Formulation and Evaluation of Microsponge Gel for Topical Delivery of Antifungal Drug

Jitendra Shinde [1*], Rakesh Patel [2], Shweta Shriwas [3]

[1] *Ph.D. Scholar, School of Pharmacy, Dr. A. P. J. Abdul Kalam University, Indore, Madhya Pradesh, India.* *jitushinde29@gmail.com*

[2] *Professor, School of Pharmacy, Dr. A. P. J. Abdul Kalam University, Indore, Madhya Pradesh, India.*

[3] *Associate Professor, School of Pharmacy, Dr. A. P. J. Abdul Kalam University, Madhya Pradesh, India.*

Abstract: The quasi emulsion solvent diffusion technique was used to create the clotrimazole microsponges, which were eventually recognized as an efficient carrier for the topical delivery of the medicine. The characteristics of the created system were significantly affected by the drug:polymer ratio. It was discovered that microsponges made for prolonged release formulation were effective, and clotrimazole microsponges with gel produced results that were equivalent. Microsponge gel compositions that were prepared beforehand showed regulated medication release. It has been shown that microsponges can transport medications for topical antifungal therapy successfully. Given how well the formulations kept the medication on the skin, it appears that microsponge gel is a more effective drug delivery mechanism than ordinary gel.

Keywords: Microsponge gel, clotrimazole, topical, antifungal.

1. INTRODUCTION

The topical drug delivery system has been used predominantly in the treatment of localized skin diseases and other injuries. Local treatment requires only that, the drug permeate the outer layers of the skin to treat the specific area with the hope that this occurs with little or no systemic accumulation. The industries produce a chemical entity-specific for dermal or transdermal are ideally suited to retain on to the skin and should not uptake into and through the skin. This means that considerable effort has to be expended on the appropriate design of a formulation or a device to deliver enough of the medicine with a controlled, extended and target manner at its site of action [1-3]. Drug Delivery Systems that control the release rate and target to a specific site of the body has an immense impact on the health care system [4]. The invention of microsponges has become a significant step toward overcoming these problems. These tiny sponges give the action at a specific target site and stick on the surface and begin to release the drug in a controlled and predictable manner for drugs with poor solubility [5]. The development of novel microsponges based drug delivery systems, to modify and control the release behavior of the drugs. By incorporation into a carrier system, it is possible to alter the therapeutic index and duration of the activity of drugs [6]. Microsponges are polymeric delivery systems composed of porous microspheres [7]. Moreover, they may enhance stability, reduce side effects and modify drug release favorably [8]. Depending upon their particle size, these porous systems can be divided into microporous microbeads (particle below 50μm) and microporous macro beads (particle range of 100-200 μm) [9]. Microsponges release their active ingredients upon application, producing a highly concentrated layer of active ingredient that is rapidly absorbed [10]. Microsponges can also entrap active ingredients with certain special characteristics. It is widely regarded as a leading technology for addressing skin conditions such as acne, hyperpigmentation, keratosis, aging and photodamage [11]. The existing formulations in the market are having huge side effects and adverse effects in the treatment. Conventional formulations of topical drugs are intended to apply to the outer layers of the skin. Potentially, the Microsponge system can reduce significantly the irritation of effective drugs without reducing their

efficacy [12]. Topical antifungal preparations sometimes cause skin irritation, stinging, burning, edema, blistering pruritis, and sensitization. Theses side effects could occur due to the burst release of the drug on application. Modification of release pattern in such a fashion to control the delivery rate of the active ingredient to the predetermined site in the human body is a challenging area of research. Clotrimazole is a broad spectrum antifungal which is used as a drug of choice in fungal infections. Clotrimazole is practically insoluble in water, has a half-life of only 2 h, it is poorly absorbed from GIT and it is metabolized into inactive compounds by hepatic metabolism. Hence, it is necessary to manipulate the drug delivery system of Clotrimazole for topical administration. The marketed formulation is cream, lotion, trouche, lozenges and solution those are not sustained release, and therefore it is suitable to design in sustained release formulation [13-16]. Releasing of active ingredient from conventional topical formulation over an extended and controlled predetermined rate is quite difficult. Application of topical drugs suffers many problems such as ointments, cream which is aesthetically unappealing, greasiness, stickiness, etc. that often results in lack of patient compliance. Hence, Clotrimazole is used in microsponge's preparation to deliver the drug in a controlled and sustained manner to improve to the therapeutic system. The present study is based on the hypothesis that incorporation of Clotrimazole into microsponge's will improve amount and time of drug residence on to the skin which increases therapeutic efficacy of the drug and reduces toxicity occur due to burst release. Microsponge can provide sustained and controlled release of the entrapped drug. Microsponge system allows for a high accumulation of the drug in the skin, with relatively low permeation flux as compared to conventional dosage forms [17-18].

