International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 15, Issue 1, 2023

Original Article

DEVELOPMENT AND EVALUATION OF MICROSPONGE GEL OF AN ANTIFUNGAL DRUG

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Received: 13 Oct 2022, Revised and Accepted: 20 Dec 2022

ABSTRACT

Objective: The objective of the present study was to compare the release effect of Luliconazole from different polymeric (Hydrophilic and Hydrophobic) microsponges prepared using varying concentrations. The best microsponge was selected and incorporated into different gel (Natural and synthetic) and drug release is determined and compared with marketed formulation.

Methods: Polymers such as EC, HPMC, Eudragit RSPO and PVA as emulsifier, and solvent DCM is used as solvent. Microsponge were prepared by using the quasi emulsion solvent diffusion technique. FTIR was studied to estimate the incompatibility. Microsponges were evaluated for SEM, particle size, drug content, and *In vitro* diffusion studies. Optimized microsponge incorporated gel was prepared by using different gel (flax seed gel and Aerosil gel) were evaluated for pH, spreadability, extrudability, drug content and *in vitro* diffusion studies.

Results: Theresults obtainedshowed no physical-chemical incompatibility between the drug and the polymers. EC, HPMC and EC combination was found to be a suitable polymer compared to Eudragit RSPO and other combination in preparation of microsponge. From the evaluation of microsponge, the optimized F1 formulations was incorporated into different gel (flax seeds, aerosil) and compared with marketed formulation in which MG-I (flax seed gel) was considered as good topical anti-fungal microsponge gel based on there physical parameters and drug release kinetics.

Conclusion: Microsponge and microsponge gel were successfully prepared for Luliconazole and their evaluation studies of each dosage form revealed that topically applied microsponge gel possess immense potential to control the release rate of medicament to improve the bioavailability as well as patient compliance.

Keywords: EC, HPMC, Eudragit RSPO, Gel topical drug delivery

DOI: https://dx.doi.org/10.22159/ijcpr.2023v15i1.2069 Journal homepage: https://innovareacademics.in/journals/index.php/ijcpr

INTRODUCTION

Microparticulate drug delivery system

Microparticles are small spherical entities with a diameter ranging from 1-1000μm size range in the form of free-flowing powders. They are developed from different components as inorganic, polymeric and minerals [1]. In addition, MP's can be exist in various structural design,for example, microgranules, micro pellets, microcapsules, microsponges, microemulsions, magnetic MP's and lipid vesicles as liposomes and niosomes [2].

Porous materials can be classified according to their pore sizes: microporous materials (less than 2 nm), mesoporous materials (2–50 nm), macro-porous materials (50–200 nm), and giga-porous materials (more than 200 nm). The diversities in pore sizes meet requirements in many practical applications and are intensively studied for their promising virtues [3].

Microsponge drug delivery system

The Microsponges technology was developed by Won in 1987 and the original patents were assigned to advanced polymer system. This company developed a large number of variations of the technique and applied to the cosmetic as well as over the counter (OTC) and prescription pharmaceutical product. At present, this technology has been licensed to Cardinal Health, for use in topical products [4, 5].

The microsponges Delivery system (MDDS) is a polymeric system consisting 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 through which active ingredient are released in a controlled manner [6]. The size of the micro sponge's ranges from 5-300 μm in diameter and a typical 25 μm sphere can have up to 250000 pores and an internal pore structure equivalent to 10 feet in length, providing a total pore volume of about 1 ml/g for extensive drug retention [7-13].

Fungal infection [14-18]

A fungal infection is also known as mycosis. Fungi are microorganisms characterized by a substance in their cell walls called chitin. Some fungi, like many types of mushrooms, are edible. Other types of fungi, like aspergillus, can be extremely dangerous and lead to life-threating diseases. Fungi reproduce by releasing spores that can be picked up by direct contact or even inhaled. The prevalence of fungal infections of the skin has increased rapidly, affecting around 40 million people in developing as well as under developed countries across the globe. Fungal infections can affect various parts of the body and thus, are, named accordingly. The etiological agents comprise of dermatophytes and yeast infections, involving Candidiasis and Pityriasis versicolor. In case of children, tinea capitis and tinea corporis are the most frequent type of fungal infections demonstrated; whereas in adults, tinea pedis and tinea versicolor are the prevalent form of infections. Candida species invade the deeper tissues and reach to the systemic circulations leading to life-threating systemic Candidiasis infection. Fungal infections (mycoses) can be both superficial and systemic. However, superficial mycosis of the skin is among the most commonly occurring human infectious disease observed in clinical practice. Superficial and systemic fungal infections have been treated well by both topical and systemic therapies.

The two classes of antifungal medications used most commonly to treat tinea cruris are the azoles and the Allylamines. Azoles inhibit the enzyme lanosterol 14-alpha-demethylase, an enzyme that converts lanosterol to ergosterol, which is an important component of the fungal cell wall. Membrane damage results in permeability problems and renders the fungus unable to reproduce. Allylamines

inhibit squalene epoxidase, which is an enzyme that convertssqualene to ergosterol, resulting in the accumulation of toxic levels of squalene in the cell and cell death [19, 20].

MATERIALS AND METHODS

Materials

Drug luliconazole and polymers are (ethylcellulose, HPMC k15, eudragit RSPO), solvent (dichloromethane), emulsifier (PVA), preservative(sodium benzoate), gelling agents (aerosil,flaxseeds gel). Luliconazole was obtained by glenmark bangalore private limited as gift samples. All the excipients were of laboratory grade. Double distilled water was used throughtout the study. The microsponge were prepared by the quasi-emulsion solvent diffusion method.

