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A discussion on the formulation and an analysis of the topical antifungal gel that contains itraconazole

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Abstract
The current research was carried out with the intention of developing a topical gel formulation of itraconazole, which is the study's stated objective. Itraconazole is a kind of imidazole derivative that is used in the treatment of both systemic and local forms of fungal infection. Itraconazole shouldn't be taken by mouth too often since it might cause a lot of unpleasant side effects. This formulation was created for better patient compliance, to reduce the dose of the drug, and to avoid side effects such as liver damage and kidney damage, which are not available in commercially available itraconazole topical gel preparations on the market. Commercially available itraconazole topical gel preparations do not exist. Changing the polymer ratio was one step in the process of formulating the gel. By making use of an appropriate polymer, a number of formulations (F1, F2, F3, F4, and F5) were produced (carbopol 934p and HPMC). The formulation was analysed for its percentage yield, spread ability, extrudability, wash ability, and viscosity. Additionally, it underwent stability testing, a skin irritation research, and drug release testing. One of the steps in the process of creating the gel was changing the proportion of the polymer. The use of an appropriate polymer allowed for the production of a number of formulations, which were denoted by the letters F1, F2, F3, F4, and F5 (carbopol 934p and HPMC). The formulation was evaluated in a number of different ways, including its % yield, spread ability, extrudability, wash ability, and viscosity. In addition to that, it was examined for its stability, its potential to irritate the skin, and its potential to release drugs.

Keywords: itraconazole, carbopol 934p, HPMC

Introduction
One of the most prevalent dermatological issues seen in modern times is a fungal infection of the skin. The doctors have a broad variety of therapy options available to them, including solid dosage, semisolid dosage form, and liquid dosage formulation respectively. Clear, translucent gels are among the topical formulations that have found widespread acceptance in the cosmetics and medicines industries [1]. When it comes to the topical treatment of dermatological diseases as well as general skin care, doctors and patients have access to a broad range of vehicle preparations. These preparations may take the form of solids, semisolids, or liquids. Both the cosmetics industry and the pharmaceutical industry have seen an increase in the usage of transparent gels in recent years [2]. These gels are part of the larger category of semisolid preparations. Delivery of drugs to patients in the form of various pharmaceutical dosage forms, such as tablets, capsules, pills, suppositories, cream, gel, ointments, liquids, aerosols, and injectables, has been the primary method of treatment for acute diseases as well as chronic illnesses for a number of decades now. This method has been largely successful in curing patients of acute diseases as well as chronic illnesses. It is possible to treat local dermatological conditions with a treatment that is both effective and targeted if medications are delivered directly to the skin. Because it sidesteps the first-pass effects, gastrointestinal discomfort, and metabolic degradation that are often associated with oral administration, this method of drug delivery has gained a lot of traction in recent years. Because of the first-past effect, approximately 25-45% of the amount that is orally delivered really makes it into the blood circulation. Gel compositions have been suggested for use as a topical treatment in order to get around these drawbacks. Gels are characterised as "semisolid systems in which a liquid phase is restricted inside a polymeric matrix in which a high degree of physical and chemical cross-linking is induced," according to the definition. Itraconazole is an antifungal agent that is synthetic and belongs to the imidazole class. It works by inhibiting the growth of pathogenic fungi, which is how it treats infections. It is effective in treating infections caused by fungi. The production of membrane lipids that is unique to fungi is the focus of the triazole drug. Itraconazole has the unique ability to insert itself preferentially into the membranes of fungal cells, so impairing their function. The replication of DNA in fungal cells is the target of 5-fluorocytosine [3]. Hydroxypropyl methylcellulose (HPMC), also known as Carbapol 934p, is a kind of hydrophilic polymer that has been used topically in gel drug delivery systems [4].

Materials and Methods

Material

Itraconazole, HPMC, carbopol934, trim ethanolamine, glycerine, methylparaben, and propylparaben, together with water are the ingredients in this formulation.

