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FORMULATION AND EVALUATION OF MUCOADHESIVE VAGINAL IN-SITU GEL OF ECONAZOLE NITRATE

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Abstract:

The objective of this study was to develop mucoadhesive dosage form of Econazole Nitrate. The mucoadhesive vaginal in-situ gel were prepared by thermosensitive method. Various mucoadhesive vaginal in-situ gels were prepared by using different concentration of Poloxamer188, Poloxamer 407, HPMC K4M, HPMC K100 M as a temperature sensitive polymer and as a mucoadhesive polymer respectively. The prepared in-situ gel was evaluated for weight for gelling time, gelation temp, viscosity, spreadability, pH, mucoadhesion strength and in-vitro drug release study. The formulation containing HPMC K4M show better mucoadhesive strength and in vitro drug release. The prepared mucoadhesive vaginal in- situ gel provided drug release of about 85.99 in 8 hrs, good mucoadhesive strength which indicates a potential alternative drug delivery system of econazole nitrate.

Keywords: Econazole Nitrate, Vaginal In-Situ Gel, Muco adhesion, Poloxamer

Introduction

In vaginal drug delivery system mucoadhesion means the ability of the mucoadhesive polymer to adhere the mucus layer. The mucous membrane is the moist tissue that liens body cavities and organs such as the mouth, gut, lungs, and nose. The mucosal layer is made up of mucus which is secreted by the goblet cells and is a visco-elastic fluid. The mucoadhesion has a potential to optimize controlled drug delivery in both localize as well as systemic drug delivery by keeping the formulation in intimate contact with tissue or cells at absorption site.[1]

The principle involving the in situ gelling of vaginal formulations is that the vaginal formulations absorb in the vaginal fluid after administration and forms gel into the vaginal cavity. Due to bio adhesive property the gel adheres the vaginal mucosa. Therefore, there is no need to remove the dosage form after it has been depleted of drug.[2]

In-Situ gelation is a process of gel formation at the site of action after the formulation has been applied at the site. In-Situ gel phenomenon based upon liquid solution of drug formulation and converted into semi-solid Mucoadhesive key depot. It permits the drug must be delivered in a liquid form or solution form.[3]

Econazole Nitrate is Anti-Fungal Drug. Econazole Nitrate is used mainly for vaginal infections and other diseases caused by fungi. It is usually administered topically as a pessary of 150 gm for three consecutive days or as a 1% Econazole Nitrate cream in a regimen of at least 15 days.[4] It is soluble at pH 4.5 in citrate buffer ang having molecular weight of 444.7g/mol. [5, 6]

Materials and Method:

Econazole Nitrate was obtained as a gift sample from, Yarrow Chem Products, Mumbai. Poloxamer 188, Poloxamer 407, HPMC K 4 M and HPMC K 100 M was purchased from SD fine chemicals.

Method:

- The in situ gelling polymer (Poloxamer188, Poloxamer 407, HPMC K 100 M, HPMC K4 M) as per quantity taken was added slowly in 10 ml citrate buffer (pH 5.5) with continuous stirring until completely dissolved.
- And the temperature was maintain at 4°C ± 0.5°C while preparing the solution
- Then the solution was kept overnight, after 24 hrs, the drug as per quantity taken was added in the above solution.
- And at last Benzalkonium Chloride was added as a preservative and a clear solution was formed.

Formulation Table:

Ingredients (%)	F1	F2	F3	F4	F5	F6	F7	F8
Econazole Nitrate	1	1	1	1	1	1	1	1
PLX 188	10	6	10	6	-	-	-	-
PLX 407	-	-	-	-	6	8	6	10
HPMC K 4 M	0.5	1	-	-	0.5	1	-	-
HPMC K 100 M	-	-	0.5	1	-	-	0.5	1
Benzalkonium Chloride	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Citrate Buffer (ml)	10	10	10	10	10	10	10	10

Table 1: Formulation Table.