Methods

Microsponges containing luliconazole were prepared by Quasi emulsion solvent diffusion method using ethyl cellulose, Hydroxy propyl methyl cellulose, eudragit RSPO as polymer. Internal organic phase was prepared by dissolving polymers like ethyl cellulose, Hydroxy propyl methyl cellulose, eudragit RSPO and drug in dichloromethane. External phase was prepared by PVA and 100 ml water and dissolved completely by using magnetic stirrer. The organic phase was added dropwise to the continuous stirring aqueous phase to form the discrete droplets at stirring speed 570rpm for 1hr. The solution was filtered in vacuum filter using Whatmann filter paper and dried for 24 h at room temperature and determine production yield [21-22].

Preparation of microsponge gel

Preparation of gel [23-24]

Flax seeds gel: (Natural gelling agent)

- 20g of flax seeds is added into 200 ml of water, boil until the mucilage is formed for about 30 min.
- Dry the mucilage in hot air oven. Until the mucilage is completely dried for about 24 h at 60 °C
- Separate the dried mucilage and triturate to get powder form.
- Add 200 mg of flaxseed mucilage powder to 5 ml of water (3%) and add 0.14g of sodium benzoate as a preservative.

Aerosil gel: (Synthetic gelling agent)

- Gels were prepared by dispersing the 13g of polymer in the100 ml of water and stirred continuously at 300rpm for 2h

Preparation of microsponge gel

50 mg of optimized microsponge was added to prepared each 3 % flaxseeds gel and 13 % of Aerosil gel (natural and synthetic) respectively.

Table 1: List of instruments and manufacturing company

S. No.	Equipments	Manufacturer
1	Magnetic stirrer	Remi limited
2	Analytical Balance	Sartorius
3	Vacuum filter	Norge air filter 407
4	UV/Visible spectrophotometer	ELICO Limited
5	FTIR Spectrophotometer	Shimadzu-FTIR 410 Model
6	Hot air oven	Inlab equipments
7	Franz Diffusion cell	Fabricated
8	Dissolution apparatus	Labinbia Ds 8000

Table 2: Composition of luliconazole microsponge

S. No.	FR code	Drug (mg)	EC (mg)	Eudragit RSPO (mg)	HPMC (mg)	DCM (ml)	PVA (g)	DIS water (ml)
1	F1(1:1)	250	250	-	-	5	0.1	100
2	F2(1:2)	250	500	-	-	5	0.1	100
3	F3(1:3)	250	750	-	-	5	0.1	100
4	F4(1:1)	250	-	250	-	5	0.1	100
5	F5(1:2)	250	-	500	-	5	0.1	100
6	F6(1:3)	250	-	750	-	5	0.1	100
7	F7(1:1:1)	250	250	-	250	5	0.1	100
8	F8(1:1:2)	250	500	-	250	5	0.1	100
9	F9(1:1:3)	250	750	-	250	5	0.1	100
10	F10(1:1:1)	250	-	250	250	5	0.1	100
11	F11(1:1:2)	250	-	500	250	5	0.1	100
12	F12(1:1:3)	250	-	750	250	5	0.1	100
13	F13(1:1:1)	250	250	250	-	5	0.1	100

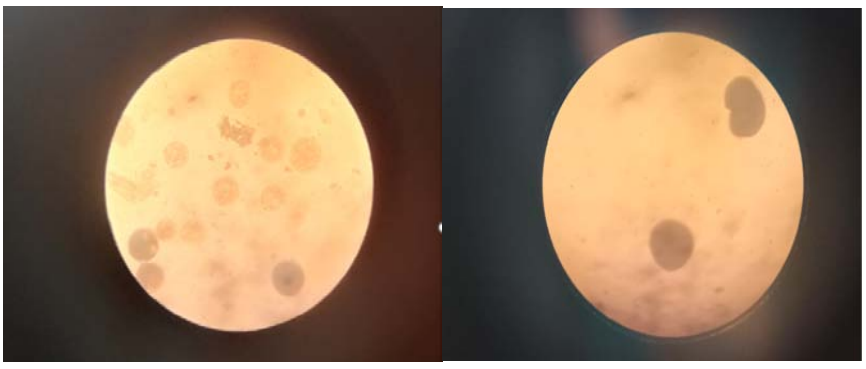

Fig. 1: Image of microsponge in light microscope

a) Flaxseeds microsponge gel **b) Aerosil microsponge gel**

Fig. 2: Image of gel loaded with microsponge

Evaluation of luliconazole drug

Preformulation studies: [25]

Melting Point Determination [26]

Solubility [27]

Drug Excipient Compatibility Studies by FTIR [28]

Determination of λ_{max} of luliconazole [29-31]

Preparation of stock solutions

Stock solution was prepared by dissolving 100 mg of Luliconazole in 20 ml methanol and make up the volume using 0.1N HCL in 100 ml volumetric flask as primary stock solution, further secondary stock solution was prepared by pipetting 10 ml from primary stock solution and diluting to 100 ml with 0.1N HCL. Further dilutions were made by transferring suitable aliquots (0.2–3 ml) into various 10 ml volumetric flasks and made up to volume with solvent. The diluted solutions prepared for calibration curve were checked for their absorbance using UV-VISIBLE spectrophotometer at 294.5 nm against buffer as blank. Standard graph was plotted between the concentration on X-axis and absorbance on Y-axis.

