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Research Article

FORMULATION AND EVALUATION OF MICROSPONGES FOR TOPICAL DRUG DELIVERY OF MOMETASONE FUROATE

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ABSTRACT

Mometasone furoate is a medium potency, synthetic, non-fluorinated topical Corticosteroid, indicated for the relief of inflammatory and pruritic manifestations of corticosteroid responsive dermatoses including psoriasis. The percutaneous absorption increases risk associated with systemic absorption of topically applied formulation. Controlled release of the drug to the skin could reduce the side effects while reducing percutaneous absorption. Therefore, the aim of present study was to produce mometasone furoate entrapped microporous microparticles (microsponges) to control the release of the drug to the skin. Mometasone furoate microsponge was prepared using an emulsion solvent diffusion method. In order to optimize the microsponge formulation, factors affecting the physical properties of microsponges were determined. Compatibility of the drug with excipients was studied by FT-IR. Production yield, loading efficiency and surface morphology of microsponges were performed. It was shown that the drug: polymer ratio, stirring rate, volume of external and internal phase influenced the particle size and drug release behaviour of microsponges. The results showed that, generally an increase in the ratio of the drug: polymer resulted in a reduction in the release rate of mometasone furoate from microsponges.

Keywords: Microsponges, Mometasone furoate, Eudragit RS 100, Quasi-emulsion solvent diffusion.

INTRODUCTION

Microsponges are polymeric delivery systems composed of porous microspheres. They are tiny, sponge like spherical particles that consist of a myriad of interconnecting voids within a non-collapsible structure with a large porous surface. Moreover, they may enhance stability, reduce side effects and modify drug release favourably[1, 2].

Skin inflammatory diseases are very frequent though they are usually transitory and do not cause serious damage. However, some peculiar skin diseases are chronic and can decrease the quality of the patient's life. Some of these conditions include atopic dermatitis, eczema and psoriasis which affect around 2% of the world population[3]. Corticosteroids are the most widely used topical agents in the management of patients with psoriasis[4].

Mometasone furoate a medium potency, synthetic, non-fluorinated topical corticosteroid[5,6,7]. is indicated for the relief of inflammatory and pruritic manifestations of corticosteroid responsive dermatoses, including psoriasis. Mometasone furoate depresses formation, release and activity of endogenous mediators of inflammation, including prostaglandins, kinins, histamine[8]. The percutaneous absorption increases risk associated with systemic absorption of topically applied formulation.

Controlled release of mometasone furoate from delivery system to the skin could reduce the side effects while reducing percutaneous absorption. The present study was designed to formulate a delivery system based on microsponges that would reduce the side effects of the drug.

MATERIALS AND METHODS

Materials

MOF sample was gifted by Amwill health care, Eudragit RS100 was a gift from Evonic India Pvt.Ltd, Mumbai, India. Poly vinyl alcohol from Loba chemie, Bangalore. All the chemicals used for analysis were of analytical grades.

Preparation of Microsponges

The microsponges were prepared by quasi-emulsion solvent diffusion method[9, 10].

The internal phase consists of Eudragit RS100 dissolved in 20 ml of dichloromethane: ethanol (1:1) under sonication. This was followed by addition of MOF with stirring. The surfactant PVA (0.75%) was weighed accurately and dissolved in 90 ml of distilled water at 60˚C. The surfactant mixture was allowed to cool to room temperature. The internal phase containing MOF and Eudragit polymer was added drop wise with stirring at 1500 rpm. After 8h of stirring, microsponges were formed due to the removal of solvent from the system by evaporation. The microsponges were washed with water, filtered and dried at 40˚ C for 12h.

For the evaluation of the effect of drug: polymer ratio on the physical characteristics of microsponges, seven different ratios of the drug to Eudragit RS100 (1:1, 3:1, 5:1, 7:1, 9:1, 11:1 and 13:1) were employed.

Compatibility studies

FT-IR spectra of MOF, Eudragit RS100, Physical mixtures of MOF and Eudragit polymer were incorporated in KBR discs and evaluated with a Shimadzu model FT-IR Spectrometer for their compatibility.

