



PHASE II STUDY OF TOPICAL NIOSOMAL UREA GEL - AN ADJUVANT IN THE TREATMENT OF PSORIASIS

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ABSTRACT

The purpose of the study was to prepare niosomal urea gel using chitosan polymer, to test the same on healthy human volunteers to check the irritation on the skin and to study its clinical effectiveness on psoriasis patients. In this present study topical niosomal gel in chitosan were prepared using urea as a model drug. The urea niosomes were prepared by both lipid layer hydration and trans membrane pH gradient method. Niosomes were prepared and characterised for various physical characters. Surfactants such as spans were used with cholesterol in 1:1 molar ratio with 5% dicetyl phosphate (DCP). The human volunteer study to test the irritancy was performed by human repeated insult patch test (HRIPT) test. PASI scoring was used to determine the severity of the lesion. Niosomes prepared using span 60 showed a better entrapment than other spans. Both the niosomes showed uniform particle size distribution. SEM analysis showed smooth outer surface. A short-term stability studies showed that niosomal gel had better stability followed by niosomes prepared using transmembrane method and lipid layer hydration method. Permeation study of niosomal gel through the human skin showed better diffusion of drug through the skin and skin deposition study showed that better deposition of drug in comparison to plain gel. The niosomal urea gel and plain gel did not produce any irritation of the human skin. The gels were tested on psoriasis patients with less than 25% severity of any category of psoriasis. The niosomal gel produced significant reduction in the lesion ($p < 0.05$) than plain urea gel. The niosomal urea gel produced greater reduction in total score and desquamation score compared to erythema and infiltration score and proved that niosomal urea in chitosan gel can be used as an adjuvant in the treatment of psoriasis.

Keywords: Urea niosomes, Transmembrane method, HRIPT, human volunteer study, PASI score, niosomal topical gel.

INTRODUCTION

Niosomes appear to have application in topical and transdermal products both containing hydrophobic and hydrophilic drugs. Besides, niosomes have also been used to encapsulate, lidocaine¹, estradiol², cyclosporin³, erythromycin⁴, alpha-interferon⁵, plasmid DNA for the human interleukin-1 receptor.⁶ In some of the studies, the non-ionic vesicles can be formulated to target the pilosebaceous glands. The topical route has been selected for some drugs to treat the localized lesions, which can be seen in case of psoriasis and eczema. Psoriasis is a rather common disease. The disease is generally chronic and persistent in nature, and the prevalence of psoriasis increases with age, sharply demarcated. Erythematous lesions and hyper proliferation of cells is the most important characteristic feature of the psoriatic lesion. Plain urea gels are used to reduce the hyper proliferation of cells and are used widely as adjuvant in the treatment of psoriasis.

Urea is used as an emollient in topical creams in concentrations of 2 to 30%; 40% urea is used for the non-surgical removal of dystrophic nails in cases of fungal infections.⁶ Topically applied urea reportedly has a hygroscopic effect; it apparently increases the ability of the skin to retain water.⁷ It may also have an antipruritic effect.⁸

Urea can bind water due to crystalline structure and the keratin layer can bind large amount of water in the presence of urea. In higher dose it can increase the diffusion of active substances in formulation.⁸⁻¹⁰

Chitosan, a natural polysaccharide, is being widely used as a pharmaceutical excipient. The polymer has also been investigated as a potential adjuvant for swellable controlled drug delivery systems. Chitosan exhibits myriad biological actions, namely hypocholesterolemic, antimicrobial and wound healing properties.¹¹

This property has been exploited in current study in the preparation of niosomal urea gel using chitosan.

MATERIALS AND METHODS

Materials and reagents

Urea, Span 40, Span 60, Span 80, Dicetyl phosphate and Cholesterol were from sigma chemicals (St. Louis, MO). All solvents used were of high performance liquid chromatography grade (HPLC), and other chemicals were analytical grade. Pharmaceutical grade Chitosan a kind gift from fisheries department, Kerala, India. PH 7.4 buffer saline was prepared as described in Indian pharmacopoeia.



