INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Research Article

TOLNAFTATE MICROSPONGES EMBEDDED BIOCOMPATIBLE GELS FOR CONTROLLED AND EFFECTIVE ANTIDERMATOPHYTIC ACTIVITY

Prashant Pandey *[1], Shashi Kiran Misra [2], Anupriya Kapoor [2], Nisha Sharma [3] and Pushpa Kumari [4]
[1]Project Assistant, University Institute of Pharmacy, C S J M University, Kanpur, Uttar Pradesh, India
[2]Assistant Professor, University Institute of Pharmacy, C S J M University, Kanpur, Uttar Pradesh, India
[3]HOD/Associate Professor, University Institute of Pharmacy, C S J M University, Kanpur, Uttar Pradesh, India
[4]Research Scholar, University Institute of Pharmacy, C S J M University, Kanpur, Uttar Pradesh, India
*Corresponding Author Email: mrpandeyprashant@gmail.com

Article Received on: 26/05/18 Approved for publication: 22/06/18

DOI: 10.7897/2230-8407.096103

ABSTRACT

The aim of this investigation was to develop potentially efficient Tolnaftate Microsponges embedded gels for effective management of dermatophytosis, which has been highly ignored skin ailment in the current era. Immunosuppressant and patients suffering from severe diseases are highly prone to dermatophytosis. Herein Tolnaftate microsponges were prepared through quassi-emulsion solvent diffusion technique applying biocompatible polymers Eudragit RL100 and Eudragit RS100. Formulated Microsponges were embedded in Carbopol 934 and HPMC to attain controlled topically effective formulation and their physical parameters like viscosity, pH, spreadibility, the in-vitro drug release kinetics were evaluated. Drug-excipient compatibility was performed by FTIR and TGA. FESEM analysis revealed micro size microsponges with numerous pores present over their surface. Several in-vitro release kinetics models were applied, and the formulated gels followed Korsmeyer Peppas model. Antidermatophytic activity against Trichophyton mentagrophytes revealed a distinct zone of inhibition and showed the potential role for the management of dermatophytosis.

Keywords: Dermatophytosis, Tolnaftate, Microsponges, Quassi emulsion technique, *Trichophyton mentagrophytes*

INTRODUCTION

Dermatophytosis is a superficial cutaneous infection is extremely common disease in last few decades is caused by filamentous dermatophytes. Mostly belongs to the genera *Trichophyton, Microsporum and Epidermophyton* which is keratinophilic fungi that encroaches keratinized layer of skin tissues (scalp, nail and hair) and causes several tinea diseases. They likely develop outwards on skin, forming a ring like pattern that's why also known as 'Ringworm'. These dermatophytes propagate only in the superficial layer of the epidermis (stratum corneum) and usually do not penetrate deeper tissue but encouraged by a damp and warm local environment. Although the complex immune system and internal temperature of human body largely protect from major life threatening fungal infections but excess use of antibiotics/steroids and altered physiological conditions are also worsen the cases.[1,2] Dermatophytes are spreaded by coming in contact with affected host or by direct or indirect contact with infected skin or hair (combs, adhered in clothing, hair brushes).[3]

Tolnaftate is a synthetic thiocarbamate used as the topical antifungal agent, reported by Noguchi and their colleagues in 1963.[4] It is a lipophilic in nature, has poor aqueous solubility with a high molecular weight (307.41 g/mol), shows poor permeability property and it comes under BCS class IV drugs. It acts by suppressing an enzyme squalene epoxidase, resulting deficiency of ergosterol in fungal membrane.[5,6] Tolnaftate is active only by topical application and inactive via intraperitoneal and other routes. In market Tolnaftate is available in various topical dosage forms like spray, powder, liquid aerosol and creams.[7,8]

Microsponges is sponge like porous polymeric delivery system that are commonly used for extended release of drug. It offers to deliver active ingredients readily at low dose and reduce allergenicity, mutagenicity, irritation and side-effects and enhanced stability and payload of drug. They are stable at variable ranges (pH 4-9).[9-11] The objective of the present investigation was to load Tolnaftate into microsponges by quassi-emulsion solvent diffusion technique in order to elevate the aqueous solubility and permeability and to evaluate them by formulating controlled release topical gels.

