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Original Article

FORMULATION AND EVALUATION OF LICORICE OIL-BASED EMULGEL FOR THE TREATMENT OF PSORIASIS

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ABSTRACT

Objective: The aim of the present research work was to develop and evaluate the topical emulgel incorporated with licorice oil for the effective management of psoriasis.

Methods: The present study involves the preparation and optimization of licorice oil-based emulsion using tween 80, span 20, propylene glycol and was loaded in gel base (carbopol 940 was used as gelling agent). The prepared emulgel were evaluated for various parameters such as particle size, zeta potential, entrapment efficiency, spreadibility, pH, viscosity, Fourier-Transform Infrared Spectroscopy (FTIR), *in vitro* release studies and *in vitro* cell line study.

Results: The optimized formulation was found to have droplet size of 54.50 nm,-14.1 V zeta potential, entrapment efficiency of 59.53±8.42 % and spreadibility of 2.901±0.12 mm. The pH and viscosity of optimized licorice oil-based emulgel was found to be 6.0±0.467 and 93,500±832 cps, respectively. Cumulative *in vitro* release was found to be 95.15±0.26 % has shown by the optimized formulation for 10 h. In (3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) MTT cytotoxicity study indicated non-toxic potential properties of licorice oil and its emulgel at lower level and caused moderate toxicity at higher level against Human Epidermal Keratinocytes (HaCaT) cell lines after the incubation period of 24 h respectively.

Conclusion: This study showed that the emulgel formulation has the potential to significantly enhance the efficacy of licorice oil in the treatment of psoriasis. These findings provide exciting new possibilities for improving psoriasis treatment and explores importance of continued research in this area.

Keywords: Licorice oil, Carbopol 934, Topical formulation, Psoriasis, Emulgel, HaCaT cell line

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INTRODUCTION

Psoriasis is a chronic autoimmune, non-communicable inflammatory, incurable, disfiguring, and life-long sickness of the skin and joints [1]. National Psoriasis Foundation (NPF) states that about 7.5 million people have been suffering from psoriasis in United States (US) [2]. The serious global problem of psoriasis in countries among 0.08–12%, making psoriasis a critical worldwide hassle [3, 4]. Psoriasis is a non-contagious hereditary skin disease expressed by sever itching, thickened, stinging, inflamed, scaly and deformed are all symptoms of lesions that in 70% of cases appear in mild-to-moderate form [5]. The condition causes of psoriatic skin to be stress, cold weather, dry skin, vaccination, beta-blocker, lithiums, Upper Respiratory Infection (URI), smoking, diet, and alcohol [6–10]. Hyperkeratosis known as the thickening of the Stratum Corneum (SC) and parakeratosis known as abnormal maturation of the SC are two typical of the SC in psoriatic skin [11]. Psoriasis can rises at any age but it generally arrives in two stages. The first stage is between the ages of 20–30 y, and the second stage is between the ages of 50–60 y [12]. Psoriasis is a skin disorder known to be characterized by genetic and environmental aspects such as mental stress, infection, alcohol, smoking, and trauma, but its causes are still not completely understood [13]. The quality of patient life with psoriasis is often spoiled because of the flawed appearance, loss of confidence and social stigmatization [14]. In Traditional Chinese Medicine (TCM), Licorice (*Glycyrrhiza glabra*) is undoubtedly an essential herbal medication. According to TCM beliefs, licorice is an indispensable ingredient in nine out of ten formulae, and it is one of the most effective herbal medicines for reducing toxicity and increasing the efficacy of other herbal medicines when used together [15-17]. Licorice is a powerful plant with a wide range of beneficial properties which known as *Glycyrrhiza glabra*, it belongs to the Leguminosae family and can be used to treat psoriasis [18]. Among the different types of licorice, *Glycyrrhiza glabra* is the most commonly used in feed and food products [19]. This plant contains a variety of nutrients such as proteins, mineral salts, starches, sterols, amino acids, gums, simple sugars, polysaccharides, resins and pectin [20]. In addition, licorice contains several key chemicals, including glycyrrhizin, isoliquiritin, and glycyrrhizic acid, glycyrrhizinic acid which have been shown to have anti-psoriatic, anti-cancer, anti-microbial, anti-atherogenic, anti-spasmodic, anti-diabetic, anti-inflammatory, and anti-asthmatic properties [21]. While there have been no reports of toxic compounds in licorice, it is important to note that high dosages over an extended period can lead to serious illnesses. Make sure to use licorice responsibly to enjoy its numerous health benefits [22]. Different formulations of are licorice prepared, such as licorice cream (good vibes), licorice capsules (nature's way), licorice lotion (licorice brightening body lotion), licorice ointment (melaglow) [23]. Topical formulations such as creams, ointments, or lotions often suffer from instability, stickiness and low spreading coefficient [24]. Fortunately, there's a new solution-the emulgel. This innovative formulation combines the best features of both emulsions and gels to create a superior product [25]. When formulating licorice oil, an emulgel was used because it offers several advantages. Emulsions have been known for the delivery of hydrophobic as well as hydrophilic therapeutic molecules. Emulgels have improved patient compliance and easy self-medication, while gels offer faster drug release and a higher spreading coefficient than other semi-solid preparations [26]. They also exhibit mucoadhesive properties that provide a longer contact time for the formulation on the skin [27]. Emulgels are dual control release systems that combine the properties of both emulsions and gels. Topical gels, like the emulgel, offer a range of benefits, such as being greaseless, easily spreadable, easily removed, emollient, and water-miscible. This makes them an excellent choice for topical applications [28]. Incorporating gel into an emulsion has been proven to significantly enhance the stability and penetration ability of the emulsion through its thixotropic behavior. Emulgel, a combination of gel and emulsion, offers several advantages over traditional topical treatments. It is highly accepted by patients due to its non-greasy nature and requires no excessive rubbing. Emulgel is a stable system and an optimal vehicle for delivering hydrophobic