Preparation of Niosomes

Lipid layer hydration and sonication

Niosomes were prepared by lipid hydration method. Surfactant, cholesterol (1:1 molar quantity) and dicetyl phosphate were dissolved in chloroform: ethanol (4:1), and the solvent was evaporated using rotary flash evaporator (BUCHI Rotavapor R-124), under reduced pressure at 60°C. The dried organic layer is rehydrated with 10ml of 7.5 pH phosphate buffer saline (PBS), which was heated to 60°C in a water bath with gentle agitation. The mixture was intermittently mixed in a vortex. The mixture thus obtained was dispersed using probe sonicator, 20-kHz, 500W vibra cell (Sonics and Materials, Inc., Co., USA) for 30 sec at 1 min intervals for a period of 2 minutes. After dispersion the suspension was maintained for 2 hours at room temperature to allow the niosomes to form and sealed.¹²

Transmembrane pH gradient (inside acidic) process (Remote loading)

In this technique surfactant and cholesterol (1:1) were dissolved in chloroform. The solvent was then evaporated under reduced pressure to get a thin film on the wall of the round bottom flask. The film was hydrated with 300 mM citric acid buffer (pH 4.0) by vortex mixing. The

multilamellar vesicles were frozen and thawed 3 times and later sonicated. To this niosomal suspension, 5 ml aqueous solution containing drug was added and vortexed. The pH of the sample was then raised to 7.0-7.2 with 1M disodium hydrogen phosphate. This mixture was later heated at 60°C for 10 minutes¹³.

Volume of hydration

The volume of hydration was optimized for 10 ml of pH 7.4 phosphate buffer saline with 2 hours of hydration time to get maximum percent entrapment.

Purification and entrapment efficiency of niosomes

The niosomes were purified by passing through Sephadex G-50 column using pH 7.4 buffer as eluent and entrapment efficiency was determined.

The entrapment efficiency was determined by adding 2.5% Triton X-100 to niosomal suspension and shaken well to lyse the vesicles to release the encapsulated urea. This was diluted to suitable concentration and determined using a spectrophotometer (UV 160A Shimadzu) at 479 nm. The plain niosomal suspension was used as blank in all the cases.¹⁴

Table 1: Different methods of urea preparation and its percentage entrapment efficiency

| Method of preparation | Formulation code | Surfactant | Surfactant: Cholesterol | % EE* with 0% DCP (±SD)** | % EE with 2.5% DCP (±SD)* | %EE with 5% DCP (±SD)* |
|---|------------------|------------|-------------------------|---------------------------|---------------------------|------------------------|
| Lipid layer hydration | Urea-1 | Span 40 | 300:300 | 13.3±1.2 | 14.5±3.1 | 16.3±2.0 |
| | Urea-2 | Span 60 | 300:300 | 10.3±1.45 | 11.4±2.1 | 13.4±1.2 |
| | Urea-3 | Span 80 | 300:300 | 9.4±2.1 | 10.1±1.3 | 11.4±1.34 |
| Transmembrane pH gradient (inside acidic) process | Urea-4 | Span 40 | 300:300 | 38.9±1.2 | 39.4±3.2 | 41.2± 1.23 |
| | Urea-5 | Span 60 | 300:300 | 46.8±0.45 | 48.3±2.11 | 52.9±2.35 |
| | Urea-6 | Span 80 | 300:300 | 34.3±1.45 | 35.6±3.20 | 37.4±1.23 |

