RESEARCH PAPER

Formulation And Evaluation Of Clotrimazole And Ketoconazole Combination Loaded Microsponge Gel Using Different Polymers For Topical Drug Delivery

Neha Sodiyal [1], Mayank Yadav [1*], Ranjit Singh [1]

[1]*Department of Pharmaceutical Sciences, Adarsh Vijendra Institute of Pharmaceutical Sciences, Shobhit University, Gangoh, Saharanpur, Uttar Pradesh, India.*

***Corresponding Author:** Mayank Yadav, Department of Pharmaceutical Sciences, Adarsh Vijendra Institute of Pharmaceutical Sciences, Shobhit University, Gangoh, Saharanpur, Uttar Pradesh, India. Email: mayankmp@gmail.com

ABSTRACT

The study focuses on the formulation and evaluation of a combination-loaded microsponge gel containing Clotrimazole and Ketoconazole for topical drug delivery. The objective is to enhance the therapeutic efficacy and minimize the side effects of these antifungal agents by developing a controlled release system. Various polymers were utilized to prepare the microsponges, including ethyl cellulose, Eudragit, and polyvinyl alcohol (PVA). The microsponges were formulated using the quasi-emulsion solvent diffusion method, optimizing parameters such as drug-to-polymer ratio, stirring speed, and solvent type. The resultant microsponges were characterized for particle size, surface morphology, drug loading efficiency, and encapsulation efficiency. The formulated microsponges were incorporated into a gel base and evaluated for their physicochemical properties, including pH, viscosity, spreadability, and in vitro drug release. The stability of the microsponge gel was assessed under various storage conditions. Results indicated that the microsponge exhibited a spherical shape with a porous surface, appropriate particle size distribution, and high drug encapsulation efficiency. The gel formulation showed desirable rheological properties and a controlled release profile, with a sustained antifungal effect over an extended period. The combination therapy of Clotrimazole and Ketoconazole in a microsponge gel provided a synergistic effect, enhancing antifungal activity and potentially reducing the frequency of application and adverse effects associated with conventional formulations. In conclusion, the study successfully developed a novel microsponge gel system for the topical delivery of Clotrimazole and Ketoconazole, demonstrating its potential as an effective treatment for fungal infections.

Key words: microsponge, polymer, skin, antifungal, ketoconazole, clotrimazole, in-vitro drug release, antifungal, diffusion method

How to cite this article: Sodiyal N, Yadav M, Singh R. Formulation and evaluation of clotrimazole and ketoconazole combination loaded microsponge gel using different polymers for topical drug delivery. Int J Drug Deliv Technol. 2026;16(7s): 232-235; DOI: 10.25258/ijddt.16.7s.26

INTRODUCTION

Noval drug delivery system is new approach for the drug delivery system. it has been increasingly investigated to achieve targeted and controlled release of drugs as many of conventional delivery systems require high concentration of active agents to be incorporated for effective therapy because of their low efficiency as delivery system. Microsponges are highly cross- linked, patented, porous, polymeric microspheres that acquire the flexibility to entrap a wide variety of active ingredients that are designed to release active agents gradually onto the skin, either over time or in response to specific triggers. Recent advancements in drug delivery technologies have focused on optimizing therapeutic efficacy and cost-effectiveness. Among these, MDS has emerged as a promising approach for controlled drug release targeting the epidermis.

Microsponge particles are microporous beads, typically ranging from 10–25 µm in diameter, capable of encapsulating a wide variety of active substances, including pharmaceutical and therapeutic agents. These systems are composed of microscopic, polymer-based microspheres that can suspend or entrap ingredients efficiently.

Microsponge technology offers several advantages:

- Sustained release of active agents
- Reduced side effects
- Enhanced stability
- Improved skin feels and texture
- Greater formulation flexibility

Importantly, microsponges can remain localized within skin cells, minimizing systemic absorption and preventing dose dumping into the bloodstream, which could otherwise lead to adverse effects. Studies have shown that microsponge systems are non-allergenic, non-irritating, non-mutagenic, and non-toxic. This technology is currently utilized in cosmetics, skincare products, sunscreens, and prescription formulations.

