Original Article

Commiphora mukul and Quercetin Loaded Liposphere Gel: Potential Treatment for Psoriasis

Madhura Mestry, Meenal Rane*, Amrita Bajaj

Department of Pharmaceutics, SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Vile Parle (W), Mumbai, Maharashtra, INDIA.

ABSTRACT

Background: Psoriasis is a chronic autoimmune skin disorder characterized by thick skin patches, which are typically red, scaly and itchy. Topical drug delivery is backbone in mild and moderate psoriasis as well as useful complementary therapy to systemic therapy in severe conditions. **Aim:** The attempt was made to formulate, optimized and evaluate novel liposhpere based drug delivery system containing anti-psoriatic herbal drug such as *Commiphora mukul* and Quercetin for treatment of psoriasis. **Materials and Methods:** Liposphere were prepared separately for both the drugs by using Precirol ATO 5, Phosphotidylcholine, poloxamer 338. Physicochemical characteristics of the liposphere such as, particle size, drug encapsulation efficiency were determined. Also, drug release and *in vitro* skin permeability were evaluated using Franz diffusion cells. **Results:** The results showed that the maximum encapsulation efficiency was 83% and 81.77% for *Commiphora mukul* and Quercetin loaded liposphere respectively. *In vitro* study was observed that F1 liposphere gel attributed 89.28 % release in 1440 min (24 hr) and F2 conventional cream batch attributed 80.24% release in 540 min (9 hr). As per the result it was observed that liposphere gel gives more sustained release as compared to conventional cream. The results substantiate that liposphere gel containing combination of *Commiphora mukul* and Quercetin can be an efficacious for the treatment of psoriasis.

Key words: *Commiphora mukul*, Combination therapy, Imiquimod induced psoriasis model, Lipospheres, Psoriasis, Quercetin.

INTRODUCTION

Topical drug delivery is backbone in mild and moderate psoriasis as well as useful complementary therapy to systemic therapy in severe conditions. However, potency of topical therapy in psoriasis have been a major concern.[1-3]

Psoriasis is the chronic autoimmune type-1 disorder generally observed in teen and adults. 2.7% population of the world suffers from this disease as per US National Institute of Health.[4-6] Psoriasis may be exaggerated by infections, injury, irritation and in those patients who already have autoimmune disorders such as rheumatoid arthritis.[7] It commonly affects trunk, elbows, knees, scalps and nails.[8,9] It takes a month for new-born dermal cells to transfer from lower layer to upper layer of surface in normal healthy skin however in case of psoriasis this process gets accomplished within few days and develop thick scaly patches which is main characteristic of psoriasis.[10,11] Many herbal anti psoriatic drugs are research like Silymarin, Quercetin.[12]

Commiphora mukul is an oleoresin derived from plant *Commiphora mukul* and well recognized for their hypolipidemic activity.[13] Recently, the study was conducted on the oxazolone-induced mouse for contact dermatitis and psoriasis to corroborate the anti-psoriatic effect of *Commiphora mukul*.[14] It consists of guggulsterone E and Z which act as actives having anti-inflammatory activity and inhibit TNF produced by macrophage cells and interferon- produced by the Th1 cells.[15]

Quercetin is a strong antioxidant and showed anti-psoriatic activity as COX antagonist

Submission Date: 23-11-2019;
Revision Date: 27-02-2020;
Accepted Date: 12-05-2020

DOI: 10.5530/ijper.54.3.115

Correspondence:
Dr. Meenal M Rane
Department of Pharmaceutics, SVKMs Dr. Bhanuben Nanavati College of Pharmacy, Vile Parle (W), Mumbai-400056, Maharashtra, INDIA.
Phone: +91 9930397679
E-mail: meenal.rane@bncp.ac.in

www.ijper.org

and COX-2 selective antagonist and provide anti-proliferative and anti-inflammatory effect.[16] A literature search of quercetin indicates that topical application of quercetin reduces the cutaneous oxidative damage caused by increased the formation of free radicals and other reactive species induced by sunlight exposure.[17-20] In spite of these promising. Although Quercetin having such a promising activity, it has low solubility in water and poor penetrability. Hence, lipid based drug delivery systems would be much preferred for enhancing the topical delivery of the drugs.[21]

In Psoriatic skin there is depletion of ceramides and normal moisturizing factors (NMFs) like water and cholesterol level increases which causes rigidization of skin.[22] Lipoidal drug delivery system being proposed for complexity of the topical delivery into the psoriatic skin as lipid may restore the normal skin conditions and results in effective delivery across the psoriatic skin barrier.[23] Conventional topical delivery systems for treatment of psoriasis such as creams and ointments have many limitations such as poor percutaneous absorption and patient's discomfort due to greasiness and stickiness.[24-26] Lately, incorporation of drugs in novel pharmaceutical carriers has been shown to provide a more useful anti- psoriatic therapy, minimizing drug's loss and increasing both patient compliance and drug bioavailability.[27-30] Safety will be another benefit for these carriers concentrating the fraction of drug at targeted tissues, while diminishing toxic side effects. *Commiphora mukul* and Quercetin are herbal drugs which have anti-psoriatic activity reported, but no novel marketed formulations are available. So, attempts will be made to incorporate the herbal drugs in lipospheres to enhance the penetration and give sustained release and targeted drug delivery.

There are various Novel drug delivery systems for psoriasis such as liposomes, noisome, microspheres nanoparticles, transferosomes being reported however, lipidic drug delivery is found to be preferred over surfactants and polymer based drug delivery.[31-32] As compared to polymeric microparticles lipidic systems have more biocompatibility which minimizes the hazards of acute and chronic toxicity, they reduce the mobility of incorporated drugs and leakage from carrier. The lipospheres are one of the novel drug delivery system that often have more advantages in topical delivery. The drug entrapped in solid hydrophobic triglycerides with monolayers of phospholipid embedded on surface of the liposphere. The lipospheres are preferred over other drug delivery systems because they offer high entrapment and better physical stability of drugs as well as ease of scale up.[33-37]

MATERIALS AND METHODS

Material

Commiphora mukul and Quercetin were obtained as a generous gift samples from Enovate Bio Life Sciences, India. Quercetin was procured as a gift sample from Otto Chemie Pvt Ltd. Compritol, Precirol ATO 5 were gifted from Gattefosse pvt ltd., Mumbai India. Stearic acid, Glyceryl monostearate, Dynasan and Cetosteryl alcohol Poloxamer 338, Poloxamer 188 were gifted from BASF, India. Soya Lecithin was gifted from Hi Media, VAV Life Sciences Pvt Ltd. Mumbai, India. Ethanol, Methanol were purchased from SD fine chemicals, India. All the other chemicals used in this study were pharmaceutical grade and were used without further treatment.

Preparation and Optimization of *Commiphora mukul* and Quercetin lipospheres

Based on the preliminary studies for *Commiphora mukul* and Quercetin, Precirol ATO 5 was selected as a lipid as solubility of both the drugs was more in it. Poloxamer 338 as a surfactant and lecithin (Soya lecithin) were selected for solubilization of drugs and Prototype formulations were prepared to study the effect of various parameters on formulation characteristics. Both *Commiphora mukul* (200mg) and Quercetin lipospheres (50mg) were prepared separately. Soya phosphotidylcholine and Poloxamer 338 were dissolved in 20 ml of water at 75ºC in a beaker. In another beaker Precirol ATO 5 was melted at 75°C and drugs were added. Both the aqueous phase and lipid phase were maintained at the same temperature. Aqueous phase was then added into lipid phase and stirred well. Emulsion was then homogenized for 20 min (7000 rpm) in Ultra Turrax, high speed homogenizer and simultaneously cooled into an ice bath with continuous stirring. Lipospheres dispersion were then lyophilized using 5% Trehalose as a cryoprotective agent. *Commiphora mukul* and Quercetin loading and particle size of lipospheres were optimized by varying Lipid: Lecithin ratios from 2:1 to 4:1 and surfactant ratio such as 10, 15, 20mg. Factorial design 3^2 was applied for optimization of lipospheres formulation (Table 1).

Characterization of Lipospheres

Entrapment efficiency (%EE)

Accurately weighed 10 mg of *Commiphora mukul* and Quercetin loaded lipospheres were dispersed in 10 ml of Methanol. The drug was extracted in Methanol by centrifugation. The prepared liposphere dispersion was centrifuged at 5000 rpm speed for 20 min at 0°C using REMI cooling centrifuge. Residue was filtered

Table 1: Optimization of formulation parameters for lipospheres preparation.