2. MATERIALS AND METHODS

Materials:

Clotrimazole obtained from Encube Pharmaceutical Pvt Ltd. Verna, Goa. All the chemicals used were of analytical grades.

Formulation of clotrimazole loaded microsponges:

Clotrimazole Microsponge was prepared by quasi emulsion solvent diffusion method. The quasi emulsion solvent diffusion method seemed to be promising for the preparation of Clotrimazole microsponge's as it is easy, reproducible, and rapid; has the advantage of avoiding solvent toxicity. To prepare the internal phase, Eudragit RS 100 is dissolved in dichloromethane (DCM) and ethanol (1:1). The drug can be then added to the solution and dissolved under ultra-sonication for 20 minutes. 1% triethylcitrate is added to provide the plasticity to the formulation. The internal phase containing drug (100mg) and 8 ml of DCM: Ethanol (1:1) was gradually added into a 200 ml distilled external phase, containing polyvinyl alcohol as an emulsifying agent. The mixture was stirred on a magnetic stirrer at 1000 rpm for 8hrs to remove DCM. The formed microsponges were filtered through Whatman filter paper no. 41 (Whatman, UK), washed with distilled water, dried at 40 °C for 12 h and weighed [19-20].

Optimization of microsponges formulation:

During the optimization of Microsponges formulation various parameters were studied like internal phase solvent and its volume, Surfactant concentration, and various drug and polymer concentration whose effect was measured during the preparation of microsponges. The final product was evaluated for their morphology, physical characteristics, production yield, actual drug content, entrapment efficiency and mean particle size [21-25].

Selection of internal phase solvent

For the selection of the internal phase; the various investigations were carried out using different internal phase solvent with the constant drug to polymer ratio of 1:1 and the stirring speed of 1000rpm for a period of 8 hrs. The composition of the external phase was kept constant for all batches i.e. 50 mg PVA in 200ml distilled water. Initial selections of the internal phase solvent were based on the solubility of the Clotrimazole and Eudragit RS 100 polymer.

Effect of volume of the internal phase

Five different volumes 4, 6, 8, 10 and 12 ml were taken to study the effect of volume of internal phase solvent (dichloromethane: ethanol) on the Microsponge formulations PB-1, PB-2, PB-3, PB-4, and PB-5 respectively. The microsponges prepared were evaluated for their morphology, physical characteristics, particle size, and production yield and entrapment efficiency.

Effect of surfactant concentration

To know the optimum concentration of surfactant required for the formation of microsponges; different concentration of polyvinyl alcohol such as 40mg, 45mg, 50mg, 55mg 60mg in 200 ml of distilled water was used as the external phase. Also, one formulation was prepared without using PVA. Drug to polymer ratio and stirring speed and other parameters were kept constant. These formulations were coded as PB-1, PB-2, PB-3, PB-4, and PB-5.

Effect of the drug to polymer ratio

The drug and polymer in the ratios 1:1, 1:2, 1:3, 1:4 and 1:5 were taken to prepare different microsponge formulations. In each formulation, the amounts of the drug (100 mg), dichloromethane (8 ml), PVA (50mg) were kept constant. The prepared batches PB-1, PB-2, PB-3, PB-4, and PB-5 were analyzed for physical properties, particle size, production yield, and entrapment efficiency.

3. EVALUATION OF MICROSPONGES:

FTIR Study:

Clotrimazole and the polymer were subjected to drug – excipients compatibility studies. FTIR measurements of the drug, individual polymer, and drug-polymer mixtures were obtained on FTIR JascoV-630. Samples were prepared by mixing with KBr and placing it in the sample holder. The spectra were scanned over the wave number range of 4000-400 cm^{-1} at ambient temperature.

Frequency Distribution Analysis:

Particle size of all the prepared batches of microsponge was determined using optical microscopy at 10X and 40X. A minute quantity of microsponges was spread on a glass slide and the average size of 100 microsponges was determined in each batch.

