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Research Article

Vaginal delivery of clotrimazole by mucoadhesion for treatment of candidiasis

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Abstract

The aim of this study was to prepare mucoadhesive vaginal tablets of clotrimazole for treatment of vaginal candidiasis. A combination of mucoadhesive polymers like HPMC K100M, Sodium CMC, and Eudragit L100 were used in different ratios prepare solid dispersions to enhance its solubility. Tablets were prepared by the wet granulation method. Solid dispersions were evaluated for saturation solubility. All tablet batches were evaluated for weight variation, hardness, friability, drug content, swelling index, *in vitro* drug release study, *ex vivo* diffusion and mucoadhesive strength. FTIR spectra showed there was no interaction between the drug and the excipients. HPMC K100 M increased the solubility of clotrimazole in simulated vaginal fluid at pH 4.5. Eudragit L100 was shown to increase the swelling and mucoadhesive strength of the tablet, i.e., 3.03 and 3.29 g. The *in vitro* and *ex vivo* release of all 9 batches showed between 61 to 78% release in 8h. *Ex vivo* diffusion studies using sheep vaginal membrane showed 43 to 59% in 6h in simulated vaginal fluid. The release and flux were nearly comparable to marketed tablet i.e., Candid-V6. The drug release of all batches followed the Korsmeyer-Peppas kinetic model, and the mechanism was found to be non-Fickian/anomalous.

Keywords: Clotrimazole, solid dispersion, HPMC K100M, Eudragit L100, Sodium CMC.

INTRODUCTION

Vulvovaginal candidiasis (VVC) is a fungal infection of the female genital tract caused by the abnormal growth of yeast-like fungi. It develops in the mucosa and usually causes a watery, white, cottage cheese-like vaginal discharge.¹ Various conventional formulations are prepared for the treatment of vaginal candidiasis, like oral and vaginal tablets. Vaginal drug delivery has many advantages as compared to oral drug delivery, like bypassing the first-pass metabolism and local drug delivery. For several years, imidazole derivatives have been used as the drugs of choice for treating this infection. Clotrimazole (CTZ) is a broad spectrum antimycotic agent which has prominent antifungal action. It operates to kill individual Candida or fungal cells by changing the permeability of the fungal cell wall.² It binds to phospholipids in the cell membrane and inhibits the biosynthesis of ergosterol and other sterols required for cell membrane production. This leads to the cell's death via the loss of intracellular elements. CTZ is available in various formulations, like tablets, creams, and gels for local treatment. However, a major difficulty with these formulations is their low residence time.³

Solubility is a major physicochemical factor that affects the absorption and onset of action of the drug and its therapeutic potency. Drugs having poor aqueous solubility may face problems with dosage form design as well as effective

therapeutic action. The low dissolution rate and aqueous solubility of the drug candidate affect the oral bioavailability of the drug. The enhancement of the solubility and dissolution rate of drugs is one of the major factors which affect the development of dosage forms.² The term solid dispersion (SD) introduces a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be both crystalline and amorphous. The drug can be dispersed molecularly, in amorphous particles (clusters) or crystalline particles. The transformation of the crystalline drug to an amorphous drug upon SD formulation increases the dissolution rate.⁴ SD techniques have been used to increase the solubility of a poorly water-soluble drug. SD is a viable and economical method to enhance the bioavailability of poorly water-soluble drugs. CTZ is a BCS class II drug that has low solubility and high permeability, which affects bioavailability. The SD technique involves different methods like fusion, solvent evaporation, lyophilization technique, extruding method, spray drying, and gel entrapment method to improve the solubility and dissolution rate.⁵

This study aimed to enhance the solubility and dissolution rate of CTZ by SD technique and formulation of a mucoadhesive CTZ vaginal tablet using a suitable mucoadhesive agent.⁶ Further, SD mucoadhesive vaginal tablets were evaluated for hardness, thickness, weight

variation, friability, *in vitro* dissolution, mucoadhesive strength, *ex vivo* studies, and stability studies.

MATERIALS AND METHODS

Materials

Clotrimazole was a kind gift of Amoli organics, Vapi, India. HPMC K100M was obtained from Aurobindo Pharma Ltd, Hyderabad, India. Sodium carboxymethyl cellulose was obtained from AET lab, Hyderabad, India. Eudragit L100 was obtained from Evonik Degussa India Private Limited, Mumbai. All chemical used in this study were the analytical grade.

Methods

Preliminary trials for the selection of polymer

Different polymers were selected for preliminary trials, such as PVP K30, HPMC K4M, HPMC E5, Eudragit S100, Chitosan, Sodium carboxymethylcellulose, PEG 6000, and Hydroxypropyl cellulose. The polymer mixture was prepared and determined the saturation solubility in simulated vaginal fluid pH 4.5.⁷ The result of saturation solubility indicated HPMC K100 M, Eudragit L100, and Sodium carboxymethyl cellulose showed higher solubility as compared to other polymers. Hence, HPMC K100 M, Eudragit L100, and Sodium carboxymethyl cellulose were selected for further studies.

Preparation of CTZ Solid dispersions

SDs of CTZ were prepared by the solvent evaporation method (Table 1).

