Formulation and development of antipsoriatic herbal gelcream

Shantanu Kuchekar and Kiran Bhise*
Department of Pharmaceutics, MCE Society’s Allana College of Pharmacy, Azam Campus, Pune 411 001, India

Received 20 September 2011; revised 29 December 2011; accepted 30 January 2012

This study presents formulation and development of patient friendly antipsoriatic topical gelcreams using Simulgel NS and Sepicide HB with Myrrh oil. Optimized formulation F5 depicted that gelcream had a viscoelastic nature with good creep recovery, and non-Newtonian behavior. Stability studies for three months at 40±2°C and 75±5% RH of Formulation F5 showed no change in colour and consistency, and pH remained between 5.7 and 5.9. Primary skin irritation test conducted on 30 healthy volunteers demonstrated nonirritating nature of F5. Thus Simulgel NS and Sepicide HB (conc., 2% w/v each) were found to give better anti-inflammatoty gelcream containing myrrh oil with good consistency and stability.

Keywords: Factorial design, Gelcream, Myrrh oil, Psoriasis

Introduction

Psoriasis is an inflammatory condition of skin, and has affected 1-2% of US population. Patients with psoriasis experience itching, scaly, painful, and disfiguring skin lesions. Although there is no cure for psoriasis, several treatments can minimize skin lesions and associated symptoms. Common triggers include alcohol, smoking, an injury to skin (cut, scrape, insect bite, sunburn), stress, antimalarial and antiinflammatory medicines including ibuprofen, ACE inhibitors and beta blockers. Some studies have addressed research on allopathic topical antipsoriatic drug. However, limited work has been performed on the formulation of antipsoriatic creams with traditional medicines. Topical antipsoriatic formulations have mostly been designed as ointments or creams that have disadvantages of stickiness, irritation, oily feeling and poor spreadability. However, gelcreams are preferred for topical application due to easy spreadability, cooling and nonoily effects. Myrrh, an oleo-gum-resin obtained from Commiphora myrrha (T. Nees) Engl., contains volatile oil (2-10%), which is composed predominantly of sesquiterpenes, sterols, and steroids. This study presents formulation of a herbal antipsoriatic gelcream.

Experimental Section

Marker Myrrh oil was purchased from Cosmochem Research Lab; Simulgel NS and Sepicide HB were obtained as gift samples from Kreglinger Supplier, Belgium, Europe and other reagents and solvents were purchased from Loba Chemie Pvt Ltd, Mumbai.

Extraction of Oil

Dried Myrrh gum (50 g) was crushed and introduced in half filled 500 ml round bottom flask with distilled water. Flask was attached to Clevenger apparatus. Mixture was heated at 80-90°C for 4-5 h. Further oil layer was separated from aqueous layer and stored in tightly sealed vials.

Characterization of Oil, Polymer and Preservative

Oil, polymer Simulgel NS and preservative Sepicide HB were analyzed for color, odour, appearance, solubility, pH and viscosity. Myrrh oil was dissolved in ethanol and phosphate buffer pH 5.8 (7:3) to prepare dilutions (conc., 1-10 µg/ml). Calibration curve was plotted by using UV/VIS spectrophotometer- JASCO V 530 at λmax (Fig. 1).

Gelcream Formulation and Evaluation

Trial batches of gelcreams were prepared by mixing together 5% of Myrrh oil with Simulgel NS and Sepicide HB in different ratios (1:1, 2:1, 1:2, 2:2, 2:3, 3:2, 3:3, 3:4, 4:3); glycerine, propylene glycol and rose oil with
continuous stirring using Ultra turrax. Final volumes of gelcreams were adjusted with distilled water. Trial batches were evaluated for appearance, pH, spreadability, phase separation, viscosity and in-vitro diffusion studies. For appearance, trial batches were inspected visually for clarity, color and particulate matter. For pH, each trial batch was measured on calibrated digital pH meter (model 802, Systronic). For phase separation, all trial batches were subjected to centrifugation at 3000 rpm for 30 min at room temperature (RT) and were inspected for creaming, flocculation and phase separation. Viscosity of trial batches was measured at 25°C with Brookfield Viscometer (Model No.CAP-2000, Brookfield Engineering Labs Inc, Middleboro, USA) at 10 rpm for 20 s run time.

Spreadability

Sample (0.5 g) was placed between two glass slides (7.5 cm x 2.5 cm) of spreadability apparatus. A weight (100 g) was put on the upper slide for 1 to 2 min to enable an expulsion of entrapped air between slides for ease of a uniform film of gelcream. Weight was removed and top slide was subjected to a pull of 5 g. Time necessary for top slide to travel premarked distance of 6.5 cm was noted to estimate relative spreadability of different gelcreams. Spreadability was calculated as

\[ S = \frac{M \times L}{T} \]

where, \( M \) = weight tide to upper slide, \( L \) = length moved on glass slide and \( T \) = time for movement.

