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# FORMULATION AND EVALUATION OF TOPICAL ANTIFUNGAL GEL CONTAINING ITRACONAZOLE

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## ABSTRACT

The objective of the present research work is to formulate and evaluate Itraconazole antifungal gel. Itraconazole is an imidazole derivative and used for the treatment of local and systemic fungal infection. The oral activity of Itraconazole is not much proven to be efficient as it has many side effects. This formulation is made for better patient compliance and to reduce the dose of the drug. The gel was formulated by changing the polymer ratio. Various formulation (F1, F2, F3, F4) were developed by using a suitable polymer (carbopol 971p and noveonAA1). The formulation was evaluated for, spreadability, extrudability and viscosity *in vitro* drug release study. Viscosity studies of various formulations revealed that formulation F4 was better to compare to others. From among all the developed formulation, F4 shows better drug diffusion, did good Rheological properties. pH of the F4 formulation is sufficient enough to treat the skin infections. Results indicated that the concentration of carbopol 971p and noveon AA1 significantly affects drug release and rheological properties of the gel. It was concluded that formulation F4 was the best formulation among this formulation. Hence formulation F4 has shown the better results compared to other batches.

**Keywords:** Itraconazole, carbopol 971 p, noveon AA1, antifungal.

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# INTRODUCTION

Fungal infection of skin is now-a-days one of the most common dermatological problems. Infection is caused by microscopic organisms that invade the epithelial tissue. The fungi kingdom includes yeasts, moulds, rusts and mushrooms which are commonly found on the skin, mouth, throat, stomach, colon, rectum and vagina. Whenever proliferation of this kind of organism occurs, it can produce symptomatic infection of the skin, mouth, vagina and intestine.[1]

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.

Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders (e.g. acne) or the cutaneous manifestations of a general disease (e.g. psoriasis) with the intent of containing the pharmacological or other effect of the drug to the surface of the skin or within the skin. Semi-solid formulation in all their diversity dominate the system for topical delivery, but foams, spray, medicated powders, solution, and even medicated adhesive systems are in use.

The term “Gel” was introduced in the late 1800 to name some semisolid material according to pharmacological, rather than molecular criteria. The U.S.P. defines gels as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. The inorganic particles form a three dimensional “house of cards” structure.[2]

Antifungal compounds works by exploiting differences between mammalian and fungal cells to kill the fungal organism without dangerous effect on host.[3]

Topical antifungal are important adjuvant in treatment of dermatophytosis. Also specific situation such as dermatophytosis in pregnancy and infants often warrant topical therapy.

Topical drug delivery is one of the most suitable routes for administration of drugs that undergo first-pass metabolism. It is generally effective against fungal infections.[4]

Itraconazole, a triazole derivative, is used for the treatment of systemic fungal infection. It is one of the triazole antifungal agents that inhibits cytocrome P-450 dependent enzyme resulting in impairment of ergosterol synthesis. It has been used against histoplasmosis, blastomycosis, cryptococcal meningitis and asperigillosis. It is a BCS class II drug having low solubility and high permeability. The extremely low solubility results into poor oral bioavailability (55%) of Itraconazole. The work described here is concerned with the formulation of topical Itraconazole

gels, using Carbopol 971p and novion AA1 as a synthetic polymers[6]

## MATERIALS AND METHOD

**Table 1 Materials**

| Sr. no. | Chemicals | Manufacturer / Provider |
|---|---|---|
| 1. | Itracanozole | Glenmark research center, Sinner, Nashik |
| 2. | Noveon AA1 | Lab grade |
| 3. | Carbopol 971P | Lab grade |
| 4. | Propyl paraben & Methyl paraben | Lab grade |
| 5. | DMSO | Adhar life science, Solapur |

### FORMULATION OF ITRACONAZOLE GEL

**Carbopol 971 P gel**

Required quantity of carbopol was added in water and it was kept 24 hrs for soaking in a beaker. In another beaker the drug was dissolved in DMSO and PEG. The drug solution was mixed in gel base. Methyl and propyl paraben was added in the gel. The pH of the gel was adjusted using triethanolamine. The final volume of the gel was adjusted with the required quantity of distilled water.

