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Formulation and Evaluation of Mucoadhesive Vaginal Film

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ABSTRACT:

Objective: The objective of the present work is to Formulate and evaluate mucoadhesive vaginal film for Treatment of vaginal infection.

Experimental Work: Women are frequently affected with vulvovaginitis, or inflammation of the vulva and vagina. In this study, a novel approach is developed to manage the vaginal infection. Mucoadhesive voriconazole vaginal films were prepared by solvent casting method. The polymers used for fabricating mucoadhesive film were HPMC-CP 50, Eudragit RS100 and Polyvinyl Pyrrolidone-K30. Polyethylene Glycol 400 was used as a plasticizer. The films were characterized for various parameters like: weight variation, thickness, folding endurance, surface pH, drug content, mucoadhesion strength and time and in-vitro drug release.

Result and Discussion: All the formulation showed pH in the range of vagina and had soft, smooth surface. Drug release of formulation batches showed sustained release pattern within 8 hrs with optimum mucoadhesive strength.

Conclusion: The mucoadhesive vaginal film is a promising novel drug delivery system for vaginal infections. The vaginal route is able to provide both local and systemic action. Hence, this system provides high permeability.

KEYWORDS: Mucoadhesion, vaginal infection, vaginal film

I. INTRODUCTION:

The vaginal route has grown in importance in contemporary medicine over the last three decades as a drug delivery system and is currently seen as a viable choice for a number of therapeutic approaches, particularly for conditions afflicting women. In order to manage local problems and achieve systemic effects, vaginal drug delivery has been said to offer a number of benefits.The vaginal route has traditionally been used to administer locally acting medications, including steroids, prostaglandins, labor-inducing and spermicidal agents, antibacterial, antifungal, antiprotozoal, and antiviral treatments.[1,2]

Mucoadhesion is the process by which a drug and an appropriate carrier adhere to the mucous membrane. Mucoadhesives are intended to extend the residence time of most of the drug administration routes, such as ocular, nasal, buccal, respiratory, gastrointestinal, rectal, and vaginal which are coated with the mucous layer. Mucoadhesion has the following mechanism:

i. Close contact (wetting or swelling phenomena) between a membrane and a mucoadhesive

ii. The mucoadhesive's interpenetration into the tissue or into the mucous membrane surface.[3]

In mucoadhesive vaginal drug delivery system, mucoadhesive molecules capable of delivering the active substance over extended periods at a predictable rate are included into a formulation. Mucoadhesive compositions are well-suited to the vagina. The vaginal mucous membrane or mucus layer lining its surface interacts with formulation ingredients to cause mucoadhesion.[3]

As a solid dosage form, vaginal film offers several benefits such as minimal product volume, discrete usage, less leakage, and no applicator is required. The vaginal thin film has significantly outperformed other topical gels and creams, making it a suitable platform to be modified to treat bacterial vaginosis (VB). Vaginal films are currently most commonly used as spermicides and on demand contraception, while they are also frequently used as lubricants and deodorants. For example, the Vaginal Contraceptive Film (VCF) is a widely available over-the-counter vaginal film that contains nonoxynol-9 as a spermicide prior to intercourse. The use of these films has been expanded to assess their ability to prevent bacterial and fungal infections of the vagina. Since BV is the most prevalent vaginal infection, a number of studies investigated innovative approaches utilizing this mucoadhesive polymeric platform.[4,5]

Women of reproductive age are most frequently affected with vulvovaginitis, or inflammation of the vulva and vagina, which can have a number of underlying causes. Candidiasis is a fungal infection

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caused by Candida albicans, a polymorphic opportunistic fungus; vulvovaginitis resulting from candidiasis is also known as vaginal candidiasis.[6,7]Infections cause severe vaginal itching and a white, curdy, or cottage cheese-like discharge.[8]

II. MATERIALS AND METHOD:

Voriconazole was obtained as a gift sample from Gufic Bioscience Ltd Navsari, India. All other excipients were used of Analytical grade.

2.1 Preparation of mucoadhesive vaginal films:

The mucoadhesive vaginal films were prepared by solvent casting method. Different mucoadhesive vaginal film formulation of voriconazole were using varying amounts of polymers along-with PEG-400 as plasticizer. The formulations F1-F4 contained HPMC cP-50, F5-F8 contained HPMC cP-50 and Eudragit RS100 in combination and formulations F9-F12 contained HPMC cP-50 in combination with Polyvinyl Pyrrolidone K-30. First voriconazole was dissolved in the solvent system (Methanol: Ethanol: Water) using a magnetic stirrer at 800 rpm at room temperature. After which polymers and plasticizer were added to the above solution by continuous stirring using magnetic stirrer at 800 rpm.This solution was then poured in a petri-plate and allowed to dry for 24 hours.After drying, the films were removed from the petri dish and placed on a butter paper backing. Dried films were cut into 3 cm × 3 cm dimensions and packed carefully by wrapping in an aluminum foil and stored at 37° C until further use.