Evaluation of microsponges [32-34]

Particle size analysis

Determination of the average particle size of Luliconazole loaded microsponges was determined with an optical microscope using a calibrated eye piece and stage micrometer. A minute quantity of microsponges was spread on a clean glass slide. The average particle size was calculated by measuring 50 particles of each batch.

$$\text{Avg PS} = \sum xi/n$$

Where, Avg PS is the average diameter of particles (µm), n is number of particles per group, and $\sum xi$ sum of particles

Production yield [35]

The Production yield of the prepared luliconazole microsponge was determined by calculating accurately the initial weight of the raw materials and the last weight of the microsponge.

% yield= (Actual weight of the product/Total weight of excipients and drug) ×100

Scanning electron microscopy [37]

Scanning Electron Microscopy of optimized luliconazole microsponge formulation was carried to determine the surface morphology. The sample was mounted directly onto the SEM sample holder using double sided sticking tape and images were recorded at different magnifications at acceleration voltage of 10 kV using scanning electron microscope.

Uniform drug content [38]

The microsponges was determined spectrophotometrically (λmax = 294.5 nm). A sample of Luliconazole microsponges (50 mg) was dissolved dissolved in 5ML of methanol and made up to volume 50 ml using 0.1N HCL to form primary stock solution. secondary stock solution was prepared by pipetting 5 ml of primary stock solution and made up to the volume with 0.1N HCL to 50 ml volumetric flask. Further serial dilutions are made 4,6,8,10,12(ug/ml). The drug content was determined and expressed as actual drug content in microsponge. The drug content of the microsponges was calculated according to the following equation,

$$\text{Loading efficiency} = \frac{\text{Actual drug content in microsponges}}{\text{Theoretical drug content}} \times 100$$

***In vitro* dissolution studies [39]**

In vitro drug release study was carried out using USP type-II dissolution test apparatus. The dissolution medium 900 ml of 7.4 phosphate buffer was maintained at 37±1 ^{0}C and stirred at 50rpm. Aliquots of samples (1 ml) at an time interval upto 6 hour were withdrawn and filtered through Whatmann filter paper and made upto volume 10 ml using 7.4 phosphate buffer. The samples were analyzed for Luliconazole content by UV-Visible spectrophotometer at 294.5 nm.

Data obtained was subjected to obtain the drug release and graph is plotted for time v/s % CDR`.

Evaluation of microsponge gel [40]

pH

The pH of the systems was measured by direct immersion of the electrode of the pH meter (Henna pH meter) in the system at room temperature.

Extrudability [41]

A collapsible tube was filled with sample gel and then pressed firmly at the crimped end. When the cap was removed, gel extruded until pressure dissipated, weight im grams required to extrude 0.5 cm ribbon of gel in 10 second was determined.

Spreadability [42]

the spreadability of the prepared Luliconazole microsponge gel was measured by spreading of 0.5g of gel on a circle of 2 cm diameter pre-marked on a glass plate and then second glass plate was employed. Half kilogram of weight was permitted to rest on the upper glass plate for 5 min. The diameter of the circle after spreading of the gel was determined.

***In vitro* drug release [43-45]**

The study was performed by modified Franz diffusion cell using dialysis membrane. Before carrying out the study, membrane was kept in buffer pH 7.4 for 6 hr and it was mounted carefully between the donor and receptor chamber. 500 mg of microsponge gel was weighed and homogencity spread on the dialysis membrane. 50 ml of phosphate buffer (pH 7.4) was placed in receptor medium as a dissolution medium both donor and receptor compartment were kept in contact with each other and whole assembly was maintained at constant temperature of 32±0.5˚ C, magnetic bead was used to

stirred the solution of receptor chamber. 1 ml of sample withdrawn after specific time intervals and equal amount was replaced with fresh dissolution media. Sample absorption was calculated spectrophotometrically at 294.5 nm and % cumulative drug permeation was calculated.

Uniform drug content of microsponge gel [46-48]

The microsponges gel was determined spectrophotometrically (λmax = 294.5 nm). A sample of Luliconazole microsponge gel (100 mg) was dissolved dissolved in 5ML of methanol and made upto volume 50 ml using 0.1N HCL to form primary stock solution. secondary stock solution was prepared by pipetting 5 ml of primary stock solution and made upto the volume with 0.1N HCL to 50 ml volumetric flask. Further serial dilutions are made 8,12,16,20,24 (ug/ml). The drug content was determined and expressed as actual drug content in microsponge. The drug content of the microsponges was calculated according to the following equation,

$$\text{ASSAY} = \frac{\text{absorbance}}{\text{Slope}} \text{X dilution factor}$$

Kinetics of drug release [49-53]

Investigation for the drug release was done by studying the release data with zero order, first order kinetics and Higuchi equation. The release mechanism was understood by fitting the data to Korsmeyer Peppas model.

RESULTS AND DICUSSION

Preformulation studies

Preformulation studies of Luliconazole was carried on the basis of following parameters

Organoleptic properties of drug

Luliconazole is a pale color; it is odorless, and appeared as crystalline powder

Melting point of drug

The melting point range of the Luliconazole was found to be 151 °C. The normal range of the melting point of Luliconazole is 150-152 °C, Melting point indicates the purity of drug.

Solubility of drug

Luliconazole was freely soluble in Dichloromethane, ethanol and methanol, it insoluble in water that shows it is lipophilic in nature.

Determination of λ_{max} of luliconazole

The λ_{max} of the Luliconazole was found to be 294.5

Calibration curve of luliconazole

For the preparation of calibration curve, samples was prepared from stock solution (4, 6, 8, 10, 12,18,20 µg/ml). The absorbance of sample was taken at 294.5 nm. The calibration curve of luliconazole is presented in fig. 3, and data are presented in table 3.

