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Formulation, development and evaluation of ketoconazole bigel for enhanced topical antifungal therapy

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Abstract

The present study aimed to develop and evaluate a Ketoconazole-loaded bigel formulation for effective topical antifungal treatment with enhanced drug release and improved patient compliance. Bigels were prepared by combining hydrogels (Carbopol-934, HPMC, and Guar Gum) with organogels containing coconut oil, lemon oil, and almond oil in a 1:1 ratio. A total of nine formulations (BG1–BG9) were developed and characterized for physicochemical properties, drug compatibility, spreadability, extrudability, in vitro drug release, stability, and antifungal activity. Preformulation studies including melting point, solubility, UV spectroscopy, FTIR, and DSC analysis confirmed the identity and compatibility of Ketoconazole with selected excipients. The prepared formulations exhibited acceptable pH (7.0–7.6), good homogeneity, and satisfactory rheological properties. Among all formulations, BG1 containing Carbopol-934 hydrogel and coconut oil organogel demonstrated superior spreadability (8 cm), excellent extrudability, and the highest cumulative drug release (25.78% within 180 minutes). Drug release kinetics indicated a diffusion-controlled mechanism following first-order release behavior. Stability studies conducted under different storage conditions for three months revealed no significant changes in physical appearance, pH, viscosity, or drug content, confirming formulation stability. The antifungal sensitivity study demonstrated effective activity against fungal strains associated with Tinea versicolor. The results suggest that Ketoconazole-loaded bigel, particularly formulation BG1, is a promising carrier system for topical antifungal therapy, offering improved drug delivery, stability, and therapeutic efficacy.

Keywords: Ketoconazole, Bigel, Topical Drug Delivery, Hydrogel, Organogel, Antifungal Activity, Carbopol-934, In Vitro Drug Release, Stability Studies, Tinea Versicolor, Diffusion-Controlled Release, Skin Drug Delivery.

Introduction

The Skin

The skin is one of the most extensive and readily accessible organs of the human body. The skin of an average adult body covers a surface area of approximately 2 m² (or 3000 inch²) and receives about one-third of the blood circulating through the body. (McGrath et al, 2004) It is elastic, rugged and under normal physiological conditions, self-regenerating,with a thickness of only a fewer mm (2.97±0.28 mm). (Williams et. Al, 2003).

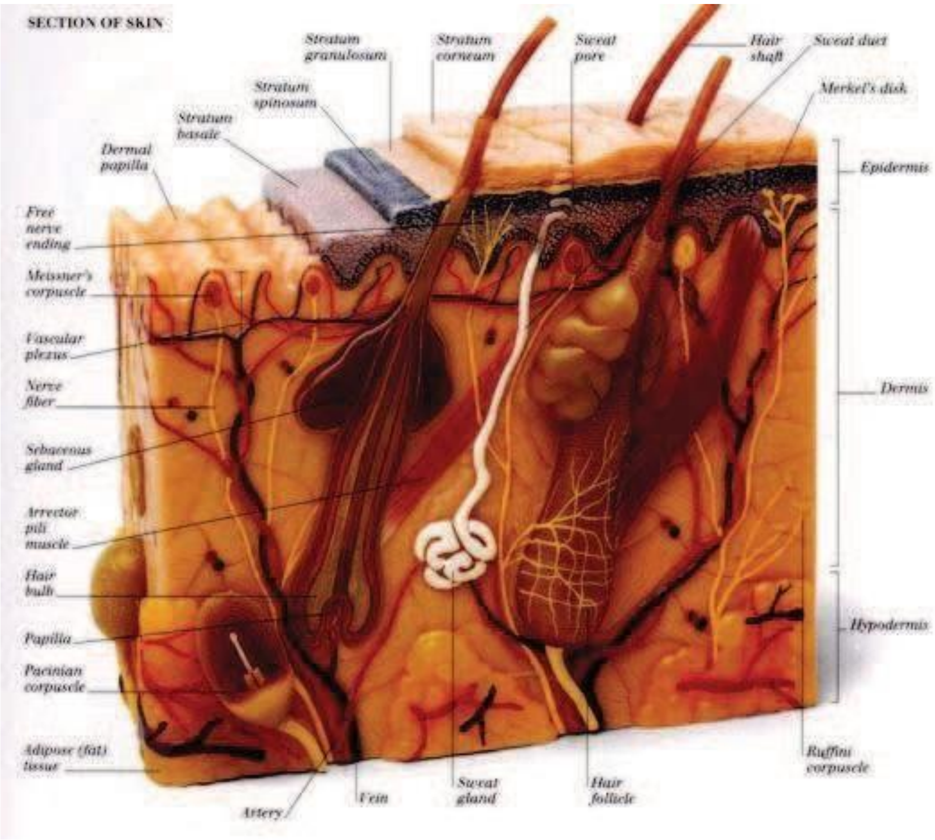


Figure 1: Structure of Skin

Methods

Analysis of Ketoconazole

1. **Differential Scanning Calorimetry** (Quadeib, et al. 2014)

Differential Scanning Calorimetry (DSC) was employed to determine the melting point of Ketoconazole sample used in present investigation. Differential scaning calorimeter equipped with a liquid nitrogen sub-ambient accessory. The instrument operated under nitrogen pure gas at a rate of 20 ml/min The DSC analysis was carried out over 20-260^{0}C at 10^{0}C/minute, using duplicate samples of 5 mg in crimped aluminum samples pans. Indium was used to calibrate the DSC instruments.