Sr No.	X_1	X_2	X_1	X_2
			Lipid: lecithin	Poloxamer 338 concentration(mg)
F1	–1	–1	02:01	10
F 2	–1	0	02:01	15
F 3	–1	1	02:01	20
F 4	0	–1	03:01	10
F 5	0	0	03:01	15
F 6	0	1	03:01	20
F 7	1	–1	04:01	10
F 8	1	0	04:01	15
F 9	1	1	04:01	20

and filtrate was scanned and absorbance was recorded using UV spectrophotometer at 368.2nm and 231 nm for analysis.

The % Entrapment of both Quercetin and *Commiphora mukul* in lipospheres were determined: %EE= (Total drug content-free drug/drug content) *100.[38,39]

Drug content

Dissolved *Commiphora mukul* and Quercetin lipospheres (10mg) in 10 ml of chloroform: ethanol (1:1). Amounts of *Commiphora mukul* active and Quercetin in lipospheres were found out by measuring the absorbance's of the solutions at 231nm and 368.2nm using liposphere placebo as a blank by developed UV spectrophotometric analytical method.

Drug release studies from lipospheres

Dialysis bag method was used to evaluate the drug release profiles of lipospheres. Dialysis membrane up to 10000 Dalton. Accurately weighed 40mg of lipospheres were placed in dialysis bag containing water (2ml) as a dispersing medium. The bag was suspended in beaker containing 40 ml of Phosphate buffer 5.5: Ethanol (1:1) as a drug release medium. The solution was stirred using magnetic stirrer for the period of 9 hr. At 1 hr interval 1 ml sample was withdrawn for 9 hr and analysed by the developed UV spectrophotometric method at 368.2 and 231 nm for two drugs. The aliquots were analysed by UV analysis using placebo lipospheres as a blank for estimation of amount of drug release at that time point. The curve was plotted for %DR vs Time (min).

Particle size analysis

Particle size distribution and Zeta potential of *Commiphora mukul* and Quercetin loaded lipospheres were determined by laser scanning technique using Malvern Zeta Seizer Instrument. The average particle size (z-average size) and polydispersity index (PDI) were measured by photon correlation spectroscopy (Malvern Mastersizer) by suitable dilutions with distilled water. Zeta potential for each sample was measured in folded capillary cells using the Nano ZS90 Zeta sizer at 25ºC. From the each liposphere dispersion the 1 ml sample was taken and diluted with 10ml of distilled water.[40,41]

SEM analysis

The prepared lipospheres of *Commiphora mukul* and Quercetin were outsourced for SEM analysis for morphological characterization. The formulations (50 mg of lipospheres/0.5ml) were then poured into aluminium stubs with the help of double adhesive tape and coated with gold in HUS -5 GB vacuum evaporator and observed in Hitachi S-3000 N SEM at an acceleration voltage of 10 Kv and a magnification of 5000X.

TEM analysis

Commiphora mukul and Quercetin-loaded lipospheres were observed under Transmission Electron Microscopy, Hitachi (H-7500). One drop of diluted *Commiphora mukul* and Quercetin-loaded lipospheres suspension was deposited on a film-coated copper grid and it was stained with one drop of 2% (w/v) aqueous solution of phosphotungstic acid. Excess of solution was drained off with a filter paper and then grid was allowed to dry for contrast enhancement. The sample was then examined by Transmission Electron Microscopy.

Differential scanning calorimetry (DSC)

DSC analyses studies were performed on *Commiphora mukul* and Quercetin loaded lipospheres, placebo lipospheres by a Mettler Toledo DSC 8220 instrument (Perkin-Elmer DSC-7). Accurately weighted 6-8 mg of samples were placed on 40 µl aluminium pans. DSC scans were recorded at a heating rate of 10°C /min and was run over the range 25-300°C, using an empty pan as reference.

Preparation of *Commiphora mukul* and Quercetin liposphere gel

Commiphora mukul (4.03%W/W) and Quercetin (3.56%W/W) liposphere gel and *Commiphora mukul* (2%W/W) and Quercetin (0.50%W/W) conventional cream were prepared. The gel phase of formulations was prepared by soaking Carbopol Ultrez 10 in distilled water and *Commiphora mukul* and Quercetin lipospheres were dispersed into it with constant stirring at a moderate speed using mechanical stirrer, then pH was adjusted to 6-6.5 using triethanolamine. The developed gels were observed for their appearance, texture and spreadability. Gel formula was tabulated in Table 2.[42,43]

Table 2: Lipospheres based gel formula.	
Ingredients	**Quantity(%W/W)**
Commiphora mukul loaded lipospheres	4.03
Quercetin loaded lipospheres	3.56
Carbopol Ultrez 10	1
Methyl paraben	0.15
Propyl paraben	0.15

Evaluation of lipospheres containing Gels

Appearance

The optimized gel formulation was inspected visually for colour, consistency and homogeneity.

Spreadability studies

Around 2gm of formulated gel was taken on ground slide which is fixed top wooden block. The gel was spread between ground slide and another glass slide. To expel the air and to provide a uniform film of gel between slides. A weight of 100g was placed on the top of the two slide for 5 min. excess of the gel was remove from the edges. Top slide was then subjected to pull 20 g of weight with the help of a string attached to the hook of fixed ground slide and provided with a hook. The time (sec) required by the top slide to cover a distance of 7.5 cm was noted. The spreadability (S) was calculated as S = M.L/t

where M is the weight (g) tied to the upper glass slide L is the length (cm) moved on the glass slide and t is time (sec). A shorter interval indicates better spreadability.[44,45]

Viscosity measurement

The rheological behaviour of the prepared gel formulations was evaluated using Brookfield Viscometer spindle number 64 at 50rpm.The viscosity of formulation was recorded and reported and rheology behaviour were noted

The pH of gel

Accurately weighed 5 g of the gel was dispersed in 45 ml. of water. The pH of the suspension was determined at 27°C using digital pH meter (Eutech instruments) which was previously calibrated using buffer of pH 4 and pH 7. The pH of the optimized gel batch was measured in triplicates and average value calculated.

Drug content of gel

The 0.5 gm of gel was dispersed and drug extracted in Chloroform: ethanol (1:1) media by keeping on sonicate (Analab instruments) for 20 min. Residue was filtered. The absorbances of drugs were taken at 231 and 372.6 nm to find out the concentration of *Commiphora mukul* and Quercetin in gel.

In-vitro diffusion studies

The Franz diffusion cell at 32°C using dialysis membrane with a molecular weight cut off 10000 Da was used for study. The membrane was soaked in hot phosphate buffer pH 5.5 for 12 hrs before using for diffusion study. The developed Liposphere dispersed gel (0.5gm) was placed on the donor compartment and 24 ml of phosphate buffer pH 5.5: ethanol (1:1) was used as the diffusion medium to fill the receptor compartment. At 1hr intervals 1 ml of sample was withdrawn for 9 hr and analysed by the developed UV spectrophotometric method at 368.2 and 231 nm for two drugs. The graph was plotted for %DR vs Time (min). Skin retention studies

Skin retention studies were carried out by the determination of the content of drugs remain in skin barrier. The pig ear skin after *ex-vivo* diffusion studies was analysed for amount of actives retained within the skin, which did not permeate through the skin. To determine Quantity of the drugs remained in skin barrier, both the drugs were extracted from the skin using Phosphate buffer 5.5: ethanol (1:1) and samples were shaken in water bath shaker for 1 hr and then subjected to sonication for 1 hr and then centrifuged at 5000 rpm for 20 min. The dilutions od aliquots were prepared using Phosphate buffer 5.5: ethanol (1:1) to determine the amount of drugs present in skin barrier. The % retention was determined using a developed Absorbance correction method.

Skin Penetration Studies Using Imiquimod Induced Psoriasis Skin

The objective of the study was to measure the Skin penetration of anti-psoriatic formulation containing Quercetin and *Commiphora mukul* loaded lipospheres incorporated in cream base/gel base using Imiquimod-Induced Psoriasis-Like skin as a Model. The experiment was carried out as per the protocol approved by Animal Ethics Committee (CPCSEA/IAEC/P-23/2017).

Female C57BL/6 mice of seven to eleven weeks' old were used as a model for inducing psoriasis. The animals were kept in animal house for at least one week for acclimatization. The mice were shaven on dorsal skin using Veet cream as a depilatory agent. After shaving dorsal skin cleaned with water so that excess cream should be removed from skin. The Imiquimod cream which contains 5% Imiquimod was used as a psoriasis inducing agent.[46] The cream is marketed by Glenmark for genital warts but its side effects are skin

Table 3: Number of sample groups with treatment.