Compatibility studies

The spectrum obtained from FTIR spectroscopy studies at wavelength from 4000 cm^{-1} to 400 cm^{-1} as shown in fig. 4,5,6,7,8 from the table 5, it was observed that characteristic peaks in the region was found to be observed in combination of drugs and polymers which were identical to that of pure drug. Thereby confirming that there are no interactions between the drug and excipients.

Table 3: Analytical data for calibration curve of Luliconazole

S. No.	Conc in mg/ml	Absorbance
1	0	0
2	4	0.3021
3	8	0.5891
4	10	0.6961
5	12	0.8164
6	18	1.1263
7	20	1.2454

The graph plotted between concentration and absorbance was found to be linear and straight line

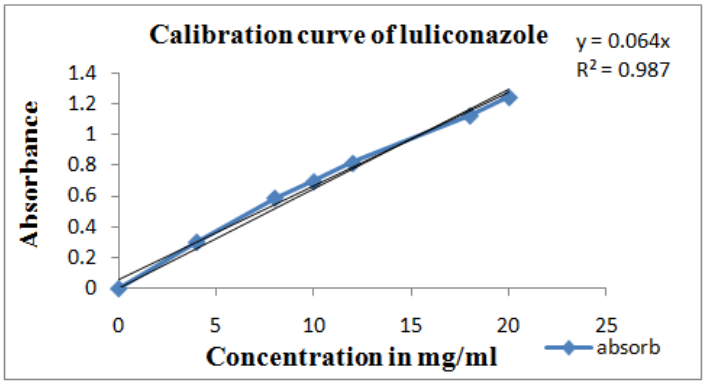

Fig. 3: Calibration curve of luliconazole

Table 4: Statistical data for calibration curve

S. No.	Parameters	Values
1	λmax	294.5
2	Linearity range µg/ml	0.1-100µg/ml
3	Slope	0.0648
4	R^2	0.9966

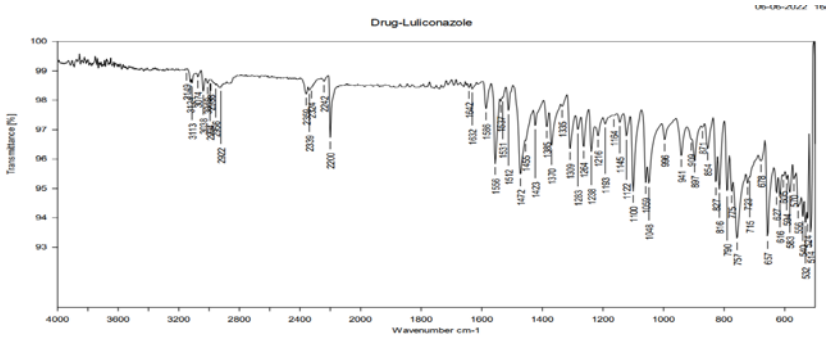

Fig. 4: FTIR spectra of luliconazole

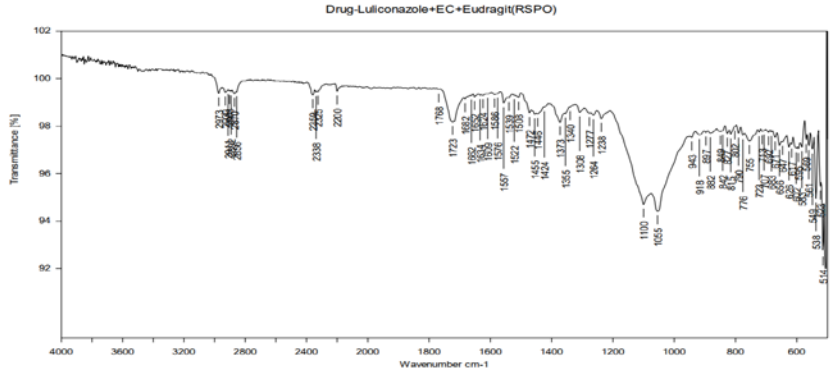

Fig. 5: FTIR spectra of luliconazole+EC+Eudragit RSPO

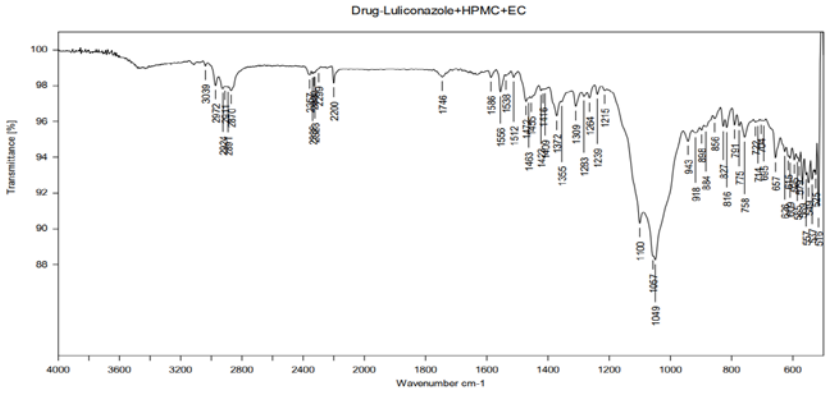

Fig. 6: FTIR spectra of luliconazole+HPMC+EC

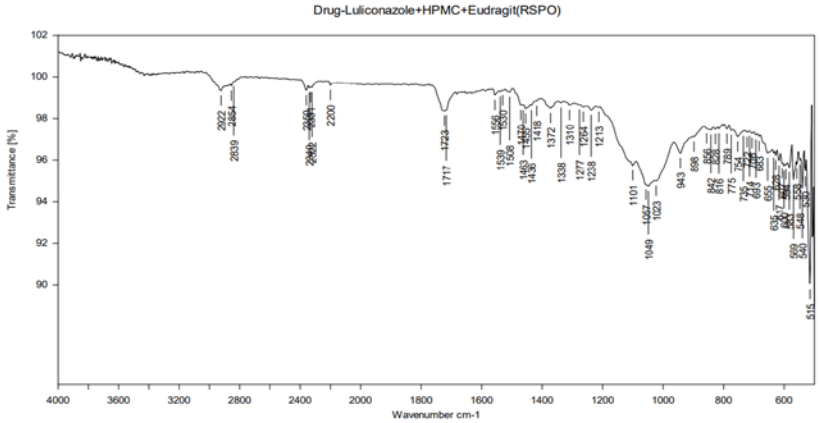

Fig. 7: FTIR spectra of luliconazole+HPMC+Eudragit RSPO

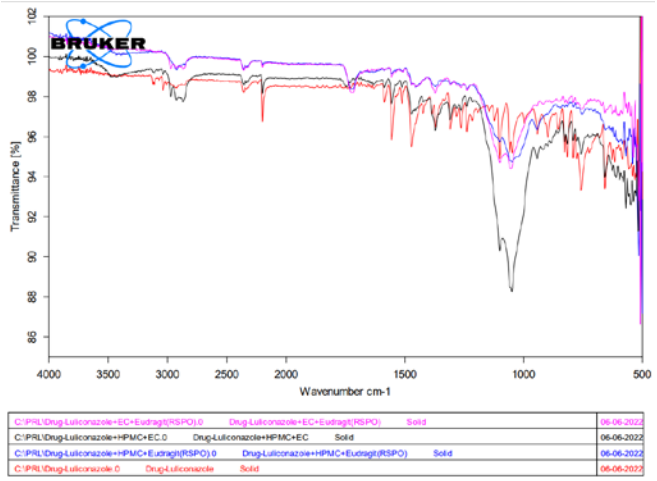

Fig. 8: Comparison FTIR spectra of all ingredients

Table 5: Interpretation of IR spectra

Functional group	Observed frequency cm^{-1}				Interactions
	Luliconazole	Luliconazole+EC+RSPO	Luliconazole+HPMC+EC	Luliconazole+HPMC+eudragit RSPO	
CN Stretching	2200	2200	2200	2200	No interaction