**Noveon AA1 Gel**

Required quantity of Noveon was added in water and it was kept 24 hrs for soaking in a beaker. In another beaker the drug was dissolved in DMSO and PEG. The drug solution was mixed in gel base. Methyl and propyl paraben was added in the gel. The pH of the gel was adjusted using triethanolamine. The final volume of the gel was adjusted with the required quantity of distilled water.

**Table 2: Formulation of gel**

| Ingradients | F1 | F2 | F3 | F4 |
|---|---|---|---|---|
| **Itraconazole (gm)** | 2 | 2 | 2 | 2 |
| **Carbopol 971p (gm)** | 1 | 1.5 | - | - |
| **Noveon AA1 (gm)** | | | 1 | 1.5 |
| **Dimethyl Sulfoxide(DMSO) (ml)** | 4 | 4 | 4 | 4 |
| **Methyl paraben (gm)** | 0.2 | 0.2 | 0.2 | 0.2 |
| **Propyl paraben (gm)** | 0.5 | 0.5 | 0.5 | 0.5 |
| **Propylene glycol** | 10 | 10 | 10 | 10 |
| **Triethanolamine** | Q.S . | Q.S. | Q.S. | Q.S. |
| **Water (ml)** | 100 | 100 | 100 | 100 |

### EVALUATION OF PREPARED GELS[2]

**1. Physical evaluation**

All the formulations of Itraconazole were evaluated for organoleptic characteristics, occlusiveness and washability.

**2. Measurement of pH**

The pH of the formulated gels was determined using digital pH meter. The electrode was immersed in the gel and readings were recorded from pH meter.

**3. Viscosity study**

Viscosity measurements were done on Brookfield viscometer by selecting suitable spindle number and rpm. 50 gm of preparation was kept in 50 ml beaker which was set till spindle groove was dipped and rpm was set and dial reading was measured after three minutes. From the reading obtained, viscosity was calculated by using factor. The procedure was repeated three times and observations are recorded as mean.

**4. Spreadability**

A sample of 0.1 g of each formula was pressed between two slides (divided into squares of 5 mm sides) and left for about 5 minutes where no more spreading was expected. Diameters of spreaded circles were measured in cm and were taken as comparative values for spreadability. The results obtained are average of three determinations.

**5. Extrudability study**

The extrudability of gel formulations were determined by filling gel in the collapsible tubes. The extrudability was determined in terms of weight in grams required to extrude a 0.5 cm. ribbon of gel.

**6. Drug content**

Weighed 10 gm of each gel formulation were transferred in 250 ml of 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 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:

$$Drug\ content = \frac{Absorbance}{Slope} \times Dilution\ factor \times \frac{1}{100}$$

**7. *In vitro* diffusion studies**

The drug release from the formulations was determined by using the apparatus, which consist of a cylindrical glass tube (with 22-mm internal diameter and 76 mm height) which was opened at both the ends. 1 gm of gel equivalent to 10 mg of Itraconazole was spread uniformly on the surface of cellophane membrane (previously soaked in medium for 24 hrs) and was fixed to the one end of tube. The whole assembly was fixed in such a way that the lower end of tube containing gel was just touches (1-2 mm deep) the surface of diffusion medium i.e. 100 ml of pH 7.4 phosphate buffer

contained in 100 ml beaker, The assembly was placed on thermostatic hot plate with magnetic stirrer and maintained at temperature 37°±2°C the contents were stirred using magnetic bar at 100rpm for a period of 6 hrs, 5 ml of samples were withdrawn at different time intervals and replace with 5 ml of fresh buffer and after suitable dilution the sample were analyzed at 260 nm for Itraconazole.

## RESULT & DISCUSSION

### 1. Physical evaluation

The prepared gel formulation was inspected visually for their colour and appearance. The developed formulations F1, F2, F3, F4 were white translucent. All the formulations were much clear.

