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FORMULATION AND EVALUATION OF HERBAL EMUGEL FOR ANTIACNE ACTIVITY

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ABSTRACT

Bacterial infections continue to pose significant threats to public health globally, leading to morbidity and mortality across diverse populations. Drug distribution through the skin is an effective treatment for bacterial infections, a frequent dermatological issue. Emugel is a novel drug delivery system that enables the controlled release of emulsion and gel for topical use. Mixing an emulsion into a gel increases its stability. In the current investigation, emulgels containing extracts of neem leaf, neem fruit oil, and peepal extract were created to treat Bacterial skin infections. neem leaf contains chemicals that constitute sugiol, nimbiol, triterpenes, stigmasterol, limonoids, nimodipine, nimbendiol, nimton. Neem fruit oil contains limonene, borneol, α-ionone, cis-β-guaiene, β-caryophyllene, carveol, and p-cymene which is utilized to generate an oil phase, which effectively stabilizes the emulsion. Initially, emulsions using the extract were made with emulsifying agents such as tween 20 and span 20. Emulgels were created by combining prepared emulsions with carbopol 934 and Na CMC at a 1:1 ratio with the help of carbopol 934 and Triethanolamine. Different formulations (F1&F2) were prepared using different ratios and different evaluation parameter such as pH, Physical appearance, stability, spreadbility and antibacterial properties were checked. All formulations produced satisfactory results for tested parameters. The result indicates formulation F2 has Better spreadability, Stability, and antibacterial properties than the other formulation. After examining these parameters, it was concluded that neem oil-based emulgel with neem and peepal leave extract can effectively cure bacterial infections on the skin along with cosmetic benefits.

KEYWORDS: Emulgel, Neem leaf extract, Peepal leaf extract , Neem fruit oil, Antibacterial activity.

INTRODUCTION

Humans coexist peacefully with microorganisms. However, infections can occur when the defense system is compromised or pathogen concentrations reach an abnormally high level. Infectious disease occurs when the infecting agents trigger a response in the body, resulting in clinically visible signs and symptoms. Infectious diseases are caused by a variety of organisms including bacteria, viruses, parasites, fungus, prions, worms, and helminths. Infections produced by bacteria were once the most dreaded, but with improved control measures, fungi now pose the greatest threat.[1]

Topical formulations include cosmetic and dermatological treatments for healthy or diseased skin.[2] These formulas vary in consistency, from solid to semisolid to liquid. Emulgel is the term used for dosage formulations that blend gels and emulsions. As the name implies, they blend emulsion micro-emulsion and gel.[3] Novel polymers are frequently employed as emulsifiers and thickeners due to their gelling capacity, which reduces surface tension and increases aqueous phase viscosity, resulting in stable emulsion formation. Drugs can be delivered to the skin via oil/water or water/oil emulsions.[4]

Emulsion gels are advantageous over traditional creams and ointments for several reasons, including improved application properties, faster and more complete drug release, and ease of application on hairy skin without greasiness or residue.[5] These vehicles can accommodate both aqueous and oleaginous chemicals, making it possible to integrate hydrophobic or poorly water-soluble medications, such as antibacterial agents, by selecting the appropriate oily phase.[6]

The skin, the body's greatest sensory organ, has a pH range of 4.0-5.6. The skin consists of four layers: non-viable epidermis, viable epidermis, viable dermis, and subcutaneous connective tissue. Topical drugs are absorbed by three separate mechanisms: transcellular, intracellular, and follicular.[7] Transcellular is the shortest and most direct route. The intercellular method is the most common, while the follicular mechanism occurs through hair follicles and sweat glands. Topical formulations are those that are delivered through the skin. Its key advantage is that it avoids first-pass metabolism.[7]

Neem leaf is frequently utilized in drug studies. Sugiol, nimbiol, triterpenes, stigmasterol, limonoids, nimodipine, nimbendiol, and nimton are important constituents found in neem leaves. Which can effectively treat skin inflammation, bacterial infections, redness and swelling. Peepal is a medicinal plant because its leaves contain phenol, glucose, asteroid, and mennos which has anti-inflammatory, anti-bacterial and anti-oxidant activity. Neem fruit oil is good for skin and hair health since it includes limonene, borneol, α-ionone, cis-β-guaiene, β-caryophyllene, carveol, and p-cymene which has increase skin glow and prevents from skin infection. For skin conditions, it may serves as medication. Neem's antiseptic qualities greatly enhance the value of a variety of goods, including pharmaceuticals and cosmetics along of meditational implementations.

