



FORMULATION AND EVALUATION OF ANTI-FUNGAL EMUGEL FOR TOPICAL DRUG DELIVERY

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ABSTRACT

Topical drug delivery systems offer a convenient and effective route for the treatment of fungal infections, particularly when localized to the skin. Emulgels, a hybrid system combining the properties of emulsions and gels, have emerged as a promising vehicle for topical antifungal therapy due to their enhanced drug penetration, stability, and patient compliance. This study focuses on the formulation and evaluation of an antifungal emulgel incorporating [insert antifungal drug name, e.g., clotrimazole or ketoconazole] for the treatment of superficial fungal infections. The emulgel was prepared using oil-in-water emulsion base integrated with a gelling agent such as Carbopol 940. Various formulations were developed and evaluated for physicochemical properties including pH, viscosity, spreadability, drug content, and in vitro drug release. Antifungal efficacy was assessed using *Candida albicans* and *Aspergillus niger* as model organisms. Among the formulations, F5 showed optimum viscosity, maximum drug release, and significant antifungal activity. The results suggest that the developed antifungal emulgel is a suitable and effective topical delivery system for treating fungal infections, with potential for further development and clinical application.

Key words:

Emulgel, topical drug delivery, antifungal activity, itraconazole, carbapol 940, skin infections.

INTRODUCTION

Emulgel are emulsions, either of the oil-in-water or water in oil type, which are gelled by mixing with a gelling agent. Emulsified gel is stable one and better vehicle for hydrophobic or poorly water-soluble drugs. They have a high patient acceptability since they possess the advantages Topical drug delivery and antifungal activity of both emulsions and gels. Direct (oil-in-water) systems are used to entrap lipophilic drugs, whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) systems. Therefore, they have been recently used as vehicles to deliver various hydrophobic drugs to the skin. In the local market, Emulgel are available: voltaren emulgel (Novartis Pharma, Switzerland), containing diclofenac diethyl amine and Miconaz-H emulgel (Medical Union Pharmaceuticals, Egypt), containing miconazole nitrate and hydrocortisone.

Topical drug administration is a localized drug deliver Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. Skin is one of the most readily accessible organs on human body for topical administration and is main route of topical drug delivery system. The emulsion gels are hydrogels containing randomly distributed oil microdroplets. Topical drug delivery systems have been used for centuries for the treatment of local skin disorders, one side the topical applications of the drug offer the potential advantages of delivering the drug directly to the site of action and delivering the drug for extended period of time at the effected site that mainly acts at the related regions. On the other hand, topical delivery system increases the contact time and mean resident time of drug at the applied site leading to an increase in local drug concentration while the pharmacological activity of Emulgel formulations may not

change as rapidly as the solution form. Several antifungal agents are available on the market in different topical preparations (e.g. creams, ointments, and powders for the purpose of local dermatological therapy). One of these antifungal agents is Itraconazole, which has both antifungal and antibacterial properties. It is applied locally in mild uncomplicated dermatophyte and other cutaneous infections.

Topical drug delivery refers to the application of a formulation to a specific body area, such as the ocular, rectal, nasal, vaginal, or skin, in order to increase bioavailability and reduce side effects.[1] Topical drug delivery refers to the local administration of medication for the treatment of dermatological problems that is not intended for systemic dispersion.

Eczema and psoriasis, for example, can be treated topically. Topical medications include corticosteroids, antivirals, antifungals, antibiotics, antiseptics, local anesthetics, and antineoplastics.

The main aim of this study is to formulate Itraconazole emulgel. By formulating Itraconazole as an emulgel we can directly deliver the drug affected skin area.

The objectives of the study include procuring the raw materials and drug, determining the λ_{max} , constructing the standard calibration curve, performing solubility studies, and formulating the emulgel for posaconazole. Additionally, the study aims to evaluate and interpret the results obtained from these experimental procedures.

MATERIALS & METHODS

All the materials used in the study including Itraconazole, various polymers (PEG, Carbopol 940), preservatives (methyl and propyl paraben), surfactants (Tween-80, Span-20), solvents (methanol), and excipients such as oleic acid and triethanolamine were procured from NCOP. Each material was of analytical grade and used as received without further purification.

Methods

Emulgel Preparation – 1

Emulgel is prepared in three steps:

Step 1: Preparation of the gel base by dispersing the gelling agent in water with constant stirring, followed by pH adjustment.

Step 2: Preparation of the emulsion by heating the oil and aqueous phases separately to 70–80°C and then slowly mixing them with emulsifiers (Span/Tween) under continuous stirring for 15–20 minutes, allowing the mixture to cool; preservatives may be added based on solubility.

