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Formulation and Evaluation of Meloxicam pH Induced *In-situ* Gels

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ABSTRACT

The traditional liquid ophthalmic delivery methods expose light pre-corneal residence time to come and also the better half retentivity to with the cornea which results in poor eye bioavailability. The aim of the present work was to formulate and evaluate an pH induced *in situ* gels for a non steroidal anti-inflammatory drug, Meloxicam, based on the concept of pH Induced *in situ* gelation. The sodium alginate was used as the gelling agent in combination with HPMC (0.25- 0.75 % w/v) which means a viscosity improving agent. Compatibility studies of the drug excipients were carried out using FTIR studies. The planned out formulations have been characterised as clarity, pH, Gelation studies, drug content, *In vitro* drug release. *In vitro* release studies determined for which MF8 formulation containing 0.3%w/v of sodium and HPMC (10cps & 15cps) with 0.5%w/v each shows sustained drug release up to 8hrs & follows zero order kinetics.

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INTRODUCTION

The current work envisaged formulating a pH-induced *in situ* gelling system of Meloxicam to attain see the light patient compliance by increasing residence time and bioavailability [1]. The advantages of *in situ* gel forming systems includes ease of administration and reduced frequency of administration. Meloxicam is a NSAID belonging to the class of oxicams. Meloxicam inhibits cyclooxygenase synthesis [2]. It has analgesic and antipyretic effect and used within the treatment containing rheumatoid arthritis, post-traumatic and postoperative pain, inflammation and swelling.

MATERIAL AND METHODS

Meloxicam was obtained from BMR Chemicals, Hyderabad. HPMC 10 cps, HPMC 15 cps were supplied by Bliss chemicals & pharmaceuticals India Ltd., Mumbai, India. Benzalkonium chloride, sodium chloride were supplied by MJ Biopharmaceuticals, Mumbai various chemical have been were using analytical grade.

Methodology

Interaction studies

Sample concentration in KBr must be within the lim-

its of 0.2% to 1%. The thickness of the pellet is much greater than a liquid film, so sample with low concentration in in-situ gelling systems [3].

Preparation of pH Induced *In-Situ* Gelling System

In situ gelling liquids had been planned out victimisation abundant concentrations of HPMC 10cps and HPMC 15cps with combination of HPMC 10cps & HPMC 15cps. Meloxicam (0.5 w/v) was weighed individually and melted within the water. HPMC 15cps & HPMC 10cps solutions. The Meloxicam solution used to be added to the alginate solution underneath constant stirring until eventually uniform, clear solution was obtained. Further, to these mixture different concentrations of HPMC 15cps & HPMC 10cps were added. Benzalkonium chloride, sodium chloride was add to the previous solutions [4]. Finally, the amount used to be adjusted with distilled water up to 100 ml (Table 1).

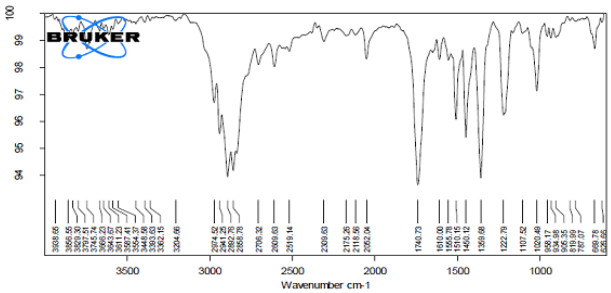

Figure 1: IR spectra of pure drug

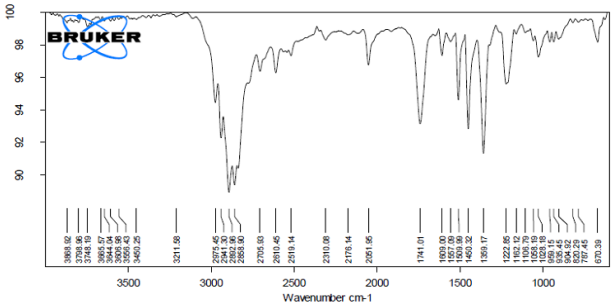

Figure 2: IR spectra of optimized formulation

Evaluation of Formulation

Visual Appearance and Clarity

It becomes done beneath fluorescent light opposed to a white and black backdrop for the reason that presence containing any particulate matter [5].

pH

The planned out in-situ gels sounded using pH meter [6].