In vitro Diffusion Studies

It was performed on a prehydrated cellophane membrane in distilled water (24 h before use), fixed to Keshary Chein cell (capacity, 10 ml). Trial batch samples (1 g each) were placed in donor compartment of diffusion cell that was immersed in 10 ml of solvent system [ethanol & PBS pH 5.8 (7:3)] in receptor compartment. Whole system was put to agitation on 8 station magnetic stirrer (Mega, 8 stations, Spectralab, India) at 37°C. Samples

![UV spectrum and calibration curve](image)
Factorial Formulations and Evaluation of Factorial Batches

A $3^2$ factorial design was used for optimization of batches. Two variables [conc. of Simulgel NS $(X_1)$ & Sepicide HB $(X_2)$ at 1.5, 2.0 and 2.5% (w/v) respectively] were fixed at three levels +1, 0 and -1. The levels were decided on the basis of trial batches and their evaluation. Nine factorial batches (Table 1) were evaluated and effect of individual variable was studied according to response surface methodology (RSM) for dependent responses including viscosity $(Y_1)$ and cumulative% drug release $(Y_2)$.

Table 1—Factorial batches of gelcream in uncoded form

<table>
<thead>
<tr>
<th>Factorial batches*</th>
<th>Simulgel</th>
<th>Sepicide</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>F2</td>
<td>2.0</td>
<td>1.5</td>
</tr>
<tr>
<td>F3</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>F4</td>
<td>1.5</td>
<td>2.0</td>
</tr>
<tr>
<td>F5</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>F6</td>
<td>2.5</td>
<td>2.0</td>
</tr>
<tr>
<td>F7</td>
<td>1.5</td>
<td>2.5</td>
</tr>
<tr>
<td>F8</td>
<td>2.0</td>
<td>2.5</td>
</tr>
<tr>
<td>F9</td>
<td>2.5</td>
<td>2.5</td>
</tr>
</tbody>
</table>

*For all batches (F1-F9), other values were as follows: myrrh oil, 5%; glycerine, 1%; propylene glycol, 1%; fragrance, 1% and water, up to 50%.

Factorial batches were evaluated for appearance, pH, phase separation, spreadability, viscosity and in-vitro diffusion drug release. For regression analysis, effect of formulation variables on responses was statistically evaluated by applying Design-Expert®, version 8.0. To describe response surface curvature, design was evaluated as $Y = \beta_0 + \beta_1X_1 + \beta_2X_2 + \beta_{12}X_1X_2 + \beta_{12}X_1X_2^2 + \beta_{22}X_2^2$, where $Y$ is response variable, $\beta_0$ is constant, $\beta_{1}, \ldots, \beta_{22}$ regression coefficients, $X_1$ and $X_2$ stand for main effect and $X_1X_2$ are interaction terms that demonstrate response changes with simultaneous changes in factors.

Evaluation of Optimized Batch of Gelcream

Rheological Studies

Rheological analyses were performed in triplicate using a stress control rheometer (Reologica Rheometer Model ViscoTech CC-K6) equipped with a cone-plate geometry (4/40) operating in oscillation mode. For Oscillation Stress Sweep (OSS) test, sample (2 g) of optimized batch was exposed to increasing stress at 25°C, at a constant frequency (1 Hz) and different ranges of stresses (0.1-10 Pa, 1-30 Pa, 1-60 Pa) and G2 values were plotted in logarithmic scale. For Oscillation Frequency Sweep (OFS) test, sample (2 g) of optimized batch was exposed to a stepwise increasing frequency at a constant stress (obtained from OSS = 15 Pa); 1-5 Hz frequency range, in the field of linear viscoelasticity, at 25°C. Frequency, G2 and G3 values were plotted in logarithmic scale. Creep recovery test was carried out at 25°C at a stress below the yield value, which was maintained constant for 10 s. It was then instantly removed and recovery was followed for 50 s. Creep compliance $J_c$ was monitored against time. The test was used to calculate sample viscosity from linear stress–strain region of retardation curve. For viscometry test, sample (2 g) of optimized batch was exposed to increasing stress from 1 Pa to 60 Pa and viscosity was recorded against stress at 25°C.