MATERIALS AND METHOD

Tolnaftate was recieved from Yarrow Chem. Products, Mumbai. Eudragit RS 100, Eudragit RL 100, Hydroxy propyl methyl cellulose (HPMC) and Carbopol 934 were purchased from Yarrow Chem. Products, Mumbai. PVA (poly vinyl acetic acid), PEG (poly ethylene glycol), dichloromethane, methanol and triethanolamine were purchased from S.D Fine Chem. Ltd, Mumbai. All other reagents and chemicals used for analysis were of analytical grade.

Preparation of Tolnaftate loaded microsponges

Tolnaftate microsponges were prepared by Quassi-emulsion solvent diffusion technique. The method consists of two step process. In first step, internal phase was prepared and in second step external phase was prepared. Internal phase was prepared by dissolving Eudragit RL 100, Eudragit RS 100 separately and their combinations, in different ratio in dichloromethane followed by addition of PEG (which was added to facilitate the plasticity),

then after Tolnaftate added into the solution and allowed for ultrasonication at 35°C. Then after external phase was prepared by dissolving PVA in deionized water and the process is carried out at room temperature. Then at room temperature, internal phase was poured into the external phase. After the completion of emulsification process, the mixture was stirred continuously for 6-7 hours at 5000 rpm. Prepared Microsponges MF1 and MF2 were separated by filtration, washing and dried in vacuum oven at 40°C for 12 hours.[12-14]

Evaluation of Tolnaftate loaded microsponges

Drug-Polymer compatibility studies

The samples of pure drug, physical mixture and Microsponges were recorded. Sample was prepared by triturating samples with KBr and samples were analyzed. Each spectrum was measured over a frequency range from 500 – 3500 cm^{-1}.[18]

DSC analysis

Samples were loaded in aluminium and the DSC thermographs were recorded at a heating rate of 10 °C/min in range of 0°C to 600°C. Nitrogen gas was purged for maintaining inert atmosphere at rate of 50ml/min. DSC thermograms were obtained using the instrumental software.[19]

Surface Morphology analysis

The morphology of microsponges was examined by SEM. The dried sample was mounted on aluminium grooved edge stub and properly coated with gold (15 nm) for one minute. The coated sample was then scanned and their images were taken.[21]

Particle size analysis

The particle size was done by using an optical microscopy by using calibrated eye piece and stage micrometer. A little amount of microsponges (MF1 and MF2) were spread on glass slide and average particle size was calculated by counting atleast 100 particles of each batch.[20]

Determination of Production yield

The production yield of prepared Tolnaftate loaded microsponges (MF1 and MF2) was determined by using following equation (1).[22]

$$\text{Production yield (\%)} = \frac{\text{Practical mass of microsponges}}{\text{Theoretical mass (Polymer + drug)}} \times 100$$

Determination of Drug content

A specific quantity (10 mg) Tolnaftate loaded microsponges (MF1 and MF2) were taken, triturated and dissolved it in 100 ml of phosphate buffer solution (pH 6.8). The volumetric flask containing microsponge solution was shaken in order to get complete solubility of drug. This solution is filtered and estimated spectrophotometrically at 257 nm using phosphate buffer solution as blank.[23]