Evaluation of mucoadhesive vaginal in situ gel

- **pH of In-Situ Gel:** pH of each formulation was determined using pH meter which was previously calibrated using standard buffer of pH 4 and pH 7.
- **Drug Content Determination:** 1 ml of formulation was taken in 10 ml volumetric flask and then diluted using citrate buffer up to 10 ml. Absorbance of prepared solution was measured at 220 nm using UV Visible spectrophotometer.[7]
- **Viscosity measurement:** The viscosity of the prepared formulation was measured with a Brookfield viscometer with spindle number 64 at 50-100 rpm at 37.5°± 0.5°C. The spindle was lowered perpendicularly into the gel in a beaker, being careful not to contact the bottom of the beaker. After 30 seconds, the readings were recorded.[8]
- **Gelling Time:** The in-situ gel forming solution timing was observed by visual examination.
- **Gelation Temp**: The in-situ gel forming solution temperature was observed by visual examination.
- **Mucoadhesive Strength:** The mucoadhesive potential of the prepared formulation is determined by measuring the force necessary to dislodge the formulation from the vaginal mucosal layer of goat vaginal mucosae from the slaughter house, with the weights gradually increasing until two mucosae are separated.

$$M=m*g/A$$

Where, M= mucoadhesive strength in dyne/cm^2

m= weight in grams

g= gravitational force (980 cm^2)

A= area in cm^2

- **Spreadability:** For the determination of spreadability excess of sample was applied in between 2 glass slide and was compressed to uniform thickness by placing 100- gram weight over the upper glass slide for 5 minutes. Weight 50 gram was added to pan. Time required separating the two slides i.e. the time in which the upper glass slide move over the lower plate was taken as measure of spreadability.[9]

$$S= (m*1)/t$$

Where,

S= Spreadability

m= weight tied to upper slide

t= time taken

1= length moved on upper glass slide

- **In Vitro Drug Release:** The drug release of the Econazole Nitrate in-situ vaginal gel was measured using Franz diffusion cell with dialysis membrane (mol. Wt. 12000 D) as a barrier. Assembly was set and the temperature was maintained at 37 ± 0.5°C, then 3 ml of in-situ gel of econazole nitrate was filled in the donor compartment, which was separated by the receptor compartment with the dialysis membrane. The receptor compartment was filled with the citrate buffer pH 5.5. One ml aliquots were withdrawn at regular time intervals and replaced with an equal volume of citrate buffer pH 5.5 as fresh receptor medium. The samples were appropriately diluted with citrate buffer pH 5.5 and analysed spectrophotometrically at 220 nm.[10]

Result:

Formulation Code	Gelling Time (sec) SD±, n=3	Gelation Temp (°C) SD±, n=3	Viscosity In-Situ Gelling Solution (cps) SD±, n=3	Viscosity In-Situ Gel (cps) SD±, n=3
F1	64.66 ± 0.51	37.33 ± 0.9	190.65 ± 0.22	1453.22 ± 1.02
F2	64.33 ± 0.41	37.16 ± 1.3	240.14 ± 0.91	1574.89 ± 1.09
F3	62.33 ± 1.53	37.71 ± 1.98	230.96 ± 0.11	1348.26 ± 0.57
F4	66.00 ± 0.64	37.21 ± 0.09	345.27 ± 0.46	1384.72 ± 1.16
F5	61.00 ± 1.1	37.53 ± 1.08	234.48 ± 0.63	1316.19 ± 1.86
F6	63.33 ± 1.52	37.68 ± 1.56	306.42 ± 0.41	1357.87 ± 0.42
F7	66.48 ± 1.6	37.39 ± 1.9	256.23 ± 0.56	1224.47 ± 0.12
F8	65.00 ± 1.60	37.31 ± 0.39	378.11 ± 0.19	1489.17 ± 0.14

Table 2: Evaluation of mucoadhesive vaginal in situ gel

Formulation Code	Spreadability (gcm/sec) SD±, n=3*	pH SD±, n=3*	Mucoadhesive Strength (dyne/cm^2) SD±, n=3*	Drug Content (%) SD±, n=3
F1	101.66 ± 0.19	5.5 ± 0.51	1458.62 ± 1.14	95.75 ± 1.23
F2	86.33 ± 1.34	4.76 ± 0.17	1247.18 ± 0.11	98.96 ± 0.76
F3	103.33 ± 1.23	4.56 ± 0.05	1284.91 ± 1.09	96.05 ± 1.02
F4	93.33 ± 1.66	5.3 ± 0.47	1491.69 ± 1.09	98.73 ± 0.68
F5	93.24 ± 1.07	5.73 ± 0.05	1879.13 ± 0.45	95.78 ± 0.55
F6	108.33 ± 2.22	4.8 ± 0.39	2565.12 ± 0.12	97.01 ± 1.68
F7	108.33 ± 2.13	5.76 ± 0.05	1898.53 ± 0.13	96.34 ± 0.98
F8	108.33 ± 2.81	4.26 ± 0.31	2718.60 ± 1.09	97.96 1.36

