International Journal of Pharmaceutical and Bio-Medical Science

ISSN(print): 2767-827X, ISSN(online): 2767-830X

Volume 02 Issue 02 February 2022

Page No: 18-22

DOI: https://doi.org/10.47191/ijpbms/v2-i2-01, Impact Factor: 5.374

Formulation and Evaluation Xylometazoline Hydrochloride Mucoadhesive Nasal in Situ Gel

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ABSTRACT

The objective of research is to develop a mucoadhesive in-situ nasal gel formulation of xylometazoline hydrochloride for the treatment of allergic rhinitis to avoid possible side effects. Mucoadhesive in-situ nasal gel of xylometazoline hydrochloride was formulated by ionic gelation method using xanthan gum as ionsensitive agent and different grades of HPMC as a viscosifying agent. The prepared batches were evaluated for drug content, pH, gelling time, spreadability, gelling strength, mucoadhesive strength and in-vitro drug release. In vitro drug release study was carried by using diffusion cell with dialysis membrane. Short term stability study was also performed for final formulation as per ICH guidelines. The drug content and pH of the formulation were found to be satisfactory. The mucoadhesive strength of the formulation was found to be from 212.55 gm/cm^2 to 490.8 gm/cm^2. The viscosity and spredability of the formulations were found to be satisfactory. Amongst all these formulations, the maximum drug release was found to be 81.46 % in formulation F8 containing 0.2 % xanthan gum and 0.5 % HPMC K15M . The developed formulations showed sustained release of drug up to 8 hrs and found to be stable.

ARTICLE DETAILS

Published On:
15 February 2022

Available on:
https://ijpbms.com/

KEYWORDS: Allergic rhinitis, In situ gel, Mucoadhesion, Xylometazoline hydrochloride

1. INTRODUCTION

Nasal route is an attractive alternative for local as well as systemic delivery of drugs specially when rapid absorption and effects are desired[1]. One of the reasons for the low degree of absorption of peptides and proteins via the nasal route is rapid movement away from the absorption site in the nasal cavity due to the mucociliary clearance mechanism[2]. In-situ gel-forming systems can be described as low viscosity solutions that undergo phase transition to form viscoelastic gels due to conformational changes of polymers in response to the physiological environment[3]. Xylometazoline hydrochloride is used for temporary relief of congestion in the nose caused by various conditions including the common cold, sinusitis, hay fever and allergies. Half life of drug is 10- 12 hrs and well absorbed through nasal mucosa[4].

Table 1: Formulation composition of nasal mucoadhesive gel

HPMC K4M (%)	-	-	-	0.3	0.5	0.7	-	-	-	-	-	-
HPMC K15M (%)	-	-	-	-	-	-	0.3	0.5	0.7	-	-	-
HPMC E15 LV (%)	-	-	-	-	-	-	-	-	-	0.3	0.5	0.7
Methyl paraben (%)	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Distilled water (ml)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

2. MATERIALS AND METHODS:

2.1. Materials:

Xylometazoline hydrochloride is obtained as a gratis sample from Luxica Pharma INC, Panoli, Gujarat. All other ingredients were used of analytical grade.

1.2. Formulation of in situ gel

In-situ gelling polymer was added slowly in distilled water with continuous stirring until completely dissolved. Other polymeric solutions were made and allowed to hydrate. After mixing and complete hydration of polymers, a separate solution of drug was added to the polymeric solution. The resultant solution was thoroughly mixed until uniform and clear solution was formed. Final volume was made up to by adding required volume of distilled water[5].