Table1: Composition of the different solid dispersions

Code	Solid dispersion	Drug: Carrier
SD1	CTZ: HPMC K100M	1:1
SD2	CTZ: HPMC K100M	1:2
SD3	CTZ: HPMC K100M	1:3
SD4	CTZ: Sodium carboxymethyl cellulose	1:1
SD5	CTZ: Sodium carboxymethyl cellulose	1:2
SD6	CTZ: Sodium carboxymethyl cellulose	1:3
SD7	CTZ: Eudragit L100	1:1
SD8	CTZ: Eudragit L100	1:2
SD9	CTZ: Eudragit L100	1:3

The SDs were prepared by using drug and polymer ratios of 1:1, 1:2, 1:3 of CTZ with HPMC K100M, Sodium carboxymethyl

cellulose, and Eudragit L100 were dissolved in methanol. The solution was stirred [CIS-24 Remi, India] until the solvent evaporated and a solid mass was obtained. After solidification, it was pulverized and sieved through #40 mesh size and stored in a desiccator for further use.⁸

Characterization of solid dispersions

Drug-excipient compatibility studies

The IR spectrum of CTZ was recorded using an FTIR spectrophotometer (Shimadzu). Sample preparation involved triturating the mixture of sample & potassium bromide (KBr) in the ratio of 1:50. The resultant triturate was placed in the sample cup and was scanned over a frequency range of 4000-400 cm⁻¹.⁹ The mixtures of HPMC K100 M, Eudragit L100, and Sodium CMC with CTZ were analyzed for IR Spectra.

Differential scanning calorimetry

The possibility of any interaction between drug and carriers during the preparation of solid dispersion was assessed by carrying out a thermal analysis of the drug. The DSC analysis was performed using [Mettler, Toledo DSC 822e] on 1 to 4 mg of sample was heated in an open aluminium pan at a rate of 20°C under a nitrogen flow of 50 mL/min.¹⁰

Saturation Solubility studies

Saturation solubility was measured by the shake flask method. The plain CTZ and SDs [in excess quantity] were placed in a glass stoppered volumetric flask containing 10 ml of simulated vaginal fluid at pH 4.5.¹¹ The sample was placed in an orbital shaker [CIS-24 Remi, India] at 37°C and 80 rpm for 24h.¹² The samples were filtered through Whatman filter paper (#11) and were diluted appropriately in simulated vaginal fluid at pH 4.5 and assayed UV spectrophotometrically (Jasco, V-730) at 263nm.¹³

Formulation of CTZ vaginal tablet

An accurately weighed quantity of, the CTZ SD equivalent to 100 mg and lactose were taken in a mortar and mixed. The wet mass formed by the addition of PVP K30 binder solution was added to the dry blend gradually with constant kneading to ensure a homogenous mass (Table 2). The mass was passed through a # 10 mesh sieve. Then granules were dried in a hot air oven [biomedica, AI-7981] at 50°C for 10 min.¹⁴ The screening of dried granules was passed through sieve # 16 and the dried granules were mixed with talc and magnesium stearate and compressed into tablets using 12 mm punches. [Rimek mini press-II MT].

Table2: Composition of the different formulations (All quantities in mg)

Sr. No	Excipient (mg)	F1	F2	F3	F4	F5	F6	F7	F8
1.	CTZSD equivalent to 100mg	200	300	400	200	300	400	200	400
2.	Lactose	290	190	90	290	190	90	290	190
3.	Magnesium stearate	3	3	3	3	3	3	3	3
4.	Talc	2	2	2	2	2	2	2	2
5.	Polyvinyl pyrrolidone K30	5	5	5	5	5	5	5	5
6.	Isopropyl alcohol	q. s	q. s	q. s	q. s	q. s	q. s	q.s	q. s

Evaluation of Mucoadhesive vaginal tablet

Hardness, thickness and uniformity of weight

The mechanical strength of tablets during shipping or breakage under conditions of storage, transportation, and handling before usage depends on their hardness. The hardness of all tablets of all batches was measured by the Monsanto hardness tester (Nevtex). The hardness was calibrated in terms of kg/cm².¹⁵ The thickness and diameter of tablets are important for the uniformity of tablet size. The thickness and diameter were calibrated using a digital Vernier Caliper.¹⁶ Weight uniformity was measured by sampling and weighing 20 tablets at random and the average weight was calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage as mentioned in IP 2018.¹⁷

Friability

Friability is a measure of tablet strength. The Roche friabilator (Veego, Mumbai) has been used for testing the friability using the following procedure. Ten tablets were weighed accurately and placed in the friabilator revolving at 25 rpm,¹⁸ dropping the tablets a distance of six inches with each revolution. After 4 min., the tablets were weighed and the percentage loss in tablet weight was measured.

Determination of drug content

Twenty tablets from each batch were randomly selected, weighed, and powdered. The quantity of powder equivalent to 25 mg of CTZ was taken and dissolved in 10 ml of methanol and filtered.¹⁸ The absorbance was measured UV spectrophotometrically (Jasco, V-730) at 263 nm after suitable dilution.