Table 3: Evaluation of mucoadhesive vaginal in situ gel

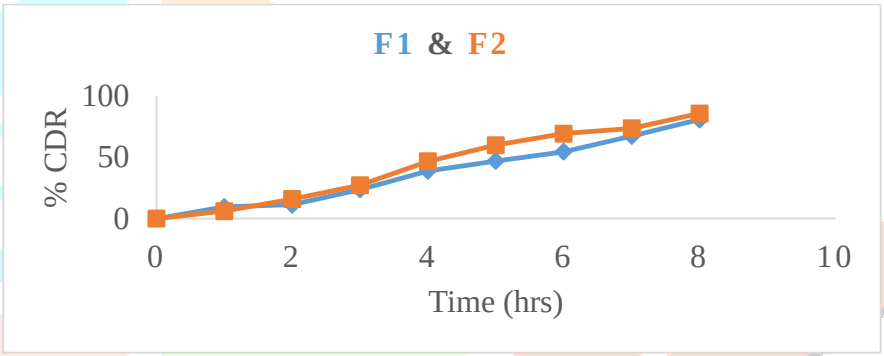

Figure 1: In-vitro drug release of F1 & F2

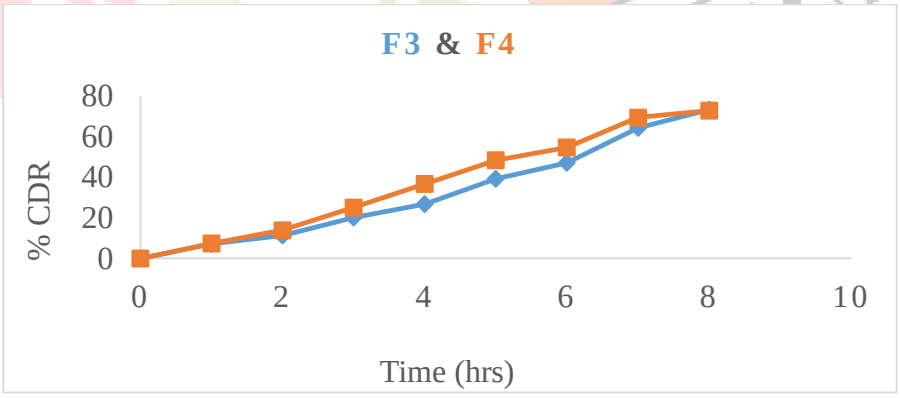

Figure 2: In-vitro drug release of F3 & F4

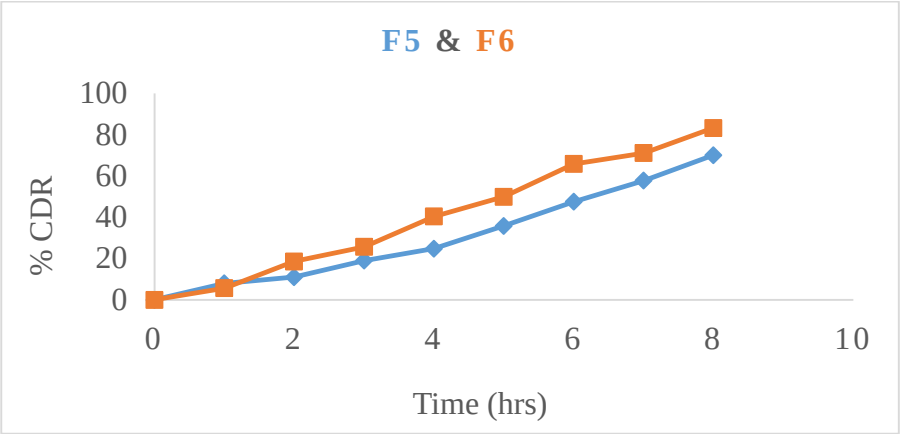

Figure 3: In-vitro drug release of F5 & F6

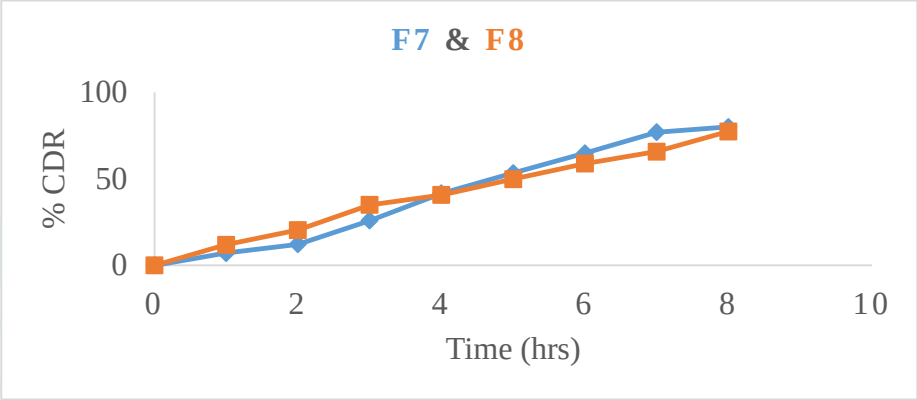

Figure 4: In-vitro drug release of F7 &F8

Discussion and Conclusion:

In-situ gel of Econazole Nitrate was successfully prepared by Thermosensitive Method to avoid first pass metabolism. Among 8 batches of Econazole Nitrate with various polymer batch F2 containing HPMC K4M (1%) shows satisfactory results. Batch F2 showing Gelation temp, satisfactory mucoadhesive properties and drug release up to (85.99%). In addition, the prepared In-situ gel meets the pharmacopoeial requirements for uniformity of Viscosity, pH, Spreadability. From the present work it can be concluded that econazole nitrate can be administered via vaginal drug delivery system which provides sustained release and reduce the frequency of drug administration and also reduce first pass metabolism of drug it can enhance the patient compliance.

References

1. Silva B, Ramos A, Bonifacio B, Negri M, Sato M, Bauab M and Chorilli M. 2014. “Nano technological strategies for vaginal administration of drugs—A review.” J. Biomedical Nanotechnology,10: 2218–2243.

2. Ensign M, Cone R and Hanes J. 2014. “Nanoparticle-based drug delivery to the vagina: A review.” Journal of Controlled Release,190: 500–514

