FORMULATION, EVALUATION AND *In-Vitro* DRUG RELEASE OF MICONAZOLE MICROEMULGEL AS ANTIMICROBIAL AGENT

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ABSTRACT

This study presents the formulation, evaluation, and in vitro drug release of Miconazole Microemulgels as a potential antimicrobial therapeutic agent. Three formulations were prepared, each utilizing a different base material: Hydroxypropyl Methylcellulose (HPMC), Carbopol 934, and Carbopol 940. These novel drug delivery systems aim to combine the benefits of microemulsions and gels, including enhanced solubility of hydrophobic drugs, improved drug stability, and ease of application. Several physicochemical properties of the microemulgels were analyzed, such as pH, viscosity, spreadability, and extrudability. Furthermore, the drug release profiles were examined over a 12-hour period. The HPMC Microemulgel demonstrated the highest drug release, smallest particle size, and most negative zeta potential, indicating its potential for enhanced drug delivery efficiency and stability. Despite promising in vitro results, further research, including in vivo studies, is recommended to validate these findings and to assess the therapeutic efficacy and safety profile of these Miconazole Microemulgels.

KEYWORDS Miconazole, Microemulgel, Antimicrobial Agent

INTRODUCTION

Microemulsion-based gel (microemulgel) systems have been recognized as potential drug delivery systems due to their promising properties, including ease of application, enhanced drug solubility and permeability, improved patient compliance, and the ability to deliver both hydrophilic and lipophilic drugs. The unique structure of microemulgel, a microemulsion within a gel matrix, allows for the efficient incorporation of a variety of drugs, particularly those used in antimicrobial therapy **[1].**

One such drug, Miconazole, a widely used antifungal agent, has shown effectiveness against a broad spectrum of fungi causing superficial mycoses. Despite its efficacy, its use has been hindered by its poor solubility and the side effects associated with conventional dosage forms. Incorporation of Miconazole into a microemulgel system, however, can overcome these limitations and improve its delivery significantly **[2].**

The formulation of an effective microemulgel requires careful selection of its components, including the oil phase, surfactant, co-surfactant, gelling agent, and the incorporation of the active pharmaceutical ingredient. In the current research, hydroxypropyl methylcellulose (HPMC), Carbopol 940, and Carbopol 934 were employed as gelling agents to formulate Miconazole microemulgels **[3].**

HPMC, a cellulose ether, offers benefits including non-toxicity, biocompatibility, and good film-forming ability. Carbopol polymers, Carbopol 934 and Carbopol 940, are acrylic acid polymers cross-linked with polyalkenyl polyether. They are extensively used in the pharmaceutical industry due to their high viscosity, excellent thickening property, and capability of forming clear gels **[4].**

Despite the emerging importance of microemulgels as drug delivery systems, literature regarding the formulation, evaluation, and comparison of Miconazole microemulgels using different gelling agents is scarce. Hence, the present study aimed to develop and compare Miconazole microemulgels using HPMC, Carbopol 934, and Carbopol 940 as gelling agents. Factors such as pH, viscosity, spreadability, extrudability, particle size, zeta potential, and drug release profiles were evaluated to ascertain the performance of each formulation. The study was envisaged to provide useful insights for the formulation and optimization of antimicrobial microemulgels in future research **[5].**

METHODOLOGY

The methodology followed for this study involves a series of steps conducted systematically. Let's explore each step in detail:

MATERIAL PROCUREMENT [6]

All the required materials including Miconazole (the active pharmaceutical ingredient), Hydroxypropyl methylcellulose (HPMC), Carbopol 934, Carbopol 940, almond oil, Tween 80 (surfactant), Co-surfactant, preservatives were obtained from verified suppliers.

PREPARATION OF MICROEMULGEL FORMULATION

HPMC-BASED MICROEMULGEL (FORMULATION 1)[7]

The formulation process commenced by creating a uniform mixture of HPMC in water. This gel-like base was then stirred continuously. Concurrently, in a different vessel, the oil phase was blended with the surfactant and co-surfactant, creating an oil-surfactant mixture. This mixture was gradually added to the gel base under continuous stirring. The active pharmaceutical ingredient, Miconazole, was then introduced at the concentration required. Finally, water was added to make up the volume.

CARBOPOL 940-BASED MICROEMULGEL (FORMULATION 2)[8]

The formulation process for this was identical to that of the HPMC-based microemulgel. The key difference lay in the gelling agent used: Carbopol 940 was used instead of HPMC.

