REVIEW: PHYSICAL CHARACTERISTICS, ANTIOXIDANT, ANTIBACTERIAL AND WOUND HEALING EFFECTS OF BASIL LEAVES IN SEVERAL TYPES OF PHARMACEUTICAL BASES

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ABSTRACT

Topical preparations are dosage forms applied to the skin for local therapy. These topical preparations contain several types of bases that are used for drug formulations. This review aimed to determine the type of base that is effective and widely used in basil leaf preparations that function as antioxidants, antibacterial agents, and in wound healing. The research method is comparative, namely, reviewing research articles on formulations of basil leaf products with various concentrations of base types, hydrogels, emulgels, lotions, hydrocarbons, water solubility, absorption, water washing, M/A-type creams, and pastes. The recommended formulation is a gel base type that has physical characteristics, non-irritating properties, antioxidant activity, antibacterial activity, and wound healing. This review contained articles published in the last 10 years.

***Keywords**: basil leaves, base type, physical characteristics, basil leaves, pharmacological activity*

INTRODUCTION

Basil leaves are herbal plants with a distinct aroma, an elevated amount of active substances, and the ability to provide aroma and flavor to food. Secondary metabolites in basil leaves such as flavonoids, ellagic acid, catechins, and tannins have therapeutic benefits (Nadeem *et al*., 2022). Basil leaves offer antibacterial, antioxidant, anti-inflammatory, and wound healing properties. The antioxidant, antibacterial, and wound-healing properties of basil leaves can be used topically to treat skin problems, such as bacterial infections and external wounds (Handoyo *et al*., 2021; Zahra & Iskandar, 2017).

Several variations of topical dosage bases are hydrogels, emulates, pastes, lotions, hydrocarbons, water-soluble, absorption, water-washed, and O/W creams (Ikhtiyarini & Sari, 2022). The differences in excipients used on different bases can affect their physical properties and pharmacological activities (Tsabitah et al., 2020; Utami & Laurany, 2019). As a result, it is necessary to create an effective topical dose form, a suitable base, and physical qualities that fulfill the needs while increasing activity. This review was conducted to establish the type of base that is effective and extensively utilized in basil leaf treatments as antioxidants, antibacterial agents, and wound healers.

RESEARCH METHOD

This article review was prepared through a comparative research strategy that entailed collecting papers from several pharmaceutical research publications available on the Internet. This article review was written with the assistance of Google Scholar, PubMed, ResearchGate, and other journal provider websites. The keywords "Ocimum basilicum", "antioxidant, wound-healing, anti-bacterial, and formulation" were used in the literature searches.

The following criteria were used to determine inclusion in this review:

1. Articles on the physical properties and antioxidant, antibacterial, and wound healing activities of basil leaves in various pharmaceutical preparations
2. Original research articles;
3. Original research articles published between 2013 and 2023
4. Articles on research in Indonesian or English.

The exclusion criteria were as follows:

1. Research articles in the form of literature reviews, systematic reviews, and meta-analyses
2. Research articles that cannot be accessed in full text.

Search results for "Ocimum basilicum", "antioxidant, wound-healing, anti-bacterial, and formulation" can help filter data for this review article. This review was conducted in four ways. First, a search was conducted using modified keywords in the Google Scholar database, PubMed, and manually. Second, the article names were filtered based on the aim of the review. Third, relevance screening was performed on the collected article abstracts. Fourth, from the relevancy screening results, we obtained a free full-text article. If it is not accessible, Google is used to find a full-text article (pdf). **Figure *1*** shows the search results.