Primary Skin Irritation Test

Skin irritation test was performed on 30 healthy human volunteers (age 22-28 y, av. wt 60 kg). Gelcream was applied topically on the arm twice daily at an interval of 12 h and were monitored for development of rashes / irritations followed by photographic imaging of skin after subsequent application for 72 h (at completion of study period) and were compared with images taken at 0 h (just prior to first application). Protocol number provided by Ethics Committee is M.C.E.S/PHARMA/EC/1-2011.

Stability Study

Optimized batch was packed in an impermeable tightly sealed container and stored for three months at 40±2°C and 75±5% RH (condition of accelerated stability testing) as per ICH guidelines and was tested for appearance, pH, change in consistency and phase separation.

Results and Discussion

Characterization of Myrrh oil, Simulgel NS and Sepicide HB

Myrrh oil (yellow amber to green oily liquid; $\lambda$ max 225 nm), Simulgel NS (whitish) and Sepicide HB (transparent) had following values, respectively: odour, balsamic, characteristic, characteristic; solubility, alcohol, cold water, cold water; pH, - , 5.6, 6.8; and viscosity, -, 23.2, 5.9 cP.
Evaluation of Factorial Batches

Viscosity of gelcream of Factorial batches (Table 2) increased as concentration of Simulgel NS increases and vice versa with Sepicide HB. Formulation F5 showed better viscosity (17 cp) with good consistency, and better drug release (84.08%) during 2 h (Fig. 2) as compared to other formulations.

Regression Analysis

Effect of Formulation Variables on Viscosity

Quadratic model was found to be significant (F value 16.71). Factorial equation for viscosity (Y) was \( Y = 17.89 + 5.67X_1 + 0.33X_2 + 2.00X_1X_2 - 3.33X_1^2 - 1.33X_2^2 \). As concentration of Simulgel NS increases gradually (Fig. 3a), viscosity of gelcreams increases. Thus thickening property of Simulgel NS improved with an increase in its concentration. As concentration of Sepicide HB increases, moisturizing capacity of gelcream also increases with decrease in viscosity. Hence optimum concentrations of Simulgel NS and Sepicide HB were used to improve viscosity and consistency respectively.

Effect of Formulation Variables on Drug Release%

Quadratic model was found to be significant (F value of 16.71). Factorial equation for drug release (\( Y_2 \)) was \( Y_2 = 81.78 - 11.83X_1 - 0.50X_2 - 4.00X_1X_2 - 4.17X_1^2 + 2.83X_2^2 \). As concentration of Simulgel NS increases, viscosity of gelcream increases causing thickening of gelcreams (Fig. 3b). Drug requires more time to get diffused from gelcream network and thus drug release retards. As concentration of Sepicide HB increases, viscosity is decreased and drug release is faster. Hence optimum concentration of Simulgel NS and Sepicide HB were used for good viscosity of gelcream and drug release respectively. F5 has optimum concentration (2%) of Simulgel NS and Sepicide HB with optimum viscosity (17 cp) and drug release (84%). On the basis of experimental (viscosity, 17; drug release, 84.089) and predicted values (viscosity, 17.88; drug release, 81.777), F5 was found as optimized formulation.
Rheology of Optimized Batch F5

OSS test allows determination of linear viscoelastic region (LVR) of the sample and therefore consequent choice of stress value to use in other oscillation tests. As LVR region (1.11E+01 - 3.03E+01) is large, gelcream was found to be more stable (Fig. 4a). Under OFS test (Fig. 4b), G2 was greater than G3, indicating viscoelastic nature of F5. Creep recovery test of F5 at 25°C (Fig. 4c) indicated that as material starts to flow, strain increased constantly as long as stress was applied and when stress is set to zero, deformation is reversible and recovered, indicating viscoelastic characteristics of gels. Under effect of shear stress on optimized batch F5 (Fig. 4d), gelcream sample showed non-Newtonian behavior.

Primary Skin Irritation Test of Optimized Batch F5

F5 was found stable and free from skin irritation on application to healthy human volunteers.

Stability Studies

Stability of optimized formulation F5 was performed at accelerated stability studies for 3 months at 40±02°C and 75±05% RH as per ICH guidelines. During 3 months, no change was observed in gel appearance (slightly white shiny gel) and consistency and there was no phase separation. pH remained 5.9 in first two months and went down to 5.7 in third month.

Conclusions

Development of antipsoriatic herbal gelcream using Simulgel NS (2% w/v), Sepicide HB (2% w/v) and Myrrh
oil gave better anti-inflammatory gelcream with good consistency and stability.

Acknowledgement
Authors thank Kreglinger Supplier, Belgium for gift samples (Simulgel NS & Sepicide HB).

References
4. www.whelehans.com
7. www.harleystreetcosmetic.com