MATHEWS

Research Article

Mathews Journal of Pharmaceutical Science

Formulation and Evaluation of Organogels of Actives from Piper Betel for Treatment of Cellulitis

Suryawanshi Prashant T*, Albhar KG

JSPM's Jayawantrao Sawant College of Pharmacy and Research, Hadapsar, Pune-411028, India

ABSTRACT

Topical drug delivery system of organogel of actives form of P Betel leaf oil is used to treat bacterial infection of cellulitis disease. The deeper layers of the skin and underlying tissues are affected by the common bacterial skin illness known as cellulitis. This study describes the organogel by using gelling agent soya lecithin and polymer Poloxamer 407 to obtain the drug released and drug content. Physicochemical characterization was performed for evaluation of the betel leaf oil on TLC, HPTLC and anti-oxidant activity. The formulation of organogel was evaluated for an organoleptic observation, measurement of pH, viscosity, spediability, *in-vitro* drug released, anti-bacterial activity, skin irritation test and stability test. Through this study, increase the drug released of organogel as increasing the concentration of gelling agent. Concentration of soya lecithin (2.5%) is then the drug released show the minimum released. Hence, gelling agent and polymer is responsible for the variation of % of drug released.

Keywords: Anti-Bacterial Activity, Antioxidant Activity, Skin Irritation Activity, Drug Released, Drug Content.

INTRODUCTION

The deeper layers of the skin and underlying tissues are affected by the common bacterial skin illness known as cellulitis [1]. It is characterized by redness, swelling, warmth, and pain in the affected area. Cellulitis typically occurs when bacteria, most commonly Streptococcus or Staphylococcus, enter the body through a break in the skin. It can occur anywhere on the body but most commonly affects the legs, arms, and face [2]. Over fourteen trillion instances of cellulitis are reported each year in the United States, making it one of the most frequent bacterial skin infections. It is responsible for over 3.7 billion dollars in ambulatory care expenses and 650000 hospital admissions per year. According to some studies, the incidence of cellulitis is around 24.6 to 50 cases per 1000 person-years, with a higher incidence among males and individuals aged 45-64 years [3]. The most common site of infection is the lower extremity.

Vol No: 09, Issue: 03

Received Date: July 13, 2025

Published Date: September 30, 2025

***Corresponding Author**

Prashant Suryawanshi

JSPM's Jayawantrao Sawant College of Pharmacy and Research, Hadapsar, Pune-411028, India, Phone: 7559390868, E-mail: prashantsuryawanshi5297@gmail.com

Citation: Prashant S, et al. (2025). Formulation and Evaluation of Organogels of Actives from Piper Betel for Treatment of Cellulitis. Mathews J Pharma Sci. 9(3):55.

Cellulitis often manifests as a warm, erythematous region that is poorly defined, edematous and sensitive to palpation. It is an acute bacterial infection that is inflaming the subcutaneous tissue around it as well as the deep dermis. There is no abscess or purulent discharge associated with the infection. Streptococcus pyogenes and methicillin-sensitive Staphylococcus aureus are the two most common beta-hemolytic streptococci that cause cellulitis. Patients who are immunocompromised, colonized with methicillin-resistant Staphylococcus aureus, bitten by animals, or have co-morbidities such as diabetes mellitus may become infected with other bacteria [4-6].

Betel leaves are commonly used in many Asian cultures for their medicinal, culinary, and cultural significance [7,8]. The betel plant, scientifically known as Piper betel is a vine belonging to the Piperaceae family and is native to Southeast Asia. The leaves of the betel plant are heart-shaped, glossy, and have a distinct spicy and aromatic flavor. Betel leaf is herbal drug with Anti-microbial, anti-inflammatory, anti-oxidant properties that has been used to treat bacterial infection of cellulitis, inflammation. Betel leaves have been used for centuries in traditional medicine systems such as Ayurveda, Siddha and Unani [9,10]. Betel leaves are rich in various phytochemicals, including alkaloids, terpenoids and phenolic compounds, which are responsible for their therapeutic properties.

Topical drug delivery systems play a vital role in delivering therapeutic agents directly to the site of application on the skin for local or systemic effects. Organogels, which are semisolid systems, composed of organic liquids immobilized within a three-dimensional network of self-assembled gelators, have emerged as promising vehicles for topical drug delivery. Organogels offer numerous advantages, including controlled release, enhanced drug stability, improved drug penetration, and prolonged drug residence time on the skin.

The organogelling of lecithin in organic phase is induced as a result of introduction of a water phase. When lecithin is dissolved in oil phase separately, it itself assembles into reverse micelles. The extension of spherical reverse micelles and their transformation into tubular and cylindrical micelle cluster which is initiated by addition of minute amounts of polar additives.

Cellulitis can lead to serious complications if left untreated or if the infection spreads. Antibiotics can help prevent the spread of bacteria, reducing the risk of complications such as abscess formation, tissue necrosis, or bloodstream infections. By addressing the underlying bacterial infection, antibiotics can accelerate the healing process. They help the body's immune system in fighting off the bacteria, allowing the affected skin and tissues to recover.

MATERIALS AND METHODS

Betel leaf oil was procured from Veda oils Wazirpur (Delhi), Soya lecithin were procured from Mahendra's pure chem laboratory, PEG 400 were procured from Pallav Chemical and Solvent Pvt Ltd Tarapur, Isopropyl palmi t a t e and Polaxomer 407 were procured from Research lab chem industries. All other chemicals used were of analytical grade.

Organogel were prepared by the dispersion method, Soya Lecithin adds in isopropyl palmitate (7%) and keep overnight at room temp (25°C) up to complete dissolved. Poloxamer 407 and methyl paraben (0.020%) propyl paraben (0.002%) dissolved in water and a store in refrigerator (2°C), then Drug and PEG 400 add in lecithin solution and Lecithin solution add in 2nd solution with continuous stirring at 400 rpm till mixed properly (Table 1).

Formulation Table

Table 1. Formulation Table

Sr. No.	Name of Ingredients (%)	F1	F2	F3	F4	F5	F6	F7	F8
1	Betel Leaf Oil (%)	1	1	1	1	1	1	1	1
2	PEG 400 (%)	10	10	10	10	10	10	10	10
3	Soya Lecithin (%)	2.5	2.5	5	10	5	5	2.5	10
4	Isopropyl Palmitate (%)	7	7	7	7	7	7	7	7
5	Polaxomer 407 (%)	10	15	10	10	15	20	20	20
6	Methyl Paraben (%)	0.020	0.020	0.020	0.020	0.020	0.020	0.020	0.020
7	Propyl Paraben (%)	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002
8	Water up to (%)	100	100	100	100	100	100	100	100

Characterization

Spectrophotometric characteristics [8]

For this,1 ml of (Betel leaf oil) was placed in a 10 ml volumetric flask and dissolved in 8 ml of ethanol, then the volume was built up to the mark using ethanol. To make a stock solution of 100 µl/ml of Betel leaf oil. This was used as final (standard) stock solution 100µl/ml. The solution was scanned in the range of 200 to 400 nm and the corresponding λmax value was reported using solvent system blank.