Production Yield:

The percentage of production yield (wt/wt) was calculated from the weight of dried microsponges (W1) recovered from batches and the sum of the initial dry weight of starting materials (W2) as the following equation:

% production yield = W1/W2 × 100

The yields of production were calculated as the percentage weight of the final product after drying, concerning the initial total amount of Clotrimazole and polymer used for preparation.

Entrapment Efficiency:

100 mg of microsponges were crushed and dissolved completely in 100 ml phosphate buffer pH 7.4 to produce a clear solution to the phosphate buffer pH 7.4. Then the solution was filtered with a 0.45-micron membrane filter. By making suitable dilutions the drug content was determined spectrophotometrically at 261 nm by using a UV spectrophotometer. Entrapment efficiency was calculated by using the following formula:

Entrapment efficiency =Actual drug loading /Theoretical drug loading× 100

Theoretical Drug Content:

Theoretical drug loading was determined by calculation assuming that the entire Clotrimazole present in the polymer solution used was entrapped in Clotrimazole microsponge's and no loss was observed at any stage of preparation of Clotrimazole microsponge's.

In-Vitro Drug Release Study [26-27]

In the present study, the USP apparatus II was used. The microsponge's equivalent to 100 mg Clotrimazole was placed directly in a dissolution basket. The dissolution test was performed using 900 ml of phosphate buffer pH 7.4, at 37±0.5 °C and 100 rpm. A sample of 1 ml of the solution was withdrawn from the dissolution apparatus at certain intervals for 9 h and the samples were replaced with fresh dissolution medium to maintain sink condition. The samples were filtered through 0.45-micron filters. The absorbance of these solutions measured at 261 nm. The cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

Formulation of gel of optimized batch [28-30]:

All the ingredients were accurately weighed. Carbopol 940 was soaked overnight with distilled water to hydrate and then hydrated Carbopol was again dispersed in distilled water by stirring on a magnetic stirrer for about 1 h, then propylene glycol along with other excipients such as Butylated Hydroxy Toluene and Methyl paraben were added with continuous stirring to the carbopol 940 solution. Then the mixture was neutralized by the drop-wise addition of triethanolamine which act as a neutralizing agent. Mixing was continued until transparent gel appeared, while the amount of base was adjusted to achieve a gel with a pH value of about 6.1.

The prepared Microsponges equivalent to 1% of Clotrimazole was weighed and dispersed into Carbopol gel with continuous stirring on a magnetic stirrer for 20 minutes to get uniformly distributed microsponges into the gel base (Table 1).

Table 1: Formulation table for gel

Sr.No.	Components	Quantity
1	Microsponges equivalent to 1% of Clotrimazole	100 mg
2	Carbopol-940	800 mg
3	Propylene glycol	1.5 gm
4	Butylated Hydroxy Toluene	10 mg
5	Methyl paraben	10 mg
6	Triethanolamine	qs
7	Distilled Water	qs

Gels are typically formed from a liquid phase that has been thickened with other components. The 0.5% Carbopol 940 Gel was prepared and microsponge's equivalent to 0.5% of Clotrimazole of optimized batch were incorporated into the Gel base and further studied for their release kinetics by using Franz diffusion cell and other evaluation parameters.

4. EVALUATION OF BASIC GEL PARAMETERS [31]:

Physical examination:

The prepared gel formulations were inspected visually for their color, homogeneity, consistency, and appearance

pH:

Weighed 10 gm of gel formulation were transferred in 10 ml of the beaker and measured it by using the digital pH meter. pH of the topical gel formulation should be between 3–9 to treat the skin infections.

Viscosity:

Brookfield digital viscometer (DVII+PRO) was used to measure the viscosity (in cps) of the prepared gel formulation. The spindle (T-D) was rotated at 10 rpm. The viscosity of formulations was more correct which was near 100% torque. Reading was reported 30 sec after putting the motor on. The determinations were carried out in triplicate and the average of three reading is recorded.

Spreadability:

Two glass slides of 20 x 20 cm were selected. The gel formulation whose Spreadability had to be determined was placed over one of the slides. The other slide was placed upon the top of the gel such that the gel was sandwiched between the two slides and 100g weight was placed upon the upper slide so that the gel between the two slides was pressed uniformly to form a thin layer. The weight was removed and the fixed to a stand without slightest disturbance and in such a way that only the upper slide without slights disturbance and in such a way only the upper slide to side off freely, to the force of weight tied to it. A 20 g weight was tied to the upper side carefully. The time taken for the upper slide to travel the distance of 7.5 cm and separate away from the lower slide under the certain of weight was noted. The determinations were carried out in triplicate and the average of three readings recorded.

