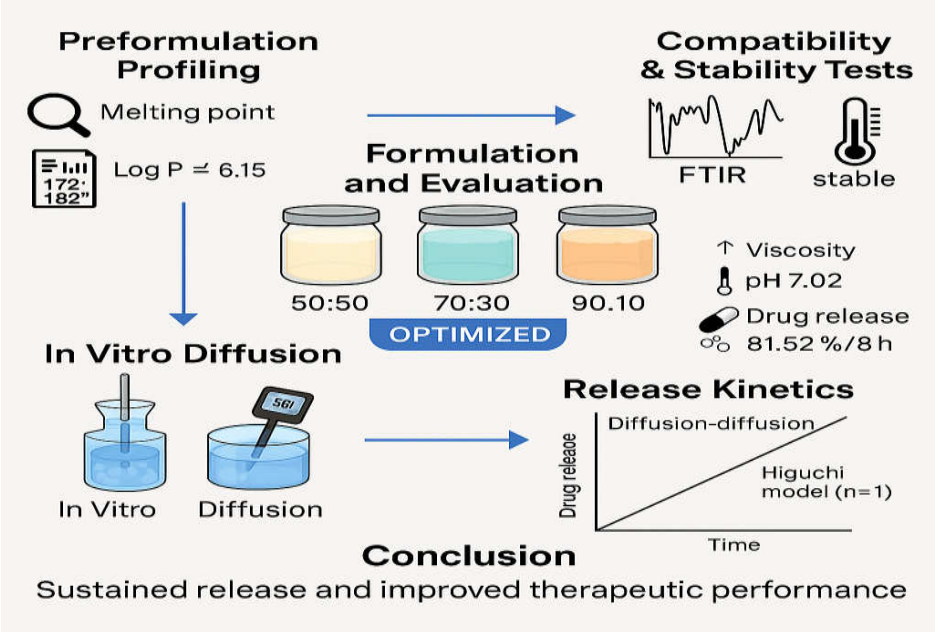
DESIGN AND CHARACTERIZATION OF MICONAZOLE NITRATE BIGEL FOR EFFECTIVE ANTIFUNGAL SKIN APPLICATION

Gursimran Kaur[1], Dr. Sandeep Kumar[2], Simran[3]
Post Graduation (M. Pharmacy) [1], HOD and Professor of Pharmaceutics[2]
[1]Department of pharmaceutics, Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial College of Pharmacy, Bela, Ropar, Punjab, India, PIN: 140111 ORCID-https://orcid.org/0009-0009-8959-8179
[2]Deprepartment of pharmaceutics , Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial College of Pharmacy, Bela, Ropar, Punjab, India, PIN: 140111, ORCID-https://orcid.org/0000-0002-0455-5711
[3]Deprepartment of pharmaceutics, Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial College of Pharmacy, Bela, Ropar, Punjab, India, PIN: 140111



Abstract: Bigel-based topical formulations containing miconazole nitrate for improved antifungal therapy are developed and evaluated in this study. Using a partition coefficient of 6.25 and a melting point of 172–182 °C, preformulation profiling validated the drug's physicochemical suitability. Using UV spectrophotometric analysis, calibration curves were created at 230 nm in phosphate buffer (pH 7.4) and 272 nm in ethanol. By using FTIR and DSC analyses, drug-excipient compatibility was confirmed.

Hydrogel-to-organogel ratios ranging from 50:50 to 90:10 was used to formulate bigels. With the best viscosity (1963 cps at 50 rpm), acceptable pH (7.02 ± 0.03), and 81.52% cumulative drug release within 8 hours, the 70:30 formulation outperformed the others. Physicochemical evaluations verified outstanding extrudability, homogeneity, and spreadability (19.62 ± 0.57 g.cm/sec). Additionally, the optimized formulation demonstrated a favorable gel-

sol transition temperature (34–38 °C) and the maximum drug content (100.00 ± 0.50%). A strong gel structure was indicated by the inversion stability, which lasted for 73 minutes. Diffusion profiles in vitro showed steady and prolonged drug release, and stability tests conducted in real-time, accelerated, and chilled conditions verified formulation integrity with minimal changes in diffusion profiles after storage.

With the potential to overcome the drawbacks of traditional topical antifungal treatments, the 70:30 bigel formulation provides a promising, stable, and efficient delivery system for miconazole nitrate.

Keywords:
Bigel, Drug release kinetics, Miconazole nitrate, Stability assessment, Topical antifungal delivery.

1. INTRODUCTION

Many skin and systemic conditions are treated with topical semi-solid formulations. In addition to minimizing serum absorption and preventing hepatic first-pass metabolism, topical administration helps to achieve a high drug concentration in the skin [1]. This is crucial for long-term treatment, such as for fungal diseases, which fall into three categories: superficial, subcutaneous, and systemic mycoses. Dermatophytosis is the most prevalent fungal infection. Fungal infections like dermatophytosis and candidiasis are frequent, especially in people with weakened immune systems. Conventional topical formulations (creams, gels, and ointments) are frequently used to treat these infections, which frequently need long-term care. Poor skin penetration, short residence time, drug instability, and greasiness are some of these systems' shortcomings, which taken together lower therapeutic efficacy and patient compliance.

Our hypothesis was that the addition of antifungal active ingredients to a gel and bigel would guarantee adequate drug-skin contact and release. Two phases make up the semi-solid formulation known as Bigel (oleo-gel/hydrogel, oleo-hydrogel, or biphasic gels [2]. Small particles of a solid mixed with a sizable volume of liquid form semi-solid matrices called gels. Regardless of the drug's solubility in water, gels may offer quicker drug release than creams and ointments [3]. Bigels are stable, non-greasy systems that combine the benefits of hydrogels and oleo gels, including their ease of preparation, ability to deliver hydrophilic and lipophilic medications, and lack of surfactants [4]. In addition to preventing water loss and promoting even dispersion of the medication on the skin, the oil phase helps hydrate the skin. Bigels and

emulgels are different in that the former have a liquid internal phase, whereas the latter have two structured phases [5].

The broad-spectrum imidazole antifungal miconazole nitrate works by preventing the synthesis of ergosterol, which causes the fungal cell membranes to rupture. Commonly found in creams, gels, and sprays for topical infections, it works well against dermatophytes, Candida, and certain gram-positive bacteria [6].

Its limited skin penetration, short residence time, and poor water solubility, however, frequently diminish therapeutic efficacy and necessitate frequent application. It is a good fit for cutting-edge delivery systems because of these drawbacks [6]. Although bigel formulations have not been the subject of published research, these substances are utilized in gel formulations. Examining suitability of bigel for introducing the tested active ingredients and producing successful therapeutic effects is pertinent.

Phase separation may cause bigels to become unstable at high temperatures, according to certain scientific articles [2]. Therefore, it is crucial to assess how temperature affects the stability of the formulation. This main goal of this article is to assess the quality and stability of bigels made with varying ratios of hydrogel and oleogel using rheological testing, antifungal activity assays, and biopharmaceutical tests conducted in vitro.

2. MATERIAL AND METHODOLOGY

2.1 Materials

Every material used was of analytical or pharmaceutical quality. Keshar Emulsion Pvt. Ltd. provided the miconazole nitrate, while Loba Chem Pvt. Ltd. in Mumbai provided the carbopol 940, ethanol, oleic acid, and other buffer salts. Merck India Ltd. supplied PEG 200 and n-octanol, while SD Fine-Chem Ltd. in Mumbai supplied Tween 20. Every chemical was used without any additional purification.

2.2 Methods

Method of Making a Bigel

The lipophilic and hydrophilic phases were extracted independently in order to prepare bigels. The hydrogel contained ethanol 95% (v/v) 10.0% (w/w), propylene glycol 5.0% (w/w)[7], Carbopol® 940 1.0% (w/w), and 84.0% (w/w) purified water. Tween was present in the organogel at 20.0% (w/w) and oleic acid at 85.0% (w/w). The weighted Carbopol® 940 was

dissolved in a solution of purified water, propylene glycol, and ethanol (at 25 °C and 400 rpm) to make the preparation, in short. When triethanolamine (pH 5.5–6.5) was added, a stable hydrogel was created. At 60°C and 100 rpm, tween 20 was dissolved in oleic acid that contained miconazole nitrate. When the heated organogel was added to the hydrogel while being continuously stirred (500 rpm) to create a homogenous mixture and allowed to cool to room temperature, a bigel was produced. Three bigel formulations, designated BG1, BG2, BG3, BG4, and BG5, were made in hydrogel/organogel ratios of 50:50, 60:40, 70:30, 80:20, and 90:10 (w/w) [8].