Evaluation of drug loaded microsponges

Determination of Production yield and loading efficiency

The production yield of the microparticles was determined by calculating accurately the initial weight of raw materials and the last weight of microsponge obtained[11]. The loading efficiency (%) was calculated according to the following equation.

$$\text{Loading efficiency} = \frac{\text{Actual MOF content in microsponges}}{\text{Theoretical MOF content}}$$

Drug content

Microsponges equivalent to 100mg of MOF were dissolved and made up to the mark in 100ml volumetric flask with methanol, further 10ml was diluted to 100ml with methanol and final dilution were made using methanol to get a concentration within beer's range of 2-20µg/ml. the absorbance was measured spectrophotometrically at 248.5 nm using blank microsponges treated in the same manner as sample.

Morphology and particle size studies

The morphology and surface characterisation of the microsponge formulation were evaluated by SEM analysis using JSM 840A SEM analyser after the sample had been gold sputtered coated using 25nm gold film thickness[12].

In-vitro Dissolution studies

In-vitro dissolution studies were carried out using USPXXI dissolution assembly (basket type) in 900 ml of pH7.4 saline phosphate buffer solution at 37℃ 1and rotated at 50 rpm. Specified amount of aliquots were withdrawn at hourly intervals up to 8h. The samples were assayed at 248.5 nm[13].

RESULTS

Effect of Drug

Polymer ratio on the physical properties of Microsponges

Free flowing powder particles of microsponges were obtained by quasi-emulsion solvent diffusion method with Eudragit RS100. The method seems to be promising for the preparation of MOF microsponges. The encapsulation efficiency and production yield increased with increase in drug: polymer ratio. The mean particle size ranged from 459 to 254µm when the drug: polymer ratio was increased from 1:1 to 13:1. The results are shown in the table no 1.

Production yield, loading efficiency and particle size analysis

The production yield, loading efficiency and mean particle size of MOF microsponge formulation are given in table no.1 It was found that production yield and loading efficiency increased with increase in the drug: polymer ratio. But the mean particle size decreased.

Characterization of microsponges

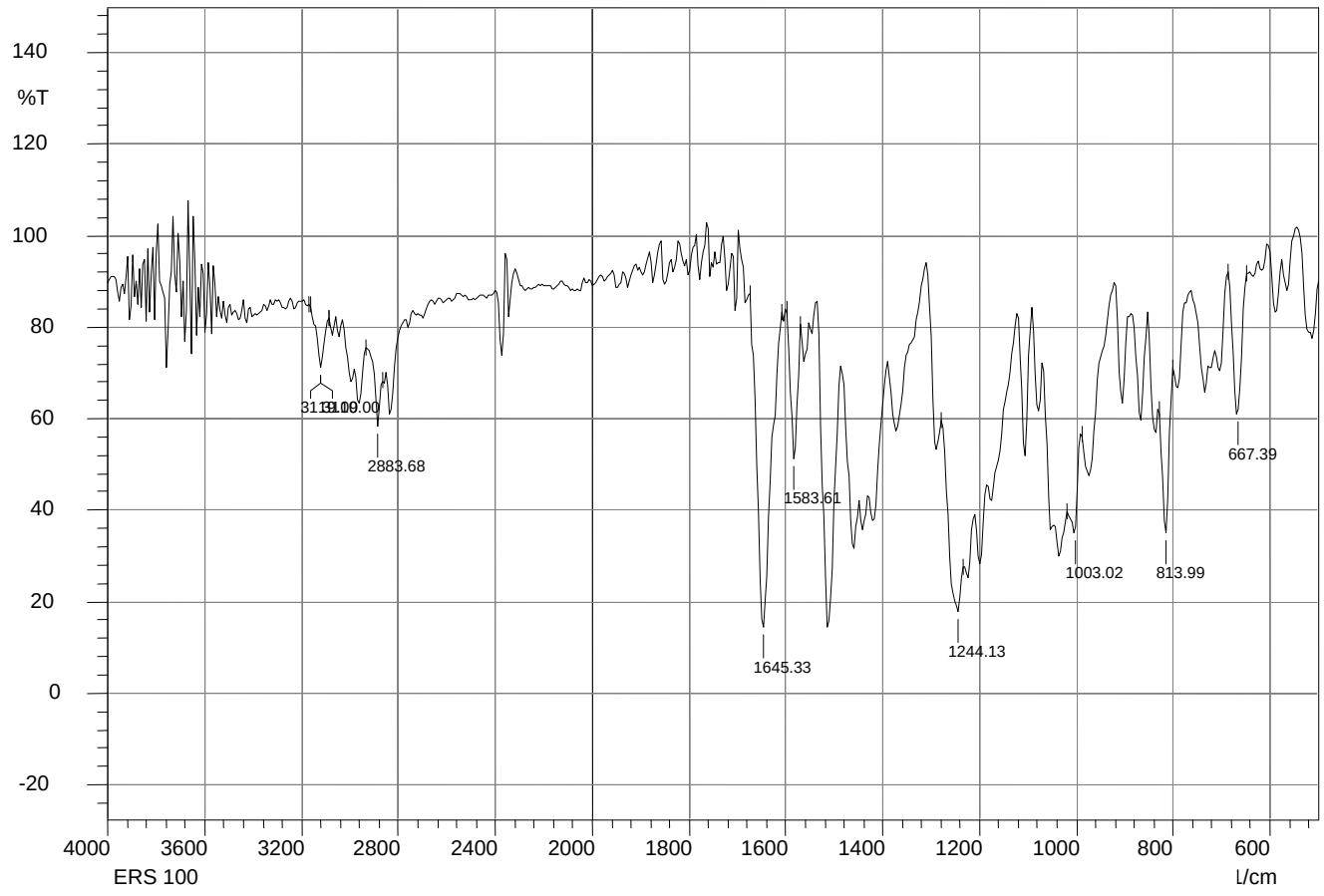
Analysis of FT-IR Spectra revealed that the peaks of pure drug and formulation were found to be identical, indicating that the drug remained in its original form without any modification when formulated as microsponge and also shows that there was no significant interaction between drug and polymer used. The spectra are shown in figure no 1.

