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
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Effectiveness of application of *Helichrysum italicum* essential oil in wound healing: report of 3 cases

Linda Julianti Wijayadi¹, Dian Pratiwi²

¹Department of Dermatovenereology, Faculty of Medicine, Tarumanagara University, Jakarta, Indonesia

²Puspa Clinic, Jakarta, Indonesia

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ABSTRACT

Helichrysum italicum (*Hi*) essential oil is commonly used in wound healing. *Hi* is an option for treating acute wounds, especially bleeding wounds. Coconut oil has also long been used for various skin disorders including wound healing and microbial infections. The high amount of antioxidants will be useful against free radicals which are considered the main cause of inflammation during the wound healing process. *Hi* essential oil was chosen because of its antimicrobial, anti-inflammatory, and wound-healing activities, all of which supported the wound-healing process in the three patients in this case report. The purpose of this case report is to determine the effectiveness of using *Hi* essential oil in healing wounds. We report 3 patients with wounds treated with topical *Hi* 10% essential oil in virgin coconut oil (VCO) applied three times daily until healed. All cases showed good wound healing without secondary infection. Despite the irritating side effects in patient 2, all three patients were satisfied with the results. The use of *Hi* 10% essential oil in VCO has advantages in terms of antimicrobial and anti-inflammatory effects on wound healing without secondary infection so it needs to be studied further as an alternative therapy option in wound healing.

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Corresponding Author:

Linda Julianti Wijayadi,
Department of Dermatovenereology,
Tarumanagara University,
5 Sawo Street, Central Jakarta, 10350, Indonesia.
Email: lindajuliantiwijayadi@gmail.com

1. Introduction

Essential oils are generally obtained from the extraction process of the roots of flowers or leaves which contain high concentrations of active plant substances and have therapeutic properties. The use of *Helichrysum italicum* (*Hi*) essential oil has been reported to be efficacious in curing inflammation and skin allergies (Ali et al., 2015; Antunes Viegas et al., 2014; Oliva et al., 2020; Orchard et al., n.d.).

Wound healing is a complex process involving inflammatory processes, including neovascularization, granulation tissue formation, reepithelialization, formation of new extracellular matrix, and remodeling. *Hi* essential oil plays a role in wound healing, increasing cell proliferation, increasing collagen synthesis, stimulating the dermis, and repairing the skin barrier (Lin et al., 2018). The use of essential oils as an alternative to topical medications is best used at low-concentration dilutions. Essential oil concentration of 4-12% provides effective results (Tisserand, 2014).

We report 3 (three) patients with various types of wounds, who consulted the clinic via teleconsultation due to the pandemic situation in Indonesia. There is informed consent from the patient to use their photos and related information. All patients are essential oil users and all chose to use essential oils as a treatment option for their wounds and reasons.

All patient wounds were treated with topical *Hi* 10% essential oil in virgin coconut oil (VCO) and applied 3 (three) times a day to the wounds until the wounds were completely healed. *Hi* essential oil from Young Living™, USA, and VCO from Niura™, Indonesia. Technical data of *Hi* essential oils used: plants come from Yugoslavia, Corsica, Croatia, and Spain. The extraction method is steam distillation of the flowers. The main constituents consist of neryl acetate (3-35%), gamma curcumene (10-28%), alpha-pinene (15-32%), beta-caryophyllene (2-9%), beta selinene (4-8%) (*Essential Oil Desk Reference*, 2019). Various negative responses from each individual to wound healing drugs, such as incomplete healing if the drug is stopped and the high number of side effects, especially on corticosteroids, make HI 10% topical essential oil in VCO can be used as an alternative.

2. Method

2.1 Case 1

Patient 1, a 35-year-old woman, with Fitzpatrick III skin type, presented with dry, thick, red left palm and itching that has been intermittent for a long time, the last recurrence was in the last 1 (one) month. A history of repeated therapy with an ointment prepared by a doctor, which is said to contain corticosteroids, usually improves but always recurs quickly once the ointment is stopped being used. The patient wants independent observation without therapy and wants to try using essential oils if the itching of the lesion is unbearable, without using the doctor's ointment anymore.

Hi 10% ointment in vaseline album (VA) is given to be applied to the lesion 2 (two) times a day after bathing. No other topical or oral medications were used during therapy. Improvements were visible after 7 days of use and almost perfect after 14 days of use. There were no complaints while using the ointment.



Figure 1. Top left photo: initial condition when coming for consultation. Top right: baseline, start using *Hi* 10% ointment in VA. Bottom left: after 7 days of using the ointment. Bottom right: after 14 days of using the ointment.

