FORMULATION AND EVALUATION OF MONTELUKAST SODIUM NASAL GEL

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ABSTRACT
The objective of the present investigation was to develop a mucoadhesive in-situ gel with reduced nasal mucocilliary clearance in order to improve the bioavailability of the antiasthamatic drug namely montelukast sodium. The in-situ gelation upon contact with nasal mucosa was conferred via the use of the thermo gelling poloxamer 407 whereas mucoadhesion and drug release enhancement were modulated using hydroxy propyl methyl cellulose, methyl cellulose and polyethylene glycol respectively. The results revealed that the mucoadhesive polymer increased the gel viscosity but reduced its sol-gel transition temperatures and the drug release. The inclusion of polyethylene glycol polymer counteracted the effect of mucoadhesive polymer whereby it decreased the gel consistency and increased the sol-gel transition as well as *In-vitro* drug release. The *In-vitro* drug release performed through cellophane membrane. The percentage drug content of all the prepared nasal gels formulations were checked and found to be in the range of 89.05-98.30%.
Key words: Montelukast sodium, Poloxamer 407.

INTRODUCTION

In recent years the nasal route has received a great deal of attention as a convenient and reliable method for systemic administration of drugs especially those which are ineffective orally and must be administered by injection. The nasal epithelium has a relatively high permeability and only two cell layers separate the nasal lumen from the dense blood vessel network in the lamina propria. The nasal route for systemic drug delivery is of interest because it provides several advantages over other routes of drug administrations. These have been suggested as follows: rapid absorption, avoidance of the intestinal and hepatic presystemic disposition, fast onset of therapeutic action, avoidance of irritation of the gastrointestinal membrane, noninvasive administration, ease of convenience, self medication and improved patient compliance. These factors make nasal drug administration an attractive delivery route. The mucosa of the nasal cavity has been examined as a possible route of administration to achieve a rapid and higher level of drug absorption[1].

Montelukast sodium is a leukotriene antagonist, effective in the treatment of asthma and allergic rhinitis. Oral bioavailability of drug is variable showing values between 64 and 68% due to extensive presystemic metabolism. The intranasal delivery seems to be an attractive alternative. However, low residence time of drug in nasal cavity is limitation of this route, which affect on absorption and in turn bioavailability of drug. Hence the design of nasal dosage forms has to consider the anatomic and physiologic characteristics of nasal mucosa and more particularly the rapid mucocilliary clearance (MCC) that limits the time available for drug absorption from the applied dosage form[2].

As compared to oral controlled release systems, mucoadhesive delivery system have several advantages by virtue of prolongation of residence time, drug targeting, intimate contact between dosage form and the absorptive mucosa. In addition, mucoadhesive dosage forms have been used to target local disorders at the mucosal surface to reduce dose and to minimize the side effects. Mucoadhesive formulations use polymers as the adhesive component. These polymers are often water soluble and when used in a dry form, they attract water from the mucosal surface and this water transfer leads to a strong interaction further increasing the retention time over the mucosal surfaces and leads to adhesive interactions. Prolonged contact time of a drug with a body tissue through the use of a bio adhesive polymer can significantly improve the performance of many drugs[3].

MATERIALS AND METHODS

Montelukast sodium was purchased from Unichem pharmaceuticals, Goa. Poloxamer 407, HPMC, Polyethylene glycol 400 was obtained from Loba Chemi., Mumbai.

METHODOLOGY:

Preparation and calibration curve of montelukast sodium:

Spectrophotometric method based on the measurement of absorbance at 283.2 nm of UV region in phos. buffer 6.4 was used in the study for estimation of montelukast sodium.

Preparation of phosphate buffer pH 6.4:

Phosphate buffer pH 6.4 was prepared according to I.P. 2007. A quantity of 50 mL of 0.2M potassium dihydrogen phosphate in a 200 mL volumetric flask and added 11.6 mL of 0.2 M sodium hydroxide was diluted with fresh distilled water to produce 200 mL.

Preparation of stock solution of montelukast sodium buffer pH 6.4 solution:

Accurately weighed 10 mg of montelukast sodium was dissolved in little quantity of phosphate buffer solution pH 6.4 and volume was adjusted to 100 mL with the same to prepare standard solution having concentration of 100 µg/ mL.

Procedure:

From the stock solution, aliquots of 2, 4, 6, 8 and 10 mL were transferred to 50 mL volumetric flasks and final volume was made to 10 mL with pH 6.4 phosphate buffer to get 2 to 10 µg/mL. Absorbance values of these solutions were measured against blank (phosphate buffer pH 6.4) at 283.2 nm using UV-visible spectrophotometer.