FTIR spectroscopy [11]

For this, potassium bromide dispersion method was used. The drug was previously dried in desiccators and the blend of betel leaf oil and potassium bromide (1:3) was prepared. The baseline correction was made using dried potassium bromide and spectrum was recorded over 4000-400cm-1. The spectrum has been used for elucidation of structure of betel leaf oil by interpreting the major peaks observed in the spectrum.

Thin Layer Chromatography [12,13]

Thin layer chromatography (TLC) is a chromatography technique used to separate mixtures. Thin layer chromatography is performed on a sheet of glass, plastic, or aluminium foil, which is coated with a thin layer of adsorbent material, usually silica gel, aluminium oxide, or cellulose (blotter paper). This layer of adsorbent is known as the stationary phase. After the sample has been applied on the plate, a solvent or solvent mixture (known as the mobile phase) is drawn up the plate via capillary action. The compounds were identified by matching color and Rf value with the parallel spot of marker compound of respective class.

HPTLC of betel leaf oil [14,15]

Procedure of sample preparation

i. Preparation of standard Eugenol:

Take a 100 µl of Eugenol and add 1ml n- hexane, shake well then two layers are formed. Take the organic fraction for a sample spotting.

ii. Preparation of betel leaf oil for a sample spotting:

Take 50 µl betel leaf oil and add 2ml n-hexane, shake well

iii. Preparation of gel formulation:

Take 1 g of gel in 15 ml of n-hexane and stir it for 2 hours. Then the solution is concentrated and its TLC is checked in 7:3:1 Toluene: Ethyl acetate: Acetic acid as a mobile phase.

***In-vitro* antimicrobial studies**

The agar plates were prepared by dissolving the nutrient agar 28 gm into the water 1000 ml and were autoclaved for 15 minutes at 121°C. Then, the agar medium was allowed to cool at 40-45°C. 25 ml of molten agar was poured into the petri dishes. The agar plates were allowed to solidify.

Preparation of inoculum Staphylococcus Aureus, Pseudomonas Aeruginosa, and Streptococcus Pyogenes were used to estimate the antibacterial efficacy of the topical formulations containing betel leaf oil and the inoculation of agar plate (Figure 2). Wells were prepared by using a sterile cork borer by making holes in the inoculated agar plates (Table 6). Each well was 5 mm in diameter. A weighed amount of the formulation was placed into each well. The plates were incubated at 37°C for 72 hours and observed for inhibition zones. The area of the inhibition zones was measured by using a ruler to the nearest millimeter.

Anti-oxidant activity [16]

Antioxidant capacity of the formulation was confirmed by the DPPH scavenging assay according to Brand-Williams et al. Different concentrations (0.01 to 0.1 mg/ ml) of the extracts and ascorbic acid (standard) were thoroughly mixed with 5 ml of methanolic DPPH solution (33 mg/L) in test-tubes and the resulting solution was kept standing for 10 minutes at 37°C before the optical density (OD) was measured at 517 nm. The measurement was repeated with three sets and an average of the reading was considered. The percentage radical scavenging activity was calculated from the following formula:

$$\% \text{ Scavenging [DPPH]} = [(A0 - A1)/A0] \times 100$$

Extrudability

Extrudability = Applied weight to extrude gel from tube (in gm) / Area (in cm2)

Drug content

1gm organogel was dissolved with little amount of ethanol in a 100 ml volumetric flask and mixture was shaken till solution was affected. The volume was made up to 100 ml with ethanol. The solution was filtered through Whatman filter paper (No. 41). Further dilute 5ml to 50 ml with ethanol (Table 3). The absorbance of the solution was measured at 355 nm

(Systronics PC based double beam spectrophotometer 2202) against reagent blank.

Drug released

All formulations were subjected to *in-vitro* diffusion through cellulose membrane by using Franz diffusion cell. The receptor compartment was filled with saline phosphate buffer pH 6.8 and kept at 32 ± 0.5°C and stirred with the help of magnetic stirrer. Phosphate buffer pH 6.8 was added to maintained sink condition. About 1 gm of organogel was placed on the cellulose membrane. 1 ml of sample was withdrawn from the receptor compartment at 1, 2, 3, 4, 5, 6, 7, 8 hours and replaced with same volume of medium (Table 4). All samples were diluted up to 10 ml with medium and analyzed for alpha lipoic acid content spectrophotometrically (Systronics PC based double beam spectrophotometer 2202) at wavelength 355 nm (Figure 11).

Skin irritation test (HET-CAM Test)

The hen's egg chorionic test (HET-CAM) is an alternative to animal testing for the identification of serious skin irritants, using embryonic chorion (Figure 3A, 3B & 3C). The skin irritation of the developed formulation has been verified by the chicken egg chorion test, a rapid, sensitive, and inexpensive test for incubated eggs, which is a case of the boundary between In-vivo systems and *In-vitro* systems, and does not conflict with ethical or legal standards or obligations (Table 7).

Stability study [8]

Short-term stability study of prepared organogel formulation was carried out by storing at 25±2°C for a period of 45 days (Table 8). At intervals of one week the organogel was visually examined for any physical changes.

RESULTS

Spectrophotometric characteristics

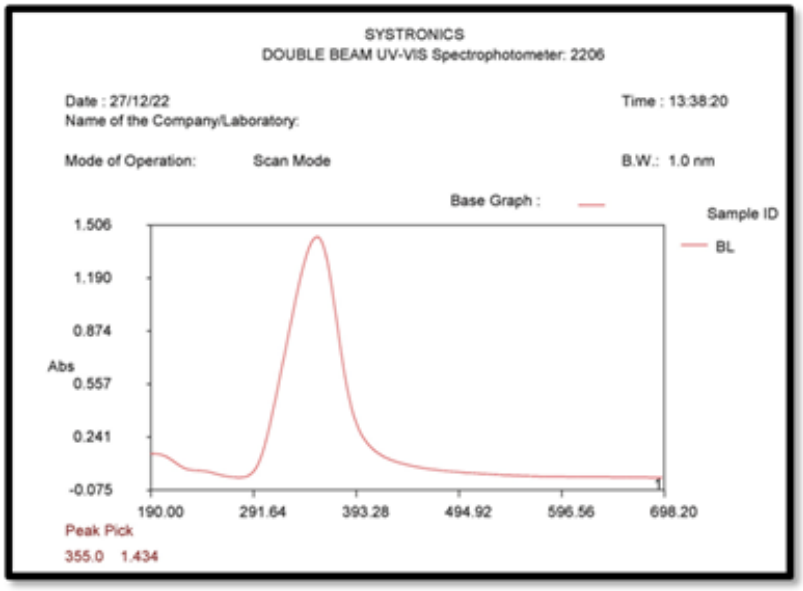


Figure 1. UV spectrum of Betel leaf oil λmax in ethanol.

