Optimization And Evaluation Of Polyherbal Topical Cream

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**ABSTRACT**

Herbal plants and their combination report therapeutic as a well synergistic effect that has been recognized in medicine. So, taking into account this factor, the polyherbal topical cream formulation was prepared by using plant extracts to improve patient compliance, enhance antimicrobial spectrum and enhance aesthetic properties. The study focused on the topical polyherbal cream formulation for delivery of the active constituents present in plants to improve skin diseases. The plant extracts of Ocimum sanctum (OS), Rubia cordifolia (RC), Glycyrrhiza glabra (GG) were utilized for the preparation of cream. The formulated cream was subjected to different evaluation parameters and the results depicted that the spreadability of the formulation was low (17.80 ± 1.10 g cm/sec) and that indicates trouble-free spreading, free from grittiness. In rheological properties all the cream formulations also exhibited the same non-Newtonian behaviour. Polyherbal topical cream showed potential antimicrobial activity against all selected microorganisms. Polyherbal topical cream (PHC-5) was ideal in terms of viscosity than other formulations and showed good drug release. Thus, the formulated polyherbal cream was found to be stable in terms of all physicochemical properties.

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**INTRODUCTION**

In the present era, the use of herbal cosmeceuicals is rapidly increasing. As these possess varied properties in terms of availability of natural resources, development of successful products and preparation of good quality, these are the potentials in the market (Parashar et al., 2013). Cosmetics are those products that cleanse, beautify or alter the appearance that is applied to the body to cleanse, change the look and enhance beauty. For most skin conditions, creams are used for the various benefits they possess (Dureja et al., 2005). The basic defence mechanism of the body against disorders is human skin. The basic three layers of the skin include the epidermis, dermis and hypodermis. These layers of skin have specific properties and role that make them act as a barrier against foreign material to enter the body through the skin (Tabassum and Hamdani, 2014). The function of the skin is to protect the underlying muscles, ligaments, internal organs etc (Marks and Miller, 2006). It also interfaces with the environment to protect against pathogens, with loss of excessive water (Proksch et al., 2008; Madison, 2003). Other functions include regulation of temperature, insulation, sensation, synthesis and storage of Vitamin D against UV, water-resistance etc (Grice et al., 2009).

So, the objective was to prepare a polyherbal cream for topical use that is useful for the management of various skin diseases by use of extracts of Ocimum sanctum (OS), Rubia cordifolia (RC), Glycyrrhiza glabra (GG).
**MATERIALS AND METHODS**

**Materials**

*Ocimum sanctum*, *Rubia cordifolia*, *Glycyrrhiza glabra* were procured from a local market and authenticated.

**Methods**

The extraction of collected plant materials was carried out using established methods. The part of the individual plant was selected, cleaned and powdered to get the crude drug. To obtain non-polar extracts, the air-dried coarse powders of *Ocimum sanctum*, *Rubia cordifolia* and *Glycyrrhiza glabra* were extracted separately by a Soxhlet extraction process using petroleum ether and chloroform. These extracts were further successively extracted with respective polar extracts hydroalcoholic (60:40) solution. The preservation of extracts was done in a refrigerator, by use of optimum pressure and temperature, to dryness. The extracts obtained were filtered, evaporated to dryness to yield semi-solid paste and preserved in a refrigerator for further study (Azwanida, 2015).

**Experimental design**

To determine the correlation between independent and dependent variables, software named DOE (Design of experiment, 12.0). At a 5% level of significance, analysis of variance was implemented. In a design expert, the model was screened out by analyzing adjusted R2 value, which has to be<1. The topical formulations of polyherbal cream were optimized by 3² factorial design. The factors were calculated by low, medium and high, at 3 levels indicating (−1, 0, +1) respectively, as given in Tables 1 and 2. Two independent formulation variables were evaluated: a) concentration of glycerin b) concentration of methylcellulose. 3² Factorial design for the formulation of polyherbal topical cream on the basis of preliminary studies, using optimization studies. The dependent factors were drug release and viscosity.