Preparation of montelukast sodium insitu nasal gel[4]:

Method:

Montelukast sodium *in-situ* gels were prepared by cold method. Small quantity of water dissolves various concentration ranges of poloxamer 407 separately such as 18, 20, 22, and 24% at cold conditions. The quantity of HPMC and MC was dissolved in that, according to the formulation chart. Later drug, PEG 400 and parabens were incorporated and stirred until clear solution was obtained. Finally make up the volume up to 10 mL with distilled water and kept it over night at (4-10°C) freezing conditions.

Table 1: Formula of montelukast sodium insitu nasal gel:

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Montelukast sodium(mg)	8	8	8	8	8	8	8	8	8
Poloxamer 407(mg)	300	100	300	100	300	300	100	200	200
HPMC E5(mg)	350	250	300	350	250	300	300	300	350
Methyl cellulose(mg)	150	150	100	150	150	200	100	150	100
Polyethylene gycol 400(ml)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Methyl parabens(mg)	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Water(ml)	10	10	10	10	10	10	10	10	10

Preformulation study:

Identification of Drug:

The preliminary studies were carried out by testing of different physical and chemical properties of drug as follows.

A. Organoleptic properties:

The organoleptic properties like physical state, colour, odour etc., of the drug was reported with help of the descriptive terminology. It helps to identify the drug.

B. Determination of Melting point:

It is the easy way to identify the drug. The melting point of montelukast sodium was tested by use of a laboratory melting point apparatus with a procedure given in the Indian Pharmacopeia 2007.

C. Solubility study[5]:

The solubility of montelukast sodium was determined by micropipette method in various solvents in order to meet the official standards. The solubility of drug was recorded by using various descriptive terminology specified in Indian pharmacopoeia, 2007.

D .Fourier Transform Infrared spectroscopy (FT-IR)[6]:

The compatibility between pure drug and polymer was detected by IR spectra obtained by using Bruker Alpha T. using Zink Selenium cells. The spectra were recorded over the wave number range of 4000 to 600 cm^{-1}.

E. UV Spectrophotometric Study:

a. Determination of λ max[7]:

The absorption maximum of the standard solution was scanned between 200-400 nm regions on Shimadzu-1700 Pharmaspec UV-visible spectrophotometer. The absorption maximum obtained with the substance being examined corresponds in position and relative intensity to those in the reference spectrum.

F. Differential scanning calorimetry (DSC) analysis[8]:

The proper design and formulation of a dosage form requires consideration of the physical, chemical and biological characteristics of all drug substances and excipients to be used in the fabricating the product. Each polymer used in the formulations was blended with the drug levels that are realistic with respect to the final dosage form. Each polymer was thoroughly blended with drug to increase drug- polymer molecular contacts to accelerate the reactions if possible.

Evaluation of montelukast sodium insitu nasal gel[9]:

A. Clarity:

The clarity of various formulations was determined by visual inspection under black and white background by using clarity test apparatus and it was graded as follows;

Turbid +, Clear ++, Very clear (glassy):+++.

B. Measurement of gelation temperature (T1)[10] :

It was determined by using method described by Miller and Donovan technique. A 2 mL aliquot of gel was transferred to a test tube, immersed in a water bath. The temperature of water bath was increased slowly and left to equilibrate for 5 min at each new setting. The sample was then examined for gelation, which was said to have occurred when the meniscus would no longer moves upon tilting through 90^{o} C.

C. Measurement of gel meting temperature (T2):

After attaining the temperature T1, further heating of gel causes liquification of gel and form viscous liquid and it starts flowing, this temperature is noted as T2 i.e. gel melting temperature. It is a critical temperature when the gel starts flowing upon tilting test tube through 90^{0} C.

D. Determination of pH[11]:

1 mL quantity of each formulation was transferred to the 10 mL volumetric flask and diluted by using distlled water to make 10 mL. pH of resulting solution was determined by using digital pH meter (LI120 pH meter, ELICO LTD)

E. Drug content[12]:

1 mL of formulation was taken in 10 mL volumetric flask, diluted with distilled water and volume adjusted to 10 mL. 1 mL quantity from this solution was again diluted with 10 mL of distilled water. Finally the absorbance of prepared solution was measured at 283.2 nm by using UV visible spectrophotometer.