In-vitro diffusion study

In-vitro diffusion study of Tolnaftate loaded microsponges were carried out by dialysis bag method using dialysis membrane in freshly prepared phosphate buffer solution (pH 6.8). Dialysis membrane was soaked overnight in the diffusion medium facilitate opening of pores for proper diffusion process. Accurately weighed Microsponges equivalent to 10 mg Tolnaftate was added in dialysis bag and allowed to hang in same diffusion media for in-vitro drug analysis. The release/diffusion profile of the drug was obtained by sampling 5ml of aliquots from the diffusion medium at predetermined interval for 8 hours. The sampled aliquot was every time replaced by fresh diffusion medium of the same quantity, to maintain the sink condition. Aliquots were analyzed through UV spectrophotometer and release kinetics were interpreted by applying DDsolver software.[24]

Preparation of Tolnaftate loaded microsponge based gel

Hydroxy propyl methyl cellulose (HPMC) and Carbopol 934 were selected for providing final form of topical gel formulation. Tolnaftate microsponges were dispersed in water and added to the drug solvent system. Triethanolamine was added dropwise in this mixture with slowly stirring, taking consideration that air bubble should not form. Prepared Tolnaftate gel was stored in an air tight collapsible tube for further study.[15-17]

Evaluation of Tolnaftate loaded microsponge based gel

Physical examination of gels

The prepared Tolnaftate microsponge based gel formulations was examined visually for its color and appearance.[25] The pH of the prepared microsponge gel formulations were measured by digital pH meter.[26]

Spreadibility

Spreadibility of gel formulations was determined by using horizontal plate method. A glass plate was stationed on the surface and an excess of gel (1g) were allocated in the slide. The gel was sandwiched between the slide and another glass slide having the fixed dimension was placed over it. A 125 g weight was positioned over the upper slide for specific time (5 min.) to expel and to provide a uniform film of the gel between the slides.[27] The spreadibility was then calculated using the following formula

$$S = M \times \frac{L}{T}$$

Where, S= spreadibility, M= weight placed on the upper slide, L= length moved by the glass slide, T= time

Viscosity measurement

Viscosity measurement was carried out by using Brookfield viscometer. Sufficient sample was placed in a cylindrical tube and measured the reading at 37°C ± 2°C and rotating the spindle no. 63 at 1.5 rpm.[28]

Extrudability

The prepared gel formulation was filled in clear, collapsible aluminum tubes. Afterward, the extrudability of gel formulations was estimated in weights in gram required to extrude out through tip of the tube.[29]

Drug content study

Tolnaftate microsponge embedded gel (100 mg) was accurately weighed and dissolved in 100 ml of Phosphate buffer solution (pH 6.8), sonicated for 10-15 minutes. The solution was filtered and absorbance was estimated by using UV/Vis Spectrophotometer at 257 nm.[30]

In-vitro diffusion study

In-vitro release of microsponge based gel containing Tolnaftate was studied by using membrane diffusion technique. The gels equivalent to 10 mg Tolnaftate was kept in the dialysis bag. The temperature of medium as maintained at 37 ± 0.5°C and stirred at 50 rpm. Aliquots of 5 ml volume of each formulation were withdrawn periodically, and medium was then replaced by equal volume. The samples were analyzed at 257 nm by UV/Vis Spectrophotometer.[31]

Anti-fungal activity

On the basis of in-vitro drug release profile the gel was selected for antifungal activity. Antifungal activity of formulated gel was carried out by Agar well diffusion method. A defined volume of *Trichophyton mentagrophyte* suspension were poured into Potato dextrose agar media (PDA) and allowed to solidify. Later the wells were made using a sterilized cork borer over that plate. The prepared wells were filled with standard solution having equal strength of control gel, Tolnaftate microsponge loaded gel. Then the petri plates were incubated at 37 °C for 24 hours.[32] The zone of inhibition were obtained, and diameter were measured.