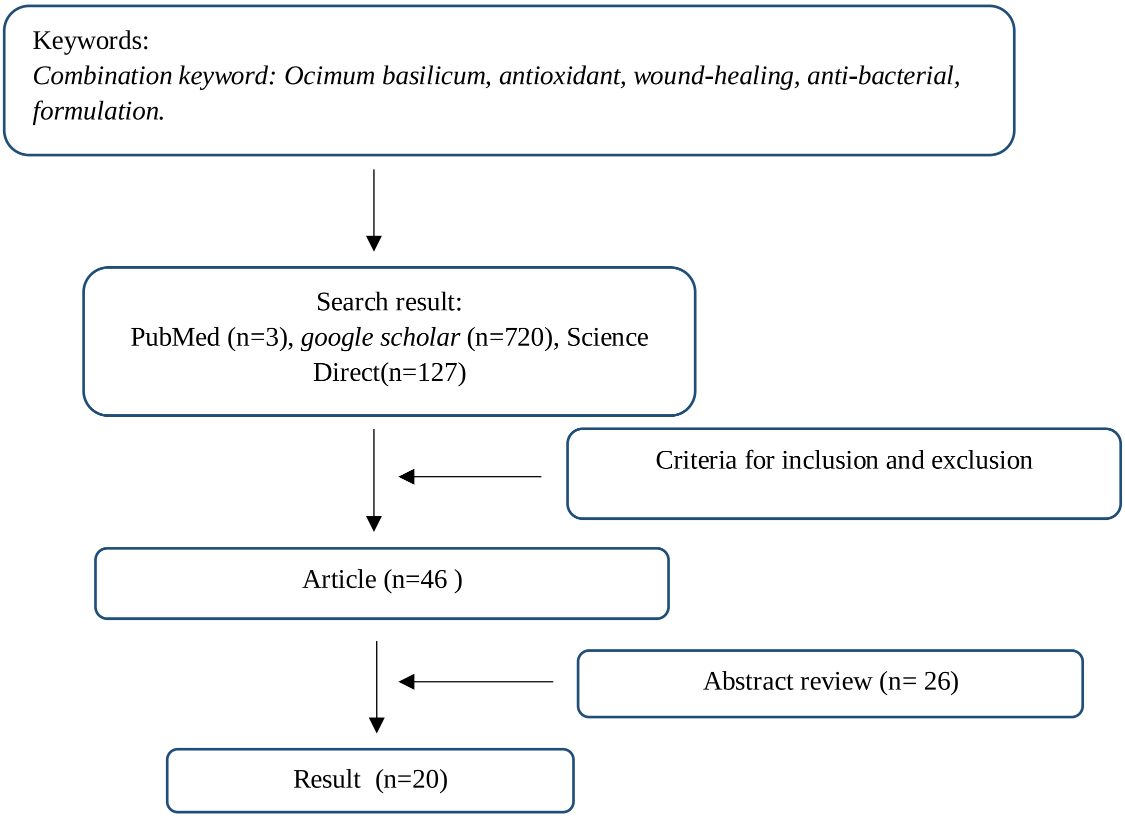

Figure 1. Process Diagram of the Literature Search

RESULTS AND DISCUSSION

An article review was conducted on 20 publications pertaining to the physical properties and antioxidant, antibacterial, and wound-healing activities of basil leaves formulated in various pharmaceutical preparation bases. The following are the findings of a review of the publications listed in **Table I**.

Table I. Characterization and Pharmacological Effects of Basil Leaves in Various Pharmaceutical Bases

Dosage form and Excipients	Method	Physical Characteristics	Result	Reference
Hydrogel Excipients: 1. Carbopol 940 2. TEA 3. Ethanol 4. Glycerin 5. Distilled water	Wound healing test 1. In vitro : Human dermal fibroblasts cells 2. In vivo: mice	-	The increase in wound healing activity in hydrogel preparations was influenced by carbopol, glycerin, and TEA which help release active substances into the skin to increase their activity. Combining Ocimum basilicum extract and Trifolium pretense can increase wound contraction time and heal wounds perfectly after 13 days of use. The in vitro test resulted in the most effective wound healing with the use of hydrogel with extract concentration of 50 μ/mL.	(Antonescu *et al.*, 2021)
Emulgel Excipients: 1. Carbopol 934 2. Liquid paraffin 3. Tween 80 4. Span 80 5. Propylene glycol 6. Methyl parabene 7. Distilled water	In vitro testing for physical qualities such as pH, spreadability, viscosity, and drug release In vivo wound healing assay using a small animal model (rabbit)	pH: 5.9 ± 0.57 Spreadability: 34 ± 0.81 mm Viscosity: 5867 ± 17.02 Over 250 minutes, the drug was released at a rate of 81.71± 1.7%.	The increase in wound healing activity in Ocimum basilicum emulgel was due to the lower concentration of carbopol used in the preparation. A wound healing test using the small animal model method showed that Ocimum basilicum emulgel had the maximum wound contraction/wound healing time equivalent to commercial drugs with a significance (p>0.05). Histopathological examination showed an improvement in the histopathological structure of the skin after 16 days of emulgel administration. The Ocimum basilicum emulgel formula with carbopol gel base has good physical characteristics.	(Ali Khan *et al.*, 2020)