F. Measurement of viscosity[13]:

The viscosity measurements were carried out by using Brookfield DV-11 Pro viscometer. The gel sample was placed in small sample adaptor. Temperature was increased in the range of 20^{0} C –34^{0}C, using a water circulation jacket. The temperature sensing probe was lowered in gel and temperature of gel was recorded. Viscosity at various temperatures was recorded.

G. *In-vitro* drug permeation studies[14]:

Drug release from gel was tested with Franz diffusion cell, using dialysis membrane (mol.wt.12000-14000) with permeation area of 2.545 cm^2. 25 ml of phosphate buffer 6.4 was added to the acceptor chamber. Gel containing drug equivalent to 10 mg was placed in donor compartment. At predetermined time points, 1 mL sample were withdrawn from the acceptor compartment, replacing the sample volume with phosphate buffer buffer pH 6.4 after each sampling for a period of 5h. The samples were suitably diluted and measured spectrophotometrically at 283.2 nm.

The obtained data was further processed for kinetic model study.

H. Stability studies[15]:

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of accelerated stability studies are adopted.

RESULTS AND DISCUSSION

Identification of drug:

1. Description:

Colour: white to off-white powder

Odour: odorless

Melting point: 146^{0}C (reported 145 to 148^{0}C)

2. Solubility study

Table 2 : The solubility of montelukast sodium in various solvents

S.No.	Name of solvent	Solubility	Parts of solvent required for 1 part of solute
1	0.1 N sodium hydroxide	Freely soluble	10
2	Distilled water	Freely soluble	10
3	Ehanol	Soluble	10
4	Methanol	Soluble	10
5	0.1 N HCl	Soluble	10
6	Phosphate buffer pH 6.4	Freely soluble	10
7	PEG 400	Soluble	20

3. UV spectrophotometric study

Calibration Curve of montelukast sodium in phosphate buffer pH 6.4:

UV absorption spectrum of montelukast sodium in phosphate buffer pH 6.4 showed λ max at 283.2 nm. The graph of absorbance Vs concentration for montelukast sodium was found to be linear in the concentration range of 2-10 µg /mL. The drug obeys Beer- Lambert's law in the range of 2-10 µg /mL.

