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DEVELOPMENT AND CHARACTERIZATION OF TOPICAL HYDROGEL CONTAINING ANTIFUNGAL DRUG

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ABSTRACT

An antifungal medication called griseofulvin is used to treat fungus infections. Griseofulvin undergoes hepatic first-pass metabolism and has a long list of possible adverse effects, hence oral usage is not advised. The purpose of this study was to develop and test a topical hydrogel formulation of griseofulvin for the treatment of cutaneous fungal infections. Several hydrophilic polymers, including carbopol 940 and guar gum, were used to develop topical hydrogel formulations of griseofulvin. Viscosity, spreadability, pH, assay, and in vitro drug release all underwent evaluation testing. An in vitro diffusion test in a Franz diffusion cell employed a cellophane membrane. The physicochemical properties of the formulations did not significantly change after exposure to accelerated temperature conditions (40 2oC). A gel formulation containing 1% w/v Guar gum and 1% w/v Carbopol 940 in a 1:1 ratio was shown to be suitable for topical administration based on an in vitro test. These results demonstrate the Griseofulvin topical gel formulation's viability.

KEYWORDS: Griseofulvin, Franz diffusion cell, Carbopol 940, Guar gum.

INTRODUCTION

For the treatment of skin conditions and to have systemic effects, the topical route of drug administration has been used.[1] Hydrogels are created for both medicinal and cosmetic purposes.[2] Gels usually provide a greater release of the active ingredient compared to creams and ointments, independent of the medication's water solubility.[3] Local application of medicinal substances offers a number of advantages over the administration of drugs orally and intravenously. A few advantages include simple skin application, the ability to target the local area of action for drugs, the elimination of hepatic first-pass metabolism, and increased patient compliance.[4,5] Due to their physical and chemical characteristics, such as their ability to manage the drug's extended release, hydrogels are frequently utilised in topical drug delivery systems.[6,7] When these formulations come into contact with the skin, a semi-occlusive skin film forms and the medication is released in a controlled manner.[8] The stratum corneum can be penetrated by lipophilic substances, but once they enter the deeper, more aqueous layers of the epidermis, their rate of diffusion reduces.[9]

Due to its affordability and accessibility, it is the drug most frequently given to treat tinea capitis in kids.[10,11] Researchers found that among antifungal therapies for tinea capitis, griseofulvin had the highest clinical and complete cure rates.[12] In the same experiment, Microsporum was more successfully treated with griseofulvin than Trichophyton. It's vital to keep in mind that Trichophyton tonsurans is the most typical cause of tinea capitis in the US. The effectiveness of griseofulvin is increased when used with selenium sulphide-containing shampoo.[3]

MATERIAL AND METHOD

Material

Griseofulvin was purchased from Sigma-Aldrich, India. Guar gum, Benzalkonium chloride, Isopropyl myristate, sodium hydroxide, and potassium dihydrogen phosphate were obtained from the laboratory of Hygia Institute of Pharmacy, Lucknow. The usage of all other substances was without further chemical alteration, and they were all of the analytical grades.

Method

The hydrophilic polymers used were guar gum and carbopol 940, and the cross-linking agent used was 0.1N NaOH solution.[13,14] Carbopol 940 is soluble in water, whereas guar gum produces colloidal dispersion in that medium. It was determined that polymeric dispersions

with concentrations between 0.1 and 5% w/v of guar gum and carbopol 940 colloidal dispersions exhibited acceptable mechanical characteristics.

The topical hydrogels were made in the following ways, utilising various ratios.

(i) Different polymeric dispersion concentrations were used to create hydrogels.

(ii) Using pure water, various carbopol940 colloidal dispersion concentrations were created.

(iii) Distilled water was used to create guar gum colloidal dispersions in various concentrations.

(iv) After full dispersion, both polymer solutions were kept in the dark for 24 hours to allow for full swelling.

(v) Polymer dispersions were created using a magnetic stirrer (500rpm). Colloidal guar gum dispersion was added to distilled water after carbopol 940 had been dissolved in it while being stirred magnetically. Benzalkonium chloride was added at 0.25% w/v and 1% v/v concentrations. The aqueous drug solution was added to the polymeric dispersion after the sodium hydroxide solution. The remaining distilled water was then added and agitated magnetically to form a homogeneous gel dispersion. In Table 1, the ingredients for various formulations were listed.

Table 1: Composition of different formulations of griseofulvin hydrogel.