Table 1: Formulation composition of Miconazole Nitrate Bigel

S. No.	Formulation no. / Name of ingredients	BG 1	BG 2	BG 3	BG 4	BG 5
		Quantity (in grams) per batch				
Oleogel part						
1.	Miconazole Nitrate	0.500	0.500	0.500	0.500	0.500
2.	Tween 20	1.875	1.500	1.125	0.750	0.375
3.	Oleic Acid	10.625	8.500	6.375	4.250	2.125
4.	**Total weight of Oleogel taken**	**12.500**	**10.000**	**7.500**	**5.000**	**2.500**
Hydrogel part						
5.	Carbopol 940	0.125	0.150	0.175	0.200	0.225
6.	Polyethylene Glycol 200	0.625	0.750	0.875	1.000	1.125
7.	Ethanol	1.250	1.500	1.750	2.000	2.250
8.	Purified water	10.500	12.600	14.700	16.800	18.900
9.	Triethanolamine	q.s	q.s	q.s.	q.s	q.s
10.	**Total weight of Hydrogel taken**	**12.500**	**15.000**	**17.500**	**20.000**	**22.500**
Bigel composition						
11.	Oleogel	12.500	10.000	7.500	5.000	2.500
12.	Hydrogel	12.500	15.000	17.500	20.00	22.500
13.	**Total weight of bigel**	**25.000**	**25.000**	**25.000**	**25.000**	**25.000**

Note: Calculation does not include the weight of active ingredient

Fig. 1: Formulations of Miconazole Nitrate Bigel

3. Preformulation of Miconazole Nitrate [9]

A crucial stage of developing a dosage form is preformulation, which evaluates a physicochemical characteristic of drug. These studies guarantee the stability, effectiveness, and safety of the medication while assisting in the identification of formulation issues.

3.12 Organoleptic Evaluation

To verify identity, miconazole nitrate was inspected for physical traits like color, odor, and appearance [4,10]

3.12 Melting Point

Using a digital melting point device and the average of three readings, the melting point is ascertained by the capillary method.

3.12 Partition Coefficient

Using an n-octanol: phosphate buffer (pH 7.4) system, the oil/water partition coefficient (Ko/w) was calculated. To determine the coefficient, the absorbance of the aqueous phase was measured at 272 nm using UV spectrophotometry.

3.12 Solubility Studies

Miconazole nitrate's solubility in solvents such as water, ethanol, and phosphate buffer was evaluated both qualitatively and quantitatively using the shake flask method. Post-equilibration, samples were filtered and analyzed spectrophotometrically at 272 nm [11–13].

3.12 UV Spectroscopy & λmax Determination

To validate identity and determine miconazole's λmax, UV absorbance was measured between 200 and 400 nm in ethanol and phosphate buffer.

3.12 Calibration Curve

Serial dilutions (5–30 µg/ml) were used to create standard curves in ethanol and phosphate buffer, which were then studied at 272 nm for ethanol and 230 nm for buffer.

3.12 FTIR Spectroscopy

The compatibility of the drug and excipient was assessed using FTIR analysis. In order to identify functional groups, samples were prepared using the KBr disc method and scanned from 400 to 4000 cm^{-1}.

3.12 Differential Scanning Calorimetry (DSC)

Using differential scanning calorimetry (DSC), thermal behaviour and the molar heat of fusion were evaluated. In order to examine phase transitions and purity, samples were heated from 20°C to 200°C while being pumped with nitrogen at a rate of 10°C per minute[11].

4. *EVALUATION OF PREPARED BIGELS*

4.12 Physical Appearance & Homogeneity

The clarity, homogeneity, and lack of aggregates of bigel were examined visually.

4.12 Color and Grittiness

Microscopic analysis verified that there was no particulate matter present. A white background was used to check color.

4.12 Consistency & Greasiness

The gel was applied to the skin to evaluate these qualities.

Viscosity

Measured in triplicate using a Brookfield viscometer Spindle no. 63 [14].

4.12 Spreadability

Using the glass slide method, spreadability (S) was calculated using the formula

$$S = (m \times l) / t,$$

Where,

m is the weight on the upper slide,

l is the length moved,

and t is the time

4.12 pH Measurement

Using a digital pH meter at room temperature, 1 g of bigel was dissolved in 10 ml of distilled water and measured [15].

4.12 Drug Content

A UV-Vis spectrophotometer was used to measure absorbance at 230 nm after 1 g of bigel was diluted with phosphate buffer (pH 7.4) and filtered[8,16].

4.12 Inversion Test

To determine whether the gel maintained its structure under its own weight, it was inverted in a beaker.

4.12 Gel-Sol Transition Temperature

The gel-sol transition temperature is measured by heating the sample in a water bath between 25-60^{o} C, raising the temperature by 5 ^{o} C at a time, and timing the gel's onset of flow [17].

4.12 *In Vitro* Drug Release

Using a Franz diffusion cell and phosphate buffer (pH 5.5) at 32 ± 0.5°C, drug release from the Miconazole Nitrate bigel was investigated. A diffusion membrane that separated the donor and receptor compartments was coated with the bigel (2 g). To calculate cumulative drug release, 1 ml samples were taken out every 8 hours, replaced with new buffer, and measured at 230 nm using a UV spectrophotometer [7].

4.12 *In vitro* release kinetic study

Different kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas, were used to analyze the in vitro drug release data of the prepared bigel formulations. Each model's correlation coefficient (R2) values were computed to identify the best fit, which revealed the drug release mechanism.

4.1.1 *In vitro* Diffusion Study for Comparative Release Analysis: Utilizing Franz diffusion cells with a dialysis membrane, an in vitro diffusion study was carried out to compare the

optimized bigel formulation (BG3) with a commercially available miconazole nitrate gel. Phosphate buffer (pH 7.4) was used to test both formulations at 37 ± 0.5°C under the same conditions. To assess cumulative drug release, samples were gathered over the course of eight hours and subjected to UV spectrophotometric analysis.

4.12 Stability Studies

Three different storage conditions were used to evaluate the Miconazole Nitrate Bigel formulation's stability:

Refrigerated (4°C ± 2 / 75% RH)

Real Time (30°C ± 2 / 75% RH)

Accelerated (40°C ± 2 / 75% RH)

Throughout the course of 30 days, samples were examined for physical characteristics, pH, viscosity, drug content, and in vitro drug release at regular intervals [18,19].

4.13 ATR-FTIR Analysis

Bigels' functional groups are identified by FTIR spectroscopy, primarily in the range of 4000–1500 cm^{-1}. Hydrogen bonding in hydrogels is demonstrated by a broad peak at 3300–3200 cm^{-3}. This bonding diminishes upon oleogel incorporation, suggesting structural interaction. At about 3330 cm^{-1}, a higher oleogel content further lowers transmittance. This demonstrates that the oleogel and hydrogel phases are effectively mixed.

4.14 Determination of Similarity Factor(f_2) and Dissimilarity Factor(f_1)

Similarity Factor (f2): It is a statistical tool used to compare the dissolution profiles of a test and a reference product. If the f2 value is between 50 and 100, the two profiles are considered similar. Using formula we calculate similarity factor:

$$f2 = 50 \log\{[1 + \frac{1}{n}\sum_{n=1}^{n}(Rt - Tt)^2]^{0.5} * 100\}$$

Dissimilarity Factor (f1): It shows the percentage difference between the test and reference profiles. If the f1 value is between 0 and 15, the profiles are considered acceptably similar. Using formula we calculate dissimilarity factor:

$$f1 = \frac{\sum_{t=1}^{n}|Rt - Tt|}{\sum_{t=1}^{n} Rt} \times 100$$

5. *RESULTS AND DISCUSSION*

5.12 *PREFORMULATION STUDIES*

5.1.1. Physical Appearance

Table 2: Physical Properties of Miconazole Nitrate

S. No.	Physical Properties	Observations
1.	Color	White to off-white crystalline powder
2.	State	Crystalline powder
3.	Odor	Odorless

5.1.2. Determination of Melting point

The capillary method was used to determine Miconazole Nitrate's melting point.

Table 3: Melting point evaluation of Miconazole Nitrate

Methodology	Experimental Value	Literature value
Capillary fusion method	172 °C - 184 °C	170 - 185 °C

Data expressed as mean ± SD (n=3)

5.1.3. pH Dependent Solubility Studies

To find the components for new formulations, tests of the drug's solubility in different solvents were conducted. The drug was analyzed using UV spectroscopy at 272 nm.

Table 4: Qualitative and Quantitative solubility data of Miconazole Nitrate

S. No.	Solvent used	Qualitative solubility	Quantitative solubility (mg/mL) (Mean ± SD)
1.	Ethanol	Freely soluble	1.105 ± 0.100
2.	Distilled water	Practical insoluble	0.019 ± 0.001
3.	Phosphate buffer pH 7.4	Soluble	0.9950.003

Data expressed as mean ± SD (n=3)

5.1.4. Partition coefficient

Miconazole Nitrate Partition Coefficient in n-Octanol: pH 7.4 Phosphate Buffer Mixture. Miconazole is lipophilic by nature since the log P value is greater than 1.