4. Fourier Transforms Infra-Red (FTIR) Spectroscopy Study:

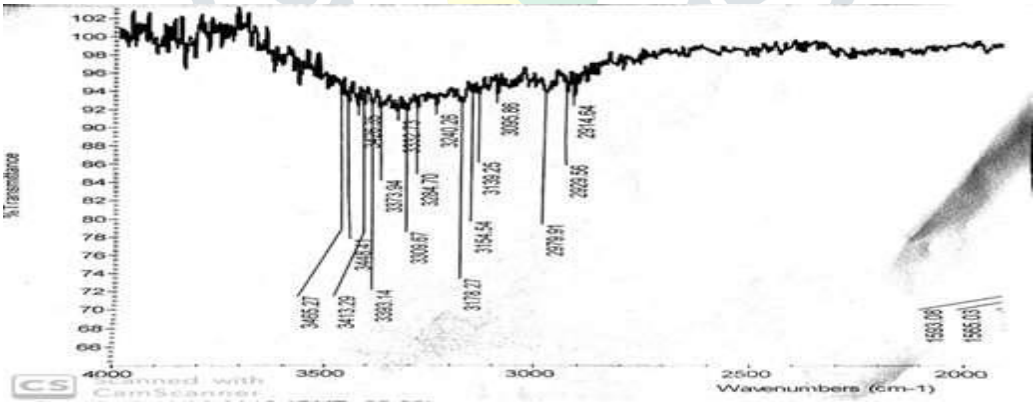

Fig.1: FTIR spectrum of montelukast sodium

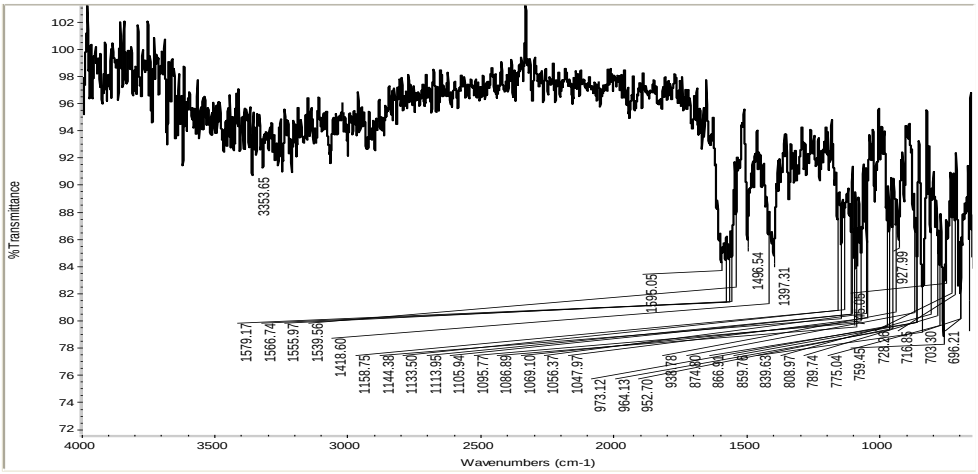

Fig.2: FTIR Spectrum of montelukast sodium+poloxamer 407

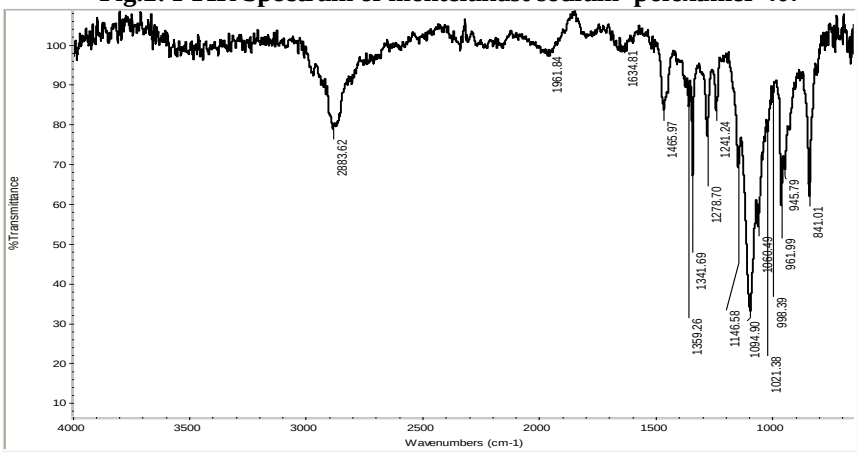

Fig.3: FTIR Spectrum of Poloxamer 407

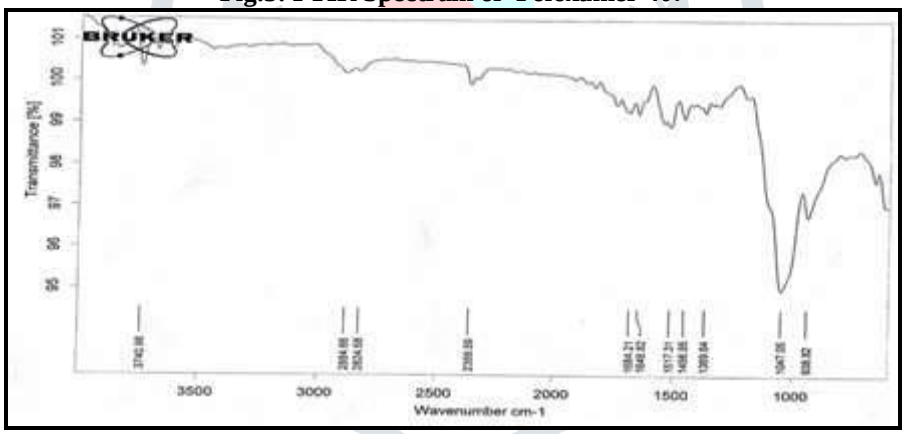

Fig.4: FTIR Spectrum of HPMC

5. Differencial scanning calorimetry (DSC) analysis:

The compatibility and interactions between drug and polymers were checked using DSC; results obtained were shown in fig.5.