Method

A beaker was filled with polymer (such as Carbopol 934p or HPMC) and sterile water, and the mixture was left to soak for twenty-four hours. In order to do this, the necessary quantity of the medication, which was two grammes, was first suspended in water, and then either Carbopol 934p or HPMC was neutralised by adding a suitable amount of triethanolamine. Glycerine was added gradually as a moistening agent, methylparaben and propylparaben were added as preservatives, and the mixture was stirred continuously and gently until it formed a homogeneous gel.

Different concentrations of carbopol934, HPMC, and itraconazole were used in the preparation of gel formulations of itraconazole.

Table 1: Optimized formulae of Itraconazole gel

Formulation code	Ingredients								
	Drug	Carbopol	HPMC	Water	Alcohol	Methyl	Propyl	Glycerine	Triethanol
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

A. Percentage Yield

The container that was empty was. After the container that the gel formulation was kept in had been weighed, the container was weighed once again while it contained the gel formulation. After that, the practical yield may be calculated by subtracting the weight of the empty container from the weight of the container containing the gel formulation. Following that, the formula was used to get the % yield.

$$Percentage\ Yield = \frac{Actual\ Yeild}{Theoratical\ Yield} \times 100\%$$

B. Drug content

It was the container that had been emptied. After the container that had the gel formulation had been weighed, it was weighed again while it still contained the gel formulation. After that, the practical yield can be computed by deducting the weight of the container that is empty from the weight of the container that is full with the gel formulation. This will provide the final result. After that, the formula was used in order to calculate the percentage yield.

$$Drug\ content = \frac{Absorbance}{Slope} \times Dilution\ Factor \times \frac{1}{1000}$$

C. Determination of Ph

A digital pH metre was used to test the solution after 50 grammes of each gel formulation had been weighed and then placed into 10 millilitres of the beaker. To treat the skin infections, the pH of the topical gel formulation that is being used should be between 3 and 9.

D. Spreadability

After first weighing 50 grammes of each gel formulation and then dispensing 10 millilitres of the beaker's contents into it, a digital pH metre was utilised in order to analyse the results of the solution's analysis. The topical gel formulation that is being used to treat the skin infections should have a pH that is between 3 and 9, according to the manufacturer's instructions.

E. Extrudability

The gel compositions were placed inside either an aluminium collapsible tube or a collapsible metal tube before being packaged. The material was forced out of the tube by applying pressure, and the extrudability of the formulation was analysed.

F. Viscosity estimation

The viscosity of gel was measured using a Brookfield viscometer DVII model equipped with a T-Bar spindle and a helipath stand. This was done in order to get an accurate reading.

a. The choice of the spindle: Spindle T 95 was used for the purpose of determining the viscosity of each and every gel.
b. The size of the sample container: The viscosity was determined using 50 gm of gel that was poured in a beaker that was 100 ml. Spindle immersion: The T-bar spindle (T95) was lowered perpendicular in the centre taking care that spindle does not touch the bottom of the jar.
c. The measurement of viscosity: The T-bar spindle (T95) was used in order to ascertain the level of viscosity present in the gels. During the procedure, the variables that are known to have an impact on the viscosity, such as temperature, pressure, and sample size, were kept constant. The T-bar spindle of the helipath was moved up and down, and viscosities were obtained at a variety of different positions along the path. The figure for the torque was consistently higher than 10%. The viscosity of gels was determined by taking three measurements within one minute and taking the average of those values.

***In vitro* Diffusion Study**

Shaving the belly skin of Albino mice that weighed 20–25 grammes and were 8–10 weeks old with a hand razor and cleaning the skin with a cotton swab dipped in hot water was performed. Five grammes of gel were spread out evenly over the surface of the skin. The donor compartment of the Frantz diffusion cell was the side of the skin that had its stratum corneum facing when it was positioned between the compartments. Phosphate buffer with a pH of 6.8 was used to fill the reservoir compartment, which was 100 ml. The temperature of the experiment was 371 degrees Celsius, and the speed was increased until the vortex made contact with the subject's skin. The experiment lasted for four and a half hours. At thirty-minute intervals, five millilitres of the sample were removed from the reservoir compartment, and the spectrophotometric measurement of absorbance at 260 nanometers was performed. In order to keep the capacity of the reservoir compartment at a consistent level, it was refilled every time with a solution of phosphate buffer pH 6.8 with a volume of 5 ml.