Swelling Index

Swelling index of all batches was determined by placing the pre weighed (W₁) tablets in petri dishes containing 4 ml of simulated vaginal fluid (pH 4.5) solution. At regular intervals (1, 2, 3, 4, 5, and 8 h), the tablets were withdrawn from the petri dishes, and gently tapped with filter paper to remove excess surface water and the weight was noted (W₂).¹⁹ The swelling index (SI) was calculated using the following formula:

$$\text{Swelling index (S.I)} = (W_2 - W_1)/W_1 \text{-----eq. (1)}$$

In vitro dissolution studies

The *in vitro* dissolution studies were carried out using USP apparatus type II (DA 8000, Lab India) at 50 rpm. The dissolution medium was 900 ml of simulated vaginal fluid maintained at 37°C ± 0.5°C. Aliquots of 5 ml were removed at 1 h intervals till 8h. The aliquots were then analyzed by a UV spectrophotometer (Jasco, V-730) at 263 nm.²⁰

In vitro release kinetics model

In order to determine the mechanism of drug release from the matrix tablet batches, data obtained from *in-vitro* drug release studies was plotted into various kinetic models like zero-order, first order, Higuchi, and Korsmeyer-Peppas models were used. The criterion for selecting the most appropriate model was chosen on the basis of the goodness-of-fit test. The zero-order kinetic describes the systems in

which the drug release rate is independent of its concentration. The first order kinetic describes the systems in which the drug release rate is concentration dependent.²¹ Higuchi described the release of a drug from an insoluble matrix as a square root of a time dependent process. In the case of the Korsmeyer-Peppas model, the drug release from such devices having constant geometry will be observed till the polymer chains rearrange to an equilibrium state.²²

Determination of mucoadhesive strength

Mucoadhesive strength was evaluated using a Texture Analyzer (CT 3 Texture Analyzer, Brookfield Engineering Labs, Inc., Model Texture Pro CT V1.4 Build 17). Fresh sheep vaginal mucosa was obtained from a local slaughterhouse and was used within 2 h of slaughtering. The mucosal membrane was cleaned with distilled water and then with acetate buffer pH 4.6. It was then carefully attached to a 10-mm cylindrical probe (TA 3/100probe) using a double-sided adhesive tape.²³ The upper platform was moved downward manually near to the tablet surface and then the mucosa was brought toward the tablet at a constant speed of 1mm/s until a predetermined compressive force of 0.5 N was used with a holding time of 60 s and a load cell of 1000 gm. The probe was then lifted with a return speed of 1 mm/s to a distance of 15 mm and the maximum detachment force (g) was determined for each sample with a data rate of 15 points/sec. For each new sample, a separate mucosa sample was used.

Ex vivo diffusion studies

Ex vivo drug permeation studies of the drug through the sheep vaginal membrane were performed using a Franz diffusion cell at 37°C ± 0.2°C. Fresh sheep vaginal tissue was fixed between the donor and receptor compartments. The vaginal tablet was put with the core facing the tissue and the compartments clamped together. Both donor and receptor compartments were filled with 8 ml of simulated vaginal fluid (pH 4.5).²³ and stirred with a magnetic bead at 50 rpm. Samples of 1 ml were withdrawn every hour (up to 8 h) and analyzed for drug content at 263 nm using an UV spectrophotometer (Jasco, V-730).

RESULTS AND DISCUSSION

Drug-excipient compatibility studies

This test was carried out to check the interaction between drugs and excipients. The FT-IR spectra of CTZ shows the absorption band at 1440 cm⁻¹, 1590 cm⁻¹, and 1674 cm⁻¹ due to C-N stretching, N-H bending, and C=O stretching of the primary amide group. It is further noted that out of plane N-H wagging, C-N stretching vibrations, N-H bending, free asymmetric and symmetric N-H stretching vibrations appear at 750 cm⁻¹, 1208 cm⁻¹ and 3062 cm⁻¹, respectively. Absorption bands at 455 cm⁻¹ and 1091 cm⁻¹ are assigned due to out of plane C=C bend and in plane C-H bend. It can be seen that absorption bands in the range of 2229-2638 cm⁻¹ are due to methyl C-H stretching. By comparing the spectra of CTZ and its physical mixtures (Fig 1) and SDs (Fig 2), it was observed that all the peaks lie in their appropriate range. No changes were observed, which indicated there was no interaction between CTZ and the excipients.