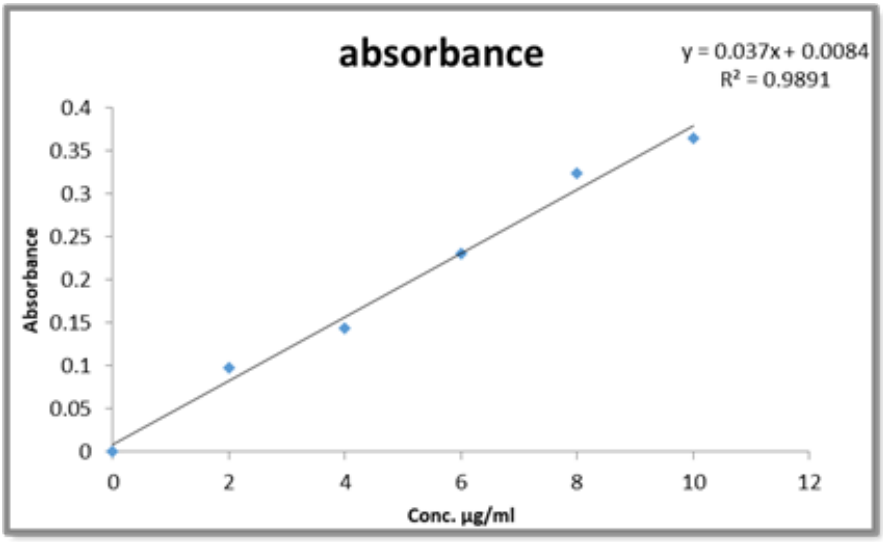


Figure 2. Calibration curve of Betel leaf oil in ethanol.

FTIR spectroscopy

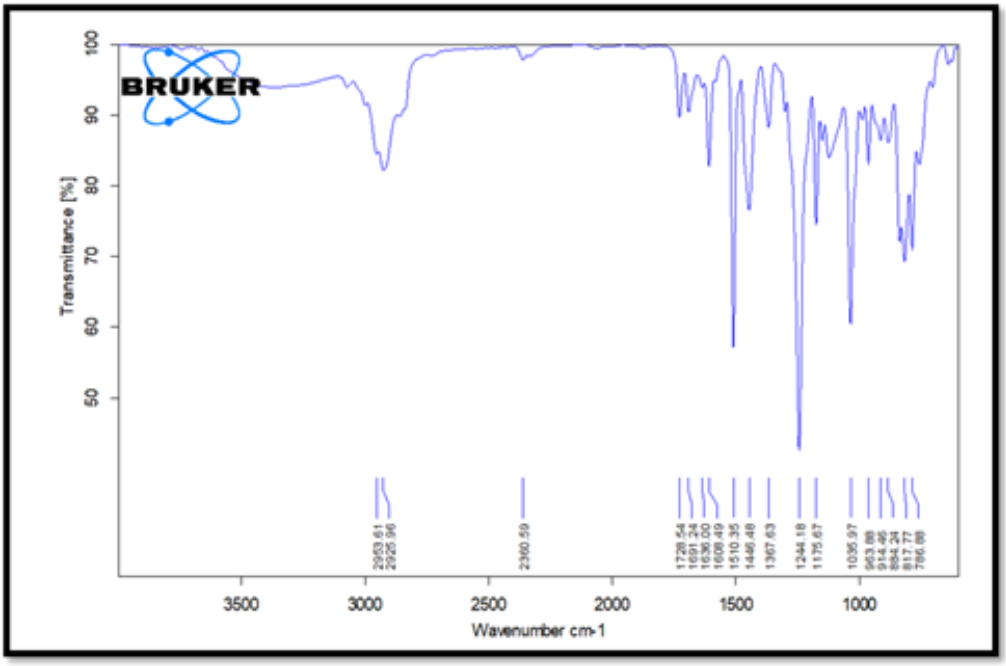


Figure 3. FTIR spectrum of Betel leaf oil.

Thin Layer Chromatography

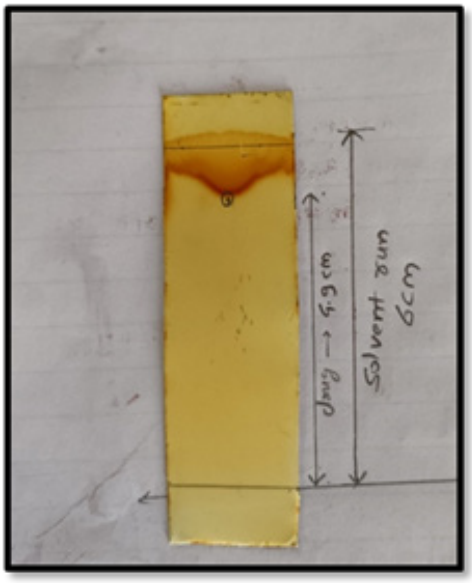


Figure 4. TLC run with mobile Methanol: Chloroform: Acetic acid.

HPTLC of betel leaf oil:

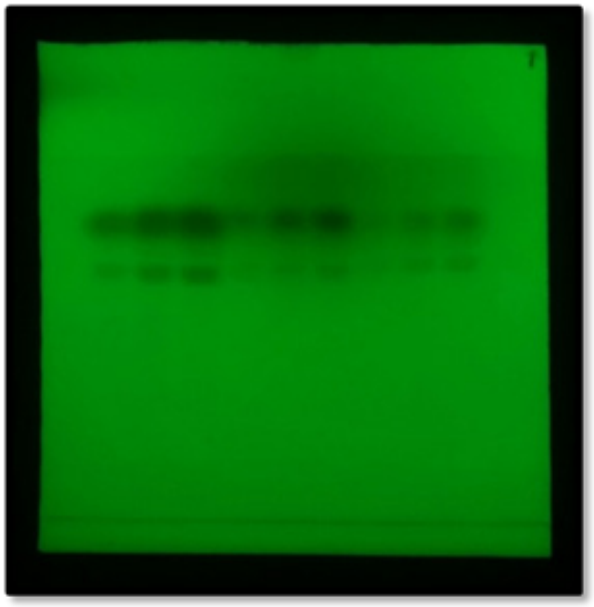


Figure 5. HPTLC Plate 1.

Figure 6. HPTLC Plate 2.