**Preparation of polyherbal cream**

Creams were formulated as given in Table 3 by first preparation of the two phases, aqueous and oil, separately. In the aqueous phase, 1gm of methylcellulose polymer was mixed in hot water (at around 75°C) further cooled at around 5°C with nonstop stirring in 100ml of water, then 1ml each of glycerin and propylene glycol was added with constant stirring. This prepared aqueous phase was added to the three preselected extracts in different concentrations. The oil phase was prepared, by melting the 0.9gm of beeswax at 70°C, with intermittent stirring and to it, 1 ml of almond oil was mixed. After preparation of both the phases, these were mixed together to get a mixture. To this, prepared above mixture, 0.1 gm of sodium benzoate as preservative and 0.8gm of zinc oxide as a skin whitener was added, with continuous stirring.

Total 9 batches were prepared, in which batches PHC 7 to PHC 9, the concentrations of glycerin were 2%w/v, propylene glycol 1%w/v, methyl cellulose 1, 1.5 and 2 %w/v, respectively, while the concentrations of other ingredients were the same as other batches.

**Phytochemical analysis of extracts**

Phytochemical analysis of different extracts was carried out to record the presence of prominent chemical constituents by the following tests: Test for steroids, Test for triterpenoids, Test for glycosides, Tests for saponins, Tests for carbohydrates, Tests for alkaloids, Tests for Flavonoids, Tests for tannins (T et al., 2015), tests for proteins as and results are depicted in Table 4.

**Evaluation of polyherbal cream**

**Physical parameter**

The physical parameters of individual topical cream studied at room temperature and at accelerated temperature.

**Homogeneity**

All the topical cream was tested individually by visual inspection and touch.

**Appearance**

It was determined for individual topical cream formulation in terms of colour, pearlescent, roughness to grade accordingly.

**pH measurement**

To measure the pH, 1 gm of respective topical cream was noted by pH meter on dilution in distilled water of 9ml.

**Spreadability**

One gram of respective topical cream individually by placing it on a plate placed on a lower plate, while the sample was with an upper plate over it. A known weight was applied to generate constant force. The observations were done thrice.

**Viscosity measurement**

The viscosity of respective topical cream was measured and compared individually before and after the accelerated test with Brookfield Viscometer, spindle 763 at100 rpm.

**Rheological studies**
The formulated respective topical cream individually was studied for its rheological property. 10 gms of respective topical cream was taken in beaker of 10 ml and kept used for 1 hr. To see whether cream existed in liquid form or not, the beaker was leaned to one side. Beaker was shaken to and fro for 5 min using a mechanical shaker to check there was a change inconsistency. The pourability was also found by titling the beaker.

As per ICH guidelines: The stability studies were performed individually for respective topical cream by keeping it at different conditions at three months period like 4 °C, 25°C ± 2 °C/60% relative humidity ± 5% RH and 40°C ± 2 °C/75% RH ± 5% RH. Various parameters were recorded.

Diffusion study
To study the drug release, Franz diffusion cell (25 ml) were utilized. 1 gm of formulation over a fixed area by use of cellophane. The receptor contained a buffer of pH 7.4 and stirred by a magnetic mechanism. The batches analyzed 270 nm, using UV spectrophotometer, and drug release determined.

RESULTS AND DISCUSSION

Pharmacognostic evaluation
Evaluation of polyherbal formulations
Physical evaluation
It includes appearance, homogeneity, Spreadability, after feeling, smear type, its removal and Rheological studies for various topical cream formulation.

Homogeneity
It was found that the cream was homogeneous and smooth and consistent in nature. Cream possessed uniformity in distribution. Visual appearance and touch confirmed this test.

Appearance
The prepared creams of individual extracts were light yellow to brown in colour, having an appropriate appearance. Also, it had a pleasant aroma.

pH of polyherbal topical cream formulation
The pH was in the range of 6.4 to 7.2, as shown in Figure 1.

Spreadability
The spreadability of the formulation was low (17.80 ± 1.10 g.cm/sec) and this indicated smooth and free from gritty nature.

Experimental Design and Statistical Analysis
Design based on $3^2$ factorial was selected, for the study, as it helps to see the effect of factors on the response, by least experimental runs. The viscosity of the formulations was found to be in the range 1546 to 1554 cps, as shown in Table 5.