3. EVALUATION STUDIES

3.1. pH of in-situ gel: pH of each formulation was determined by using pH meter which was previously calibrated using standard buffer of pH 4 and pH 7. pH was Measured by taking 1 ml formulation which was diluted with distilled water.[6]

3.2. Drug content: 1 ml of formulation was taken in 10 ml of volumetric flask and at that point diluted with distilled water up to 10 ml. Yet again 1 ml quantity from this solution was taken and diluted with 10 ml of distilled water. Lastly, the absorbance of prepared solution was measured at 217 nm against blank reagent using UV visible spectrophotometer at 217 nm.[7]

3.3. Viscosity measurement: Viscosity of prepared formulation was determined using Brookfield viscometer with spindle no. 64 at 50-100 rpm at temperature 37±0.5°C. Spindle was lowered perpendicularly into gel placed in a beaker taking care that the spindle does not touch the bottom of beaker. Reading were recorded after 30 sec.[8]

3.4. Gelling time: The in-situ gel forming solution and the artificial nasal fluid was mixed and the gelation was observed by visual examination.[9]

3.5. Mucoadhesive strength: The mucoadhesive potential of the established preparation was determined by measuring the force required to detach the formulation from goat nasal mucosal tissue which was obtained from the slaughter house. A section of goat nasal mucosa was placed on inverted beaker and formulation to be tested was applied on one of the pans of modified mucoadhesion test apparatus, on the other side weight was kept rising until two mucosa get separate from each other.[8]

M= m*g/A

Where, M= mucoadhesive strength in dyne/cm2
m= weight in grams
g= gravitational force
A= area in cm2

3.6. Gelling strength: The prepared gel was placed in 100 ml measuring cylinder the probe was placed on the gel and a weight was placed on the probe. The probe was allowed to penetrate at a distance of 5 cm and time required for penetration was noted as a gelling strength.[10]

3.7. Spreadability: For the determination of spreadability excess of sample was applied in between 2 glass slide and compressed to uniform thickness by placing 100 gram weight over the upper glass slide for 5 minutes. Weight 45 gram is 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.[11]

S= (m*1)/t

Where, S= Spreadability
m= weight tied to upper slide
t= time taken
1= length moved on upper glass slide

3.8. In vitro drug release: The drug release of the Xylometazoline hydrochloride in-situ nasal gel carried out by using Franz diffusion cell with dialysis membrane (mol. Wt. 12000 D) as a barrier. Assembly was set and the temperature was maintained at 37±1°C, then 2 ml of nasal in-situ gel of xylometazoline hydrochloride was Filled in the donor compartment, which was separated by the receptor compartment with the dialysis membrane. The receptor compartment was filled with the phosphate buffer pH 6.8. 1 ml aliquots of sample were withdrawn at regular time intervals and replaced with an equal volume of phosphate buffer as fresh receptor medium. The samples were appropriately diluted with phosphate buffer and analysed spectrophotometrically at 217 nm.[12-13]

4. STABILITY STUDY

Stability study was conducted for prepared mucoadhesive nasal in-situ gel for formulation F8 batch as per ICH guidelines, formulation was kept at 40±2°C with RH of 75 % for a period of 30 days in stability chamber. Formulation was evaluated after one-month period for drug content, pH, drug release, viscosity, gelling time, gelling strength, mucoadhesive strength, spreadability.[14-15]

5. RESULTS

Table 2. Evaluation parameters of formulation F1 to F12

Batch no.	Drug Content % (±SD)n=3	pH (±S.D.) n=3	Gelling time (sec) (±SD) n=3	Spreadability gcm/sec (±SD) n=3
F1	97.05±1.78	6.1±0.12	7.2±0.047	22.81±0.062
F2	97.75±0.89	6.3±0.01	5.3±0.163	18.30±0.082
F3	96.08±1.32	6.41±0.15	4.1±0.094	20.58±0.125
F4	95.82±0.65	5.6±0.08	10.35±0.148	53.67±0.038