Anti-oxidant activity

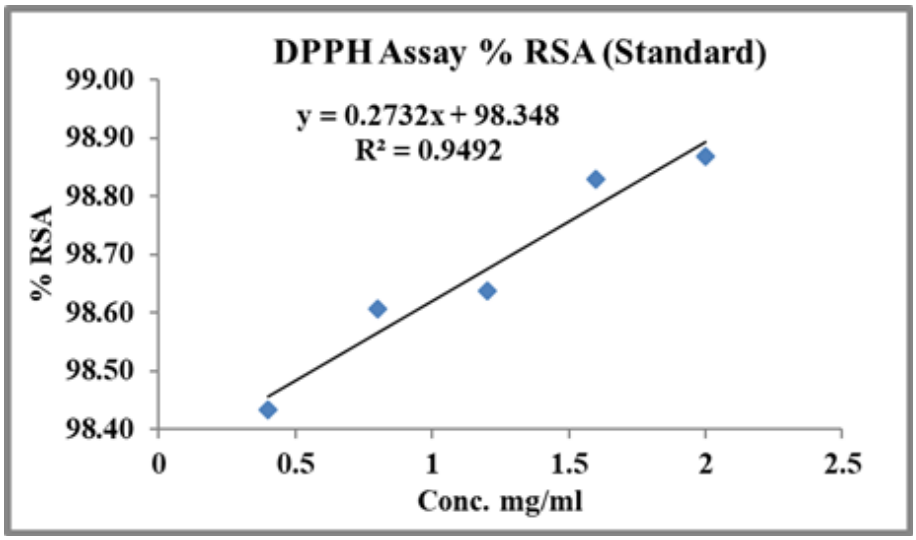


Figure 7. DPPH Assay % RSA (Standard).

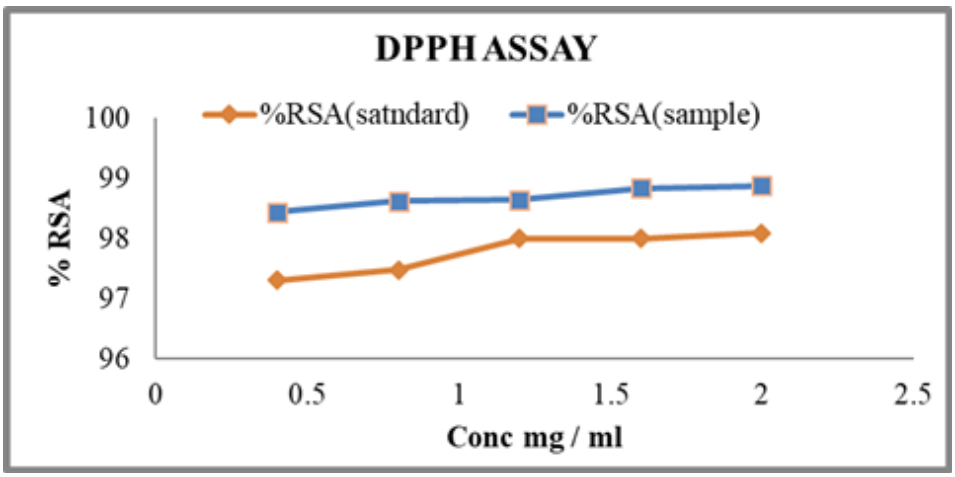


Figure 8. DPPH Assay % RSA (Standard).

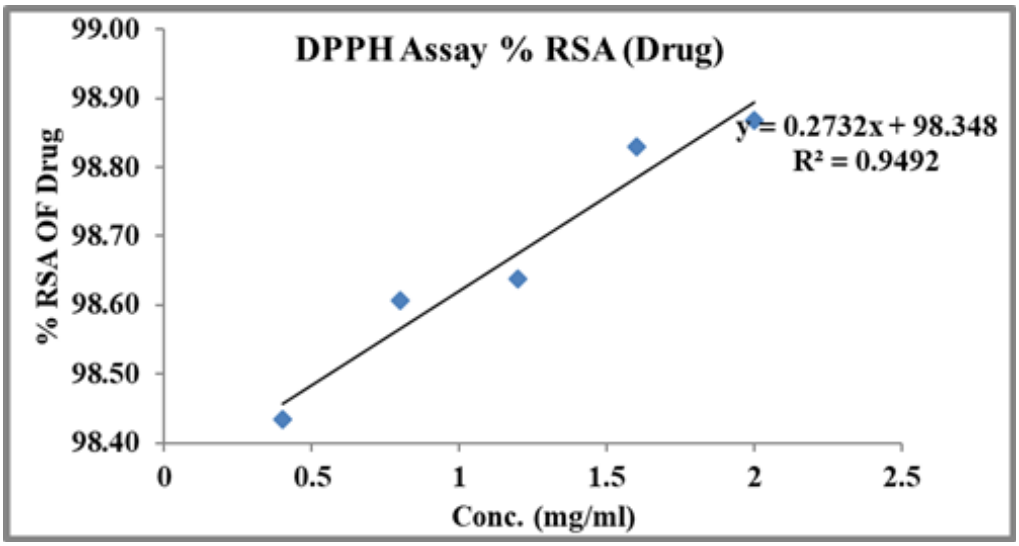


Figure 9. DPPH Assay % RSA (Drug).

Table 2. Characteristics of Preliminary trial batches organogel

Sr.No	Parameters	F1	F2	F3	F4	F5	F6	F7	F8
1	Appearance	Opaque	Opaque	Opaque	Opaque	Opaque	Opaque	Opaque	Opaque
2	Homogeneity	++	++	+++	+++	+++	+++	+++	+++
3	Colour	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow	Pale yellow
4	Odour	Odourless	Odourless	Odourless	Odourless	Odourless	Odourless	Odourless	Odourless
5	Texture	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth
6	pH	6.89±0.07	6.77±0.06	6.96±0.03	6.94±0.02	6.91±0.04	6.74±0.04	6.98±0.09	6.94±0.03
7	Viscosity (CPS)	4896±11.89	4967±12.65	5243±13.29	5497±12.76	5387±11.14	5649±13.07	5835±12.68	5735±11.32
8	Spreadability(cm)	4.7±0.12	4.4±0.08	3±0.12	3.1±0.12	3±0.09	2.8±0.12	2.3±0.16	2.5±0.09
9	Extrudability (g/ cm^2)	12.21±0.60	12.47±0.43	15±0.95	15.66±0.44	15.12±0.63	15.89±0.56	16.92±0.12	16.82±0.22

Drug Content

Table 3. Drug Content

Sr.No.	Formulation Batches	Drug Content (%)
1	F3	92 ±0.47
2	F4	94 ±0.81
3	F5	95 ±0.47
4	F6	96 ±0.47
5	F7	95 ±0.81
6	F8	96 ±0.47