Ingredients (mg)	Formulation Code				
	F1	F2	F3	F4	F5
Griseofulvin	100	100	100	100	100
Guar gum	0.05	0.5	0.375	0.375	0.375
Isopropyl myristate (ml)	1	1	1	1	1
Carbopol- 940	0.375	0.5	0.25	0.375	0.5
Benzalkonium chloride	0.25	0.25	0.25	0.25	0.25
Water (Purified)	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

CHARACTERIZATION OF HYDROGEL

Physical characteristics

The resulting hydrogel compositions' pH, colour, homogeneity, consistency, grittiness, texture, and phase separation were all assessed visually.

Determination of pH

Using a digital pH metre, the pH of hydrogel compositions was assessed. After one gramme of gel was dissolved in 25 ml of distilled water, the electrode was immersed in the gel formulation for 30 minutes to provide a reliable reading. Reading frequently was also

evident. The pH of each formulation was assessed three times, and the average findings were calculated.[15]

Washability

On the skin, formulations were applied, and the degree of water washing was manually assessed.

Extrudability study

Aluminium or metal collapsible tubes were filled with the hydrogel compositions. The material was forced through the tubes, and the formulation's extrudability was assessed.[16]

Spreadability

Two glass slides with conventional (62) dimensions were chosen. One of the slides was covered with the hydrogel preparation whose spreadability was to be tested. The formulation was sandwiched between the second slide and the slide for a distance of 6 cm along the slide when the second slide was positioned above the first slide. With the top slide receiving 100 grammes of weight, the hydrogel formulation between the two slides was drawn uniformly to create a thin layer. The extra hydrogel formulation that was sticking to the slides was scraped off once the weight was taken off. The top slide's end was attached to a string and secured to the apparatus's board so that a simple pulley could be used to convey a 20-gram weight to the top slide. Under the influence of weight, the top slide moved the 6 cm distance and separated from the lower slide in the amount of time that was measured. After repeating the experiment, the average of six such measurements for each hydrogel preparation were calculated.[17,18]

Spreadability = m.l / t

where S is spreadability (g cm/sec), m is the weight (20 grammes) tied to the upper slide, l is glass slide length (6 cm), and t is time in seconds.

Viscosity

A Brookfield digital viscometer was used to gauge the hydrogel's viscosity. At 10 rpm and 250C, the viscosity was measured using spindle number 6. Gel was adequately dispensed into the appropriate wide-mouth container. In order for the viscometer's spindle to dip gently, the hydrogel was carefully poured into the wide-mouth container. The hydrogel samples were given 30 minutes to settle at the same temperature (25 /10C) before to the measurements.[19]

Drug content

Topical hydrogel weighing precisely 100 mg was added to a beaker along with 20 cc of phosphate buffer pH 7.4. This combination was well mixed and then filtered through Whatman filter paper no. 1. After that, 1.0 ml of the filtered solution was put to a volumetric flask with a 10 ml capacity of phosphate buffer, pH 7.4. A UV spectrophotometer was used to analyse this solution at a maximum wavelength of 275 nm.

Studies on the prehydrated cellophane membrane for in-vitro drug release

The ability of the hydrogel to release medicines in vitro was tested. In a Franz diffusion cell, a cellophane membrane was utilized in an in vitro diffusion experiment. The cellophane membrane was used to protect the Franz diffusion cell. The formulation was delivered via the donor compartment on the dialysis membrane. In the reservoir compartment, 25 cc of pH 7.4 phosphate buffer was added. The experiment lasted eight hours at a speed of 100 rpm and a temperature of 37 1 °C. At one-hour intervals, samples were removed from the reservoir compartment and absorbance was measured spectrophotometrically at 275.0 nm. The reservoir compartment was constantly refilled with the same amount of 7.4 pH phosphate buffer.[20,21]

Accelerated stability studies

Stability tests on the improved formulation were carried out in accordance with the International Conference on Harmonization's recommendations (ICH). The formulation packaged in an aluminium tube was submitted to three months of accelerated stability testing at 40 0C and 75 5% relative humidity in accordance with ICH norms. Over the course of three months, samples were collected on a monthly basis and analysed for changes in pH, spreadability, drug content, and in-vitro drug release using the previously described method. Any changes to the evaluation parameters were reported. The tests were performed in triplicate, and the mean and standard deviation of the obtained data were reported.