Emulgel

When emulsions are mixed with gel bases, the dosage forms are known as emulgels. Emulgels are emulsions (oil-in-water or water-in-oil) that gel when mixed with a gelling agent. Water-in-oil emulsions are commonly used for emollients and dry skin therapy, while oil-in-water emulsions are best suited for cosmetics and medicine bases that can be washed away. Hydrophobic medications can be produced as emulgels, which comprise both oil and aqueous phases. Emulgels are gaining popularity as a medicine delivery method in dermatology.[8,9,10]

MATERIALS AND METHODS

The leaves of Neem and Peepal were collected from the SDPC (Near kim railway station, kim; olpad; surat; gujarat) garden in the locality. Carbopol 934, Span 20, Tween 20, and Propylparaben were obtained from Chemtech. Na CMC was obtained from Yarrow Chem. Propylene glycol, Ethanol, and Triethanolamine were obtained from Mahakali industries. All ingredients and reagents used are of analytical grade.

Method

Extraction of neem extract[11]

The leaf sample (Neem leaves) was washed with tap water, dried, and then chopped into small pieces or placed in a blender to be ground into powder. An adequate quantity of water (150 ml) was put into a conical flask, followed by a little piece/powder of neem leaves. Boil for 2 hours, stirring frequently. After 2 hours, the solvent is filtered with filter paper, and the filtrate is poured into the china dish. The evaporation process continues until the extract is

obtained in the dish. Dry it till it becomes fine powder, then collect and keep it in the container.

Extraction of peepal extract[12]

The young, green foliage of F. religiosa was gathered. To get rid of dust and other debris, the leaves were first washed with tap water and then distilled water. The cleaned leaves were left to air dry for one to two hours. Subsequently, about 20 g of finely chopped leaves were added to a 250 ml conical flask along with 100 ml of distilled water. Boil the flask on a magnetic stirrer for one hour at 50 °C. Once the extract had cooled, I filtered it with Whatman-1 filter paper and evaporated it on a burner until the extract was exact, and the extract was ready.

Preparation of neem fruit oil[17]

Solvent extraction is method used for extracting neem oil, which can yield a higher quality and more refined product. Neem seeds or fruits are crushed or ground to increase the surface area for extraction. A solvent (Typically hexane or ethanol) is used to dissolve the oil from the seeds or fruits. This step is done under controlled conditions to ensure efficiency and safety. The solvent-oil mixture is separated from the solid residue through filtration or centrifugation. The solvent is evaporated from the oil-solvent mixture, leaving behind crude neem oil. Finally neem oil is collected and stored for further process.

Phytochemical analysis

The phytochemical analysis of neem and peepal leaf was performed for extract and included tests for alkaloids (Mayer's test), phenols (Ferric chloride test), flavonoids (Lead acetate test), tannins (Braymer's test), saponins (Foam test), cardiac glycosides (Keller killiani test), and terpenoids and steroids.

Preparation of emulsion

1. **Oil phase:** The oil phase of the emulsion was prepared by mixing span 20 with light liquid paraffin and neem leaf oil.

2. **Aqueous phase:** aqueous was prepared by mixing tween 20 with purified water. Propylparaben was added to propylene glycol, whereas the extract was added to ethanol, and both the solution were mixed with the prepared aqueous phase.

- Both prepared oily and aqueous phases were separately heated to 70°c to 80°c.

Preparation of emugel containing extract of Neem and Peepal

The gel bases were created using Na CMC and Carbopol 934. Na CMC was disseminated in filtered water heated to 80°C, then cooled and left overnight. Carbopol 934 was mixed with distilled water and aggressively swirled for some time. Triethanolamine was added drop by drop to get the pH to 6 - 6.5 and left for one day. To make the emulsion, mix Span 20 with light liquid paraffin for the oil phase and Tween 20 with purified water for the aqueous phase. For the oil phase, Neem fruit oil is also used to improve the solubility of other ingredients and provide the ideal atmosphere for further procedures. Propylparaben was added to propylene glycol, while the extract was put into ethanol. Both solutions were then mixed with the prepared aqueous phase. The oily and aqueous phases were heated separately to 70° to 80°C. The oily phase was then added to the aqueous phase while stirring and cooled to room temperature. To create the emulgel, mix the resultant emulsion with the prepared gel bases in a 1:1 ratio while gently stirring.

Table 1: Formulation batch of emulgel.

