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Research Article

FORMULATION, OPTIMIZATION AND EVALUATION OF MUCO-ADHESIVE VAGINAL FILMS OF TIOCONAZOLE

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ABSTRACT

Vaginal candidiasis is considered a frequent opportunistic mucosal infection and the second most common cause of vaginitis after bacterial vaginosis. In this work, different vaginal films based on different concentrations of polymer chitosan, hydroxyl propyl methyl cellulose containing tioconazole, were developed and thoroughly characterized to improve the conventional therapeutics of vaginal candidiasis. Mechanical properties, swelling, adhesiveness and antifungal activity were evaluated. The purity of drug was analyzed by Differential scanning calorimetry (DSC) and Fourier transform infrared spectroscopy (FT-IR). Films showed homogeneous surfaces and presented similar mechanical properties and adhesiveness. Time-kill studies displayed that films were active against *Candida albicans* and does not cause any harm to natural vaginal flora *i.e. Lactobacilli Acidophilus*. The system based on 2% chitosan and 1% hydroxyl propyl methyl cellulose with 20% PEG 400 as plasticizer presented fast antimicrobial activity as well as the lowest swelling these indicates that films based on chitosan and hydroxyl propyl methylcellulose could be a promising alternative dosage form for the treatment of vaginal candidiasis.

Keywords: Tioconazole, chitosan, HPMC, Vaginal Candidiasis.

1. INTRODUCTION

Vaginal candidiasis is considered a frequent opportunistic mucosal infection in women, being the second most common cause of vaginitis after bacterial vaginosis. The disease affects 70-75% women at least once in their lifetime and around 50% of patients experience a recurrence. Although different Candida species may produce this disease, *Candida albicans* is the most prevalent yeast causing this infection. Vaginal candidiasis is commonly treated using azole antifungals, such as fluconazole, miconazole, itraconazole, clotrimazole, econazole, ketoconazole and tioconazole [1].

Tioconazole (TCZ), (1[2-(2-chloro-3-thienyl) methoxy-2-(2,4-dichlorrophenyl) ethyl]-H-imidazole) is an imidazole antifungal agent with a broad spectrum of activity against a variety of microorganisms. This drug has been shown to hold higher activity against *C. albicans* than clotrimazole, econazole, ketoconazole and miconazole [2]. This could be due to the fact that TCZ possesses antifungal activity even when yeast cells are in the stationary phase, while common antifungal agents such as ketoconazole and miconazole display with antimicrobial activity only when yeasts are in the growth phase.

The effectiveness of a treatment is not only determined by the antifungal compound type, but also by the development of an adequate dosage form, which is determinant in the biological activity of a therapeutic system. Particularly, pharmaceutical dosage forms for local vaginal delivery need to remain in the site of infection as long as possible and to be able to release the active compound according to the treatment. The use of conventional vaginal formulations such as creams, gels, pessaries, and foams is discouraged due to their poor retention in the vaginal tract by the tract's self-cleansing action. Other conventional formulations such as vaginal tablets and ovules show good retention abilities, but both are rigid and may produce discomfort. Alternative bioadhesive vaginal formulations such as films are suitable forms to achieve effective drug release for extended periods of time [3, 4]. In addition; these films present more flexibilitythan tablets and ovules, which may improve patient's compliance. Several biocompatible polymers such as chitosan (CH) and hydroxyl propylmethyl cellulose (HPMC) have been employed to develop mucoadhesive films. Hydroxypropyl methyl cellulose (HPMC) is a non ionic polymer, is a semi-synthetic cellulose derivative usually employed in the

pharmaceutical industry, mainly as gelling agent and to control the release of pharmaceutical drugs. Chitosan is a cationic natural polymer widely used in pharmaceutical applications shows attractive biological properties including biocompatibility, biodegradability, non toxicity, and physiological inertness [5].

The aim of this work was to develop, optimize and thoroughly characterize novel TCZ film dosage forms in order to improve the therapeutics of vaginal candidiasis.

2. MATERIAL AND METHODS

2.1. Chemicals

TCZ raw material of pharmaceutical grade (BP 2002) was acquired from Themis Medicare Pvt Ltd. (Uttarakhand, India.) During the experiments, the drug was kept in a desiccator. Double-distilled water was used for the preparation of aqueous solutions. CH (230 KDa average molecular weight and 80% of N-deacetylation) and HPMC E4M was purchased by Research lab fine chem industries (Mumbai, India) and PEG 400 was purchased from Analab fine chemicals (Mumbai, India) All other chemicals were of analytical grade.

2.2. Methods

2.2.1. Optimization Study -Experimental Design

Based on result obtained for preliminary batches 3^2 factorial design was used.

X_1= Chitosan concentration (% w/v)

X_2= HPMC E4M concentration (% w/v)

The responses for the Muco-adhesive films were Y_1 - Drug Release, Y_2 - Swelling index and Y_3 - Thickness

Table 1: Actual and Coded value for preparation of films, as per 3^2 factorial design

Factor	Name	Unit	Coded levels with the concentration		
			-1	0	+1
X_1	Chitosan	% w/v	2	2.5	3
X_2	HPMC E4M	% w/v	0.6	0.8	1

2.2.2. Film preparation

Films were prepared by solvent evaporation method as shown in Table 1. CH solutions (2, 2.5 and 3% w/v) were obtained dispersing CH in 1.5% v/v acetic acid (v/v). TCZ was suspended in PEG 400 used as plasticizer and added to the CH solution. Aqueous solutions of HPMC E4M (0.6, 0.8 and 1% w/v) were prepared and stirred overnight. Then, CH solution was dripped over HPMC E4M solution at 40°C to avoid precipitation and stirred at 200 rpm for 1 h on mechanical stirrer (Remi 1mL). Finally, the solutions were casted on 10 cm diameter Petri dishes and dried in oven at 40°C. Unloaded films were developed following the sameprocedure but without adding TCZ to the mixtures. Dried films were removed from the Petri dishes and conditioned in a chamber at 25°C and 80% RH for 24 h [6].