Drug Content Analysis

The assay all these formulations transmit mostly by pipetting 0.1 ml of optimized formulation, as well as it was once diluted equal to 100 ml containing Simulated Tear Fluid [7]. The absorbance used to be sounded at 293 nm with a UV-Visible spectrophotometer.

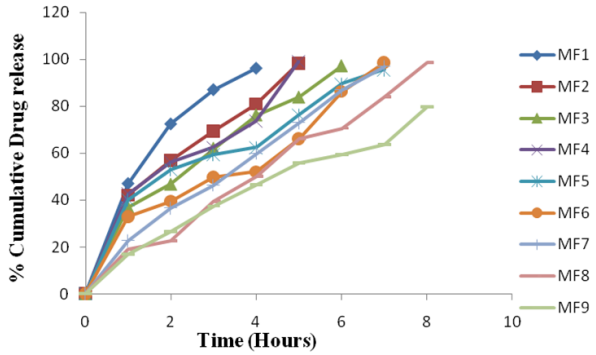

Figure 3: *In-Vitro* Release Profile of Meloxicam pH-induced *in situ* gels

Gelation Temperature

In a beaker containing cold sample solution at low temperature, immersed thermometer inside the sample. The beaker kept in a magnetic bar at 200 rpm. The melting point from which the magnetic bar flashed moving due to gelation was reported as the gelation melting point (Table 2).

Rheological Studies

The viscosity purpose transmits mostly by using a Brookfield viscometer [8].

In-Vitro Release Studies

In Franz diffusion cell used to be stuffed with 10 mL fresh simulated tear fluid in receptor compartment [9]. The receptor fluid used to be kept at 37 $\pm$ 0.5°C as well as constant moving employing Teflon coated magnetic stir. Spectracular samples had been examined absorbance at 293 nm within a spectrophotometer.

Drug Release kinetic Studies

In the present study, data of the *In vitro* release were fitted to different equations and kinetic models to explain the release kinetics of meloxicam in-situ gels [10].

Zero-order model: $Qt = Q0 + K0t$

First Order Model: $\text{Log } C = \text{Log } C_o - kt/2.303$

Higuchi model: $Q = K_H - t^{1/2}$

Korsmeyer-Peppas model: $Mt / M\infty = Kt^n$

RESULTS AND DISCUSSION

FTIR Studies

Spectacular peaks acquired in the spectra going from optimized formulation have been correlative

Table 1: Formulation of Meloxicam pH-Induced *In situ* Gels

Ingredients (%w/v)	MF1	MF2	MF3	MF4	MF5	MF6	MF7	MF8	MF9
Meloxicam	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Sodium alginate	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
HPMC 10cps	0.25	0.5	0.75	–	–	–	0.25	0.5	0.75
HPMC 15cps	–	–	–	0.25	0.5	0.75	0.25	0.5	0.75
Benzalkonium chloride	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
sodium chloride	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9
Water (ml)	100	100	100	100	100	100	100	100	100

Table 2: Evaluation of pH, Drug Content Analysis, gelation temperature

Formulations	Gelation temperature	pH	Drug content
MF1	26.92±0.15	7.5±0.01	96.14±0.22
MF2	26.52±0.45	6.9±0.07	93.27±0.56
MF3	25.15±0.22	6.9±0.06	98.39±0.01
MF4	29.92±0.50	7.2±0.09	99.78±1.86
MF5	31.18±0.33	6.9±0.04	96.65±0.52
MF6	30.46±0.48	7.2±0.03	97.19±0.48
MF7	38.36±0.12	7.0±0.20	96.45±1.89
MF8	37.68±0.28	7.1±0.15	95.36±2.46
MF9	35.43±0.72	7.3±0.05	98.52±0.66

Table 3: Rheological studies of all the formulations

Shear Rate (RPM)	Viscosity (cps) of Formulations								
	MF1	MF2	MF3	MF4	MF5	MF6	MF7	MF8	MF9
2	102.1	105.0	106.5	101.0	103.0	107.1	98.6	100.2	102.2
4	96.0	97.4	99.2	94.2	98.5	99.6	91.2	94.3	97.5
6	81.2	84.5	88.4	78.5	82.3	85.4	80.4	82.1	85.4
10	63.7	66.0	68.5	61.0	64.0	69.0	61.5	64.5	66.2
20	39.5	41.2	46.4	38.0	40.2	43.2	38.0	41.6	43.7
30	29.4	31.3	36.0	29.0	31.5	34.5	27.1	30.0	32.0

with spectacular peaks consisting of the drug spectrum.