3. Bajpai V. 2014. “In - situ gel nasal drug delivery system-A review.” International Journal of Pharmaceutical Science and Research,4(3):577- 580.

4. Esra, B and Sinem Y. 2011. “In-situ formulation of econazole nitrate: preparation and in-vitro and in-vivo evaluation.” Journal of Pharmacy and Pharmacology,63:1274-1282.

5. Tasdighi E, Azar J and Seyed A. 2011. “Development and in-vitro evaluation of a contraceptive vagino-adhesive propranolol hydrochloride gel.” Iranian Journal of Pharmaceutical Research,11(1):13.-26.

6. Dolci L, Beatrice A and Filippo M. 2020. “Development and in-vitro evaluation of mucoadhesive gelatin films for the vaginal delivery of econazole.” International Journal of Pharmaceutics,1-12.

7. Randa Z, Khaled H, Ahmed K and Ahmed A. 2011. "Ketorolac tromethamine in-situ ocular hydrogel; preparation, characterization and in-vivo evaluation." International Journal of Drug Delivery,3:535-545.

8. Mittal N and Kaur G. 2013. "In situ gelling ophthalmic drug delivery system: formulation and evaluation." Journal of Applied Polymer Science,1-9.

9. Ranch K, Patel H, Chavda L, Koli A, Maulvi F and Parikh K. 2017. "Development of in situ ophthalmic gel of dexamethasone sodium phosphate and chloramphenicol: a viable alternative to conventional eye drops." Journal of Applied Pharmaceutical Science,7(3):101-108.

10. Shaikh K, Kshirsagar V and Patil G. 2015. "Mathematical models for drug release characterization: a review." World Journal of Pharmacy and Pharmaceutical Sciences,4(4):324-338.