It is calculated using the formula:

$$S = M \times L / T$$

Where, S = is the spreadability, M = is the weight in the pan (tied to the upper slide), L = is the Length moved by the glass slide and T = represents the time in seconds taken to separate the slide completely.

Percentage Extrudability:

The gel formulation was filled in the standard caped collapsible tube and sealed. The tube was weighted recorded. The tube was placed between two glass slides and was clamped. A 500g weight was placed over the glass slide and then glass slide was clamped. A 500g weight was placed over the glass slide and then the cap was opened. The amount of gel extruded was collected and weighted. The % of gel extruded was calculated.

Extrudability = Amount of gel extruded from the tube/Total amount of gel-filled in the tube× 100

In-vitro diffusion study:

The % cumulative release of formulation was determined by using Franz (vertical) diffusion cell with area 3.14 cm^2 for 9 hrs. Cellophane membrane was mounted on the receptor compartment with facing upwards into donor compartment. The donor compartment was filled with the 1 gm of topical gel formulation. A 50 mL aliquot of phosphate buffer pH 7.4 was used as receptor medium to maintain sink condition. The available diffusion area of cell was 3.14 cm^2 .The receptor compartment was maintained at 37 ±0.5 ^{0}c and stirred by Teflon coated magnetic bars at 100 rpm. The donor compartment was kept in contact with the receptor compartment. At predetermined time intervals for 9 h, pipetted out 1 ml of solution from the receptor compartment and immediately replaced with the fresh 1 ml phosphate buffer. The drug concentration of the receptor fluid was measured at 261 nm by using UV spectrophotometer against appropriate blank. The experiment was carried out in triplicate. The results of cumulative release for the drug were reported.

5. RESULTS AND DISCUSSION:

Optimization of microsponges formulation:

Selection of internal phases:

The mixture of ethanol and DCM in the ratio of 1:1 in 8ml was selected as it showed the optimum drug entrapment without the solubility issue of the polymer. The rate of diffusion of this solvent mixture was high when compared to other solvents, thus decreasing the time required for preparation. The polymer was found to be freely soluble in DCM but sparingly soluble in ethanol. From the result obtained it was found that dichloromethane: ethanol as an internal phase gives characteristic product, Thus it was selected as an internal phase solvent for the preparation of clotrimazole microsponges.

Effect of volume of the internal phase (Table 2):

Internal phase volume less than 4 ml was found to insufficient to dissolve polymer and drug. While the Milky phase was formed with more than 10, 12 ml of Dichloromethane and production yield was also decreased. While 8 ml of the volume shows good solubility with entrapment efficiency and production yield. Thus 8 ml of inner phase solvent volume was selected for further formulation of Microsponges. When the amount of internal phase was increased from 4 to 8ml, the production yield and encapsulation efficiency of microsponges were increased. At the volume of 10 and 12 ml, there is dominant emulsification of both phases with less solidification of drug and results in decreased all factors. It was found that by decreasing the solvent volume (dichloromethane: ethanol) the particle size increases. It was found that when drug and polymer dissolved in the minimum amount of solvent, it is beneficial concerning production yield, particle size, and entrapment efficiency but also shows the problem for solubility.

Table 2: Effect of volume of the internal phase

Formulation Code	Internal phase volume (ml)	Production yield (%)	Entrapment efficiency (%)	Mean particle size (um)
PB1	4	82.20	77.07	60.13
PB2	6	78.39	90.72	54.75
PB3	8	76.44	93.56	48.24
PB4	10	66.12	68.12	42.58
PB5	12	54.85	49.12	22.19

Effect of surfactant concentration (Table 3):

When the amount of surfactant (polyvinyl alcohol) was increased, the production yield and drug content and entrapment efficiency of microsponge's increased up to 50 mg and then started to decrease. At the concentration of 40-50 mg of PVA in 200 ml external phase, the entrapment efficiency of microsponges was found to be increased up to 92.56%, while in case of 50-60mg of PVA it was found to be decreased up to 71.52%, further increasing the concentration shows the no product formation. The PVA significantly prevented the aggregation of the droplets with solidified particles during the process. The dispersion of the internal phase containing drug and polymer depended on the concentration of PVA in the external phase medium; hence when PVA concentration was increased, The particle size of microsponges decreased but up to the certain concentration of PVA; further increased in PVA concentration; increases the viscosity of external phase which lead to no formation of the solid particle. Increased PVA concentration increases the solubilization of drug into the external phase. Due to increased solubilization of drug in water, less amount of drug is made available for encapsulation thus decreases production yield and encapsulation efficiency so the 50 mg concentration of PVA in 200 ml Distilled water was found to be optimum and selected for further formulation of microsponges.