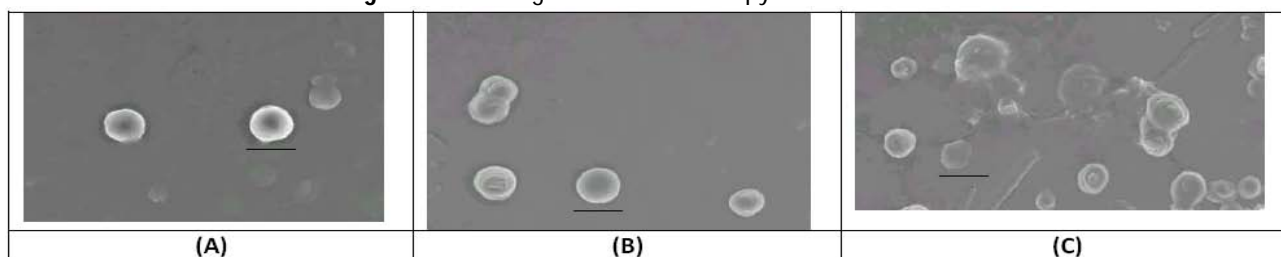
The other molar ratios of surfactant and cholesterol were not shown as it produced less entrapment ratio. 100mg of urea was used for the entrapment; EE-Encapsulation efficiency

Table 2: Mean size and poly dispersity index of niosomes

| Formulation code | % Entrapment of urea (mean±SD)* | Particle size (µm) (mean±SD)* | Poly dispersity Index (PI)** |
|------------------|---------------------------------|-------------------------------|------------------------------|
| Urea-4 | 41.2± 1.23 | 4.305 ±1.26 | 0.292 |
| Urea-5 | 52.9±2.35 | 8.127±1.01 | 0.124 |
| Urea-6 | 37.4±1.23 | 6.123 ±1.13 | 0.180 |

*Mean of 3 batches; **PI- standard deviation/vesicle size

Figure 1: Scanning electron microscopy of urea niosomes



Bar indicates 10 µm; (A) Scanning electron micrograph of Urea-4 niosomes; (B) Scanning electron micrograph of Urea-5 niosomes; (C) Scanning electron micrograph of Urea-6 niosomes

Table 3: Physical stability of niosomes and niosomal gel with different surfactants

| Surfactant | Storage Temperature | Percent leakage over time (Weeks) \pm STD | | |
|-----------------------|---------------------|---|---------------|---------------|
| | | 2wk | 4wk | 6wk |
| Urea-4 | Room | 38 \pm 3.4 | 86 \pm 2.4 | - |
| | Refrigerator | 18 \pm 3.2 | 56 \pm 1.3 | 85 \pm 0.8 |
| Urea-5 | Room | 26 \pm 1.2 | 38 \pm 0.12 | 48 \pm 0.91 |
| | Refrigerator | 4 \pm 3.1 | 18 \pm 1.2 | 24 \pm 1.1 |
| Urea-6 | Room | 68 \pm 2.3 | 96 \pm 1.2 | - |
| | Refrigerator | 30 \pm 1.4 | 58 \pm 2.1 | 87 \pm 2.3 |
| Niosomal gel (Urea-5) | Room | 8 \pm 1.3 | 16 \pm 2.2 | 20 \pm 1.8 |
| | Refrigerator | 2 \pm 0.8 | 10 \pm 1.2 | 14 \pm 2.1 |

Table 6: Frequency of dermal response in human repeated insult patch test (HRIPT) at each evaluation interval

| Formulation code** (N=10) | Observed Reaction* | Induction Phase Readings | | | | | | | | | Challenge phase readings | |
|---------------------------|--------------------|--------------------------|------|------|------|------|------|------|------|------|--------------------------|-------|
| | | 24 hrs reading | | | | | | | | | 24hrs | 72hrs |
| | | Ind1 | Ind2 | Ind3 | Ind4 | Ind5 | Ind6 | Ind7 | Ind8 | Ind9 | cha1 | cha2 |
| Placebo | 0 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% |
| | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Plain Urea gel | 0 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% |
| | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Niosomal Urea gel | 0 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% |
| | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

*Scoring of patch sites; 0 = No visible skin reaction; 1= Barely perceptible or spotty erythema; 2= Mild erythema covering most of the test site; 3= Moderate erythema, possible presence of mild edema; 4= Marked erythema, possible edema; 5= Severe erythema, possible edema, vesiculation, bullae and / or ulceration; Scoring level 2-5 results were not shown, as the formulations did not produce any reaction above level 1. The healthy human volunteers did not produce any skin irritation with the tested gel formulations.