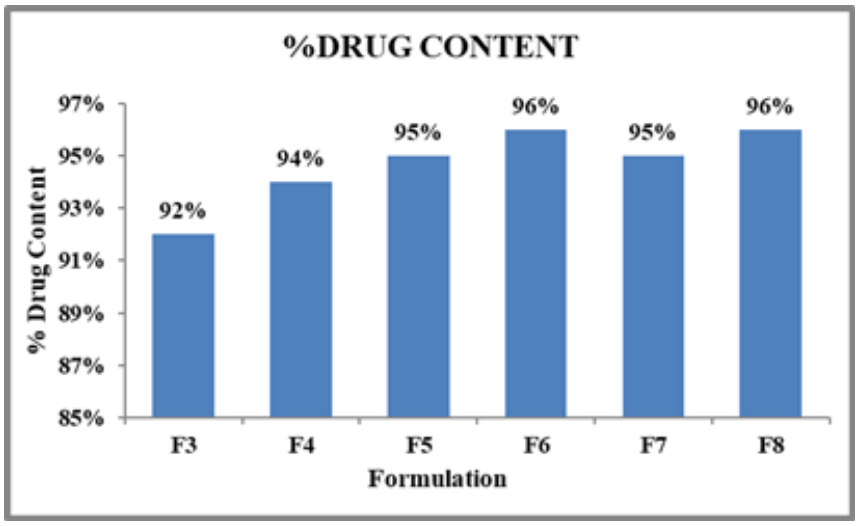


Figure 10. % Drug Content.

***In-Vitro* Drug Release**

Table 4. *In-Vitro* Drug Release

SR.NO	Formulation Batches	Cumulative Drug release (%)
1	F3	75.68 ±0.49
2	F4	79.34 ±0.85
3	F5	73.68 ±0.79
4	F6	84.21 ±0.35
5	F7	71.3 ±0.46
6	F8	86.34±0.95

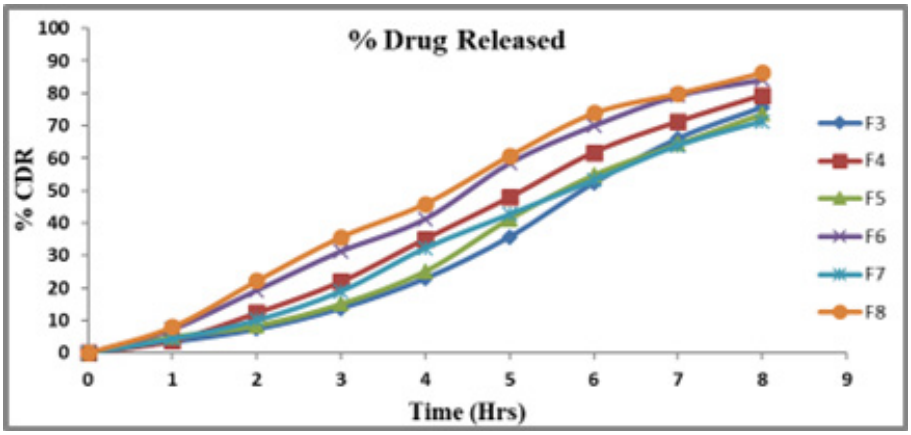


Figure 11. *In-Vitro* Drug Release.

Texture Analysis

Table 5. Deformation study of organogel

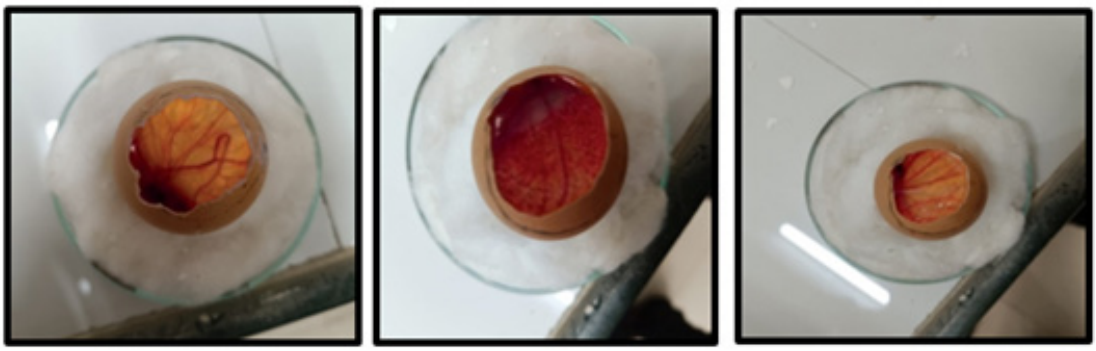
Sr.No.	Formulation Batches	Deformation (mm)
1	F3	3.81
2	F4	3.86
3	F5	3.94
4	F6	3.97
5	F7	3.96
6	F8	3.91

Antibacterial Activity

Table 6. Antibacterial activity

Sr.No.	Test organism	Sample marked as	Result (Zone of inhibition) mm
1	*Staphylococcus Aureus*	F6 batch	14
2	*Pseudomonas Aeruginosa*	F6 batch	16
3	*Streptococcus Pyogenes*	F6 batch	12

Zone of Inhibition of prepared formulation against Figure 12. *1) Staphylococcus Aureus, 2). Pseudomonas Aeruginosa, 3) Streptococcus Pyogenes*



HET CAM test

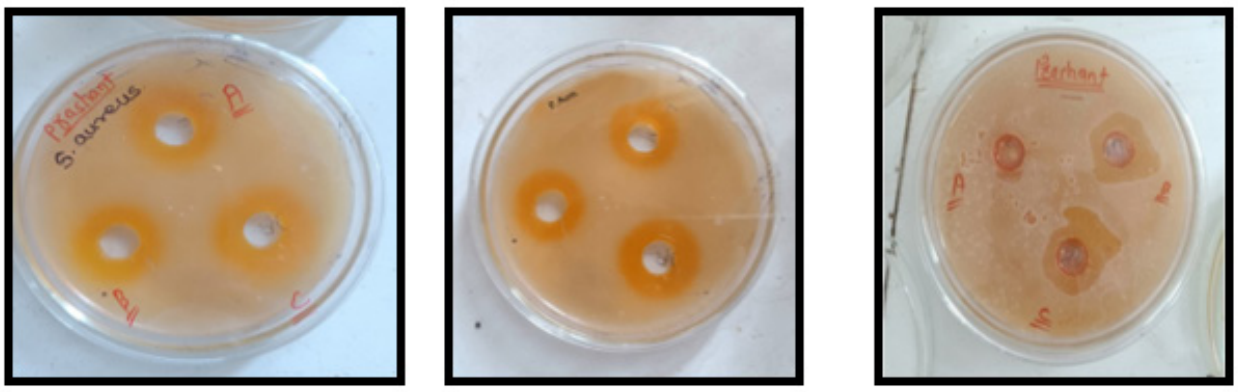


Figure 13. A) NaCl 0.9 % 1 %. B) SLS Solution (Positive control). C) Optimized batch (F6) (Negative control).