In-vitro drug release

The release profiles obtained for the microsponge formulations are presented in figure. The profiles showed a biphasic release with an initial burst effect. In the first hour, about 29- 36% of the drug was released. Cumulative release from microsponge after 8h ranged from 78-95% and is shown in fig no 2.

Table 1: Effect of different Drug: polymer ratios on microsponge properties and the drug release from the formulations

Formulation code	Drug: polymer ratio	Production yield %	Loading efficiency %	Mean particle size	Drug content %	% CDR
MS1	1:1	37.51	38.03	459	43.94	95.47
MS2	3:1	58.26	44.22	414	51.06	92.34
MS3	5:1	68.71	54.03	387	61.99	86.85
MS4	7:1	76.41	70.93	352	77.19	87.55
MS5	9:1	78.41	78.04	339	83.37	85.43
MS6	11:1	83.33	86.13	301	88.59	83.09
MS7	13:1	89.28	84.73	254	91.21	78.42



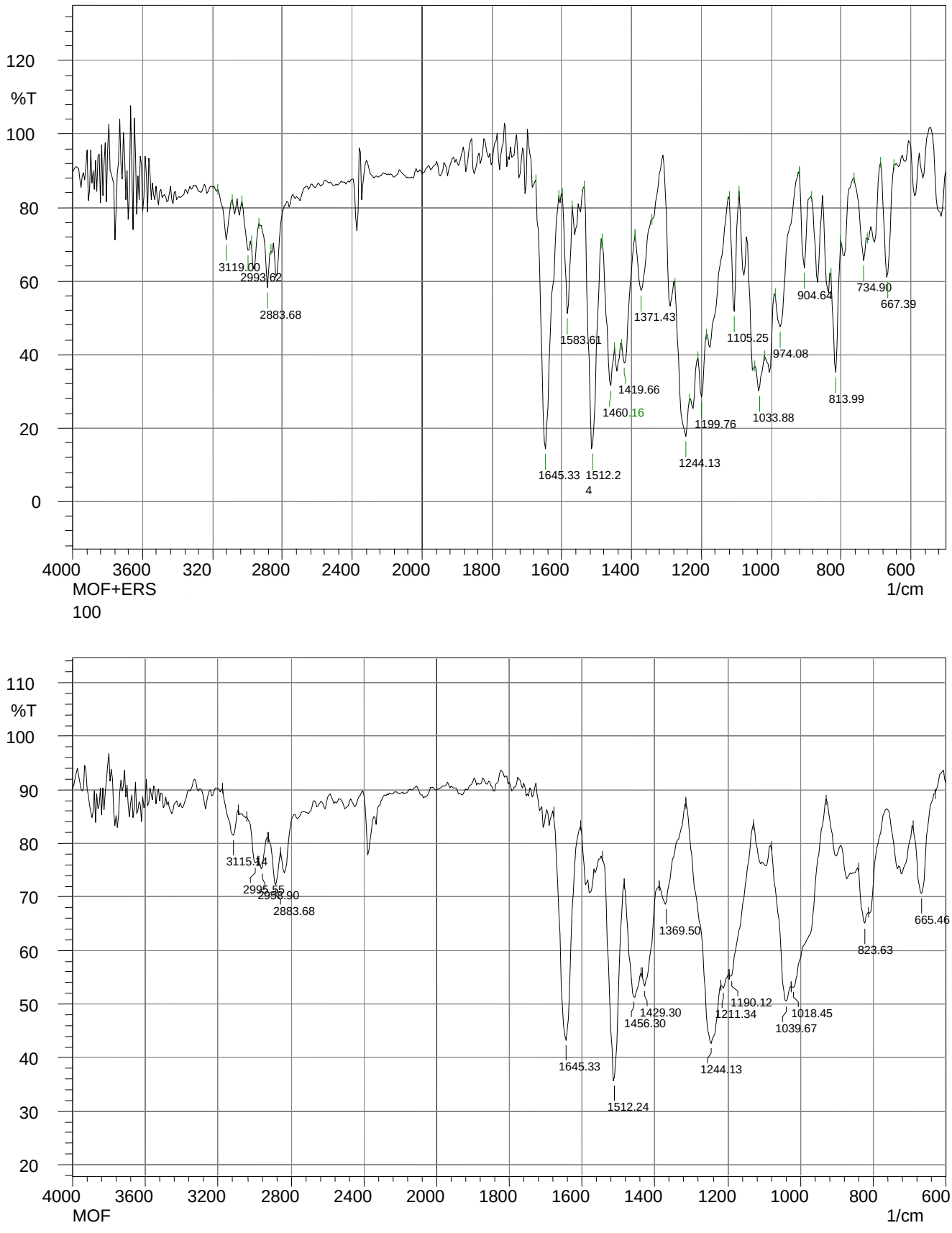
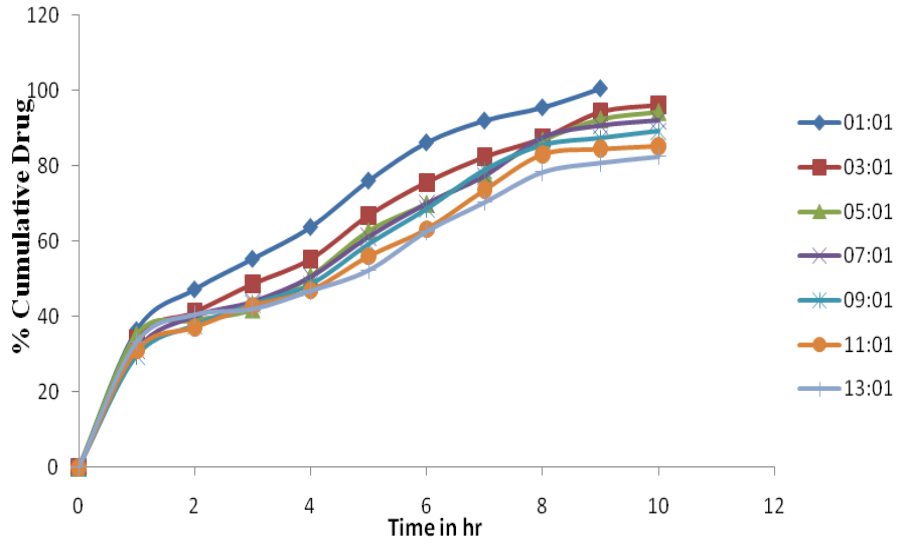
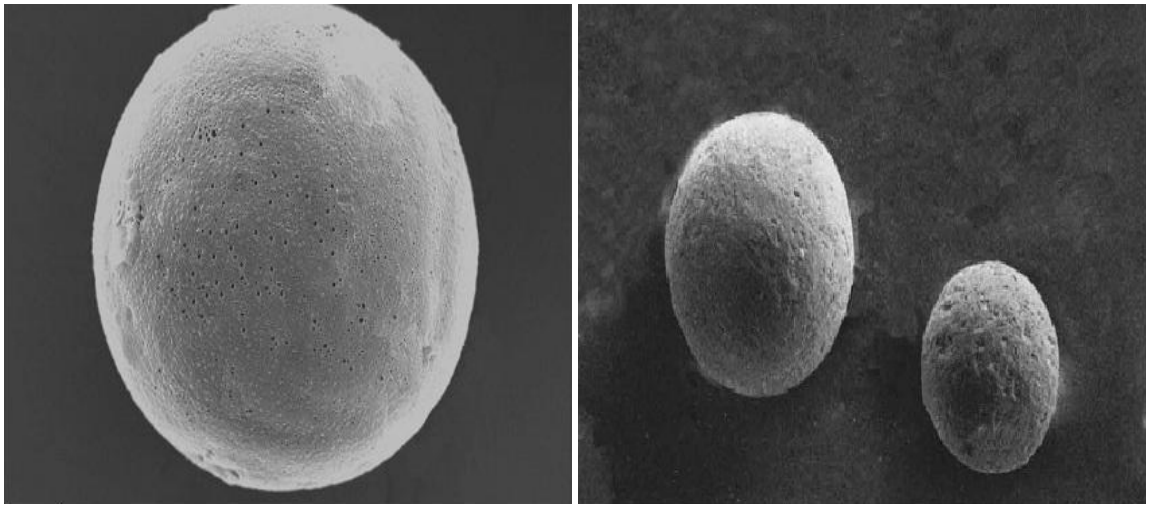
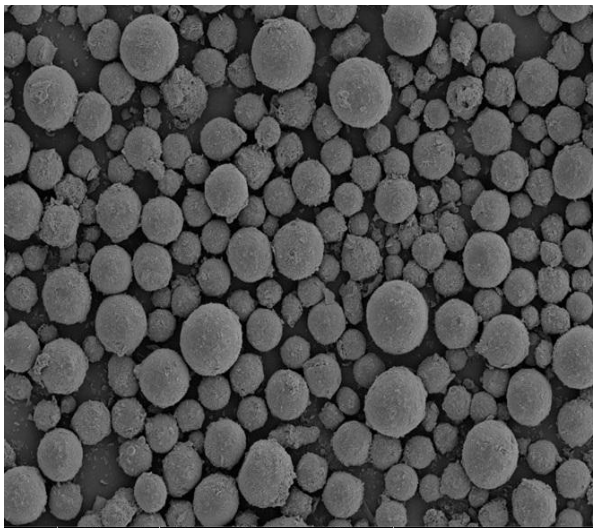