Gel Formulation

Gels are semi-solid formulations characterized by a high liquid content. Upon application, the liquid phase evaporates, leaving a thin layer of drug-loaded gel on the skin. Gels are defined as dilute, cross-linked systems that remain in a steady state and do not exhibit flow.

Compared to creams and ointments, gels offer:

- Superior application properties
- Enhanced stability
- Better skin adherence

Method of Preparation

Ketoconazole-loaded microsponges were prepared using the quasi-emulsion solvent diffusion method:

1. **Inner Phase**: Ethyl cellulose was dissolved in 20 mL of dichloromethane. Ketoconazole was added and dissolved using ultrasonication at 35°C.
2. **Outer Phase**: The resulting solution was poured into an aqueous polyvinyl alcohol solution while stirring at given rpm for 3 hours.
3. **Formation**: Microsponges formed as dichloromethane evaporated from the system.
4. **Post-Processing**: The microsponges were filtered, washed with distilled water, and dried at room temperature for 24 hours.

Formulation of ketoconazole and clotrimazole microsponges

Table no. 1: Composition of Microsponge

Chemical Name	F1	F2	F3	F4	F5
Drug (ketoconazole) (mg)	200	200	200	200	200
Drug (clotrimazole) (mg)	-	200	-	200	200
Ethyl cellulose (mg)	400	800	1200	1600	2000
Eudragit RS 100	-	400	-	800	-
HPMC	-	-	400	-	800
Dichloromethane (ml)	10	10	10	10	10
Glycerin (ml)	0.1	0.1	0.1	0.1	0.1
PVA (mg)	100	100	100	100	100
Distill water (ml)	100	100	100	100	100
Stirring speed	1000	1500	1000	1500	1500

Evaluation parameter of ketoconazole and clotrimazole microsponges

RESULT

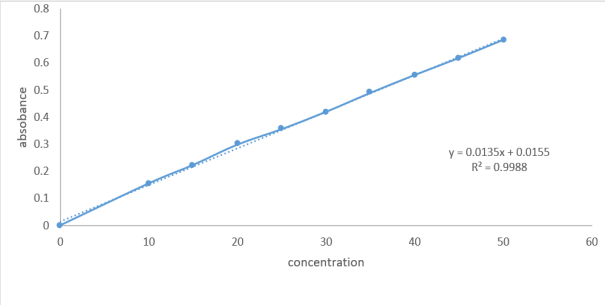
- **Preformulation study for ketoconazole**

Colour	White powder
Odour	Odourless
Appearance	Crystalline

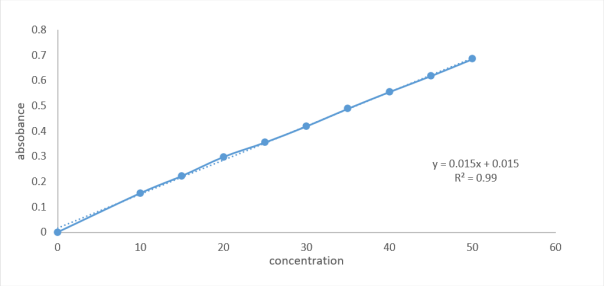
- **Preformulation study for clotrimazole**

Colour	White powder
Odour	Odourless
Appearance	Crystalline

- Calibration curve of ketoconazole using phosphate buffer pH 7.4 as medium at 287nm.