Scoring scale

Table 7. Scoring scale

Sr.No	Test solution	Score	Inference
1	NaCl 0.9 % (Negative control)	0	Non irritant
2	1 % SLS Solution (Positive control)	3	Severe irritant
3	Optimized batch (F6)	0	Non irritant

Stability Studies

Table 8. Stability data of organogel of betel leaf oil

Sr. No.	Parameters assessed	Observations						Inference
		0 day			15 day			
		4°C ±2°C	25°C/60% RH	40°C ±2°C	4°C ±2°C	25°C/60% RH	40°C ±2°C	
1	Colour	Opaque	Opaque	Opaque	Opaque	Opaque	Opaque	No change
2	Viscosity	5649±12.07	5649±12.07	5649±12.07	5727±12.71	5646±13.09	5567±9.84	No change
3	Drug content (%)	96±0.47	96±0.47	96±0.47	95 ±0.47	95±0.47	95±0.94	No significant change
4	Drug release (%)	84.21±0.35	84.21±0.35	84.21±0.35	84.08±0.23	84±0.47	83.9±0.73	No significant change

Sr. No.	Parameters assessed	Observations						Inference
		30 day			45 day			
		4°C ±2°C	25°C/60% RH	40°C ±2°C	4°C ±2°C	25°C/60% RH	40°C ±2°C	
1	Colour	Opaque	Opaque	Opaque	Opaque	Opaque	Opaque	No change
2	Viscosity	5731±12.56	5647±11.77	5563±10.19	5731±12.22	5650±12.36	5565±9.09	No change
3	Drug content (%)	93 ±0.81	95±0.81	95±0.81	94±0.81	95±0.94	95±0.94	No significant change
4	Drug release (%)	83.88±0.73	83.8±0.73	84.22±0.33	84±0.71	84±0.35	83.88±0.73	No significant change

DISCUSSION

The current study was undertaken to develop a medicated organogel formulation incorporating betel leaf oil for potential use as a topical antibacterial agent. Topical delivery systems are advantageous for localized infections, offering improved patient compliance and minimized systemic effects [17-37].

To begin with, the identity and purity of betel leaf oil were confirmed through physical, organoleptic, spectroscopic, and thermal characterization, along with chromatographic techniques such as TLC and HPTLC. These evaluations ensured that the oil used was of pharmaceutical grade and suitable for formulation. Compatibility studies with excipients, especially the gelling agents, demonstrated that there were no negative interactions, indicating their suitability for stable formulation development [38-44].

Preliminary batches of the organogel were formulated using different concentrations of soya lecithin and poloxamer 407 to identify the optimal combination for desired consistency and stability. Among all the batches, formulation F6 emerged as the most promising based on physical attributes such as homogeneity, viscosity, and spreadability [45-58].

The optimized formulation (F6) was composed of 1% betel leaf

oil, 5% soya lecithin, 10% PEG 400, 7% isopropyl palmitate, and 20% poloxamer 407, along with suitable preservatives. This composition provided a balanced gel structure, which was easy to apply and had a pleasant feel on the skin. Evaluation of pH, viscosity, spreadability, and extrudability confirmed that the formulation was stable and user-friendly [59-68].

In vitro drug release studies showed that the F6 organogel allowed controlled and sustained release of the active compound, potentially enhancing therapeutic action at the site of application. The inclusion of PEG 400 and poloxamer 407 likely facilitated this release by improving solubility and skin penetration [69-73].

Moreover, the antibacterial activity of the formulated gel indicated that the inherent properties of betel leaf oil were well preserved and effectively delivered. This supports its role in inhibiting the growth of pathogenic bacteria when applied topically.

Stability testing conducted over a 15-day period under standard storage conditions revealed that there were no significant changes in physical appearance, pH, viscosity, drug content, or drug release profile. This confirms the short-term stability and robustness of the F6 formulation.

In summary, the findings demonstrate that the developed organogel formulation offers a stable and effective platform for the topical delivery of betel leaf oil. The F6 batch, in particular, meets all the essential criteria for topical application and shows promise as a potential natural-based antibacterial product.

Therefore, it was concluded that organogel of betel leaf oil is a good for the treatment of cellulitis.

CONCLUSION

The study successfully developed a stable and effective betel leaf oil-based organogel for topical antibacterial use. The optimized formulation (F6) showed good spreadability, viscosity, and sustained drug release while retaining antibacterial activity. Overall, it presents a promising natural alternative for treating localized infections through topical application.

ACKNOWLEDGEMENTS

None.

CONFLICT OF INTERESTS

The Authors declare that there is no conflict of interests.

REFERENCES

1. Gunderson CG. (2011). Cellulitis: definition, etiology, and clinical features. Am J Med. 124(12):1113-1122.
2. Dong SL, Kelly KD, Oland RC, Holroyd BR, Rowe BH. (2001). ED management of cellulitis: a review of five urban centers. Am J Emerg Med. 19(7):535-540.
3. Brown BD, KL HW. Cellulitis.
4. Jørgensen MG, Hermann AP, Madsen AR, Christensen S, Ingwersen KG, Thomsen JB, et al. (2021). Cellulitis is associated with severe breast cancer-related lymphedema: an observational study of tissue composition. Cancers. 13(14):3584.
5. Maitre S. (2006). Cellulitis: definition, etiology, diagnosis and treatment. AMA Journal of Ethics. 8(12):831-833.
6. Phoenix G, Das S, Joshi M. (2012). Diagnosis and management of cellulitis. BMJ. 345:e4955.
7. Biswas P, Anand U, Saha SC, Kant N, Mishra T, Masih H, et al. (2022). Betelvine (Piper betle L.): A comprehensive insight into its ethnopharmacology, phytochemistry, and pharmacological, biomedical and therapeutic attributes. J Cell Mol Med. 26(11):3083-3119.
8. Nagar A, Nema RK, Vyas A. (2020). Formulation and evaluation of herbal antibacterial gel of betel leaf extract. World Journal of Pharmaceutical Research. 9(15):962-977.
9. Guha P, Nandi S. (2019). Essential oil of betel leaf (Piper betle L.): A novel addition to the world food sector. Essential Oil Research: Trends in Biosynthesis, Analytics, Industrial Applications and Biotechnological Production. 2019:149-196.
10. Preethy TT, Elsy CR. Characterization of betel vine (piper betle L) types of Malappuram district (Doctoral dissertation, Department of Plant Breeding and Genetics, College of Horticulture, Vellanikkara).
11. Bhanja S, Kishore P, kumar Das A, Pradesh A. (2013). Formulation and evaluation of Diclofenac transdermal gel. J Adv Pharm Edu & Res. 3(3):248-259.