CARBOPOL 934-BASED MICROEMULGEL (FORMULATION 3)[9]

The steps involved in this formulation mirrored those of Formulation 1. Here, Carbopol 934 replaced HPMC as the gelling agent.

EVALUATION OF MICROEMULGEL [10]

Subsequent to their preparation, the microemulgels underwent a rigorous evaluation process.

DETERMINATION OF MICONAZOLE'S λMAX (nm)[11]

The spectrophotometric analysis was performed to identify the λmax of Miconazole. In this process, Miconazole samples were subjected to varied wavelengths, and the absorbance of each was recorded.

pH EVALUATION[12]

The pH of all Microemulgel formulations was gauged using a well-calibrated pH meter. This measurement provided critical insights into the acidity or alkalinity of the formulations, which can significantly impact their stability and efficacy.

VISCOSITY MEASUREMENT[13]

The viscosity of the Microemulgel, indicative of their flow and spread properties, was evaluated using a Brookfield viscometer. The viscometer spindle was immersed in the microemulgel, and the resistance to its movement was translated into viscosity values.

SPREADBILITY ASSESSMENT[14]

A test was carried out to evaluate the spreadability of the microemulgels. It involved placing a sample of each formulation on a glass slide and recording the diameter of the spread sample.

EXTRUDABILITY TESTING[15]

*T*he ease with which each Microemulgel could be squeezed from a collapsible tube was measured. This property, known as extrudability, is crucial for patient comfort and ease of application.

MEASUREMENT OF PARTICLE SIZE AND ZETA POTENTIAL[16]

The particle size and zeta potential were assessed using a particle size analyzer. These parameters could significantly influence the drug release rate, stability, and absorption.

***In Vitro* Drug Release Study[17]**

Finally, the *in vitro* release profiles of Miconazole from each microemulgel were studied using a diffusion cell. At predetermined time intervals, samples were collected, and the quantity of drug released was measured using a UV-Vis spectrophotometer.

The tests were conducted in triplicates to maintain accuracy and consistency in results. The generated data were then analyzed statistically for mean and standard deviation to evaluate the performance of each formulation. The results were used to compare the effectiveness and quality of the different microemulgel formulations.

RESULTS

The results obtained from the series of tests conducted on the microemulgel formulations are explained in detail below:

Determination of Miconazole'sλmax (nm):

Spectrophotometric analysis of the Miconazole samples provided the λmax values. The observed λmax values ranged from 276 to 280 nm, demonstrating a slight variation among the samples but overall consistent absorbance wavelength, which is a crucial indicator of the compound's identity and purity.

Table 1- Miconazole: λmax value

Sample Number	λmax (nm)
Sample 1	277
Sample 2	280
Sample 3	278
Sample 4	276
Sample 5	279

pH EVALUATION

The pH of all microemulgel formulations was evaluated to understand their acidity or alkalinity, a key factor affecting the stability and effectiveness of the formulations. The HPMC Microemulgel showed a mean pH of 6.23 with a standard deviation of 0.05, indicating slight acidity. Carbopol 934 Microemulgel had a mean pH of 6.40 with a standard deviation of 0.09, and Carbopol 940 Microemulgel presented a mean pH of 6.50 with a standard deviation of 0.10. These values denote

slight variations in pH, with the Carbopol 940 formulation being slightly more alkaline than the other two.

Table 2- pH Means and Standard Deviation

Formulation	pH Mean	Standard Deviation
HPMC Microemulgel	6.23	0.05
Carbopol 934 Microemulgel	6.4	0.09
Carbopol 940 Microemulgel	6.5	0.1