Table 7: Mean change (\pm SD) in psoriasis severity total scores from baseline- Placebo

| Treatment period | Erythema | Infiltration | Desquamation | Total score |
|------------------|-------------------|------------------|-------------------|-------------------|
| Baseline | 0.656 \pm 0.269 | 0.76 \pm 0.403 | 0.644 \pm 0.292 | 2.056 \pm 0.964 |
| Week 2 | 0.656 \pm 0.269 | 0.76 \pm 0.403 | 0.644 \pm 0.292 | 2.06 \pm 0.964 |
| Week 4 | 0.589 \pm 0.310 | 0.76 \pm 0.403 | 0.644 \pm 0.292 | 1.993 \pm 1.005 |
| Week 6 | 0.556 \pm 0.357 | 0.76 \pm 0.403 | 0.644 \pm 0.292 | 1.96 \pm 1.052 |
| Week 8 | 0.511 \pm 0.401 | 0.76 \pm 0.403 | 0.644 \pm 0.292 | 1.915 \pm 1.096 |
| Week 10 | 0.511 \pm 0.401 | 0.76 \pm 0.403 | 0.644 \pm 0.292 | 1.915 \pm 1.096 |
| Week 12 | 0.511 \pm 0.401 | 0.70 \pm 0.464 | 0.652 \pm 0.295 | 2.133 \pm 1.16 |

Table 8: Mean change (\pm SD) in psoriasis severity total scores from baseline-Niosomal urea 5% gel

| Treatment period | Erythema | Infiltration | Desquamation | Total score |
|------------------|-------------------|-------------------|-------------------|-------------------|
| Baseline | 0.656 \pm 0.166 | 0.611 \pm 0.169 | 0.633 \pm 0.164 | 1.900 \pm 0.499 |
| Week 2 | 0.633 \pm 0.195 | 0.478 \pm 0.249 | 0.470 \pm 0.155 | 1.581 \pm 0.599 |
| Week 4 | 0.533 \pm 0.174 | 0.412 \pm 0.169 | 0.310 \pm 0.147 | 1.255 \pm 0.49 |
| Week 6 | 0.522 \pm 0.159 | 0.412 \pm 0.169 | 0.290 \pm 0.267 | 1.224 \pm 0.595 |
| Week 8 | 0.422 \pm 0.190 | 0.406 \pm 0.169 | 0.190 \pm 0.162 | 1.018 \pm 0.521 |
| Week 10 | 0.389 \pm 0.157 | 0.406 \pm 0.169 | 0.140 \pm 0.151 | 0.935 \pm 0.477 |
| Week 12 | 0.389 \pm 0.153 | 0.372 \pm 0.155 | 0.120 \pm 0.199 | 0.881 \pm 0.507 |

Table 9: Mean change (\pm SD) in psoriasis severity total scores from baseline-Plain Urea 10% gel