drug molecules to the skin [29]. The study aimed to demonstrate that emulgel is an effective method of administering licorice for the management of psoriasis.

MATERIALS AND METHODS

Materials

The following chemicals was obtained such as span 20 and carbopol from Research –lab fine chem industries (Mumbai, India), liquid paraffin, propylene glycol and tween 80 from chemco, licorice oil and glycyrrhizic acid was purchased from stallion while other ingredients and solvents were of analytical grade.

Gas chromatography/Mass spectrometry (GC/MS) analysis

The Thermo Finnigan Trace GC/Trace DSQ/A1300, equipped with an SGE-BPX5 MS fused silica capillary column was used to analyze the essential oil. The GC-MS detection system utilized an electron ionization process with an ionization energy of 70 eV and helium as the carrier gas with a flow rate of 1 ml/min. The injector and MS transfer line temperatures were set to 220 °C and 290 °C, respectively [30]. The oven temperature was programmed to gradually increase from 50 °C to 150 °C at a rate of 3 °C per minute and held at a constant temperature for 10 min before being raised to 250 °C at a rate of 10 °C/min. The diluted samples of 1.0 l were manually injected in the split less mode. Individual compounds were identified by precisely comparing their relative retention times with those of authentic samples on the SGE-BPX5 capillary column. Mass spectra were matched with those obtained from authentic samples, the Wiley 7N, and TRLIB libraries spectra, as well as published data [31].

Selection of surfactants and co-surfactants

The excipients were selected for the development of emulsion by optimal mixing, 10 ml licorice oil was added to each vial containing 1 ml of an acceptable medium. The solution was kept at 25 °C for 48 h in an orbital shaking incubator to ensure solubility and equilibrium. After centrifuging at 500 rpm for 15 min, the filtered sample was mixed with ethanol. Ultra Violet (UV) spectrophotometer was used to determine the concentration of licorice oil by measuring its absorbance at 261 nm. This approach showed accurate results and a superior solution [32].

Formulation of gel

To make the gel base, carbopol 934 was stirred into water until it swelled and formed a uniform gel. This base was mixed with a solution to create the final homogeneous gel. For a more thorough understanding of the gel infused with licorice oil, which has been showed in table 1 [33].

Table 1: Composition of licorice oil-based gel

Composition	F1	F2	F3	F4	F5	F6	F7
Carbopol 934 (gm)	1.00	1.50	1.00	1.50	1.00	1.50	1.00
Ethanol (ml)	2.00	2.50	2.00	2.50	2.00	2.50	2.00
Water (ml)	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.

Development of licorice oil-loaded emulsion and loading into gel

The spontaneous method is the simplest way to prepare an emulsion. In this method, the emulsion mixture is stirred directly to create a uniform mixture. Accurately weighed licorice oil, tween 80, propylene glycol and methanol. First, mix licorice oil with span 20 and liquid paraffin to form the oil phase [34]. Then, vortex the mixture and add the surfactant propylene glycol and co-surfactant. Finally, 20 ml of water was added with constant stirring to obtain a perfect emulsion. To produce an emulgel, a measured amount of gelling reagent was dissolved in water to create the base of the gel. Then it was gradually mixed with the emulsion by magnetic stirrer for 5 min at 700 rpm to get a uniform emulgel [35]. The details of the specific compositions of licorice oil-based emulgel are shown in table 2.

Table 2: Composition of licorice oil-based emulgel formulations

Composition	F1	F2	F3	F4	F5	F6	F7
Licorice oil	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Liquid paraffin	1.50	2.00	1.50	2.00	1.50	2.00	1.50
Methanol	0.75	1.00	0.75	1.00	0.75	1.00	0.75
Span 20	0.25	0.30	0.25	0.30	0.25	0.30	0.25
Propylene glycol	1.25	1.50	1.00	1.25	1.5	1.00	1.25
Tween 80	0.25	0.3	0.25	0.3	0.25	0.3	0.25
Water	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.

Characterization of emulgel

Physical appearance

The emulgel formulations were visually assessed for physical appearance, color, and consistency. The formulation exhibiting desirable results underwent further examination and characterization [36].

pH determination

The pH values were measured using a calibrated meter at room temperature. 1g of emulgel was distributed in 100 ml of distilled water. Digital pH meter was used to determine the dispersion's pH value [37].