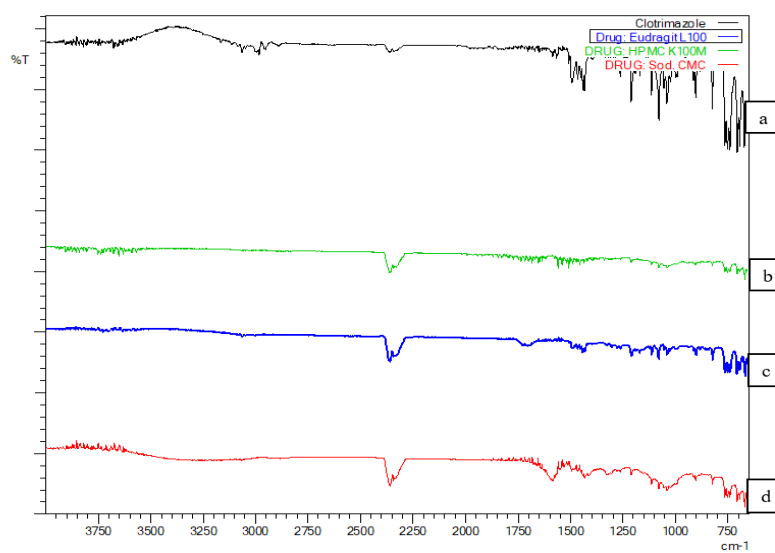


Figure 1: a) CTZ b) CTZ+HPMC K100 M c) CTZ+Eudragit L100 d) CTZ+Sodium CMC

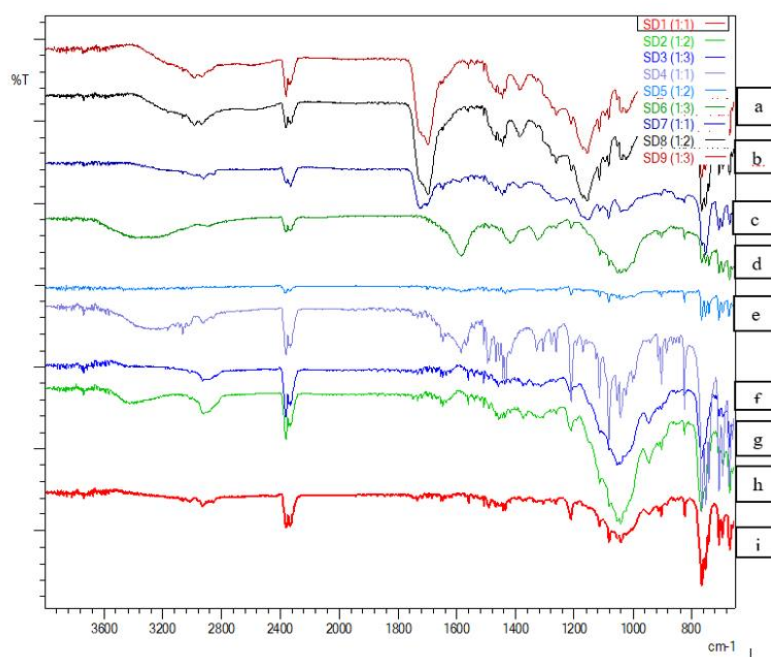


Figure 2: FTIR of solid dispersion a) drug+HPMC K100 M(1:1) b) drug+HPMC K100 M(1:2) c) drug +HPMC K100 M(1:3) d) drug +Sodium CMC (1:1) e) drug+ Sodium CMC (1:2) f) drug+Sodium CMC (1:3) g) drug+Eudragit L100(1:1) h) drug+Eudragit L100 (1:2) i) drug+Eudragit L100(1:3)

Differential scanning calorimetry

The pure drug and the SDs were analyzed by DSC to study the thermal behaviour. The DSC thermogram of drug and solid dispersion are shown in (Fig 3). The DSC analysis provided additional evidence that solid dispersions were formed. When solid dispersions are formed, their melting,

boiling, and sublimation points shift to different temperatures or disappear. The DSC thermogram of CTZ shows a sharp endothermic peak at 147.8 °C, which is the melting endotherm of the CTZ and also reflects its crystallinity (Fig 3). The thermograms of SDs did not show the sharp endothermic peak, suggesting that the drug is molecularly dispersed in the polymers.