SR.NO.	GROUP (no. of samples group n=6)	TREATMENT
1	Normal Control group	Vanishing Cream/Placebo gel
2	Disease Control group	Psoriasis induced by 5%Imiquimod Cream
3	Treatment group	Psoriasis induced group treated with Quercetin (0.16%)and *Commiphora mukul* containing (0.6%) lipospheres incorporated in cream base/gel base
4	Comparison group	Psoriasis induced by 5%Imiquimod Cream and will be treated with Conventional Cream containing Quercetin (2%) and *Commiphora mukul* (0.5%).

inflammation, skin lesions, red patches which are similar to psoriasis symptoms. The mice were divided in four groups viz Normal Control group, Disease Control group, Treatment group, Comparison group. The groups description was given in Table 3. The normal control group were used to compare with psoriasis induced groups to determine the intensity of the skin inflammation, redness, lesions by comparing with the skin of normal control group. The Imiquimod cream was applied to all the groups except control. The Imiquimod cream with dose 62.5 mg was topically applied on the dorsal part of mice every day for 7-8 consecutive days.

After induction of psoriasis the mice were sacrificed for penetration measurement of drugs through Psoriasis skin. The mice were sacrificed by spinal dislocation method. The penetration evaluation was done using Franz diffusion apparatus.

Skin was excised from Female C57BL/6 mice of seven to eleven weeks' old procured from ACTREC, Kharghar. The skin was wiped with tissue paper and was immediately mounted on the Franz diffusion cell or frozen at −20°C for a maximum period of 4 weeks. The skin was placed horizontally on Franz diffusion cells, between the donor and receptor compartments. The Optimized formulation and conventional cream was applied on psoriasis induced skin in donor compartment and placebo gel was applied to the control group. Sink conditions were obtained in the receptor compartment with ethanolic phosphate buffer pH5.5(1:1), with a volume of receptor fluid of 22ml. The receptor compartment was continuously stirred using a stirring magnetic bead and the temperature was kept at 32°C using a water circulation system. Serial sampling was performed after 1hr up to 9 hr and 1-hr time interval between each aliquot.

UV determination of *Commiphora mukul* and Quercetin contents were determined spectrophotometrically as per the Absorbance correction method. The concentration of *Commiphora mukul* was found to be very low, so standard addition method was used to quantify the drug.[47]

Skin retention studies

Skin retention studies for the formulation was carried out by the determination of the content of drugs remain in skin barrier. The mice skin after *ex-vivo* diffusion studies was analysed for amount of actives retained on the skin, which did not permeate through the skin.[48] To determine Quantity of the drugs remained in skin barrier, both the drugs were extracted from the skin using Phosphate buffer 5.5: ethanol (1:1) and samples were shaken in water bath shaker for 1 hr and then subjected to sonication for 1 hr and then centrifuged at 5000 rpm for 20 min. The dilutions od aliquots were prepared using Phosphate buffer 5.5: ethanol (1:1) to determine the amount of drugs present in skin barrier.

Stability Studies as Per ICH Guidelines

With the help of ICH guidelines, the stability studies were carried out for 3 months to assess the stability studies of *Commiphora mukul* and Quercetin.Three replicates of optimized formulation were sealed in aluminium coated inside with polyethylene pack and stored at 8°C±2°C, 25±2°C/60% RH±5%, 40°C±2°C/75% RH±5% in the humidity chambers. Specimens were gathered following from storage and estimated the physical evaluation parameters, pH, viscosity, spreadability.

RESULT AND DISCUSSION

Preparation and Optimization of *Commiphora mukul* and Quercetin lipospheres

Various liposphere were formulated (Table 1) comprising of central lipid structure, phospholipids, solvent and drug combination, surfactants. To select optimized formulation and for better penetration into skin particle size of lipid based system plays major role. Central lipid system is a significant component of liposphere which is responsible for encapsulation of lipophilic drug. Surface coated lipid is another component of liposphere that influence the surface properties of liposphere. The central lipid core and surface lipid which is responsible for the drug release. The release can alter by varying the proportion of both type of lipid using 3^2 factorial design for the optimization of quercetin and *Commiphora mukul* liposphere. Entrapment efficiency and particle size evaluated for quercetin and

Table 4: Evaluation of liposphere's dependent variables for factorial design.

Formulation No.	*Commiphora mukul* loaded lipopsheres		Quercetin loaded lipospheres	
	Entrapment efficiency (%)	Particle size(μm)	Entrapment efficiency (%)	Particle size(μm)
F 1	78	3-6 μm	32	2-4 μm
F 2	79.38	2-5μm	38.99	2-5 μm
F 3	64.06	2-6 μm	22.65	3-5 μm
F 4	69.64	2-5 μm	74.3	2-4 μm
F 5	73.7	2-4 μm	29.82	2-3 μm
F 6	75.76	2-4 μm	17.73	2-4 μm
F 7	83.63	2-3 μm	76.28	2-4 μm
F 8	81.506	2-5 μm	Batch failed	2.9-3.7 μm
F 9	72.32	2-4 μm	84.77	2-4 μm

Commiphora mukul loaded liposphere mentioned in (Table 4).

Statistical analysis of *Commiphora mukul* loaded lipospheres

Optimization of both drug's lipospheres were done using Design Expert 10.0 software

Response of Entrapment efficiency (%EE)

Statistical equation was obtained for investigating the effect of lipid lecithin ratio (lipid: lecithin) and concentration of Poloxamer 338 surfactant concentration on response of %EE as depicted in equation 1

Polynomial equation

Response of % EE (R1) = + 75.89 + 2.66 * A – 3.188 * B + 0.66 *AB + 3.44 * A^2 – 4.29 B^2 1

Where, A=Ratio of Lipid: Lecithin and B=Concentration of Poloxamer-338. From the polynomial equation and Figure 1 it can be observed that ratio of Lipid: lecithin had a positive effect on the %EE, which means that as the ratio of Lipid: lecithin is increased, %EE of the lipospheres formulation is increased. The concentration of Poloxamer 338 had negative effect on %EE which means that increasing concentration of poloxamer decrease the %EE. Both the ratio of lipid: lecithin and poloxamer appropriate optimized concentration may increase the %EE of the drug in lipospheres.

Response of particle size

Statistical equation was obtained for the effect of lipid lecithin ratio (lipid: lecithin) and concentration of Poloxamer 338 surfactant concentration on response of particle size as depicted in equation 2.

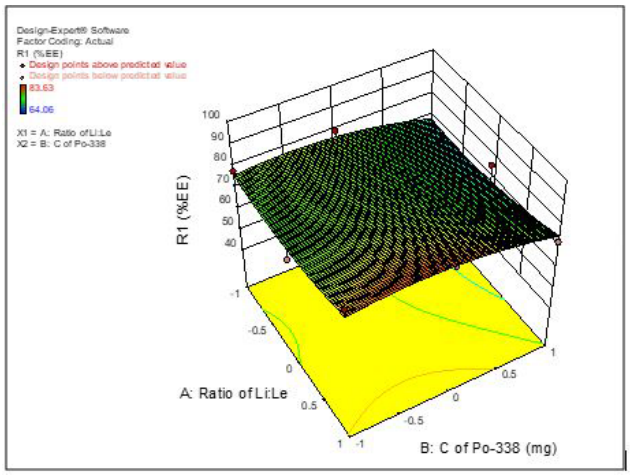


Figure 1: Resoibse surface graph for %EE *Commiphoral mukul* loaded lipospheres.

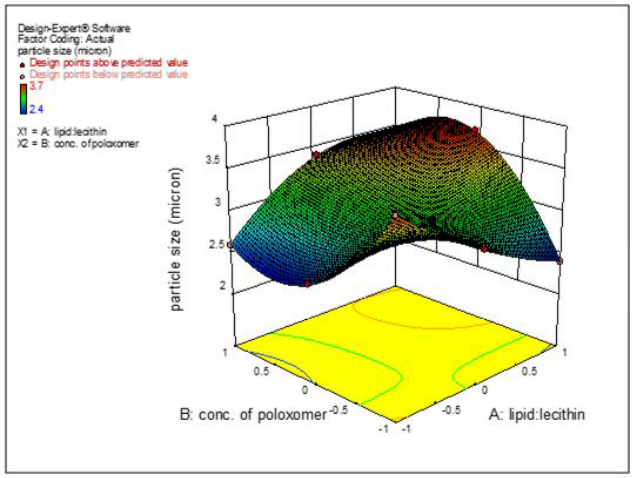


Figure 2: Response surface graph for particle size of *Commiphora mukul* loaded lipospheres.

Polynomial equation:

Response of particle size (R2) =+3.22+0.6*A+0.5*AB-0.13*A^2-0.083B^2-0.25A^2B -0.7AB^2 2

Where, A = Ratio of Lipid: Lecithin and

B = Concentration of Poloxamer-338

From the polynomial equation and Figure 2. It can be observed that ratio of Lipid: lecithin had a positive effect on the particle size, which means that as the ratio of Lipid: lecithin is increased, particle size of the lipospheres formulation is also increased. The concentration of Poloxamer 338 also had positive effect up to certain level on particle size which means that twice increasing concentration of poloxamer decreased the particle size because as a surfactant it will decrease the increase in the surface area and decrease the particle size. Increase in lecithin concentration decrease the

particle size as lecithin also acts as a surfactant which decreases the particle size by increasing surface area of lipospheres particle. Both the ratio of lipid: lecithin and the poloxamer appropriately optimized concentration may give desired appropriate particle size of lipospheres.