Viscosity determination

The cone and plate viscometer with spindle seven was used to determine the viscosity of formulations. Temperature was maintained at 25 °C using a thermostatically controlled water flow [38, 39].

Spreadability determination

The spreadability apparatus is a device which specifically designed to measure the spreadability of transdermal preparations. 1g of emulgel was taken with the combination between two horizontal glass slides (25 × 25 cm), 500 gm load was applied for a minute and spreadability was calculated using the formula:

Spreadability = Mass (g) × Length (cm)/Time (Sec) [40].

Centrifugation test

To evaluate stability, emulgel formulations undergo a centrifugal test. Both formulations were subjected to 5000 rpm for 10 min at 25 °C. After the process, the products were visually inspected for signs of phase separation or creaming [41].

Particle size, polydispersity index (PDI) and zeta potential

The particle size and PDI and zeta potential are crucial factors to consider when assessing the quality of a licorice oil-based emulgel [42]. Therefore, a dynamic light scattering instrument was used to investigate these vital parameters after diluting the compositions over 100 times with distilled water to ensure accurate results. The light scattering was evaluated at 90° room temperature for optimal performance. Laser Doppler Electrophoresis also measures the zeta potential after vigorous mixing and a 200-fold dilution in distilled water [43].

FTIR studies

FTIR was conducted to evaluate the medication's interaction and compatibility with other ingredients. A spectrometer was used to observe FTIR spectra of licorice oil and excipients mixed with potassium bromide. The analysis used transmission mode scanning with wavenumbers ranging from 4000 to 400 cm^{-1} [44].

Drug content

1 gram of emulgel was dissolve in 1 ml of methanol. Dilute the resulting solution and measure its absorbance by UV spectrometer at 261 nm. The formula was used to find the amount of drug present in each formulation. The formulation with the most drug content was taken for further examination and characterization [45].

Drug content = (concentration × dilution factor × volume taken) × conversion factor

***In vitro* drug release studies**

Drug release was studied by Franz diffusion cells or egg membranes. 1 g of formulation was applied to the membrane and clamped between the donor and receptor chambers. The medium used was 200 ml of 25% methanol phosphate buffer at pH 7.4, warmed and stirred at 37±1 °C and 100 rpm. Samples were taken and replaced with fresh medium at fixed intervals and analyzed at 261 nm using a UV spectrophotometer [46].

Stability studies

Stability assessments evaluated the physicochemical properties of licorice oil-based products. Gel and emulgel formulations were stored for three months at 4 °C and 25 °C with 60% relative humidity. Physical analysis was conducted to evaluate the samples [47].

Determination of *in vitro* anti-psoriatic effect of extract on cultured HaCaT cell line

MTT assay was used to determine cell viability in HaCaT cells. Licorice oil-based emulgel was used for this purpose [48]. The cells cultured of Dulbecco Eagle medium supplemented with heat-activated fetal bovine serum using 10% (v/v). The cells were maintained at 37 °C with a CO_2 concentration of 5% and harvested by trypsinization technique. In every three days, the growth media was replaced. The experiment showed that the licorice oil-based emulgel accurately determined cell viability in HaCaT cells [49, 50].

Statistics

Data presented as mean values with standard deviation, based on n=3. The statistical analysis was conducted using Graph Pad Prism 5 software. The data have been expressed as mean±Standard Error Mean (SEM). A one-way Analysis Of Variance (ANOVA), followed by post-Dunnett's analysis, was performed. Significance was determined at p-value<0.05.

RESULTS AND DISCUSSION

GC-MS analysis

The hydrodistillation of the analysis of *Glycyrrhiza glabra*, a yellowish oil was obtained with a yield of 0.19% (w/w). The oil was then subjected to GC-MS analyses, which resulted in the detection of 25 components, exhibiting about 100% of the complete oil. Chromatograms of the GC-MS analysis of licorice oil showed in fig.1. The list of identified components, including their retention time and relative percentages, are described below in table 3. Licorice oil was characterized by relatively high content of carbonic acid, eicosyl vinyl ester representing 14.84 % of the oil.1-Bromotridecane (12.94 %) and Piperidinone (9.59 %) are the main active constituents of the oil. Furthermore, heptane (7.07 %), dihydroandroaterone (5.29 %), tricosaze (5.37 %) were found to be predominant monoterpenes in licorice oil. As far as our literature survey could ascertain, one report on chemical composition of licorice essential oil has been previously reported [51]. Carbonic acid, octadecyl prop-1-en-2-yl ester (4.38), cyclotetradecene (3.97 %), Styrene (3.75%), (Z)-3-oxo-6-octenoic acid methyl ester (3.70 %), methylcyclopentane (3.59 %), carbonic acid, eicosane (3.49 %), octadecyl prop-1-en-2-yl ester (2.54 %), toluene (2.34 %),(1R)-2,6,6 trimethylbicyclo[3.1.1]hept-2-ene (1.36 %), oxalic acid, cyclobutyloctadecyl ester (1.83), oxalic acid, cyclobutylheptadecyl ester (1.23 %), Dotriacontylperfluorobutyrate (1.19 %), octacosyltrifluoroacetate (1.09 %), methyl azetidine-2-carboxylate (1.09%), ethyl 2-chloropropionate (0.89 %), oxalic acid, hexadecyl hexyl ester (0.87 %).