| Treatment period | Erythema | Infiltration | Desquamation | Total score |
|------------------|-------------------|-------------------|-------------------|-------------------|
| Baseline | 0.750 \pm 0.032 | 0.520 \pm 0.024 | 0.640 \pm 0.012 | 1.910 \pm 0.068 |
| Week 2 | 0.650 \pm 0.042 | 0.502 \pm 0.045 | 0.522 \pm 0.023 | 1.674 \pm 0.011 |
| Week 4 | 0.632 \pm 0.020 | 0.502 \pm 0.010 | 0.402 \pm 0.024 | 1.536 \pm 0.054 |
| Week 6 | 0.540 \pm 0.042 | 0.480 \pm 0.024 | 0.380 \pm 0.035 | 1.400 \pm 0.101 |
| Week 8 | 0.482 \pm 0.021 | 0.440 \pm 0.012 | 0.342 \pm 0.036 | 1.264 \pm 0.069 |
| Week 10 | 0.462 \pm 0.024 | 0.422 \pm 0.023 | 0.302 \pm 0.067 | 1.186 \pm 0.114 |
| Week 12 | 0.420 \pm 0.052 | 0.400 \pm 0.012 | 0.282 \pm 0.045 | 1.102 \pm 0.109 |

Characterization of urea niosomes

The niosomes prepared using Trans membrane pH gradient method was taken for the characterisation and for further study.

Particle size determination

The particle size was analysed using Mastersizer 2000 ver.3.20 from Malvern instruments Ltd, Malvern, UK. The table 2 provides the particle size, percentage entrapment of the final formulations prepared using 5% DCP and poly dispersity index. The smaller poly dispersity index shows that the vesicles were of uniform size.¹⁵

Scanning electron microscopy (SEM)

The surface morphology of the vesicles of niosomes composed of surfactants, cholesterol, DCP (5%) in the molar ratio 300:300 prepared by Transmembrane pH gradient method was shown (Figure 1). They were uniform spherical in shape.

Stability

10 ml of the sample was sealed in a glass vial (niosomes suspended in phosphate buffer pH 7.4). The temperature studies were carried out in 4°C, 25°C (RT). Both niosomes and niosomal gel was stored at the same temperatures and percentage leakage over time for 6 weeks was determined (table 3).

Preparation of niosomal gel

Span 60-niosomal urea was taken for the study and incorporated in chitosan gel. Various proportion of chitosan was tried and one with optimum viscosity was chosen for the preparation of gel. The gel was prepared using 0.5%, 1%, 1.5% Chitosan which was dispersed using 10% of glacial acetic acid. The dispersion was hydrated for 4-5 hours. 5% equivalent of urea niosomal suspension, 1% glycerin, 2.5% propylene glycol and required distilled water was added to make 100g. The gel was allowed to stand overnight to remove the entrapped air. The residual acetic acid was determined in the gel. The plain gel was prepared using same formula with 10% urea.¹⁶

The stability of niosomal gel was determined at room temperature and refrigeration temperature. The formulation was found to be stable compared to Urea niosome suspension.

Skin permeation study

The release rate of niosomal gel was determined using modified Franz diffusion cell.^{17, 18} Vertical Franz diffusion cell essentially as described by Chien was used for the study. This upright diffusion cell consists of receiving chamber, which was water-jacketed; maintaining a constant 32°C temperature, simulating the temperature of skin *in vivo*. The receiving chamber was magnetically stirred to minimize diffusion boundary layers. An approximately 20mmX20mm portion of human skin (obtained from patients who had undergone abdominal fat reduction plastic surgery from the hospital) was

mounted on top of the Franz cell and clamped in place such that the dermis is in contact with the PBS in the receiving chamber and stratum corneum exposed to the air. The surface area of skin exposed to drug treatment in this diffusion cell was 9 mm in diameter.

On this 0.1g of known concentration of drug containing niosomal gel, plain and placebo gels were added. The receptor compartment, filled with 10 ml of isotonic phosphate buffer solution maintained at pH 7.4. The solution was maintained at 32°C and rotated at 50 rpm. At specified interval of time 1 ml of the solution withdrawn from the cell and replaced with fresh buffer solution. The samples were withdrawn at specified intervals and analysed at 479nm for Urea in UV 160A Shimadzu spectrophotometer. All experiments were performed for 24 hours at 32°C in triplicates (table 4).

