ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

FORMULATION AND EVALUATION OF OLOPATADINE HYDROCHLORIDE NASAL IN - SITU GEL

Mijbabanu Shaikh, Femin Sailor, Hitesh Jain*, Satyajit Sahoo, D. B. Meshram

Pioneer Pharmacy Degree College, Vadodara, Gujarat, India

*Corresponding author Email: **hitesh_hitachi@rediffmail.com**

ARTICLE INFO

Key words:
Mucoadhesion,Nasal in-situ gel, Olopatadine, pH induced method

Access this article online
Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

To develop a mucoadhesive in-situ nasal gel formulation of Olopatadine hydrochloride for the treatment of allergic rhinitis to avoid possible side effects. Mucoadhesive in-situ nasal gel of Olopatadine hydrochloride was formulated by pH-induced method using carbopol 934 aspH sensitive agentand HPMC as a viscosifying agent. The formulated batches were evaluated for drug content, pH, gelling time, spreadability, gelling strength, and mucoadhesive strength and in-vitro drug release. Ex- vivo permeation study was performed for the batchB8. During experiment it was concluded that viscosity and mucoadhesive strength increases with increasing the concentration of polymer. Amongst all these formulations, the maximum drug release was found to be 99.5 % and it was also observed that drug release decreases by increasing the concentration of polymer. Ex- vivo permeation study of formulation B8 was found to be95.8%. The mucoadhesive in-situ nasal gelling system is a promising novel drug delivery system for an allergic rhinitis drug Olopatadine hydrochloride which could enhance nasal residence time with increased viscosity and mucoadhesive character and provided better release profile of drug.

INTRODUCTION

Nasal drug delivery which has been accomplished for thousands of years has been given a new contract of life. Nasal therapy, has been known form of treatment in the Ayurvedic systems of Indian medicine, it is also called "NASAYA KARMA". Nasal route is permeable to more compounds than the gastrointestinal tract due to lack of pancreatic and gastric enzymatic activity, neutral ph of the nasal mucus and a smaller amount of dilution by gastrointestinal contents. It is a useful delivery method fordrugs that are active in little doses and show no least oral bioavailability such as proteins, peptides, hormones andsteroids[1].

The nasal mucosa itself and the drug delivery systems affect drug absorption through the nasal route, is priceless. A stable, safe and effective nasal product can be developed through suitable and adequate Pre-formulation studies ofdrug[2]. Olopatadine Hydrochloride is an antihistamine used to relieve sneezing and a stuffy, runny or itchy nose caused by allergic rhinitis (hay fever) and allergies. It is white, crystalline powder, Sparingly Soluble in Water, Freely soluble in Alcohol, Olopatadine acts as a selectiveantagonist of the histamine H1 receptor, thus stabilizing mast cells and inhibiting histamine release. This agent also blocks histamine h1

receptors, thereby preventing histamine from binding to these receptors. Both actions prevent the effects of histamine on capillaries, bronchial smooth muscle, and gastrointestinal (GI) smooth muscle, including histamine- induced vasodilation, increased capillary permeability, bronchoconstriction, and spasmodic contraction of GI smooth muscle. This drug also prevents histamine-induced pain and itching of mucous membranes.

MATERIALS AND METHODS

Materials:

Olopatadine hydrochlorides obtained as a gratis sample from flax laboratories, all other ingredients were used of Analytical grade.

Methods:

The in situ gelling polymer was added slowly in distilled water with continuous stirring until completely dissolved. Other polymeric solution 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 inform and clear solution was formed. Final volume was made upto 10 ml by adding required volume of distilled water.

EVALUATION STUDIES:

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 measure from this solution was taken and diluted with 10 ml of distilled water. Lastly, the absorbance of prepared solution was measured at 300 nm against blank solution using uv visible spectrophotometer.[4]

pH of in situ gel: Formulation of drug was transferred and 1 ml formulation diluted with distilled water. pH was determined using phmeter which was previously calibrated using standard buffer of pH 4 and pH 7.[5]

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

Spreadability: For the determination of spreadability excess of samplewas applied in between 2 glass slide and compressed to uniform thickness by placing 100 gram weight over the upper glass slide for 5 minutes. Weight45 gram is added to pan. Time required separating the two slides i.e. Thetimein which the upper glass slide move over the lower plate was taken as measure of Spreadability.