2.2 Case 2

Patient 2, a 47-year-old woman, Fitzpatrick III skin type, consulted via teleconsultation with abrasions rubbed on the right waist area due to a fall. The skin looks eroded, with a little crusting, and feels very painful. A history of repeated therapy with an ointment prepared by a doctor, which is said to contain corticosteroids, usually improves but always recurs quickly once the ointment is stopped being used. The patient has an allergy to antibiotic ointment of unknown content and refuses to be given antibiotic ointment.

The patient chooses to use essential oils at home first, and if it doesn't improve then he will use the prescribed antibiotic ointment containing 2% fusidic acid. The patient uses *Hi* essential oil which is applied directly without dilution to the lesion 3 (three) times a day, and sends photos via teleconsultation. On the 3rd day afterward, the lesion appeared to have healed with the size of the erosion lesion decreasing. The surrounding skin looks red due to the allergy to the plaster used by the patient. On the 6th day, all the erosion lesions had been fully epithelialized, but the skin in the lesion area and surrounding areas appeared dry, peeling in the plaster area, and a little itchy. There were no ointments or other oral medications used by the patient. The patient did not return to control afterward.



Figure 2. Patient 2, left photo: baseline, middle: after 3 days, and right: after 6 days using *Hi* essential oil directly without dilution.

2.3 Case 3

Patient 3, a 23-year-old woman, with a Fitzpatrick III skin type, was consulted via teleconsultation with a torn nail on her left big toe and continuing to bleed due to being hit by a fallen chair. The patient refused to go to the clinic directly because of the COVID-19 pandemic situation. The top 1/3 of the left toenail appears to have separated from the nail bed, and the bleeding has not stopped. The patient decided to use the essential oil at home first while waiting for the delivery of the antibiotic ointment containing 2% fusidic acid prescribed by the clinic. The patient uses *Hi* essential oil which is applied directly without dilution to the lesion 3 (three) times a day, and sends photos via teleconsultation. On the 3rd day afterward, healing appeared and the surrounding skin area looked a little dry. Because on the first day, the bleeding stopped immediately and the wound appeared to be healing, the patient did not take the prescribed antibiotic ointment. No ointments or other oral medications were used by the patient. The patient did not return to control afterward.



Figure 3. Patient 3, left photo: first day and right photo after 3 days of using *Hi* essential oil directly without dilution. The wound healing process in all three patients was good and there were no secondary infections.

3. Results and Discussion

Phytochemical studies report *Hi* subsp. *Italicum* has three chemotypes. The first contains many monoterpenes, with the main constituents being neryl acetate, neryl propanoate, and alpha-pinene. The second contains the main constituents geraniol and geranyl acetate. The third one contains lots of sesquiterpenes. The diverse phytochemical content of *Hi* underlies its anti-inflammatory and antimicrobial effects (Fraternale et al., 2019; Sarkic et al., n.d.). There is no information on the subspecies and chemotypes of the *Hi* essential oil used in this case report, where the main constituents include neryl acetate, gamma-curcumene, and alpha-pinene. Thus, it is likely included in *Hi* subsp. *Italicum* chemotype monoterpene.

Hi essential oil (EO) is widely used in skincare products, because of its antimicrobial, antioxidant, and anti-inflammatory activities (Antunes Viegas et al., 2014; Djihane et al., 2017). This is the reason for choosing *Hi* EO in this case report. In addition, *Hi* EO from Corsica and Yugoslavia is reported to be good for use in wounds and scar therapy (Antunes Viegas et al., 2014). The *Hi* essential oil used in this case report comes from the same area.

According to Djihane (2017), *Hi* EO has antimicrobial activity and is more effective against the Gram-positive bacteria *Staphylococcus aureus* than the Gram-negative *Escherichia coli*, *Enterobacter aerogenes*, and *Pseudomonas aeruginosa*, which is caused by differences in the structure of the bacterial cell walls (Djihane et al., 2017). In this case report, no there was secondary infection in the wound healing phase of all three patients, which may be related to the antimicrobial activity of *Hi* EO.

Hi EO also has significant in vitro anti-inflammatory effects against protein denaturation. Polyphenols are natural products known to have important biological properties. Three phenols (thymol, eugenol, and 3-isopropylphenol) and 27 volatile carboxylic acids have been identified in *Hi* EO. The in vitro anti-inflammatory activity of *Hi* EO can be attributed to its polyphenol content, which is more of a synergistic effect of the overall content, rather than a single constituent (Djihane et al., 2017; Djihane & Mihoub, 2016). Patient 1 had signs of inflammation that improved with the use of *Hi* EO in VCO.