Table 3: Effect of surfactant concentration – polyvinyl alcohol [PVA]

Formulation Code	surfactant concentration (mg)	Production yield (%)	Entrapment efficiency (%)	Mean particle size (um)
PB1	40	68.36	65.03	232.4
PB2	45	75.85	72.12	60.56
PB3	50	82.47	92.56	52.70
PB4	55	71.49	77.94	73.47
PB5	60	68.08	71.52	54.76

Effect of the drug to polymer ratio (Table 4):

Table 4: Effect of the drug to polymer ratio

Formulation Code	Drug: Polymer Ratio (mg)	Production Yield (%)	Entrapment Efficiency (%)	Mean Particle size (um)
PB1	1:1	77.71	71.52	37.65
PB2	1:2	80.23	82.95	43.97
PB3	1:3	83.14	91.04	54.66
PB4	1:4	88.72	92.45	123.79
PB5	1:5	93.65	89.37	164.76

With an increase in drug: polymer ratio leading to an increase in production yield & entrapment efficiency and an increase in mean particle size. Increased Production yield & Entrapment is the due fact that the amount of polymer is increased with an increased ratio of drug to the polymer. It was observed that as a drug to polymer ratio increases the particle size increased ; this is probably due to fact that at higher relative drug content ; the amount of polymer available per microsponge to encapsulate the drug become more, thus increases the thickness of the polymer wall and hence larger the size of microsponges

6. EVALUATION OF MICROSPONGES:

Compatibility Study:

Differential scanning calorimetry:

The DSC thermogram of the microsponge of Clotrimazole is shown below:
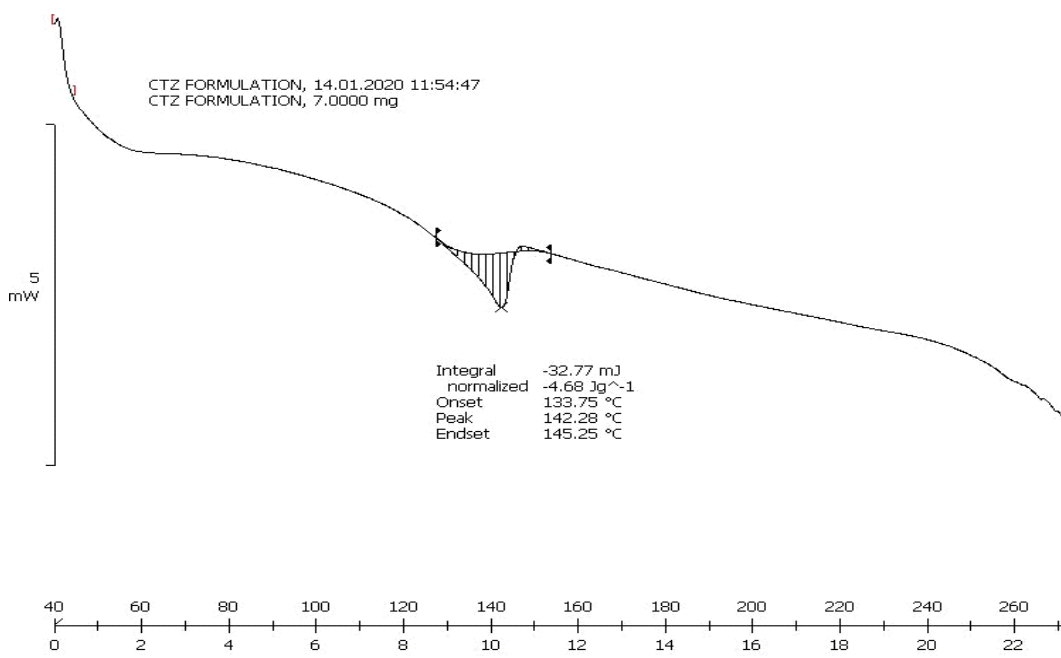