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

Where,

S=Spread ability

M= weight tied to upper slide

T= time taken

L= length moved on upper glass slide

Viscosity: Viscosity of prepared formulation was determined using brookfield viscometer with spindle no. 64 at 50-100 rpm at temperature 37±0.5℃. Spindle was lowered perpendicularly into gel placed in a beaker taking care that the spindle does not touch the bottom of beaker.[6]

Gelling strength: The prepared gel was placed in 100ml 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 gellingstrength.[7]

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 situated 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 increasing until two mucosa get separate from eachother.[8]

***In vitro* drug release:** The drug release of the Olopatadine Hydrochloride in situ gel was carried out by using Franz diffusion cell. Assembly can be set and the

temperature was maintained at 37±0.5°C, then 2 ml of nasal in situ gel of Olopatadine Hydrochloride was filled in the donor compartment, which was separated by the receptor compartment with the dialysis membrane (mol. Wt. 12000D). 1 ml aliquots of sample was 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 analyzed spectrophotometrically.[9]

Ex-vivo permeation study for batch (B8):

The drug permeation study of the Olopatadine hydrochloride in-situ nasal gel was measured using Franz diffusion cell with goat nasal mucosal tissue as a barrier, which was obtained from the slaughterhouse. Assembly was set and temperature was maintained at 37±1°C, then 2 ml of nasal in-situ gel of Olopatadine hydrochloride was filled in the donor compartment, which was separated by the receptor compartment with the goat nasal mucosa. The receptor compartment was filled with the phosphate buffer pH 6.4. One 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 300 nm.[10]

Table 1: Formulation composition of nasal in situ gel

Ingredients	B1	B2	B3	B4	B5	B6	B7	B8	B9
Olopatadine hcl (%)	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Carbopol 934 (%)	0.1	0.1	0.1	0.2	0.2	0.2	0.3	0.3	0.3
HPMCE50 LV(%)	0.2	0.3	0.4	0.2	0.3	0.4	0.2	0.3	0.4
MethylParaben(%)	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