Table 2: Composition of loaded films as per 3^2 factorial designs

Ingredients	Batches								
	B1	B2	B3	B4	B5	B6	B7	B8	B9
Tioconazole (mg)	220	220	220	220	220	220	220	220	220
Chitosan (% w/v)	2.5	2	3	3	2.5	2	2.5	3	2
HPMC E4M (% w/v)	0.6	0.6	0.6	1	1	0.8	0.8	0.8	1
PEG 400 (% w/w)	20								

2.3. Film characterization

2.3.1. Pre-formulation Studies

Testing is the first step in the rational development of dosage form of a drug. It can be defined as the investigation of physical and chemical properties if drug substances alone or in combination with excipients. The overall objective of pre-formulation studies is to generate information useful to formulator in developing stable and bio-available dosage form which can be mass produced. The goals of pre-formulation studies are: To establish the necessary physicochemical characteristics of a new drug substances.To establish its compatibility with different excipients.

2.3.2. Characterization of Tioconazole

Tioconazole powder sample was analyzed for physical properties like color, odor and appearance.

2.3.3. Solubility Analysis

The solubility of drug was checked in different solvents like, water, methanol ethanol, chloroform, ethyl acetate etc [7].

2.3.4. Detection of Melting Point

The sample was loaded in to sealed capillary (melting point capillary) which was then placed in melting point apparatus. The sample was then heated and as the temperature increase the sample was observed to detect the phase change from solid to liquid phase. The temperature at which the phase changes occur gives the melting point.

2.3.5. Calibration Curve of Tioconazole

Accurately weighed 50 mg of drug was dissolved in 50 ml of methanol and thus 1000 mcg solution was prepared. The UV spectrum was recorded in the range of 200-400 nm using shimadzu UV 1700. The Wavelength of maximum absorption (λ max) was determined. From stock solution different concentrations were prepared in the range of 1-25 mcg/ml of Tioconazole in methanol for standard curve. Then these solutions are analyzed by UV- Visible spectrophotometer at λ max of drug. The calibration curve was plotted as concentration on X- axis and absorbance on Y- axis.

2.3.6. Drug - Excipient Compatibility Study

2.3.6.1. FTIR Spectroscopy

The objective of this investigation was to identify a stable storage condition for drug in solid state and identification of compatible excipients for its information. This can be confirmed by carrying out by infrared light absorption scanning spectroscopy studies (IR). Drug and polymer was mixed in the equal ratio and finally grounded and intimately mixed with approximately 100 mg of dry potassium bromide powder. Grinding and mixing can be done with mortar and pestle. The mixture is then pressed into a transparent disk in an evacuable die at sufficiently high pressure. Suitable KBr disks or pellets can often be made using a simpler device such as a hydraulic press. The base line correction was done using dried KBr. Then, the spectrum of dried mixture of drug and potassium bromide was scanned from 2000cm^{-1} to 400 $cm^{-1.}$

2.3.6.2. Differential Scanning Colorimetry

DSC studies of pure Tioconazole were carried out. Accurately weighed sample were carefully added in DSC aluminum cup and heating curve were recorded in temperature range 40-280°C at heating rate of 10°C/ min under inert atmosphere. The study was carried out using different scanning calorimeter [8].

2.3.7. Thickness Uniformity

Micrometer was utilized to measure the thickness with a least count of 0.01 mm. Films were tested from five different positions, Mean and standard deviation (SD) values were calculated.

2.3.8. Uniformity of Weight

The film was cut into portions of size 2×2 cm^2 and weight of each portion was taken individually, mean and standard deviation values were calculated.

2.3.9. Folding Endurance

Folding endurance was determined by repeated folding of the film at the same place till it broke. The number of times the film can be folded without breaking was considered as folding endurance [9].

2.3.10. Swelling Index

Film swelling study was carried out in a 2% agar media plates prepared in a simulated vaginal fluid pH 4.5 (SVF). Each film sample with a surface area of 3×3 cm^2 was weighed (Wo) and placed in agar plate. The films were reweighted (Wt) after specific time interval upto 3 hrs. The swelling index was determined by taking 3 films of each formulation and the films were allowed to swell for 3 h on the surface of 2% agar plate [10].

The degree of swelling was calculated as follow:

$$\textbf{Swelling Index} = (W_t - W_0)/\ W_0 X\ 100$$

2.3.11. Drug Content Uniformity

A square piece of film measuring 4 $cm^2$was cut and drenched in a beaker containing 100 ml of SVF. The contents were stirred by ultra-sonicator for 24 h to dissolve the patch. Suitable aliquots were made and filtered. The absorbance of the filtered solution was found out by using UV-visible spectrophotometer at 240 nm.

2.3.12. In vitro diffusion study

A section of dialysis membrane was positioned between donor and receptor compartment of Franz diffusion cell. A strip of muco-adhesive film (2×2 cm^2) was placed on it which was wetted with 1 ml of SVF. The receptor compartment was filled with 15 ml of SVF, which was magnetically stirred. The aliquots (1 ml) were withdrawn at predetermined time intervals and replaced with same volume of SVF of pH 4.5. The samples were analyzed for drug content using UV-Spectrophotometer at 240 nm [7, 11].

2.3.13. Surface pH

The surface pH was determined by taking 3 films of each formulation and the films were allowed to swell for 2 h on the surface of 2% agar plate. The surface pH was measured by using a pH paper placed on the surface of the swollen film. A mean of 3 readings was recorded.

2.3.14. Antifungal activity and Lactobacillus inhibition

Antifungal studies were performed for *C.albicans* in sabouraud's agar medium by the cup plate method. The cups cut in the inoculated solidified media were filled with different formulations using sterilized syringes. The optimized mucoadhesive film swelled in 2 mL of sterile water applied into the cups. The covered Petri plates were incubated at 22°C in the biological oxygen demand incubator for 48 h. The zone of inhibition was measured at the end of 48 h. Lactobacillus is nonpathogenic bacteria normally present in the vagina to maintain its acidic pH. The formulation should not adversely affect the flora of the human vagina. Lactobacillus inhibition was also studied using Lactobacillus acidophilus by the same procedure described previously [11].