2. **Fourier Transform Infra-Red Spectroscopy (FTIR)** (Chonkar, et al. 2014)

The IR analysis of the sample was carried out for qualitative compound identification. The IR analysis provides complete description regarding the interactions between drug and excipients. The pellet of approximately 01 mm diameter of the drug was prepared grinding approximately 5 mg of sample with 100-120 mg of Potassium Bromide in pressure compression machine. The sample pellet was mounted in IR compartment and scanned at wavelength 4000 cm^{-1} – 400 cm^1.

3. **Ultraviolet absorption** (Lalima, et al. 2020)

Ultraviolet spectroscopy analysis of the drug was carried out for wavelength maxima and absorbance determination and calibration of standard curve of the drug. It is performed by preparing various conc. of solution (methanolic Phosphates

Buffer, pH 7.4) of drug and run the spectroscopy in the range of 240 to 400 nm to obtain the absorbance for their relative concentration.

4. **Solubility** (Lilian et al. (2019)

The solubility of Ketoconazole was determined in different solvents. An excess quantity of the drug was added in 10 ml of each solvent in screw capped glass test tubes and shaken or 12 hours at room temperature. The solution was filtered, diluted and the solubility was determined at 415 nm spectrophotometrically.

5. **Partition coefficient** (Lilian et al. (2019)

The partition coefficient of Ketoconazole was determined in n-octanol: phosphates buffer pH 7.4 system. An accurately weighed (500mg) amount of Ketoconazole was added into 10 ml each of n- octanol and aqueous phase in a screw capped tube. The mixture was shaken for 20 hours until equilibrium was reached. Phases were separated; the aqueous phase was filtered, diluted and the amount of Ketoconazole solubilized in aqueous phase was determined by measuring the absorbance at 415 nm spectrophotometrically.

The partition coefficient of Ketoconazole was calculated from the ratio between the concentration of Ketoconazole in organic and aqueous phase using following equation.

$\mathbf{P_{o/w} = (C_{Oil} / C_{pH\ 7.4})}$ **equilibrium**

Calibration curve of Amphotericin-B

- **Determination of Absorption maxima**

A UV absorption maxima was determined by scanning a 2 to 10 ug/ml solution of Ketoconazolein 5% (v/v) methanolic Phosphate buffer pH 7.4 between 240- 500nm.

- **Preparation of Calibration Curve**

10 mg of Ketoconazolewas weighed accurately and dissolved 5ml methanol in a 100 ml of volumetric flask and volume was made up to with the Phosphate buffer pH 7.4. Two ml of this solution was diluted to 10 ml with pH 7.4 Phosphate buffer to obtain a stock solution of 20ug/ml.

From this stock solution, samples of 1ml, 2ml, 3ml, 4ml……10ml were transferred to 10 ml volumetric flasks and volume was made up to 10ml Phosphate buffer pH 7.4. The absorbances of these solutions were measured at 415 nm against a blank phosphate buffer pH 7.4. The calibration curve was plotted between concentration and absorbance.

Preparation Methods (Panchagnula, et al., 1997) (Ram et al., 2020)

Topical gels are semisolid formulations used for the localized delivery of drugs or active ingredients to the skin. They provide a convenient and controlled means of delivering therapeutic agents and can be formulated using various methods. Here are some common formulation methods for topical gel preparation:

- Cold Mixing Method: This is a simple and commonly used method for preparing topical gels. It involves dispersing the gelling agent, such as a polymer, in a suitable solvent or mixture of solvents. The active ingredient(s) and other excipients are then added while stirring until a homogenous gel is obtained. Cooling may be necessary to facilitate gel formation if the gelling agent is temperature-sensitive.

- Hot Mixing Method: In this method, the gelling agent and other ingredients are mixed in a suitable solvent and heated to a temperature above the gelling agent's melting point. The mixture is stirred until all components are dissolved or dispersed, and then allowed to cool to form a gel. This method is often used for gelling agents that require higher temperatures to dissolve or for better homogeneity.
- In situ Gelation Method: Some gelling agents can undergo gelation in response to changes in temperature, pH, or ion concentration. In the in situ gelation method, the gelling agent is incorporated into a liquid or semisolid formulation, and gelation occurs upon application to the skin due to environmental triggers. For example, a sol-to-gel transition may occur when the formulation is exposed to body temperature.
- Polymer Swelling Method: This method involves dispersing a gelling agent, such as a crosslinked polymer, in a suitable solvent. The polymer absorbs the solvent and swells to form a gel-like consistency. The active ingredients and other excipients are incorporated into the swollen polymer matrix to create the topical gel. This method is commonly used with polymers such as Carbopol®.
- Solvent Evaporation Method: In this method, a polymer or combination of polymers is dissolved in a volatile organic solvent to form a clear solution. The active ingredients and other excipients are added to the polymer solution, and the mixture is mixed and stirred until homogenous. The gel is then obtained by evaporating the solvent, either under reduced pressure or by allowing it to evaporate at room temperature.
- Rheological Modification Method: This method involves modifying the rheological properties of an existing gel base by incorporating a gelling agent or thickening agent. The base gel may already contain some polymers or structuring agents, and the additional gelling agent helps enhance the viscosity and gel-like consistency. This method allows customization and modification of existing gel formulations.

Preparation of projected Bigel (Agne et al., 2018)

Hydrogel: All the ingredients were collected according to the formula the given above table Required amount of gelling agents Carbopol-934, HPMC, and Guar Gum were added in water with constant stirring at 500 rpm for about 2 hours. Propylene glycol, methyl paraben, propyl paraben and Triethanolamine were added to it with maintaining 25°C. Final weight was made with water. All the samples were allowed to equilibrate for 24 h at room temperature prior to performing evaluation test.

Organogel: All the Chemical/ingredients were collected according to the formula the given above table required amount. Add span-60 in DMSO solution than added above given oils separately with constant stirring at 500 rpm for about 1 hour. Propylene glycol, methyl paraben, propyl paraben and Triethanolamine were added to it with maintaining 60°C. Final weight was made with Oil. All the samples were allowed to equilibrate for 24 h at room temperature prior to performing evaluation test.