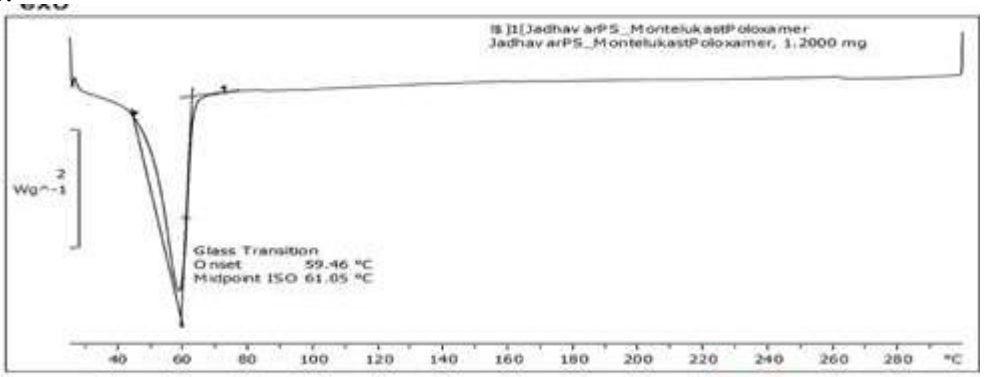

Fig.5: DSC Thermogram of montelukast sodium+poloxamer 407

Table 3 : DSC Thermogram of montelukast sodium+poloxamer

Sr.No.	DSC Thermogram sample	Onset temp.(^{0}C)	Peak temp.(^{0}C)
1	Montelukast sodium+poloxamer 407	59.46^{0}C	61.05^{0}C

6. Evaluation of mucoadhesive *in situ gels*:

Clarity:

The clarity of nine formulations of montelukast sodium mucoadhesive nasal *gels* were recorded in Table 4.The clarity of various formulations were determined by visual inspection under black and white background. All the prepared formulations were found to be clear (+) and very clear (+++ glassy). The very clear transparent solution was found to be F4 with the grade of +++ under the visual inspection of both black and white background.

Table 4: Clarity of mucoadhesive nasal gel

Sr. no	Formulation code	Visual appearance	
		Black background	white background
1	F1	++	++
2	F2	++	++
3	F3	+++	+++
4	F4	+++	+++
5	F5	++	++
6	F6	+++	+++
7	F7	++	++
8	F8	++	++
9	F9	++	++

Measurement of gelation temperature (T1):

The physiological range of the nasal mucosal temperature lies between 32-34ºC. Poloxamer 407 undergo thermal gelation or sol-gel transition at a temperature of about 25-37 ºC.

The gelation temperature study shows that loading of drug montelukast sodium and polymers like HPMC and PEG 400 alters the T1 of HPMC gel formulation that F1,F2, F3 having gelation temperature of 28.53, 31.23, 32.53 having low level (0.25%) of HPMC whereas F4,F5, F6 having gelation temperature of 34.86, 36.13, 35.00 having middle level (0.5%) of HPMC where as F7, F8,F9 having the gelation temperature of 37.93, 36.00, 38.53. It indicates that mucoadhesive polymer HPMC has increased T1 whereas the addition of water soluble PEG 400 increased the T1. The phenomenon may be mediated through modification of miceller association of the poloxamer 407 molecule. In addition the PEG molecules may form mixed micelles with Poloxamer. The hydrophilic end chains of Poloxamer 407 the same PEO chains that are present in PEG. It is suggested that esters binds to these chains, promoting dehydration and causing an increase in entanglement of adjacent micelle. In the presence of PEG, association of poloxamer molecules were hindered and mixed miceller system with different physicochemical properties found.

Measurement of gel melting temperature (T2):

The gel-sol effect depends on the addition of water soluble polymer PEG 400. The mucoadhesive polymer HPMC increases the T2 of the formulations. The gel melting temperature of the formulations F1,F2, F3 having 56.2, 52.2, 47.56 whereas F4, F5, F6 having 48.00, 47.8, 53.13 where as F7, F8, F9 having 54.26, 55.16, 58.2. It indicates that addition of water soluble PEG 400 produces increase in T1 while decrease in T2.

The gelation temperature (T1) and gel melting temperature T2 of nine formulations of Montelukast sodium mucoadhesive nasal *gels* were recorded in Table 5.

Table 5 : Gelation Temp.(T1) and Gel Melting Temp. (T2) of mucoadhesive insitu nasal gel

S.N0	FORMULATION CODE	GELATION TEMPERATURE (T1°C) ± SD	GEL MELTING TEMPERATURE (T2°C) ± SD
1	F1	28.53±0.94	56.20±0.03
2	F2	31.23±0.66	52.60±0.01
3	F3	32.53±0.13	47.56±0.35
4	F4	34.86±0.30	48.00±0.52
5	F5	36.13±0.30	47.80±0.38
6	F6	35.00±0.38	53.13±0.44
7	F7	37.93±0.46	54.26±0.17
8	F8	36.00±0.34	55.26±0.33
9	F9	38.45±0.15	58.20±0.91

Determination of pH:

The pH of nine formulations of montelukast sodium mucoadhesive nasal gels were recorded in Table 6.