- Calibration curve of clotrimazole using phosphate buffer pH 7.4 as medium at 254nm



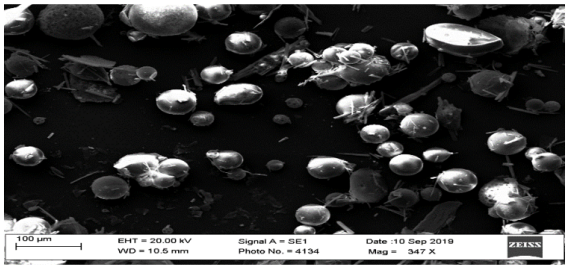
Characterization and evaluation of the ketoconazole and clotrimazole microsponges

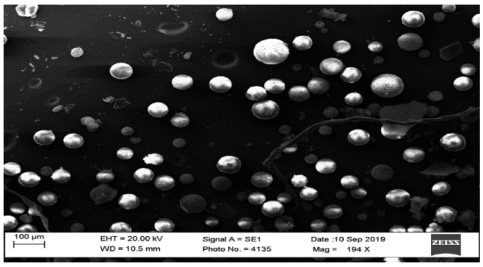
Production yield, drug content and entrapment efficiency

Formulation	Production yield (%)	Drug content (%)	Entrapment efficiency (%)
F1	62	46	44
F2	65	51	50

F3	67	58	56
F4	71	67	61
F5	73	74	68

Scanning Electron Microscopy





SEM image of formulation F1

SEM image of formulation F2

- **Micromeretics evaluation**

Code	**Particle size (µm)**	**Bulk density**	**Tapped density**	**Carr's index (%)**	**Hausner's ratio**	**Angle of repose**	**Flow character**
F1	24.27	240	302.12	20.521	1.258	25.60	Excellent
F2	27.06	301.12	332.32	9.388	1.103	29.12	Excellent
F3	35.25	318.03	345.22	7.876	1.085	31.50	Good
F4	45.32	325..65	354.16	8.050	1.087	33.41	Good
F5	52.05	224.32	324.48	30.867	1.446	35.25	Fair

CONCLUSION

The microsponge delivery system represents a novel and versatile technology that has gained significant attention in both pharmaceutical and cosmetic industries due to its remarkable ability to provide controlled and sustained release of active ingredients. By entrapping drugs within a porous, polymeric microsphere network, this system not only enhances formulation stability but also minimizes undesirable side effects, thereby improving overall therapeutic efficacy. Its unique architecture allows for precise modulation of drug release kinetics, making it particularly valuable in topical applications where prolonged activity and reduced irritation are desired. Furthermore, studies have consistently demonstrated that microsponges are biocompatible, non-toxic, non-allergenic, and non-mutagenic, which underscores their safety for long-term use. Beyond dermatological and cosmetic formulations, the potential of microsponges extends into advanced biomedical fields such as bone regeneration and tissue engineering, where they can act as scaffolds for cell growth while simultaneously delivering therapeutic agents. With these multifaceted advantages, microsponge technology holds immense promise for the future, offering innovative solutions for the treatment of diverse diseases and paving the way for next-generation drug delivery systems.

REFERENCE

1. Swati J, Dhaval B, Mahesh G. Formulation and evaluation of fluconazole soap strip for dermal infections. International Journal of Pharma Tech Research. 2011; 3(4): 2215-2221
2. Jain V, Singh R. Devlopment and characterization of drug loaded microsponge and its colonic delivery system containing paracetamol microsponge. Arch Pharma Research 2011; 34(5):733-740
3. John I. Topical Anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsponge delivery system. Research J. Pharma and Tech. 2008; 1(4): 502-506
4. Nokhodchi A, Jelvehgari M, Siahi M. Factors affecting the morphology of benzoyl peroxide microsponges. Micron Online Journal. 2007; (38): 834-840
5. Swati J, Dhaval B, Mahesh G. Formulation and evaluation of fluconazole soap strip for dermal infections. International Journal of Pharma Tech Research. 2011; 3(4): 2215-2221
6. Jain V, Singh R. Devlopment and characterization of drug loaded microsponge and its colonic delivery system containing paracetamol microsponge. Arch Pharma Research 2011; 34(5):733-740
7. John I. Topical Anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsponge delivery system. Research J. Pharma and Tech. 2008; 1(4): 502-506

