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Formulation and Evaluation of Betel Leaf Antifungal Emulgel

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ABSTRACT

The utilization of natural compounds in pharmaceutical formulations has gained momentum due to their perceived safety and efficacy. Betel leaf, known for its medicinal properties, possesses antifungal attributes. This study aims to formulate and evaluate a novel antifungal emulgel incorporating betel leaf extract. The emulgel was formulated using suitable emulsifiers and gelling agents to achieve optimum stability and rheological properties. Various physicochemical parameters, including pH, viscosity, spreadability, were assessed to characterize the emulgel. Additionally, in vitro antifungal activity against common fungal pathogens was evaluated using standard microbiological techniques. The results demonstrated the successful formulation of a stable emulgel with desirable rheological properties. Moreover, the emulgel exhibited potent antifungal activity against tested fungal strains, indicating its potential application in the management of fungal infections. Thus, the formulated betel leaf antifungal emulgel presents a promising alternative for the treatment of fungal skin infections, warranting further investigation for its clinical efficacy and safety.

INTRODUCTION:

Nowadays, Modern pharmaceutical technology is being combined with traditional health medicines to increase the efficacy. Fungal skin infection has increased in the last two decades. It is now the fourth most common infection in the world. Immobility, mucositis, use of antibiotics, radiation therapy, certain immunosuppressive agents, and intensive care units are the various factors responsible for the fungal infections. Candida species are responsible for the variety of infections ranging from superficial, cutaneous-mucosal to deep-seated infections. There are various types of candidiasis or yeast infections which is caused by C. albicans out of which reoccurrence rate of cutaneous candidiasis is more and it is rarely cured. In the present study Candida albicans is selected to assess the susceptibility patterns against the phytochemical extracts.[1]

Emulgel is a new field for topical medication administration, with few commercialized products to date, therefore focusing on it is both exciting and demanding. Before moving on to emulgel, it's important to understand the benefits of emulsion and gel for topical drug administration. Emulsions are controlled-release systems that comprise two immiscible phases, one of which is dispersed (internal or discontinuous phase) into the other (external or discontinuous phase) with the help of an emulsifying agent. The drug particle captured in the internal phase travels through the exterior phase and then gently absorbs into the skin to deliver a regulated effect.

Gel which are used for dermatological properties have a few positive properties for example being emollient, greaseless, easily removable, non-staining, and compatible with various excipient. The emulgel may provide a better option when it is concerned with topical delivery of poorly water-soluble drug. It is provided better and stable formulation for water soluble or hydrophobic drug.[2]

The topical drug delivery system has followed the first pass metabolism there are the chances of degradation of medicament. So, emulgel formulation has been fruitful importance in the pharmaceutical field under the category of semisolid dosage form.

Betel leaf has been referred to as an aromatic stimulo carminative, astringent, and aphrodisiac since ancient times. The leaf secretes an aromatic volatile oil that contains chavicol, a phenol with potent antibacterial effects.

Scientific research on the leaf of this plant reveals that it possesses many beneficial bioactivities and its extract from betel leaves has a great potential to be used in developing commercial products. Due to the numerous benefits, betel vine is grown for its leaves. The best conditions for commercial betel vine cultivation are those of tropical rain forests, which provide cool shade, considerable humidity and an adequate supply of soil moisture like Indonesia, Malaysia, Philippines, Thailand, Cambodia, Vietnam and India.[3]

The role this formulation is to evaluation the antimicrobial and antifungal activity in form of drug gel of piper betel. The gel formulation topically show higher drug release than ointment and creams. It has many advantages of emulsion and gels. Major disadvantages are their inability to deliver hydrophobic drug and instability during storage. Such type dermatological gels contain a number of advantageous characteristics, such as being greaseless, emollient, easily removable, non-staining, and compatible with different excipients. When it comes to the topical administration of poorly water-soluble medications, the emulgel might be a preferable choice. For drugs that are hydrophobic or weakly soluble in water, it offers a more reliable and better carrier. The topical drug delivery system has adhered to the first pass metabolism, which increases the likelihood of medication destruction. Under the category of semisolid dosage form, emulgel formulation has been beneficially important in the pharmaceutical industry despite the discomfort associated with intravenous therapy and the gastrointestinal system. This formulation's purpose is to assess the drug gel of paper antibacterial and antifungal properties. The benefits of gels and emulsions are numerous. Their fragility during storage and incapacity to administer hydrohobic drugs are major drawbacks.