Antifungal study

The antifungal activity of the gels generated was tested against the Candida albicans strain using the nutrient agar cup technique. To inoculate the aseptically prepared nutrient agar cups, a tested fungal suspension strain was dispersed. Wells were made in the cups with a sterile borer, and sterile syringes were used to fill each well with the prepared gels. The zone of inhibition in each cup was checked, the radius was calculated, and the results were compared to the control using an antibiotic zone reader.

RESULTS AND DISCUSSION

The spectra of the drug solution were conducted in a double-beam ultraviolet spectrophotometer using a concentration range of 5-25 g/ml of griseofulvin in 7.4 phosphate buffers to detect the absorption maxima. In phosphate buffer pH 7.4, griseofulvin demonstrated a linear relation with a correlation coefficient of 0.999 at concentrations ranging from 5 to 25 g/ml. Figure1. The drug's melting point was discovered to be 148–1490°C, as opposed to the 149–150°C stated in the conventional monograph. All of the pre-formulation study's findings were discovered to be identical to those in the standard monograph, indicating that the medication was genuine and pure in form and could be utilised to construct the formulation of a hydrogel loaded with griseofulvin.

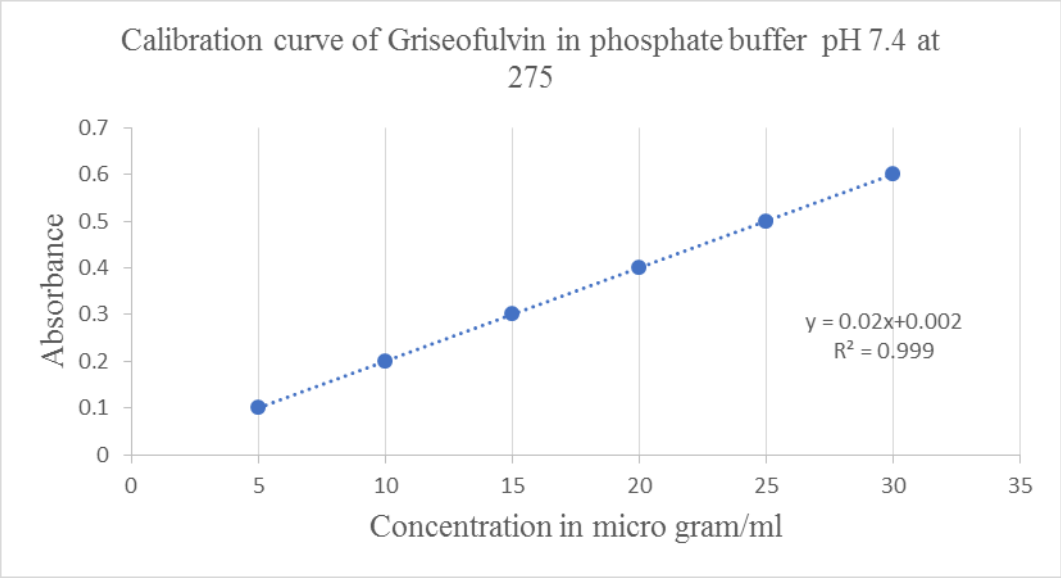

Fig.1: Griseofulvin calibration curve in phosphate buffer pH 7.4 at 275nm.

The hydrogel formulations were white, thick, and creamy, with a uniformly smooth texture and glossy appearance. Table 2 provides a discussion of the findings. Table 3 contains the findings for all formulations' spreadability, extrudability, and washability. According to the findings, formulations F1–F5 have strong washability properties, whereas formulations F2–F3 have good All formulations were found to have extrudability and spreadability ranging from 11.98 to 14.33. The viscosity of the hydrogel was measured with a Brookfield digital viscometer. The viscosity of the formulations increases as their polymer concentration increases. A pH metre was used to assess the hydrogel's pH. The pH of the hydrogel

formulation was 6.78 to 7.03, which was regarded acceptable to prevent skin irritation when applied to the skin, and table 4 revealed that the medication concentration of F5 was larger than 99.3.

Table 2: Physical parameters of formulations.

Physical parameter	Formulation Code				
	F1	F2	F3	F4	F5
Homogeneity	Very good	Very good	Very good	Very good	Very good
Colour	Colourless	Colourless	Colourless	Colourless	Colourless
Phase separation	None	None	None	None	None
Consistency	Excellent	Excellent	Excellent	Excellent	Excellent

Table 3: Outcomes of extrudability washability and spreadability study.