12. Muneeswari VS, Karthick S, Akanksha D, Sushma G, Hasheem SA, Vasimunni S, et al. Extraction and identification of phytochemical active constituents in leaves of catharanthus roseous, carica papaya and piper betel by using TLC method. World Journal of Pharmaceutical Research. 11(10):891-937.

13. Annegowda HV, Tan PY, Mordi MN, Ramanathan S, Hamdan MR, Sulaiman MH, et al. (2013). TLC–bioautography-guided isolation, HPTLC and GC–MS-assisted analysis of bioactives of Piper betle leaf extract obtained from various extraction techniques: In vitro evaluation of phenolic content, antioxidant and antimicrobial activities. Food Analytical Methods. 6(3):715-726.

14. Banerjee B, Bhardwaj LK, Agrawal N, Lalhlenmawia H, Datta S, Bhowal A, et al. (2018). Lupeol And Eugenol Enriched Fraction from Piper Betel Leaf Oil and Their Quantitative Estimation by HPTLC for Quality Control Purposes. EJPMR. 5(8):352-355.

15. Das S, Ray A, Nasim N, Nayak S, Mohanty S. (2019). Effect of different extraction techniques on total phenolic and flavonoid contents, and antioxidant activity of betelvine and quantification of its phenolic constituents by validated HPTLC method. 3 Biotech. 9(1):37.

16. Milardović S, Iveković D, Grabarić BS. (2006). A novel amperometric method for antioxidant activity determination using DPPH free radical. Bioelectrochemistry. 68(2):175-180.

17. Raff AB, Kroshinsky D. (2016). Cellulitis: a review. Jama. 316(3):325-337.

18. Hadzovic-Cengic M, Sejtarija-Memisevic A, Koluder-Cimic N, Lukovac E, Mehanic S, Hadzic A, et al. (2012). Cellulitis--epidemiological and clinical characteristics. Med Arch. 66(3 Suppl 1):51-53.

19. Sullivan T, de Barra E. (2018). Diagnosis and management of cellulitis. Clin Med (Lond). 18(2):160-163.

20. Castellano-Tejedor C. (2022). Non-Pharmacological Interventions for the Management of Chronic Health Conditions and Non-Communicable Diseases. Int J Environ Res Public Health. 19(14):8536.

21. Edmund Daniel Co, Marangoni AG. (2012). Organogels: An alternative edible oil-structuring method. Journal of the American Oil Chemists' Society. 89:749-780.

22. Gökçe EH, Yurdasiper A, Korkmaz E, Özer Ö. (2013). A novel preparation method for organogels: high-speed homogenization and micro-irradiation. AAPS PharmSciTech. 14(1):391-397.

23. Khan F, Maurya R, Ramteke S. Organogel controlled release formulation: a novel approach.

24. Bystritsky RJ. (2021). Cellulitis. Infect Dis Clin North Am. 35(1):49-60.

25. Vijayalakshmi B, Ganapathy D. (2016). Medical management of cellulitis. Research Journal of Pharmacy and Technology. 9(11):2067-2070.

26. Yang M, Quah BL, Seah LL, Looi A. (2009). Orbital cellulitis in children—medical treatment versus surgical management. Orbit. 28(2-3):124-136.

27. Bailey E, Kroshinsky D. (2011). Cellulitis: diagnosis and management. Dermatol Ther. 24(2):229-239.

28. Bhagat TS, Kumar L, Garg P, Goel A, Aggarwal A, Gupta S. (2023). To Study the Clinical Profile and Management of Cellulitis of Lower Limb in Northern India. Int J Low Extrem Wounds. 22(1):44-47.

29. Deshpande SG, Grover A, Shahapurkar VV, Shinde RK. (2017). Limb cellulitis in rural setting in India: a case control study. International Surgery Journal. 4(8):2751-2755.

30. Ferguson MP, McNab AA. (1999). Current treatment and outcome in orbital cellulitis. Aust N Z J Ophthalmol. 27(6):375-379.

31. Sengupta R, Banik JK. (2013). A review on betel leaf (pan). International Journal of Pharmaceutical Sciences and Research. 4(12):4519-4524.

32. Pawar PL, Nabar BM. (2010). Effect of Plant Extracts Formulated in Different Ointment Bases on MDR Strains. Indian J Pharm Sci. 72(3):397-401.

33. Toh SC, Lihan S, Bunya SR, Leong SS. (2023). In vitro antimicrobial efficacy of Cassia alata (Linn.) leaves, stem, and root extracts against cellulitis causative agent Staphylococcus aureus. BMC Complement Med Ther. 23(1):85.

34. Lao RCC, Yabes AM, Tobias-Altura M, Panganiban LCR, Makalinao IR. (2023). In Vitro Antibacterial and Antibiofilm Activities of Piper betle L. Ethanolic Leaf Extract on Staphylococcus aureus ATCC 29213. Acta Med Philipp. 57(12):53-60.

35. Jørgensen MG, Toyserkani NM, Hansen FG, Bygum A, Sørensen JA. (2021). The impact of lymphedema on health-related quality of life up to 10 years after breast cancer treatment. NPJ Breast Cancer. 7(1):70.

36. Rehman K, Zulfakar MH. (2014). Recent advances in gel technologies for topical and transdermal drug delivery. Drug Dev Ind Pharm. 40(4):433-440.

37. Nadig PA, Mandira TG, Kumar JR. (2021). Comparative studies on the antioxidant, anti-inflammatory and phyto-chemical constituents of piper betel leaves from the Western Ghats and northern region of Karnataka. IJPSR. 12(6):3165-3175.

38. Singh VK, Singh PK, Sharma PK, Srivastava PK, Mishra A. (2013). Formulation and evaluation of topical gel of acelofenac containing piparine. Indo Am J Pharm Res. 3(7):5268-5278.

39. Kumar L, Verma R. (2010). In vitro evaluation of topical gel prepared using natural polymer. International Journal of Drug Delivery. 2(1):58-63.

40. Hurler J, Engesland A, Poorahmary Kermany B, Škalko-Basnet N. (2012). Improved texture analysis for hydrogel characterization: Gel cohesiveness, adhesiveness, and hardness. Journal of Applied Polymer Science. 125(1):180-188.

41. Ng SF, Rouse J, Sanderson D, Eccleston G. (2010). A comparative study of transmembrane diffusion and permeation of ibuprofen across synthetic membranes using Franz diffusion cells. Pharmaceutics. 2(2):209-223.