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 formulatins

Formulation	Ph
F1	6.98
F2	7.01
F3	6.98
F4	6.5
F5	6.79

Table 5: Spreadability of get formulations

Formulation	Spreadability	
	R1	R2
F1	1.3	1.9
F2	2.1	2.9
F3	19	2.8
F4	1.7	2.3
F5	1.5	2.1

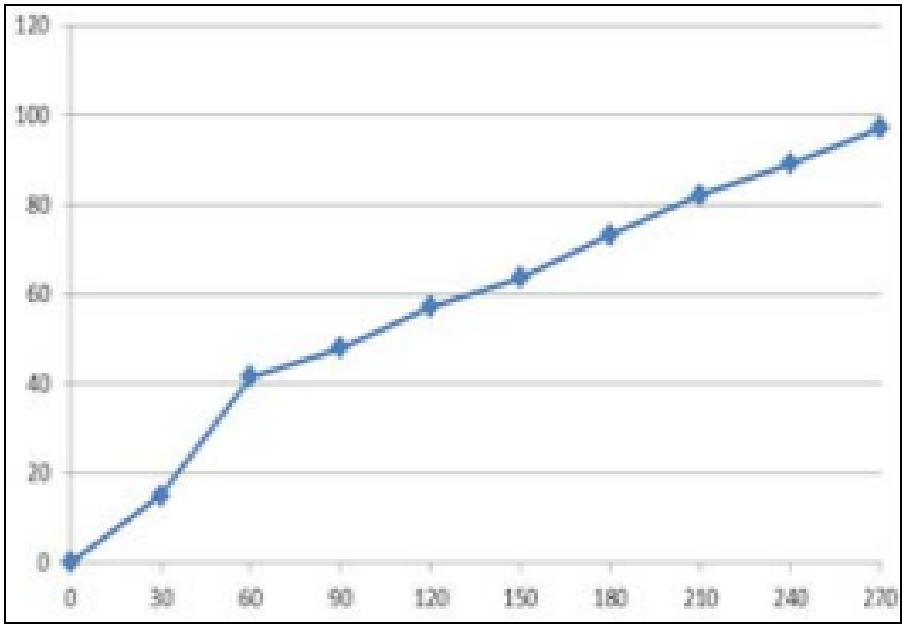

Fig 1: *In vitro* diffusion for F3 formulation

Conclusion

By making use of an appropriate polymer, a number of formulations (F1, F2, F3, F4, and F5) were produced (carbopol 934p and HPMC). Itraconazole formulations that were developed were tested for a variety of physiochemical properties, including % yield, drug content, pH, viscosity, Spread ability, extrudability, and *in vitro* drug diffusion, amongst others. Viscosity tests performed on a number of different formulations showed that formulation F3 was superior to the others when compared to its viscosity. Out of all the different formulations that were produced, F3 had the best rheological qualities and showed the best drug diffusion. It has been determined that the pH of the F3 formulation is enough to treat the skin infections. According to the findings, the concentration of carbopol-934 and HPMC K4M has a substantial impact on the gels' rheological characteristics as well as the rate at which drugs are released. In comparison to HPMC K4M gels, carbopol-934 gels had a much higher viscosity; nevertheless, the amount of medication that was released from either kind of gel decreased with an increase in the polymer concentration. Therefore, gels that are appropriate for topical application may be effectively made by utilising carbopol-934 and hydroxypropyl methylcellulose as the gelling agents in the ratio of 1:3 (carbopol-934 and hydroxypropyl methylcellulose). As a result, formulation F3 ought to go through further development for further scale-up to industrial manufacturing.