2.3.15. Mucoadhesive Strength

A strip of mucoadhesive film (2×2 cm^2) was cut and smeared onto the surface of flat faced disk attached to the top pan balance. The disk was then placed to the dialysis membrane wetted with SVF pH 4.2 attached to a flat immovable surface.

After a contact time of 2 min, weights were gradually added on the other side of the top pan balance and the weight required for detaching the mucoadhesive film from mucosa was calculated as the strength [12].

Mucoadhesive Strength (dyne/ cm^2) = mg/A

Where,

m= Weight required for detachment in gram

g= Acceleration due to gravity

A= Area of mucosa exposed

2.3.16. Stability Studies

Stability studies of films were performed at 5±3°C and 25±2°C and 65±5% RH for 3 months. Tiocnazole films were sealed in sachets prepared by heat sealing of aluminum foil placed in cartons, and stored at accelerated stability conditions (5°C and 25°C and 65±5% RH). Samples were evaluated periodically at the end of 3 months for color, odor, softening time, swelling index, folding endurance and drug content characteristics of Tioconazole in film.

Fig. 1: Modified Muco-adhesive Tester

3. RESULTS AND DISCUSSION

3.1. Pre-formulation study - Organoleptic properties of drug

The color, odor and taste of the drug were characterized and recorded using descriptive terminology; the results are shown below:

Table 3: Results of Organoleptic Properties of Tioconazole

Sr. No.	Parameter	Observation
1	Color	White
2	Taste	Tasteless
3	Odor	Odorless
4	Appearance	Whitish Powder

3.2. Solubility of drug

The solubility of the drug was checked in different solvents. This might be helpful in selection of a suitable solvent to dissolve drug as well as excipients used in formulations. Solubility of drug depends on pH, ionic strength, temperature, buffer concentration.

Table 4: Solubility data of Tioconazole

Sr. No.	Solvent	Solubility
1	Methanol	Very soluble
2	Ethanol	Very soluble
3	Ethyl acetate	Soluble
4	Chloroform	Soluble
5	Water	Very slightly soluble

3.3. Melting point

The Reported melting point of Tioconazole was found to be 165-172°C by capillary method.

Table 5: Melting point of Tioconazole

Property	Observation	
	Reported M.P.	Observed M.P.
Melting point	82-83°C	82-84°C

3.4. Partition Coefficient

The partition coefficient of drug was found to be 6.77.

3.5. Calibration Curve of Tioconazole

Tioconazole solution which was scanned in range of 400 nm to 200 nm showed maximum absorption at 240 nm. Absorbance of prepared solution was measured at 240 nm using UV Spectrophotometer.

3.6. *FTIR Spectroscopy*

The peaks show that the characteristics peaks of Tioconazole which shows that the drug is Tioconazole. The FTIR spectra of pure drug Tioconazole and physical mixture of Tioconazole samples are shown in Fig.3 and Fig. 4 respectively. The characteristic of IR absorbance peaks of Tioconazole compared with IR spectra of Tioconazole physical mixture, which shows similarity in peaks of physical mixture and indicates no interaction between drug and polymers.