Bigel: A bigel was obtained when the heated organogel was added to the hydrogel under continuous stirring (500 rpm) to obtain a homogeneous mixture and with cooling to ambient temperatures. Nine bigel formulations were prepared by using various ratios of hydrogel and Organogel. The prepared bigels were inspected/ evaluated visually for their color, homogeneity, consistency, and phase separation.

Formulation of Gel

Drug Free Gel

Table 1: Hydrogel

Ingredients (mg)	DFH1	DFH2	DFH3
Ketoconazole	-	-	-
Carbopol-934	100mg	-	-
HPMC	-	100mg	-
Guar Gum	-	-	100mg
Propylene Glycol	500mg	500mg	500mg
Triethanolamine	10mg	10mg	10mg
Methyl Paraben	10mg	10mg	10mg
Propyl Paraben	0.25mg	0.25mg	0.25mg
Water	9.380ml	9.380ml	9.380ml
Total	≈10gm	≈10gm	≈10gm

All the ingredients were collected according to the formula the given above table Required amount of gelling agents Carbopol-934, HPMC, and Guar Gum were added in water with constant stirring at 500 rpm for about 2 hours. Propylene glycol, methyl paraben, propyl paraben and Triethanolamine were added to it with maintaining 25°C. Final weight was made with water. All the samples were allowed to equilibrate for 24 h at room temperature prior to performing evaluation test.

Table 2: Organ gel

Ingredients (mg)	DFO1	DFO2	DFO3
Ketoconazole	-	-	-
Coconut Oil	2000mg	-	-
Lemon Oil	-	2000mg	-
Almond Oil	-	-	2000mg
DMSO	3000mg	3000mg	3000mg
Span-60	4980mg	4980mg	4980mg
Triethanolamine	10mg	10mg	10mg
Methyl Paraben	10mg	10mg	10mg
Propyl Paraben	0.25mg	0.25mg	0.25mg
Total	≈10gm	≈10gm	≈10gm

All the Chemical/ingredients were collected according to the formula the given above table required amount. Add span-60 in DMSO solution than added above given oils separately with constant stirring at 500 rpm for about 1 hour. Propylene glycol, methyl paraben, propyl paraben and Triethanolamine were added to it with maintaining 60°C. Final weight was made with Oil. All the samples were allowed to equilibrate for 24 h at room temperature prior to performing evaluation test.

Preparation of Bigel:

Drug Containing Gel:

Table 3: Hydrogel

Ingredients (mg)	DCH1	DCH2	DCH3
Ketoconazole	200mg	200mg	200mg
Carbopol	100mg	-	-
HPMC	-	100mg	-
Guar Gum	-	-	100mg
Propylene Glycol	500mg	500mg	500mg
DMSO	2ml	2ml	2ml
Triethanolamine	10mg	10mg	10mg
Methyl Paraben	10mg	10mg	10mg
Propyl Paraben	0.25mg	0.25mg	0.25mg
Water	7.180ml	7.180ml	7.180ml
Total	≈10gm	≈10gm	≈10gm

Table 4: Organ gel

Ingredients (mg)	DCO1	DCO2	DCO3
Ketoconazole	200mg	200mg	200mg
Coconut Oil	2000mg	-	-
Lemon Oil	-	2000mg	-
Almond Oil	-	-	2000mg
DMSO	3000mg	3000mg	3000mg
Span-60	4780mg	4780mg	4780mg
Triethanolamine	10mg	10mg	10mg
Methyl Paraben	10mg	10mg	10mg
Propyl Paraben	0.25mg	0.25mg	0.25mg
Total	≈10gm	≈10gm	≈10gm

All the Chemical/ingredients were collected according to the formula the given above table. Add 200mg Ketoconazole in 500mg DMSO and dissolve completely and tagged name label-A. Now add Span-60 in solution –A. Required amount of coconut oil/ Lemon oil and Almond oil added in solution-A and continuously stirring at 500 rpm for about 1 hour. Propylene glycol, methyl paraben, propyl paraben and Triethanolamine were added to it with maintaining 60°C. Final weight was made with Oil. All the samples were allowed to equilibrate for 24 h at room temperature prior to performing evaluation test.

Table 5: Preparation of Bigel of Ketoconazole and Ketoconazole:

Formulation	BG1	BG2	BG3	BG4	BG5	BG6	BG7	BG8	BG9
Ratio	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1
Hydrogel+ Organogel Code	DCH1+ DCO1	DCH1+ DCO2	DCH1+ DCO3	DCH2+ DCO1	DCH2+ DCO2	DCH2+ DCO3	DCH3+ DCO1	DCH3+ DCO2	DCH3+ DCO3

A bigel was obtained when the heated organogel was added to the hydrogel under continuous stirring (500 rpm) according above given table to obtain a homogeneous mixture and with cooling to ambient temperatures. Nine bigel formulations were prepared by using various ratios of hydrogel and Organogel. The prepared bigels were inspected/ evaluated visually for their color, homogeneity, consistency, and phase separation.

Evaluation of Ketoconazole Gel:

Standard curve of Ketoconazole

100 mg of accurately weighed Ketoconazole was dissolved in little amount of 0.1M hydrochloric acid and made up to required volume 100 ml with 0.1M hydrochloric acid. So that each ml of stock solution required concentration of 0, 2, 4, 6, 8, 10 and 12 µg/ml was made up with 0.1M hydrochloric acid. The absorbance of the dilute sample was measured pectrophotometrically at 415nm using 0.1M hydrochloric acid in UV- spectrophotometer. The standard plot was made with concentration (µg /ml) on X axis and Absorbance on Y axis.