F5	96.78±0.79	5.9±0.02	7.2±0.016	47.09±0.125
F6	96.94±1.56	5.7±0.04	7.08±0.089	45.55±0.098
F7	97.84±0.75	6.5±0.04	8.72±0.183	49.24±0.174
F8	98.96±0.86	5.5±0.19	4.1±0.081	51.42±0.095
F9	98.06±0.31	6.2±0.07	6.3±0.124	37.33±0.056
F10	97.92±0.68	6.07±0.09	9.9±0.028	51.42±0.142
F11	96.36±1.05	6.3±0.12	7.56±0.171	43.15±0.089
F12	95.72±0.98	6.1±0.16	5.14±0.047	48.36±0.132

Table 3: Evaluation parameters of formulation F1 to F12

Batch no.	Viscosity cps (±SD) n=3		Mucoadhesive strength (gm/cm^2) (±SD) n=3	Gelling strength (sec) (±SD) n=3
	Solution	Gel		
F1	328±1.25	1978±0.61	212.55±0.48	56±0.99
F2	390±1.07	1368±0.05	228.92±1.09	63±1.24
F3	368±0.82	1734±0.38	261.62±1.12	75±0.48
F4	345±1.01	1325±0.75	310.65±0.96	58±0.31
F5	360±0.29	1692±0.41	359.7±0.16	60±0.98
F6	388±1.23	1978±0.61	392.4±0.09	72±1.32
F7	415±0.09	1475±0.45	375±1.13	41±0.48
F8	448±0.03	1886±0.58	490.8± 0.19	57±0.94
F9	590±1.22	2025±0.35	474.15±1.12	67±1.65
F10	216±0.02	1248±1.1	196.2±0.08	39±1.30
F11	239±0.08	1469±0.05	235.44±1.01	48±1.23
F12	269±0.19	1768±0.07	300±1.15	52±0.95