Ideal properties of emulgel:

1. Good Spreadability
2. Greaseless
3. Thixotropic
4. Good shelf life
5. Odorless & a pleasant appearance

Rationale for using emulgel: [2]

There are numerous medicated products available in the market that are applied to the skin or mucous membrane to enhance its quality or restore its fundamental function or

pharmacologically alter an action in the underlined tissues etc. but these topical or dermatological products that are available mostly in the form of ointments, creams or lotions, have plenty of disadvantages. These products are sticky in nature and cause uneasiness to the patient when applied, they also have minimal spreading coefficient that is why they need to be rubbed when applied and these preparations also exhibit the problem of stability. They are also sometimes time consuming to apply and regimen may also become difficult when lots of formulations are prescribed. The use of transparent gels has increasingly expanded in the pharmaceutical and cosmetic preparations because there are lots of limitations within the major group of semisolid preparations. But in spite of many advantages of gels, their biggest limitation is the delivery of hydrophobic drugs. That is why to overcome this sole limitation an emulsion based approach is being developed and used so that even the hydrophobic drugs could be successfully incorporated and delivered through gels.

MATERIALS AND METHODS:

1. PIPER BETLE (BETEL LEAF):

Botanical Name: Piper siriboa L.

Kingdom: Plantae

Family: Piperaceae

Part typically used: Leave

Color: Green

Chemical Constituents: Chavibetol, Caryophyllene, Chavibetol acetate, Allylpyrocatechol Diacetate, Chavibetolmethylether, Campene, f-Pinene, Eugenol, u-Limonene, a-Pinene, 1,8-Cineol, Saprobe, Allylpyrocatechol Monoacetate.

Uses: Stimulant, Antiseptic, Antifungal, to treat dry skin and wrinkles.

2. LEMON OIL:

Botanical Name: Citrus limon

Kingdom: Plantae

Family: Rutaceae

Part typically used: Fruit peel

Color: Pale yellow

Chemical Constituents: Lemon oil mainly contains d-limonene (about 90 percent) and citral (about 4 percent). It also contains small quantities of citronella), geranyl acetate, terpineol, a sesquiterpene and aldehydes.

Uses: Lemon oil is principally used as a flavouring agent. It also possesses stimulant, carminative and stomachic properties.

3. LAVENDER OIL:

Botanical Name: Lavendula angustifolia, Lavendula officinalis

Kingdom: Plantae

Family: Lamiaceae

Part typically used: Leaves and flower buds

Color: Clear with a Tinge of Yellow

Chemical Constituents: Linalyl Acetate, Linalool, (Z)-B-Ocimene, Lavandulyl acetate, Terpinene-4-ol, B-Caryophyllene, (E)-B-Farnesene, (E)-B-Ocimene, 3-Octanyl Acetate

Uses: Soothes inflammation. Lavender oil has a calming effect that helps reduce itching, swelling, and redness caused by infections, insect bites, and skin disorders like eczema and psoriasis, Anti- Aging, Fights Acne, Promotes Wound healing, Fights Infections.

4. MENTHOL:

Botanical Name: Mentha piperita

Kingdom: Plantae

Family: Lamiaceae

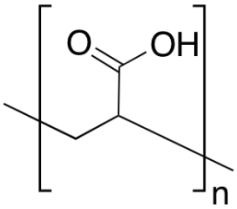
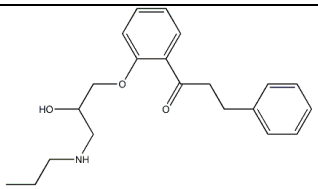
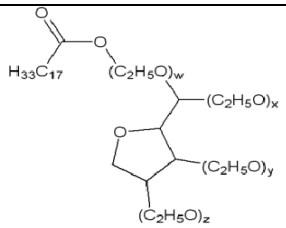
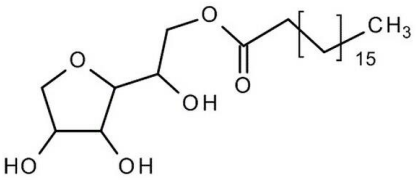
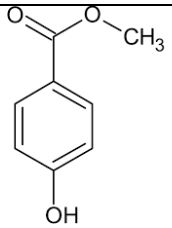
Part typically used: Flowers

Color: White crystals

Chemical Constituents: Monoterpenoids

Uses: as a denaturant, flavouring agent and fragrance ingredient

Chemicals:

Sr. No.	Name of Chemical	Structure	Use
1.	Carbopol 934		Gelling agent
2.	Liquid paraffin		To treat dry skin
3.	Tween 80		Surfactant
4.	Span 60		Emulsifier and stabilizer
5.	Methyl paraben		Increase shelf life and inhibit bacterial and fungal growth in formulation.

Method:

1. Plants

The plant of betel leaf was obtained from the farm.

2. Vehicle

The vehicle use for the formulation of emulgel is water.

3. Emulsifier

The emulsifying agent are used to reduce interfacial tension in between water & oil.