Table 5: Partition coefficient value of Miconazole Nitrate

Methodology	Experimental Value	Literature value
n - octanol/ Phosphate buffer pH 7.4	6.15 ± 0.01	6.25

Data is expressed as Mean ± SD (n=3)

5.1.5. Determination of Absorption maxima (λ_{max}) for analysis

Miconazole nitrate's absorption maxima (λmax) in ethanol and phosphate buffer (pH 7.4) were determined. Their spectrums are shown in Fig. 2 and Fig. 3.

Fig.2: spectrum of Miconazole Nitrate in Ethanol

Fig. 3: Spectrum of Miconazole Nitrate in Phosphate Buffer pH 7.4

❖ Calibration curve for miconazole nitrate in ethanol

Table 6: Absorbance value of different dilutions of Miconazole Nitrate in Ethanol

Concentration (µg/mL)	Absorbance (Mean ± SD)
0	0.000 ± 0.000
5	0.215 ± 0.002
10	0.415 ± 0.002
15	0.612 ± 0.005
20	0.816± 0.005
25	1.015 ± 0.005

Data expressed as mean ± SD (n=3)

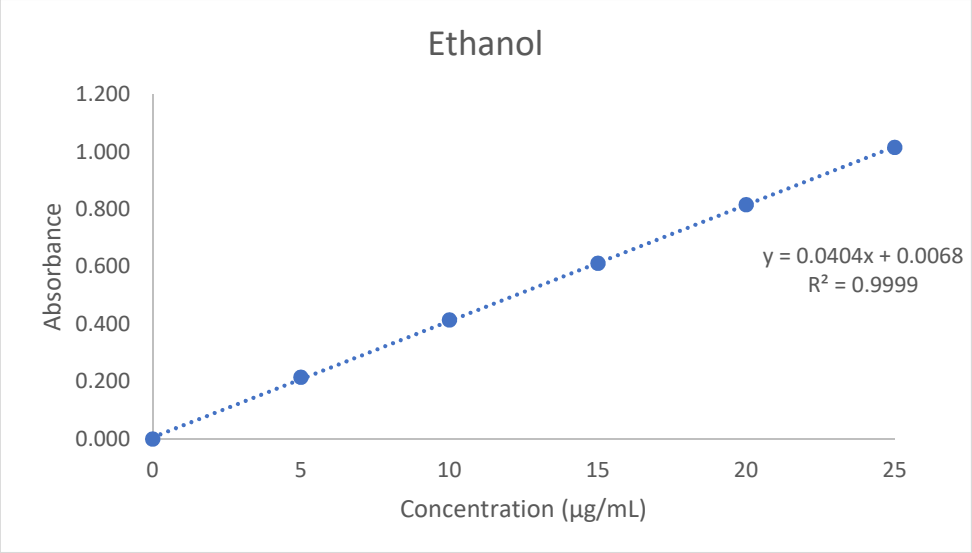


Fig. 4: Standard Curve of Miconazole Nitrate in ethanol

❖ Calibration curve for Miconazole Nitrate in pH 7.4 Phosphate Buffer

Table 7: Absorbance value of different dilutions of Miconazole Nitrate in Phosphate buffer pH 7.4

Concentration (µg/mL)	Absorbance (Mean ± SD)
0	0.000 ± 0.000
5	0.152 ± 0.002
10	0.252 ± 0.001
15	0.354 ± 0.003
20	0.453 ± 0.002
25	0.552 ± 0.005
30	0.653 ± 0.004
35	0.751 ± 0.006
40	0.851 ± 0.005
45	0.998 ± 0.002

Data expressed as mean ± SD (n=3)

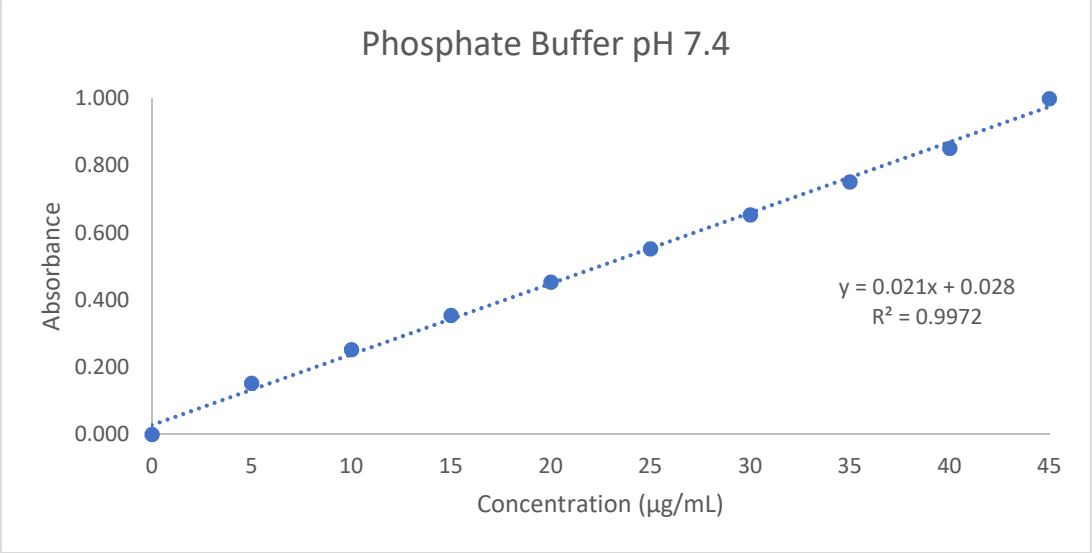


Fig. 5: Standard Curve of Miconazole Nitrate in Phosphate Buffer pH 7.4

5.1.6. Fourier Transform Infrared Spectroscopy

Compatibility and potential interactions between drug excipients were investigated using Fourier transform infrared (FTIR) analysis. From 400 cm^{-1} to 4000 cm^{-1}, the prepared samples were scanned.