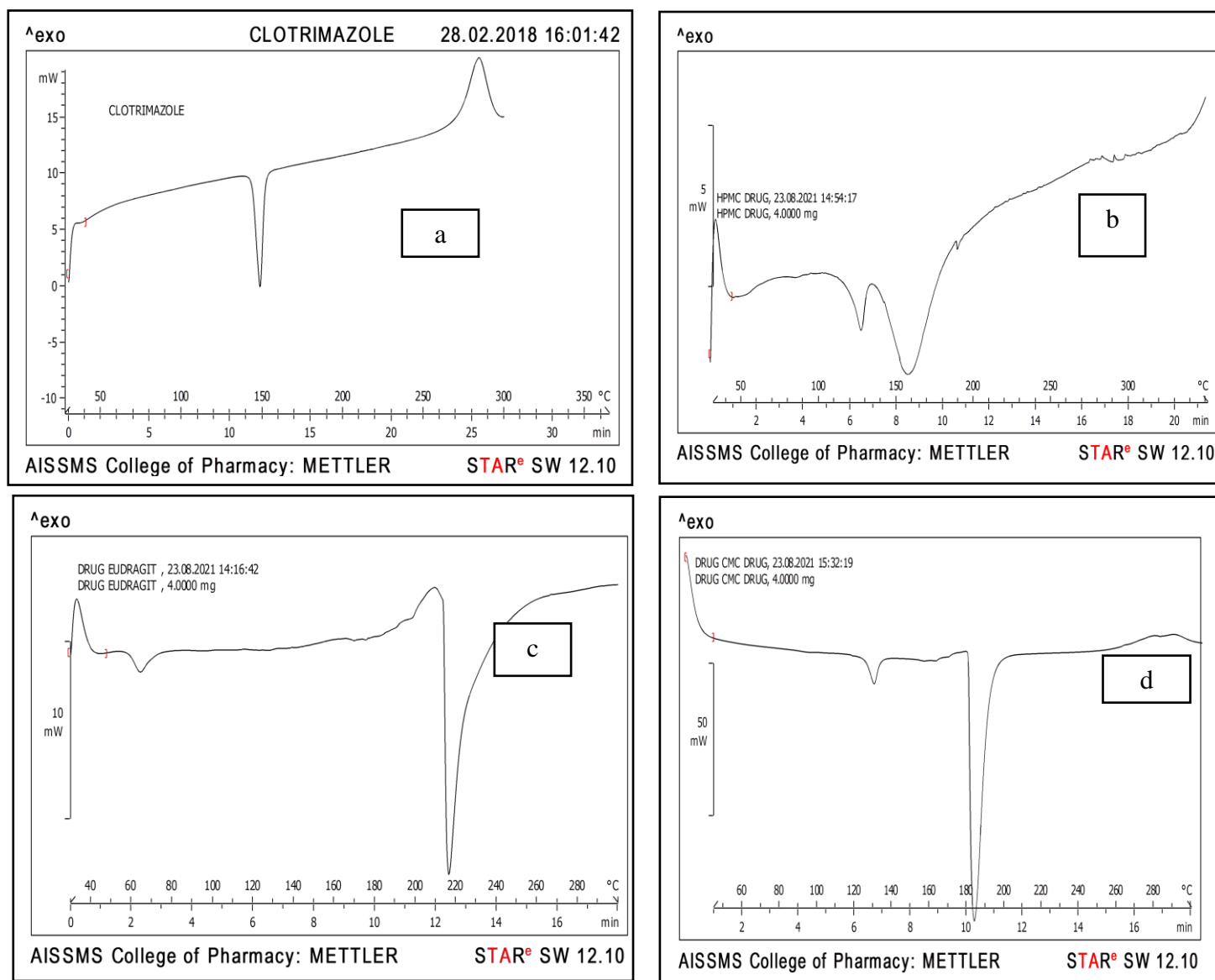


Figure 3: DSC of solid dispersions a) Clotrimazole b) CTZ+HPMCK100M b) CTZ+Sod.CMC c) CTZ+Eudragit L100

Saturation solubility studies of SDs

Solubility studies of SDs were performed in simulated vagina fluid pH 4.5. The solubility of CTZ was highest in SDs of HPMCK 100M than Eudragit L100 and sodium CMC (Fig4). Increase in polymer concentration caused a marginal increase in saturation solubility. An 18-fold increase in

solubility was observed at 1:3 CTZ-HPMC ratio whereas at same ratio of sodium CMC the increase was 12 folds and with Eudragit L 100 the increase was 8 folds. Among all formulations, SD3, SD6 and SD9 showed the highest solubility in simulated vaginal fluid (pH 4.5), i.e., 25.54 ± 3.21 $\mu\text{g/mL}$, 17.1 ± 9.87 $\mu\text{g/mL}$ and 11.98 ± 9.81 $\mu\text{g/mL}$.

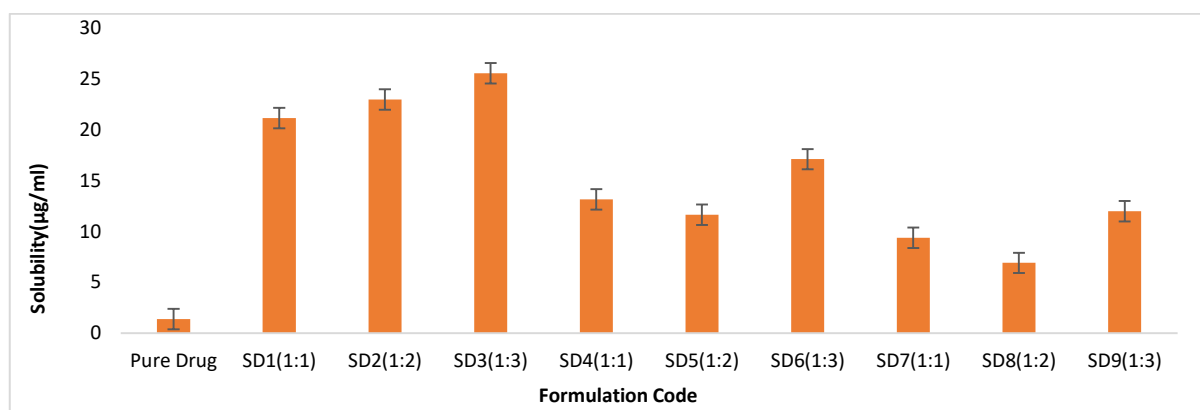


Figure 4: Saturation solubility of SDs of CTZ at different polymer ratio (Mean \pm SD (n=3))

Evaluation of mucoadhesive vaginal tablets

Wet granulation technique was employed for the preparation of nine different formulations, i.e., F1 to F9. The

(Table3) shows various quality parameters for the tablets. All properties were found to fulfil compendial specifications.²⁴

Table 3: Evaluation Tests for Formulations Expressed as (Mean±SD (n=3))