Cream Excipients: 1. Stearic acid 2. Cetyl alcohol 3. Liquid paraffin 4. Tween 80 5. Span 80 6. Glycerin	Spreadability, pH, and adhesion tests are performed. Method for testing antibacterial activity: diffusion Bacteria: *Propionibacterium acnes*	pH:5.2 Spreadability: 5cm Stickiness: 4.42 minutes	The antibacterial activity of the cream preparations increased along with the greater concentration of extracts (basil and green betel) used. Cream with an active ingredient concentration of 45% has an inhibition zone of 25.05 mm. This inhibition is greater than the concentration of 15%, 20.02 mm, and 30% concentration which is 21.24 mm.	(T *et al*., 2021)
Gel Excipients: 1. Carbomer/ carbopol 940 2. TEA 3. Alcohol 70% 4. Methyl parabene 5. Glycerin 6. Aquadest	pH, syneresis, and homogeneity tests are performed on physical properties. Agar diffusion method for testing antibacterial activity Bacteria: *Eschericia coli*	pH: 6.0 Syneresis: no syneresis occurs Homogeneity: the state of being homogeneous.	The concentration of carbopol base increases the pH and syneresis, rendering the preparation unstable. The smallest concentration of carbopol, 0.1%, generates physically stable preparations that inhibit bacterial growth. The resulting inhibition zone measures 15,6 millimeters. The gel that did not contain basil leaf essential oil had an inhibition of 9.67 mm. Gel preparations containing basil leaf essential oil were significantly more inhibitive than those that did not contain these substances ($p<0.05$).	(Arisanty *et al*., 2019)
Cream type O/W (Body Scrub) Excipients: 1. Liquid paraffin 2. Tween 60 3. Propylene glycol 4. Methyl parabene 5. Prophyl paraben 6. Adeps lanae	Emulsification is the manufacturing method. pH homogeneity, spreadability, and viscosity tests are performed.	pH: 5.0 homogeneity: the state of being homogeneous Spreadability is 39.5 mm and the viscosity is 12500.	In tests for pH, homogeneity, spreadability, and viscosity, the body scrub cream containing basil leaf extract and white rice at concentrations of 3% and 10% exhibited the finest and most stable physical properties ($p>$ 0.05).	(Yunita *et al*., 2021)

7. Stearic acid 8. Cetyl alcohol 9. Aquadest				
Gel (Serum) Excipients: 1. Carbomer 2. Glycerin 3. TEA 4. Na Benzoat 5. Dinatrium EDTA 6. Aquadest	Viscosity, pH, and spreadability tests were performed. Method of activity testing: diffusion Bacteria: *Staphylococcus aureus*	pH: 5.04 Spreadability: 5.3 cm Viscosity: 1996	The greater concentration of basil leaf extract in gel preparations (serum) and the use of carbopol as a gelling agent in small concentrations to facilitate the release of the active substance increased antibacterial activity. A concentration of basil leaf serum of 3% produced an inhibition zone of 17.4 mm, indicating that the formulation was potent.	(Fikayuniar *et al.*, 2021)
Gel Excipients: 1. HPMC 2. Glycerin 3. TEA 4. Propylenglycol 5. Aquadest	pH, adhesion, homogeneity, and spreadability are all physical parameters to be tested. Agar diffusion method for testing antibacterial activity Bacteria: *Staphylococcus aureus*	pH: 6.33±0.15 Homogeneity: Homogeneous Adhesion: 2.26±0.03 sec Spreadability: 4.27±0.37 cm	Basil leaf gel preparations with a concentration of 1.5% inhibited Staphylococcus aureus more effectively than 0.5% and 1% concentrations. Antibacterial activity of a preparation is proportional to its concentration. At a concentration of 1.5% extract, the gel inhibition zone measured 19.1 millimeters (strong category).	(Kindangen *et al.*, 2018)
Ointment Excipients: Hydrocarbon base: 1. Cera alba 2. White Vaseline Absorption base: 1. Lanolin anhydrous 2. Cera alba 3. White Vaseline Water	pH, homogeneity, and spreadability tests Antibacterial activity testing in vivo (back skin infection) Rabbits were used as test subjects. Bacteria: *Staphylococcus aureus*	pH: 5.5 homogeneity: the state of being homogeneous Spread: 4.2 cm	Basil leaf ointment is formulated using various bases, including hydrocarbon, absorption, and water extraction. The physical properties test revealed that the various types of bases affected the pH and spreadability of the preparations but had no effect on their homogeneity. The antibacterial test conducted on the skin of the rabbit's back revealed that the variety of base affected the antibacterial activity. The hydrocarbon base has the greatest	(Naibaho *et al.*, 2013)