Table 6: Standard curve of Ketoconazole

Sn	Concentration (µg/ml)	Mean Absorbance* ± S.D
1	2	0.0776 ± 0.00046
2	4	0.1466 ± 0.00011
3	6	0.2136 ± 0.00013
4	8	0.2816 ± 0.00026
5	10	0.3506 ± 0.00029

* Mean of five values

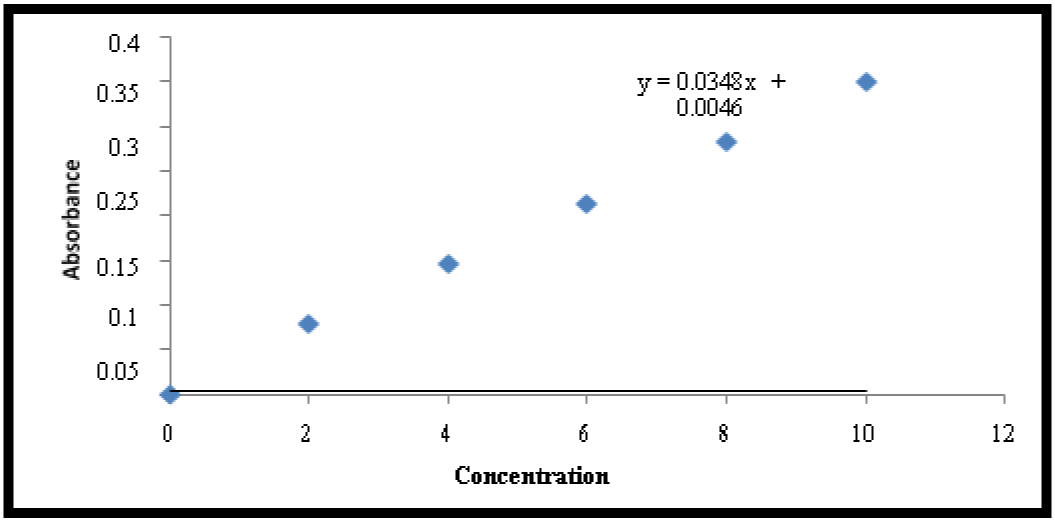


Figure 2: Calibration Curve of Ketoconazole

Results

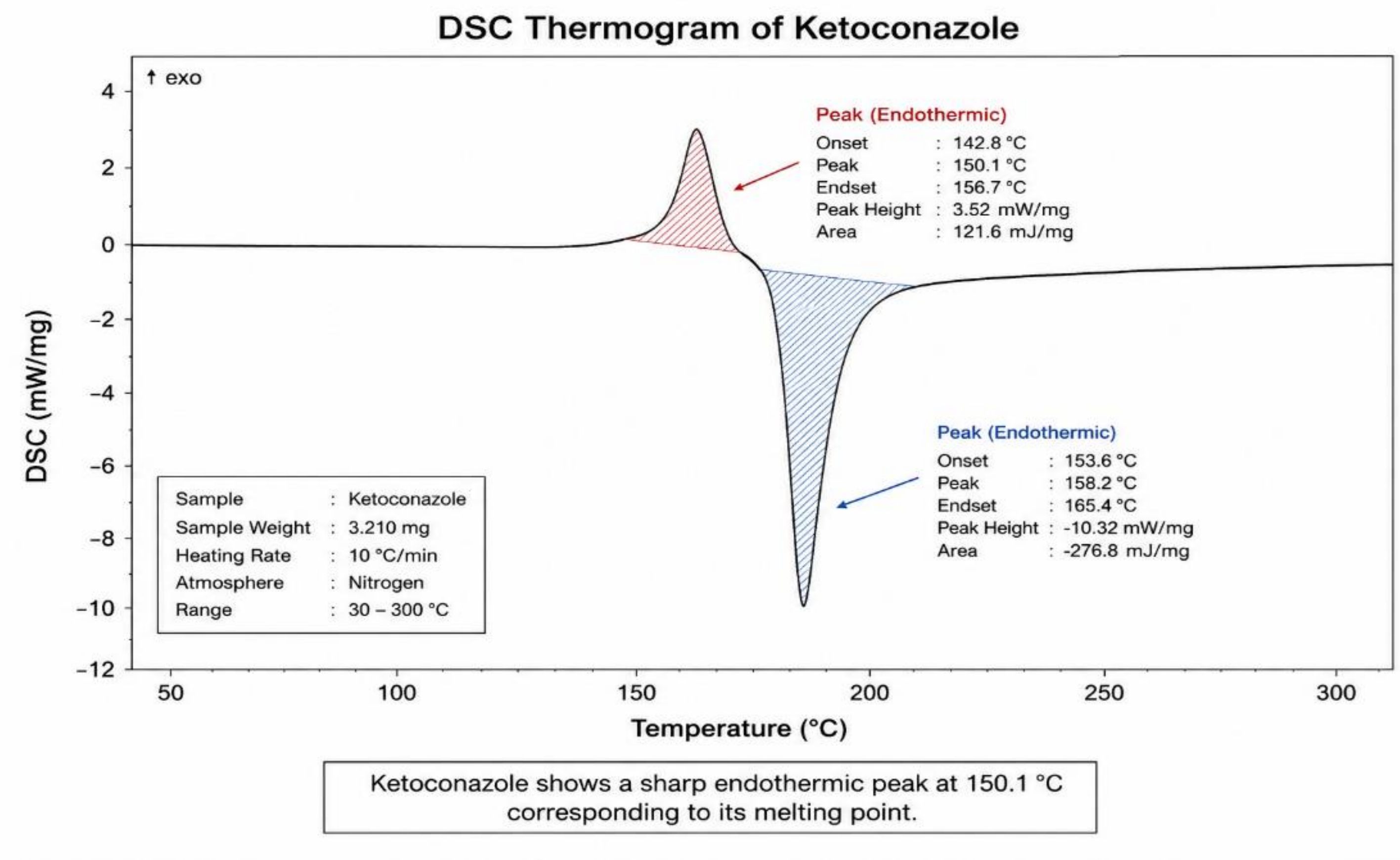
In the proposal study Bigel of Ketoconazole was prepared and evaluated for their use to obtain Local Fast release and Increased bioavailability by preventing from first pass metabolism