CH Bending	1100	1100	1100	1101	No interaction
C-Cl Stretching	775	776	775	775	No interaction
CH Bending	816	815	816	816	No Interaction

Characterization and evaluation of microsponge

The particle size of the prepared Luliconazole microsponges was determined using microscopic method and the particle size was in the range of 50 to 300 mm. Based on the polymer ratio the particle size was less in case of 1:1 and 1:1:1 ratio and was bigger in case of 1:3, 1:1:3 ratio. Considering this we can say that increase in polymer ratio increases the particle size.

The microscopic image of the prepared microsponge showed that they are spherical and discrete in shape. Table 6: Shows the particle size and fig. 9 shows the graph of particle size distribution of microsponge.

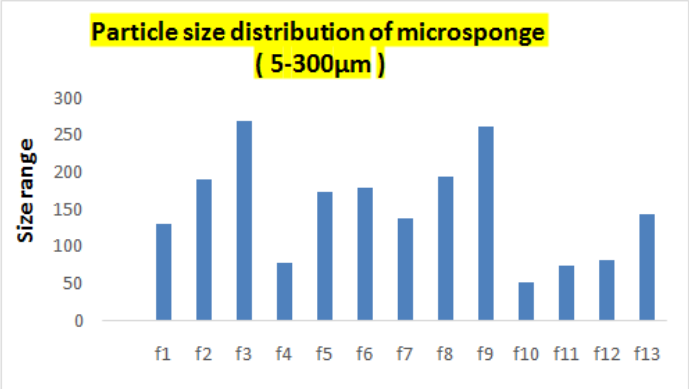

Fig. 9: Graph showing particle size distribution of microsponge

Table 6: Shows the particle size and fig. 9 shows the graph of particle size distribution of microsponge

S. No.	FR	Average particle size (µm)
1	F1	129
2	F2	189
3	F3	269
4	F4	76.1
5	F5	171.8
6	F6	178
7	F7	136
8	F8	193
9	F9	261
10	F10	51.5
11	F11	73
12	F12	80.5
13	F13	143

Percentage yield

The percentage yields of Microsponge prepared by Quasi emulsion solvent diffusion method were found to be in between 25 to 90% as shown in table 7. The percentage yield was very less in 1:1 HPMC k15 and Eudragit RSPO (F10) formulation, because HPMC is water soluble polymer most of the polymer is dissolved in water. The yield was 90% in drug and Eudragit RSPO (f4) formulation due insoluble in water, The graph of percentage yield is as shown in the fig. 10.