References

1. Provost C. A review on transparent oil-water gels. Int J Cosmet Sci,1986:8:233-47.
2. Gupta A, Mishra AK, Singh AK, Gupta V, Bansal P. Formulation and evaluation of topical gel of diclofenac sodium using different polymers. Drug Invention Today,2010:2:250-3.
3. Gerry Fink, the Fink lab. How antifungal drug kill fungi and cure disease; 2005. Available from: URL: http://www. medscape.com/viewprogram/296 3-pn. [Last accessed on 09 Feb 2005].
4. Golinkin HS. Process for fracturing well formulation using aqueous gels. US Patent, US 4137182, 1979.
5. Singh MP, Nagori BP, Shaw NR. Formulation development and evaluation of topical gel formulations using different gelling agents and its comparison with marketed gel formulation. Int J Pharm Erud,2013:3:1-10.
6. Niyaz Basha B, Kalyani P, Divakar G. Formulation and evaluation of gel containing fluconazole-antifungal. Int J Drug Dev Res,2011:3:109-12.
7. Doaa AH, Dalia AE, Sally AA, Mohamed AE. Formulation and evaluation of fluconazole topical gel. Int J Pharm Pharm Sci,2012:4:176-83.
8. Sudipta DA, Arnab SA, Ananya BO. Design, development and evaluation of fluconazole topical gel. Asian J Pharm Clin Res,2015:8:132-13.
9. Ashni VE, Sukhdev SI, Rupinder KA, Upendra KJ. A review: topical gels as drug delivery systems. Int J Phrm Sci Rev Res,2013:23:374-82.
10. Prateek CH, Rajesh ST, Umesh RA. A review on the topical gel. Int J Pharm Bio Agric,2013:4:606-13.
11. Loveleen PR, Tarun KG. Topical gel: a recent approach for novel drug delivery. Asian J Biomed Pharm Sci,2013:3:1-5.
12. Debjit B, Harish G, B Pragati, S Duraivel, KP Sampath Kumar. Recent advances in novel topical drug delivery system. Pharma Innovation,2012:1:12-31.
13. Roychowdhury S, Singh DH, Gupta R, Masih D. A review on the pharmaceutical gel. Int J Pharm Res Bio Sci,2012:1:21-36.

14. Loveleenpreet K, Prabhjot K. Formulation and evaluation of topical gel of meloxicam. Int J Res Pharm Chem,2014:4:619-23.
15. PK Lakshmi, Marka KK, Aishwarya S, Shyamala B. Formulation and evaluation of ibuprofen topical gel: a novel approach for penetration enhancement. Int J Appl Pharma,2011:3:25-30.
16. Joshi B, Gurpreet AC, Saini S, Singla V, Emulgel A. Comprehensive review on the recent advances in topical drug delivery. Int Res J Pharm,2011:2:66-70.
17. Arun RR, Elwin J, Jyoti H, Sreerekha S. Formulation and evaluation of Ketoprofen solid dispersion incorporated topical gels, Eur J Biomed Pharm Sci,2016:3:156-64.
18. Swetha CH, Sellappan VP, Narayana RG, Nagarjuna R. Formulation and evaluation of clarithromycin topical gel. Int J Drug Dev Res,2013:5:194-202.
19. Ganesh M, Gouri D, Vijay G. Formulation and evaluation of herbal gels. Int J Nat Prod Res,2012:3:501-5.
20. Marwa HS, Ghada FM. Evaluation of topical gel bases formulated with various essential oils for antibacterial activity against methicillin-resistant staphylococcus aureus. Trop J Pharm Res,2013:12:877-84.
21. Aejaz A, Azmail K, Sanaullah S, Mohsin AA. Formulation and *in vitro* evaluation of aceclofenac solid dispersion incorporated gels. Int J Appl Pharm,2010:2:7-12.
22. Barhate SD, Potdar MB, Nerker P. Development of meloxicam sodium transdermal gel. Int J Pharm Res Dev,2010:2:1-7.
23. Bazigha AK, Eman AF, Sahar FA, Heyam SS, Saeed KA, Development and evaluation of Ibuprofen transdermal gel formulations. Trop J Pharm Res,2010:9:355-63.
24. Jain S, Padsalg BD, Patel AK, Mokale V. Formulation, development and evaluation of fluconazole gel in various polymer bases. Asian J Pharm,2007:1:3-8.