Preformulation Studies

- **Physical Appearance:** Physical appearance of pure drug was studies and was found a white (Ketoconazole) powder.
- **Melting Point:** Melting point of the drug was observed within the range of 150 °C (Ketoconazole)
- **Solubility:** Ketoconazole is Soluble in dimethyl sulphoxide; slightly soluble in dimethyl formamide and in methanol; insoluble in benzene, in ethanol (95%), in ether and in water.

Analytical Profile of Active Drug (DSC & FTIR)

Ketoconazole: The DSC thermogram of Ketoconazole is shown in Figure 8.1. The DSC thermogram of Ketoconazole showed sharp peak at 150^0C. The identity of a compound was confirmed by comparison with that of an authentic sample and verification of the presence of functional groups in an unknown molecule was done by IR spectra**.** The IR spectra obtained was elucidated for important chromophore groups. The IR spectra showed peaks at 3240, 1650, 1280,950,840 and 510 cm^{-1}. The various peaks are depicted in Figure 2.



Ketoconazole shows a sharp endothermic peak at 150.1 °C corresponding to its melting point.

Figure 3: DSC Thermogram of Ketoconazole

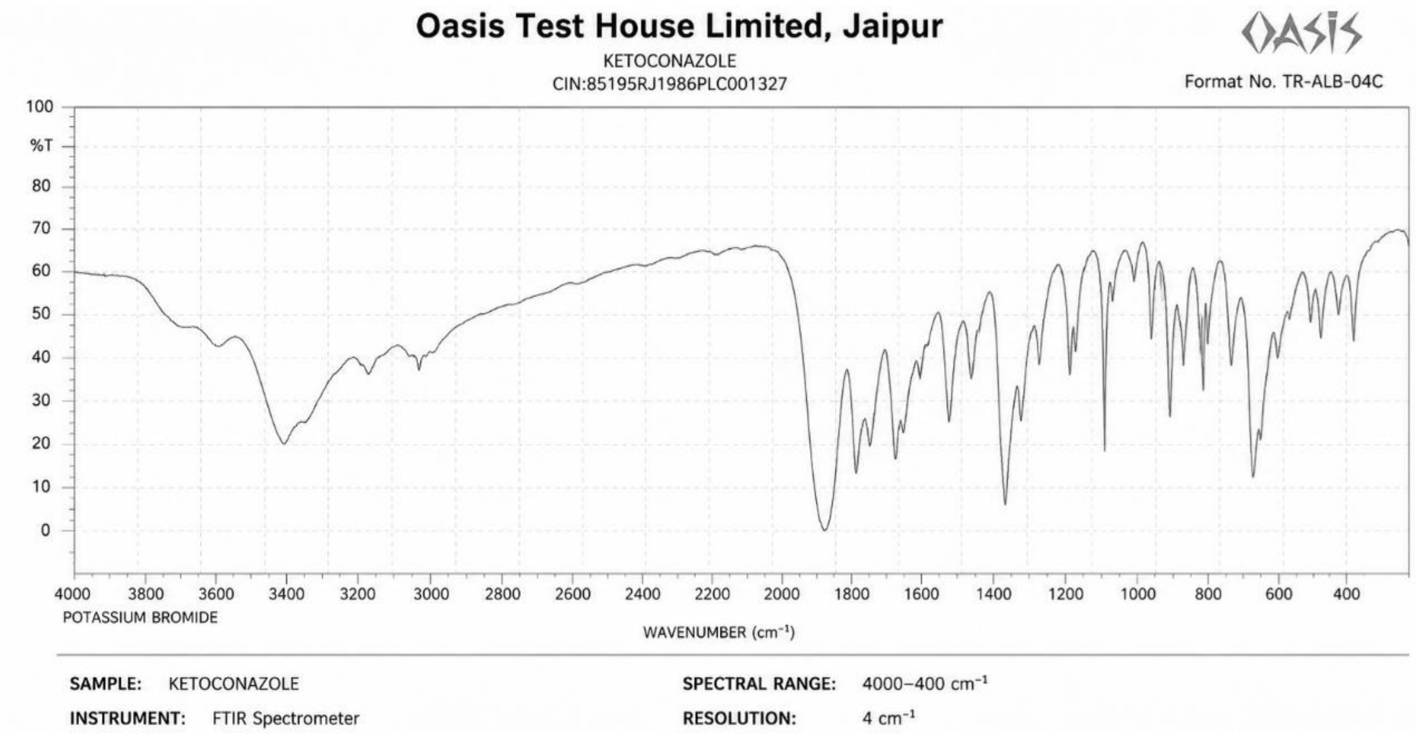
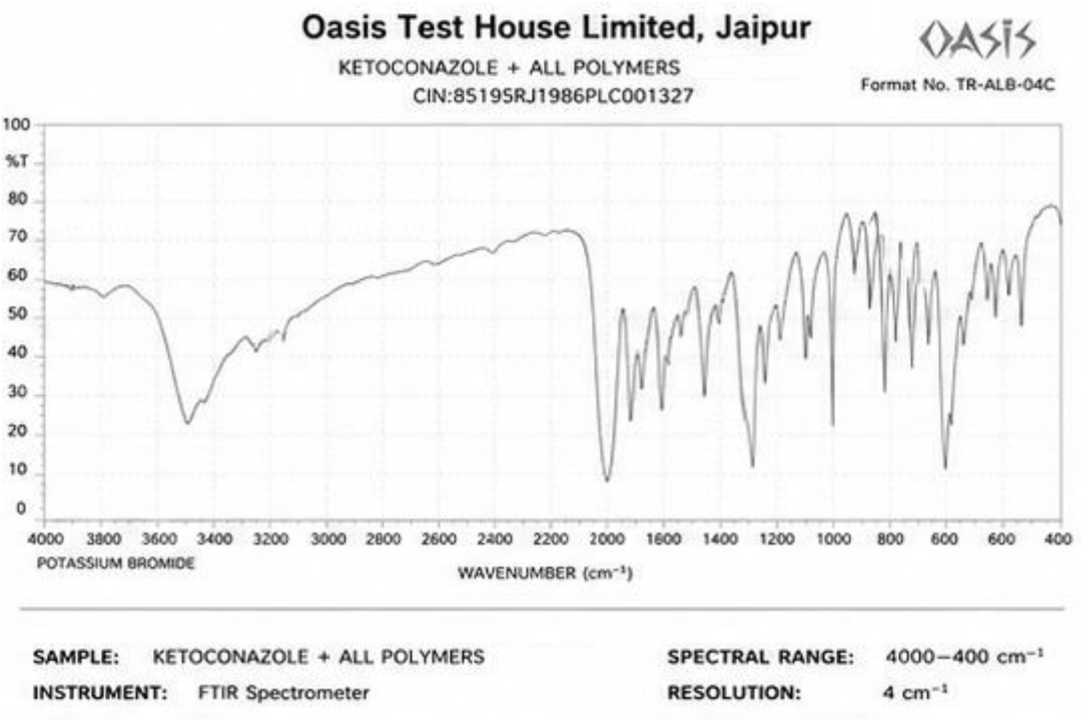