8. Nokhodchi A, Jelvehgari M, Siahi M. Factors affecting the morphology of benzoyl peroxide microsponges. Micron Online Journal. 2007; (38): 834-840
9. Roop K Khar, S P Vyas, Farhad J Ahmad, Gaurav K Jain. The theory and practice of industrial pharmacy. CBS Publishers. 2013; 4th edition:714-756
10. Mikari B. Formulation and evaluation of topical liposomal gel for fluconazole. Indian J Pharm. Sci. 2010; 44(4): 324-325
11. Chadawar V, Shaji J. Microsponge Delivery System. Current Drug Delivery. 2007;4: 123-129
12. Pradhan SK. Microsponge as the versatile tool for drug delivery system. Int J Res Pharma Chem. 2011; 1(2): 243-258.
13. RJ. (2012). Patel EK, Oswal Microsponges: a novel drug delivery system. *IJRPC*, 2(2), 237-238.
14. A.P. Pharma, Inc. Microsponge Technology, Topical Technology December 2001. Available at: http://www.appharma.com/PDFs/topicalsht.pdf.
15. Hainey P, Huxham I M, Rowatt B, Sherrington D C. Synthesis and ultrastructural studies of styrene-divinylbenzene polyhipe polymers macromolecules. A.C.S Publishers. 1991; (24): 117-121
16. Abdellatif AAH. A novel controlled release microsponges containing albendazole against haemonchus contortus in experimentally infected goats. Journal of Drug Delivery Science and Technology. 2018 (43): 469-476.
17. Kumari P, Mishra S. A comprehensive review on novel microsponges drug delivery approach. Asian J Pharm Clin Res. 2016;9(1):25-30.
18. Aldawsari H. Microsponges as promising vehicle for drug delivery and targeting: preparation characterization and applications. Afr J Pharm Pharmacol. 2013 May 8;7(17):873-81.
19. Kumar L, Chadha M, Rana R, Kukreti G, Kaundal AK, Aggarwal V. Polymeric microsponges: an emerging prospect in topical delivery of therapeutic agents. International Journal of Polymeric Materials and Polymeric Biomaterials.
20. Sah S, Kohri A, Patil S. A comprehensive review on microsponges drug delivery systems. J Res Appl Sci Biotechnol. 2024;3(3):59-66.
21. Halder S, Behera US, Poddar S, Khanam J, Karmakar S. Preparation of microsponge drug delivery system (MSDDS) followed by a scale up approach. AAPS PharmSciTech. 2024;25(6):162.
22. Tiwari A, Mishra MK, Shukla A, Yadav SK. Micro sponge: an augmented drug delivery system. Am J Pharm Tech Res. 2016;6(6):79-95.
23. Pentewar R, Kazi S, Bharti R, Pulgamwar G. MDS technology: an approach for topical oral controlled and cosmetic formulations. Res J Pharm Biol Chem Sci. 2014;5(3):1170-90.
24. Rajeswari S, Swapna V. Micro sponges as a neoteric cornucopia for drug delivery systems. Int J Curr Pharm Res. 2019;11(3):4 12.
25. Saxena S, Nacht S. Delivery system handbook for personal care and cosmetic products: technology applications and formulations. New York: William Andrew Publishing; 2005. p. 333-51.
26. Naga Jyothi K, Dinesh Kumar P, Arshad P, Karthik M, Panneerselvam T. Micro sponges: a promising novel drug delivery system. J Drug Deliv Ther. 2019 Oct;9(5):188-94.
27. John I. Topical Anti-inflammatory gels of fluocinolone acetonide entrapped in eudragit based microsponge delivery system. Research J. Pharma and Tech. 2008; 1(4): 502-506.
28. Swati J, Dhaval B, Mahesh G. Formulation and evaluation of fluconazole soap strip for dermal infections. International Journal of Pharma Tech Research. 2011; 3(4): 2215-2221
29. Pradhan SK. Microsponge as the versatile tool for drug delivery system. Int J Res Pharma Chem. 2011; 1(2): 243-258.
30. RJ. (2012). Patel EK, Oswal Microsponges: a novel drug delivery system. *IJRPC*, 2(2), 237-238.