washable base: 1. PEG 400 2. PEG 4000			antibacterial effect based on the shorter time required for the infection on the rabbit's back skin to recover when compared to other bases.	
Cream Excipients: 1. Glycerin 2. TEA 3. Stearic acid 4. Cethylalcohol 5. Liquid paraffin 6. Aquadest	pH, adhesion, and spreadability tests are performed on physical attributes. Diffusion method for determining antibacterial activity Bacteria: *Staphylococcus aureus*	Spreadability: 3.3±0.0 cm pH: 4.92±0.27 Adhesion: 7.92±0.29 seconds	The increased antibacterial activity of the product against Staphylococcus aureus corresponded to the higher basil leaf concentration employed. This was demonstrated at the highest basil leaf concentration, 15%, which resulted in an inhibition of 16.23 4.16 mm. There was a statistically significant difference between the 15% concentration and the other concentrations ($p<0.05$).	(Tondolambung *et al.*, 2021)
Gel Excipients: 1. Carbomer 2. TEA 3. Propylene glycol 4. Methyl parabene 5. Prophyl parabene 6. Aquadest	pH, adhesion, homogeneity, and spreadability are all tested for physical qualities. Antibacterial activity testing: The Disk Diffusion Method Bacteria: *Staphylococcus aureus*	pH: 5.4±0.50 Adhesion: 7.08±0.47 seconds Homogeneity: homogeneous Spreadability: 5.24±0.25cm	Compared to concentrations of 6% and 4%, the antibacterial activity of basil leaf gel against Staphylococcus aureus was most effective at a concentration of 8%. At an extract concentration of 8%, the gel inhibition zone measured 19.1 mm, placing it in the category of "strong." This is larger than gels with concentrations of 4% and 6%, which have inhibition zones measuring 9.0 2.87 mm and 10.0 2.57 mm, respectively.	(Turrohmah & Shoviantari, 2021)
Lotion Excipients: 1. Etanol 2. Stearic acid 3. TEA 4. Liquid paraffin 5. Cethyl alcohol	pH, homogeneity, adhesion, and spreadability tests are performed. DPPH technique for testing antioxidant activity (in vitro)	pH: 5.5 4.65 seconds for adhesion Homogeneity: the state of being homogeneous Spreadability: 5.7cm	The increase in antioxidant activity of lotion formulations paralleled the increase in basil leaf extract concentration. Basil leaf extract lotion with a concentration of 1.5% has an IC50 value of 18.36 ppm, placing it in the extremely potent (<50	(Ambari *et al.*, 2021)

6. Methyl parabene 7. Glycerin 8. Aquadest			ppm) range.	
Gel Excipients: 1. Carbopol 2. CMC Na 3. HPMC 4. Prophylen glycol 5. TEA 6. Glycerin 7. Aquadest	pH, viscosity, and spreadability should all be tested. Diffusion method for testing antibacterial activity Bacteria: *Escherichia coli* and *Staphylococcus aureus*	pH: 5 viscosity: 16500 cps 6.16 cm in spreadability	Basil herb essential oil emulsion was formulated using various bases, including HPMC, CMC-Na, and Carbopol. On a carbopol premise, it was most effective to increase the antibacterial activity of gel preparations against Staphylococcus aureus and Escherichia coli. The optimization results demonstrate that the carbopol base produces a material with the specified physical properties. Basil herb gel with a 7.5% concentration exhibited antibacterial activity with an inhibition zone of 6.6 mm against Staphylococcus aureus and 5.2 mm against *Escherichia coli.*	(Legowo *et al.*, 2020)
Pasta Excipients: 1. CMC Na 2. Glycerin 3. Aquadest 4. Na sacarin 5. Nipagin 6. Ca carbonat 7. Aerosil 8. Na lauryl sulfat 9. Menthol	Diffusion method for testing antibacterial activity Bacteria: *Streptococcus mutans*	-	In the antibacterial activity test, the inhibition zone was altered by the basil leaf paste's calcium carbonate content. The activity increases as the amount of calcium carbonate used decreases. Basil leaf paste containing an extract of 50 mg/mL is the most effective paste for inhibiting Streptococcus mutans.	(Nurmashita *et al.*, 2015)
Gel Excipients: 1. Na alginate 2. Glycerin 3. Alcohol 4. Methyl parabene 5. Aquadest	In vitro antioxidant activity test using the DPPH method	-	Using the DPPH assay, a gel containing basil and aloe vera leaf extracts demonstrated antioxidant activity. The IC50 value of basil leaf extract gel and aloe vera with a 2:1 ratio was calculated to be 41.97 ppm. The IC50 value of these	(Robiyun *et al.*, 2022)