Statistical analysis of Quercetin loaded lipospheres

Response of Entrapment efficiency (%EE)

Statistical equation was obtained for the effect of lipid lecithin ratio (lipid: lecithin) and concentration of Poloxamer 338 surfactant concentration on response of %EE as depicted in equation 3.

Polynomial equation

Response of %EE (R1) = +29.82-19.45*A-28.28*B+4.46*AB-10.37*A^2+16.19 B^2+28.05A^2B+46.05AB^2 3

Where, A = Ratio of Lipid: Lecithin and

B = Concentration of Poloxamer-338

From the polynomial equation 3 and Figure 3. It can be observed that ratio of Lipid: lecithin had a negative effect on the %EE, but as lipid lecithin ratio is increased twice the %EE of the lipospheres formulation was also found to be increased due to increase in the solubility of Quercetin in lipid because of lecithin as lecithin acts as a surfactant and emulsifier. The concentration of Poloxamer 338 had negative effect on %EE but increase in concentration of poloxamer 338 increased the %EE because poloxamer is surfactant and increases the solubility of Quercetin and form stable primary emulsion in liposphere preparation. Both ratio of lipid: lecithin and poloxamer concentration may increase the %EE of drug in lipospheres.

Response of particle size

Statistical equation was obtained for investigating the effect of lipid lecithin ratio (lipid: lecithin) and concentration of Poloxamer 338 surfactant concentration on response of particle size as depicted in equation 4.

Polynomial equation:

Response of particle size (R2) =+4.13+3.25*A-0.05 *B -0.3*AB+1.15*A^2-2.25 B^2+0.3A^2B -3.4 AB^2 4

Where, A = Ratio of Lipid: Lecithin and

B = Concentration of Poloxamer-338

From the polynomial equation 4 and Figure 4 it can be observed that ratio of Lipid: lecithin had a positive effect on the particle size, which means that as the ratio of Lipid: lecithin is increased, particle size of the lipospheres formulation is increased. The concentration of Poloxamer 338 also had positive effect up to certain level on particle size which means that increasing concentration of poloxamer may decrease the particle size because as a surfactant it will increase the surface area and decrease the particle size. Increased poloxamer concentration and appropriate ratio of lipid: lecithin concentration may give desired particle size of lipospheres.

Characterization of Lipospheres

Drug content

Drug content of *Commiphora mukul's* formulation batch F7, F8, F9 shows 130 mg, 120mg and 115mg respectively. Batch F7, F8 was selected as a drug content and % entrapment was more as compared to F9 for *Commiphora mukul*. Drug content of Quercetin's formulation batch F4, F7, F9 shows 34.93mg, 30.463mg and 35.93mg respectively. Although for Quercetin F4 and F9 batch

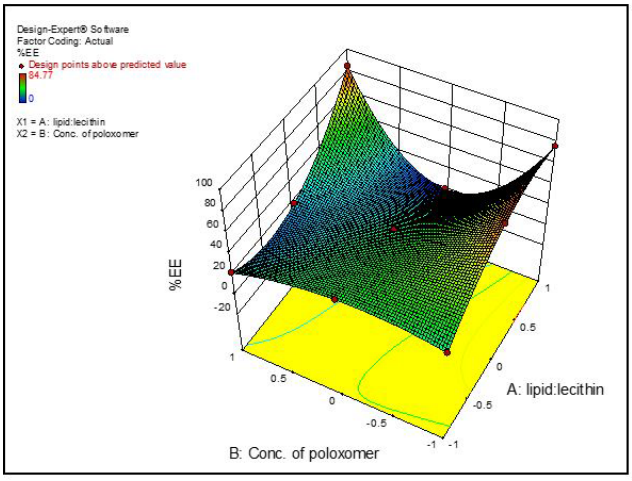


Figure 3: Response surface graph for %EE of Quercetin loaded lipospheres.

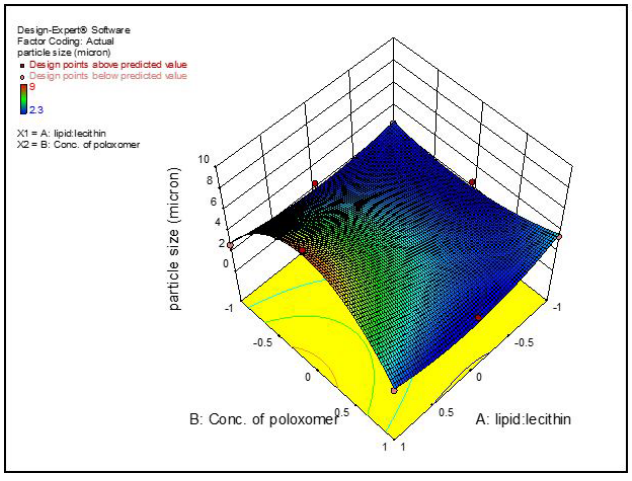


Figure 4: Response surface graph for particle size of Quercetin loaded lipospheres.

possesses higher drug content but % entrapment for F7 was more as compared to F4 batch therefore F9 and F7 was selected for further evaluations.

Drug release studies from lipospheres

As observed in Figure 5, Drug release properties of *Commiphora mukul* and Quercetin lipospheres was investigated to study the release pattern of drugs interpreted from lipospheres. The dialysis bag method was used for drug release studies. Drug release of Quercetin and *Commiphora mukul* in various poloxamer and lipid: lecithin ratio were studied. It was observed that G1 gives 54.5% release in 480 min (8 hr) and G2 batch gives 87.9% release in 420 (7hr) min. The G1 [Lipid: lecithin (4:1) poloxamer 338(10 mg) *Commiphora mukul*] batch was selected for further evaluation as G2 was giving more release and in skin disorders the formulation should retained on skin as targeted site is skin barriers so drugs should not pass the skin barrier it should remained in skin barrier for activity.

Formulation G3 gives 54.8%release in 540 min (9hr). and G4 batch gives 55.9 % release in 540 min (9hr). Both the batches gave sustained release effect which is desired in treatment of Psoriasis. The G4 [Lipid: lecithin (4:1) poloxamer 338 20 mg Quercetin] batch was selected as both the batches exhibited similar release profile but entrapment efficiency and drug content of G4 batch was better than G3 because surfactant concentration may increase the entrapment of Quercetin due to increase the solubility in lipids.

Particle size analysis

Particle size distribution and zeta potential of lipospheres was determined by laser scanning technique using Malvern Zeta Seizer Instrument. The results mentioned in Table 5. *Commiphora mukul* and Quercetin lipospheres were spherical. Zeta potential allows for prediction about the storage stability of colloidal particles, as the particle aggregation will be less to the charged particles. The zeta potential of *Commiphora mukul* and Quercetin loaded lipospheres was found to be -32 .4 mV and -24.5mV respectively which states that no agglomeration in particles.

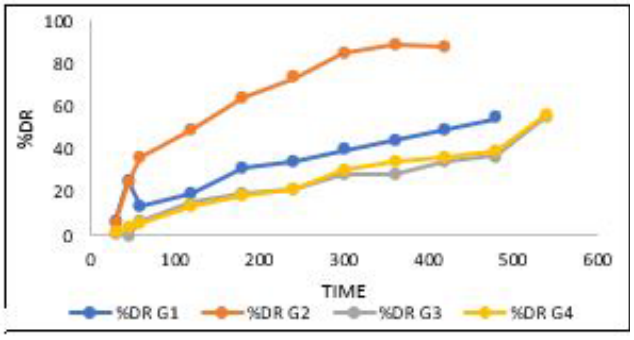


Figure 5: Drug release of Quercetin and *Commiphora mukul* in various poloxmer and lipid;lecithin ratio G1 (*n*=3): Lipid lecithin (4:1) poloxamer 338(10 mg) *Commiphora mukul*; G3 (*n*=3): Lipid: lecithin (4:1) poloxamer 338 10 mg Quercetin; G4 (*n*=3): Lipid: lecithin (4:1) poloxamer 338 20 mg Quercetin.

Table 5: The particle size and zeta potential of lipospheres.