Table 6: pH of mucoadhesive insitu nasal gel

Sr.No.	Formulation code	pH ± S.D.
1	F1	6.27±0.04
2	F2	5.59±0.02
3	F3	6.32±0.02
4	F4	6.47±0.01
5	F5	6.40±0.09
6	F6	6.26±0.07
7	F7	5.48±0.09
8	F8	6.68±0.02
9	F9	5.98±0.01

It is known that the normal physiological pH of nasal mucosa is 4.5-6.5. However the nasal mucosa can tolerate solutions within pH range of 3-10. pH of all the nine formulations were found to be within 5.48-6.68 that is between physiological range of pH of nasal mucosa.

Determination of drug content:

The drug content of nine formulations of montelukast sodium mucoadhesive nasal in situ gels were recorded in Table 7.

Table 7: Drug Content of mucoadhesive insitu nasal gels

S.NO	FORMULATION CODE	DRUG CONTENT±S.D. (%)
1	F1	89.05±0.08
2	F2	90.22±0.04
3	F3	92.45±0.07
4	F4	98.30±0.02
5	F5	96.22±0.01
6	F6	94.64±0.05
7	F7	90.26±0.07
8	F8	89.99±0.04
9	F9	94.92±0.03

The percentage drug content of all the prepared nasal gels formulations were checked and found to be in the range of 89.05-98.30%.

Measurement of Viscosity:

The measurement of of nine formulations of montelukast sodium mucoadhesive nasal gels were recorded in Table 8.

Table 8: Viscosity of mucoadhesive insitu nasal gels

TEMP ^{0}C VISCOSITY MEASUREMENTS (cPs)±S.D.									
	FORMULATION CODE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
20 °C	840.00 ±1.54	810.33 ±1.45	835.33 ±1.54	910.00 ±1.00	958.00 ±1.00	998.66 ±1.52	1040.33 ±1.25	1265.00 ±1.00	1298.66 ±1.15
22 °C	854.00 ±1.15	825.00 ±1.00	868.33 ±1.52	968.00 ±1.00	1021.0 0±1.00	1045.33 ±0.57	1094.66 ±1.52	1299.33 ±1.52	1454.66 ±0.57
24 °C	870.66 ±1.15	896.00 ±0.57	910.00 ±1.00	1042.6 6±0.57	1145.3 3±1.52	1298.00 ±1.73	1312.00 ±1.73	1542.00 ±1.00	1845.33 ±1.52
26 °C	926.66 ±0.98	910.00 ±0.57	960.66 ±1.52	1092.6 6±0.57	1415.0 0±1.00	1615.00 ±1.00	1640.33 ±1.52	1964.33 ±1.52	2045.00 ±1.00
28 °C	1060.6 6±0.78	936.33 ±1.52	998.66 ±1.52	1112.6 6±1.52	1845.6 6±1.52	2245.00 ±1.73	1975.00 ±1.00	2211.33 ±1.52	2541.00 ±1.00
30 °C	1098.6 6±1.00	981.00 ±1.00	1041.6 6±1.15	1742.0 0±1.00	2015.0 0±1.73	2402.33 ±1.52	2320.00 ±1.00	2621.66 ±1.52	2987.66 ±1.15
32 °C	1140.0 0±1.00	1042.0 0±0.57	1165.6 6±1.50	2054.6 6±0.57	2350.0 0±1.00	2750.00 ±1.00	3510.33 ±1.52	3244.33 ±1.52	3124.33 ±1.15
34 °C	1196.6 6±1.52	1140.3 3±1.00	1237.0 0±1.73	2545.0 0±1.00	2610.6 6±1.52	2910.66 ±1.52	3321.00 ±1.00	3268.00 ±1.00	3321.00 ±1.00

The table (8) shows the viscosity profile of formulations at 34ºC. Viscosity measurement of the nine formulations at various temperatures shows that there was increase in viscosity with increase in temperature. This indicates the temperature induced gel structure formation of poloxamer 407.

In-vitro drug permeation studies

Table 9: *In-vitro* drug permeation profile of formulation F4, F5, F6.