Figure 4: IR Spectra of Ketoconazole

Table 7: FTIR Spectra of Ketoconazole

Functional Group	Observed Value (cm^{-1})
C-O stretch	1718
O-H stretch	3227
N-H	3327
S=O	1044
C-N stretching	1510.28–1451.28
C-F stretching	1587.44–1451.28

a) FTIR of Ketoconazole and various polymers (Compatibility Study)



Oasis Test House Limited, Jaipur

KETOCONAZOLE + ALL POLYMERS

CIN:85195RJ1986PLC001327

Format No. TR-ALB-04C

SAMPLE: KETOCONAZOLE + ALL POLYMERS

INSTRUMENT: FTIR Spectrometer

SPECTRAL RANGE: 4000–400 cm^{-1}

RESOLUTION: 4 cm^{-1}

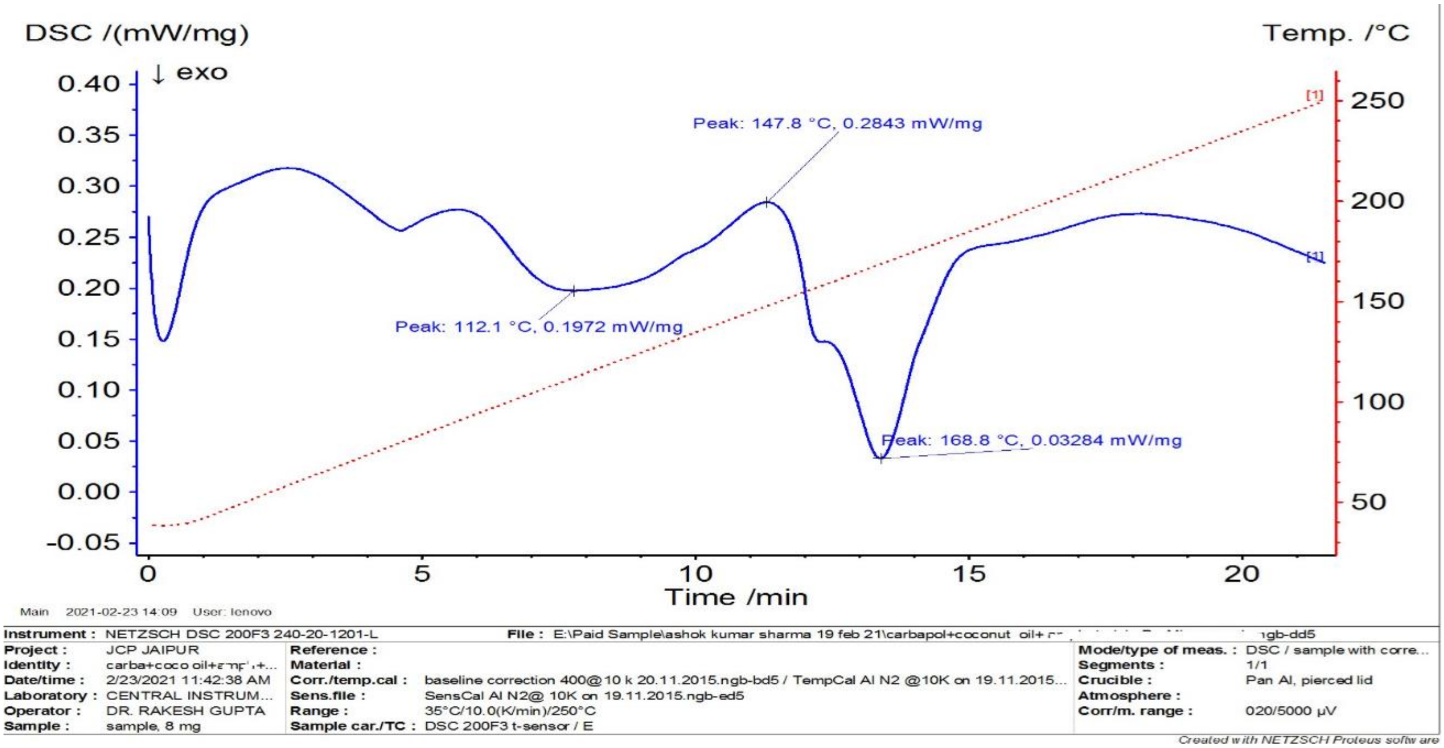
Figure 5: DSC Ketoconazole

Physical Evaluations

Ph: Ph of prepared formulation was evaluated by Digital pH meter. The pH of prepared formulations observed in range 7.0 to 7.6.

Viscosity measurements

- **DSC of Bigel Formulation**



Instrument : NETZSCH DSC 200F3 240-20-1201-L
File : E:\Paid Sample\ashok kumar sharma 19 feb 21\carbapol+coconut oil+
Project : JCP JAIPUR
Identity : carba+coco oil+...
Date/time : 2/23/2021 11:42:38 AM
Laboratory : CENTRAL INSTRUM...
Operator : DR. RAKESH GUPTA
Sample : sample, 8 mg
Reference :
Material :
Corr./temp.cal : baseline correction 400@10 k 20.11.2015.ngb-bd5 / TempCal Al N2 @10K on 19.11.2015...
Sens.file : SensCal Al N2@ 10K on 19.11.2015.ngb-ed5
Range : 35°C/10.0(K/min)/250°C
Sample car./TC : DSC 200F3 t-sensor / E
Mode/type of meas. : DSC / sample with corre...
Segments : 1/1
Crucible : Pan Al, pierced lid
Atmosphere :
Corr/m. range : 020/5000 µV

Created with NETZSCH Proteus software

Figure 6: DSC Bigel Formulation

Extrudability

The extrudability of the gel formulations were checked as per the procedure. Extrudability of carbopol and HPMC gels were excellent than Guar gum gel and the results were shown in Table 8.2