Step 3: Incorporation of the prepared emulsion into the gel base in a 1:1 ratio with gentle stirring to obtain a uniform emulgel.

Emulgel Preparation – 2

Step 1: Gel Base Preparation

The gel base is prepared by dispersing Carbopol 934 in purified water with constant mechanical stirring, followed by pH adjustment to 6–6.5 using triethanolamine (TEA).

Step 2: Emulsion Preparation

- **Oil phase:** Span 80 is dispersed in oleic acid.
- **Aqueous phase:** Tween 80 is dispersed in purified water.
- Posaconazole is dissolved in methanol, while methyl and propyl paraben are dissolved in propylene glycol along with Transcutol P; these solutions are then added to the aqueous phase.

Step 3: Mixing of Phases

Both the oil and aqueous phases are heated to 70–80°C, after which the oil phase is added to the aqueous phase under continuous stirring until the mixture cools to room temperature. The resulting emulsion is stored in a tightly closed container.



Fig 1: Itraconazole Formulation

Table 1: Formulation Composition of Itraconazole-Loaded Gel/Emulgel Systems (F1–F6)

Formulation	F1	F2	F3	F4	F5	F6
itraconazole	1g	1g	1g	1g	1g	1g
Carbapol 940	-	-	0.5	1	-	-
HPMC	-	-	-	-	0.5	1
Poly vinyl alcohol	0.5	1	-	-	-	-
Span 80	0.5	0.5	0.5	0.5	0.5	0.5
Tween	0.6	0.6	0.6	0.6	0.6	0.6
Methyl paraben	0.2	0.2	0.2	0.2	0.2	0.2
Propyl paraben	0.1	0.1	0.1	0.1	0.1	0.1
Triethanol amine	1	1	1	1	1	1
Water	2	2	2	2	2	2

Pre-formulation studies**Drug – excipient compatability(FTIR)**

FTIR analysis for Itraconazole was done by FTIR spectrometer Shimadzu (Model: FTIR-8400S). Each sample was mixed with potassium bromide in 1:100 and compressed to observed at the range from 4000 to 400 cm⁻¹.

Organoleptic properties

“The pure ketoconazole sample was studied for their organoleptic properties like color, odor, taste and crystallinity and pH”.

Determination of Melting Point

Melting point of ketoconazole sample was determined by using melting point apparatus. “Itraconazole was filled in one end open capillary tube. The capillary was placed in melting point apparatus and gradually temperature rises when drug was melted the melting point of Itraconazole powder was recorded”.

Evaluation Methods**Physical Appearance**

Color, homogeneity, consistency, and pH of the produced Emulsion compositions were visually evaluated.

Spreadability

Mutimer et al (1956) suggested an equipment for determining spreadability, which was adapted in the lab and used for the investigation. It's built out of a wooden block with a pulley on one end. Spreadability is measured using this method based on the emulgel's 'Slip' and 'Drag' qualities. On this block a ground glass slide is fixed. This ground slide has an excess of emulgel (approximately 2 gm) under observation. After that, the emulgel is placed between this slide and a second glass slide with the same size as the fixed ground slide, as well as a hook. For 5 minutes, a 1 kg weight is placed on top of the two slides to release air and provide a consistent emulgel coating between the slides. The excess emulgel is scraped away from the edges. After that, an 80-gram pull is applied to the top plate. The time (in seconds) required by the top slide to cover a distance of 7.5 cm should be recorded with the help of string tied to the hook. The shorter interval, the

better the spreadability. The formula was used to calculate spreadability.

$$S = M.L/T$$

S = spreadability.

M = Weight tied to upper slide.

L = Length of glass slides.

T = Time taken to detach the slides

Extrudability study

It's a common empirical test to determine how much force is required to extrude material from a tube. When the shear rate is greater than the yield value, the procedure for determining the amount of applied shear in the rheogram zone that results in plug flow. The method used to evaluate emulgel formulations for extrudability in this study is based on the percentage of emulgel and emulgel extruded from a lacquered aluminum collapsible using the gramme weight required to extrude at least a 0.5 cm emulgel ribbon in 10 seconds. Extrudability improves as the quantity extruded increases. Each formulation's extrudability is measured three times and the average values are reported. After that, the extrudability is computed using the formula: **Extrudability = Weight used to extrude emulgel from tube (in gm) / Area (in cm²).**

Rheological studies

A Brookfield viscometer with spindle no.18 at 100 rpm is used to determine the rheological properties of the various emulgel compositions at 250° C.