Figure 1: DSC thermogram of the microsponge formulation

Compatibility study was carried out to check for any possible interaction between drug and excipients used. In DSC studies, a pure Clotrimazole thermogram (Figure 1) reflected an endothermic peak at 145.43°C corresponding to its standard melting point range depicted in Figure 8.5. Physical mixture showed similar thermal behavior as that of the pure drug but with lower intensity 145.58°C Figure 8.7. However, the melting endotherm of microsponge formulation was suppressed due to the partial protection of Clotrimazole and its encapsulation in the polymer system that's why it shows a sharp peak at 142.28°C as depicted in Figure 8.8. It was also observed that drug crystallinity altered significantly in microsponge formulation confirming its dispersion in the system. Clotrimazole is entrapped in Eudragit RS 100 is concluded from the above study as well as it is compatible with Eudragit RS 100 as no any significant changes are seen in thermograms.so it's clear that it doesn't hamper the physicochemical property of drug, polymer and formulation mixture.

FTIR study:

From the spectra of Clotrimazole, physical mixture and formulation (Figure 2), it was observed that all characteristics peaks of Clotrimazole were present in the combination spectrum and in the formulation, thus indicating compatibility of the drug and polymer (Table 5). The process used for the formulation is also compatible as no changes in the drug purity occur as microsponge formulation of the drug takes place.
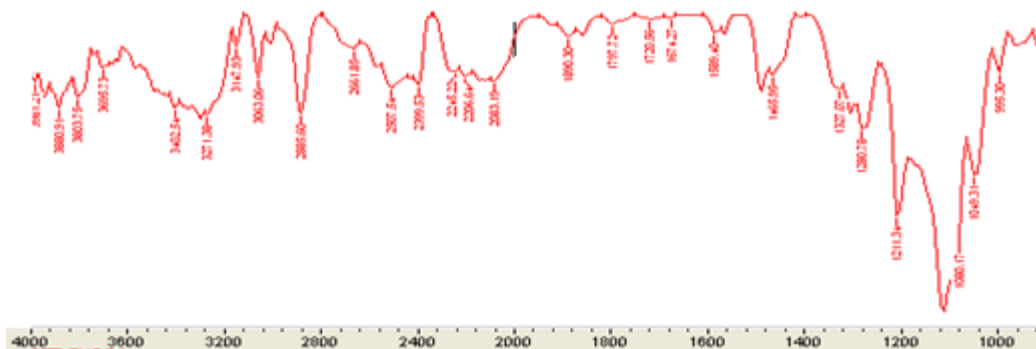
Figure 2: IR spectra of microsponge formulation

Table 5: Interpretation of IR spectra of microsponge formulation

Sr.no.	The peak observed(cm^{-1})	Peak interpretation
1	3063.06	C–H stretch (aromatic)
2	1589.40	C=N stretch of imidazole ring (aromatic)
3	1080.17,1049.31	C–N stretch of imidazole ring(aromatic)
4	1671.27	C=C stretch of imidazole ring(aromatic)
5	1211.34	C–H bend (in-plane)
6	910.43	C–H bend (out-of-plane)
7	1720.56	-COO-(easter)
8	2885.60	-CH Aliphatic (stretch)

FTIR study clearly indicated that no interaction occurred between the drug and the polymer. It also indicated that the drug was loaded in the microsponges as it showed desired peaks of both drug and polymer. It indicates that the drug having compatibility with the components of Microsponge formulation. These results indicate the method used to prepare microsponge does not affect the physicochemical properties of the systems.

In vitro drug release study

Table 6: In Vitro Drug Release profile for Clotrimazole microsponge Formulation

Time (h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	20.46±0.231	22.34±0.345	24.34±0.455	8.56±0.332	10.46±0.221	14.54±0.442	16.44±0.236	5.85±0.701	18.45±0.346
1	36.56±0.451	38.45±0.452	26.34±0.452	12.6±0.421	14.86±0.231	20.43±0.441	24.68±0.442	13.03±0.720	22.46±0.987
2	42.66±0.542	44.45±0.354	28.45±0.423	26.8±0.442	18.96±0.231	28.67±0.421	30.88±0.462	29.14±0.788	30.68±0.956
3	48.74±0.452	50.54±0.423	30.34±0.462	32.6±0.342	26.94±0.212	34.66±0.421	40.8±0.431	36.74±0.904	42.67±0.945
4	52.42±0.535	54.44±0.562	34.36±0.432	42.8±0.232	34.88±0.241	44.68±0.24	46.34±0.341	41.06±0.969	48.8±0.978
5	62.44±0.432	56.43±0.442	45.24±0.561	56.7±0.234	47.04±0.424	52.89±0.423	50.67±0.425	51.67±0.806	56.8±0.453
6	64.65±0.453	60.56±0.532	52.34±0.442	76.45±0.442	52.08±0.243	64.98±0.241	54.86±0.434	66.02±0.876	64.24±0.967