Table 8: Extrudability of gel formulations

Formulation	Extrudability
BG1	++++
B2	++++
BG3	+
BG4	++
BG5	++
BG6	++
BG7	++
BG8	+
BG9	++

++++Excellent, ++Good, +Not satisfactory

Determination of Spreadability

The Spreadability of gels was determined as per the procedure. From spreadability data is observed that the formulation with carbopol-934 showed maximum (8cm), whereas the formulations with carbopol-940, HPMC and Guar gum were showed significant spreadability. The results were tabulated in Table 8.

Table 9: Spreadability of gel formulations

Formulation	Time taken (minutes)	Spreadability (cm)
BG1	30	8.0
BG2	30	7.8
BG3	30	5.4
BG4	30	4.7
BG5	30	5.5
BG6	30	6.3
BG7	30	5.4
BG8	30	5.6
BG9	30	5.2

Scanning And Determination of Maximum Wavelength (λ_{MAX})

Table 10: Scanning of Ketoconazole in different solvents

Sn	Solvent Used	Concentration of final aliquots solution (10 µg/ml)	
		λ_{max}	Absorbance
1.	DMSO	255	0.772
2.	Ethanol	255	0.616
3.	Methanol	255	0.720
5.	Phosphate Buffer (pH 6.8)	255	0.672

Standard curve of Ketoconazole

100 mg of accurately weighed Ketoconazole was dissolved in little amount of DMSO, Ethanol, Methanol and Phosphate Buffers volume 100 ml. So that each ml of stock solution required concentration of 0, 2, 4, 6, 8, 10 and 12 µg/ml was made up with particular solvent. The standard plot was made with concentration (µg /ml) on X axis and Absorbance on Y axis.

Table.11: Curve for the Estimation of Ketoconazole

Sn	Concentration (µg/ml)	Mean Absorbance* ± S.D
1	2	0.0776 ± 0.00046
2	4	0.1466 ± 0.00011
3	6	0.2136 ± 0.00013
4	8	0.2816 ± 0.00026
5	10	0.3506 ± 0.00029