***In- vitro* drug release (B1-B9):**

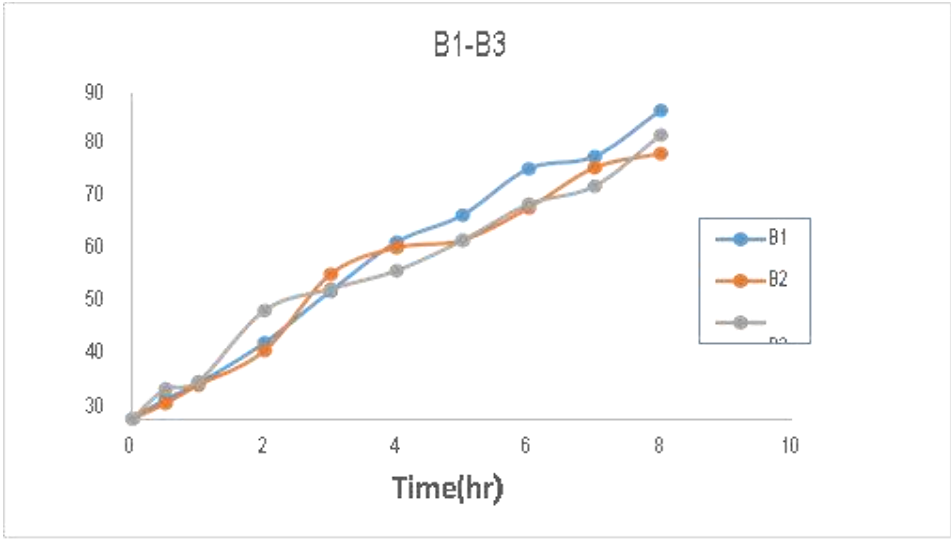

Figure 1: *In- vitro* drug release from B1-B3

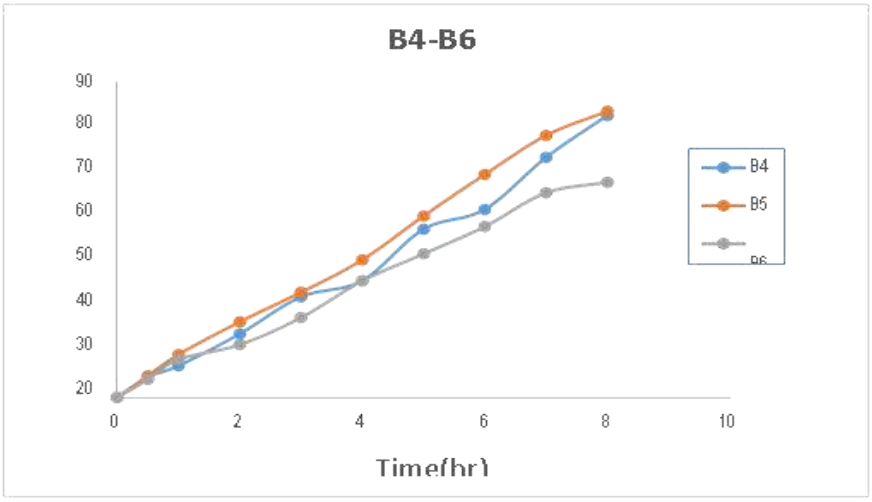

Figure 2: *In- vitro* drug release from B4-B6

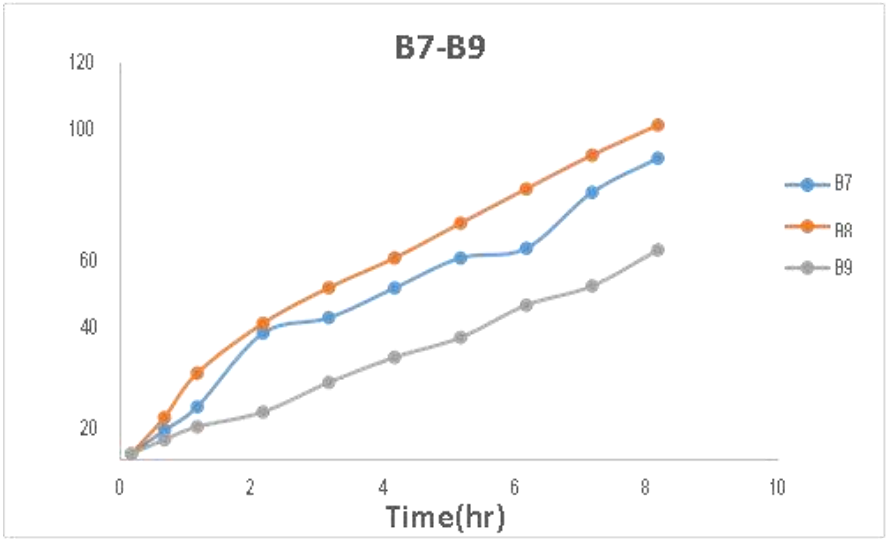

Figure 3: *In-vitro* drug release (B7-B9)

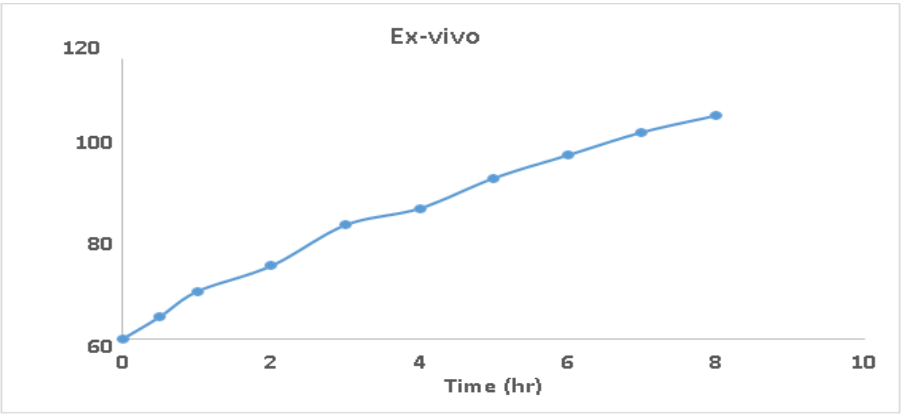

Figure 4: *Ex-vivo* permeation study of batch (B8)