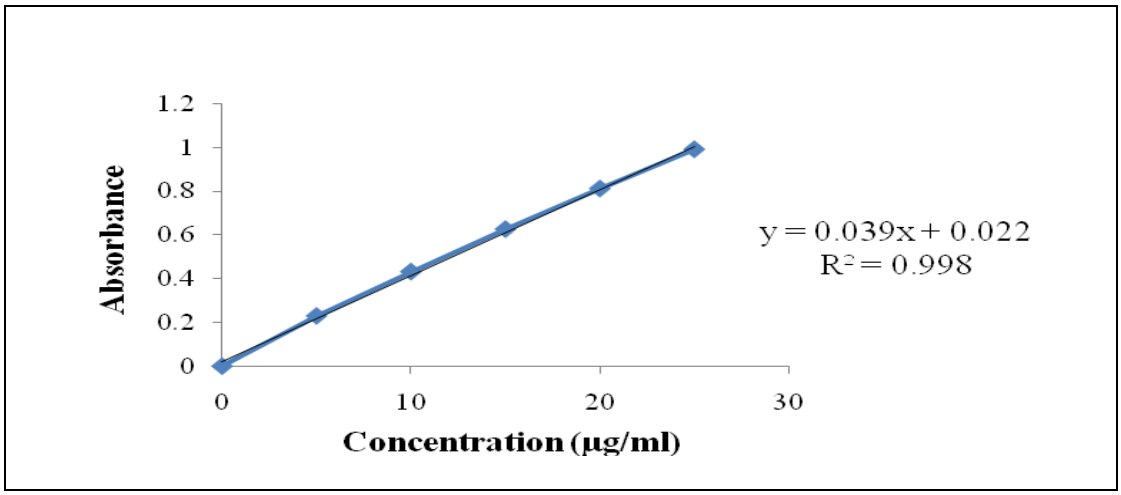

Fig. 2: Calibration Curve of Tioconazole

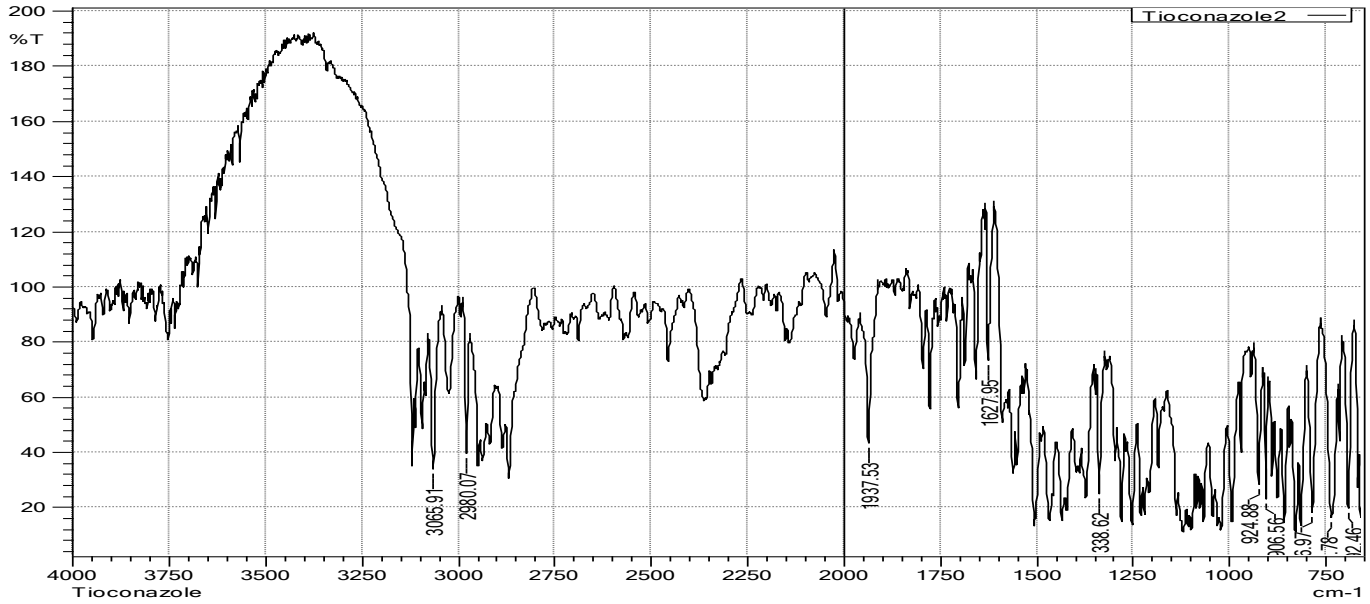

Fig. 3: FTIR Spectrum of Tioconazole

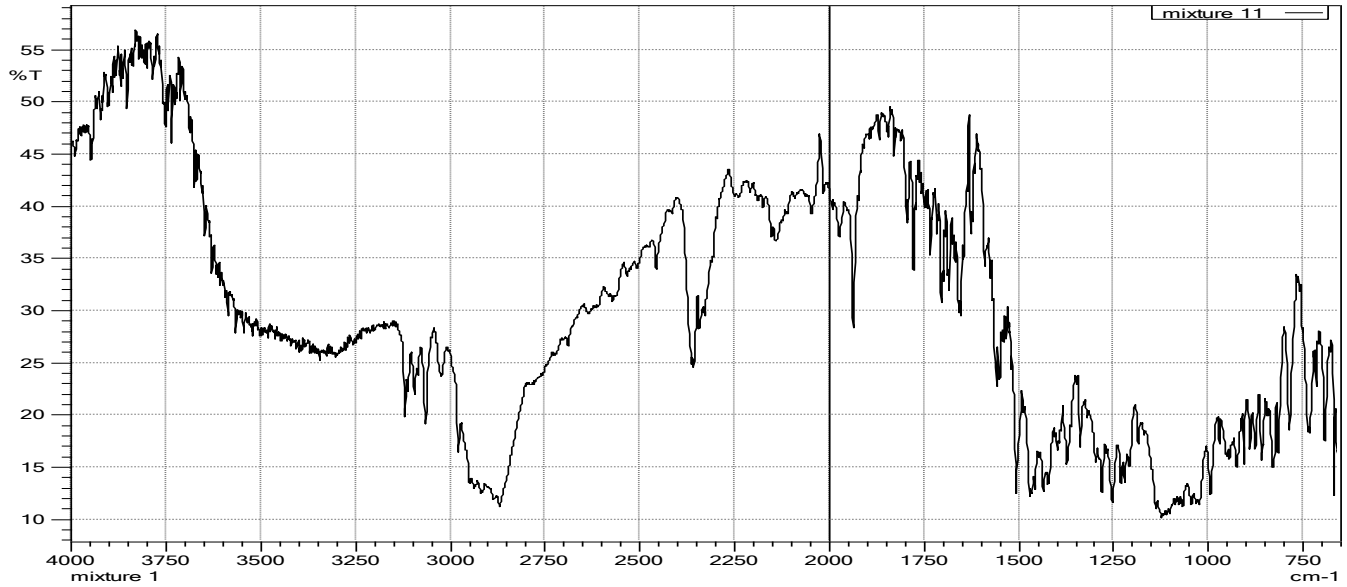

Fig. 4: FTIR Spectrum of Physical Mixture of Tioconazole

Table 6: FT-IR Peaks of Tioconazole

Reference Peaks (cm^{-1})	Obtained peaks (cm^{-1})	Functional groups	Stretching/ Bending
1675-1600	1627.95	C=C (Alkenes)	Stretching
1470-1430	1470.85	C-H	Deformation
1335-1250	1290.28	C-N	Stretching
1450-1300	1340.62	C=C	Stretching
750-650	737.78	C-S	Stretching
800-600	692.46	C-Cl	Stretching

Table 7: FT-IR Peaks of physical mixture

Obtained peaks (cm^{-1}) drug	Obtained peaks (cm^{-1}) sample	Functional groups	Stretching/ Bending
1627.95	1627.95	C=C (Alkenes)	Stretching
1470.85	1470.85	C-H	Deformation
1290.28	1290.28	C-N	Stretching
1340.62	1340.62	C=C	Stretching
737.78	737.78	C-S	Stretching
692.46	692.46	C-Cl	Stretching

3.7. DSC of Tioconazole

The purity of Tioconazole drug was confirmed by comparison of the differential scanning calorimetry with the spectrum of the standard drug. Differential scanning calorimetry studied indicated a sharp endothermic peak at 84.33°C for Tioconazole which was also detected in the thermograms of physical mixture, signifying no interaction between drug and polymers

3.8. Evaluation on Mucoadhesive Vaginal Films

The different batches of muco-adhesive vaginal films prepared using 3^2 factorial designs were evaluated for following parameters.

