INTRODUCTION

Fungal infection of the skin is nowadays one of the common dermatological problems. The physicians have a wide choice for treatment from solid dosage to semisolid dosage form and to liquid dosage formulation. Among the topical formulation, clear transparent gels have widely accepted in both cosmetics and pharmaceuticals [1]. Topical treatment of dermatological disease as well as skin care, a wide variety of vehicle ranging from solids to semisolids and liquids preparations is available to clinicians and patients. Within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparation [2]. For many decades treatment of an acute disease or a chronic illness has been mostly accomplished by delivery of drugs to patients using various pharmaceutical dosage forms, including tablets, capsules, pills, suppositories, cream, gel, ointments, liquids, aerosols and injectable, as drug carriers. Delivery of drugs to the skin is an effective and targeted therapy for local dermatological disorders. This route of drug delivery has gained popularity because it avoids first-pass effects, gastrointestinal irritation, and metabolic degradation associated with oral administration. Due to the first pass effect, only 25-45% of the orally administered dose reaches the blood circulation. In order to bypass these disadvantages, the gel formulations have been proposed as a topical application. Gels are defined as “semisolid system in which a liquid phase is constrained within a polymeric matrix in which a high degree of physical and chemical cross-linking introduced”.

Itraconazole, syntho antifungal agent of the imidazole class; it works by slowing the growth of fungi that cause infection. It is used to treat fungal infection. Triazole drug targets the fungal-specific synthesis of membrane lipids. Itraconazole inserts preferentially into fungal membranes and disrupts their function. 5-fluorocytosine targets fungal-specific DNA replication [3]. Hydroxypropyl methylcellulose (HPMC), Carbopol 934p, has been used as hydrophilic polymers topically in gel drug delivery system [4].

MATERIALS AND METHODS [5, 6]

Material

Itraconazole, HPMC, carbopol934, trimethanolamine, glycerine, Methylparaben, propylparaben, water.

Method

Polymer (like Carbopol 934p or HPMC) and purified water were taken in a beaker and allowed to soak for 24 h. To this required amount of drug (2 gm) was dispersed in water and then Carbopol 934p or HPMC was then neutralized with sufficient quantity of Triethanolamine. Glycerine as a moistening agent, methylparaben and Propylparaben as preservatives were added slowly with continuous gently stirring until the homogenous gel was formed.

Table 1: Optimized formulae of Itraconazole gel

| Formulation code | Ingredients | Drug | Carbopol | HPMC | Water | Alcohol | Methyl | Propyl | Glycerine | Triethanolol |
|-----------------|-------------|------|---------|------|-------|---------|--------|--------|-----------|-------------|
| F1              |             | 2    | 1       | -    | 60    | 4       | 0.1    | 0.05   | 10        | 4           |
| F2              |             | 2    | 1       | -    | 60    | 4       | 0.1    | 0.05   | 10        | 4           |
| F3              |             | 2    | 0.5     | 0.75  | 60    | 4       | 0.1    | 0.05   | 10        | 4           |
| F4              |             | 2    | 0.5     | 0.5   | 60    | 4       | 0.1    | 0.05   | 10        | 4           |
| F5              |             | 2    | 0.75    | 0.5   | 60    | 4       | 0.1    | 0.05   | 10        | 4           |
Evaluation of itraconazole gel [7-24]

**Percentage Yield**

The empty container was weighed in which the gel formulation was stored then again the container was weighed with gel formulation. Then subtracted the empty container weighed with the container with gel formulation then it gives the practical yield. Then the percentage yield was calculated by the formula.

\[
\text{Percentage yield} = \left(\frac{\text{Practical yield}}{\text{Theoretical yield}}\right) \times 100
\]

**Drug content**

Weighed 10 gm of each gel formulation were transferred in 250 ml of the volumetric flask containing 20 ml of alcohol and stirred for 30 min. The volume was made up to 100 ml and filtered. 1 ml of the above solution was further diluted to 10 ml with alcohol and again 1 ml of the above solution was further diluted to 10 ml with alcohol. The absorbance of the solution was measured spectrophotometrically at 260 nm. Drug content was calculated by the following formula

\[
\text{Drug content} = \frac{\text{Absorbance}}{\text{Slope}} \times \text{Dilution factor} \times 1000
\]

**Determination of pH**

Weighed 50 gm of each gel formulation were transferred in 10 ml of the beaker and measured it by using the digital pH meter. pH of the topical gel formulation should be between 3 – 9 to treat the skin infections.