5.1 In vitro drug release

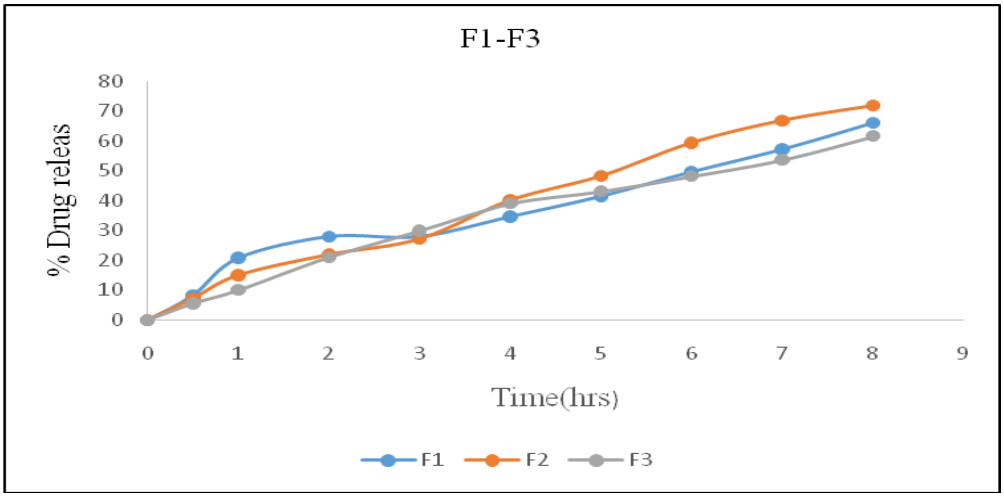

Figure 1: In-vitro drug release from F1-F3

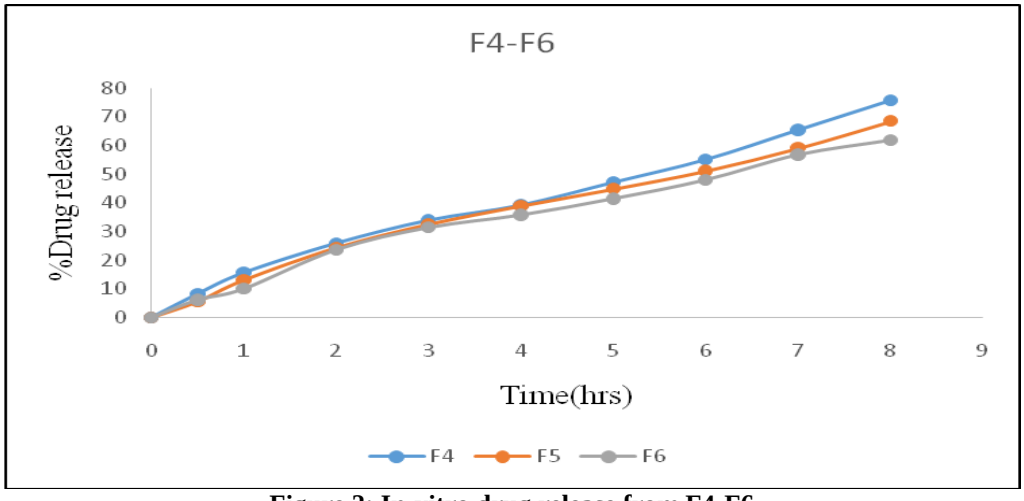

Figure 2: In-vitro drug release from F4-F6

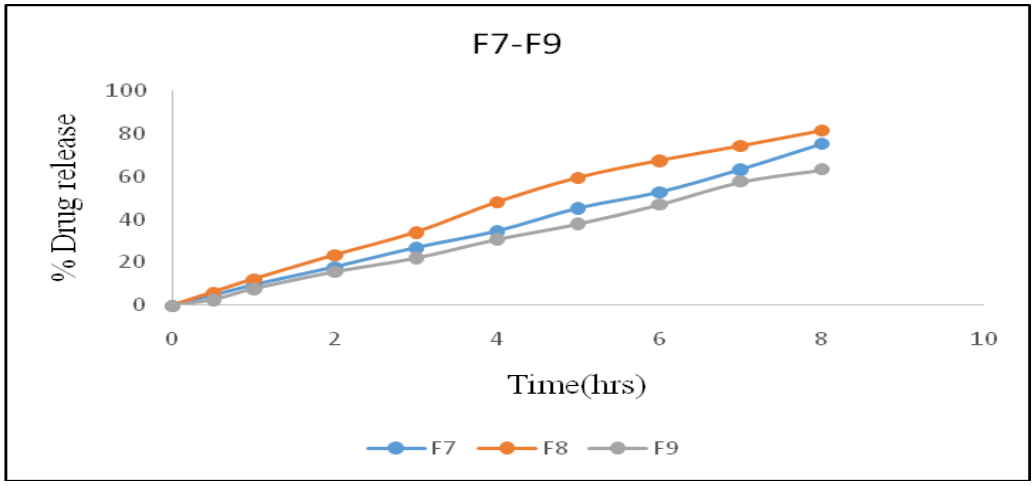

Figure 3: In-vitro drug release from F7-F9

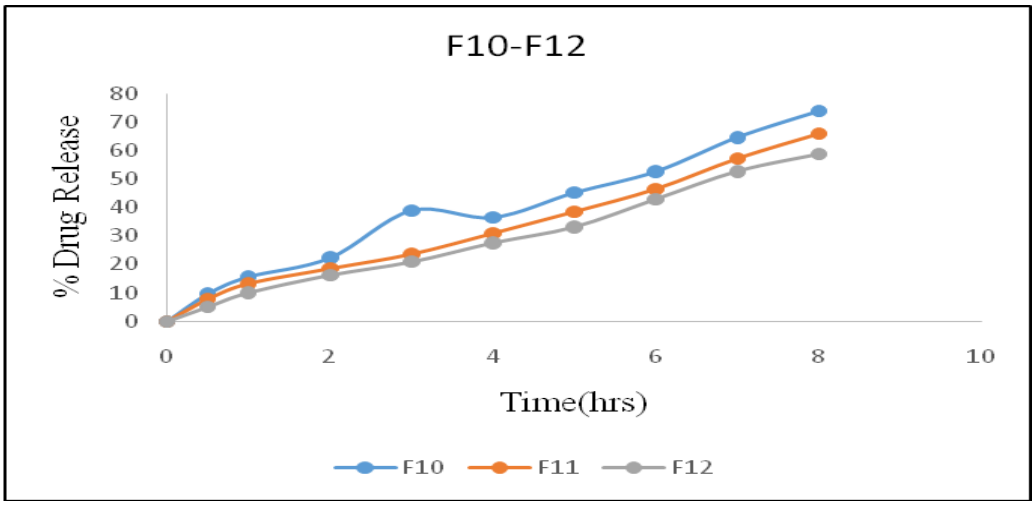

Figure 4: In-vitro drug release from F10-F12

5.2 Stability study of batch F8

Table 4: Stability Study of F8

Physical properties	Initial		At 40±2 °C/75±5%RH	
Drug Content (%)	98.96±0.86		99.2±0.959	
pH	5.5±0.19		6.2±0.08	
Viscosity (cps)	448±0.03	1886±0.58	411±1.247	1758±1.699
Gelling time (sec.)	4.1±0.0.081		5.3±0.124	
Spreadability(gcm/sec)	51.42±0.095		41.87±1.61	
Gelling strength (sec.)	57±0.94		55±0.249	
Mucoadhesive strength (gm/cm^2)	490.8±0.19		459.51±3.07	