4. Gelling agent

Consistency the gelling property can be increase by using various gelling agent such as Carbopol 934.

5. Preservative

The substance which preserves the preparation for the long period such as methyl paraben and propyl paraben.

6. Extraction method

Take betel leaf and dry it at room temperature. After proper drying of leaves they are was powdered with the help of blender. Then Soxhlet apparatus is used for extraction process. 20gm of betel leaf powder placed it into thimble and take RBF containing the 150ml ethanol as a solvent for 3 hours after betel leaf extraction filter it and keep it on water bath for 1hours for the evaporation process and collect the residue.

Fig. 1: Extraction of Betel leaf

Table no. 1: Formulation table:

Sr. No	Name of Ingredient	Formulation I F1 (20gm)	Formulation II F2 (20 gm)
1	Carbopol 934	0.16 gm	0.16 gm
2	Betel extract	02 mg	2.5 mg
3	Liquid paraffin	8.2 ml	8.2 ml
4	Tween 80	0.10 mg	0.10 mg
5	Span 60	0.5 mg	0.5 mg
6	Methyl paraben	0.10 mg	0.10 mg
7	Lemon oil	0.16 ml	0.16 ml
8	Lavender oil	0.16 ml	0.16 ml
9	Menthol	0.10 mg	0.10 mg
10	Water	q.s	q.s

1. **Aqueous phase**:-Dissolve Tween 80 in purified water then add methyl and propyl paraben add in it whereas extract of betel leaf also dissolves in water for preparation the Aqueous phase.

2. **Oily phase** :- Add Span 60 in liquid paraffin. Then add Lavender oil and lemon oil in it to make an oily phase.

3. **Gel phase:-** Gel phase can be prepared by the addition of Carbopol 934 in purified water with constant stirring. Finally, both aqueous and oily phase heat at 70℃ and add oily phase into aqueous phase to make an emulgel.

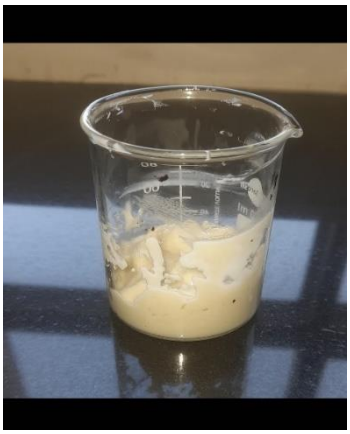
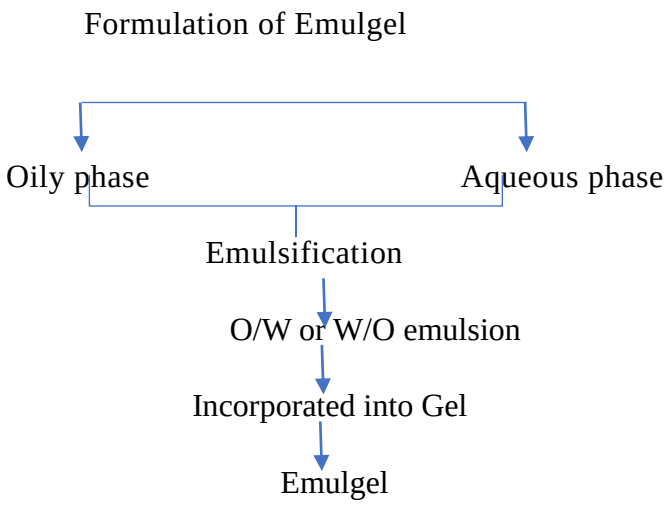


Fig. 2: Emulgel formulation

Flow Chart for formulation:[4]



Evaluation parameters: [4,5]

a) Color: The gel formulation's colour was examined against a background of black and white.

b) Odour: We tested the gel's odour by dissolving it in water and inhaling the resulting mixture.

c) Measurement pH: By using digital pH meter.

1gm of gel in 100 ml of distilled water

↓

Keep aside for two hours

After determining the mean pH of the gel formulation, the pharmaceutical product's pH was measured three times.

d) Homogeneity:

After the gel was put in a container, the homogeneity of each generated gel formulation was visually examined. They underwent tests to check for aggregate appearance and existence. Table reports on the gel formulation's homogeneity.

e) Spreadability:

Spreadability was determined by glass slide and wooden block apparatus.

About 20 gm of weight was added to the pan

↓

The time were noted for upper slide to move

↓

Separate completely from the fixed slide

↓

An express amount of gel 2gm under study was placed on this lower slide

↓

Then the gel was sandwiched between two slides

↓

Another glass slide has the fixed at lower slide

To create a consistent gel layer and eliminate air between the slides, a 1 kg weight was applied to each slide for five minutes. The borders had extra gel removed. The top plate was

then pulled using the string that was fastened to the hook, and the number of seconds it took for the top carriage to move 7.5 cm was noted. The sweepability improves with decreasing interval length. The spreadability of the gel was calculated using the following formula:

$$\text{Spreadability} = M \times L/T$$

Where, M = Weight in the pan which is tied to the upper slide, L= Length moved by the glass slide

T = Time in seconds taken to separate the slide completely each other. The malleability of the gel is listed.