Fig. 2: %Cumulative drug release plot of MoF:ERS100 Microsponge formulation





A) **B)**



C)

Fig. 3: SEM Photo of MoF: ERS100 Microsponge formulations A) 5:1 B) 7:1 and C) 11:1

DISCUSSION

Quasi –emulsion solvent diffusion method seems to be promising for the preparation of MOF microsponges as it is a rapid, easy, reproducible method and has an advantage of avoiding solvent toxicity[14, 15]. In this method there is formation of quasi-emulsion droplets. The rapid diffusion of solvent in to the aqueous medium might reduce the solubility of polymer in the droplets, since the polymer is insoluble in water. The instant mixing of the ethanol and water at the interface of the droplets induce precipitation of the polymer thus forming a shell enclosing the solvent and dissolved drug. Counter diffusion of solvent and water through the shell promotes further crystallization of the drug in the droplets of the polymer from the interior/core. The finely dispersed droplets of the polymer solution of the drug were solidified in the aqueous phase via diffusion of solvent[16].

Furthermore, it was observed that as drug: polymer ratio increased, particle size decreased. This is probably due to the fact that at higher relative drug content, the amount of polymer available per microsponge to encapsulate the drug becomes less, thus reducing the thickness of the polymer wall and hence, smaller microsponges[17].