Time (h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
7	66.67±0.865	62.56±0.423	60.24±0.232	80.34±0.443	77.68±0.521	74.88±0.442	64.56±0.673	71.29±0.809	74.87±0.978
8	68.98±0.654	65.56±0.121	64.46±0.456	82.45±0.563	85.98±0.223	86.76±0.432	70.46±0.987	78.8±0.948	76.67±0.968
9	70.65±0.986	68.66±0.342	72.56±0.427		95.78±0.231	90.65±0.223	78.65±0.687		82.56±0.987

Where ±SD = standard deviation (n=3)

The decrease in the rate and extent of drug release was observed with the increase in polymer concentration in microsponges and is attributed to increase in the density of the polymer matrix and also an increase in the diffusional path length which the drug molecules have to traverse (Table 6, Figure 3-5).
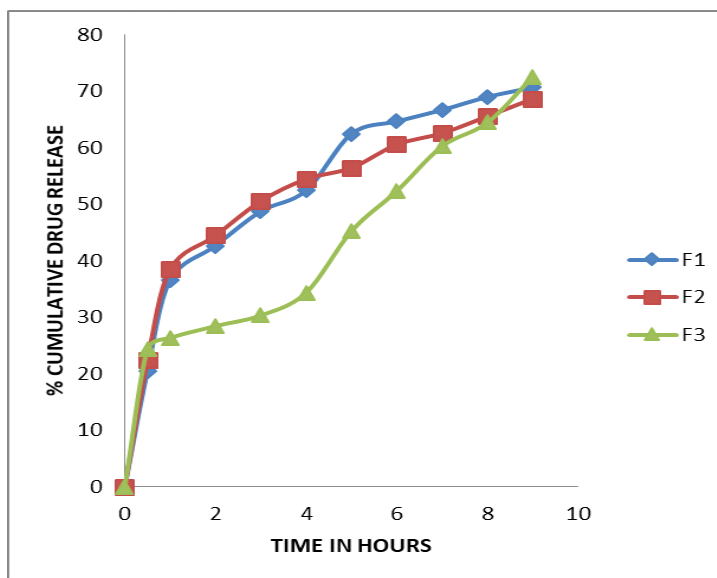
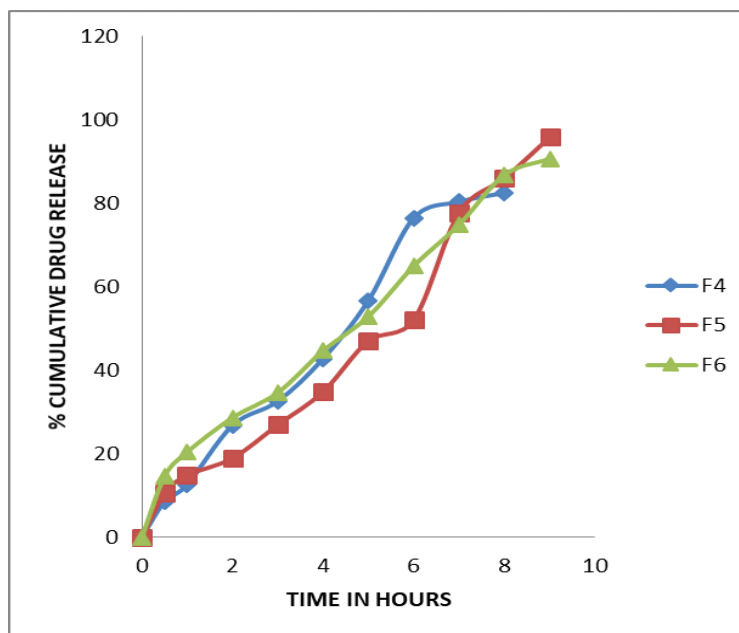**Figure 3:** *In vitro* drug release profile of Clotrimazole microsponges. (Batch F1 to F3)