Screening and selection of different surfactants and co-surfactants

The solubility of licorice oil has been extensively investigated across various mediums such as oils, surfactants, and co-surfactants [52]. Moreover, among the surfactants tested, tween 80 has shown remarkable potential for enhancing the solubility with licorice oil compared to other surfactants, as illustrated in fig. 2A. Additionally, the use of propylene glycol as a co-surfactant has been discovered to significantly increase the solubility with licorice oil, as indicated in fig. 2B. Due to the fact that it is non-ionic, tween 80 is frequently used in topical nanoemulsions, as was discovered in a previous study [53]. Non-ionic surfactants such as Tween 80 are widely used in topical nanoemulsions due to reduce interfacial tension. These findings can have a significant impact on the development of new and effective formulations for licorice oil-based products. By using the appropriate combination of oils, surfactants, and co-surfactants, safe and effective nanoemulsions can be developed to enhance the bioavailability and efficacy of glycyrrhizic acid in licorice oil.

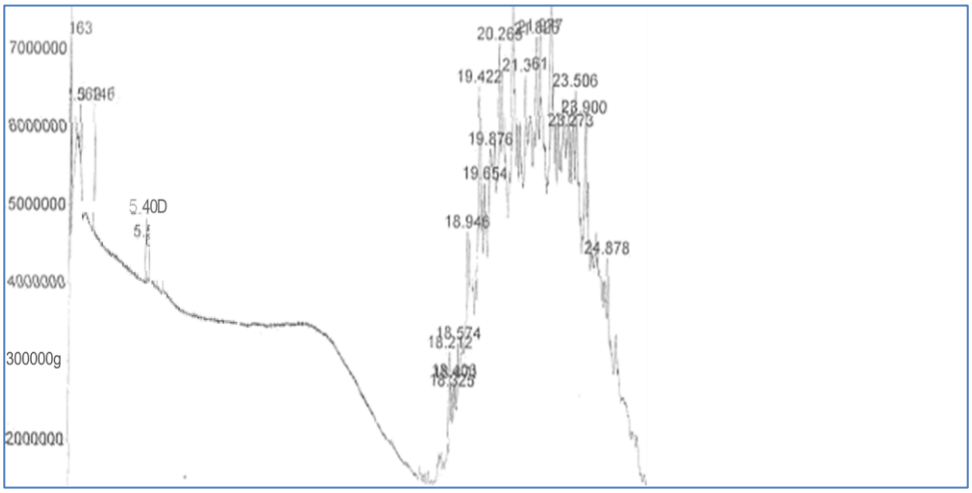


Fig. 1: Chromatograms of the GC-MS analysis of licorice oil

Table 3: Chemical composition of the essential oil of licorice

S. No.	Retention time (min)	Name of compound	(%)
1.	2.163	Methylcyclopentane	3.59
2.	2.562	Methyl azetidine-2-carboxylate	1.09
3.	3.146	Toluene	2.34
4.	5.409	(1R)-2,6,6-Trimethylbicyclo[3.1.1]hept-2-ene	1.36
5.	5.571	Ethyl 2-chloropropionate	0.89
6.	6.095	N-ethyl-N-methyl-2-(2-methylpropoxy)ethanamine	0.89
7.	18.212	(Z)-3-oxo-6-octenoic acid methyl ester	3.70
8.	18.325	Oxalic acid, hexadecyl hexyl ester	0.87
9.	18.406	Oxalic acid, cyclobutylheptadecyl ester	1.23
10.	18.471	Octacosyltrifluoroacetate	1.09
11.	18.574	Oxalic acid, cyclobutyloctadecyl ester	1.83
12.	18.946	Styrene	3.75
13.	19.422	Piperidinone	9.59
14.	19.654	14-Bromo-1-tetradecene	1.99
15.	19.876	Octadecyl prop-1-en-2-yl ester	2.54
16.	20.265	Heptane	7.07
17.	20.821	1-Bromotridecane	12.94
18.	21.361	Carbonic acid	4.38
19.	21.826	Dihydroandroaterone	5.29
20.	21.977	Cyclotetradecene	3.97
21	22.431	Carbonic acid, eicosyl vinyl ester	14.84
22.	23.273	Dotriacontylperfluorobutyrate	1.19
23.	23.506	Dihydroandroeterone	4.71
24.	23.900	Tricosaze	5.37
25.	24.878	Eicosane	3.49