3.8.1. Muco-adhesive Strength of different formulation

Use of polymers with strong bioadhesive capacities can significantly limit the total clearance of the formulation from the vaginal cavity. An optional system for vaginal drug delivery would therefore be film enough for easy administration yet would not undergo rapid initial clearance, and would have sufficient interaction with the mucosal surface to limit its clearance for extended time periods. Residence time of any formulation in vaginal cavity depends on the mucoadhesive strength of polymers. Formulation B9 was found to be 127.67gm /cm^2 and it show sufficient mucoadhesive strength.

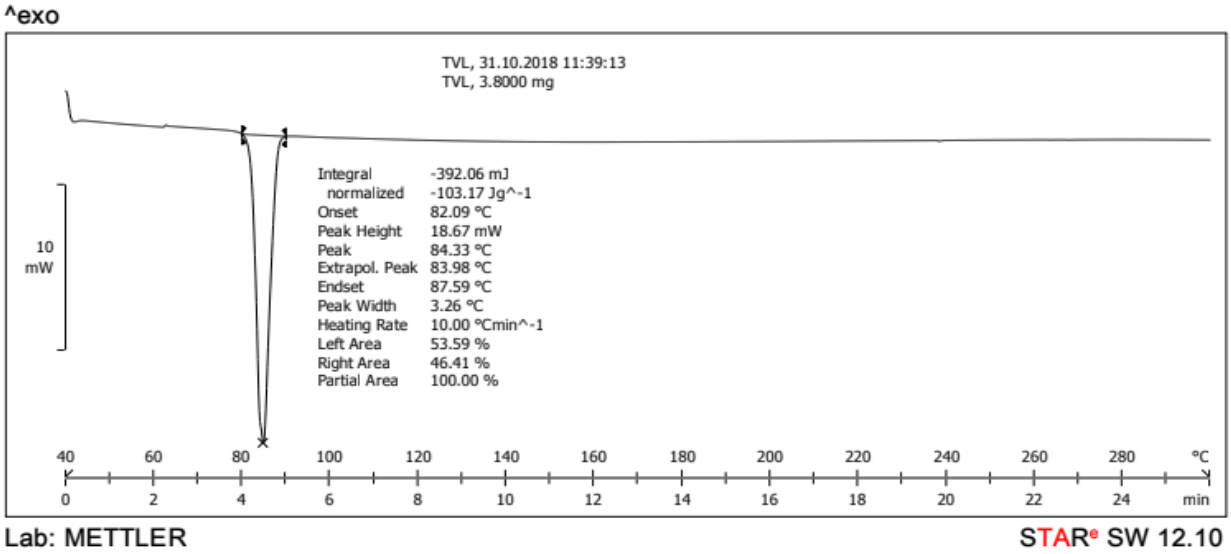

Fig. 5: DSC Spectrum of Sample Tioconazole

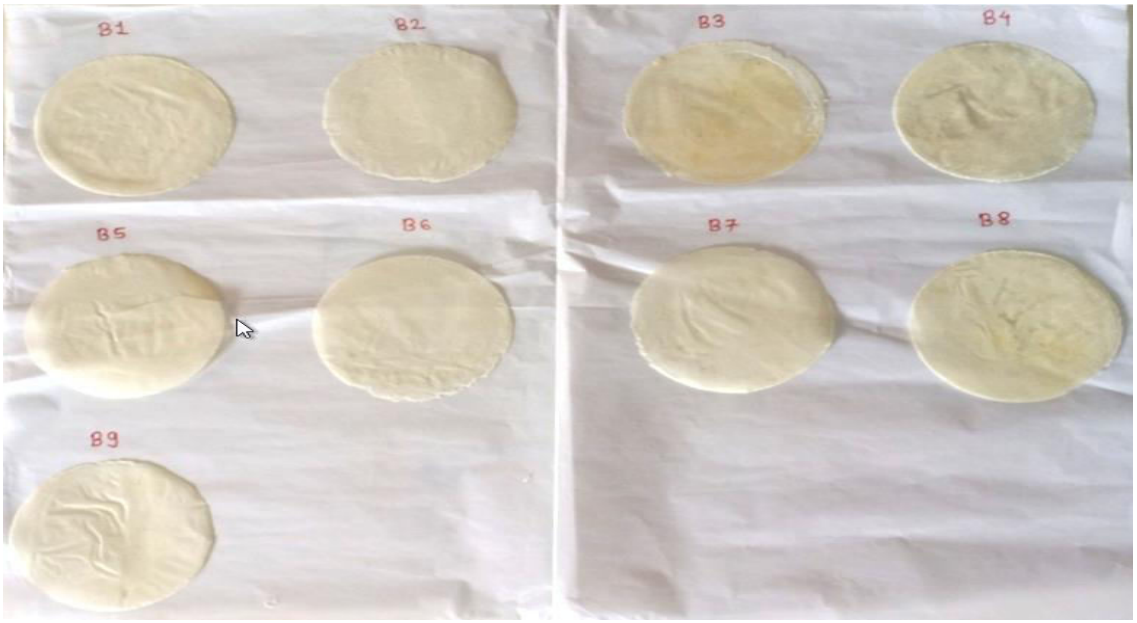

Fig. 6: Formulated vaginal patches for all different batches (B1 to B9)