Swelling Index

Weighing 1 gramme of prepared topical emulgel on porous aluminium foil and depositing it separately, undisturbed, in a glass beaker with a capacity of 50 ml and 10 ml of 0.1 N NaOH determined the swelling index. The samples are then withdrawn from the beakers at various time intervals and placed in a dry place for a period of time before being reweighed. The swelling index was calculated by using the equation:

$$SW \% = [Wt - W_o / W_o] \times 100$$

SW % = Equilibrium percent swelling

Wt = Swollen Weight emulgel after time t,

Wo = Initial weight of emulgel at time **Skin irritation study**

In the formulation, 0.5 g of each is uniformly placed over a 4 cm² area on the hairless skin of rabbits. After 24, 48, and 72 hours of application of the formulation, the skin surface is examined for any obvious changes such as erythema (redness).

The following are the erythema scores: no erythema=0, minimal erythema (barely perceptible-light pink) =1, moderate erythema (dark pink) =2, moderate to severe erythema (light red) =3, and severe erythema (dark red) =4 (extreme redness).

In-vitro drug release

Release of itraconazole from emulgel formulation was measured through dialysis membrane by using Franz diffusion cell. Dialysis membrane was soaked in diffusion media for overnight and then placed on support screen of diffusion cell assembly. Phosphate buffer at pH 5.5 was used as the receptor medium and 1g of gel was placed on the donor side. At predetermined time interval, 2ml of sample was withdrawn from the receptor compartment and replaced with same volume of phosphate buffer at pH 5.5. The aliquots were analyzed by UV spectrophotometer at 226nm.

Stability study

The emulgels are packed in aluminium collapsible tubes (15 gramme) and tested for three months at 50°C,

250°C/60 percent relative humidity, 300°C/65 percent relative humidity, and 400°C/75 percent relative humidity. Each month, samples are taken and evaluated according to ICH requirements for physical appearance, pH, rheological properties, drug content, and drug release profile, among other things.

To assess the physical, chemical, and performance stability of Itraconazole emulgel over time under different storage conditions as per ICH guidelines.

Dilution test

By introducing Continuous phase to a 50 to 100 times aqueous dilution of emulgel, phase separation and clearness were visually verified.

Determination of PH

A digital pH meter was used to determine the pH of the formulation. The pH meter electrode was cleaned in distilled water before being put into the mixture to measure

RESULTS & DISCUSSION

Physical appearance

emulgel preparation were thick creamy preparation with smooth homogeneous texture, the color of formulation was examined against a white, and the consistency of emulgel was verified by applying it to the skin.

Table 2: Organoleptic and Physical Characteristics of Itraconazole Formulations

Formulation code	colour	Phase separation	Homogeneity	Consistency
F1	White	No	Homogenous	Creamy
F2	White	No	Homogenous	Creamy
F3	White	No	Homogenous	Creamy
F4	White	No	Homogenous	Creamy
F5	White	No	Homogenous	Creamy
F6	White	No	Homogenous	Creamy

Drug-Excipient compatibility (FTIR)

FTIR Spectrum of ketoconazole was obtained by scanning the drug in the range of 4000 to 400cm⁻¹. Observed FTIR

spectra and standard values. The observed value was within the range or very close to the characteristic peaks of standard value confirming drug as Itraconazole.

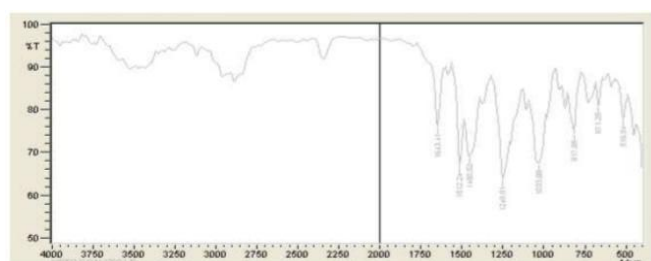


Fig 2: FTIR spectra of itraconazole

An FTIR spectrum of formulation shows significant peaks of Itraconazole indicating no interaction between ketoconazole and carbapol 934.

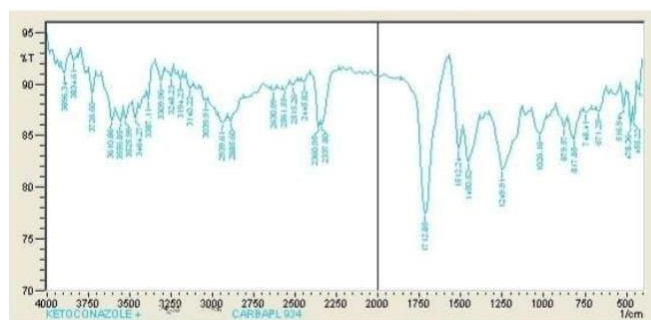


Fig 3: FTIR spectra of itraconazole + carbapol 940

Organoleptic properties

The drug was studied for their organoleptic properties like odour, taste, crystalline was observed.