Ingredients	Category	F1	F2	F3	F4	F5	F6	F7	F8
Neem Extract (g) & Peepal Extarct	Anti-Bacterial	1 g	2 g	1g	1g	1g	1g	1g	1g
Carbopol (g)	Gelling agent, emulsifier	0.5 g	1 g	1.5 g	2 g	-	-	-	-
Na CMC	Thickening agent, gelling agent	-	-	-	-	0.5 g	1 g	1.5 g	2 g
Span 20 (ml)	Co-surfactant	1.25 ml	1.25 ml	1.25 ml	1.25 ml	1.25 ml	1.25 ml	1.25 ml	1.25 ml
Light liquid paraffin (ml)	Softening / soothing agent	1.25 ml	2.25 ml	1.25 ml	2.25 ml	1.25 ml	2.25 ml	1.25 ml	2.25 ml
Tween 20 (ml)	Non-ionic detergent	1.5 ml	2.5 ml	1.5 ml	2.5 ml	1.5 ml	1.5 ml	2.5 ml	1.5 ml
Propylparaben (g)	Preservative	0.25 g	0.25 g	0.25 g	0.25 g	0.25 g	0.25 g	0.25 g	0.25 g
Propylene glycol (ml)	As an emollient, prevents water loss	0.5 ml	2.5 ml	0.5 ml	2.5 ml	0.5 ml	2.5 ml	0.5 ml	2.5 ml
Ethanol (ml)	Antiseptic, astringent	4 ml	5 ml	4 ml	5 ml	4 ml	5 ml	4 ml	5 ml
Triethanolamine (ml)	Buffer, pH indicator	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Water (s.q.)	As vehicle	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

Evaluation of emugels

Physical appearance[13]

The prepared emulgel is visually inspected for colour, consistency, and phase separation.

pH[12]

The pH evaluation is a crucial criterion for topical formulations. Emulgel's pH should be between.[5-8] A calibrated digital pH meter was used to measure the aqueous gel solution at a steady temperature.

Stability of herbal emulgels [14]

The base and formulation were tested for stability at various storage circumstances, including color, appearance, and odor, over 1 Month. After 1 Month, formulation F2 showed no significant changes in appearance, odor, or color.

Spreadability[15]

The spreadability of emulgel is assessed by the diameter of the circle formed when it is placed between two weighted glass plates. A weighed amount of emulgel is placed on one glass plate and another is dropped from a distance of a few cm. Measure the diameter of the emulgel circle after spreading.

Calculated using the following formula

S=m.l/t

Where, s = spreadability

m = weight tied to upper slide

l = length of glass slide

t = time taken to spread

Extrudability study[16]

The emulgel formulation was packed into a conventional caped collapsible lami-tube and sealed. The tube was weighed and documented. The tube was inserted between two glass slides and clamped. A 500 g weight was placed on the glass slide and the cap was opened. The emulgel was collected and weighed. The percentage of emulgel extruded was computed and grades were assigned (+ + Excellent, + + Very Good, + Good).

Anti-bacterial[17]

The Zone of Inhibition test evaluates the antibacterial effectiveness of products. Neem leaf and peepal leaf oil has a good antibacterial property. A Zone of Inhibition test involves spreading bacteria culture over a nutrient agar-based petri dish. Evenly distribute a swab of pure bacterial culture across Mueller-Hinton agar plates. The treated product sample is put on the agar media plate using sterile forceps. This petri plate is incubated for 18 to 24 hours at 36°C, in addition to other ideal circumstances that promote the growth of bacteria. Following the incubation period, the antibacterial product sample is surrounded by a clear region, or zone of inhibition, which indicates the antimicrobial activity of a material or solution of E. coli and S. aureus, which is quantified and monitored. A greater zone of inhibition is formed by treated items with potent antibacterial action, or vice versa. A product sample is placed on nutrient agar. Notice after a few days.

RESULTS AND DISCUSSIONS

In the present study, a total of eight formulations of herbal emulgels were prepared from the extract of neem leaf and peepal leaf. The extraction was performed using the solvent extraction method. Neem fruit oil is an extract of neem oil used in the oil phase preparation. The aqueous phase was created with various ingredients in sufficient quantities. Formulation batches were optimized by the try and error method and In the case of antibacterial activity; it was determined Out of 8 batches, the F2 batch showed significant result.

Fig. 1: Neem extract.

Fig. 2: Neem Oil.

Fig. 3: Peepal extract.

Fig. 4: Aqueous phase.

Fig. 5: Oil phase.

Fig. 6: Final product.

The results obtained from the experiments conducted are as follows

Phytochemical analysis of leem extract

Phytochemical analysis showed the presence of phytochemicals namely;

1. Alkaloids
2. Phenols
3. Flavonoids
4. Tannins
5. Cardiac glycoside
6. Terpenoids
7. Steroid

Table 2: Phytochemical Test for Neem and Peepal extract.