Multiple Regression Analysis
To make possible the response parameters, by the effect of the independent variables, a mathematical model predicts the value of response and that generates the polynomial equations, that is useful for evaluation.
Table 1: Independent variables and their corresponding levels for optimization studies

| Independent variables (%w/w) | Levels          |
|------------------------------|-----------------|
| Concentration of glycerin A  | -1  0 +1        |
| Concentration of methylcellulose | 1.0  1.5  2.0  |
### Table 4: Phytochemical Screening of Ocimum sanctum, Rubia cordifolia, Glycyrrhiza glabra

| Plant Constituents | Test performed | Ocimum sanctum | Rubia cordifolia | Glycyrrhiza glabra |
|--------------------|----------------|----------------|------------------|-------------------|
| Steroids Test      | Test of Salkowski | +             | +                | +                 |
|                    | Test of Liebermann-Buchard | +             | +                | +                 |
| Triterpenoids Test | Test of Salkowski | -             | +                | +                 |
|                    | Test of Liebermann-Buchard | +             | +                | +                 |
| Glycosides Test    | Test of Balget’s | -             | +                | +                 |
|                    | Test of Keller-Killiani | -             | +                | +                 |
|                    | Test of Legal | -             | -                | +                 |
|                    | Test of Borntrager’s | -             | -                | +                 |
| Saponin Test       | Test of Foam | ++            | +                | +                 |
| Carbohydrates Tests | Test of Molisch’s | -             | +                | -                 |
|                    | Test of Barfoed’s | -             | -                | -                 |
|                    | Test of Fehling’s | -             | +                | -                 |
|                    | Test of Benedict’s | -             | -                | -                 |
| Alkaloids Test     | Mayer’s Reagent | +             | -                | +                 |
|                    | Hager’s Reagent | +             | +                | +                 |
|                    | Dragendorff’s Reagent | +             | +                | +                 |
| Flavonoids Tests   | Test of Ferric-chloride | +             | +                | +                 |
|                    | Test of Shinoda | +             | +                | +                 |
| Tannins Test       | Solution of FeCl3 | +             | +                | +                 |
|                    | Test of Gelatin | +             | +                | +                 |
| Proteins Test      | Test of Millon’s | -             | -                | -                 |
|                    | Test of Xanthoproteic | -             | -                | -                 |
|                    | Test of Biuret | -             | +                | -                 |
|                    | Test of Ninhydrin | -             | -                | -                 |

*Present(+) Absent (-)*

### Table 5: Viscosity and Drug release for the prepared polyherbal cream

| Formulation number | Factor 1 (A) | Factor 2 (B) | Viscosity (cps) | Drug release (%) |
|--------------------|--------------|--------------|-----------------|------------------|
| PHC1               | -1           | -1           | 1546±0.57       | 87.4±0.57        |
| PHC 2              | -1           | 0            | 1550±2.30       | 91.2±0.60        |
| PHC 3              | -1           | +1           | 1550±1.52       | 96.5±1.05        |
| PHC 4              | 0            | -1           | 1554±1.73       | 93.3±0.64        |
| PHC 5              | 0            | 0            | 1554±0.57       | 93.1±0.45        |
| PHC 6              | 0            | +1           | 1548±1.15       | 90.1±0.45        |
| PHC 7              | +1           | -1           | 1552±1.52       | 86.4±0.62        |
| PHC 8              | +1           | 0            | 1551±0.57       | 89.2±0.47        |
| PHC 9              | +1           | +1           | 1544±1.52       | 90.3±0.45        |

*Data are mean values (n=3)±SD*
Table 6: ANOVA Analysis on Viscosity

| Basis                  | Sum of Squares | Degree of freedom | Square Mean | Value of F | Value of P |
|------------------------|----------------|-------------------|-------------|------------|------------|
| Type Model             | 72.28          | 5                 | 16.86       | 9.88       | 0.0479     |
|                        |                |                   |             |            | significant|
| A-Con Of Glycerin      | 2.49           | 1                 | 2.49        | 0.8670     | 0.4205     |
| B-Conc Of Methyl       | 44.46          | 1                 | 44.46       | 15.50      | 0.0292     |
| Cellulose AB           | 11.18          | 1                 | 11.18       | 3.90       | 0.1428     |
| A²                     | 0.6033         | 1                 | 0.6033      | 0.2103     | 0.6777     |
| B²                     | 2.07           | 1                 | 2.07        | 0.7215     | 0.4581     |
| Residual               | 8.60           | 3                 | 2.87        |            |            |
| Cor Total              | 92.89          | 8                 |             |            |            |