			preparations falls within the extremely potent range (<50 ppm).	
Krim Excipients: 1. Tween 80 2. GMS 3. SLS 4. Light liquid paraffin 5. White petroleum jelly 6. Paraffin wax 7. Cetyl alcohol 8. Stearyl alcohol 9. Aquadest	Examine the viscosity, adhesion, and spreadability. Agar diffusion test for antibacterial activity Bacteria: *Staphylococcus epidermidis*	Viscosity: 28150 cps Adhesion: 1.66 seconds Spreadability: 2.93 ± 0.15cm	The antibacterial activity of cream formulations against Staphylococcus epidermidis is enhanced when GMS, tween 80, and SLS emulsifiers are combined. Basil leaf essential oil cream formulated with a base of GMS: Tween 80 (1: 3.45) and GMS: SLS (3.68: 1) can function as an antibacterial with an inhibition zone ranging from 5.0–11.3 mm against bacteria and 4.3–7.4 mm against fungi.	(Yadav *et al*., 2013)
Gel Excipients: 1. Carbomer 2. TEA 3. PEG 6000 4. Glycerin 5. Ethanol 96% 6. Na metabisulfit 7. Na2EDTA 8. Methyl parabene 9. Prophyl parabene 10. Aquadest	pH and viscosity tests are performed on physical properties. In vitro antioxidant activity testing using the DPPH method	pH: 7,03 Viscosity: 16310 cps	Basil herb gel was prepared using a carbomer base with several concentrations. The gel formula with a carbomer concentration of 0.75% has the characteristics of a gel that meets the requirements. The use of carbomer with a concentration of 0.75% resulted in a physically stable preparation with the most potent antioxidant activity with an IC50 value of 149.94 ppm (100-150 ppm).	(Rustiani *et al*., 2013)
Cream Excipients: 1. Stearic acid 2. Cetyl stearyl alcohol 3. Liquid paraffin 4. Triethanol amine	pH and viscosity tests for physical properties Test for antioxidant activity using the in vitro DPPH technique	pH: 7.06 ±0.03 Viscosity: 1009±2.34 cps	The antioxidant activity of a cream containing basil and guava leaf extracts increases in proportion to its concentration. The combination cream composition with a ratio of (1:1) yields an IC50 value of 80,1 g/mL, which is comparable to commercially available	(Ilomuanya *et al*., 2018)

5. Hard paraffin 6. Soft paraffin 7. Methyl paraben 8. Propyl paraben 9. Purified water			antioxidant creams.	
Cream Excipients: 1. Ceto stearyl alcohol 2. Liquid paraffin 3. Tween 80 4. Span 60 5. Cetyl palmitate 6. Purified water	pH, spreadability, and viscosity tests Antioxidant activity testing using the DPPH technique (in vitro)	pH: 7.06 ±0.03 Spreadability: 44.19mm The viscosity is 5668.1 cps	The viscosity of the cream formulation decreases as the volume of oil phase increases. Nonetheless, there is a strong relationship between the quantity of emulsifier and the cream's viscosity. 800 g/ml of a polyherbal cream formulation containing basil, rosella, and betel leaf extracts demonstrates antioxidant activity. However, the antioxidant potential is lower than that of ascorbic acid, the comparator compound.	(Ilomuanya *et al*., 2021)
Ointment Excipients: 1. Vaselin album 2. Cera flava	Stickiness and spreadability are tested as physical qualities. Agar diffusion test for antifungal activity Fungi: *Candida sp*	Adhesion: very strong Spreadability: 5,67 cm^2	The hydrocarbon base utilized in ointment formulations has superior adhesion. The semisolid-based hydrocarbon base has stronger adhesion than the water-soluble base. The 50% concentration of basil leaf ethanol extract ointment inhibits the growth of Candida sp more effectively than 2% ketoconazole.	(Stiani *et al*., 2015)
Gel Excipients: 1. Carbopol 2. Glycerin 3. TEA 4. Methyl paraben 5. Aquadest	pH, viscosity, spreadability, and homogeneity tests Antibacterial test: diffusion method Bacteria: *Pseudomonas aeruginosa* and *Staphylococcus epidermidis*	pH: 6.8 Spreadability: 7.2cm Homogeneity: homogeneous 27 poises of viscosity	The greater the concentration of the extract, the greater the viscosity increase prior to the stability test. In the test for spreadability, as the concentration of the extract increases, so does the consistency of the preparation, resulting in a decrease in the gel's spreadability. With	(Rumanti *et al*., 2023)