2.2 Formulation Table

Table 2.2: Composition of mucoadhesive vaginal film

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Voriconazole (mg)	50	50	50	50	50	50	50	50	50	50	50	50
HPMC cP-50 (%)	1%	2%	3%	4%	1%	2%	3%	4%	1%	2%	3%	4%
Eudragit RS100 (%)	-	-	-	-	1%	1%	1%	1%	-	-	-	-
PVP-K30 (%)	-	-	-	-	-	-	-	-	1%	1%	1%	1%
PEG-400 (ml)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Methanol (ml)	3	3	3	3	3	3	3	3	3	3	3	3
Ethanol (ml)	6	6	6	6	6	6	6	6	6	6	6	6
Water (ml)	3	3	3	3	3	3	3	3	3	3	3	3

III. EVALUATION OF MUCOADHESIVE VAGINAL FILM:

Uniformity of weight:[9]

To evaluate the weight of the films, the weight of each film was obtained individually and the mean and standard deviation values were calculated.

Thickness uniformity:[9]

Thickness uniformity was measured using a micrometer screw gauge, with a minimum count of 0.01 mm. The mean and standard deviation values are calculated.

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Folding endurance:[10]

Folding endurance was tested by repeatedly folding the film at the same place until the film was broken. The number of times the film was folded without breaking was considered as folding endurance.

Surface pH:[11]

The surface pH of the films was determined using a pH meter. The films were contacted with 5 mL of distilled water to swell for one hour at room temperature. Then, the surface pH was measured by touching the electrode with the surface of the films. A mean of three readings were recorded.

Drug content:[9]

A square piece of film measuring 3 cm × 3 cm was cut and drenched in a beaker containing 10 ml of SVF. The contents were stirred by ultrasonicator for 24 hours to dissolve the film. Suitable aliquots were made and filtered. The absorbance of the filtered solution was found out by using UV-visible spectrophotometer at 256 nm.

In-vitro drug release:[9]

The drug release from mucoadhesive film was determined using the USP Type-I Dissolution apparatus. The 3×3 cm^2 film was placed in the basket mesh. The 250 ml SVF (pH 4.5) was used as dissolution media and the study was continued for 8 hours. Stirring rate was maintained at 50 rpm and temperature 37 ± 2º C. The aliquots (5 ml) were withdrawn at predetermined time intervals and replenished with the same volume of SVF of pH 4.5 to maintain the sink condition. The samples were analyzed using a UV-visible spectrophotometer at 256 nm against SVF as a blank.

Ex-vivo mucoadhesive strength:[11]

The mucoadhesive strength of the film was determined by using modified physical balance method. Goat vaginal mucosa was obtained from local slaughter house. The mucosa was cleaned, washed and kept in SVF prior to use. The mucosa was cut in a square piece (surface area equal to film the area). The section of vaginal goat mucosa was placed on an inverted beaker and film was stick on one of the pan of modified mucoadhesive test apparatus, on the other side weights were slowly added to the pan until two mucosa get detached from other.

Ex-vivo mucoadhesion time:[12]

For determination of mucoadhesion time goat vaginal mucosa was used which was obtained from the local slaughter house. The mucosa was cleaned, washed and kept in SVF prior to use. The mucosa was glued to the inner surface of 100 ml beaker. The mucoadhesive film was hydrated using SVF and this hydrated film was brought in contact with the mucosal membrane. The beaker was filled with 30 ml SVF and stirring speed was kept 50 rpm and temperature 37 ± 2º C. The time taken for the mucoadhesive film to completely detach from the membrane was noted.