Chemical test	Observation	Results
Test for alkaloids	Red precipitate	Positive
Test for phenols	Blue or green or violet colour	Positive
Test for flavonoids	Deep yellow colour	Positive
Test for tannins	Dark blue	Positive
Test for cardiac glycoside	Pink colour	Negative
Test for terpenoids	Reddish brown colour (two	Positive

		layer separate)	
Test for steroids	Red colour (two layer separate)	Positive	

Fig. *7: Test* for Alkaloids, Phenols and Flavonoids.

Fig. 8: Test for tannins.

Fig. 9: Test for cardiac glycoside.

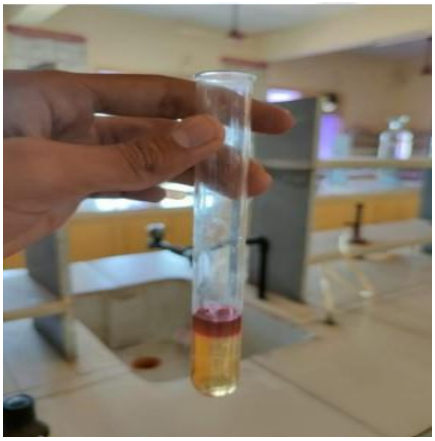

Fig. 9: Test for terpenoids.

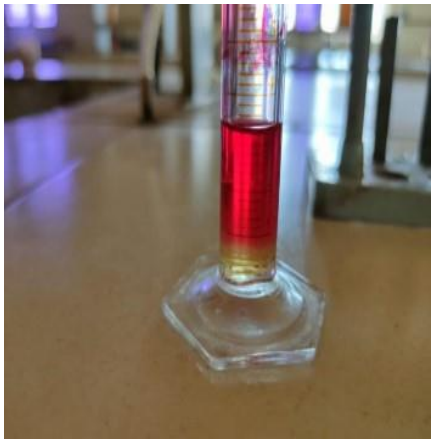

Fig. 10: Test for steroids.

Physical appearances of the formulation

The prepared formulations were yellow and pale pink in colour. The consistency was found to be good to excellent and there was no phase separation in the formulations. Observed results are below table.

Table 3: Physical appearances of the formulation.

Formulation code	Colour	Consistency	Phase separation
F1	Yellow	Good	Slightly separation
F2	Pale Pink	Excellent	No phase separation
F3	Yellow	Good	No phase separation
F4	Pale Pink	Good	No phase separation
F5	Yellow	Excellent	No phase separation
F6	Yellow	Good	No phase separation
F7	Pale Pink	Good	No phase separation
F8	Yellow	Good	No phase separation

pH, Spreadability, Extrudability

Prepared emulgels were evaluated for pH, spreadability, and antibacterial activities. pH of all the formulations was found in the range of 5.8 to 6.1. Which suits the skin pH indicating skin compatibility. Results indicate that gelling agent concentration affects emulgel spreadability and extrudability. Lower polymer concentrations resulted in improved spreadability and extrusion.

Table 4: pH, Spreadability, Extrudability of Formulation.

Formulation code	pH	Spreadability (cm)	Extrudability
F1	5.9	6.6	+++
F2	6.1	9.8	+++
F3	5.8	5.9	++
F4	6.0	7.2	++
F5	5.9	8.5	+++
F6	6.0	5.3	+++
F7	6.0	6.8	++
F8	5.8	9.4	++

(Where: + Good, ++ Very Good, +++ Excellent

Among all the formulations F2 show Ideal pH, spreadability, and Extrudability.)

Table 5: Stability study of optimized Batch F2.

Stability study	Temperature (°c)	Humidity (%RH)	Time period
Accelerated Stability study	40°C± 2°C	75%RH± 5%RH	1 month

Table 6: Antibacterial activity of emugel formulation.

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8
Zone of inhibition (mm)	3	6, 5.6, 6.1	2	2	3	4	5	4

Fig. 11: Zones of Inhibition of F2 batch (3 spot) Against Bacteria.

CONCLUSION

Present study successfully developed an herbal emulgel using Neem extract, peepal extract and neem fruit oil for anti-bacterial activity. Emulgel formulas containing Neem extract and peepal extract were successfully prepared Physical parameter, pH, Stability, Spreadability, Extrudability and anti-bacterial activity were evaluated. Total 8 formulations (F1-F8) demonstrate among them formulation F2 showed more significant and promising results along with good antibacterial effect. The claimed antibacterial effect was might be because of chemical constituents of Neem and Peepal leaves present in extract. Hence, topical Emulgel of Neem and peepal extract would have to be a better alternative as a topical drug delivery system for treatment of acne.

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