Liposphere Batch	Particle size(nm)	Zeta potential	Polydispersity Index(PdI)
Lipid: lecithin (4:1) poloxamer 338(10 mg) *Commiphora mukul* (200mg)	368.4	-32.4 mV	0.653
Lipid: lecithin (4:1) poloxamer 338(20mg) Quercetin(50mg)	405	-24.5mV	0.636

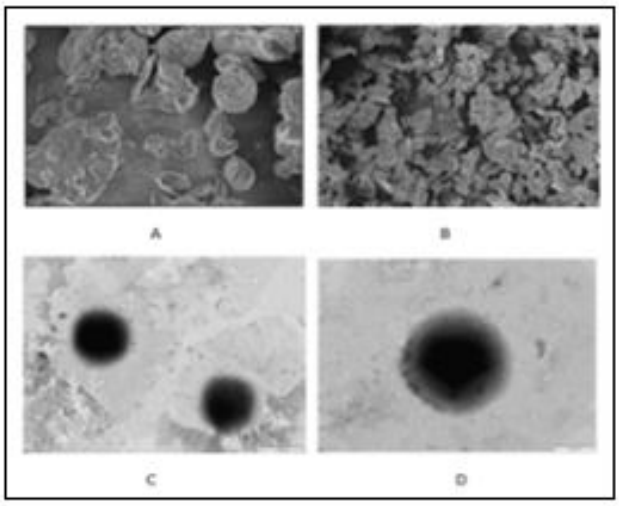


Figure 6: SEM and TEM Analysis of liposphere.
A: SEM analysis of *Commiphora mikul* loaded liposphere, B: SEM analysis of Quercetin loaded loposhere, C: TEM analysis of *Commiphora mikul* loaded liposphere, D: TEM analysis of Quercetin loaded loposhere.

SEM and TEM analysis

The Scanning electron microscopy (SEM) was performed for *Commiphora mukul* and Quercetin loaded lipospheres for morphological characterization. The images of SEM are presented in Figure 6. The SEM images of optimised formulation of *Commiphora mukul* and Quercetin loaded lipospheres reveals that lipospheres were spherical and moderately uniform. TEM is employed for visualizing the surface morphology and size of the drug encapsulated lipospheres in water at room temperature. TEM analysis is ultimate for quantitatively visualizing the surface texture of the substance. TEM image of lipospheres is shown in Figure 6C and 6D, wherein Nano sized particles with average size of 200–500 nm was observed. These results suggest that phospholipids

may serve as efficient delivery carriers for hydrophobic drugs.

Differential scanning calorimetry (DSC)

DSC analysis was done in order to find the effect of heat on the formulation and results. From formulation DSC endotherm, it can be observed that whether the drug is in molecular dispersion form or free form. If the drug is giving its own peak in formulation endotherm, then it might be in free form and not entrapped in the formulation (liposphere). The results of the DSC endotherm of placebo which carried out done for comparison with *Commiphora mukul* and Quercetin loaded liposphere is also described in Figure 7-9.

The confirmation of desired physical state of matrix lipid is crucial which can be determined by the DSC. When the DSC thermograms of the lipids and corresponding lipospheres were compared the difference in the position and shape of the signals are usually observed. Figure 7 showed DSC curves of placebo lipospheres and Figure 8 and 9 showed the DSC endotherms of *Commiphora mukul* and Quercetin loaded lipospheres. The *Commiphora mukul* and Quercetin did not show peaks at 172°C and 314°C which is melting points of the two drugs respectively. Therefore, it is confirmed that *Commiphora mukul* and Quercetin were entrapped in lipospheres.

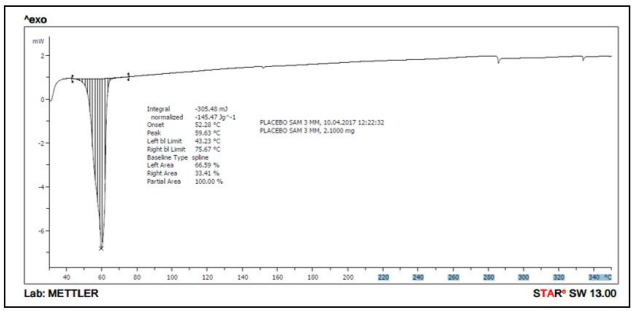


Figure 7: DSC endotherm of placebo lipospheres.

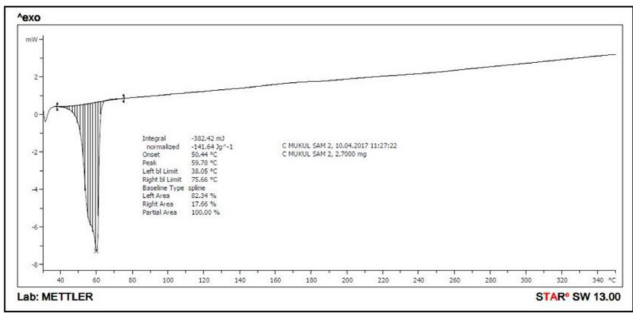


Figure 8: DSC endotherm of *Commiphora mukul* loaded lipospheres.

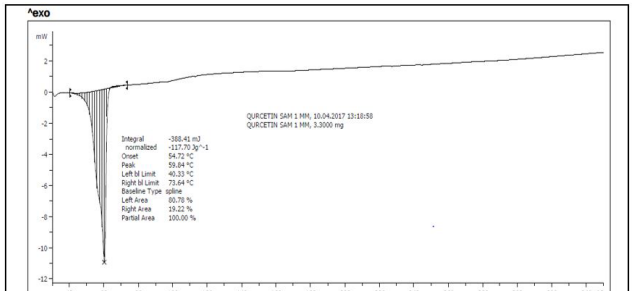


Figure 9: DSC endotherm of Quercetin loaded lopospheres.

Gel Formulation

Optimized batch of lipospheres were incorporated in gel base. Various gelling agents like Carbopol 980, Carbopol 971p, Carbopol 71 G, Carbopol Ultrez 10, HPMC E-5 were screened. The gels were prepared as per the method described in 2.4. Carbopol 971 p and 71 G are low viscosity polymers and gave less viscous gels as compared to other polymers. It was observed that the lipid systems incorporated gels became stiff after storage. Low viscosity polymer was selected so that after storage it will regain the proper consistency of gel but after storage the consistency was not reached up to desired level. Therefore, Carbopol 971 p and 71 G were not selected as gelling base. HPMC E-5 gave sticky gel which would not be patient compliant. Carbopol 980 and Carbopol Ultrez 10 resulted in the formation of clear, smooth, easily spreadable, homogenous gels. But, after storage it was observed that Carbopol 980 gel became stiff which exhibited poor spreadability while Carbopol Ultrez 10 gel remained soft and smooth after storage. Therefore, Carbopol Ultrez 10 was selected as a gel base and optimized liposphere formulation of drugs were incorporated into the gels to form final liposphere based gel delivery

Evaluation of lipospheres containing Gels

Yellow coloured smooth gel was formed having Spreadability 96±1.36 gm cm/sec. It indicated shorter interval to spread the gel means better is the spreadability. The rheological study of the prepared gel formulation was evaluated using Brookfield Viscometer and viscosity of optimized formulation was found to be 65000cPs. The pH of the gel dispersion in water was determined using digital pH meter and it exhibited 6.5±0.34 which is non-irritant to psoriatic skin. Drug content of *Commiphora mukul* and Quercetin loaded lipospheres in gel was found to be 96.56% and 97.23%.

In-vitro diffusion profile of Liposphere based gel

From Figure 10, it was observed that F1 gel attributed 89.28 % release in 1440 min (24 hr). And F2 conventional

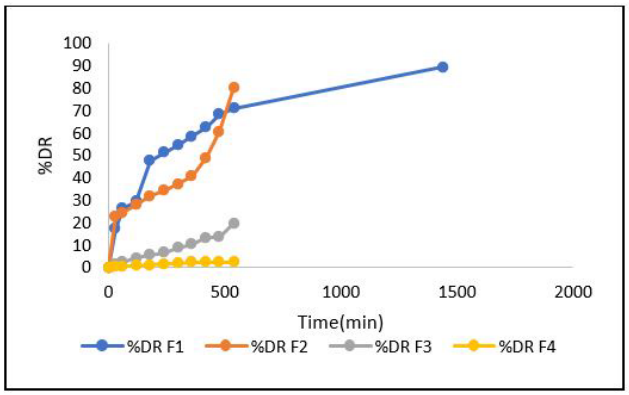


Figure 10: *In vitro* diffusion profiles.

F1 (*n*=3): *Commiphora mukul* release form optimized lipospheres batch in gel, F2 (*n*=3): *Commiphora mukul* release form Conventional cream, F3 (*n*=3): Qurecetin release form optimized lipospheres batch gel, F4 (*n*=3): Qurecetin release form Conventional cream.