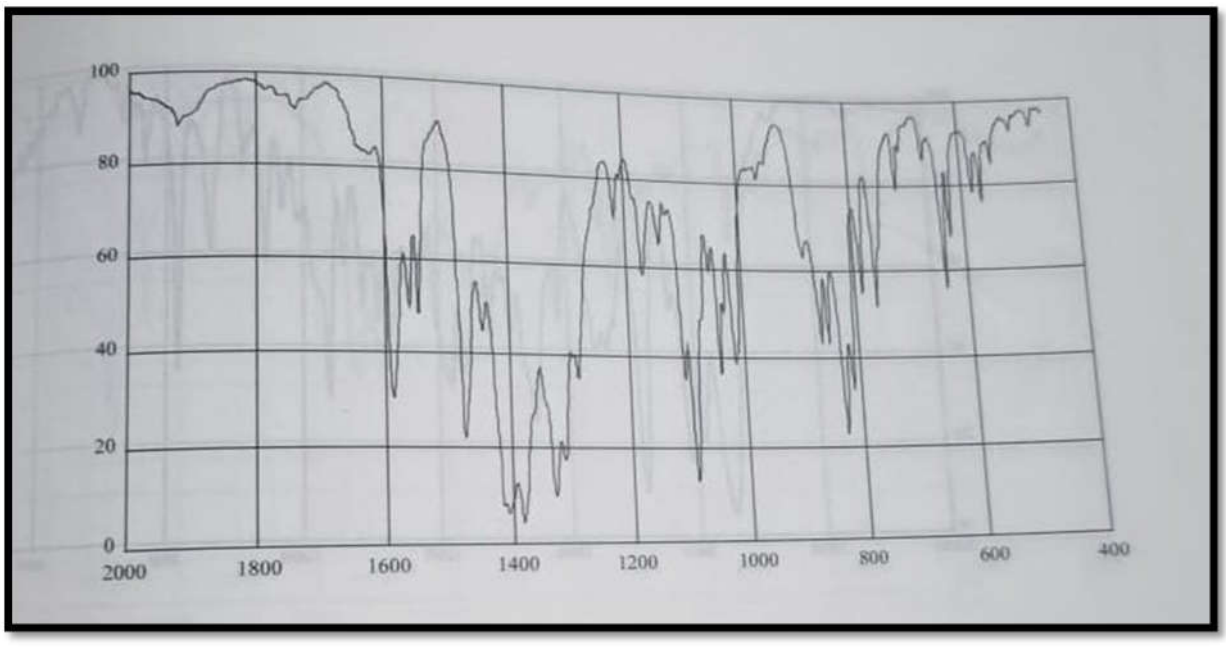


Fig. 6: Standard FTIR of Miconazole Nitrate

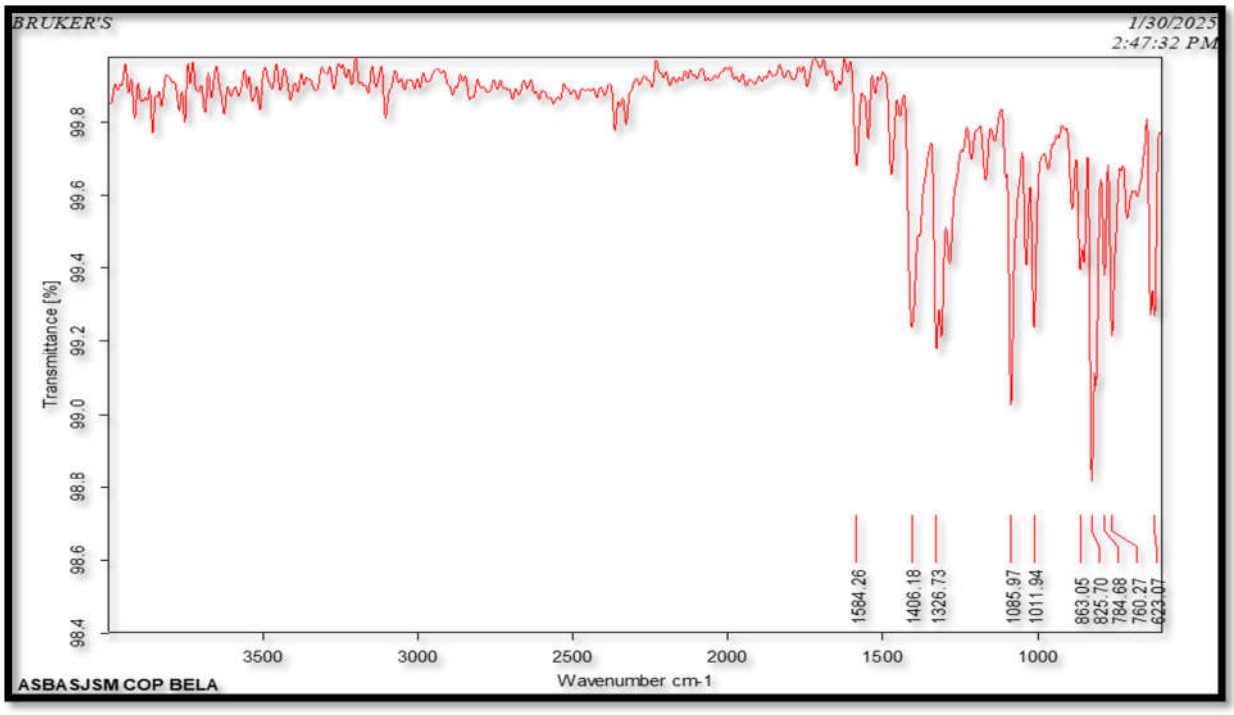


Fig. 7: FTIR spectrum of pure Miconazole Nitrate

5.1.7. Molar Heat of Fusion

Differential Scanning Calorimetry (DSC)

The DSC instrument was used to study the drug's thermal behavior. Heat flow's temperature range was measured.

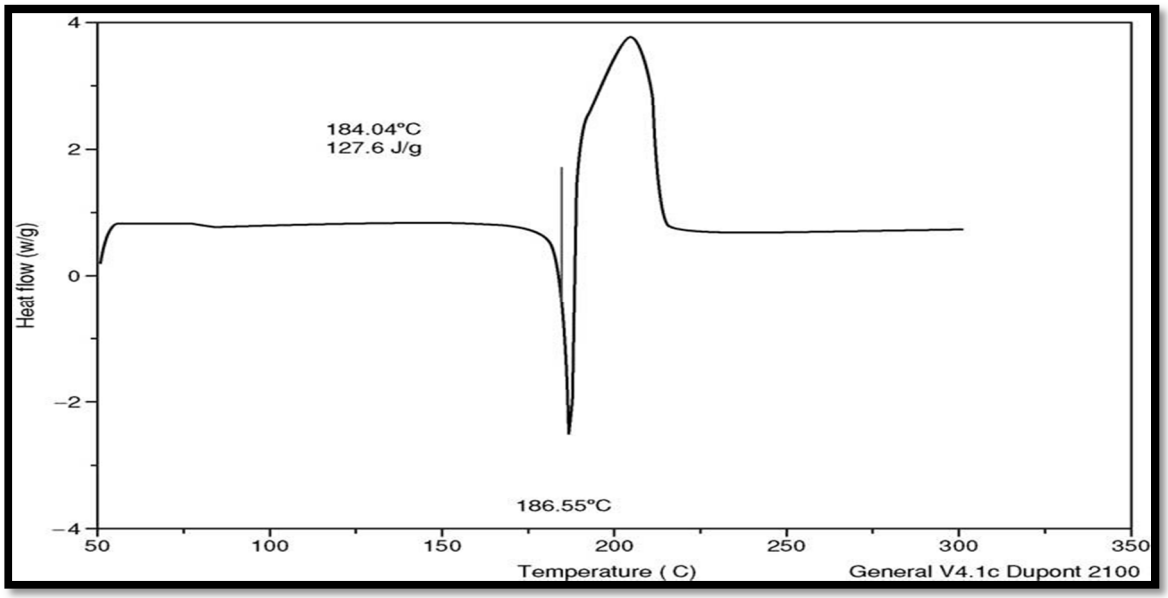


Fig. 8: Differential Scanning Calorimetry (DSC) thermogram of miconazole Nitrate

5.2 *EVAULATION OF BIGEL*

5.2.1 Physicochemical study of bigel formulation

Bigels were assessed for spreadability, grittiness, and homogeneity. It was determined that the bigel formulation had good spreadability and homogeneity.

Table 8: Physical properties of Miconazole Nitrate Bigel

Formulation no.	Homogeneity	Grittiness	Extrudability
BG 1	+++	-	++
BG 2	+++	-	++
BG 3	+++	-	++
BG 4	+++	-	++
BG 5	+++	-	++

+ Satisfactory, ++ Good, +++ Very Good, - No irritation.

5.2.2 Measurement of pH

The pH of the prepared formulations was measured, and it is neutral enough to be suitable for skin.

Table 9: pH values of prepared Miconazole Nitrate Bigel

Formulation no.	pH (Mean ± SD)
BG 1	6.31 ± 0.01
BG 2	6.82 ± 0.03
BG 3	7.02 ± 0.03
BG 4	6.92 ± 0.03
BG 5	6.51 ± 0.02

Data expressed as mean ± SD (n=3)

5.2.3. Viscosity

The Brookfield viscometer was used to measure the gel's viscosity. The viscosity of these bigels demonstrated Pseudoplastic flow as the rate of shear increased.

Table 10: Viscosity of prepared Miconazole Nitrate Bigel

Formulation no.	Viscosity (cps)	
Speed	50 RPM	100 RPM
BG 1	1219	1157
BG 2	1785	1236
BG 3	1963	1368
BG 4	2189	1439
BG 5	2298	1523

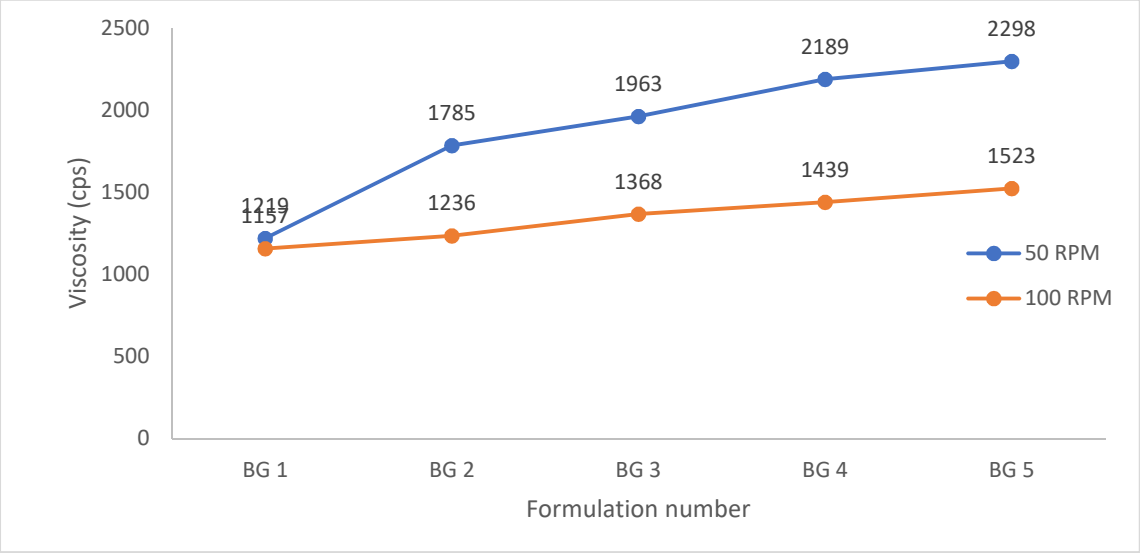


Fig. 9: Viscosity of prepared Miconazole Nitrate Bigel

5.2.4. Spreadability

Determined using the glass slide method.