**Spreadability**

The spreadability of the gel formulation was determined, by measuring the diameter of 1 gm gel between horizontal plates (20×20 cm²) after 1 minute. The standardized weight tied on the upper plate was 125 gm.

**RESULTS AND DISCUSSION**

| Table 2: Percent yield of gel formulations |
|-------------------------------------------|
| **Formulation** | **Percent yield** |
| F1 | 99.59% |
| F2 | 98.34% |
| F3 | 97.44% |
| F4 | 99.81% |
| F5 | 98.76% |

| Table 3: Drug content of gel formulations |
|-------------------------------------------|
| **Formulation code** | **Drug content** |
| F1 | 94.41 |
| F2 | 97.38 |
| F3 | 98.24 |
| F4 | 96.52 |
| F5 | 95.07 |

| Table 4: pH of gel formulations |
|--------------------------------|
| **Formulation** | **pH** |
| F1 | 6.98 |
| F2 | 7.01 |
| F3 | 6.98 |
| F4 | 6.5 |
| F5 | 6.79 |
Table 5: Viscosity of gel formulations

| Formulation | Viscosity (cp) |
|-------------|----------------|
| F1          | 8476           |
| F2          | 4259           |
| F3          | 4450           |
| F4          | 4544           |
| F5          | 6.79           |

Table 6: Spreadability of gel formulations

| Formulation | Spreadability |
|-------------|--------------|
|             | R1           | R2           |
| F1          | 1.3          | 1.9          |
| F2          | 2.1          | 2.9          |
| F3          | 4.9          | 2.8          |
| F4          | 1.7          | 2.3          |
| F5          | 1.5          | 2.1          |

Table 7: Extrudability of gel formulations

| Formulation | Extrudability |
|-------------|--------------|
| F1          | +            |
| F2          | +++          |
| F3          | +++          |
| F4          | ++           |
| F5          | ++           |

Excellent (+++), Good (++), Average (+), Poor (-)

Table 8: In vitro diffusion chart

| Time  | % CDR F1 | % CDR F2 | % CDR F3 | % CDR F4 | % CDR F5 |
|-------|----------|----------|----------|----------|----------|
| 0     | 0        | 0        | 0        | 0        | 0        |
| 30    | 12.95    | 16.87    | 14.88    | 14.03    | 13.67    |
| 60    | 39.51    | 44.39    | 41.39    | 40.76    | 40.05    |
| 90    | 47       | 48.49    | 47.95    | 47.02    | 46.91    |
| 120   | 56.59    | 56.01    | 57.18    | 56.24    | 55.74    |
| 150   | 62.84    | 61.28    | 63.59    | 62.31    | 61.89    |
| 180   | 71.84    | 72.69    | 73.26    | 72.13    | 71.84    |
| 210   | 80.17    | 79.37    | 82.15    | 81.68    | 80.86    |
| 240   | 87.27    | 86.16    | 89.07    | 88.19    | 87.98    |
| 270   | 95.98    | 94.09    | 97.03    | 96.83    | 96.03    |

Fig. In vitro diffusion for F3 formulation

CONCLUSION

Various formulation (F1, F2, F3, F4, F5) were developed by using a suitable polymer (carbopol 934p and HPMC). Developed formulations of Itraconazole were evaluated for the physiochemical parameters such as percentage yield, drug content, pH, viscosity, spreadability, extrudability, in vitro drug diffusion. Viscosity studies of various formulations revealed that formulation F3 was better to compare to others. From among all the developed formulation, F3 shows better drug diffusion, did good Rheological properties. pH of the F3 formulation is sufficient enough to treat the skin infections. Results indicated that the concentration of carbopol-934 and HPMC K4M significantly affects drug release and rheological properties of the gels. The viscosity of carbopol-934 gels was very high as compared to HPMC K4M gels but both gels showed a decrease in drug release with an increase in polymer concentration. Thus, gels can be successfully prepared using carbopol-934 and Hydroxypropyl methylcellulose as gelling agents in the ratio 1:3(carbopol-934 and Hydroxypropyl methylcellulose) suitable for topical application. Hence formulation F3 should be further developed for scale-up to industrial production.

AUTHORS CONTRIBUTIONS

All the author have contributed equally

CONFLICT OF INTERESTS

Declared none

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