Table 1. Tolnaftate Microsponge Formulations Prepared by Quassi-Emulsion Solvent Diffusion Method

Constituents	Microsponge formulations	
	MF1	MF2
Tolnaftate (gm)	0.25	0.25
Eudragit RL 100 (gm)	0.05	0.15
Eudragit RS 100 (gm)	0.15	0.05
Dichloromethane (ml)	5	5
Polyvinyl alcohol (gm)	0.08	0.08
Polyethylene glycol (ml)	0.5	0.5
Deionized water (ml)	10	10

Table 2. Formulation of Tolnaftate Gels Containing Microsponges Entrapped Drug

Ingredients	TMG 1	TMG 2
Tolnaftate microsponge equivalent 100 mg drug (mg)	100	100
HPMC (gm)	0.3	
Carbopol 934 (gm)		0.3
Polyethylene glycol (ml)	2	2
Ethanol (ml)	3	3
Triethanolamine (ml)	2	2
Methyl paraben (mg)	0.8	0.8
Deionized water q.s. (ml)	50	50

Table3. Production Yield, Drug Content, Particle Size And % Cumulative Drug Release of Microsponge Formulations

Formulation code	Production yield (%)	Drug content (mg)	Particle size (µm)	% Cumulative drug release
MF 1	68.9	27.3	0.8	70.4
MF 2	71.7	39.3	1.0	89.2

Table 4. Physical Evaluation of Gel Characteristics for Prepared Gel Formulations

Formulation code	pH	Spreadibility (g cm/sec)	Extrudability (g/cm^2)	Viscosity (cp)	Drug content (mg)	% Cumulative drug release
TMG 1	6.74	18.33	0.97	6079	29.50	69.3
TMG 2	6.92	24.81	1.03	6059	15.22	60.1

Table 5. Release Kinetic Models for Tolnaftate Microsponge Gel Formulations

Formulation Code	Zero order		First order		Korsmeyer Peppas		Higuchi	
	K_0	R^2	K_1	R^2	N	R^2	K_h	R^2
TMG 1	0.205	0.878	0.004	0.896	0.423	0.974	3.721	0.968
TMG 2	5.75	0.899	0.003	0.805	0.478	0.973	3.174	0.946

Table 6. Observation of in-vitro Antifungal activity

Antifungal Strain	Formulation	Zone of inhibition (mm)
T. mentagrophytes	Control gel	-
T. mentagrophytes	TMG1	8.8 ± 0.7

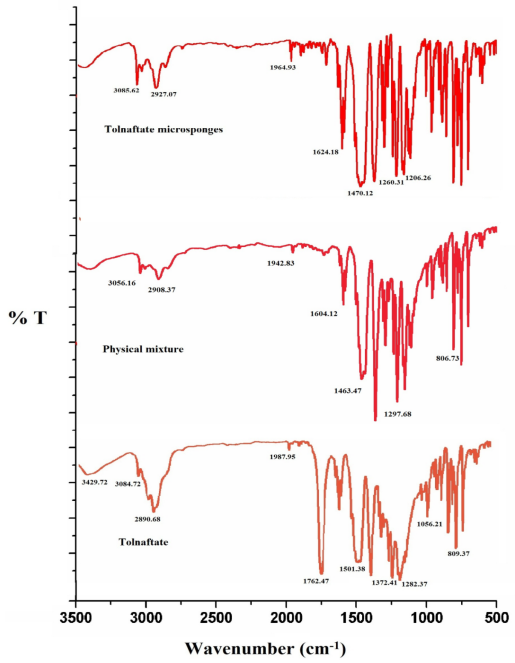

Figure 1. FTIR Spectra of Tolnaftate, Physical Mixture and Tolnaftate Microsponge