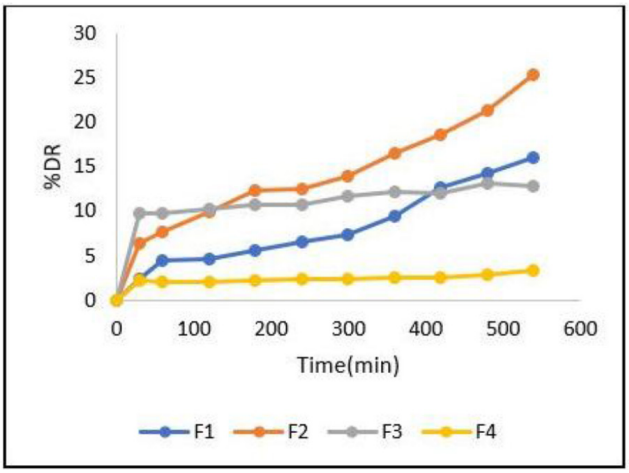


Figure 11: *Ex-vivo* diffusion profiles.

F1 (*n*=3): Release of *Commiphora mukul* form lipophere gel, F2 (n=3): Release of *Commiphora mukul* form Conventional cream, F3(*n*=3): Release of Qurecetin form lipophere gel, F4(*n*=3): Release of Qurecetin form Conventional cream.

cream batch attributed 80.24% release in 540 min (9 hr). It can be calculated that liposphere gel gives more sustained release as compared to conventional cream. Flux of the *Commiphora mukul* loaded lipospheres in gel were found to be 62.473 $\mu g/cm^{-2}hr^{-1}$ in 24 hr whereas flux in cream was found to be 666.76 $\mu g/cm^{-2}hr^{-1}$. It was observed that flux of the drug was less in gel as compared to cream which exhibited that less penetration of the drug through membrane in gel as compared to cream and drug may retained in the skin surface and skin barrier. F3 attributed 19.69 %release in 540 min (9 hr). And F4 batch attributed 2.5% release in 540 min (9 hr). Quercetin has poor penetrability through it was not able to reach the till dermal barrier to give the activity. From above result it can be calculated that due to lecithin coat of liposphere Quercetin is able to penetrate the membrane and conventional cream gives poor penetrability of Quercetin. Flux of the Quercetin loaded lipospheres in gel was found to be 18.6 $\mu g/cm^{-2}hr^{-1}$ in 9 hr whereas flux in cream was found to be 5.052 $\mu g/cm^{-2}hr^{-1}$. It was observed that flux of the drug was more in gel as compared to cream which exhibited that the drug was able to diffuse through hydrophobic membrane in gel as compared to cream which means the penetrability of Quercetin enhanced by incorporating into lipospheres. But less flux indicated that drug may have retained in the skin surface and skin barrier.

It was observed that the *Commiphora mukul* (R^2=0.96) and Quercetin (R^2=0.92) were following Higuchi model in gel because the drug is entrapped in lipospheres based gel system the release and the drug is slowly releasing through lipid matrix. The *Commiphora mukul* and Quercetin followed first order kinetics in conventional cream means the diffusion of the drug was depending upon the drug concentration.

Ex-vivo diffusion studies

From Figure 11, *ex-vivo* skin penetration and permeation experiments was performed on Franz diffusion apparatus using pig ear skin. From above results it can be observed that F1 gel attributed 15.93 % release in 9hr. and F2 conventional cream attributed 25.23% release in 9 hr. So, from this it can be concluded that the release of *Commiphora mukul* from gel was less as compared to conventional cream and penetration through skin barrier was less so it may be retained in the skin barrier which was essential for the activity of the drug in the skin.

F3 gel attributed 12.7 % release in 9hr. and F4 Conventional cream batch attributed 3.4% release in 9 hr. Quercetin has poor penetrability through skin. So, Quercetin loaded lipospheres increases the penetrability of drug through skin layer and retained the in-skin barrier to release the drug whereas in case of Quercetin release from conventional cream was poor so it won't be able to cross the skin barrier and reach the psoriatic skin barrier. 20

Skin retention studies

Skin retention studies were carried out by the determination of the amount of drugs remain in skin barrier. The pig ear skin after *ex-vivo* diffusion studies was analysed for amount of actives retained on the skin, which did not permeate through the skin. The % retention for *Commiphora mukul* in gel and conventional cream was found out be 40% and 15% whereas % retention for Quercetin in gel and conventional cream was found out to be 20 % and 3% respectively which indicated that gel has more potential to treat the psoriasis than

conventional cream % retention of both the drugs was more from gel as compared to conventional cream. It can be concluded that the drug loaded lipospheres based gel would be more effective as compared to conventional cream in treatment of psoriasis.

Skin penetration studies using Imiquimod induced psoriasis skin

The objective of the study was to measure the Skin penetration of anti-psoriatic formulation containing Quercetin and *Commiphora mukul* loaded lipospheres incorporated in cream base/gel base using Imiquimod-Induced Psoriasis-Like skin as a Model. The experiment was carried out as per the protocol approved by Animal Ethics Committee (CPCSEA/IAEC/P-23/2017).

The Imiquimod cream was applied to all the groups except control. The Imiquimod cream with dose 62.5 mg was topically applied on the dorsal part of mice every day for 7-8 consecutive days. The induction of psoriasis and normal shaved skin for comparison was indicated in Figure 12. Skin penetration of both the drugs were evaluated by Franz diffusion studies. UV determination of *Commiphora mukul* and Quercetin contents were determined spectrophotometrically as per the Absorbance correction method. The % drug release for *Commiphora mukul* in gel and conventional cream was found out be 0.5 and 15% whereas for Quercetin in gel and conventional cream was found out to be 15.3 % and 1.45% respectively which indicated that gel has more potential to treat the psoriasis than conventional cream % retention of both the drugs was more from gel as compared to conventional cream. From above results it was observed that the penetration of both the drugs from gel through skin barrier was very less as compared to drugs from conventional cream. It can be concluded that drugs may retained in skin barrier which was essential for the activity of skin.

Skin retention studies

Skin retention studies were carried out by the determination of the amount of drugs remain in skin barrier. The dilutions of aliquots were prepared using Phosphate buffer 05.5: ethanol (1:1) to determine the amount of drugs present in skin barrier. The % retention was determined using a developed Absorbance correction method and mentioned in Table 6.

From above results it was observed that the retention of drugs in skin barrier was more in gel as compared to conventional cream. This indicated that more drugs retained in skin barrier and available at site of action from gel as compared to conventional cream. The gel has more potential to treat the psoriasis than conventional cream. It can be concluded that the liposphere gel would give more effect as compared to conventional cream in treatment of psoriasis.

Table 6: Retention studies of drugs.

Drugs	%Retention(*n*=3)	
	Gel	Conventional cream
Commiphora mukul	55.69%	17%
Quercetin	36%	8%

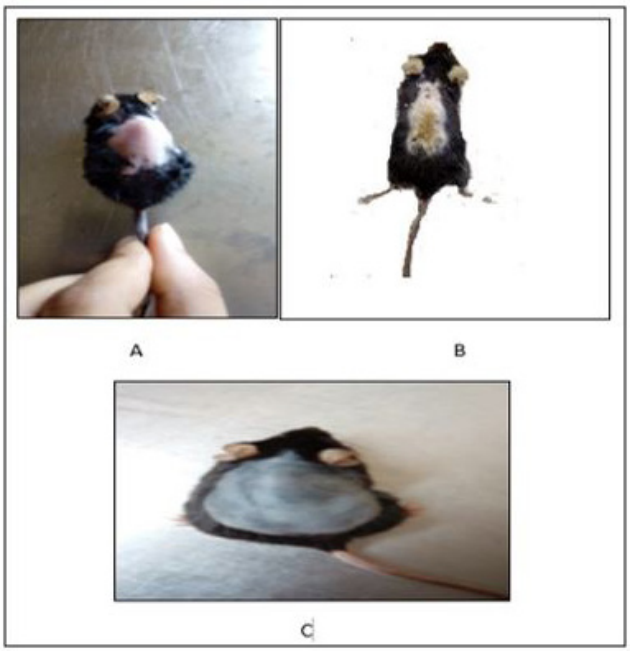


Figure 12: Comparison between normal skin and Psoriasis induced skin. A: Shaved mice B: Psoriasis like symptoms induction in mice C: Treatment with optimized gel formulation.

Treatment of mice using optimized gel formula on Psoriasis induced mice

After induction of psoriasis the treatment was given by topically applying optimized gel formulation to the dorsal skin of mice every day with dose 0.2 gm for 1 week. The evaluation was done visually like intensity of lesion, inflammation, red patches. The images of psoriasis induced mice and after treatment were shown in Figure 12.

After 1-week application of optimized lipospheres based gel formulation it was observed that the erythema, skin thickening, scaling, epidermal alterations were disappearing so it can be concluded that the optimized gel formula has potential to treat the psoriasis.

Stability Studies

From Table 7, it was observed that the optimized lipospheres based gel formulations were stable, showing minute changes in the physicochemical parameters

Table 7: Stability studies of *Commiphora mukul* and Quercetin liposphere gel.