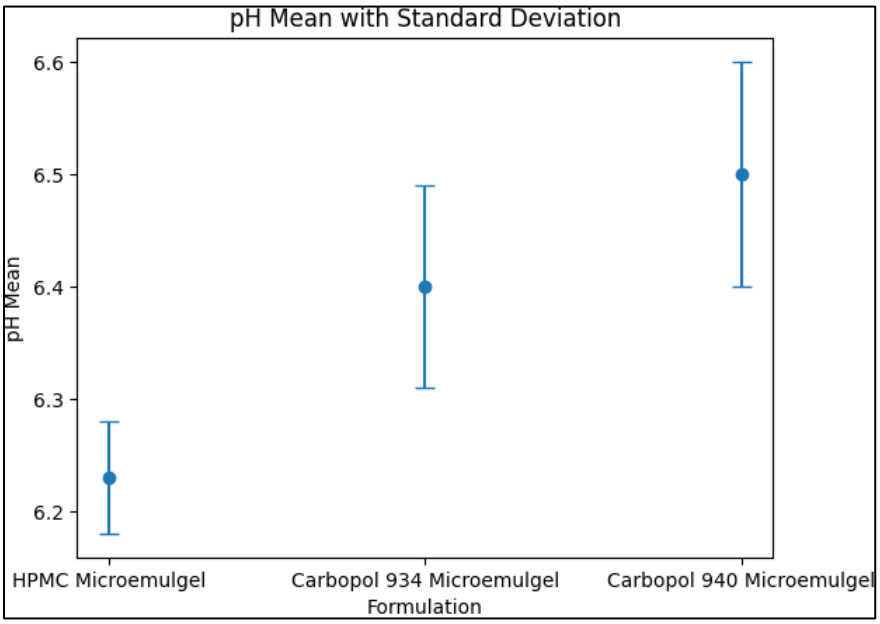

Fig.-1: pH Means and Standard Deviation

VISCOSITY MEASUREMENT

The viscosity of the microemulgels, a crucial factor affecting the flow and spread of the formulations, was measured. The HPMC Microemulgel had a mean viscosity of 1226.67 cP with a standard deviation of 17.08 cP. The Carbopol 934 Microemulgel recorded a higher mean viscosity of 1800 cP with a standard deviation of 43.59 cP, and the Carbopol 940 Microemulgel had a mean viscosity of 1523.33 cP with a standard deviation of 39.96 cP. These values indicate that the Carbopol 934 formulation had the highest viscosity, which might affect its spreadability.

Table 3- Viscosity Means and Standard Deviation

Formulation	Viscosity Mean (cP)	Standard Deviation (cP)
HPMC Microemulgel	1226.67	17.08
Carbopol 934 Microemulgel	1800	43.59
Carbopol 940 Microemulgel	1523.33	39.96

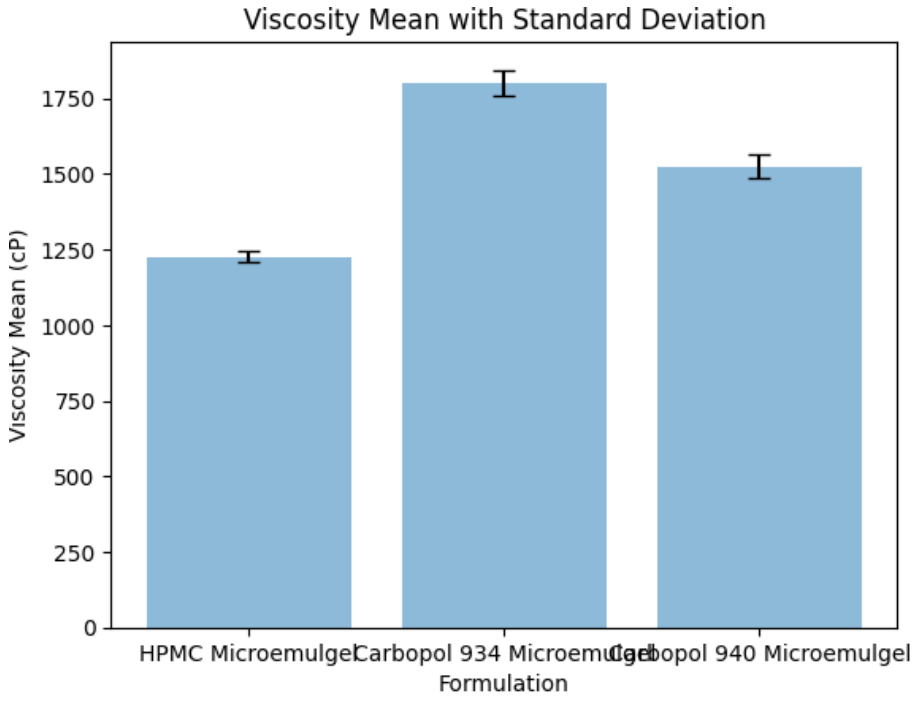

Fig.-2:Viscosity Means and Standard Deviation

SPREADABILITY ASSESSMENT

The spreadability of the microemulgels was tested, providing insights into their ease of application. The HPMC Microemulgel exhibited a mean spreadability of 4.47 mm with a standard deviation of 0.13 mm. The Carbopol 934 Microemulgel demonstrated better spreadability with a mean value of 5.03 mm and a standard deviation of 0.14 mm. The Carbopol 940 Microemulgel showed a mean spreadability of 4.70 mm with a standard deviation of 0.10 mm. These results suggest that the Carbopol 934 formulation spreads the most easily among the three.