42. Pandey M, Belgamwar V, Gattani S, Surana S, Tekade A. (2010). Pluronic lecithin organogel as a topical drug delivery system. Drug Deliv. 17(1):38-47.

43. Sharma J, Agrawal D, Sharma AK, Khandelwal M, Aman S. (2022). New topical drug delivery system pharmaceutical organogel: A review. Asian Journal of Pharmaceutical Research and Development. 10(1):75-78.

44. Shaikh IM, Jadhav KR, Gide PS, Kadam VJ, Pisal SS. (2006). Topical delivery of aceclofenac from lecithin organogels: preformulation study. Curr Drug Deliv. 3(4):417-427.

45. Madhumita M, Guha P, Nag A. (2019). Extraction of betel leaves (Piper betle L.) essential oil and its bio-actives identification: Process optimization, GC-MS analysis and anti-microbial activity. Industrial Crops and Products. 138:111578.

46. Vintiloiu A, Leroux JC. (2008). Organogels and their use in drug delivery--a review. J Control Release. 125(3):179-192.

47. List GR. (2015). Soybean lecithin: Food, industrial uses, and other applications. Polar Lipids. 2015:1-33.

48. Ezzat SM, Salem MA, El Mahdy NM, Mahfouz MM. (2022). Lecithin. In Antioxidants Effects in Health. Netherlands: Elsevier. pp. 375-386.

49. Sangale PT, Manoj G. (2015). Organogel: A novel approach for transdermal drug delivery system. World J Pharm Res. 4(3):423.

50. Choukse R, Agrawal A, Sangameswaran B, Sharma M. (2012). Formulation and evaluation of pluronic lecithin organogel of non steroidal anti-inflammatory drug for topical application. Int J Pharm Bio Arch. 3(6):1538-1543.

51. Pande DS, Atram SC, Joshi AV, Bobde NN, Wankhade VP. (2019). Formulation And Evaluation Of Pluronic Lecithin Clotrimazole Organogel For Topical Delivery. Indo American Journal of Pharmaceutical Research. 9(1):1860-1864.

52. Alighiri DA, Cahyono E, Eden WT, Kusuma E, Supardi KI. (2018). Study on the improvement of essential oil quality and its repellent activity of betel leaves oil (Piper betle l.) from Indonesia. Oriental Journal of Chemistry. 34(6):2913.

53. Garg SC, Jain R. (1992). Biological Activity of the Essential Oil of Piper betle L., Journal of Essential Oil Research. 4(6):601-606,

54. Shah H, Jain A, Laghate G, Prabhudesai D. (2021). Pharmaceutical excipients. In Remington. Netherlands: Academic Press. pp. 633-643.

55. Bvg ZV. = VcYWdd ` d [E] VgbVXZji ^ XVa : mX ^ e ^ Zcih.

56. Verma S, Rawat A, Kaul M, Saini S. (2011). Solid dispersion: a strategy for solubility enhancement. International Journal of Pharmacy and Technology. 3(2):1062-1099.

57. Patil MP, Shinde GP, Kshirsagar SJ, Parakh DR. (2015). Development and characterization of ketoconazole loaded organogel for topical drug delivery. Inventi J. 3:1-0.

58. Saifee M, Gosavi PP. (2022). Organogels in topical drug delivery system: a systematic review. 11(16):1810-1833.

59. McKenzie B, Kay G, Matthews KH, Knott RM, Cairns D. (2015). The hen's egg chorioallantoic membrane (HET-CAM) test to predict the ophthalmic irritation potential of a cysteamine-containing gel: Quantification using Photoshop® and ImageJ. Int J Pharm. 490(1-2):1-8.

60. Swartz MN. (2004). Clinical practice. Cellulitis. N Engl J Med. 350(9):904-912.

61. Bhargava P, Uppoor A, Pralhad S, Nayak D. (2015). An Invitro Study Of Determination Of Anti-Bacterial, Antioxidant, Anti-Inflammatory Potential Of Piper Betel Essential Oil. National Journal of Integrated Research in Medicine. 6(2):37-44.

62. Amorati R, Foti MC, Valgimigli L. (2013). Antioxidant activity of essential oils. J Agric Food Chem. 61(46):10835-10847.

63. Ahuja SC, Ahuja U. (2011). Betel leaf and betel nut in India: History and uses. Asian Agri-History. 15(1):13-35.

64. Sarma C, Rasane P, Kaur S, Singh J, Singh J, Gat Y, et al. (2018). Antioxidant and antimicrobial potential of selected varieties of Piper betle L. (Betel leaf). An Acad Bras Cienc. 90(4):3871-3878.

65. Lim PF, Liu XY, Kang L, Ho PC, Chan SY. (2008). Physicochemical effects of terpenes on organogel for transdermal drug delivery. Int J Pharm. 358(1-2):102-107.

66. Sahoo S, Kumar N, Bhattacharya C, Sagiri SS, Jain K, Pal K, et al. (2011). Organogels: properties and applications in drug delivery. Designed monomers and polymers. 14(2):95-108.

67. Caburian AB, Osi MO. (2010). Characterization and Evaluation of Antimicrobial Activity of the Essential Oil from the Leaves of Piper betle L. E-International Scientific Research Journal. 2(1):2-13.

68. Ting TC, Rahim NF, Zaudin NA, Abdullah NH, Mohamad M, Shoparwe NF, et al. (2020). Development and Characterization of Nanoemulgel Containing Piper betle Essential Oil as Active Ingredient. InIOP Conference Series: Earth and Environmental Science. 596(1):012032).

69. Mei KR. (2021). Physicochemical, antioxidant and antibacterial properties of betel leaf and kaffir lime essential oil nanoemulsions (Doctoral Dissertation, Universiti Sains Malaysia).

70. Sarjuni NI. (2010). The fabrication of antibacterial composite from bacterial cellulose and betel leaves. Faculty of Chemical and natural resources engineering. University Malaysia Pahang.

71. Hamka A, Fatimawali F, Datu OS, Tallei TE. (2021). Antibacterial activity of betel (Piper betle L.) fruit against Pseudomonas aeruginosa. Acta Biochimica Indonesiana. 4(1):10.

72. Schendel KU, Erdinger L, Komposch G, Sonntag HG. (1994). Investigation of the potential to irritate mucous membranes of orthodontic substances with the HET-CAM test. Fortschritte der Kieferorthopädie. 55(1):28-35.

73. Sharma U, Patidar D, Sharma N. (2022). Design Development And Characterization Of Chitosan Sodium Alginate Biodegradable Transdermal Hydrogel For The Controlled Delivery Of Curcumin. Journal of Pharmaceutical Negative Results. 13(10):2186-2194.