	inhibition area diameters of 25.5 mm and 26.6 mm, Pseudomonas aeruginosa and Staphylococcus epidermidis could be inhibited by an antiseptic gel containing 4.5% (F3) basil leaf extract. This antiseptic gel's antibacterial activity is of the robust variety.

Basil leaves, formulated in several bases, have pharmacological activities such as antioxidants, antibacterials, and wound healing (Qamar et al., 2021). The higher the concentration of basil used, the higher the antioxidant, antibacterial, and wound-healing activities. Several pharmaceutical bases have been studied, including hydrogels, emulgels, pastes, lotions, hydrocarbons, water-soluble, absorbent, water-washed, and O/A cream types. Based on **Table I**. Basil leaves formulated on an emulgel and hydrogel basis have effective wound-healing activity. Hydrogels with an extract concentration of 50µg/ml could heal wounds in 13 days, and emulgel with an extract of 5% could heal wounds in 16 days. Basil leaves are formulated into creams, gels, pastes, and ointments at different concentrations that produce different bacterial inhibition powers. The base that had the most potent antibacterial activity was gel extract 4.5% (B6) against Pseudomonas aeruginosa and Staphylococcus epidermidis with an inhibition zone of 25.5 mm and 26.6 mm (very strong) (Rumanti et al., 2023). The most potent antioxidant activity was produced by a gel with a combination of basil and aloe vera extracts, with an IC50 value of 41.97 ppm (very strong). The pharmacological activity of each base is shown in **Figure 2Figure 3Figure** 4.

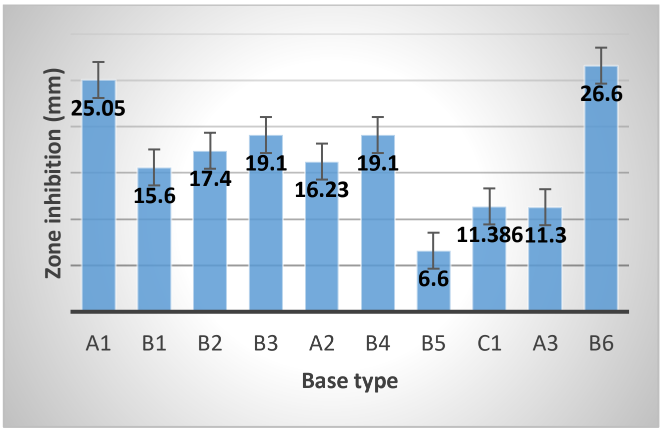

Figure 2. Antibacterial Action on Various Bases (A1: Cream Basil Leaf Extract (BLE); A2: Cream BLE 15%; A3: Cream BLE 4%; B1: Gel Combination; B2: Gel BLE 3%; B3: Gel BLE 1,5%; B4: Gel BLE 8%; B5: Gel BLE 7,5%; B6: Gel BLE 4,5%)

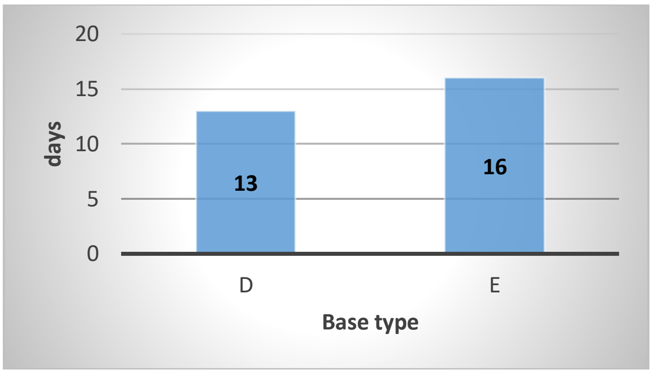

Figure 3. Wound-Healing Action on Various Bases (D: Hydrogel BLE 50µg/ml; E: Emulgel BLE 5%)