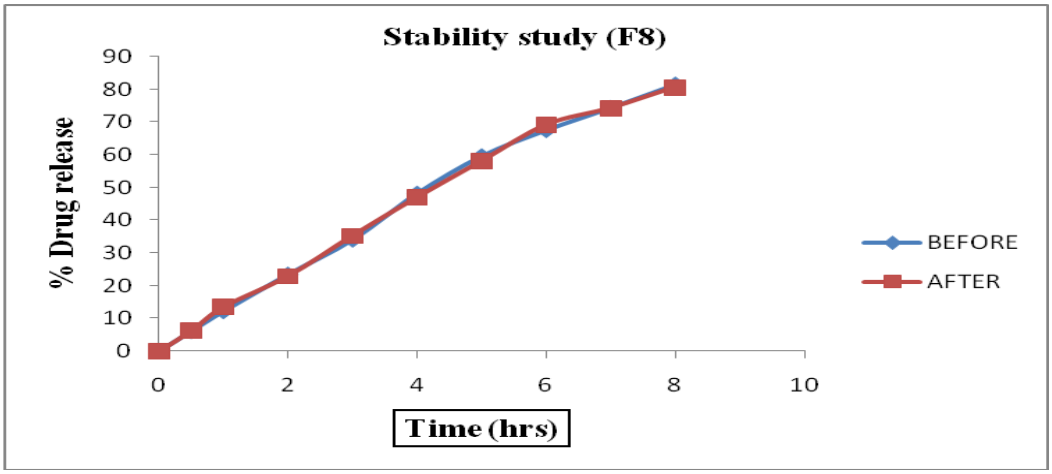

Figure 5: In-vitro drug release of F8

6. CONCLUSION

In present investigation, attempt was made to prepare mucoadhesive nasal in-situ gel of Xylometazoline hydrochloride with different polymer concentration and polymer grades using ionic gelation method. Mucoadhesive nasal in-situ gel of xylometazoline hydrochloride are designed to reduce dose related side effect and it also avoid first pass metabolism of drug. Different polymers were used for preparing batches of mucoadhesive in- situ gel. The study conclusively demonstrated that xylometazoline hydrochloride can be successfully formulated into mucoadhesive nasal in-situ gel by ionic gelation method using HPMC K15 M to obtain sustain release over the extended period of 8 hrs.

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