Formulation code	Diameter (mm)	Thickness (mm)	Hardness (Kg/cm ²)	Friability (%)	Weight variation (mg)	Drug Content (%)
F1	8.01±1.2	2.45±0.9	6.3±1.4	0.47±0.5	503±1.39	98.3±1.1
F2	7.97±0.9	2.96±1.2	7.2±1.3	0.47±0.4	504.9±2.34	97.4±1.2
F3	7.97±1.1	2.96±1.1	6.6±1.7	0.34±0.6	503.5±1.94	98.1±1.5
F4	7.96±1.2	2.72±1.3	6.9±1.5	0.34±0.6	505.6±1.75	99.2±0.9
F5	8.13±1.4	2.81±1.2	7.4±1.2	0.56±0.3	503.3±2.04	99.5±0.8
F6	7.99±1.1	2.39±0.9	6.0±1.3	0.38±0.4	501.3±1.73	96.7±1.6
F7	7.88±1.1	3.19±1.1	7.1±1.1	0.49±0.2	504.7±2.04	99.2±0.9
F8	7.94±1.3	3.01±1.3	7.8±0.9	0.46±0.3	503.1±2.09	99.4±0.5
F9	7.98±1.2	3.08±0.9	7.5±1.2	0.52±0.1	504.3±1.98	99.5±0.8

Swelling index

The swelling index of all batches were calculated and it was found that the swelling index ranged between 2-3 with tablets containing Eudragit L 100 having greater swelling than other polymers (Fig 5). Batches F1 to F3 containing HPMC K100M had swelling index in the range of 1.8 to 2.63, Swelling index for F4 to F6 batches containing sodium CMC ranged between 2.46 to 2.6. For F7 to F9 (Eudragit L100) the index was highest in the range of 2.83 to 3.03. Swelling

capacity is of importance since it regulates the mucoadhesive property of the formulation and enhances the adhesive material's adsorption onto the mucosa.²⁴ The concentration of mucoadhesive agent increases the swelling. For all batches a slow and gradual increase in swelling of the vaginal tablets was observed. The swelling polymer forms a matrix with a numerous tortuous channel through which the drug diffuses. Thus, swelling of polymer will not only affect mucoadhesion but also release of drug from the polymer matrix.²¹

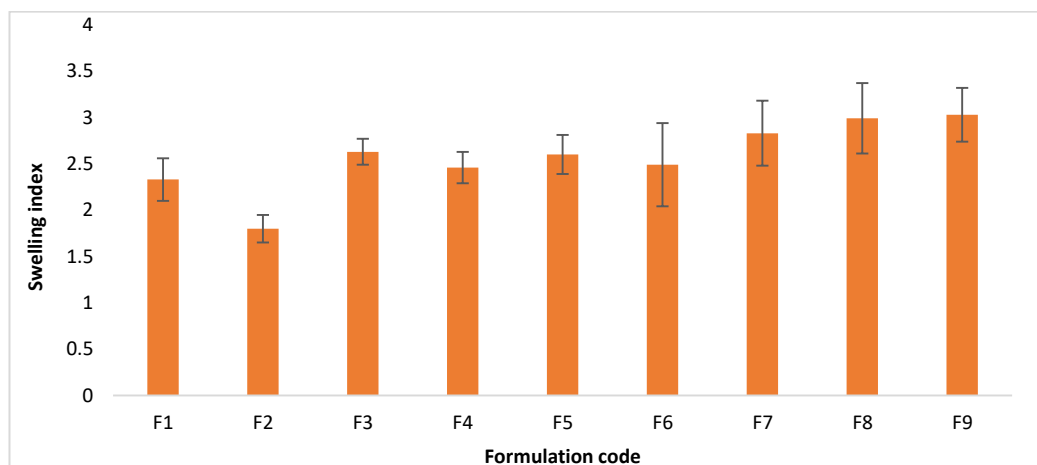


Figure 5: Swelling index of batches F1-F9 (Mean±SD (n=3))

In vitro dissolution studies

The dissolution studies of all batches were carried out in simulated vaginal fluid at pH 4.5. The dissolution data shows the effect of the polymer type and ratio on the dissolution of CTZ mucoadhesive vaginal tablets. In all the formulations, around 9 to 31 % release of CTZ was observed within the first 1 h and which gradually increased up to 8 h. The release of

the drug from F1 to F3 batches was 78.84%, 71.25% and 65.31% in 8h. In formulation F4, F5 and F6 containing sodium CMC in different ratios the release was approximately 61 to 69% in 8h. In formulations F7 - F9 containing Eudragit the release ranged from 65 to 70% in 8 h (Fig 6). The release of the marketed vaginal tablet, i.e., Candid-V6, was 75.45% at 8h. All batches showed nearly comparable release to the marketed tablets.