Table 11: Spreadability of prepared Miconazole Nitrate Bigel

Formulation no.	Spreadability (g.cm/sec) (Mean ± SD)
BG 1	28.12 ± 0.18
BG 2	22.78± 0.16
BG 3	19.62± 0.57
BG 4	17.47 ± 0.17
BG 5	15.26 ± 0.68

Data expressed as mean ± SD (n=3)

5.2.5. Drug Content

Before being suitably diluted and examined using a UV spectrophotometer, 1 g of bigel was weighed in a 100 ml volumetric flask and dissolved in phosphate buffer (7.4). Percentage drug content of prepared Miconazole Nitrate Bigel shown in Table 12. Bar graph depicted % Drug Content of prepared bigel formulations shown in Fig. 10

Table 12: Percentage drug content of prepared Miconazole Nitrate Bigel

Formulation no.	Percentage Drug content (Mean ± SD)
BG 1	98.76 ± 0.04
BG 2	99.52 ± 0.03
BG 3	100.00 ± 0.50
BG 4	99.20 ± 0.10
BG 5	98.66 ± 0.11

Data expressed as mean ± SD (n=3)

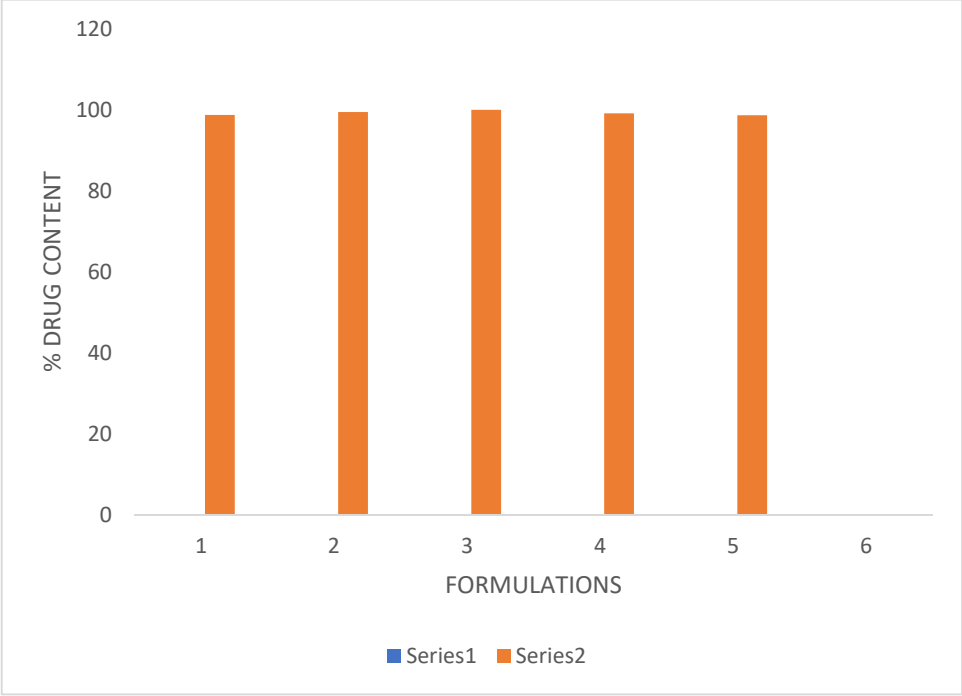


Fig. 10: % Drug Content of prepared bigel formulations

5.2.6. Inversion Test

The most widely used diagnostic test for gelation involves inverting a beaker containing the sample and observing if the sample flows under its own weight. It was done for bigels.

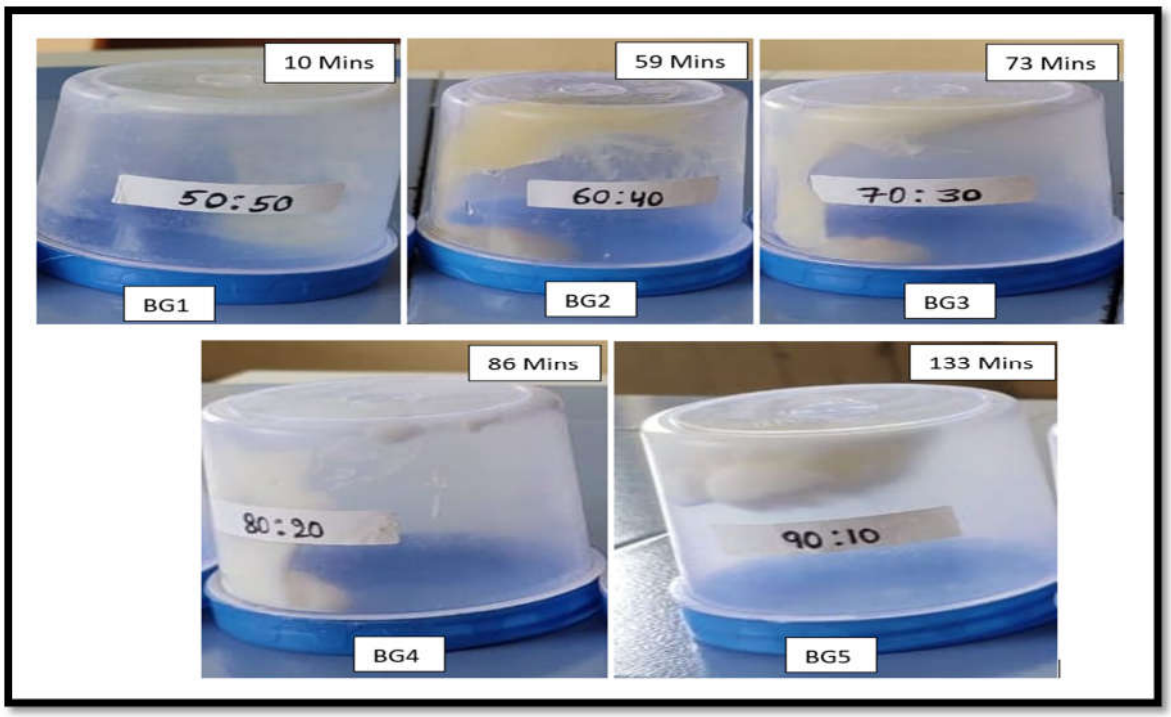


Fig. 11: Bigel formulations shows inversion test

Table 13: Inversion test of bigel

Formulation Number	Time (Minutes) mean± SD
BG1	10±0.002
BG2	59±0.001
BG3	73±0.003
BG4	86±0.002
BG5	133±0.003

Data is expressed as mean ± SD (n=3)

5.2.7. Gel-sol phase transition temperature

All gels are incubated in a constant temperature bath between 25-60°C to determine their gel-sol transition temperature. Every 5 minutes, the water bath's temperature is raised by 5°C. After

that, the beaker is left upside down, and the temperature at which the gel begins to flow is noted.

Table 14: Gel-Sol Transition Temperature of Bigel Formulations

Formulation Number	Temperature of Gel-Sol Transition
BG1	42-45ºC
BG2	38-42ºC
BG3	34-38ºC
BG4	30-34ºC
BG5	28-32ºC

5.2.8. *In-Vitro* Diffusion Studies

Conducted over eight hours using Franz diffusion cells and a receptor medium of phosphate buffer (pH 5.5). Analysis of the samples was done at 230 nm. Percentage cumulative drug release vs Time intervals data of prepared Miconazole Nitrate Bigel shown in Table 15. And a graph depicting % Cumulative Drug diffusion of bigel containing miconazole nitrate shown in Fig. 12.