**Table 3: Evaluation of Gel**

| Sr.no. | Batches | Physical evaluation | Extruded amount (%) | Spreadability (gm.cm/sec) | pH | Viscosity (cps) | Drug Content (%) |
|---|---|---|---|---|---|---|---|
| 1. | F1 | White | 83.84 | 11.60 | 6.8 | 47856 | 97 |
| 2. | F2 | White | 85.02 | 11.2 | 7.1 | 64249 | 98 |
| 3. | F3 | White | 87.63 | 12.25 | 6.9 | 49353 | 97.5 |
| 4. | F4 | White | 88.57 | 12.75 | 6.8 | 66063 | 98.5 |

### 2. Measurement of pH

The pH of gel was determined using digital pH meter. The F1 to F4 batches shows 6.8 to 7.1 pH. The pH results are given in Table no. 3

### 3. Viscosity study

The F1 to F4 batches shows 47856 to 66063 cps of viscosity. As the polymer concentration increases, the viscosity also increases. The viscosity results are given in Table no.3

### 4. Spreadability

The value of Spreadability indicates the degree of shear required to apply the gel. The spreadability results are given in table no.3

### 5. Extrudability study

Extrudability of all formulations was higher than 80%. So, it can be said that extrudability of all formulations shows acceptance property. The Extrudability results are given in table no.3

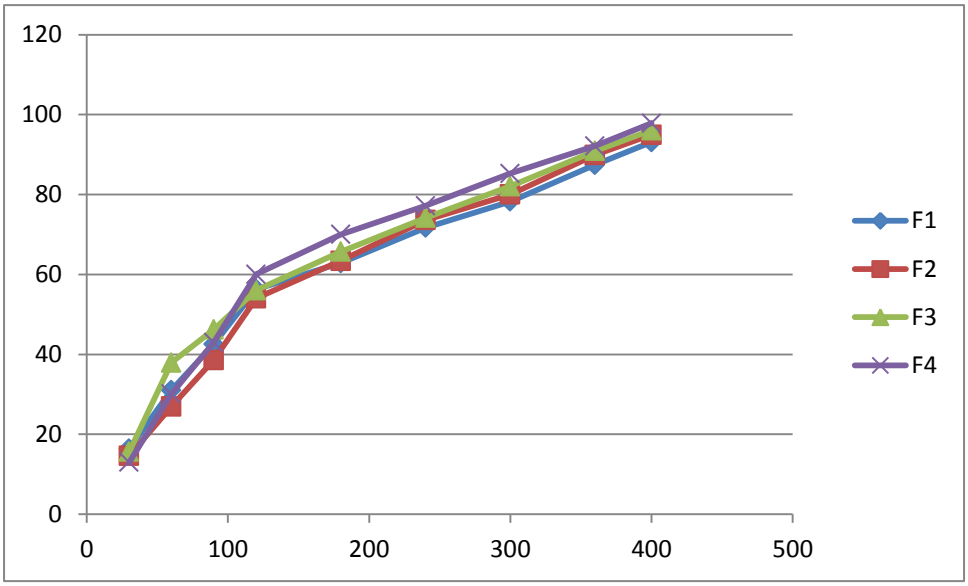
### 6. Drug content

The drug content of all batches of all formulations were in the range of 97 to 98.5%. The F3 batch shows maximum 98.5% and F1 batch shows minimum 97% drug content. The drug content determination showed that the drug was uniformly distributed throughout the Gel. The drug content results are given in table no.3

**7. *In vitro* diffusion studies**

Itraconazole antifungal gel containing the formulations F1-F4, in which formulation F1 and F2 containing carbopol 971(P) shows drug release of 93.13 & 94.97% upto 7 hrs. Formulation F3 and F4 containing noveon AA1 shows drug release is about 96.09% and 97.84% upto 10 hrs. Formulations F3 and F4 shows the highest drug release with prolonged period of time.

**Table no. 4 % Drug release of Antifungal gel**




## CONCLUSION

Various formulation (F1, F2, F3, F4) were developed by using a carbopol 971p and noveon AA1. Developed formulations of Itraconazole were evaluated for the physiochemical parameters such as drug content, pH, viscosity, spreadability, extrudability, *in vitro* drug diffusion. Viscosity studies of various formulations revealed that formulation F4 was better to compare to others. From among all the developed formulation, F4 shows better drug diffusion, did good Rheological properties. pH of the F4 formulation is sufficient enough to treat the skin infections. The viscosity of noveon AA1 gels was very high as compared to carbopol-971 gels but both gels showed a decrease in drug release with an increase in polymer concentration. Thus, gels can be successfully prepared using Carbopol-971p and Noveon AA1 as gelling agents suitable for topical application Hence formulation F4 should be further developed for scale-up to industrial production.

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