Table 4: Diffusion of Urea across the human skin

| Time (hrs) | Percentage of drug diffusion (Mean±SD) | |
|------------|--|-------------------|
| | Plain urea gel | Niosomal urea gel |
| 2 | 16.36 ±1.45 | - |
| 4 | 25.24 ±2.34 | 7.34 ±1.56 |
| 6 | 32.26±1.23 | 12.45±2.33 |
| 8 | 46.34±3.21 | 18.23 ±2.03 |
| 24 | 68.21 ±4.23 | 24.12±1.45 |

Skin retention studies

The skin mounted on the Franz diffusion cell was carefully removed. The remaining gel adhered to the skin was scraped using a spatula and then wiped with tissue paper. The skin piece was mashed by adding 10ml of methanol and mechanically shaken in a shaker bath at 37±1°C for 36 hours for the complete extract of the drug. The filtrate was removed and analysed spectrophotometrically.¹⁸ Student t test was performed and the all the formulations were significantly different from each other. The percent retained on the skin was shown in table-5.

Table 5: Percent of drug contained on the human skin (mean±SD)

| Formulation | Percent of drug retained on human skin mean ± std |
|-------------------|---|
| Plain urea gel | 18.14 (±0.45) |
| Niosomal urea gel | 40.90 (±0.33) |

Human repeated insult patch test (HRIPT)

This test was performed on healthy human volunteers to determine the irritation and/or allergic contact sensitization potential of a test article (gel) after repetitive patch applications to the skin of human subjects before subjecting formulations on patients.¹⁹ Ten human volunteers were selected for the study. Approval was obtained from ethical clearance committee of the hospital to conduct human volunteer study (Victoria hospital, Bangalore, India). An informed consent from human volunteers was obtained before start of the study.



Human volunteers were randomly assigned. There were 7 males and 3 females with age ranging from 25 to 55 years. There were 3 different formulations tested on these human volunteers.

The HRIPT test performed on human volunteers did not produce any irritation or sensitization of the skin. The 3 formulations were taken for the double blind placebo controlled study.

Methodology

Induction Phase

Approximately 0.2 grams of each gel was applied to the subject's back, using occlusive patches. Semi-occlusive tape was applied. Twenty-four hour patch applications were made on a Monday, Wednesday, Friday schedule. Twenty-four hour rest periods followed Tuesday and Thursday removals and a 48-hour rest period followed the Saturday removal. The site was scored by a dermatologist just prior to the next patch application. This procedure was repeated until nine inductions of the test article were made on the same skin site.

Challenge Phase

Approximately 2 weeks after application of the last induction patch, a challenge patch was applied to a previously unpatched (virgin) site, adjacent to the original induction patch site.

The challenge site was scored 24 and 72 hours after application. The subjects were asked to report any delayed reactions, if any after the final challenge patch reading.

Scoring

The area was scored with 0-5 point scale. In case a subject developed a level 2 reaction or greater during the induction phase, the patch was applied to an adjacent fresh site for the next application. If a level 2 or greater reaction occurred on the new site, no further induction applications were made. However, any reactive subjects were subsequently patched with the test article on a virgin test site during the challenge phase of the study.

Double blind placebo controlled study

The study was a single centered double blind placebo controlled which compared 3 treatments.

Extent and severity was measured by Psoriasis Area and Severity Index (PASI). The severity of the erythema, infiltration, desquamation and overall severity was assessed for the presence of lesions on the trunk, upper arm or lower arm. The PASI score was calculated as the sum of severity of main symptoms multiplied by the numerical value of the areas involved with various percentages of the 3 main body areas. The scoring was done depending on the area of the lesion.²⁰

a. Inclusion criteria: Patients with stable plaque psoriasis involving <25% of the body surface area and or palmoplantar psoriasis were included in the study.

b. Exclusion criteria: Patients with psoriatic lesions on face and or scalp, administration of other systemic therapy or intralesional therapy or UV radiation for at least 2 months prior to inclusion in the study, children, pregnant and lactating mothers, patients with above 25% lesion were excluded from the study.

c. Patient population: 40 patients between ages of 22 and 60 years having psoriasis from 2- 8 years were chosen for the study to determine the efficacy of niosomal gel formulations.