Table 15: Percentage cumulative drug release vs Time intervals data of prepared Miconazole Nitrate Bigel

time intervals (Hours)	BG 1	BG 2	BG 3	BG 4	BG 5
0	0.00± 0.00	0.00± 0.00	0.00± 0.00	0.00± 0.00	0.00± 0.00
1	3.33± 0.04	8.00± 0.03	10.62± 0.02	6.52± 0.04	4.33± 0.03
2	4.00± 0.03	18.25± 0.02	22.52± 0.03	15.26± 0.03	10.26± 0.04
3	15.33± 0.02	25.61± 0.03	29.60± 0.04	22.54± 0.04	20.33± 0.02
4	19.00± 0.03	33.50± 0.04	42.36± 0.04	32.50± 0.02	24.67± 0.01
5	23.67± 0.04	50.26± 0.01	56.23± 0.03	45.62± 0.01	39.33± 0.04
6	27.00± 0.02	59.62± 0.03	65.32± 0.02	55.42± 0.03	45.62± 0.03
7	38.00± 0.04	72.10± 0.02	75.22± 0.01	70.58± 0.04	55.26± 0.02
8	50.00± 0.03	78.25± 0.04	81.52± 0.04	77.52± 0.02	65.52± 0.04

Data is expressed as mean ± SD (n=3)

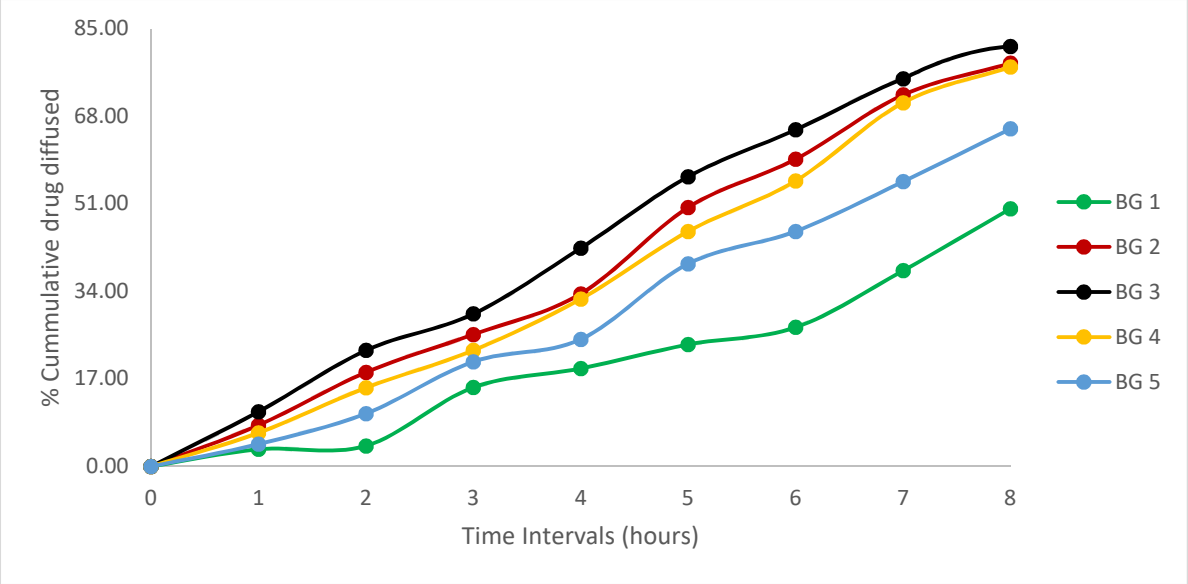


Fig. 12: % Cumulative Drug diffusion of bigel containing miconazole nitrate

5.2.9. *In-Vitro* Drug Release Kinetic Study

In vitro drug release data were fitted to kinetic models (zero-order, first-order, Higuchi, and Korsmeyer–Peppas), and the model with the highest R^2 value was selected to determine the drug release mechanism. The Korsmeyer–Peppas model for BG3 showed an n value of 0.9944 with $R^2 = 0.9956$, indicating a strong fit and suggesting a Case-II transport mechanism, where drug release is governed by polymer relaxation rather than diffusion.