* Mean of five values

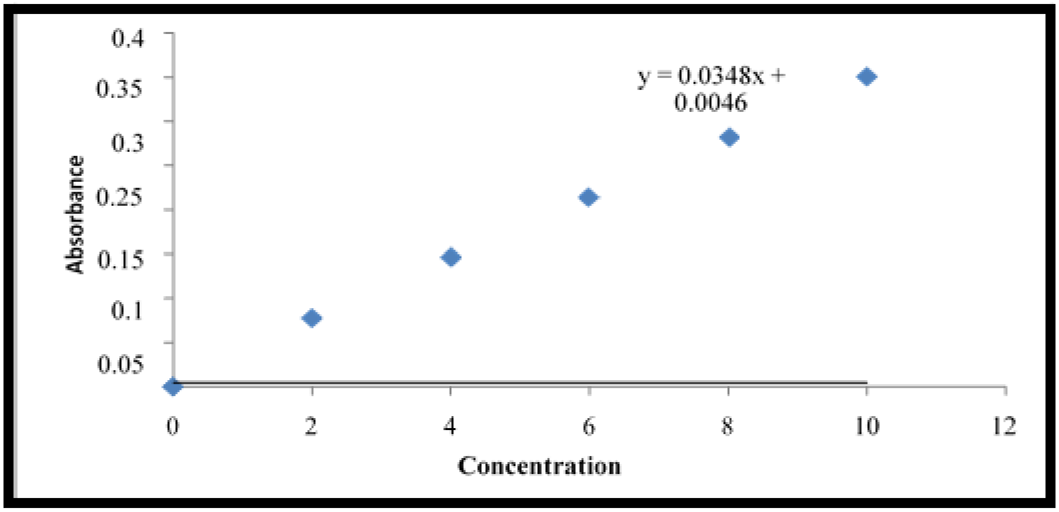


Figure 7: Calibration Curve of Ketoconazole

In-Vitro Release

Table 12 – a: Drug release profile of Formulation BG1

Ketoconazole

Time (minutes)	Absorbance at 255nm	Concentration (µg/ml)	Amount of drug release(mg)	Percentage drug release*
30	0.215	1.651	0.33	3.3
60	0.471	6.879	1.375	13.75
90	0.601	9.475	1.895	18.95
120	0.715	11.856	2.371	23.71
150	0.757	12.591	2.518	25.18
180	0.771	12.894	2.578	25.78

Table 12 – b : Drug release profile of Formulation BG2

Ketoconazole

Time (minutes)	Absorbance at 255nm	Concentration (µg/ml)	Amount of drug release (mg)	Percentage drug release*
30	0.162	0.522	0.104	1.04
60	0.312	3.609	0.721	7.21
90	0.396	5.337	1.067	10.67
120	0.443	6.304	1.26	12.6
150	0.503	7.539	1.507	15.07
180	0.532	8.135	1.627	16.27

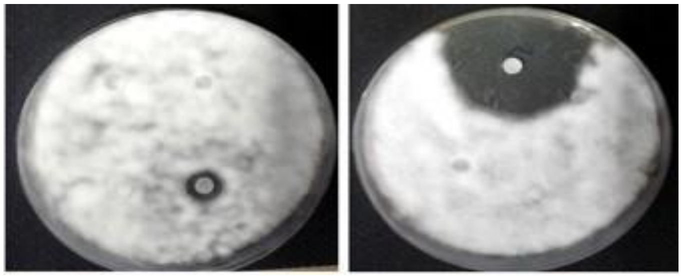
Table 13: Release kinetics and release mechanism of from various Formulations

Model	BG1	BG2	BG3	BG4	BG5	BG6	BG7	BG8	BG9
Zero Order	0.925	0.898	0.865	0.934	0.905	0.885	0.861	0.834	0.775
First Order	0.941	0.923	0.909	0.942	0.919	0.908	0.975	0.939	0.953
Higuchi	0.933	0.899	0.892	0.929	0.892	0.874	0.969	0.978	0.956
Korsmeyer Peppas	0.969	0.960	0.957	0.964	0.954	0.952	0.984	0.979	0.958

Next the Release data obtained were subjected for Kinetic treatment to know the type and order of drug release. From the in-vitro drug release profile it is evident that the kinetic of drug release is first order for all the prepared formulations as the plot between log percent drug retained versus time showed good linearity. The coefficient of determination of R^2 values much closer to 1 for Kosmayer plots, thus indicating the drug release followed a diffusion controlled mechanism.

Skin irritation test: The primary skin irritation test was performed on healthy albino rabbits, weighing between 2.0-3.5 kg. The gel formulation film was prepared and used as test patches, while adhesive tape (USP) was used as control. The test was conducted on unbraided skin of the rabbits. The control and test patches were placed on the left and right dorsal surfaces of the rabbits respectively. The patches were removed after 24 hours with the help of alcohol swab and the skin was examined for erythema and edema[45],

Antifungal sensitivity: The antifungal sensitivity test is employed on to the all the fungi colony of Tinea Versicolor under present study. For this experiment 6 mm diameter wells, stock of bigel applied on it. A SDA plate is seeded with Tinea Versicolor with the help of spread plate technique and left for 5 minutes then incubated for 24 hours at 37°C. After incubation, plates were observed to see the sensitivity of formulation towards test at particular concentration in the form zone of inhibition.



Marketed Product BG1

Figure 8: Stability studies for the formulation BG1 (carbopol-934 with coconut oil)

Stability study for the best formulation was done as per the procedure. The gel was both physically and chemically stable at 4-5^{0}c, Room temperature and 37±5^{0}c.

Table 14: Drug content of formulation BG1

Parameters	Room Temperature	37±5^{0}C	4-5^{0}C
Visual appearance	Transparent	Transparent	Transparent
Initial	Transparent	Transparent	Transparent

Final			
Ph InitialFinal	6.9 7.1	6.9 7.0	6.9 6.9
Viscosity (cps)Initial Final	43,000 43,000	43,000 43,500	43,000 43,000
ExtrudabilityInitial Final	+++ +++	+++ +++	+++ +++
Phase separation	Not found	Not found	Not found
Leakage	Not found	Not found	Not found
Nature Initial Final	 Smooth Smooth	 Smooth Smooth	 Smooth Smooth

Chemical evaluation

The drug content of the formulation was estimated over a period of 3 months. The results were tabulated as follows.

Table 15: Drug content of formulation BG1

Storage condition	Withdrawal period (monthly)			
	0	1	2	3
4-5^{0}C	101.72	101.54	100.04	99.36
Room Temperature	101.72	100.86	99.48	98.93
37±5^{0}C	101.72	100.55	99.08	98.24

Conclusion

The present study successfully developed and evaluated Ketoconazole-loaded bigel formulations for topical antifungal delivery. Among all formulations, BG1 exhibited the best physicochemical properties, excellent spreadability and extrudability, and the highest drug release profile. Compatibility studies confirmed the stability of Ketoconazole with selected excipients, while stability testing demonstrated that the formulation remained stable under different storage conditions. The developed bigel showed promising antifungal potential and can be considered an effective and stable topical drug delivery system for the treatment of fungal skin infections.

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