Table 3: Organoleptic and Physical Characteristics of Itraconazole

Odour	Odourless
Taste	Tasteless
Crystalline	Amorphous

Determination of Melting point

Melting point of drug was determined by capillary method was found to be 148.6°C (Table 4). The observed value

was found to be in between the range of reported value i.e., 148 °C to 152°C. The observed melting point confirmed the drug as Itraconazole.

Table 4: Melting Point Determination of Itraconazole

Drug	Observed	Reference
Itraconazole	149±2	148.0 °C to 152.0 °C
Itraconazole	148±2	148.0 °C to 152.0 °C
Itraconazole	149±2	148.0 °C to 152.0 °C

Spreadability

A ground glass slide approximately 20 cm in length was mounted to the table. This ground slide was treated with an excess of emu gel (about 1 g). A 500-gram weight was put on top of the two slides for 5 minutes to evacuate air and

create a homogenous coating of emu gel between the slides. The top plate was then pulled by a weight of 50 g linked to the upper slide at a distance of 7 cm. The shorter the time it takes for the slides to move the necessary distance of 7 cm, the better the emulgel spreads.

Table 5: Spreadability Evaluation of Itraconazole Formulations

Formulation	Time (sec)	Length (cm)	Weight (gm)	Spreadability $S=M.L/T$
F1	25	7	50	14
F2	23	7	50	15.21
F3	26	7	50	13.46
F4	21	7	50	16.66
F5	24	7	50	14.58
F6	23	7	50	15.21

Extrudability study

Extrudability is indicative of ease with which product could be easily removed from the collapsible tube. The effect of polymer concentration and consistency were

observed on the extrudability of the product. The extrudability was found to be in the range of 69-75 % for the Carbapol gels whereas from 76.8 to 84.2 for the tamarind gum gels.

Table 6: Extrudability (%) and Grading of Prepared Itraconazole Formulations

Formulation	Extrudability (% gel Extruded)	Grade
B1	79	Fair
F2	77.4	Fair
B3	72.8	Fair
B4	83.1	Good
B4	81.3	Good
B5	76.8	Good

Rheological Study

The viscosity of the produced emu gel was measured with a Brookfield viscometer (Brookfield viscometer).

Viscosity was measured at 2365 cps. As the concentration of gelling agent grew, so did its viscosity.

Table 7: Viscosity Profile of Itraconazole Formulations (F1–F6)

Formulation code	Viscosity Cps
F1	2151±9.01
F2	2160±4.58
F3	2190±6.50
F4	2262±7.54
F5	2287±7.93
F6	2295±5.29

Swelling Index

The swelling index of different formulations was observed and the data.

Table 8: Swelling Index of Itraconazole Formulations (F1–F6)

Time	F1	F2	F3	F4	F5	F6
0	1	1	1	1	1	1
15	1.15	1.12	1.22	1.13	1.15	1.08
30	1.10	1.14	1.30	1.19	1.17	1.21
45	1.20	1.10	1.16	1.1	1.15	1.24
60	1.4	1.22	1.29	1.25	1.3	1.7
120	1.2	1.8	1.98	1.26	1.23	1.29

Skin irritation

The results of skin irritation test of the optimized selected emulgel formula (F6), there is no irritation signs on the rat skin like erythema, oedema and ulceration after application of the emulgel and monitoring of the irritation signs for 6 days, this result indicates that this formula is safe and suitable for the topical drug delivery.

In-vitro drug release

At predetermined time interval, 2ml of sample was withdrawn from the receptor compartment and replaced with same volume of phosphate buffer at pH 5.5. The aliquots were analyzed by UV spectrophotometer at

226nm. At the end of 6 hours the total amount of drug release from the F5 batch was found to 39 which is the better %drug release as compare to other emulgel formulation.

In-Vitro Drug Release Profile of Formulations F1–F6 (Up to 6 Hours)

An *in-vitro* dissolution study was performed for six different formulations (F1 to F6) to evaluate and compare their drug release profiles over a period of 6 hours (360 minutes). The cumulative percentage of drug released at various time intervals was measured.