SR.NO.	TIME IN HRS	MEDIUM	F4(%)	F5(%)	F6(%)
1	0	PHOSPHATE BUFFER 6.4	0.00	0.00	0.00
2	1		19.45	17.25	18.56
3	2		25.25	21.56	22.75
4	3		34.36	27.56	26.76
5	4		39.44	35.87	34.65
6	5		46.55	48.46	50.45
7	6		72.29	70.68	69.45
8	7		79.77	81.25	82.45
9	8		98.87	97.78	96.12

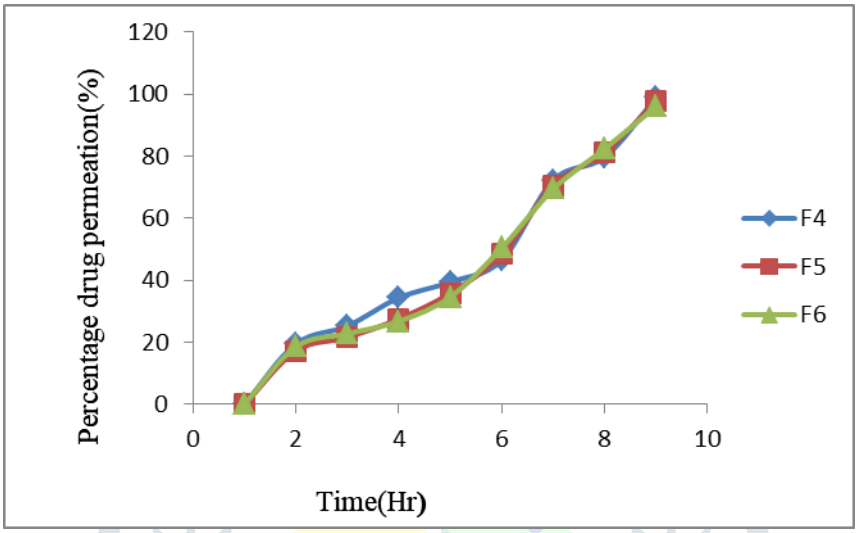

Fig.6: *In-vitro* drug permeation profile of formulations F4,F5,F6

In-vitro diffusion studies revealed that the release of montelukast sodium from different formulations varies with the characteristics and composition of polymers.

The formulated mucoadhesive gels showed a most favorable release within 5 hours. But in the 8th hour, the drug permeation was 87.23%, 88.34%, 85.21%, 98.87%, 97.87%, 96.12%, 84.95%, 88.41% and 91.10% for F1, F2, F3, F4, F5, F6, F7, F8 and F9 respectively. This was followed by a steady drug release pattern.

From these above data, it showed formulation F4 permeated drug mostly at the end of 8 hours. The *In-vitro* drug permeation rate of Montelukast sodium shows that with increasing HPMC concentration influences the diffusion of drug particle while addition of PEG 400 enhances the drug permeation.

Among all the nine formulations, formulation F4 (composed of montelukast sodium 8mg, 100 mg poloxamer 407, 350mg HPMC,150mg Methyl cellulose,0.5ml PEG 400) exhibited the highest *In-vitro*drug permeation of 98.87% at 8 hours, while the lowest drug release of 84.95% was recorded for formulation containing (composed of montelukast sodium 8mg, 100 mg poloxamer 407, 300mg HPMC,200mg methyl cellulose,0.5ml PEG 400).

From the above evaluation parameters it was concluded that the formulation F4 having a maximum percentage of drug release in acontrolled manner, so the formulation F4 was selected as the optimized formulation.

Kinetics of *In-vitro* drug permeation:

Table 10: Drug release Kinetics for montelukast sodium insitu nasal gel formulation F4

Sr.No	Time (Hr)	Square root of time	Log time	Cum % DR	% DR remaining	Log Cum %DR	log cum %DR remaining
1	0	0		0	0	0	0
2	1	1	0	19.45	80.55	1.288919606	1.906065545
3	2	1.414	0.150449	25.25	74.75	1.402261382	1.873611197
4	3	1.732	0.238548	34.36	65.64	1.536053155	1.817168572
5	4	2	0.30103	39.44	60.56	1.595936906	1.782185866
6	5	2.236	0.349472	46.55	53.45	1.667919685	1.72794771
7	6	2.449	0.388989	72.29	27.71	1.859078225	1.442636526
8	7	2.645	0.422426	79.77	20.23	1.901839592	1.305995883
9	8	2.828	0.451479	98.87	1.13	1.995064534	0.053078443