Table no 2: Observation and evaluation of gel formulation

Evaluation parameter	F1	F2	F3
Colour	Greenish	Greenish	Greenish
Odour	Characteristics	Characteristics	Characteristics
Consistency	Semi-solid	Semi-solid	Semi-solid
Spreadability	3.28gm.cm/sec	4.64gm.cm/sec	3.38gm.cm/sec
Extrudability	Good	Good	Good
pH	6.5	6.71	6.7

1. Antifungal activity:

The antifungal activity of every created batch of formulation, or blank formulation, was tested using the Cup-plate method and compared to commercially available antifungal formulation (marketed gel). Candida albicans was one of the bacterium cultures used. Agar well diffusion was utilized to conduct the antifungal test. In sterile petri dishes, prepared nutrients were brought, poured, and allowed to cool and dry. Next, micron wire loops were used to disperse each bacterial culture. To drill holes 4 mm deep, a sterile cork borer with a 6 mm diameter was utilized. Afterwards, 0.5 g of gel from every batch is added to these holes. Next, the plates were incubated for 48 hours at 27℃. Following that, the diameter in millimetres (mm) of any formed zone of inhibition for each fungal strength was evaluated for that specific chemical.

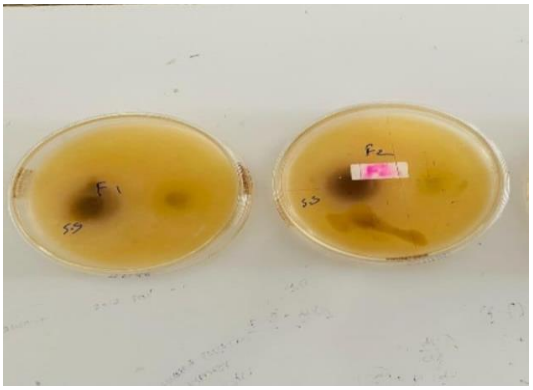


Fig 3. Antifungal activity

Result of activity: Anti – fungal (Candida *Albicans)*

Sr.no.	Zone of Inhibition(mm)	
F1	20.3mm	10.6mm
F2	20.3mm	10.3mm

RESULT AND DISCUSSION:

After being manufactured, the herbal gel was evaluated according to several parameters. The herbal gel felt smooth and cold to the touch after application. It had a dark greenish color. The gel has a pH of 6-7. When the gel was applied using water and cotton gauze, it was discovered to be non-oily, non-irritating, and readily removed. The herbal gel was applied with a cold, smooth sensation and had a translucent, dark greenish tint. According to the study, PH remained steady and was found to be 6-7. After conducting a stability study, spreadability was also measured and discovered to be less variable than the previously prepared gel. The gel is safe, nongreasy, and nonstick. After application, these can be effortlessly removed using cotton gauze and water. Stability study: - All the prepared emulgel formulations were found to be stable upon storage for 3 week at room temperature no change was observed in their physical appearance, pH Spread ability, viscosity, phase separation are not observe.

Conclusion:

In the recent years, topical drug delivery will be used extensively due to better patient compliance. Since emulgel possesses an edge in terms of spreadibility, adhesion, viscosity

and extrusion, they will become a popular drug delivery system. Moreover, they will become a solution for loading hydrophobic drugs in water-soluble gel bases it was observed that the gel formulation of the aqueous extract of betel leaves exhibited clear color, odor, and clarity. Additionally, the study that the gel showed antibacterial and activity against Bacillus, mixed strains, and yeast. This suggests potential applications for the betel leaf extract gel in various antimicrobial treatments.

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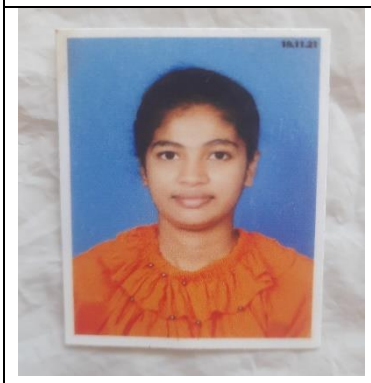 **Image Author -3**	Author Name: Snehal B. Borade Author Affiliation: SMBT Institute of D. Pharmacy Author Address/Institute Address: SMBT Institute of D. Pharmacy, Nandi Hills. Dhamangaon, Nashik, Maharashtra, India.