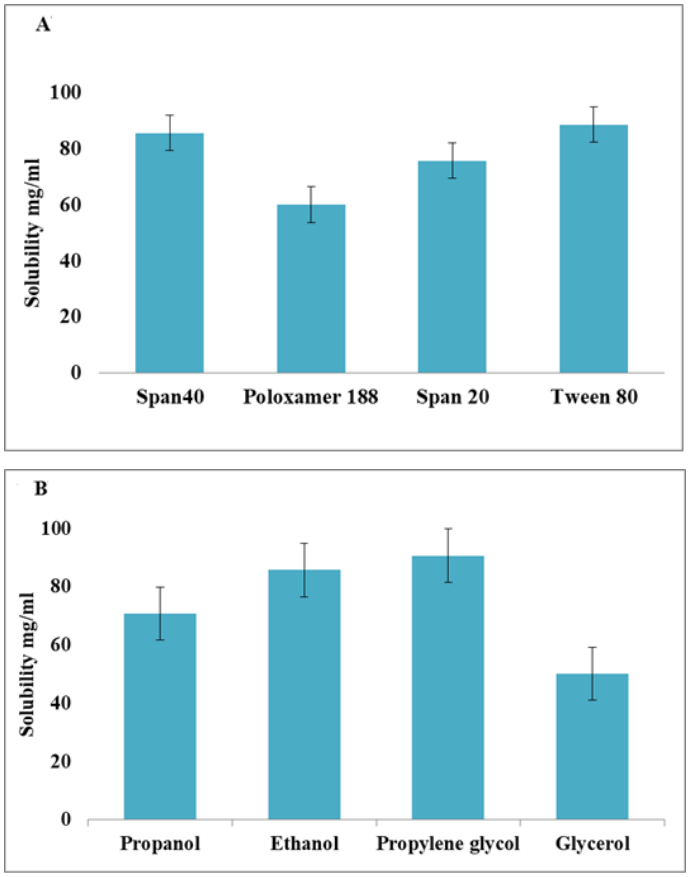


Fig. 2: Displays the solubility of licorice oil of (A) surfactants and (B) co-surfactants, values are expressed as mean±SD, n=3. Error bars indicate the SD values

Physical appearances

The transdermal licorice oil-based emulgel was meticulously evaluated for its physical properties such as color, consistency, and homogeneity. The result was found to be an off-white color emulgel that boasts excellent uniformity and consistency, providing a smooth and even application. The emulgel does not produce unpleasant odour or oily residue; after a month of development, optimized formulation (F5) showed no signs of change or deterioration, proving to be a reliable and long-lasting product.

Measurement of pH

pH of the optimized formulation (F5) was adjusted with triethanolamine and measured between 6.0±0.467. It was revealed that the formulation has an optimum pH which is required for topical delivery of drug from emulgel (5.5-6.5) [54].

Viscosity measurement

Viscosity of the optimized formulation (F5) was measured between 93,500±832 cps. It was observed that on increasing the concentration of gelling agent (carbopol), the viscosity of the formulation was increased as the gelling agent was responsible to reduce interfacial as well as surface tension the flow of gel and thereby increases the viscosity. The produced topical optimization formulations were assessed, as shown in table 4. Optimized formulation has shown desired viscosity for topical delivery of drug [55].

Spreadability

Spreadability of the optimized formulation (F5) was found to be 2.901±0.12 mm. Gel treatment effectiveness is determined by its spread. Emulgels prepared for topical application must meet the optimal quality for topical application, improving patient compliance and have high spreadability [56]. Table 4 displays the results of spreadability study.

Table 4: Viscosity, spreadability, entrapment efficiency and pH of licorice oil-based emulgel

Formulations	Viscosity (cps)	Spreadability (mm)	Entrapment efficiency	pH
F1	89, 233± 438	1.901±0.18	56.43±0.21 %.	6.2±0.44
F2	82,489±983	2.203±0.56	54.33±0.89 %.	6.1±0.53
F3	90,174±267	1.241±1.34	51.21±1.35 %.	6.2±0.78
F4	83,374±198	1.345±1.35	52.45±1.56 %.	6.1±1.67
F5	93,500±832	2.901±0.12	59.53±0.76 %.	6.0±0.467
F6	85,233±233	2.267±0.88	49.62±1.25 %.	5.9± 0.34
F7	91,394±437	2.802±0.79	58.59±0.67 %.	6.1±0.48

Value are expressed as mean±SD, n=3

Percentage entrapment efficiency

The encapsulation efficiency of optimized formulation (F5) was found to be 59.53±8.42%. These results propose that a relatively high amount of licorice oil was entrapped emulgel [57].

Centrifugation test

After conducting the visual centrifugation test, it was confirmed that all formulations were stable. No phase separation was observed, indicating excellent stability [58].

Particle size, PDI and zeta potential

Particle size, PDI and zeta potential of optimized emulgel was measured 54.5±0.21 nm, 0.04±0.34 and −14.1±0.22 V, respectively. This indicated that stable dispersion with a smaller globular size [50]. The results of the each formulations has been shown in table 5. Zeta potential and globule size of the optimized formulation have been depicted in fig. 3 (A and B) [60].