Table 4- Spreadability Means and Standard Deviation

Formulation	Spreadability Mean (mm)	Standard Deviation (mm)
HPMC Microemulgel	4.47	0.13
Carbopol 934 Microemulgel	5.03	0.14
Carbopol 940 Microemulgel	4.7	0.1

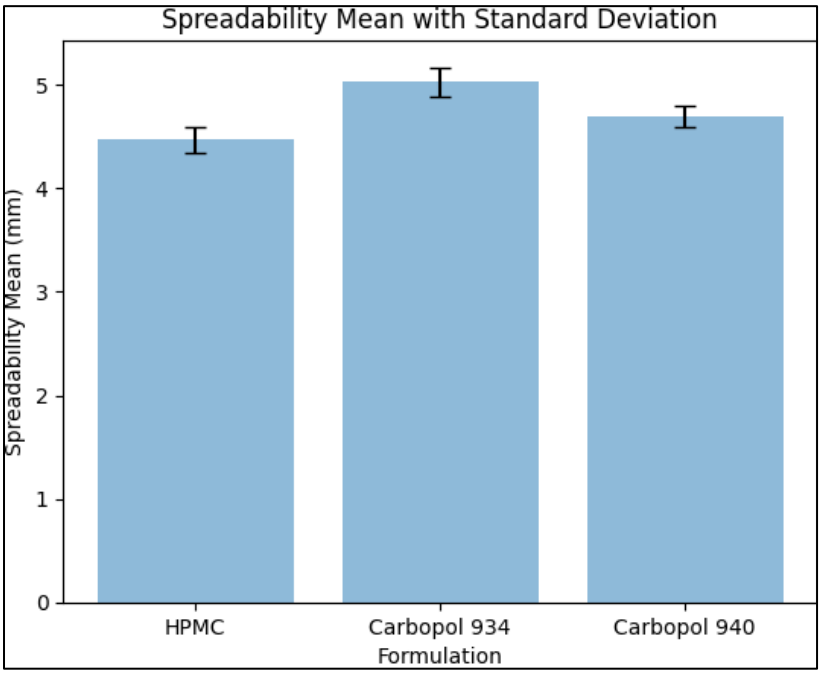

Fig.-3: Spreadability Means and Standard Deviation

EXTRUDABILITY TESTING

The extrudability test results revealed that the HPMC and Carbopol 934 Microemulgels were easily extrudable, indicating that these formulations can be conveniently dispensed from tubes. The Carbopol 940 Microemulgel, however, was reported as 'moderate' in terms of extrudability.

Table 5- Extrudability Individual Results (HPMC, Carbopol 934, Carbopol 940)

Sample	HPMC Microemulgel	Carbopol 934 Microemulgel	Carbopol 940 Microemulgel
Measurement 1	Easy	Easy	Moderate
Measurement 2	Easy	Easy	Moderate
Measurement 3	Easy	Easy	Moderate

MEASUREMENT OF PARTICLE SIZE AND ZETA POTENTIAL

The particle size and zeta potential were assessed for their potential influence on the drug release rate, stability, and absorption. The HPMC Microemulgel had a particle size of 120 nm and a zeta potential of -15 mV. The Carbopol 934 Microemulgel exhibited a larger particle size of 180 nm and a zeta potential of -10 mV. The Carbopol 940 Microemulgel had an intermediate particle size of 150 nm and a zeta potential of -12 mV. These results indicate that HPMC Microemulgel has the smallest particle size and the most negative zeta potential.