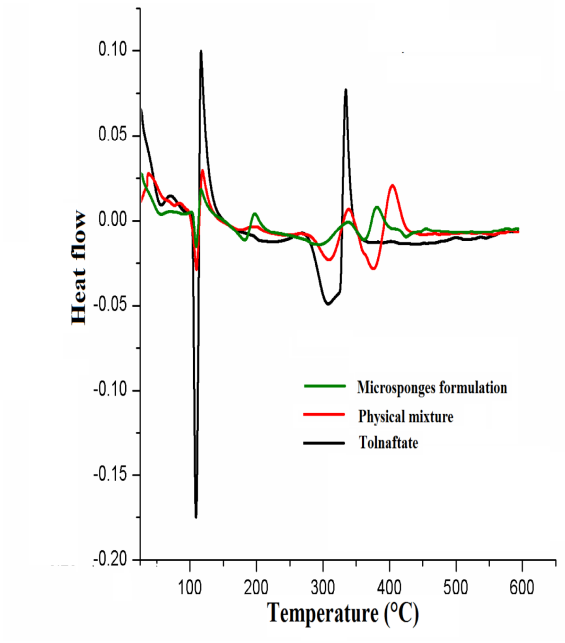

Figure 2. DSC thermogram of Tolnaftate (Drug), Physical Mixture and Microsponge Formulation

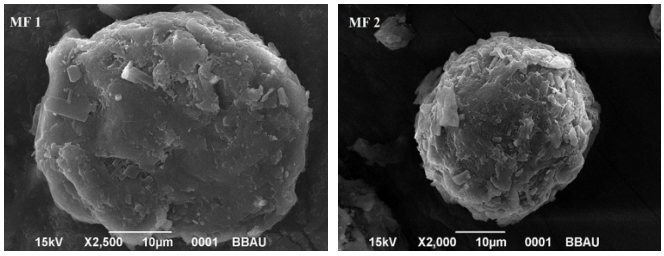

Figure 3. SEM Images of Tolnaftate Microsponges (MF1 and MF2)

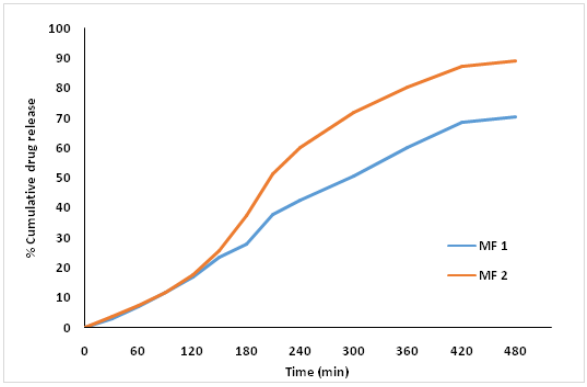

Figure 4. Drug Release Profile of Tolnaftate Microsponges Formulations

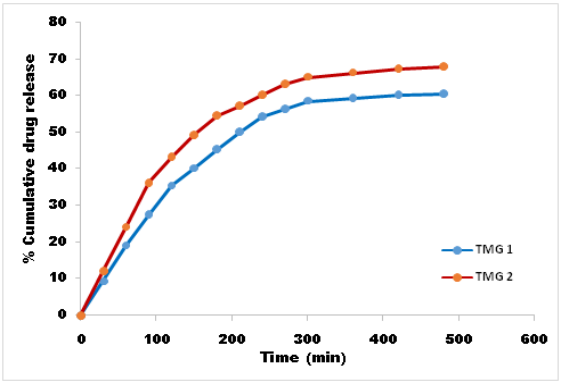

Figure 5. % Cumulative Drug Release of Tolnaftate Microsponge Gel Formulations

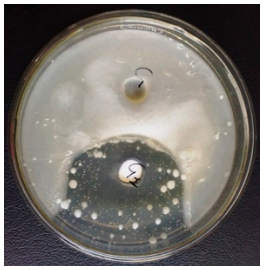

Figure 6. In-vitro antifungal activity against *T. mentagrophytes*

RESULTS AND DISCUSSION

Evaluation of Tolnaftate loaded microsponges

Drug polymer compatibility study

Drug polymer compatibility study was done by FTIR spectroscopy. The FTIR spectrum of pure drug, physical mixture and microsponges were obtained and compared to identify specific peaks by virtue of respective functional groups present in their chemical structures. Distinctive peaks of asymmetric C-H stretching at 3084.72 cm^{-1}, symmetric C-H stretching at 2890.68 cm^{-1}, C-N-C stretching vibration at 1501.38 cm^{-1}, O-H stretching peak at 1282.37 cm-1 and C-O-H stretching vibration at 1056.21 cm^{-1}were seen. It shows that there was no chemical interaction between the drug and the polymers. This illustrated that Tolnaftate was compatible with polymers and it was stable in microsponge formulations.