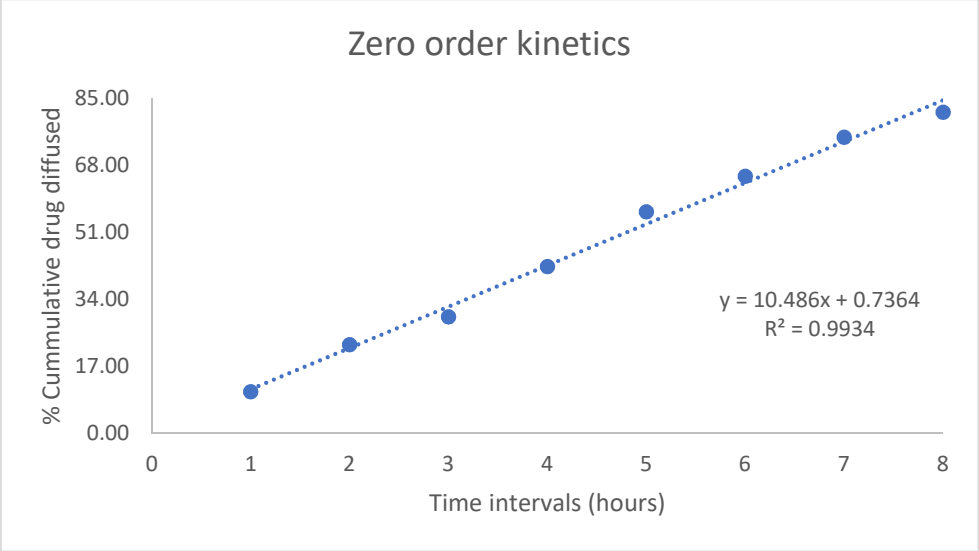


Fig 13: Zero order kinetics of drug release

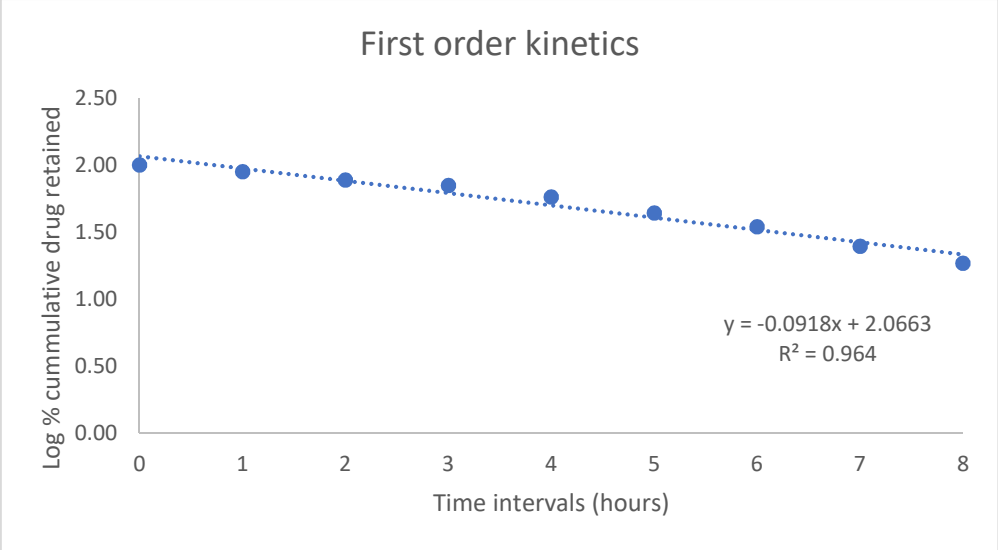


Fig 14: First order kinetics of drug release

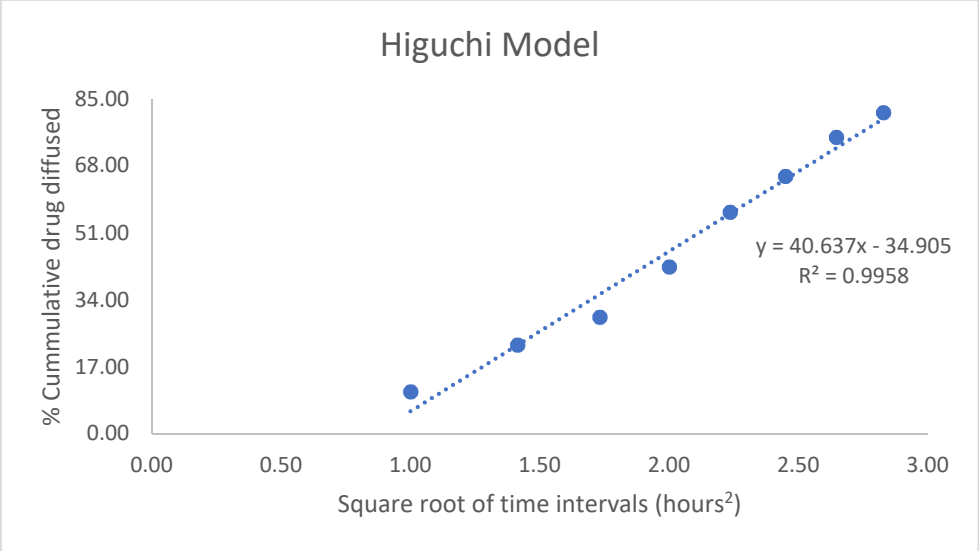


Fig 15: Higuchi model for drug release

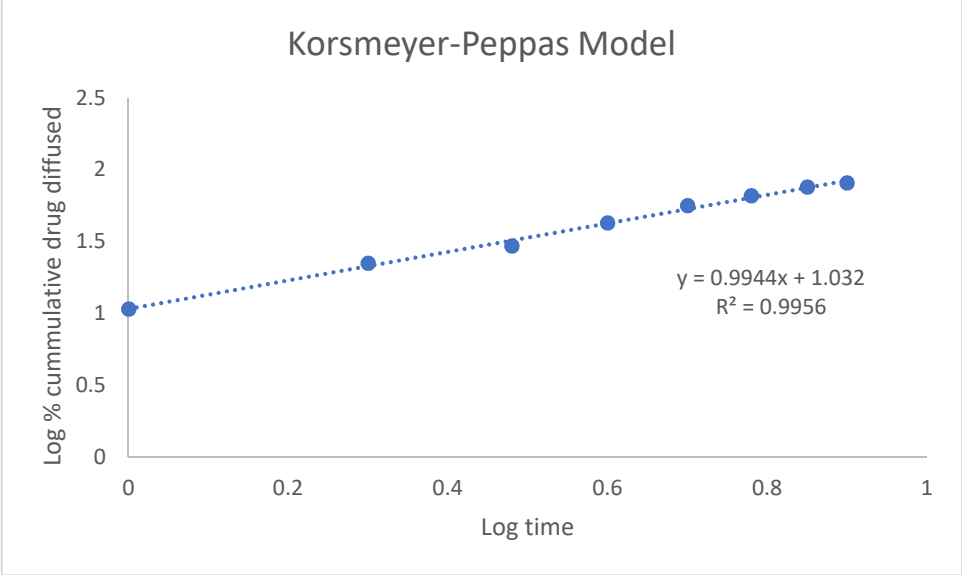


Fig 16: korsemeyer-peppas model for drug release

Table 16: kinetic analysis of the *in-vitro* diffused data of BG3 formulation

Formulation Code	Zero Order		First Order		Higuchi Order		Korsmeyer Peppas	
BG3	R^2	k°	R^2	k°	R^2	k°	R^2	k°
	0.9934	10.486	0.964	0.0918	0.9958	40.637	0.9956	0.9944

5.3.0. *In Vitro* Diffusion Study for Comparative Release Analysis

BG3 bigel and a commercial miconazole gel were compared in an in vitro diffusion study using Franz diffusion cells. Under the same conditions, BG3 demonstrated improved drug release over an 8-hour period.

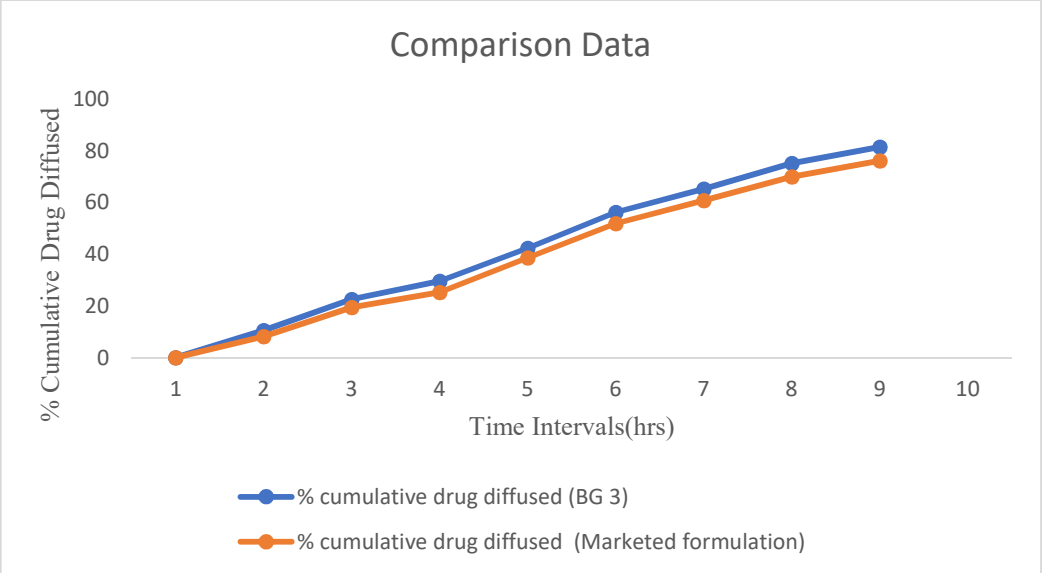


Figure 17: Comparative % Cumulative Drug Diffused Between BG3 and Marketed Formulation

Table 17: Comparative % Cumulative Drug Diffused Between BG3 and Marketed Formulation

Time intervals (hrs)	% cumulative drug diffused (BG 3)	% cumulative drug diffused (Marketed formulation)
0	0.00± 0.00	0.00± 0.00
1	10.62± 0.01	8.24± 0.02
2	22.52± 0.02	19.53± 0.02
3	29.60± 0.02	25.34± 0.01
4	42.36± 0.03	38.68± 0.03
5	56.23± 0.04	51.89± 0.02
6	65.32± 0.03	60.78± 0.01
7	75.22± 0.02	69.95± 0.02
8	81.52± 0.03	76.21± 0.03

Data expressed as mean ± SD (n=3)

5.3.0. Stability Studies

Stability of the Miconazole Nitrate bigel formulation was assessed under **three storage conditions**:

Refrigerated (4°C ± 2 / 75% RH)
Real Time (30°C ± 2 / 75% RH)
Accelerated (40°C ± 2 / 75% RH)

Evaluation data of BG3 formulation during storage period (Refrigerated condition, real condition and accelerated condition) shown in Table 18 and Stability Profile of formulation at Different Temperature and Humidity Conditions shown in Table 19 and % Cumulative drug release vs Time intervals data of prepared Miconazole Nitrate Bigel before storage and after storage shown in Table 20 and % Cumulative Drug diffusion of bigel containing miconazole nitrate before and after storage shown in Fig. 17.

Table 18: Evaluation data of BG3 formulation during storage period

Time (Days)	Refrigerated (4°C±2°C/75%RH±5%RH)			Real time (30°C±2°C/75%RH±5%RH)			Accelerated (40°C±2°C/75%RH±5%RH)		
	Physical	pH	Drug content	Physical Appearance	pH	Drug content	Physical Appearance	pH	Drug content

	Appearance		(%)			(%)			(%)
0	Pale white to creamy	7.02 ± 0.03	100.0± 0.50	Pale white to creamy	7.02 ± 0.03	100± 0.50	Pale white to creamy	7.02 ± 0.03	100± 0.50
7	No change	7.01 ± 0.02	99.5± 0.04	No change	7.00 ± 0.01	99.6± 0.03	Slight creamy tint	6.95 ± 0.02	99.1± 0.04
14	Slight stiffening, Smooth	6.98 ± 0.01	99.1± 0.02	No change	6.98 ± 0.02	98.9± 0.03	Slightly creamy appearance	6.90 ± 0.03	98.0± 0.04
21	No change	6.96 ± 0.02	98.8± 0.03	No change	6.96 ± 0.02	98.5± 0.02	Slight yellowish	6.85 ± 0.02	97.2± 0.04
28	Slight increase in firmness	6.95 ± 0.03	98.4± 0.03	No change	6.95 ± 0.01	98.3± 0.02	Slight yellowish	6.80 ± 0.01	96.5± 0.03

Data is expressed as mean ± SD (n=3)

Table 19: Stability Profile of formulation at Different Temperature and Humidity Conditions

Time in Days	Refrigerated (4°C±2°C/75%RH±5%RH) % Cumulative drug diffused	Real time (30°C±2°C/75%RH±5%RH) % Cumulative drug diffused	Accelerated (40°C±2°C/75%RH±5%RH) % Cumulative drug diffused
0	81.52± 0.00	81.52± 0.00	81.52± 0.00
7	81.45± 0.04	81.30± 0.04	81.40± 0.03
14	81.38± 0.03	81.18± 0.02	81.30± 0.02
21	81.30± 0.02	81.05± 0.03	81.22± 0.04
28	81.20± 0.01	80.92± 0.02	81.12± 0.01

Data is expressed as mean ± SD (n=3)

Table 20: % Cumulative drug release vs Time intervals data of prepared Miconazole Nitrate Bigel before storage and after storage

Time (hrs.)	% cumulative drug diffused before storage	% cumulative drug diffused After storage (real time condition)	% cumulative drug diffused After storage (refrigerated condition)	% cumulative drug diffused After storage (accelerated condition)
0	0.00±0.000	0.00±0.000	0.00±0.000	0.00±0.000
1	10.62±0.002	10.45±0.001	10.21±0.001	10.02±0.002
2	22.52±0.003	22.10±0.002	22.00±0.002	21.59±0.003
3	29.60±0.005	29.00± 0.002	28.84±0.002	28.64±0.004
4	42.36±0.004	41.96±0.003	41.83±0.003	41.40±0.002
5	56.23±0.003	55.79± 0.004	55.67±0.001	55.48±0.001
6	65.32±0.002	64.86± 0.004	64.72±0.003	64.36±0.003
7	75.22±0.001	74.94± 0.003	74.77±0.002	74.51±0.002
8	81.52±0.004	80.93± 0.002	80.75±0.001	80.46±0.002

Data is expressed as mean ± SD (n=3)