Table 8: Evaluation parameters of the prepared vaginal films

Batches	Appearance	Weight (gm)	Thickness (mm)	Tensile Strength	Surface pH	Folding Endurance	Drug Content (%)
B1	Opaque	0.031±0.01	0.19 ±0.01	100.67±5.77	5	> 300	96.03
B2	Opaque	0.031±0.05	0.14 ±0.01	91.67±2.88	4.5	> 300	95.98
B3	Opaque	0.035±0.06	0.234±0.016	99.67±1.52	4.5	> 300	97.88
B4	Opaque	0.037±0.05	0.154±0.015	101±3.60	4.5	> 300	97.79
B5	Opaque	0.030±0.01	0.204±0.005	110±6.22	5	> 300	98.27
B6	Opaque	0.032±0.02	0.104±0.015	105±5.9	4.5	> 300	96.84
B7	Opaque	0.033±0.09	0.13 ± 0.01	94.34±4.04	4.5	> 300	98.76
B8	Opaque	0.036±0.05	0.193±0.005	98.67±4.15	4.5	> 300	97.97
B9	Opaque	0.027±0.01	0.143±0.015	115±5.06	4.5	> 300	98.85

3.8.2. Swelling Index

Use of HPMC E4M with Chitosan can significantly limit the swelling of the formulation in the vaginal cavity. As the excess swelling of the films due to the chitosan may cause the rapid clearance of the formulation from the vaginal cavity and may cause the difficulty in drug release in vagina. This developed formulation with the combination of chitosan and HPMC E4M shows less swelling index as compared to other batches. Residence time of any formulation in vaginal cavity affected by the swelling index of polymers. Formulation B9 was found to be 47.33% swelling index.

3.8.3. In vitro drug release studies

From permeability study it was observed that the drug permeation increases with an increase in chitosan concentrations and decrease in mucoadhesive polymer, HPMC E4M. The result clearly showed that chitosan and HPMC E4M affect the drug release. As the concentration of chitosan and HPMC E4M affect the drug release. The drug release for the formulated films was between 81.37 ±0.3 to 95.93±0.3. The optimized batch was B9.

3.8.4. Effect of Chitosan and HPMC E4M on Drug release

Final Equation in terms of Coded factors:

Drug Release =+84.22+11.02*A1+0.2700*A2+ 0.8650*B1+0.3050*B2

The graph reveals the contribution of Chitosan and HPMC E4M to drug release. As the sign of Chitosan and HPMC E4M both are positive, it is concluded that the as the both polymer have direct relation with the drug release.

The independent and response variable were related using polynomial equation with statistical analysis through Design-Expert software. The values of the coefficients X1 and X2 are related to the effect of these variables on the response. A positive sign of coefficient indicates a synergistic effect while a negative term indicates an antagonistic effect upon the response. The larger coefficient means the independent variable has more potent influence on the response.

Table 9: ANOVA for response surface linear model

Source	Effect on Muco-adhesive Strength	
	P- Value Prob>F	R- Squared
Model	0.0065	0.9528 Significant
A: Concentration of Chitosan	0.0023	
B: Concentration of HPMC E4M	0.3126	