DSC study

In DSC thermogram of pure drug, at 25 °C the endothermic peak was seen which indicated the glass transition of the drug, a exothermic peak were also observed at 355 °C which showed the crosslinking and the sharp endothermic peak was also observed at 111 °C which is corresponding to the melting point of the drug reflecting the purity of drug and its crystalline form. In DSC thermograph of physical mixture and formulated microsponges, exothermic peak at 111 °C were observed.

Surface morphology analysis

The morphology and surface topography were observed by Scanning electron microscopy (SEM) MIRA3 TESCAN. The scanned images of formulated microsponges are shown in Figure 3 and it revealed that microsponges were spherical in shape, smooth and porous. The surface topography study revealed that microsponges consisted tiny pores. From the surface of microsponges diffusion of volatile solvent induced pores.

Particle size analysis

Particle size of the formulated microsponges varied due to the change in the concentration of polymers. The average particle size distribution of formulated microsponges of MF1, MF2 was 0.8 µm & 1.0 µm respectively.

Determination of Production yield

The production yield of Tolnaftate microsponge formulations was determined and it ranged from 63.4 to 71.7%. From the production yield of Tolnaftate microsponge formulations, it was indicated that on increasing the ratio of drug: polymer production yield was also increased.

Determination of Drug content

The drug content of Tolnaftate microsponges was determined and reported in Table 3. The obtained drug content were in ranges of 27.3-39.3 mg. The results revealed that drug was distributed in microsponges.

In-vitro diffusion study

In-vitro diffusion profile of the formulated Tolnaftate microsonges are presented in Table 3 and Figure 4. Amongst the formulated microsponges after 8 hours, MF2 exhibited prolonged release i.e. 89.2 %. This may be due to higher permeability of Eudragit RL 100 owing to high concentration of quaternary ammonium compound in their chemical structure with respect to Eudragit RS 100.

Evaluation of Tolnaftate loaded microsponge gels

Physical examination of gels

Formulated gels (TMG1 and TMG2) were subjected for evaluations i.e. color, appearance, pH, spreadibility, viscosity, extrudability and drug content. Both formulated gels were white in color, gel prepared from HPMC (TMG1) was translucent, having skin compatible pH of 6.74 and sufficient spreadibility (Table 4).

In-vitro drug release study

In-vitro drug release profile of TMG1 and TMG2 gels are being shown in figure 5. The diffusion study showed enhanced release of drug in TMG1 as compared to formulation TMG2. Microsponge loaded gel having HPMC exhibited higher amount of drug diffusion as compared to formulation having Carbopol for 8 hours. The results of various drug release kinetic models are shown in Table 5.

Antifungal activity

In-vitro antifungal activity of formulated Tolnaftate loaded microsponge gel (TMG1) against control are shown in figure 6. The gel TMG1 was selected for activity on the basis of in-vitro release profile. The formulated gel showed promising antifungal activity (Zone of inhibition of gel was 8.8 ± 0.7 mm) against selected dermatophyte *T. mentagrophyte.*

CONCLUSION

The present study concluded successfully formulation of Tolnaftate loaded microsponge by using quassi-emulsion solvent diffusion technique. The implemented technique was found to be easy, reproducible and rapid. Formulated microsponges were spherical in shape, have pourous and regular surface. Varied ration of drug-polymer showed remarkable effects on drug content, particle size, entrapment efficiency and drug release. The in-vitro drug release study of formulated Tolnaftate microsponge loaded gel TMG1 followed KorsmeyerPeppas kinetic model on their regression (r^2) values. The in-vitro antifungal study of gel showed effective results against *T. mentagrophyte* dermatophyte. Thus, it found to have potential management of nosocomial infections for better patient compliances.