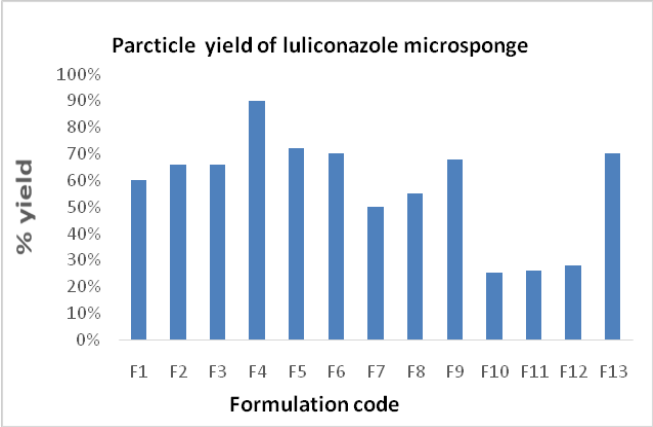

Fig. 10: Graph showing particle yield of microsponge

Table 7: Percentage yield of luliconazole microsponge

S. No.	FC	% Yield
1	F1	60%
2	F2	66%
3	F3	66%
4	F4	90%
5	F5	72%
6	F6	70%
7	F7	50%
8	F8	55%
9	F9	68%
10	F10	25%
11	F11	26%
12	F12	28%
13	F13	70%

Sem analysis of microsponge

Scanning Electron Microscopy of optimized luliconazole microsponge formulation was carried to determine the surface morphology. The sample was mounted directly onto the SEM sample holder using double sided sticking tape and images were recorded at 11.8 mm X 100SE magnifications at acceleration voltage of 10 kV using scanning electron microscope. Fig. 11 shows the SEM image of microsponge F1 formulation. The porous image of microsponge can be seen in fig. 12 which is recorded at 11.5 X 50.0 SE. So, by this we can say that all microsponge pores are lies in the given range.

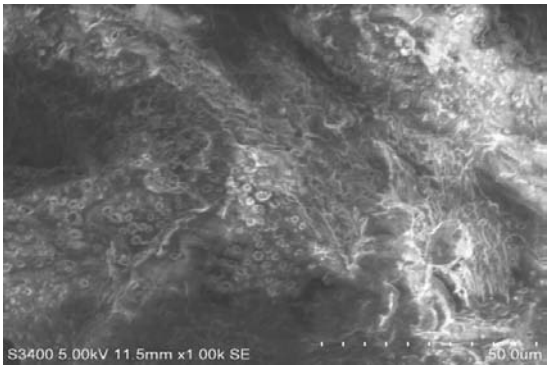

Fig. 11: SEM image of F1 microsponge

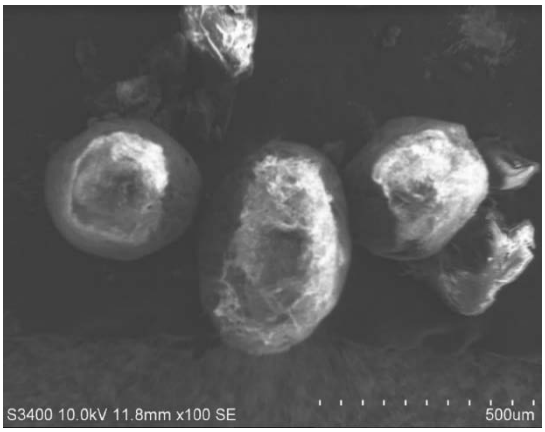

Fig. 12: SEM image of porous structure of F1 microsponge

Drug content

The percentage drug content of all the 13 formulations was done and found to be between 65.61%-97.26 % as shown in table 8 and fig. 13. The F1 formulation showed maximum drug content of all the formulation. Because the EC is water insoluble polymer and polymer and drug ratio is (1:1), increase in polymer ratio and water-soluble polymers drug content decrease.

Table 8: Drug content in luliconazole microsponge

S. No.	FC	% Drug content
1	F1	**97.26**
2	F2	94.81
3	F3	88.64
4	F4	70.34
5	F5	79.83
6	F6	65.61
7	F7	95.83
8	F8	87.99
9	F9	80.55
10	F10	91.76
11	F11	90.66
12	F12	87.49
13	F13	74.93

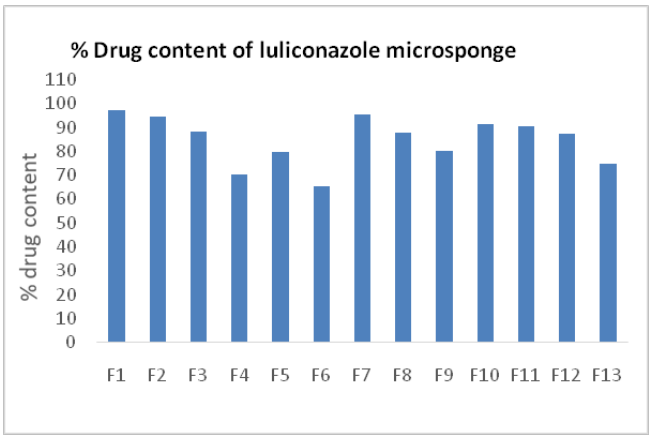

Fig. 13: Graph showing % drug content of microsponge

***In vitro* dissolution studies**

All the formulations prepared Microsponge of Luliconazole were subjected to *in vitro* release studies. The release data obtained for formulations F1–F6 were tabulated in table 9 and formulation F7–F13 in table 9 and 10 and fig. 14 and 15 shows the plot of cumulative % drug released as a function of time for different formulations respectively. Cumulative % drug release at 6th h was high in formulation (F1) 72.45% which and low in (F12) 56.87% respectively, depending on type of polymer and concentration of polymer.