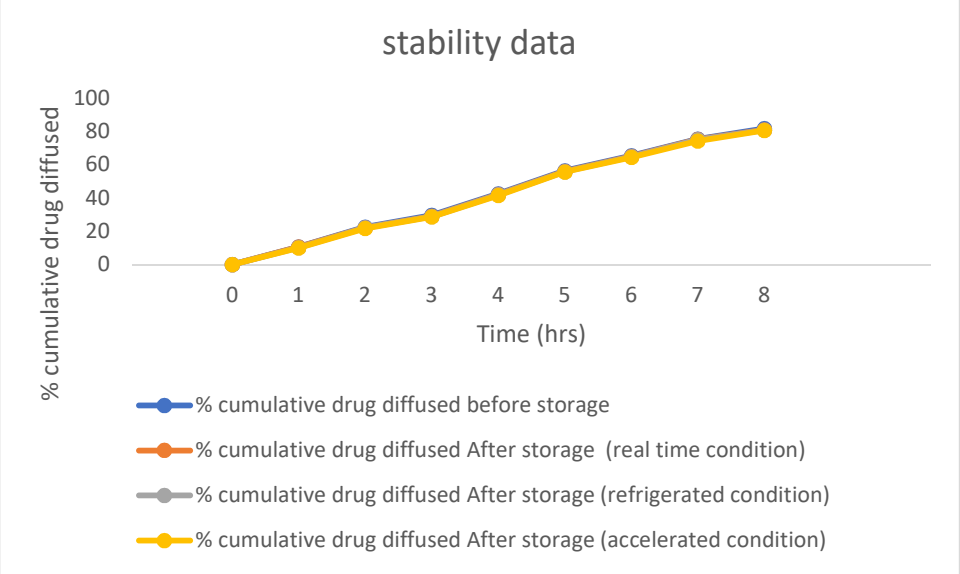


Fig. 18: % Cumulative Drug diffusion of bigel containing miconazole nitrate before and after storage

5.3.1. ATR-FTIR Analysis

The broad peak in this FTIR spectrum, located at about 3300 cm^{-1}, indicates that the hydrogel has strong hydrogen bonds and O–H stretching. The C–H stretching from lipophilic substances like oleic acid is represented by the peak close to ~2920 cm^{-1}. The presence of esters or acids is suggested by a sharp peak near ~1700 cm^{-1}, which shows C=O stretching. The distinct

structure is confirmed by the fingerprint region, which is between 1500 and 500 cm^{-1}. Overall, the spectrum verifies that the bigel contains both hydrophilic and lipophilic components.

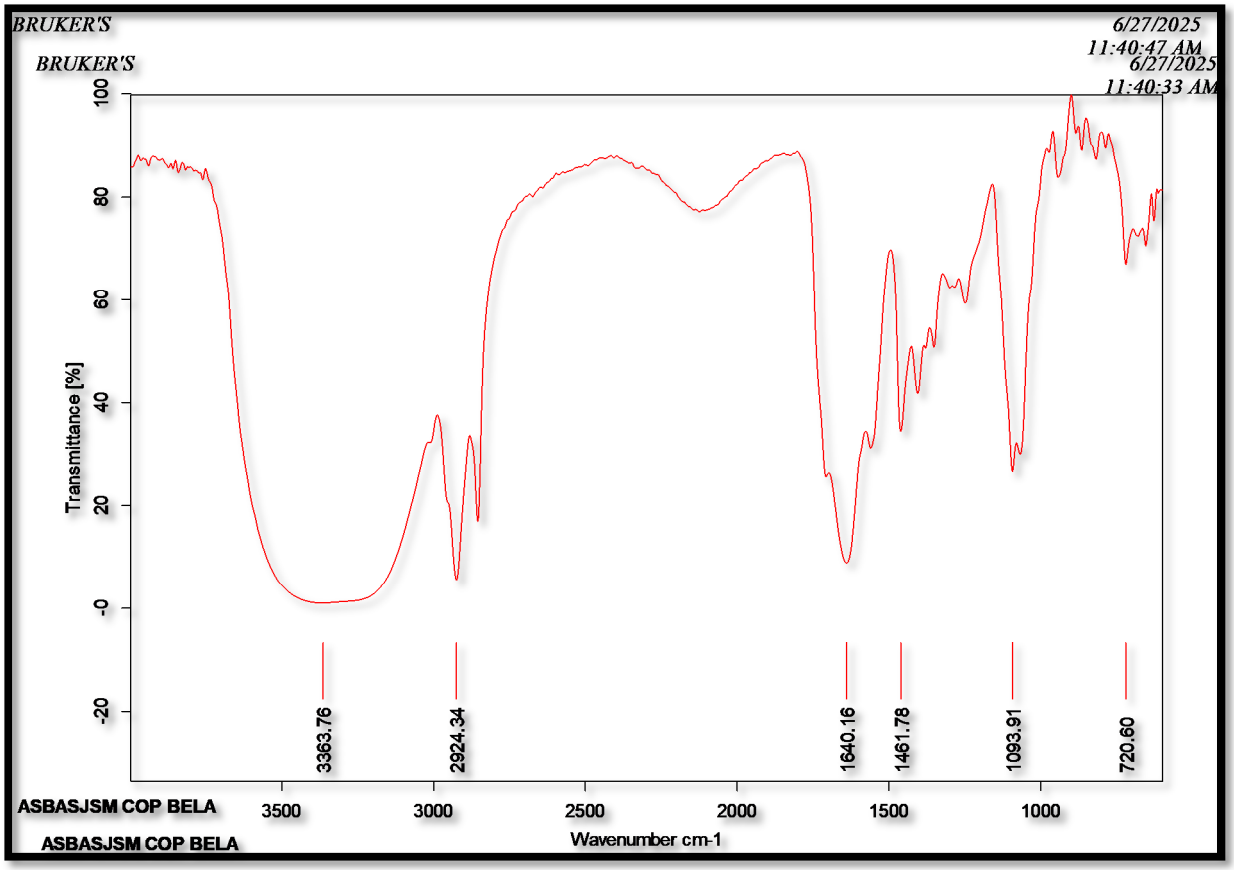


Fig. 19: FTIR of final formulation (BG3)

5.3.2. Determination of Similarity Factor(f_2) and Dissimilarity Factor(f_1)

Table 21: similarity and dissimilarity factor of formulation with respect to storage conditions

Condition	Similarity factor (f_1)	Dissimilarity (f_2)
Real time condition	0.88	98.27
Refrigerated condition	1.25	97.06
Accelerated condition	1.93	94.17

For the miconazole nitrate bigel (BG3), the similarity factor calculated before and after storage indicating that the drug release profiles of the two formulations are very similar.

6. *DISCUSSION*

A bigel system containing miconazole nitrate for topical antifungal treatment was successfully developed and assessed by the study. The identity and physicochemical suitability were

validated by preformulation studies of drug. The bigel showed good consistency, homogeneity, and spreadability, among other physical qualities. For extended antifungal action, the in vitro drug release profile demonstrated consistent and effective release over an 8-hour period. The formulation's stability in terms of appearance, drug content, and release behavior was validated by stability studies conducted in real-time, accelerated, and refrigerated environments. The dual-phase nature of bigel, which combines the advantages of hydrogels and organogels, allowed it to perform better than traditional topical formulations.

7. *CONCLUSION*

Bigels were effectively created in this study using oleogel made of oleic acid and Tween 20 as well as hydrogel based on carbopol. The microstructure showed that the phases were evenly distributed, creating a stable biphasic system. Research on drug release and antifungal properties showed that the bigel exhibited good activity against fungal strains and could release a significant amount of Miconazole Nitrate. The formulation's internal structural integrity and long-term consistency were validated by rheological and stability studies. Organoleptic characteristics did not significantly alter while being stored in accelerated, real-time, or refrigerated conditions. According to these results, the developed Miconazole Nitrate bigel is a promising option for improved topical antifungal treatment, which calls for additional clinical testing.

- **Ethics Statement**

  The present study did not involve any human participants or animal subjects. All experimental procedures were conducted using in vitro methods and complied with institutional, national, and international ethical guidelines for research integrity and good laboratory practices. No ethical approval was required as the study was limited to laboratory-based formulation and evaluation work.

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- **Conflict of Interest**

  Authors are declaring there is no conflict of interest in relation to this article.

- **Funding**

  The research did not receive grant funding from any source (public, commercial, or not-for-profit).

- **Data Access**

  All data generated or analyzed during this study are included in this published article. Additional raw data supporting the findings of this work are available from the corresponding author upon reasonable request.

- **Author's ORCID Numbers**

  Gursimran Kaur (GK)

  ORCID: 0009-0009-8959-8179

  Dr. Sandeep Kumar (SK)

  ORCID: 0000-0002-0455-5711

- **Specific Contribution of Each Author**

  Gursimran Kaur: Study conception and design, literature review and manuscript drafting.

  Dr. Sandeep Kumar: Supervision, Review

  Simran: literature review

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