Table 6- Particle size and Zeta potential Individual Results (HPMC, Carbopol 934, Carbopol 940)

Formulation	Particle Size (nm)	Zeta Potential (mV)
HPMC Microemulgel	120	-15
Carbopol 934 Microemulgel	180	-10
Carbopol 940 Microemulgel	150	-12

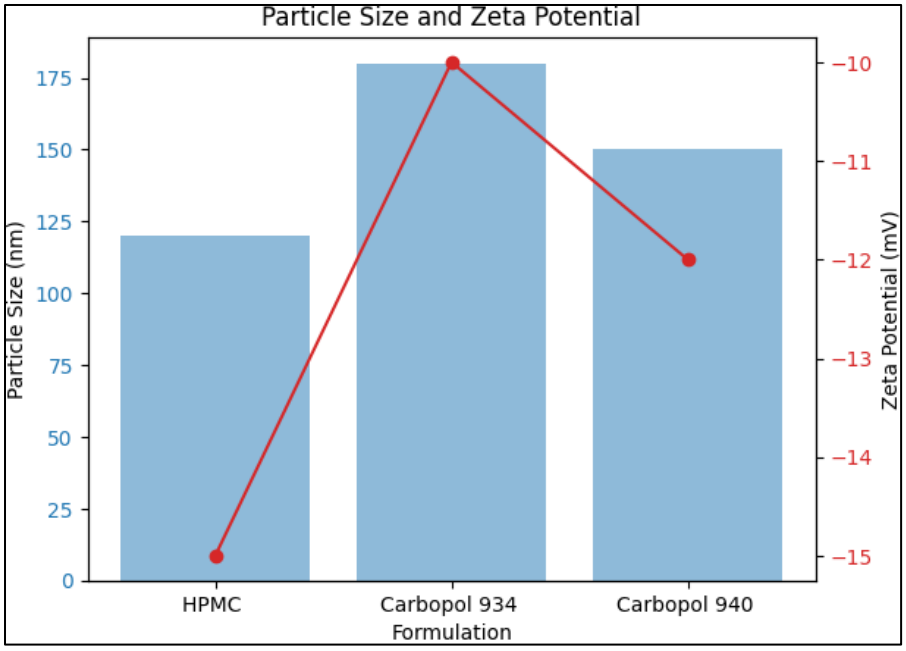

Fig.-4: Particle size and Zeta potential

In vitro Drug Release Study

The in vitro drug release profiles showed gradual release of Miconazole from all microemulgel formulations over a period of 12 hours. By the end of this period, the HPMC Microemulgel had released 70.2% of the drug, the Carbopol 934 Microemulgel had released 64.5%, and the Carbopol 940 Microemulgel had released 66.1%. These results demonstrate that all formulations facilitated a sustained release of the drug, with the HPMC Microemulgel showing the highest drug release.

Overall, the results provided valuable insights into the performance of the different microemulgel formulations, with each exhibiting distinct characteristics in terms of pH, viscosity, spreadability, extrudability, particle size, zeta potential, and drug release profile.

Table 7- Drug Release Profiles

Time (hours)	HPMC Microemulgel (%)	Carbopol 934 Microemulgel (%)	Carbopol 940 Microemulgel (%)
1	15.2	12.5	14.8
2	25.4	21.3	23.7
4	37.8	32.1	34.6