p-value less than 0.050 indicates model A and B are found to be significant

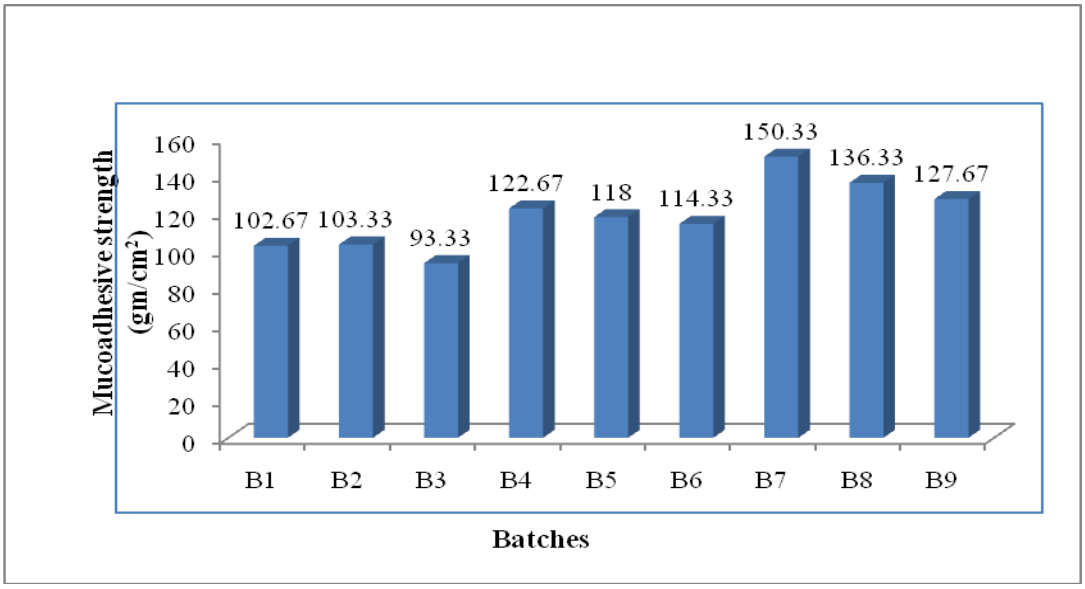

Fig. 7: Comparison of Muco-adhesive Strength of Different Formulations

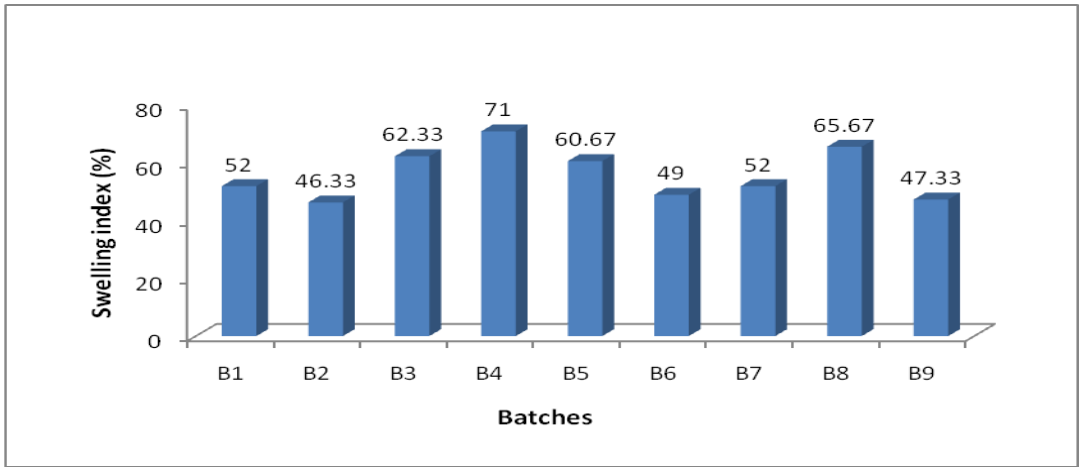

Fig. 8: Comparison of swelling index of different formulations

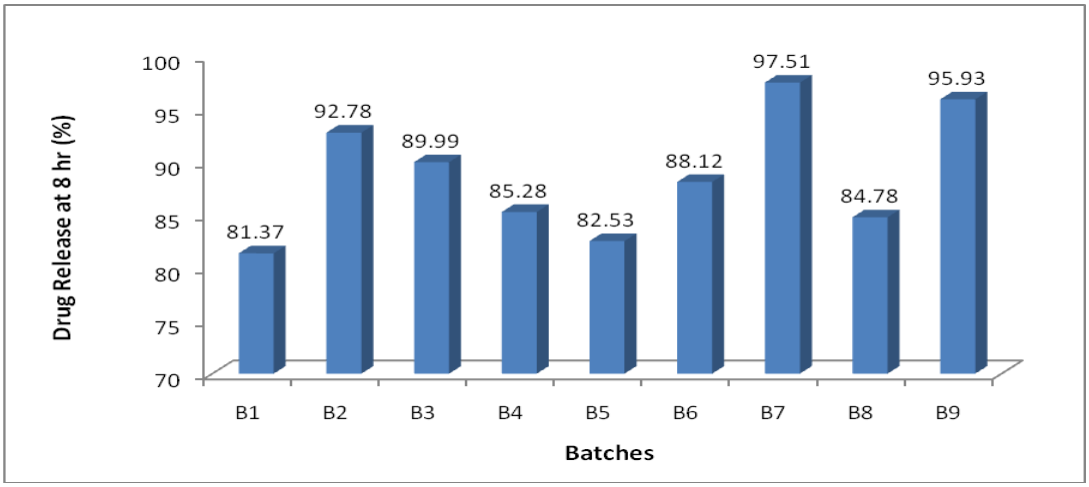

Fig. 9: Comparison of In vitro permeability of different formulations

3.8.5. Effect of Chitosan and HPMC E4M on Swelling Index

Final Equation in terms of Coded factors:

Swelling Index=

+56.62+10.02*A1+0.5611*A2+3.47*B1+0.1111*B2

The graph reveals the contribution of Chitosan and HPMC E4M to swelling index. As chitosan increases and HPMC E4M decreases the swelling index. It is concluded that the as the concentration of chitosan polymer have direct relation with the Swelling index.

Final Equation in terms of Coded factors:

Thickness= +0.1647+0.0233*A1- 0.0003*A2+ 0.0395*B1+0.0035*B2

The graph reveals the contribution of Chitosan and HPMC E4M to thickness. As chitosan increases and HPMC E4M decreases the thickness. It is concluded that the as the concentration of chitosan polymer have direct relation with the thickness.

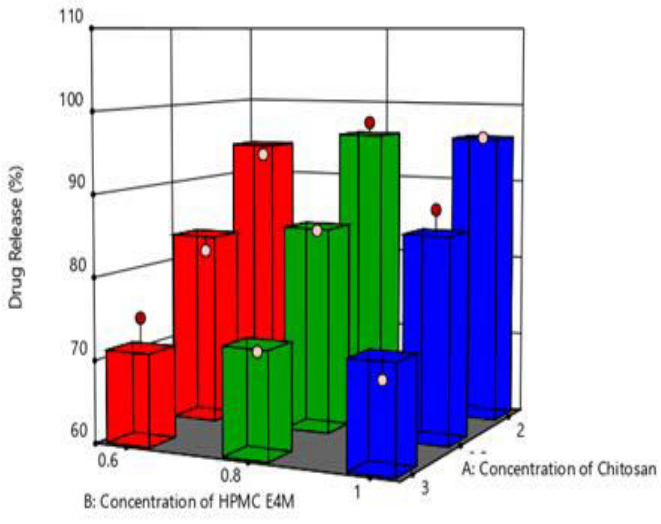

Fig. 10: 3D response surface plot showing effect of polymers on drug release

Table 10: ANOVA for response surface linear model

Source	Effect on Swelling Index	
	P- Value Prob>F	R- Squared
Model	0.0010	0.9819 Significant
A: Concentration of Chitosan	0.0004	
B: Concentration of HPMC E4M	0.0218	

p-value less than 0.050 indicates model A and B are found to be significant.

Table 11: ANOVA for response surface linear model

Source	Effect on Thickness	
	p-Value Prob>F	R- Squared
Model	0.0052	0.9576 Significant
A: Concentration of Chitosan	11.48	
B: Concentration of HPMC E4M	33.66	

p-value less than 0.050 indicates model A and B are found to be significant.