Table 9: Cumulative % drug release of microsponge F1–F6

Time in min	Cumulative % drug release					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
15	1.140867	0.659946	0.768975	0.296678	0.557567	0.593477
30	3.851694	4.767006	2.307778	1.147485	2.178614	1.738699
45	7.278569	6.708137	4.334782	19.7406	3.975699	3.754211
60	12.70576	16.39478	10.33446	22.31394	9.050481	7.955106
120	14.90176	19.55137	17.9572	25.99771	14.53164	14.68294
180	20.56556	28.16699	27.80115	30.4569	21.72642	24.32202
240	37.41613	38.81598	40.37096	40.20189	31.3511	38.40167
300	54.85581	52.95248	53.81782	52.25197	46.2659	54.19257
360	**72.45741**	68.99646	68.64488	68.36997	63.41005	68.30529

Table 10: Cumulative % drug release of microsponge F7-F13

Time in min	Cumulative % drug release						
	F7	**F8**	**F9**	**F10**	**F11**	**F12**	**F13**
0	0	0	0	0	0	0	0
15	1.436877	0.933282	0.84635	0.485211	0.79804	0.492948	1.076703
30	3.383335	2.326332	2.315447	1.228728	1.965293	1.638407	3.231304
45	6.884939	4.132203	4.131623	2.625072	3.778411	3.4212	8.45133
60	12.88682	8.265372	7.901599	4.917572	7.757457	6.303176	12.50762
120	21.92875	13.87423	14.66389	11.77663	14.79495	9.951621	22.28607
180	32.14182	24.34553	22.47002	21.9033	24.84825	17.15016	30.90584
240	44.68843	36.75828	32.89293	36.57488	36.55481	28.20484	41.0945
300	59.03412	49.73841	48.5264	51.92989	50.57637	42.24537	54.97008
360	71.90368	67.98459	66.5435	68.9698	66.28626	56.8739	71.03298

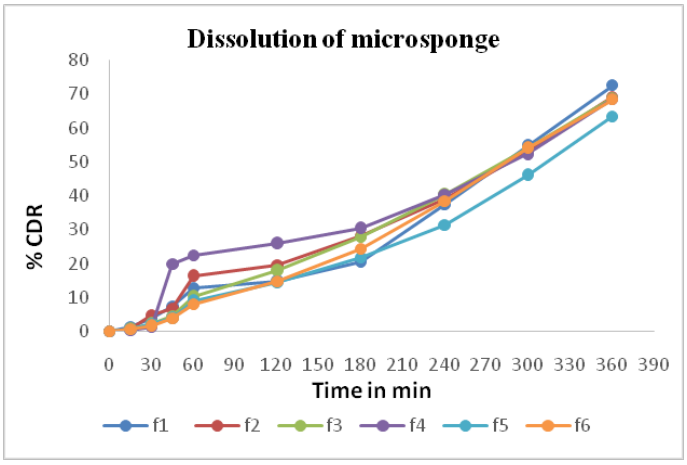

Fig. 14: Graph showing % drug release of microsponge F1-F6

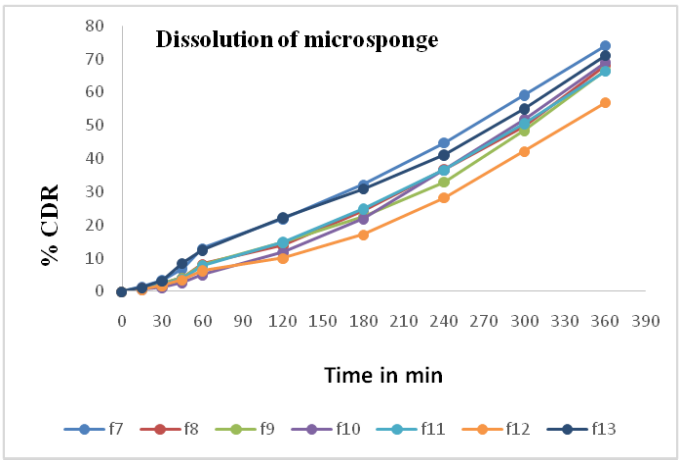

Fig. 15: Graph showing % drug release of microsponge F7-F13

Evaluation of microsponge topical gel

The evaluation of Microsponge gel was performed for gels prepared from F1 formulation of microsponge with different gelling agent (Natural and synthetic). Flax seed gel and aerosol gel.

pH

The pH of microsponge gel was performed for optimized formulation was found to be pH 4.1 to 6.3 for Luliconazole. The pH of microsponge gel was found to be in the range of 5.2-6.2. From table 11

Extrudability

The extrudability of luliconazole microsponge gel was found to be good. The prepared gel from natural and synthetic gelling agent shows better good extrudability

Spreadability

The spreadability of Luliconazole microsponge gel was found to be 5.1. The microsponge gel has good spreadability and having good appearance. Other was brown transparent in appearance. Spreadability range 1-8.5. refer spreadability table 11

Drug content

The percentage drug content of MGI and MGII formulations was done and found to be 97.6–87.8 and marketed formulation of luliconazole gel found to be 99.8 as shown in table 11. The MGI formulation showed maximum drug content of the microsponge gel formulation.

***In vitro* drug release**

In vitro drug release for Luliconazole microsponge gel was performed using modified Franz diffusion cell. From table 12 and fig. 16 the drug release for Microsponge gel of shows 65-63 % at 6 h respectively. Formulated Microsponge gel also shows better penetration and higher drug release, in this highest drug release Flaxseed gelling was having good consistency, appearance, transparency.