Figure 4: *In vitro* drug release profile of Clotrimazole microsponges. (Batch F4 to F6)
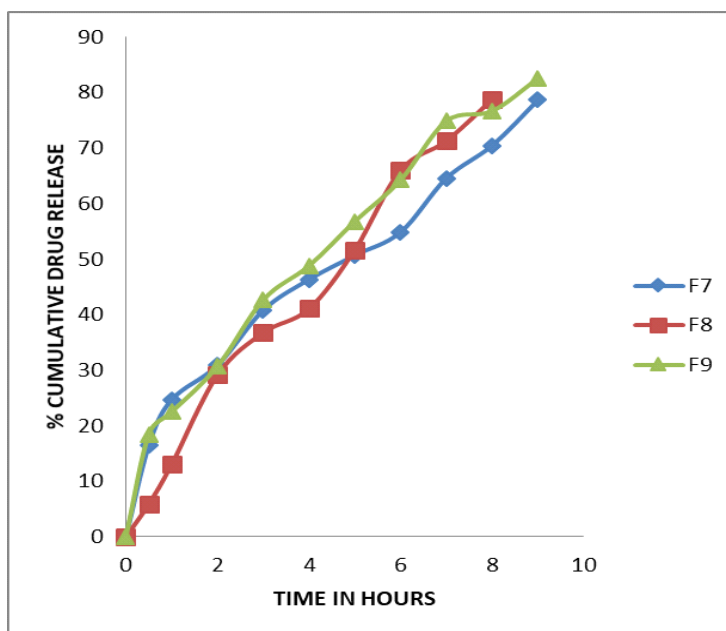
Figure 5: *In vitro* drug release profile of Clotrimazole microsponges (Batch F7 to F9)

Drug release from the formulations decreased with an increase in the amount of polymer in the microsponges. The present study showed that increase in the ratio of drug: polymer resulted in a decrease in the release of Clotrimazole from microsponges. While the higher concentration of polymer decreases the release of drug from microsponges; this could be due to the formation of a thicker matrix wall in microsponges with the smaller drug: polymer ratios lead to a longer diffusion path, and consequently slower drug release rate. Batch F5 showed 95.78 % drug release at 9 hours, it indicated that the formulation F5 was found to be an optimized batch. Formulation F1, F4, and F7 showed an unsatisfactory drug release pattern.

Table 7: Release kinetic data of Clotrimazole microsponges

Formulation	Zero Order	First Order	Highuchi Matrix	Korsmeyer Peppas
F5	0.9563	0.916	09859	0.9892

The optimized batch evaluated kinetically by Zero Order, First Order, Highuchi Matrix, and Korsmeyer Peppas Model (Table 7). The model with a higher correlation coefficient (R^2) was considered the best fit as presented in table no.8.15 formulation F5 fitted well to the Korsmeyer- Peppas release model, this model suggested that the drug release was by diffusion mechanism. The diffusion of the drug from the formulation into the diffusion medium depends upon the concentration. As gradient varies, the drug is released, and the distance for diffusion increases. To confirm the diffusion mechanism, the data were fitted to Korsmeyer's equation;

$Q_t /Q\alpha = K t^n$

Where, Q is the amount of drug released at time t, Qα is overall released amount, K is a constant incorporating the properties of the macromolecular polymeric system and the drug, and n is a kinetic constant or diffusion exponent that depends on the transport mechanism. The exponent n gives information about the release mechanism; n = 0.5 characterizes diffusion Controlled release, 0.5<n < 1.0 indicates anomalous (non-Fickian transport), and n = 1.0 indicates swelling controlled release (zero-order kinetics). Formulation F5 showed a diffusion controlled-release mechanism as reflected by their n value which indicating drug release by the non-fickian mechanism.

7. CONCLUSION

The development of clotrimazole microsponges, which were later defined as an effective carrier for the topical delivery of the medication, was accomplished using the quasi emulsion solvent diffusion technique. The drug:polymer ratio had a discernible impact on the developed system's attributes. It was found that microsponges designed for prolonged

release formulation were successful, and a comparable result was seen with microsponges for clotrimazole that included gel. Preparation-ahead microsponge gel formulations showed controlled drug release. It has been demonstrated that microsponges can effectively carry drugs for topical antifungal therapy. The formulations' outstanding success at keeping the medicine on the skin suggests that microsponge gel is a better drug delivery method than regular gel.

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