Table 2: Evaluation parameters of formulation B1-B9

Batch No	Viscosity cps (± S.D.)		Mucoadhesive Strength (gm/cm^2)(± S.D.)	Gelling strength (sec)(± S.D.)
	Solution	Gel		
B1	110±0.52	1224±0.163	160.1±2.07	29±0.32
B2	155±0.21	1430±0.183	180.2±5.3	38±0.21
B3	480±0.17	1790±0.18	360.9±6.1	49±0.08
B4	210±0.24	1581±0.124	215.12±7.6	39±0.26
B5	548±0.047	1884±0.24	480.25±0.12	60±0.291
B6	690±0.247	2000±0.21	590.32±0.11	69±0.312
B7	410±0.210	1610±0.18	495.15±1.43	51±0.314
B8	580±0.371	1917±0.29	703.7±3.07	74±0.329
B9	720±0.318	2021±0.39	525.3±4.07	62±0.216
***Each observation value are expressed as mean ±S.D. of n=3**				

***Ex-vivo* permeation study of batchB8**

Table 4: *Ex-vivo* permeation study of batch (B8)

Time(hrs)	0	0.5	1	2	3	4	5	6	7	8
%drug permeation	0	9.51	20.3	31.25	48.8	55.9	68.9	78.8	88.6	95.8

CONCLUSION:

In present investigation, attempt was made to prepare mucoadhesive nasal in-situ gel of Olopatadine hydrochloride with different polymer concentration using pH induced method. The formulation has longer residence time and contact time with nasal mucosa due to its high viscosity and release the drug in sustained manner.

REFERENCES:

1. Alagusundaram M, et al., "Nasal drug delivery system -an overview." *Int. J. Res. Pharm. Sci.* 2010; 4:1454-465.
2. Chaturvedi AK, Singh UK and Verma AK, "Intranasal Drug Delivery System An overview." *Inventi Impact Ndds*. 2011; 3:127-133.
3. John C, Yong OC, "True melting point determination."*Chem Educator*.2013; 18: P. 203- 208.
4. Parekhhb,etal.,"Novelinsitupolymericdrugdeliverysystem:areview."*Journal of Drug Delivery System and Therapeutics*. 2012; 2(5): p. 136-145.
5. Godbolemd,therepwanddangrepv,"Formulationandoptimization of prolonged released nasal in-situ gel for treatment of migraine." *Indo American Journal of Pharmaceutical Research*. 2014; 4(2):1320-1332
6. Nirmalhb,bakliwalsrandpawars" In-situgel:newtrendincontrolled and sustained drug delivery system." *International Journal of Pharmatech Research*. 2010; 2(2):1398-1408.

7. Ahmed VA and Goli D, "Xyloglucan based in-situ gel: formulation development and evaluation of in-situ ophthalmic gel of brimonidine tartrate." *Indo Global Journal of Pharmaceutical Sciences*. 2018; 8(3):92- 103.
8. Nirmalhb,bakliwalsrandpawarsp ,"Insitugel:newtrendincontrolled and sustained drug delivery system." *International Journal of Pharmatech Research*. 2010; 2(2):1398-1408.
9. Valavi MP, Tadavi SA, Shaikh A and Pawar SP, "Review on insitu gel a novel drug delivery system." *World Journal of Pharmacy and Pharmaceutical Sciences*. 2019; 8(2):1288-1309.
10. Nerella A, Dontha P, Uppuluru A and Konda SK, "Formulation and evaluation of in- situ mucoadhesive nasal gel of montelukast sodium." *Der Pharmacia Sinica*. 2014; 5(2):1-8