FTIR studies

FTIR analysis was conducted to investigate the possible conflict between licorice oil and other inactive components used in the composition of the emulgel. The study revealed that licorice oil is a rich source of keto and enol functional groups at the peak 1642.00 cm^{-1}, the peak of 1464.02 cm^{-1} showed the presence of O-H bending and carboxylic acid functional groups, and the peak of 1238.6 cm^{-1} showed the presence of C-O stretching and aliphatic ether functional groups. These properties make licorice oil a highly effective and versatile ingredient in the formulation of emulgel [61]. Refer to fig. 4A for a clear illustration of the results. The FTIR spectra graph in fig. 4B reveals the impressive complexity of licorice oil. Its spectrum is a testament to the many functional groups present within the oil. The peak at 1458.28 cm^{-1} indicates both keto and enol functional groups, while the peak at 1376.46 cm^{-1} suggests the presence of O-H bonding and carboxylic acid functional groups. Additionally, the peak at 720.53 cm^{-1} indicates C-O stretching and aliphatic ether functional groups [62]. The richness of licorice oil's molecular composition is genuinely remarkable. The functional groups in the nanoemulsions formulation have been successfully identified by analyzing the recorded peaks in fig. 4C. The peak at 1456.84 cm^{-1} indicates the presence of keto and enol functional groups, while the peak at 3437.57 cm^{-1} confirms the existence of free hydroxyl alcohol and phenol functional groups. Additionally, the peak at 1375.03 cm^{-1} indicates the presence of the O-H bending functional group, and the peak at 1176.96 cm^{-1} signifies the presence of C-O stretching and aliphatic ether functional groups [63]. Remarkably, all the drug peaks were found in the nanoemulsions formulation, which indicates that the drug is entirely intact in the formulation and there are no potential interactions between the drug and the formulation ingredients.

Drug content

Drug content of optimized formulation (F5) was found to be 97.20±0.67 %. The results indicated that higher drug content compared to other formulations [64]. The drug content of each formulation of licorice-based emulgel has been listed in table 6.

Table 5: Particle size, PDI and zeta potential of licorice oil-based emulgel

Formulations	Particle size	PDI	Zeta potential
F1	34.04± 0.56 nm	1.24±1.45	-56.20 ±1.23V
F2	47.89±1.24 nm	0.50±0.23	-45.80± 0.56 V
F3	33.56±0.67 nm	0.90± 1.67	-10.20±0.12 V
F4	34.04±0.76 nm	1.12±0.89	-56.10± 1.45V
F5	54.5±0.21 nm	0.04±0.34	−14.1±0.22 V
F6	49.89 ±1.67 nm	0.34±1.35	-32.4 ±1.89V
F7	52.67±1.25 nm	1.34±0.22	-12.4±0.23V

Value are expressed as mean±SD, n=3

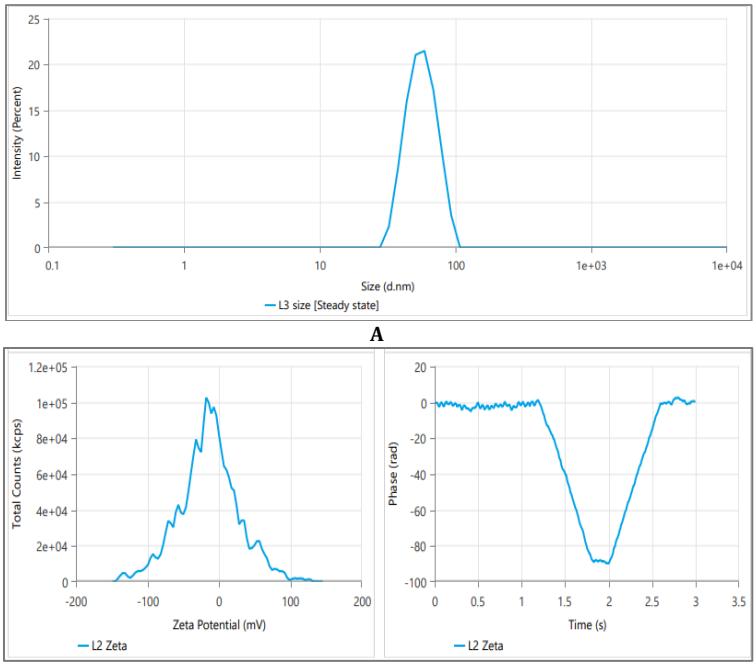


Fig. 4: Illustrates the optimized formulation of (A) particle size and (B) zeta potential