This means therefore the drug was compatible using the formulation components as shown in Figures 1 and 2.

Rheological Studies

The formulation must have optimal viscosity for straight forward installation into the eye, which is able to submit to a quick sol-to-gel transition, hence the virtue solidify capacity (Table 3).

In-Vitro Release Studies

Total nine formulations were designed by using two different polymers and gelling agent, among them MF1 to MF3 formulations, were formulated using HPMC 10cps as viscosity enhancer with three different proportions (0.25, 0.5, & 0.75%) in which maximum concentration shows sustain release up to 6hrs. Further formulations were formulated using HPMC 15cps with the same proportions. MF4-MF6 formulations were formulated using HPMC 15cps as a viscosity enhancer. Among them, HPMC 15cps with the highest concentration shows maximum sustain release up to 7hrs. Further 3 formulations were designed with a combination of HPMC 10cps & 15cps. MF7-MF9 formulation was formulated using HPMC 10cps & HPMC 15cps in combination. MF7 formulations show a maximum drug release

Table 4: *In-Vitro* Release Profile of Meloxicam pH-induced *in situ* gels

Time (hr)	MF1	MF2	MF3	MF4	MF5	MF6	MF7	MF8	MF9
0	0	0	0	0	0	0	0	0	0
1	46.95± 0.16	42.08± 0.86	36.95± 0.32	42.69± 0.15	40.05± 0.15	32.95± 0.16	22.64± 0.46	19.06± 0.12	16.85± 0.20
2	72.37± 0.24	56.94± 0.95	46.75± 0.56	56.09± 0.26	52.94± 0.23	39.46± 0.24	36.53± 0.23	22.63± 0.26	26.37± 0.62
3	86.95± 0.53	69.37± 0.32	62.08± 0.80	62.38± 0.33	59.36± 0.46	49.61± 0.85	46.25± 0.52	39.38± 0.48	37.31± 0.23
4	96.08± 0.63	80.92± 0.10	76.34± 0.43	73.64± 0.84	62.38± 0.86	52.06± 0.36	59.76± 0.89	49.85± 0.84	46.38± 0.15
5	-	98.34± 0.31	83.96± 0.26	98.96± 0.56	76.48± 0.22	66.08± 0.95	72.84± 0.66	66.07± 0.62	55.82± 0.01
6	-	-	97.34± 0.16	-	89.38± 0.46	86.34± 0.42	86.84± 0.34	70.49± 0.31	59.31± 0.62
7	-	-	-	-	95.61± 0.29	98.68± 0.54	96.81± 0.21	83.94± 0.20	63.68± 0.23
8	-	-	-	-	-	-	-	98.52± 0.46	79.64± 0.15

Table 5: Drug release kinetics

	r^2 values				n values
Formulation	Zero-order	First-order	Higuchi	Korsmeyer - Peppas	Korsmeyer- Peppas (n)
MF8	0.991	0.725	0.921	0.698	1.490

of 96.81% up to 7 hrs. Whereas MF8 formulation shows 98.52% of drug release at then of 8th hour and MF9 formulation shows 79.64% drug release at the end of 8^{th} hour due to higher proportion of polymer. So MF8 formulation displays level best drug release subsequently of 8 hours therefore its far selected as an optimized choice of words futher drug release kinetics report were carried out for MF8 formulation as shown in Figure 3 & Table 4.

Release Order kinetics

The in vitro drug release data expedient formulation MF8 were fitted in different kinetic models i.e., zero order, first order, and Higuchi and Korsmeyer-Peppas equation. Optimized formulation MF8 shows r^2value 0.991. As its value nearer to the '1', it is confirmed as it follows the zero-order release (Table 5). The steering mechanism of drug discharge is further unalterable individually Korsmeyer plus Peppas plot line, if n = 0.45 it truly is called Fickian diffusion, 0.45 < n < 0.89 suggest anomalous propriety. The 'n' worth is 1.490 for the optimized formulation (MF8) i.e., n value was n > 0.89 which indicates Super case II transport.

CONCLUSION

Meloxicam was successfully formulated as an *in situ* gel using HPMC as a polymer. Sodium alginate as a gelling agent is used in combination with HPMC as a viscosity-improving agent. The phrasing used to be liquid and performed speedy gelation consequent to approaching toward tear up fluid. Spectacular MF8 gel shaped *in situ* accorded sustained drug waiver over the eight hours period.

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Conflict of interest

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