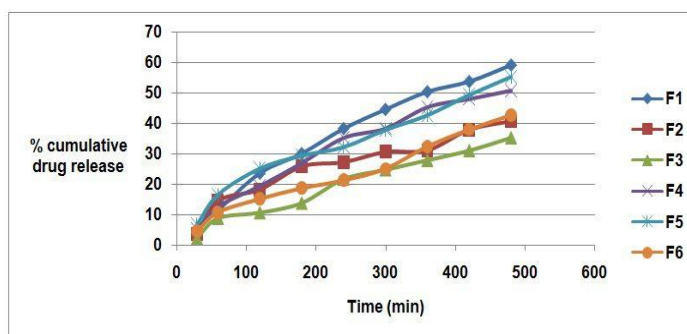


Figure 4: *In Vitro* Cumulative Drug Release Profile of Itraconazole Formulations (F1–F6)

Stability studies:

The stability studies data was represented in Table. All the prepared emulgel formulations were found to be stable upon storage for three months, no change was observed in their physical appearance, clarity, pH, viscosity, spreadability and **Drug content, *in vitro* release studies:**

Stability studies of F6 emulgel formulations

Physical appearance and drug content showed minimal changes over 3 months, confirming good stability. The formulation was stable under accelerated conditions with no microbial growth. The emulgel maintained acceptable pH, viscosity, and drug release profile as per pharmacopeial limits. Thus, the Itraconazole emulgel formulation complies with ICH stability requirements.

Table 9: Effect of Storage on Homogeneity, pH, Spreadability, Viscosity, and Drug Content of Itraconazole Formulation

Time period	Homogeneity	PH	Spreadability	Viscosity	Drug content
Before	Good	6.23±0.10	17	2295±5.29	89.56±4.29
After	Good	6.12±0.11	17	2190±4.21	87.47±5.13

Stability studies of F6 emulgel formulation-drug release:

Table 10: Stability Evaluation of Optimized Itraconazole Formulation Before and After Storage (F6)

Time (hr)	Before storage	After storage
5	12.91±2.56	11.61±1.04
10	24.26±2.94	22.61±1.74
15	37.45±2.01	35.42±2.74
20	45.12±3.56	43.21±2.08
25	55.25±1.73	51.24±1.96
30	62.15±2.20	62.15±2.20

Dilution test

Dilute the emulgel with distilled water in ratios like **1:10**, **1:20**, or even **1:50**

Table 11: Observation for clarity, phase separation, precipitation, and homogeneity

Dilution ratio (emulgel:water)	Appearance	Phase separation	Precipitation	Homogeneity
1:1	Uniform, semi-solid	No	No	Good
1:5	Slightly thinner gel	No	No	Good
1:10	Flowable, still uniform	No	No	Good
1:20	Very flowable	No	No	Acceptable
1:50	Watery consistency	No	Slightly traces	Poor

PH determination

The pH of the produced emulgel was measured using a pH meter. The pH of the emulgel formulation was in the range of 5.7-6.3, which was regarded adequate to avoid the risk of skin irritation upon application to the skin.

Table 12: pH values of Formulations

Formulation code	pH
F1	9.20
F2	8.9
F3	8.31
F4	9.15
F5	8.6
F6	8.8

CONCLUSION

In the present study, an attempt has been made to formulate the topical drug delivery system of Itraconazole Emulgel. Itraconazole is an antifungal medicine made up of triazole that is used to treat a variety of fungal infections. Tinea, cutaneous candidiasis, pityriasis versicolor, dandruff, and seborrheic dermatitis are all fungal skin infections. When taken by mouth, this medication has a low absorption rate. To counter this, topical drug delivery is favored, as it prevents the drug's first-pass metabolism.

The itraconazole was firstly characterized for its identification by using physical characterization test like:

- Melting point was obtained 149 ± 2 .
- Emulgel was developed using gelling agent's carbapol 940 and hydroxy propyl methyl cellulose. Span and tween 20 used as Emulsifiers. Propylene glycol used as penetration enhancer. Methyl paraben and propyl paraben used as preservative and Itraconazole as a Hydrophobic drug.
- The major objective behind this formulation is to enhance topical delivery of hydrophobic drug (Itraconazole) by formulating Itraconazole emulgel by using carbopol 934 as gelling agent.
- The prepared emulgel were evaluated for their physical appearance, pH determination, viscosity, spreadability, in-vitro drug release and drug content. Physical characteristics of all the prepared emulgels were acceptable.
- To investigate the rate and duration of drug release from emulgel, in vitro drug release and drug content of the test formulation was done. In vitro testing

reveals a maximum release of 98 percent in 6 hours in ideal (F5) formulations.

- When compared to all other formulations, the formulation batch F5 shows better drug release.

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