REFERENCES

1. Martinez DA, Oliver BG, Gräser Y, Goldberg JM, Li W, Martinez-Rossi NM, et al. Comparative genome analysis of *Trichophytonrubrum* and related dermatophytes reveal candidate genes involved in infection. mBio; 2012; 43(5):e00259-12; doi:10.1128/mBio. 00259-12.
2. Wagner DK, Sohnle PG. Cutaneous Defenses against Dermatophytes and Yeasts. Clinical Microbiology Reviews; 1995; p. 317-335.
3. Divers TJ, Peek SF, Rehbun's Disease of Dairy Cattle, 2nd Edition, Elsevier Inc., Health Sciences Division, 2008.
4. Noguchi T, Igarashi Y, Shigemtsu A, taniguchi K. Antitrichophyton activity of naphthiomate. Antimicrobial Agents and Chemotherapy; 1962; 25:259-267.
5. Ryder NS, Frank I, Dupont MC. Ergosterol biosynthesis inhibition by the thiocarbamate antifungal agents Tolnaftate

and tolciclate. Antimicrobial Agents and chemotherapy; 1986; 29 (5):858-60.
6. Misra S. K, Pandey H, Patil S, Pramod WR, Pandey AC. Tolnaftate-Loaded Polyacrylate Electrospun Nanofibers for an Impressive Regimenon Dermatophytosis. Fibers; 2017; 5(4): 41; doi:10.3390/fib5040041.
7. Weinstein MJ, Oden EM, Moss E. Antifungal properties of Tolnaftate in vitro and in vivo. Antimicrobial Agents and chemotherapy; 1964; 10:595-601.
8. Yamaguchi H, Uchida K, Tanaka T, Yamaguchi T. Therapeutic efficacy of a topical Tolnaftate preparation in guinea pig model of tineapedis. The Japanese journal of antibiotics; 2001; 54(6):323-330.
9. Souza AC, Amaral AC. Antifungal therapy for systemic mycosis and the Nanobiotechnology Era: Improving Efficacy, Biodistribution and Toxicity. Frontiers in Microbiology; 2017; 8:336; doi:10.3389/fmicb.2017.00336
10. Howard YA, Galen WR. Remington: The Science and Practice of Pharmacy, 20th edition; Mack Publishing Company; 2000; p. 700
11. Kumari P, Misra SK and Pandey S. Formulation and Evaluation of Tolnaftate Microsponges Loaded Gels for Treatment of Dermatophytosis. European Journal of Pharmaceutical and Medical Research; 2017; 4(06):326-335.
12. Kiliçarslan M, Baykara T. The effect of drug & polymer ratio on the properties of the Verapamil hydrochloride loaded microspheres. International Journal of Pharmaceutics; 2003; 252(1-2): 99-109.
13. Chadawar V, Shaji J. Microsponge delivery system. Current Drug Delivery; 2007; 4(2):123-129.
14. Comoğlu T, Gönül N, Baykara T. Preparation and in vitro evaluation of modified release ketoprofen microsponges. II Farmaco; 2003; 58(2): 101-106.
15. Cooper and Gunns. Dispensing for pharmaceutical students. 11thed, pitman medical and scientific publishing company LTD; 1987. p. 214-222.
16. Farhan JA, Mohd AA, Zeenat IK, Roop KK, Mushir A. Development and in vitro evaluatiaon of an acid buffering bioadhesive vaginal gel for mixed vaginal infections. Acta Pharmaceutical; 2008; 58: 407-419.
17. El-Houssieny B, Hamouda HM. Formulation and evaluation of clotrimazole from pluronic F127 gels. Drug discovery and therapeutics; 2010; 4(1): 33-43.
18. Vikas J, Ranjit S. Development and characterization of Eudragit RS 100 loaded microsponges and its colonic delivery using natural polysaccharides. Acta Poloniae Pharmaceutica-drug research; 2010; 67(4): 407-415.