Formulation Code	Extrudability	Washability	Spreadability (gcm/sec)
F1	Good	Excellent	11.98
F2	Excellent	Excellent	12.34
F3	Excellent	Excellent	13.21
F4	Good	Excellent	12.43
F5	Good	Excellent	14.33

Table 4: Drug content, pH, and viscosity.

Formulation Code	pH	Viscosity (cps)	Drug Content	Zone of inhibition
F1	6.91	9255	97.8	16
F2	7.01	9481	97.4	15
F3	6.78	9137	98.7	18
F4	6.81	9231	96.1	21
F5	7.03	9563	99.3	23

The somewhat extended drug release rate was validated by the substantially slower drug release from griseofulvin hydrogel. The drug's release rate was impacted by the incorporation of carbomer. The medication's release rate was reduced when the quantity of carbomer was raised, which may have been due to the formulation's increased stiffness and subsequently decreased permeability to the drug. The medication release rate for the enhanced formulation F2 is much better, as shown in Table 5.

Table 5: Cumulative % of drugs released from various formulations.

Time (min.)	Cumulative % of drug release				
	F1	F2	F3	F4	F5
5	71.1	31.4	74.3	54.2	47.8
10	73.8	39.2	78.3	57.9	56.8
15	75.7	41.5	82.1	69.4	63.5
20	77.4	48.2	82.8	72.4	69.4
30	81.2	87.8	83.9	79.8	77.5

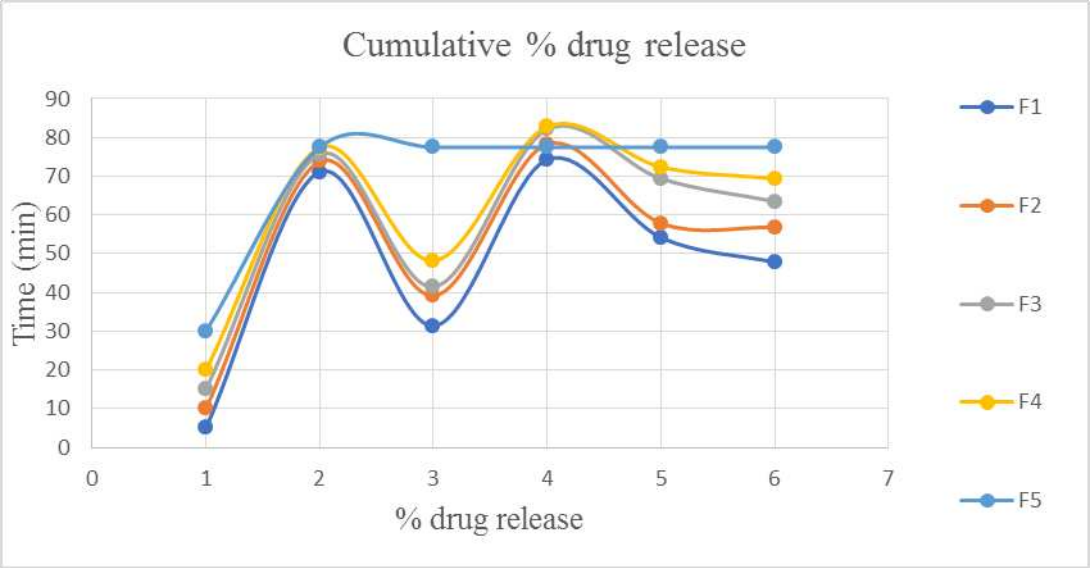

Fig.1: Cumulative % drug release profile of topical hydrogel.

Zone of inhibition

Table 3 lists the antifungal properties of griseofulvin in various gel formulations. Its antifungal activity was determined by measuring the zone of inhibition. The findings from each preparation were good; the preparation with the most activity had an inhibition zone of 23 mm, while the formulation with the lowest activity had an inhibition zone of 15 mm. Figures are displayed in table 4.

CONCLUSION

The Griseofulvin hydrogel for topical application was made with guar gum and Carbopol 940, and evaluation studies were carried out. A transdermal medicine delivery system must be designed and developed with the proper polymer choices and ratios. The gels' homogeneity, stability, and drug release rates were all excellent. All of the aforementioned parameters produced good results and were discovered to be inside the permitted bounds. Conclusion: The drug release study, consistency, and homogeneity were all improved by formulation F5. The generated gels showed promising antifungal efficacy against C. albicans species. Therefore, it was found that the developed formulation might be a good topical treatment for fungus infections of the skin. Using topical gels will help you avoid the adverse effects of taking Griseofulvin pills orally.

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