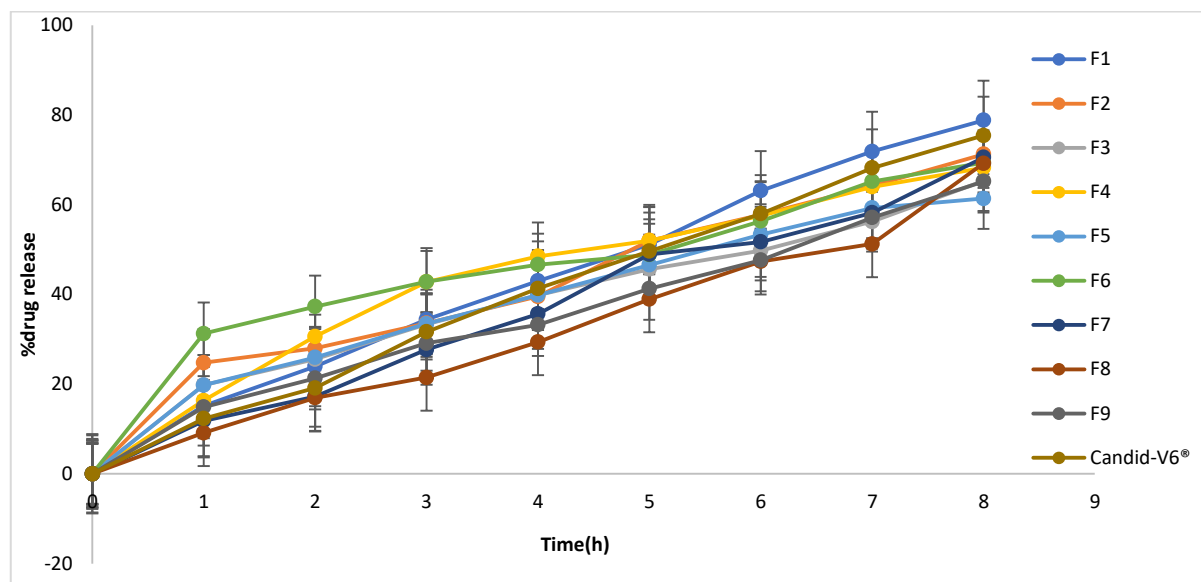


Figure 6: *In vitro* drug release of CTZ (Mean±SD (n=3))

***In vitro* release kinetics model**

The *in vitro* release data was fitted to different kinetic models such as zero-order, first order, Higuchi and Korsmeyer-Peppas as shown in (Table 4). The regression coefficient indicated that all formulations followed Korsmeyer- Peppas dissolution model. The value of n (release exponent) $0.45 < n < 0.89$ indicated non-Fickian drug release. When the formulation is in contact with the

dissolution media, the media penetrates the polymer matrix leading to disentanglement and subsequent dissolution/erosion of polymer chains resulting in the release of the drug molecules from the dosage form. According to another theory, the glass-rubbery transition of the polymer matrix leads to an increase in the mobility of polymeric chains allowing the drug molecules to dissolve and diffuse through the gel layer.²⁵

Table 4: Values of Correlation Coefficient (r^2) and Release Exponent (n) of Clotrimazole vaginal Tablet Formulations

Formulation Code	Zero order	First order	Higuchi	Korsmeyer-Peppas		Best fit model
	R^2	R^2	R^2	R^2	Slope(n)	
F1	0.893	0.915	0.958	0.996	0.595	Peppas
F2	0.974	0.983	0.974	0.982	0.748	Peppas
F3	0.965	0.972	0.96	0.988	0.504	Peppas
F4	0.956	0.969	0.978	0.992	0.606	Peppas
F5	0.974	0.974	0.982	0.989	0.602	Peppas
F6	0.976	0.935	0.975	0.997	0.669	Peppas
F7	0.954	0.915	0.981	0.986	0.593	Peppas
F8	0.958	0.958	0.953	0.978	0.519	Peppas
F9	0.964	0.923	0.964	0.989	0.786	Peppas

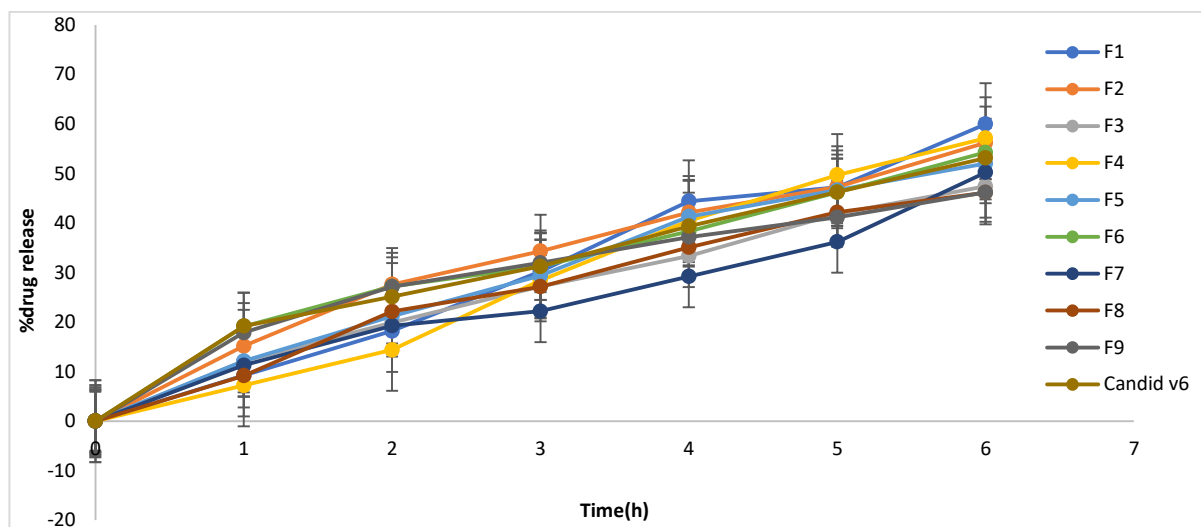
***Ex vivo* diffusion studies**

The diffusion studies of all batches were carried out in simulated vaginal fluid at pH 4.5 using Franz diffusion apparatus at 50 rpm. Formulations F1 to F9 contain different mucoadhesive polymers. The release of the drug form F1 to F3 batches was 59 to 47% in 6h and the flux was calculated (table 5). In formulation F4, F5 and F6 containing sodium CMC in different ratio the release was approximately 51 to 57% in 6h. In formulations F7-F9 containing Eudragit L100 the release ranges from 43 to 50%. The release of the marketed vaginal tablet, i.e., Candid-V6, was 53.12% at 6h