Temperature		Parameters				
		pH	Viscosity (cPs)	Spreadability (gm cm/sec)	*In vitro* drug release (%)	
					Commiphora mukul	Quercetin
	Initial	6.5	65000	96±1.36	89.28	19.69
8°C±2°C	1 month	6.57	65000	96.4±1.74	87.26	22
	2 month	6.54	65000	96.351±1.23	85	23
	3 month	6.54	65000	98±1.5	86.32	24.65
25±2°C/60%RH±5%	1 month	6.52	65076	98±0.38	88.6	17.3
	2 month	6.52	65077	97±0.45	88	18
	3 month	6.54	65000	96±0.49	88.63	18.72
40°C±2°C/75%RH±5%	1 month	6.52	65076	98±0.26	88.6	23.6
	2 month	6.58	65077	97±0.22	88.45	20.3
	3 month	6.55	65074	96.5±0.40	89	22.5

over. The pH, viscosity, spreadability and *in-vitro* drug diffusion parameters exhibited a minimal change. Hence it can be concluded that the optimized formulations showed stability over the study duration, carried out as per ICH guidelines. Hence *Commiphora mukul* and Quercetin loaded lipospheres based gels have potential to be marketed for therapy of psoriasis.

Liposphere based gel formulations were developed and optimized for treatment of psoriasis using 3^2 factorial designs containing anti-psoriatic herbal drugs *Commiphora mukul* and quercetin in combination. The optimized formulation had high entrapment efficiency and particle size which was necessary for topical delivery. Central lipid system is a significant component of liposphere which is responsible for encapsulation of lipophilic drug. Surface Coated lipid is another important excipient of liposphere that influence the surface properties. *Commiphora mukul* and Quercetin lipospheres were observed nearly 200-500 nm. Liposphere gel system advantageous in the aspects of application, deeper penetration and slow release of drugs. The formulated liposphere gel of *Commiphora mukul* and Quercetin illustrated an improved *in vivo* anti-psoriatic efficacy on IMQ induced psoriatic mice model. From the above studies, the conclusion made was that *Commiphora mukul* and Quercetin liposphere gel has better anti-psoriatic potential of developed formulation.

ACKNOWLEDGEMENT

The authors feel privileged to thank the E novate Bio Life Sciences, Otto Chemie Pvt Ltd., VAV Life Sciences Pvt Ltd for providing the gift samples.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

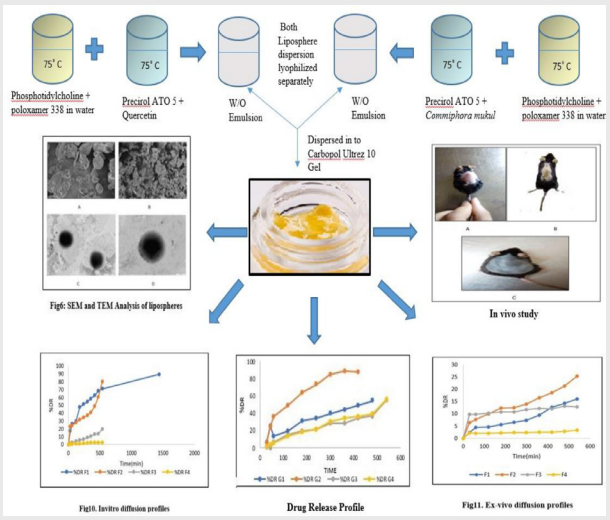
SEM: Scanning Electron Microscope; **TEM:** Transmission Electron Microscope; **Kv:** Kilo Volt; **DSC:** Differential Scanning Calorimetry; **CPCSEA:** Committee for the Purpose of Control and Supervision of Experiments on Animals; **IAEC:** Institutional Animal Ethics Committee; **COX:** Cyclooxygenase; **%EE:** % Entrapment Efficiency; **% DR:** % Drug Release; **ICH:** International Conference on Harmonization; **IQM:** Imiquimod.

REFERENCES

1. Raza K, Singh B, Mahajan A, Negi P, Bhatia A, Katare OP. Design and evaluation of flexible membrane vesicles (FMVs) for enhanced topical delivery of capsaicin. J Drug Target. 2011;19(4):293-302.
2. Dwarampudi LP, Palaniswamy D, Nithyanantham M, Raghu PS. Antipsoriatic activity and cytotoxicity of ethanolic extract of *Nigella sativa* seeds. Pharmacogn Mag. 2012;8(32):268-72.
3. Katare O, Raza K, Singh B, Dogra S. Novel drug delivery systems in topical treatment of psoriasis: Rigors and vigors. Indian J Dermatology, Venereol Leprol. 2010;76(6):612.
4. Krueger JG. The immunologic basis for the treatment of psoriasis with new biologic agents. J Am Acad Dermatol. 2002;46(1):1-26.
5. Deng S, May BH, Zhang AL, Lu C, Xue CCL. Topical herbal medicine combined with pharmacotherapy for psoriasis: A systematic review and meta-analysis. Arch Dermatol Res. 2013;305(3):179-89.
6. Kuchekar AB, Pujari RR, Kuchekar SB, Dhole SN, Mule PM. International Journal of Pharmacy and Life Sciences Psoriasis: A comprehensive review. Int J Pharm Life Sci. 2011;2(6):857-77.
7. Ernst E. Complementary and alternative medicine in rheumatology. Best Pract Res Clin Rheumatol. 2000;14(4):731-49.