The drug release profile of the microsponge formulation showed that cumulative percent drug release was maximum in the 1st hour for all formulations. Burst release was observed which could be due to the surface adsorbed drug and porous nature of microsponges which provides a channel for the release of the drug[18] and formulation MS3 to MS6 showed a controlled drug release.

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REFRENCES

1. 1. Jain V, Singh R. Dicyclomine-loaded Eudragit-based Microsponge with Potential for Colonic Delivery: Preparation and Characterization. Tropical Journal of Pharmaceutical Research. 2010; 9 (1): 67-72.
2. Jelvehgari M, Siahi-Shadbad M, Azarmi S, Martin GP, Nokhodchi A. The microsponge delivery system of benzoyl peroxide: Preparation, characterization and release studies. International journal of pharmaceutics. 2006; 308(1-2):124-32.
3. Lebwohl M Psoriasis. Lancet. 2003; 361:1197-1204.
4. Greaves M W, Weinstein G D. Treatment of Psoriasis. NEJM.1995; 332:581.
5. Medansky R, Bressinck R, Cole G, Deeken J, Ellis C, Guin J, et al. Mometasone furoate ointment and cream 0.1 percent in treatment of psoriasis: comparison with ointment and cream formulations of fluocinolone acetonide 0.025 percent and triamcinolone acetonide 0.1 percent. Cutis; Cutaneous medicine for the practitioner. 1988; 42(5):480.
6. Koo J, Cuffie CA, Tanner DJ, Bressinck R, Cornell RC, DeVillez RL, et al. Mometasone furoate 0.1%--salicylic acid 5% ointment versus mometasone furoate 0.1% ointment in the treatment of moderate-to-severe psoriasis: a multicenter study. Clinical therapeutics. 1998; 20(2):283-291.
7. Crim C, Pierre LN, Daley-Yates PT. A review of the pharmacology and pharmacokinetics of inhaled fluticasone propionate and mometasone furoate. Clinical therapeutics. 2001; 23(9):1339-54.
8. Smith C, Kreutner W. In vitro glucocorticoid receptor binding and transcriptional activation by topically active glucocorticoids. Arzneimittel-Forschung. 1998; 48(9):956.
9. Orlu M, Cevher E, Araman A. Design and evaluation of colon specific drug delivery system containing flurbiprofen microsponges. International journal of pharmaceutics. 2006; 318(1-2):103-17.
10. Omu glu C T, G Onul N, Baykara T. The effect of the drug: polymer ratio on the properties of the verapamil Hcl loaded microspheres. International journal of pharmaceutics.2003; 252(1-2):99-109.
11. D'Emanuele A, Dinarvand R. Preparation, characterisation, and drug release from thermoresponsive microspheres. International journal of pharmaceutics. 1995; 118(2):237-42.
12. KIlIçarslan M, Baykara T. The effect of the drug/polymer ratio on the properties of the verapamil HCl loaded microspheres. International journal of pharmaceutics. 2003; 252(1-2):99-109.
13. Klose D, Siepmann F, Elkharraz K, Krenzlin S, Siepmann J. How porosity and size affect the drug release mechanisms from PLGA-based microparticles. International journal of pharmaceutics. 2006; 314(2):198-206.
14. Kawashima Y, Niwa T, Handa T, Takeuchi H, Iwamoto T, Itoh K. Preparation of controlled release microspheres of ibuprofen with acrylic polymers by a novel quasi emulsion solvent diffusion method. Journal of pharmaceutical sciences. 1989; 78(1):68-72.
15. Perumal D, Dangor C, Alcock R, Hurbans N, Moopanar K. Effect of formulation variables on in vitro drug release and micromeritic properties of modified release ibuprofen microspheres. Journal of microencapsulation. 1999; 16(4):475-487.
16. Ré M, Biscans B. Preparation of microspheres of ketoprofen with acrylic polymers by a quasi-emulsion solvent diffusion method. Powder Technology. 1999; 101(2):120-133.
17. Nokhodchi A, Jelvehgari M, Siahi MR, Mozafari MR. Factors affecting the morphology of benzoyl peroxide microsponges. Micron. 2007; 38(8):834-840.
18. Mandal T, Bostanian L, Graves R, Chapman S, Idodo T. Porous biodegradable microparticles for delivery of pentamidine. European Journal of Pharmaceutics and Biopharmaceutics. 2001; 52(1):91-96.