

LGP group: lamellar gel phase emulsion with calendula essential oil,

CAL group: calendula essential oil only (does not contain lamellar gel phase emulsion),

GEL group: only lamellar gel phase emulsions,

CONTROL group: no lamellar gel phase emulsion and no calendula essential oil.

6. Castor Essential Oil (*Ricinus communis*)

This plant, which belongs to the Euphorbiaceae family, is commonly known as castor. This plant is grown worldwide in commercial quantities for the production of castor essential oil which is rich in ricinoleic acid (the seeds contain about 40% oil). The oil is a thick liquid that

is colorless or slightly yellow, and almost odorless (Okafo et al., 2024). Castor essential oil contains palmitic acid (1%), palmitoleic acid (0.1%), oleic acid (3.2%), linoleic acid (4.7%), ricinoleic acid (90%), and stearic acid (1%). This oil is known to reduce lipid peroxidation and act as an antioxidant such as increasing collagen fibril viability, collagen fiber strength, increasing blood circulation, DNA synthesis and preventing cell damage (Abomughaid et al., 2024). This has been proven in many studies, one of which is in the study of Sharma *et al.* in mice, which showed a significant decrease in wound area with a p value <0.001 in the control group compared to the group given a formulation containing 25% castor essential oil and a mixture of other ingredients, namely on the 2nd day of healing of 17.30 ± 0.14 to 13.84 ± 0.14 mm^2 and a percentage reduction of 35.21 ± 0.49 compared to 6.08 ± 0.15 to 2.11 ± 0.09 mm^2 and 58.19 ± 0.44, which then on the 6th day obtained a percentage reduction of 69.57 ± 0.61 compared to 89.07 ± 0.50, and increased to 99% in the treatment group on the 9th day, as shown in Figure 8 (Sharma et al., 2020).

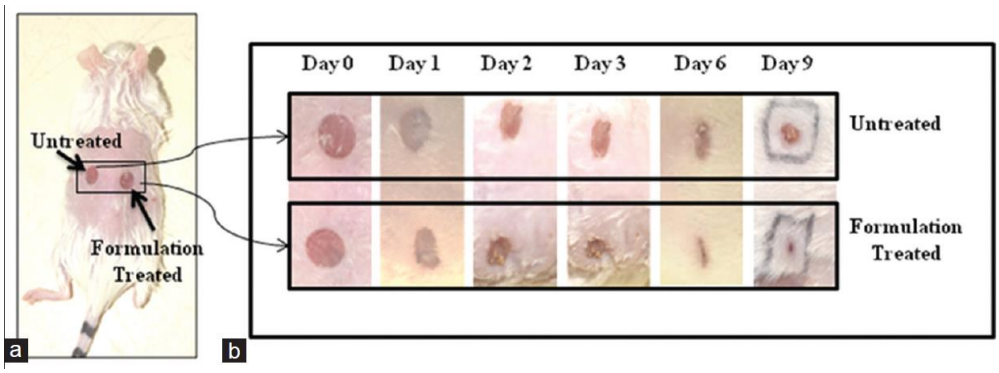

Figure 8. Wound healing process in two treatment groups on days 0 to 9 (Sharma et al., 2020)

CONCLUSION

Various studies on herbal essential oils for wound healing have been conducted. Wound healing itself consists of four phases, each of which involves a series of cells and biochemical processes mediated by various growth factors, cytokines and enzymes. Several herbal essential oils discussed in this literature review have been shown to have significant results on wound healing. However, the research used in this literature review is limited to animal studies and there are still many other herbal essential oils that have not been discussed. It is hoped that in the future, this literature review can be a reference in larger-scale research and can make herbal oils an alternative in healing cutaneous human wounds.

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