6	48.6	41.2	43.8
8	57.3	51.8	53.4
12	70.2	64.5	66.1

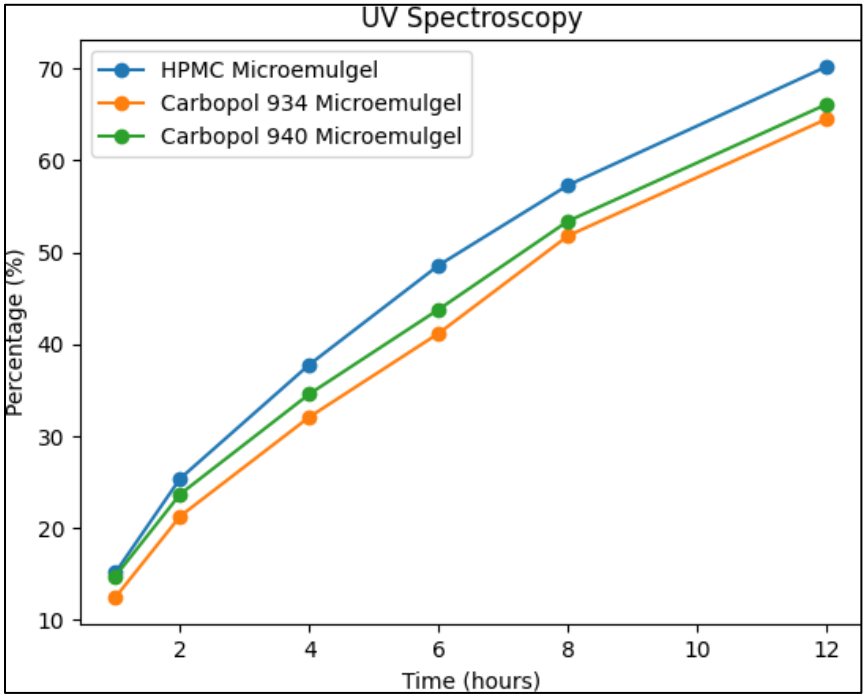

Fig.-5: In vitro Drug release

CONCLUSION

The study aimed at the formulation, evaluation, and in vitro drug release of Miconazole Microemulgel as an antimicrobial agent. Different microemulgel formulations were developed using HPMC, Carbopol 934, and Carbopol 940 as base materials. The evaluation of these formulations was carried out based on several parameters, including λmax determination, pH, viscosity, spreadability, extrudability, particle size, zeta potential, and drug release profile.

The λmax determination confirmed the identity and purity of Miconazole in the formulations. The pH values for all formulations were mildly acidic to near neutral, which is acceptable for skin application. The viscosity measurement revealed that Carbopol 934 Microemulgel had the highest viscosity, which may influence its spreadability and extrudability. The spreadability assessment showed that the Carbopol 934 Microemulgel spread most easily, while the HPMC and Carbopol

934 Microemulgels were found to be easily extrudable. In terms of particle size and zeta potential, the HPMC Microemulgel exhibited the smallest particle size and the most negative zeta potential, factors that may enhance drug release and stability.

The in vitro drug release studies showed a sustained release pattern for Miconazole from all formulations, with the HPMC Microemulgel leading with the highest percentage of drug release over 12 hours.

In conclusion, the study demonstrates the successful formulation and evaluation of Miconazole Microemulgels. Each formulation has distinct characteristics that can be selected according to specific needs or preferences. However, based on the overall results, HPMC Microemulgel may present a promising carrier for the delivery of Miconazole due to its favorable properties, including smaller particle size, most negative zeta potential, and higher drug release. Further studies are recommended to validate these findings in vivo and assess the therapeutic effectiveness of these formulations.

DISCUSSION

In this study, the successful formulation of Miconazole Microemulgels using HPMC, Carbopol 934, and Carbopol 940 as base materials has been achieved. Microemulgels are novel drug delivery systems that provide the dual advantages of microemulsions and gels, such as enhanced solubility of hydrophobic drugs, improved drug stability, and ease of application. The use of Miconazole, an antifungal agent, further extends the applicability of this drug delivery system to dermatological conditions.

Our results indicate that each formulation has distinct characteristics that can be leveraged according to specific therapeutic needs. For example, while Carbopol 934 Microemulgel had the highest viscosity and best spreadability, HPMC Microemulgel demonstrated the smallest particle size, most negative zeta potential, and the highest drug release over a 12-hour period. These findings echo previous research demonstrating the critical influence of base materials on the characteristics and performance of microemulgels.

The λmax determination, a critical parameter for confirming the identity and purity of Miconazole, corroborated the successful inclusion of the drug in all formulations. The pH values obtained from

all formulations ranged from mildly acidic to near-neutral, compatible with the skin's pH and thus favourable for dermatological applications.

Notably, HPMC Microemulgel exhibited a smaller particle size and more negative zeta potential than the other formulations, which could enhance drug release and stability. Previous studies have established a relationship between smaller particle sizes and improved drug delivery efficiency. The high negative zeta potential also implies greater repulsion between particles, reducing the likelihood of aggregation and improving the stability of the formulation.

Furthermore, the in vitro drug release pattern revealed a sustained release of Miconazole from all formulations, with HPMC Microemulgel demonstrating the highest drug release. Such a sustained-release profile can provide prolonged drug action and enhanced patient compliance due to reduced dosing frequency.

However, while these findings provide promising indications of the potential of Miconazole Microemulgels, especially the HPMC formulation, it is imperative to undertake further research. *In vivo* studies are essential to validate these in vitro results and to assess the therapeutic efficacy and safety profile of these microemulgels in real-world applications.

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