19. Bodmeier R, Chen H. Preparation and characterization of microspheres containing the anti-inflammatory agents, indomethacin, ibuprofen and ketoprofen. Journal of Controlled Release; 1989; 10(2):167-175.
20. Swati KV, Shalini R, Kanchan M, Ashwini C, Eknath P. Microsponge: Comprehensive Review of application. International Journal of Pharmacy and Biological Science; 2013; 3(1):214-226.
21. D'Emanuele A, Dinarvand R. Preparation, characterization and drug release from thermoresponsive microspheres. International Journal Pharmacaceutics; 1995; 118(2): 237-242.
22. Mohan KV, Veena NM, Manjula BP. Formulation and evaluation of microsponges for topical drug delivery of mupirocin. International Journal of PharmTech Research; 2013; 5(3): 1434-1440.
23. Gao Y, Fu-de C, Ying G, Lei Y, Yong SW, Li-na Z. Preparation of Roxithromycin polymeric microspheres by the emulsion solvent diffusion method for taste masking. International Journal of Pharmaceutics; 2006; 318(1-2):62-69.
24. Srilatha R, Aparna C, Srinivas P, Sadanandam M. Formulation, evaluation and characterization of glipizide nanoemulsion; Asian Journal of Pharmaceutical and Clinical Research; 2013; 6: 66-71.
25. Setty CM, Babubhai SR, Pathan IB. Development of valdecoxib topical gel effect of formulation variables on the release of valdecoxib. International Journal of Pharmacy and Pharmaceutical Sciences; 2010; 2(1):70-73.
26. Thakur NK, Bharti P, Mahant S, Rao R. Formulation and characterization of Benzoyl Peroxide Gellified Emulsions. Scientia Pharmaceutica; 2012; 80(4):1045-1060.
27. Joshi B, Singh G, Rana AC, Saini S. Development and Characterization of Clarithromycin Emulgel for topical delivery. International Journal of Drug Development & Research; 2012; 4(3): 310-323.
28. Harish NM, Prabhu P, Charyulu RN, Gulzar MA, Subrahmanyam EV. Formulation and evaluation of in situ gels containing clotrimazole for oral candidiasis. Indian Journal of Pharmaceutical Sciences; 2009; 71(4): 421-427.
29. Katkade M, Kalkotwar R, Jain N, Patil P, Gadakh R, Naikwade J. Ethyl cellulose based microsponge delivery system for anti-fungal vaginal gels of tioconazole. Journal of Drug Delivery & Therapeutics; 2013; 3(6): 14-20.
30. Sekhara B, Reddy CH, Tirupati SR, Rao RK, Duppada DR, Sarubudeen M. Formulation and evaluation of topically applied acyclovir loaded microsponges for the treatment of viral skin disorders. International Journal of Innovative Pharmaceutical Sciences and Research; 2014; 2(10): 2412-2424.
31. Shazly G, Nawroth T, Langguth P. Comparison of dialysis and dispersion methods for in vitro release determination of drugs from multilamellar Liposomes. Dissolution technologies; 2008; 15:79.
32. Chaman S, Sharma G, Anil S, Reshi K. Study of antimicrobial properties of *Catharanthus roseus* by agar well diffusion method. International Research Journal of Applied and Basic Sciences; 2013; 5: 65-68.

Cite this article as:

Prashant Pandey *et al*. Tolnaftate microsponges embedded biocompatible gels for controlled and effective antidermatophytic activity. Int. Res. J. Pharm. 2018;9(6):128-133 http://dx.doi.org/10.7897/2230-8407.096103

Source of support: Nil, Conflict of interest: None Declared