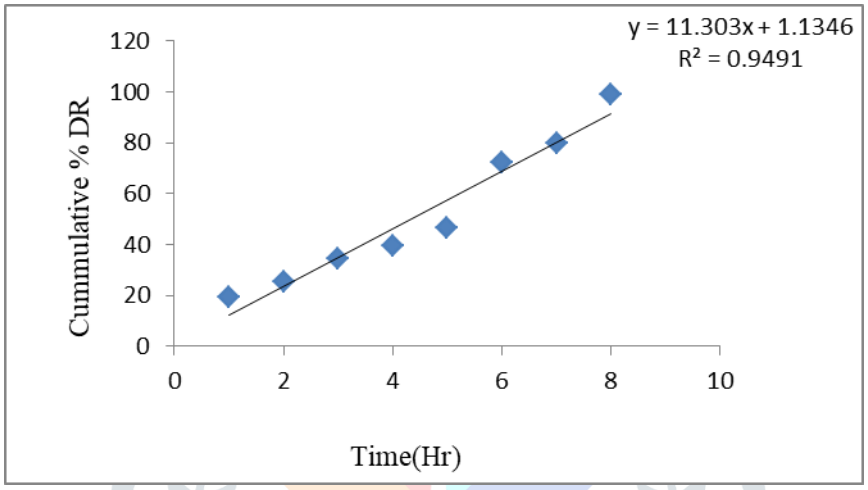

Fig.7: Zero order plot of montelukast sodium insitu nasal gel F4

Table 11: Different kinetic models for montelukast sodium nasal in situ gels(F4)

S.NO	F. Code	Zero order	First order	Higuchi	Korsemeyer-Peppas	Best fit model
		R^2	R^2	R^2	R^2	
1	F4	0.9491	0.0.6433	0.0.884	0.0.7824	Zero order

7. Stability studies:

Procedure:

The study was carried out to observe the effect of temperature on optimized formulation (F4). Stability studies were carried out at 40°C ±2°C at 75% RH ± 5% for the formulation F4 for 3 months. A quantity of montelukast sodium *in situ gel* in cillin bottles were stored in a dessicator containing a saturated solution of sodium chloride, which provided a relative humidity of 75 ±5%. The dessicator was placed in a hot air oven maintained at 400C ± 20C, and the samples were withdrawn at 1, 2 and 3 months.

After exposure to stability conditions (40ºC ±2ºC at 75% RH ±5% RH) the formulation was analyzed for various evaluation parameters; results are shown in Table 12.

Table 12: Stability studies of optimized formulation F4

Characteristic	Initials	1st Month	2nd Month	3rd Month
Clarity	+++	+++	+++	+++
Gelation Temperature (T1)	34.86±0.30	34.86±0.30	34.85± 0.36	34.84± 0.41
Gel Melting Temperature (T2)	48.00±0.52	48.00±1.42	47.99±1.61	47.98±0.25
pH	6.47±0.02	6.46 ±0.05	6.44 ±0.02	6.42± 0.02
Drug Content	98.30±0.02	98.28±0.11	98.26±0.14	97.24±0.02
Invitro Drug Permeation at 8 h (%)	98.87	98.80	98.72	98.40

Table 13: Percentage *In-vitro* drug permeation of selected formulation F4 after stability studies at 40°C ±2°C at 75% RH ± 5%.

S. No	Time in Hrs	$40^0C±2^0C$ at 75%RH±5%			
		Initial	1st month	2nd month	3rd month
1	1	19.45	19.42	19.40	19.39
2	2	25.25	25.23	25.20	25.18
3	3	34.36	34.34	34.31	33.30
4	4	39.44	39.42	39.41	39.38
5	5	46.55	46.53	46.51	46.49
6	6	72.29	72.27	72.26	72.24
7	7	79.77	79.76	79.72	79.70
8	8	98.87	98.85	98.83	98.79

The studies revealed that, there were no much significant changes in was intimate between the evaluated data from initial after stability studies of Clarity, pH, gelation temperature (T1) and gel melting temperature (T2), drug content and *In-vitro* drug permeation studies and all the values were found in worth accepting limits after the stability studies at 40°C ±2°C at 75% RH ± 5% for optimized formulation F4.

CONCLUSION

The studies revealed that, there were no much significant changes in percentage clarity, gelation temperature and gel melting temperature, pH, drug content and *In-vitro* drug permeation studies for three months at 40ºC. Out of the nine formulations, it appears that formulation F4 has the maximum potential in providing In situ gel nasal delivery system. This formulation was considered as best formulation for temperature induced nasal in situ gelling system for the treatment of allergic rhinitis with respect to its evaluation parameters like clarity, gelation temperature and gel melting temperature, pH, drug content and *In-vitro* drug release and this formulation may give patient friendly and needle free dosage form**.**

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