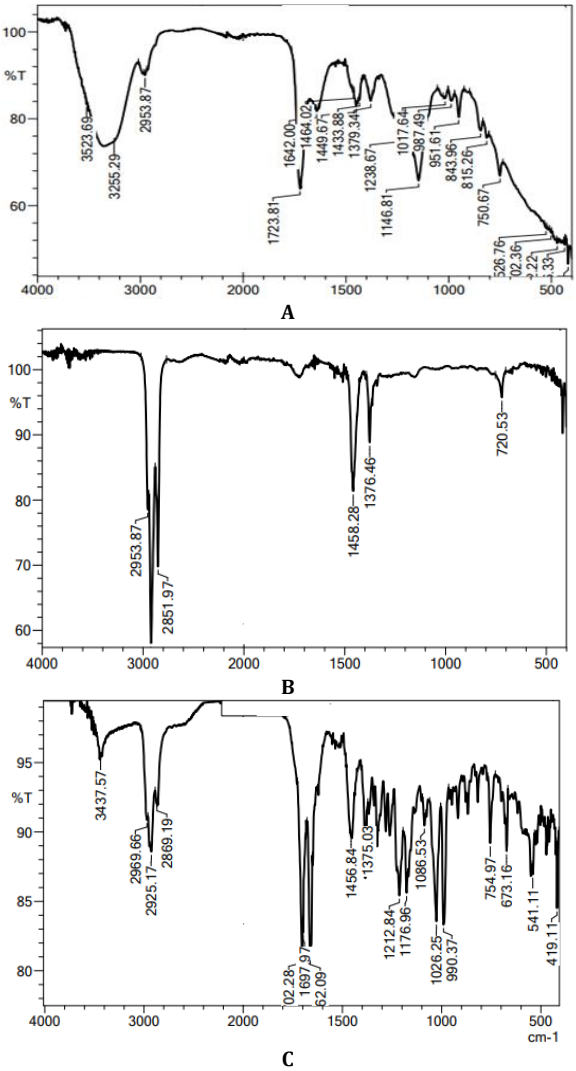


Fig. 5: FTIR spectra of (A) optimized formulation (B) licorice oil (C) glycyrrhizic acid

Table 6: Drug content of various formulation of emulgel

S. No.	Formulation	Drug content in emulgel
1.	F1	88.50±1.05%
2.	F2	92.00±0.67%
3.	F3	86.70±1.56%
4.	F4	84.21±00.89%
5.	F5	97.20±0.67%
6.	F6	88.00±1.45%
7.	F7	90.45±1.23%

Value are expressed as mean±SD, n=3

In vitro release study

In this study, we examined the impact of licorice oil based emulgel by an *in vitro* approach, utilising Franz diffusion cell to measure drug release. The release of licorice oil-based emulgel, as seen *in vitro*, ranged from around 85.03±0.5 1% to 95.15±0.26 % after 24 h, as shown in table 7 and fig. 5. The optimized formulation (F5) showed higher release and better performance than other formulations. It was revealed upon increasing the concentration of carbopol, % release time was also increasing [65]. The lipid nanosystem's occlusive behavior changed the arrangement of corneocytes, resulting in the dilation of inter-corneocyte openings. This led to an increase in skin hydration and the deposition of nano-sized drug carriers in both the epidermis and dermis. Additionally, excipients used in the formulation contributed to enhanced penetration. In a prior study, it was reported that the release of curcumin-loaded gel was lower compared to that from emulgel, with levels ranging from around 87.58 % to 94.48 % at 12 h [66]. Furthermore, it was discovered that the rate of optimized formulation release was significantly influenced by the licorice oil phase employed. The observed phenomenon may be attributed to the inclusion of surfactants and co-surfactants [67]. The findings of this study provide evidence that the integration of licorice oil based emulgel is more advantageous compared to the utilization of gel delivery systems.

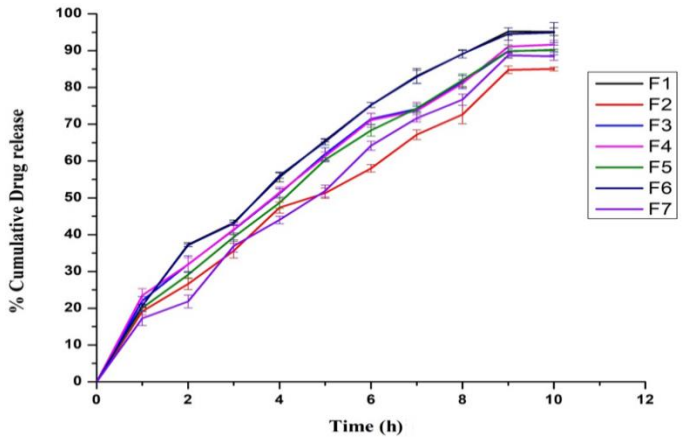


Fig. 5: Percentage cumulative drug release of formulations, values are expressed as mean±SD, n=3. Error bars indicate the SD values

Table 7: *In vitro* release study of various formulation of emulgel

Time	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
1	20.68±0.39	19.18±0.94	22.06±1.10	23.49±1.82	20.07± 1.01	20.68± 0.39	17.23±1.93
2	37.30 ±0.56	26.59±1.50	31.97±2.26	31.89±1.84	29.10± 0.85	37.11± 0.28	21.82±1.74
3	43.23 ±0.71	35.62± 2.01	41.23±1.19	41.42±1.44	39.33± 1.15	43.05± 0.43	36.91±1.66
4	55.66 ±1.33	47.33± 1.52	51.18±1.28	51.45± 1.50	48.67±1.53	56.05± 0.73	43.99±1.01
5	65.56±0.38	51.26± 1.42	61.93± 1.70	61.26± 1.22	60.33±0.58	65.25± 0.84	51.87±1.62
6	75.23 ±0.68	58.01± 1.01	71.44±1.50	71.11± 1.93	68.33± 1.53	75.23± 0.68	64.16±1.22
7	83.13 ±2.01	67.2± 1.31	74.18 ±0.74	73.67± 2.31	74.33±1.17	82.92± 1.73	71.65±1.00
8	89.06±1.01	72.67± 2.52	81.48±1.78	81.12± 1.02	81.96±1.70	89.15± 1.13	76.67±1.53
9	94.21±1.06	88.79± 1.02	89.97±0.61	91.12± 1.73	94.85±1.69	94.56± 1.69	88.49±0.77
10	94.89 ±1.04	85.03± 0.51	90.22±1.35	91.63± 1.15	95.15±0.26	94.92± 2.74	88.76±1.09