Table 11: pH, extrudability, spreadabilityand drug content of microsponge gel and gel

Gel code	pH	Extrudability (g/cm²)	Spreadability (cm)	% Drug content
MGI	6.0	*	5.0	97.6
MGII	6.1	*	5.5	87.8
MF	6.3	***	6.0	99.8

*Satisfactory, **Good, ***Excellent

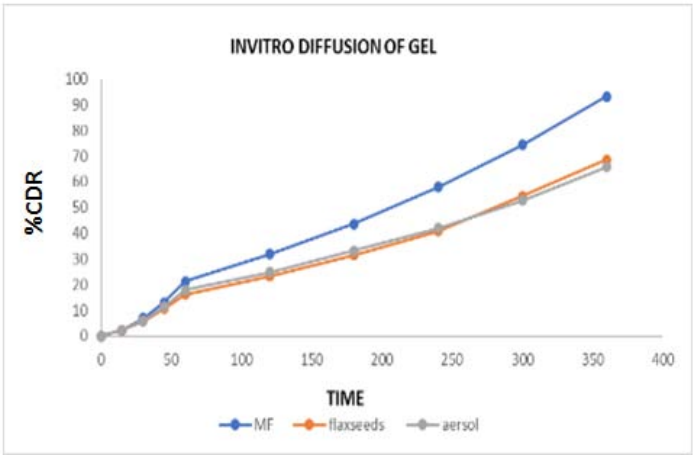

Fig. 16: Graph showing drug release of microsponge gel and marketed gel of luliconazole

Table 12: Comparision study of *in vitro* drug release of microsponge gel and marketed gel of luliconazole

Time in min	% Drug release		
	MF	Flaxseeds MGI	Aersol MGII
0	0	0	0
15	2.377011	2.322404	2.324926
30	7.018643	5.811229	6.09763
45	13.1893	10.71424	11.38179
60	21.27494	16.2192	17.91613
120	32.01038	23.37631	24.82759
180	43.70355	31.6192	33.15241
240	57.97512	40.94234	42.03828
300	74.46596	54.37981	52.8411
360	93.28595	68.64628	65.80336

Kinetics of drug release

The *in vitro* drug release data of all formulations were analyzed for determining kinetics of drug release is shown in table 13 and fig. 17. The obtained data were fitted to zero order kinetics, first order kinetics and Higuchi model, korsmeyer peppas. The highest correlation coefficient (r^2) obtained from these method gives an idea about model best fitted to the release data. From the results of kinetic studies, the examination of correlation coefficient r^2indicated that the drug release followed zero order kinetics. It was found that the value of r^2 for zero order is 0.9894 and 0.9859 respectively for MGI and MGII, it was understood to be following zero order release pattern. It was found that the optimized formulation MGI and MGII follows a zero-order kinetics as it has the highest R^2 value and it was further concluded by the n exponent value of karsmeyer-peppas model which shows the zero-order drug release mechanism with time independent and case II transport mechanism.

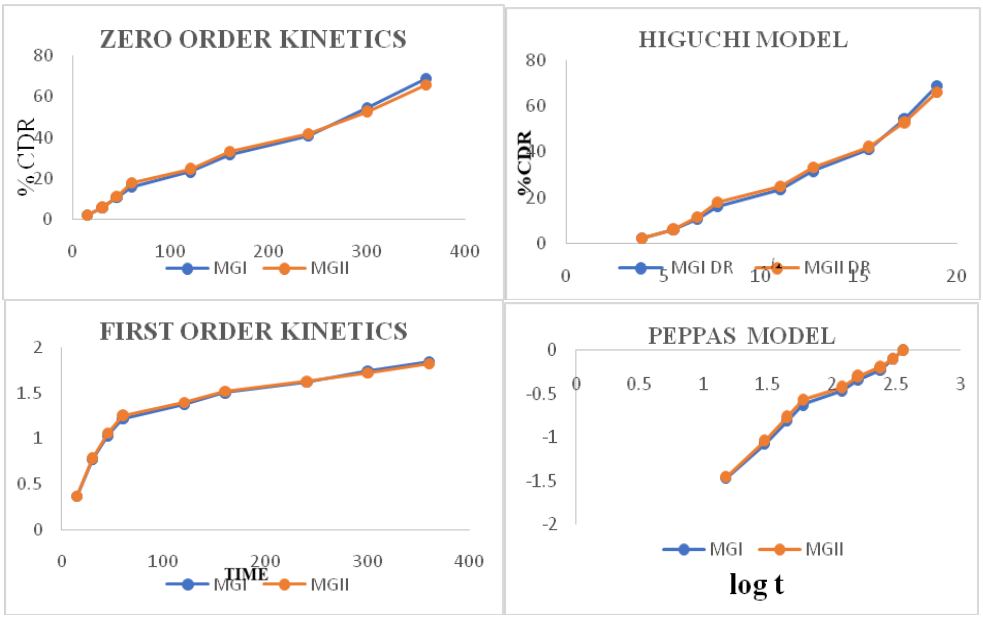

Fig. 17: Graph showing Zero order, Higuchi, first order and peppas model kinetics of microsponge gels MGI and MGII

Table 13: Kinetic study of microsponge gel and marketed gel

Formulation code	Zero order	First order	Higuchi model	Peppas model	
				R value	n-value
MGI	0.9894	0.792	0.9666	0.9774	0.9901
MGII	0.9859	0.7597	0.9798	0.967	0.9724

CONCLUSION

The Microsponge based delivery system has been developed using quasi emulsion solvent diffusion method to provide a sustained release medication for topical delivery of luliconazole. The drug content and the size of the prepared microsponges were affected by the drug: polymer ratio. Microsponge formulation MS I which showed good results incorporated in natural gel (flaxseeds)andsynthetic (Aerosil) and formulated as gels MG I-II respectively. Among the two gels, MG I showed better *in vitro* drug release. A fickian diffusion which is controlled by the porosity of the microsponges is the mechanism of the drug release from the flax seed gel loaded with the selected microsponge formulation. As the gel has sustained-release characteristics the side effects have been minimized.

ACKNOWLEDGEMENT

The author gratefully acknowledged the East point college of Pharmacy for support and providing good laboratory with materials and equipment's.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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