8. Rahman M, Zaki AM, Kazmi I, Akhter S, Beg S, Gupta G, *et al*. Insight into the Biomarkers as the Novel Anti-Psoriatic Drug Discovery Tool: A Contemporary Viewpoint. Curr Drug Discov Technol. 2012;9(1):48–62.
9. Aydin SZ, Castillo-Gallego C, Ash ZR, Marzo-Ortega H, Emery P, Wakefield RJ, *et al*. Ultrasonographic assessment of nail in psoriatic disease shows a link between onychopathy and distal interphalangeal joint extensor tendon enthesopathy. Dermatology. 2013;225(3):231-5.
10. Cuesta-Montero L, Belinchón I. Connective tissue diseases and psoriasis. Actas Dermosifiliogr. 2011;102(7):487-97.
11. Oostveen AM, Beulens CA, DeKerkhof PCMV, DeJong EMGJ, Seyger MMB. The effectiveness and safety of short-contact dithranol therapy in paediatric psoriasis: A prospective comparison of regular day care and day care with telemedicine. Br J Dermatol. 2014;170(2):454-7.
12. Sabir S, Arshad M, Asif S, Chaudhari SK. An insight into medicinal and therapeutic potential of *Silybum marianum* (L.) Gaertn. Int J Biosci. 2014;4(11):104-15.
13. Masten SA. Gum Guggul and some of its steroidal constituents. Review of Toxicological Literature. 2005;(2):6-12.
14. Sundar R, Francis S, Hiradhar PK, Rajesh N, Devada S. Effect of *Commiphora mukul* in Chronic Oxazolone Induced Mouse Dermatitis Model. Int J Vet Sci. 2016;5(1):1-4.
15. Saelee C, Thongrakard V, Tencomnao T. Effects of thai medicinal herb extracts with anti-psoriatic activity on the expression on NF-κb signaling biomarkers in hacat keratinocytes. Molecules. 2011;16(5):3908-32.
16. Vijayalakshmi A, Ravichandiran V, Velraj M, Nirmala S, Jayakumari S. Screening of flavonoid "quercetin" from the rhizome of *Smilax china* Linn. for anti-psoriatic activity. Asian Pac J Trop Biomed. 2012;2(4):269-75. Available from: http://dx.doi.org/10.1016/S2221-1691(12)60021-5
17. Paleco R, Vučen SR, Crean AM, Moore A, Scalia S. Enhancement of the *in vitro* penetration of quercetin through pig skin by combined microneedles and lipid microparticles. Int J Pharm. 2014;472(1-2):206-13.
18. Casagrande R, Georgetti SR, Verri WA, Dorta DJ, DosSantos AC, Fonseca MJV. Protective effect of topical formulations containing quercetin against UVB-induced oxidative stress in hairless mice. J Photochem Photobiol B Biol. 2006;84(1):21-7.
19. Fabiana TMCV, Yris MF, Dimitrius LP, Mamie MI, Vitória LBBM, Maria JVF, *et al*. Evaluation of protective effect of a water-in-oil microemulsion incorporating quercetin against UVB-induced damage in hairless mice skin. J Pharm Pharm Sci. 2010;13(2):274-85. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L360199032%0Ahttp://ejournals.library.ualberta.ca/index.php/JPPS/article/download/7166/7202
20. Bonina F, Lanza M, Montenegro L, Puglisi C, Tomaino A, Trombetta D, *et al*. Flavonoids as potential protective agents against photo-oxidative skin damage. Int J Pharm. 1996;145(1-2):87-94.
21. Hatahet T, Morille M, Hommoss A, Devoisselle JM, Müller RH, Bégu S. Quercetin topical application, from conventional dosage forms to nanodosage forms. Eur J Pharm Biopharm. 2016;108:41-53. Available from: http://dx.doi.org/10.1016/j.ejpb.2016.08.011
22. Wertz PW, Madison KC, Downing DT. Covalently bound lipids of human stratum corneum. J Invest Dermatol. 1989;92(1):109-11. Jan [cited 2019 Sep 14] Available from: http://www.ncbi.nlm.nih.gov/pubmed/2909622
23. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, *et al*. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. J Am Acad Dermatol. 2009;60(4):643-59. Available from: http://dx.doi.org/10.1016/j.jaad.2008.12.032
24. Badıllı U, Şen T, Tarımcı N. Microparticulate Based Topical Delivery System of Clobetasol Propionate. AAPS Pharm Sci Tech. 2011;12(3):949.
25. Gupta M, Agrawal U, Vyas SP. Nanocarrier-based topical drug delivery for the treatment of skin diseases. Expert Opin Drug Deliv. 2012;9(7):783-804.
26. Suresh K. Novel topical drug carriers as a tool for treatment of psoriasis: Progress and advances. African J Pharm Pharmacol. 2013;7(5):138-47.
27. Abdelgawad R, Nasr M, Hamza MY, Awad GAS. Topical and systemic dermal carriers for psoriasis. Int J Curr Pharm Rev Res. 2016;8(1):4-9.
28. Pradhan M, Singh D, Singh MR. Novel colloidal carriers for psoriasis: Current issues, mechanistic insight and novel delivery approaches. J Control Release. 2013;170(3):380-95. Available from: http://dx.doi.org/10.1016/j.jconrel.2013.05.020
29. Akhtar N, Pathak K. Cavamax W7 Composite Ethosomal Gel of Clotrimazole for Improved Topical Delivery: Development and Comparison with Ethosomal Gel. AAPS Pharm Sci Tech. 2012;13(1):344-55.
30. Tokudome Y, Saito Y, Sato F, Kikuchi M, Hinokitani T, Goto K. Preparation and characterization of ceramide-based liposomes with high fusion activity and high membrane fluidity. Colloids Surfaces B Biointerfaces. 2009;73(1):92-6.
31. Bhagwat RR. Novel drug delivery systems: An overview R.R. Bhagwat* and I.S. Vaidhya Department of Quality Assurance, Dr. L.H. Hiranandani College of Pharmacy, C.H.M. College Campus, Opp. Rly Stn., Ulhasnagar- 421003, Maharashtra, India. 2013;4(3):970-82.
32. Dwarakanadha RP, Swarnalatha D. Recent advances in novel drug delivery systems. Int J PharmTech Res. 2010;2(3):2025-7.
33. Attama AA, Okafor CE, Builders PF, Okorie O. Formulation and *in vitro* evaluation of a PEGylated microscopic lipospheres delivery system for ceftriaxone sodium. Drug Deliv. 2009;16(8):448-57.
34. Jadhav SV, Sadgir DP, Patil MP. Liposphere Review: Methods and Its Applications in Bio-Compatible Drug Delivery System. 2014;3(9):1023-43.
35. Raza K, Kumar M, Kumar P, Malik R, Sharma G, Kaur M, *et al*. Topical delivery of aceclofenac: Challenges and promises of novel drug delivery systems. Biomed Res Int. 2014;2014.
36. Singh M, Singh D, Drug SS-IJ of, 2009 undefined. Development and *in vitro* evaluation of polar lipid based lipospheres for oral delivery of peptide drugs. International Journal of Drug Delivery. 2009;1(1). pdfs.semanticscholar.org. [cited 2020 Mar 9]; Available from: https://pdfs.semanticscholar.org/39b2/b0967872ece6771dfba431f9711f4fa73537.pdf
37. body distribution of SLN nanoparticles.pdf.
38. Momoh MA, Esimone CO. Phospholipon 90H (P90H)-Based PEGylated microscopic lipospheres delivery system for gentamicin: An antibiotic evaluation. Asian Pac J Trop Biomed. 2012;2(11):889-94. Available from: http://dx.doi.org/10.1016/S2221-1691(12)60248-2
39. Bhise KS, Mohammed N, Khan A. Formulation and Development of Fenofibrate Loaded Liposphere System. J Drug Deliv Ther. 2013;3(1):1-10.
40. Preeti K, Priyanka M. Formulation and evaluation of vinpocetine loaded lipospheres. Int J Pharm Pharm Sci. 2012;4(Suppl 3):470-3.
41. Chime SA. Recent advances in lipospheres drug delivery system. J Pharm Res. 2012;5(3):1743-8. [cited 2019 Sep 14]Available from: http://jprsolutions.info
42. Kute SB, Saudagar RB. Emulsified gel A Novel approach for delivery of hydrophobic drugs: An overview. J Adv Pharm Educ Res. 2013;3(4):368-76.
43. Singh RP, Parpani S, Narke R, Sinhgad RC. Www.Ajprd.Com 111. Asian J Pharm Res Dev. 2014;2(2):112-23.
44. Maitri S, Modi D, Shah D. A New Future Approach in Novel Drug Delivery System Through Micro-Emulgel: Review. World J Pharm Pharm Sci. 2016;5(5):243–59.
45. Article R. Topical Gel: A Recent Approach for Novel Drug delivery. Asian J Biomed Pharm Sci. 2013;3(17):1.
46. DerFits LV, Mourits S, Voerman JSA, Kant M, Boon L, Laman JD, *et al*. Imiquimod-Induced Psoriasis-Like Skin Inflammation in Mice Is Mediated via the IL-23/IL-17 Axis. J Immunol. 2009;182(9):5836-45.
47. Jean J, Pouliot R. *In vivo* and *in vitro* Models of Psoriasis. Tissue Eng. 2010;359-82.
48. Andrews SN, Jeong E, Prausnitz MR. Transdermal delivery of molecules is limited by full epidermis, not just stratum corneum. Pharm Res. 2013;30(4):1099-109.

PICTORIAL ABSTRACT



About Authors

Ms. Madhura is a Post graduate with Master in Pharmaceutics completed from SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai. This article is part of her research work carried out during her Masters degree.

Dr. Amrita Bajaj has more than 40 International and 50 national research publications in her tenure of forty years as a Pharma Professional. Received Best Teacher Award by Govt of Maharashtra 2002.

SUMMARY

Psoriasis is a chronic autoimmune skin disorder characterized by thick skin patches, which are typically red, scaly and itchy. Topical drug delivery is backbone in mild and moderate psoriasis as well as useful complementary therapy to systemic therapy in severe conditions. *Commiphora mukul* and Quercetin are herbal drugs which have anti-psoriatic activity reported, but no novel marketed formulations are available. This study gives an account of the anti-psoriatic efficacy of *Commiphora mukul* and Quercetin loaded liposphere gel formulation. Novel drug delivery systems for psoriasis such as liposomes, niosomes, microspheres nanoparticles, transferosomes being reported however, lipidic drug delivery is found to be preferred over surfactants and polymer based drug delivery. Liposphere gel showed slow release of both the drugs which is beneficial property of topical formulation. Skin penetration study was performed on imiquimod induced psoriasis skin model and retention of both drugs in dermal layer was evaluated by Franz diffusion studies. Results indicated improvement in retention of both the drugs in dermal layer with *Commiphora mukul* and Quercetin loaded liposphere gel as compared to conventional cream. These results substantiate that liposphere gel containing combination of *Commiphora mukul* and Quercetin can be an efficacious for the treatment of psoriasis.

Dr. Meenal M. Rane is a Doctorate in Pharmaceutics currently working as Assistant Professor in Pharmaceutics at SVKM's Dr. Bhanuben Nanavati College of Pharmacy, Mumbai. Research work has been appreciated at various National and International conferences. Received 2nd prize and Merit Award for the Best Research Paper at the 11th and 13th International symposium on Advances in Technology and Business Potential of NDDS organized by CRS-Indian Chapter held at Mumbai, Received 1st prize at Avishkar Interuniversity research festival organized by Maharashtra in 2010. Received 3rd prize at 5th International Annual conference on "Drug Discovery and Development–Challenges in Partnership" SACCP, Mumbai, 2011. Our research activity focuses on Pulmonary, Oral, Topical and Targeted Drug delivery using Nano carriers.

Cite this article: Mestry M, Rane MM, Bajaj AN. *Commiphora mukul* and Quercetin Loaded Liposphere Gel: Potential Treatment for Psoriasis. Indian J of Pharmaceutical Education and Research. 2020;54(3):654-67.