Value are expressed as mean±SD, n=3

Stability studies

The optimized formulation underwent rigorous three-month testing at 60 % relative humidity and temperatures of 4 °C and 25 °C, with the results showed in table 8. Upon comparing the stored formulations to the fresh ones, no significant difference was observed in crucial physical characterizations, including colors, pH, spreadability, viscosity, homogeneity and drug content. Therefore, the consistency and stability of this formulation, even under extreme storage conditions [68].

Determination of *in vitro* anti-psoriatic effect of extract on cultured HaCaT cell line

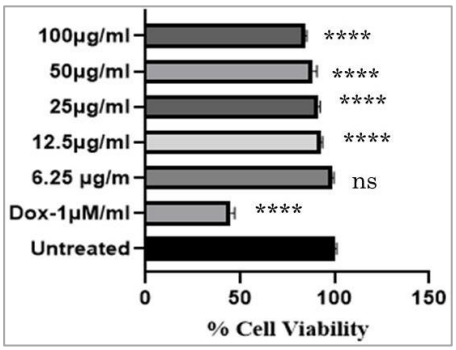
The MTT cytotoxicity study indicated non-toxic potential properties of licorice oil and its emulgel at lower level and caused moderate toxicity

at higher level against HaCaT cell lines [69]. Fig. 6 (A and B) showed significant decrease in the cell viability in the group treated with licorice oil and emulgel at100 µg/ml compared to the untreated group. Licorice oil and its emulgel showed the anti-psoriatic activity [70].

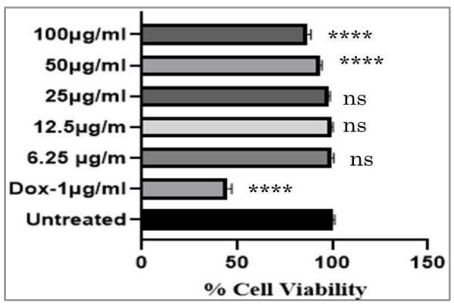
Table 8: Stability study of various formulations of emulgel

Properties	Temperature	Licorice oil-based emulgel
Color and homogeneity	4 °C	Off-white color and homogenous
	25 °C	Off-white color and homogenous
pH*	4 °C	6.0±0.46
	25 °C	6.0±0.52
Viscosity (cps)*	4 °C	93,500±832
	25 °C	91,154±178
Spreadability (mm)*	4 °C	2.901±0.12
	25 °C	2.601±0.67
Centrifugation test	4 °C	No phase separation
	25 °C	No phase separation
Drug content*	4 °C	91.42±1.98 %
	25 °C	93.08±0.34 %

*value are expressed as mean±SD, n=3



A



B

Fig. 6: Overlaid bar graph showed the % cell viability values of HaCaT cell lines treated with different concentrations of (A) licorice oil by MTT study and (B) optimized formulation by MTT study. *Data are presented as mean±SEM (n = 3). ***p<0.001 vs. control group. Error bars indicate the SD values

LIMITATIONS

The present study was performed by licorice oil based emulsion for the treatment of psoriasis. Further, there is requirement of studied with the isolated bioactive compounds. The preclinical and clinical studied must be performed for the evaluation of various crucial parameters of safety and efficacy of the formulations.

CONCLUSION

Licorice oil-based emulgel may aid in autoimmune skin disease such as psoriasis due to their anti-inflammatory properties and anti-psoriatic activity. Emulgel is a novel drug delivery system that can deliver lipophilic and hydrophilic ions of drugs in two phases. The optimized formulation (F5) has the highest cumulative drug release, pH 6.0±0.467, and viscosity 93,500±832 cps. Licorice oil are useful for the treatment of psoriasis, skin infection, and burn. The licorice oil-based emulgel has undergone a series of rigorous tests and evaluations, which include particle size, zeta potential, PDI, and FTIR spectra, *in vitro* release and *in vitro* cell line study. The results have demonstrated its remarkable colloidal stability, high encapsulation efficiency, and biocompatibility with human keratinocytes making it a strong candidate for combating psoriasis. The research also opens fresh avenues for further studies on the mechanisms of action of licorice oil in the treatment of skin infections like psoriasis. This study introduces a new, cost-effective topical emulgel containing licorice oil that can be used for the treatment of psoriasis. Further, safety and toxicity profiles must be explored through clinical studied.

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AUTHORS CONTRIBUTIONS

All authors, Priyanka Jurel, Shiv Bahadur, Meenakshi Bajpai, have contributed equally to the development and execution of this work. Each author actively participated in the conceptualization, data collection, analysis, and manuscript preparation. All authors have reviewed and approved the final version of the manuscript for publication.

CONFLICTS OF INTERESTS

All authors have none to declare

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