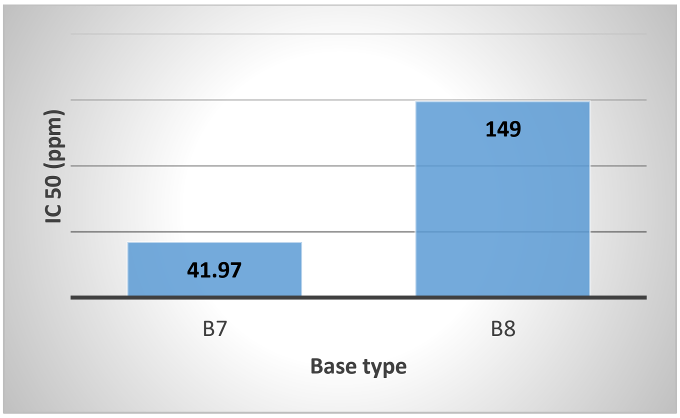

Figure 4. Antioxidant Action on Various Bases (B7: Gel Combination BLE, B8: Gel BLE 0,226%)

Basil leaves, formulated in a hydrocarbon base, are water-soluble, absorbent, and water leached, and have a wound-healing effect. Ointments with a hydrocarbon base heal wounds faster in the presence of bacterial infections. This was evidenced by the disappearance of pus and erythema faster than the ointment with the other three bases. Hydrocarbon bases exhibit better adhesion than water-soluble, absorbent, and water-washable bases. Good adhesion greatly influences drug absorption through the membrane. The longer the preparation is attached, the more drug can diffuse through the membrane (Hasyim *et al*., 2012; Stiani *et al*., 2015).

Combining glycerin and tween 80 emulsifiers in O/W cream resulted in a stable formulation and vigorous antibacterial activity. The combination of emulsifiers in the cream also resulted in a stable viscosity, spreadability, and adhesion during three months of testing. The irritation test also showed that basil leaf cream using a combination of glycerin and tween 80 emulsifiers showed that this cream formula did not irritate the skin (Yadav *et al*., 2013).

Preparations of basil leaves with a lotion and paste base exhibit antioxidant and antibacterial activities. The antioxidants in the preparations become more powerful as the concentration of basil used increases. Using calcium carbonate in a paste base can reduce the diameter of the bacterial inhibition zone. The smaller the concentration of calcium carbonate used, the greater the antibacterial activity (Nurmashita et al., 2015).

The use of carbopol as a gelling agent on a gel, hydrogel, and emulgel basis has been shown to improve wound healing and antibacterial and antioxidant properties because of its ability to optimally release active substances in the skin and increase oxygen entry into the wound (Demirci et al., 2016; Francesko et al., 2019). Optimization of the use of the gelling agent was also carried out for carbopol, HPMC, carbomer, and CMC-Na, indicating that the gelling agent chosen was carpool because it produced the best physical evaluation, especially in dosage forms that did not foam during stability tests (Legowo et al., 2020). The use of a gelling agent also affects the viscosity of the preparation; the higher the concentration, the higher the viscosity. This also affects the spreading power, the higher the concentration of the gelling agent used, the smaller the spreading power (Ali Khan et al., 2020).

The gel base type is an adequate and widely chosen base for formulating basil leaves with various pharmacological activities, such as wound healing and antioxidant and antibacterial activities, which is in line with previous research (Antonescu et al., 2021; Kindangen et al., 2018; Robiyun et al., 2022), which states that the penetration of basil leaf gel base preparations has physical characteristics, stability, and pharmacological effects as antioxidants, antibacterial agents, and wound healing. Basil leaf gel base type with carbopol as a gelling agent has the most vigorous antibacterial activity against Pseudomonas aeruginosa and Staphylococcus epidermidis with an inhibition zone of 25.5 mm and 26.6 mm (very strong) (Rumanti et al., 2023).

CONCLUSION

According to the findings of this review, the gel base type with carbopol as an excipient is an acceptable and commonly used base for manufacturing basil leaves with various pharmacological activities, such as antioxidant, antibacterial, and wound healing. The physical characteristics test findings revealed that basil leaf preparations with a gel base type had better properties and more decisive pharmacological action than other base types.

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