and the calculated flux was $0.1895 \text{ mg h}^{-1}\text{cm}^{-2}$ (Table 5). Among the all batches F7-F9 containing Eudragit L100 showed the greater flux to compare sodium CMC and HPMC K100 M (Fig 7). The Eudragit L100 containing batches were slow *in vitro* and *ex vivo* drug release because they have more swelling index compare to other polymer, because they have required more distance travelling in their matrix as compare to sodium CMC and HPMC K100 M. The marketed tablet i.e., Candid-V6 release was 53% and the calculated flux was $0.1895 \text{ mg h}^{-1}\text{cm}^{-2}$ are nearly comparable F2 batch containing HPMC K.

Table 5: Flux of vaginal tablets (Mean±SD (n=3))

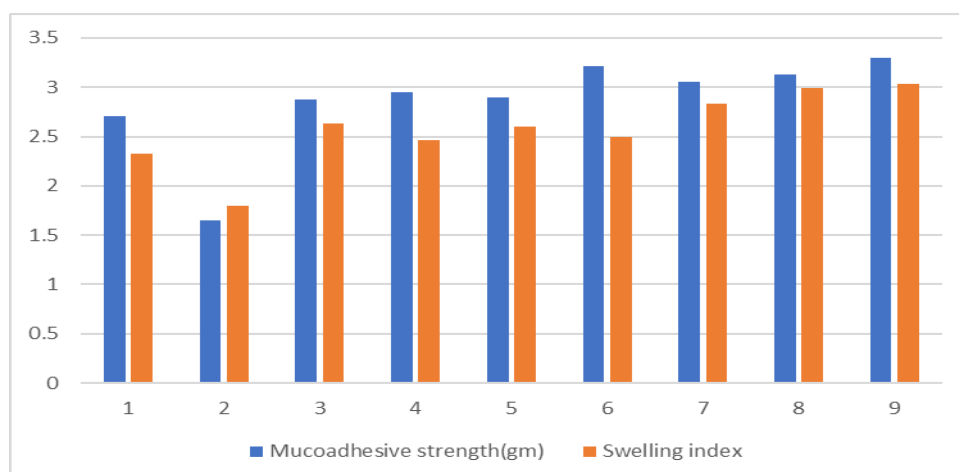
Formulation code	Flux($\mu\text{g}/\text{cm}^2/\text{min}$)
F1	0.2905±0.54
F2	0.1945±0.78
F3	0.1423±0.82
F4	0.1564±0.91
F5	0.1613±0.87
F6	0.1478±0.82
F7	0.1246±0.54
F8	0.1176±0.72
F9	0.1486±0.98
Candid-V6	0.1895±0.65

**Figure 7: Ex vivo drug release of CTZ (Mean±SD (n=3))**

Mucoadhesive strength

The concentration of mucoadhesive agent had an obvious positive effect on mucoadhesive strength. As the amount of mucoadhesive agent increases, the mucoadhesion strength also increases. The high mucoadhesive agent concentration indicated stronger mucoadhesion on sheep vaginal tissue. HPMC K100 M, Sodium CMC, and Eudragit L100 are anionic polymers which form strong hydrogen bonds with mucin, hence attachment to the mucosal layer is strong. Additionally, the polymer chains of the polymer interpenetrate the mucin lining the mucosal membrane, giving better mucoadhesivity. The mucoadhesive strength of

the tablets ranged from 1.654 to 3.294 g. The F3, F6 and F9 with higher concentration of polymers showed greater mucoadhesive strength. Amongst all polymerstables prepared with Eudragit L100 displayed greater mucoadhesive strength than sodium CMC and HPMC K100 M. There is a correlation between the percentage of swelling and the mucoadhesive strength.²⁵ The initial swelling is due to hydration, which aids the adhesion of tablets. A further increase in swelling is induced by over extension of hydrogen bonds and other forces such as van der Waals force and electrostatic forces.²⁶ These will result in lower mucoadhesion as represented by (Fig 8).

**Figure 8: Correlation between swelling index and mucoadhesive strength of vaginal tablet (Mean±SD (n=3))**

CONCLUSION

In the present work mucoadhesive vaginal tablets of clotrimazole were prepared wherein polymers were used to prepare solid dispersions of the drug for solubility enhancement. The same polymers also functioned as matrix polymers thereby playing a dual role. Solid dispersion technique is a simple and effective method for improving dissolution of clotrimazole. *Ex vivo* diffusion studies revealed good diffusivity of the drug through all polymer matrices with highest flux recorded with HPMC K100M. The mucoadhesive strength was good for all polymers with highest adhesion observed in case of Eudragit L100. Mucoadhesion will ensure longer residence of the drug in the vaginal cavity thereby showing improved therapeutic efficacy than conventional oral tablets.

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Conflict of interest

The authors report no conflict of interest, financial or otherwise.

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