The antimicrobial, anti-inflammatory, and wound-healing activities of *Hi* essential oil are the reasons for its use in wound healing (Sarkic et al., n.d.). In this case report, *Hi* essential oil was chosen because of its antimicrobial, anti-inflammatory, and wound healing activities which all supported the wound healing process in the three patients in this case report.

As a distillation product, EO constituents generally have a maximum molecular weight of 225 Daltons (rarely reaching 250 Daltons). The molecular size and shape of each constituent is related to the speed of its penetration into the skin. Small molecules easily pass through the sebaceous follicle ducts, and the smaller the molecules the faster their penetration (Price et al., 2012). Therefore, the use of pure essential oils without dilution on the skin is still controversial, especially in vulnerable groups such as babies, children, or the elderly. First, the risk of skin reactions increases with essential oil concentration.

Second, when applied undiluted to skin with a large surface area, percutaneous absorption can result in relatively high concentrations of constituents in the bloodstream, increasing the risk of systemic toxicity.

The exceptions where pure essential oils can be applied directly to the skin are small localized infections and small localized skin lesions, such as in patients 2 and 3 in this case report. In wound healing indications, therapeutic concentrations that do not cause irritation or toxicity are one or two times higher than in vitro cytotoxic concentrations, namely 4-12%. This dilution concentration is safe and effective (Tisserand, 2014). The concentration of *Hi* EO used in patient 1 in this case report was 10%, while patients 2 and 3 used it pure without dilution. There were no visible side effects in patients 1 and 3. In patient 2 there were signs of irritation in the form of dry, peeling, and itchy skin, but the shape matched the plaster used by the patient. Thus, it is possible that the patient experienced an allergic reaction or irritation from the plaster and it cannot be confirmed that there was irritation due to *Hi* essential oil. The 10% concentration appears to be safer to use than pure use without dilution.

Natural plant oils are commonly used in skin care therapies throughout the world because they are relatively cheap and easily available. Some oils have specific compounds with antimicrobial and antioxidant properties. VCO comes from the *Cocos nucifera* tree from the India-Indonesia region and is obtained directly from coconut milk using a wet process under controlled temperatures. Wet processing can avoid the loss of biologically active components such as vitamins and polyphenols. Coconut oil has long been used by several Ngada ethnic groups in Flores, to treat wounds (Ahmad et al., 2017).

Coconut oil has antimicrobial activity and improves the skin barrier because it contains monolaurin, a monoglyceride formed from lauric acid, a short-chain fatty acid with antibacterial activity against *Cutibacterium acnes*, *Staphylococcus aureus*, and *Staphylococcus epidermidis* (Deen et al., 2021; Vaughn et al., 2018). Kevin, et al reported the benefits of VCO for components of intracellular and extracellular matrix and antioxidant activity in healing skin wounds of treated animals. The benefits of VCO are what underlie the choice of VCO as a diluent oil in this case report. VCO contains high amounts of antioxidants, catechins, ferulic acid, p-coumaric acid, caffeic acid, phenolic acid, flavonoids, vitamin E, and provitamin A, all of which are beneficial for wound healing (Nevin & Rajamohan, 2010).

The natural process of wound healing consists of four phases, namely hemostasis, inflammation, proliferation, and remodeling (Akbik et al., 2014). *Hi*'s wound healing activity is associated with its biochemical effects such as its anti-inflammatory and antimicrobial activities, which possibly help wound healing by reducing the inflammatory response during the inflammatory stage and protecting against bacterial infection during the stages of hemostasis, inflammation, and proliferation until complete epithelialization. VCO also supports this process and its high amount of antioxidants will be beneficial against free radicals which are considered to be the main cause of inflammation during the wound healing process. In this case report, all cases showed good wound healing without secondary infection. Despite the irritating side effects in patient 2, all three patients were satisfied with the results.

Hidayat, et al reported a formulation of *Azadirachta indica* and *Hypericum perforatum* extracts as supporting therapy for patients with diabetic ulcers. *Hypericum perforatum* flower oil extract is quite popular as a medicine for excoriations, wounds, and bruises, which is anti-infective, helps wound healing, and is anti-inflammatory (Hidajat et al., 2020).

4. Conclusion

The use of *Hi* 10% in VCO for wound healing in this case report shows good wound healing without secondary infections, this is due to the antimicrobial, anti-inflammatory and antioxidant properties contained. Various compounds in the three *Hi* chemotypes are responsible for this. This is also supported by VCO which is antimicrobial. So it can be concluded that this treatment can contribute to the science, especially as an ideal alternative therapy for wound healing, as well as being a guide in further research. However, the small number of subjects, variations in healing time, and heterogeneous wound characteristics are limitations in this case report, so further large-scale research with homogeneous data is needed.

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