Table 4.1: Weight variation, Thickness, Folding endurance, Surface pH, Drug content

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Formulation code	Weight variation (mg) ±SD (n=3)	Thickness (mm) ±SD (n=3)	Folding endurance ±SD (n=3)	Surface pH ±SD (n=3)	Drug content (%) ±SD (n=3)
F1	148.44 ± 6.33	0.19 ± 0.027	>200 times	4.43 ± 0.31	97.30±0.18
F2	157.74 ± 5.44	0.21± 0.015	>200 times	4.32 ± 0.36	92.35±0.14
F3	162.68 ± 6.78	0.24 ± 0.015	>200 times	4.33 ± 0.35	91.48 ± 0.94
F4	206.54 ± 5.66	0.31± 0.029	>300 times	4.32 ± 0.21	90.68 ± 0.54
F5	212.06 ± 3.53	0.20 ± 0.017	>300 times	4.54 ± 0.06	95.09 ± 0.81
F6	220.02 ± 1.44	0.22 ± 0.021	>300 times	4.26 ± 0.16	98.13 ± 0.55
F7	229.24 ± 3.29	0.31 ± 0.015	>300 times	4.42 ±0.17	94.56 ± 0.15
F8	227.08 ± 4.88	0.36 ± 0.020	>300 times	4.59 ± 0.09	96.03 ± 0.96
F9	208.26 ± 4.26	0.12 ± 0.036	>300 times	4.51 ± 0.03	93.78 ± 0.34
F10	213.26 ± 4.32	0.13 ± 0.039	>300 times	4.23 ±0.03	95.90 ± 0.85
F11	333.36 ± 5.29	0.42 ± 0.027	>400 times	4.32 ±0.02	98.01 ± 0.59
F12	288.46 ± 4.92	0.32 ± 0.033	>300 times	4.52± 0.02	91.16 ± 0.11

IV. RESULTS:

N-vitro Drug Release

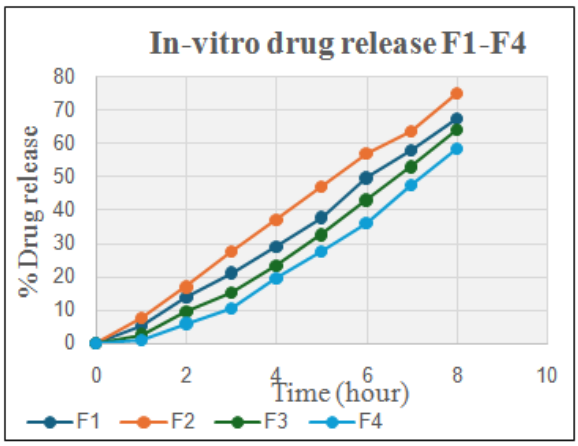

Figure 1: In-vitro drug releaseof batches F1-F4

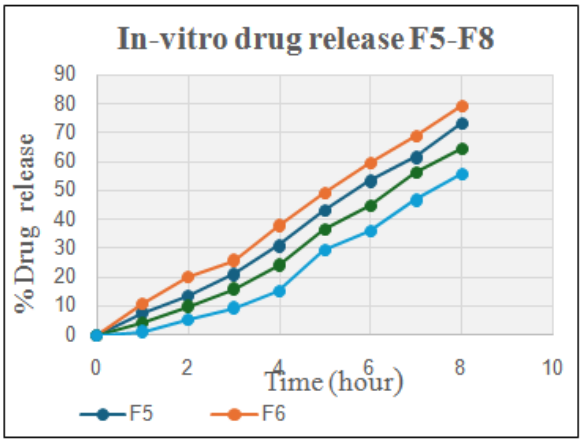

Figure 2: In-vitro drug release of batches F5-F8

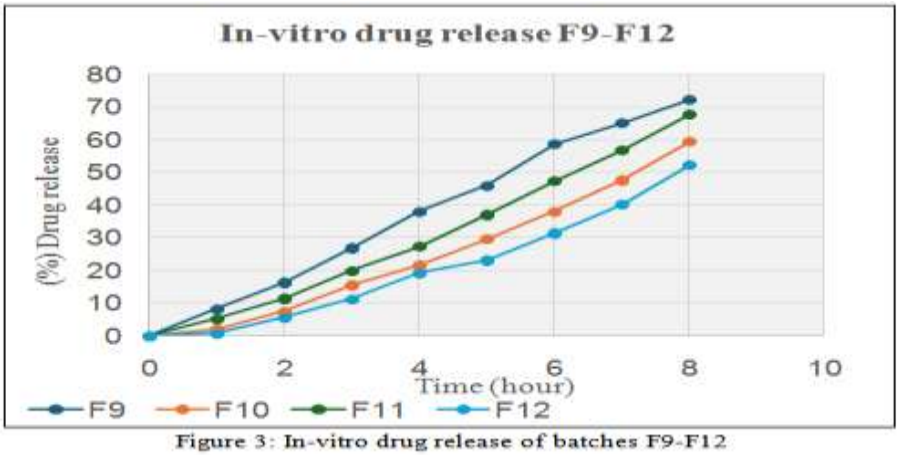

Figure 3: In-vitro drug release of batches F9-F12

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Mucoadhesion Strength:

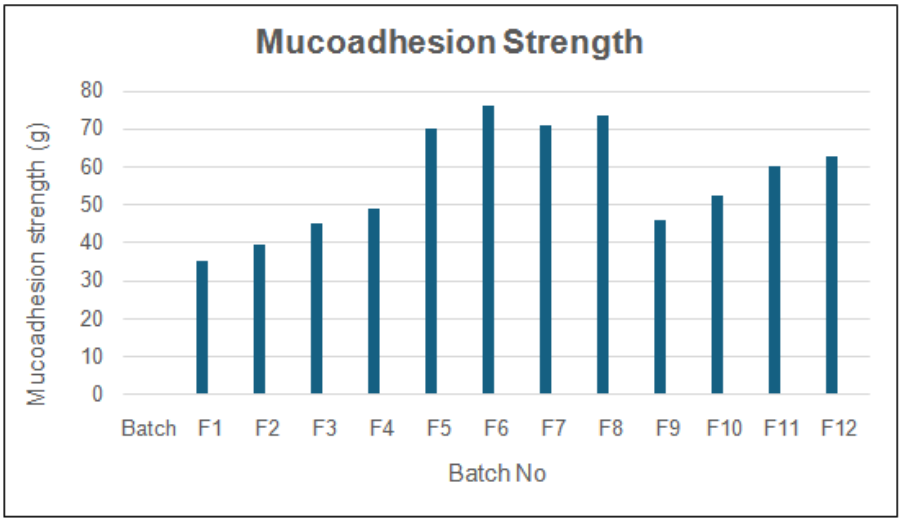

Figure 4: Mucoadhesion strength of batches F1-F12

Mucoadhesion Time:

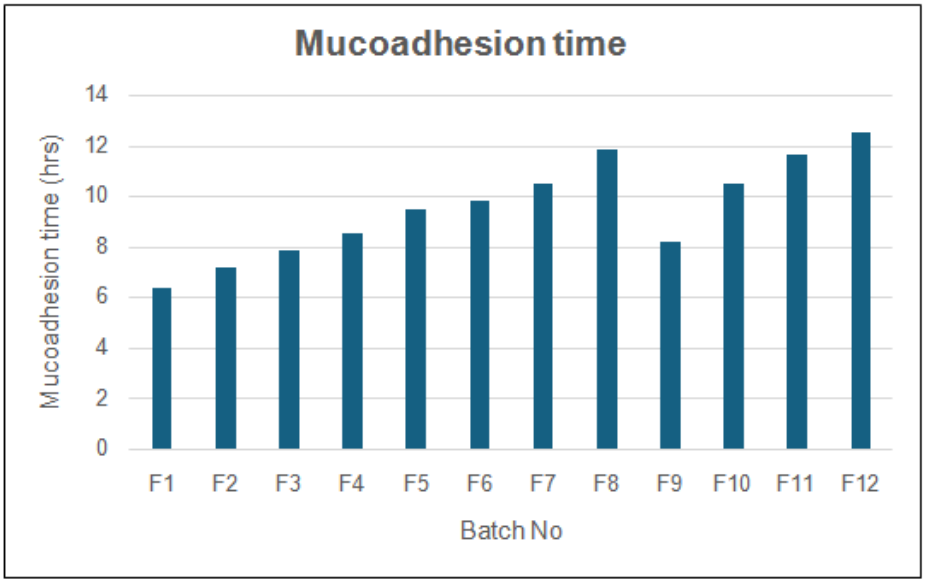

Figure 5: Mucoadhesion time of batches F1-F12

V. CONCLUSION:

In this study, voriconazole mucoadhesive vaginal films have been developed to provide a sustained release of the drug for up to eight hours. The films were prepared using HPMC cP-50 and combination of HPMC cP-50 with Eudragit RS100 and PVP-K30.Voriconazole mucoadhesive vaginal films made with a combination of Eudragit RS100 and HPMC cP-50 demonstrated better drug release. The mucoadhesive vaginal films were assessed for weight variation, folding endurance, surface pH, drug content, in-vitro drug release, ex-vivo mucoadhesion strength and time. Studies of surface pH reveal that the films' pH in acidic vaginal media does not have any irritating effects. Ex-vivo mucoadhesion studies indicates the prolong retention of the film on the mucosal membrane. Overall, the results of the research indicate that mucoadhesive vaginal film had the best possible

physico-mechanical, pharmaceutical, and biological properties.

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