Clinical efficacy, tolerability of the formulations was checked by the physical inspection and overall response of the patients to the treatment. The progress of the treatment was determined by PASI scoring on biweekly assessment. A fresh tube of coded gel was replaced in every visit. Plain urea gel and placebo were given twice a day application and niosomal urea gel was given once a day application. The niosomal urea gel group was given placebo for second application. The PASI scoring was used to assess the remission of desquamation, erythema and infiltration. The placebo, plain gel and niosomal gel were compared using analysis of variance (ANOVA), and differences greater than $p < 0.05$ were considered significant.

The tables 7-9 shown below provides the total score of psoriatic patients from baseline to 12 weeks.

The efficacies of niosomal formulations were significantly ($P < 0.05$) different from the placebo and plain gel. The formulations made were better and once-a-day application also improved the patient compliance compared to other marketed preparations which are applied twice or thrice daily.

RESULTS AND DISCUSSION

Urea niosomes was prepared by lipid layer hydration and transmembrane pH gradient method. The transmembrane pH gradient method with span 60 produced better entrapment efficiency compared to other method and other spans. In transmembrane method a pH differential exists across the niosome membrane with a lower pH inside niosomes. The amine drug added external to the niosome and crosses the membrane barrier in the unionized state. Once inside the niosome the drug becomes protonated and is unable to leave the niosomes. The acid pH inside the niosome acts as an internal trap. In case of lipid layer hydration method since the urea molecule was small the entrapment efficiency may be less compare to transmembrane methods.²¹ In general, span 60 and span 40 found have highest entrapment efficiency and produced less leaky niosomes. The span 60 niosomes produced slightly bigger niosomes than span 40 and span 60, which was also the reason for the increase in entrapment ratio. But still higher entrapment ratio was not achieved may be due to niosomes membranes were permeable to low molecular weight compounds and do release encapsulated solutes with time.^{21, 22}



The poly dispersity index showed that there was uniform distribution of particles. The short-term stability studies showed that span 60 niosomes prepared using trans membrane method was stable and gel was much stabler than the niosomes. The morphology of urea niosomes was found to be spherical. The retention study showed that compared to plain gel, niosomal gel retention on the skin was higher. Urea increases the diffusion of active substances in formulations. This may be reason for plain urea gel deposited lesser concentration of urea on the skin compare to niosomal gel. Chatoyant, a biocompatible polymer, possesses anti microbial, anti fungal and anti-inflammatory property. Hence these two properties were an added advantage to the treatment.¹¹

The healthy human volunteers study (HRIPT) of placebo, plain gel and niosomal gel did not produce any irritation on human volunteers.

The PASI scoring was used to determine the improvement of lesions. Urea gels did not produce significant improvement in psoriasis patients. But the desquamation has reduced significantly compared to erythema and infiltration in all the formulations and also in comparison to placebo ($p < 0.05$). But both plain gel and niosomal gel were equally effective in reducing the erythema and infiltration. Also the amount of urea used for the niosomal gel was only 5%. This niosomal gel can be given once daily along with other antipsoriatic formulations and this may act as a best adjuvant for the treatment of psoriasis also in other dry skin conditions.

CONCLUSION

The urea niosomes prepared using Transmembrane pH gradient method was found to be higher entrapment efficiency using 5% of DCP. The human volunteer study did not produce any skin irritation. Chitosan with its antifungal and anti-inflammatory effect supported the action of urea.

The desquamation denotes superiority of niosomal urea gel in reducing the hyperproliferation cells. The study conclusively proved that niosomal urea could be used as adjuvant in the treatment of psoriasis. The clinical study could be extended to multicenters to prove the efficacy of the formulation.

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