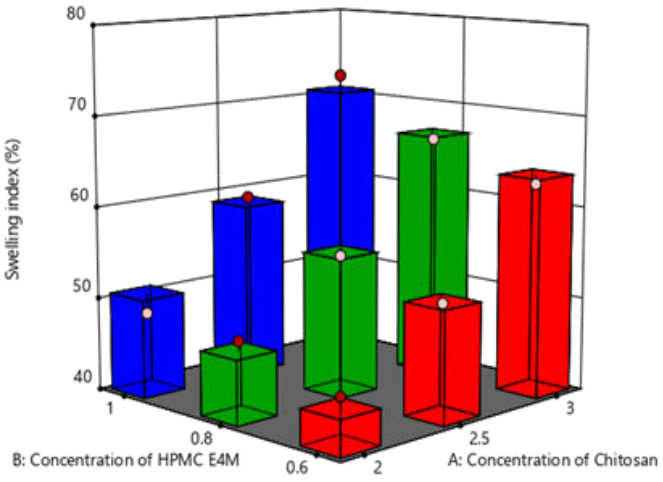

Fig. 11: 3D response surface plot showing effect of polymers on Swelling Index

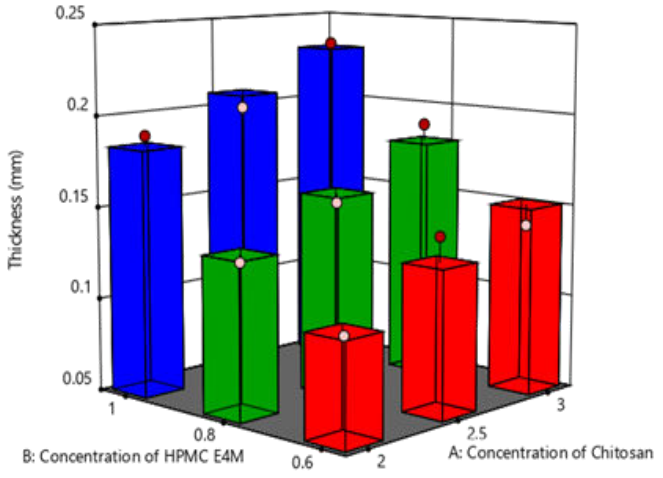

Fig.12: 3D response surface plot showing effect of polymers on Thickness

3.9. Antifungal Activity

The antifungal activity of Tioconazole films was evaluated by cup-plate method. The results were found encouraging. The zone of inhibition was found with the optimized formulation containing Tioconazole.

Antifungal study with Sabouraud culture showed that the Tioconazole was capable to control the growth of *C. albicans* for more than 12 h. Tioconazole had prolonged drug release and provided better contact with the wells cut in the plate. Microbial activity and *in vitro* safety profile of Tioconazole were not negatively affected by formulating Tioconazole films. Like bulk powder, Tioconazole effectively inhibited *C. albicans* growth. The Tioconazole showed significantly higher antifungal activity. The Zone of inhibition of optimized formulation batch (F9) was found to be 17.7±0.48 mm.

3.9.1. Compatibility of Films with Lactobacillus

Lactobacillus is a part normal flora in human vagina and maintains its acidic pH 4.2. Thus, optimized batch F9 should not adversely affect normal flora of vagina and should not inhibit growth of Lactobacillus. Tioconazole film did not induce any deteriorating effects on several strains of Lactobacillus as no loss of bacterial viability was observed.

3.10. Stability Study

Studies were carried out after storing the promising formulation (F9) at two different temperatures 5±3°C and 25±2°C temperature with 65±5% RH for 3 months. Table 12 and 13 Shows data for Appearance, Drug content, Swelling index, and folding endurance. The formulation F9 showed no change in appearance

after at 5±3°C temperature conditions. The drug content decreased from 98.85% to 97.76% after 90 days study. Also the swelling index of the formulation changed.

For storage condition of 25°C ± 2°C temperature with 65%±5% RH, there was no change in the appearance, folding endurance after 3 months. The drug content decreased from 98.85% to 96.78% after 90 days study. Also the swelling index of the formulation was changed.

Table 12: Optimized B9 formulation subjected to stability study at 5°C ± 3°C

Time Period	Appearance	% Drug Content	Swelling Index	Folding Endurance
Initial	White	98.85	47.34	<300
After 3 Months	White	97.76	48.21	<300

Table 13: Optimized B9 formulation subjected for stability study at 25±2°C

Time Period	Appearance	% Drug Content	Swelling Index	Folding Endurance
Initial	White	98.85	47.34	<300
After 3 Months	White	96.78	49.32	<300

4. CONCLUSION

Vaginal candidiasis is a fungal or yeast infection of the vulva and/or vagina. It causes a smelly, thick, white-yellow discharge that might be accompanied by itching, burning and swelling. It can also make walking, urinating and/or sex very painful. Vaginal candidiasis can be an occasional problem for even the healthiest woman. However, it's more common and severe in women with weakened immune systems. For many, a repeating or worsening vaginal yeast infection is the first symptom of HIV infection. Vaginal candidiasis (VC) is the most common reason why women look for the help of a gynecologist. It is estimated that nearly 75% of all adult women have had at least one genital yeast infection in their lifetime; at least 50% of these women will experience one or more recurrent episodes of VC. Of the 150 members of the yeast-like genus Candida, only 10 members are pathogenic in humans. *Candida albicans*is responsible for 90% of vaginal fungal infection cases; however, the noxious role in the genesis of VC has recently been stressed also for other Candida species, for example *C. glabrata*and *C. parapsilosis*.In this work, vaginal films based on combination of Chitosan and HPMC using PEG as plasticizer were successfully developed and characterized as an alternative dosage form for the treatment of vaginal candidiasis. Formulated films showed similar mechanical properties and adhesiveness. The films were able to swell for 24 h without suffering disintegration; however, films having higher concentration of Chitosan showed the highest swelling and, therefore, may produce discomfort after application. The developed films displayed faster activity against *Candida albicans* than TCZ pure drug, which is probably associated with the fact that TCZ is inside the films in amorphous state. Additionally, films presented controlled release of TCZ. The system based on Chitosan and HPMC with 20% PEG 400 as plasticizer *i.e.* formulation F9 showed fast and sustained antimicrobial activity and also the lowest swelling value. This formulation F9 showed good folding endurance and tensile strength. The swelling index, drug release and was found to be 47.34% and 95.93% for tioconazole respectively. Additionally, this formulation produced good mucoadhesive strength 127.67gm/cm^2, showing that this film is a promising alternative dosage form for the treatment of vaginal candidiasis with increased patient compliance.

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Conflict of Interest

The author declares manuscript has no conflict of interest.

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