Table 7: Results of Regression Analysis for Response Viscosity

| Std. Dev. | Mean  | C.V. % | R²     | Adjusted R² | Predicted R² | Adeq. Precision |
|-----------|-------|--------|--------|-------------|--------------|-----------------|
| 1.69      | 1549.89 | 0.1093 | 0.9074 | 0.7530      | 0.0470       | 7.6046          |

Table 8: ANOVA Analysis on Drug Release

| Basis                  | Sum of Squares | Degree of freedom | Square Mean | Value of F | Value of P |
|------------------------|----------------|-------------------|-------------|------------|------------|
| Type Model             | 74.33          | 5                 | 14.87       | 10.97      | 0.0383     |
|                        |                |                   |             |            | significant|
| A-Conc Of Glycerin     | 1.23           | 1                 | 1.23        | 0.9086     | 0.4108     |
| B-Conc Of Methyl       | 7.88           | 1                 | 7.88        | 5.82       | 0.0949     |
| Cellulose AB           | 6.58           | 1                 | 6.58        | 4.85       | 0.1149     |
| A²                     | 47.12          | 1                 | 47.12       | 34.76      | 0.0097     |
| B²                     | 11.32          | 1                 | 11.32       | 8.35       | 0.0630     |
| Residual               | 4.07           | 3                 | 1.36        |            |            |
| Cor Total              | 78.40          | 8                 |             |            |            |

Table 9: Results of Regression analysis for response drug release

| Std. Dev. | Mean  | C.V. % | R²     | Adjusted R² | Predicted R² | Adeq. Precision |
|-----------|-------|--------|--------|-------------|--------------|-----------------|
| 1.16      | 90.83 | 1.28   | 0.9481 | 0.8617      | 0.4916       | 9.5799          |

3.22509 CONC OF METHYL CELLULOSE²

The equations I term of actual factors can be used to make predictions about the response for given levels of each factor. The results are shown graphically in Figure 2.

Study of Rheology

It was non-Newtonian. Most topical formulations, when applied on the surface of the skin, show non-Newtonian behaviour. Thus, all the cream formulations also exhibited the same Non-Newtonian behaviour.

The F-value of 10.97 implies the model is significant. The 3.83% high value of F-value may be due to noise. Model is found to be significant from the P-values that is lesser than 0.05, as shown in Table 8.

Above Table ?? tells about the predicted R² - 0.4916 that is not close to the adjusted R² - 0.8617.

Coded form final equation

Drug release = +95.94 -0.4214 A +1.14 B +1.64 AB
Actual form final equation

\[
\text{Drug release} = +55.28451 + 37.672 \ \text{CONC OF GLYCERIN} + 15.09623 \ \text{CONC OF METHYL CELLULOSE} + 6.54099 \ \text{CONC OF GLYCERIN} \times \text{CONC OF METHYL CELLULOSE} - 16.10884 \ \text{CONC OF GLYCERIN}^2 - 7.54410 \ \text{CONC OF METHYL CELLULOSE}^2.
\]

The equation gives a prediction about the response, result of drug release is shown graphically in Figure 3.

Finalization of Optimized Formula

The results proved the selection of the final optimum formulation by the results of the evaluation tests. Thus, the optimized formulation was PHC5 which had a pH of 7.0, viscosity of 1554 cps and drug release of 93.1%.

Stability studies

When the formulations were examined for stability, and it was found that there existed no change in the formulations. Hence, polyherbal creams were found to be stable in terms of colour, pH and viscosity.

CONCLUSIONS

The polyherbal cream was formulated and evaluated by the use of excipients. Thus, this cream proved to be of great potential for topical application due to the properties it possessed. The pH range was observed to be between 6.4 to 7.2. The polyherbal cream also possessed good spreadability, with good emollient property and viscosity. Thus, it can be concluded that the use of a combination of plant extracts for the formulation of polyherbal cream could provide synergistic effect of all these individual plants.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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