ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF EXPERIMENTAL AND BIOMEDICAL RESEARCH

Published by Pharma Springs Publication Journal Home Page: https://pharmasprings.com/ijebr

Formulation and Evaluation of a pH Induced *In Situ* Occular Gelling System of Ketorolac

Sravya B*[1], Mandalapu Ruchitha[2], Kankala Soujanya[2], Nimmala Raveena[2], Syed Ahmed Hussaini[2], Modugula Jayaram[2]

[1]Department of Pharmacology, St. Mary's Pharmacy College, Deshmukhi (Village), Pochampally (Mandal), Yadadri Bhuvanagiri (Dist)-508284, Telangana, India
[2]St. Mary's Pharmacy College, Deshmukhi (Village), Pochampally (Mandal), Yadadri Bhuvanagiri (Dist)-508284, Telangana, India

Article History:

Received on: 25 Mar 2022
Revised on: 12 Apr 2022
Accepted on: 13 Apr 2022

Keywords:

Ketorolac,
Sodium Alginate,
HPMC,
FTIR

ABSTRACT

A traditional fluid ophthalmologic delivery mechanisms illustrate concise pre-corneal retention time as well as the relates impermeability toward the cornea which results in low class ocular bioactivity. An objective of a current work-place would be to establish but also analyze a kind optometric delivery mechanism for just a non-steroidal anti-inflammatory substance, ketorolac, founded on the principle like pH Induced through in situ gelling. A sodium alginate was being used as a gelation operative in combination by HPMC (0.25 - 0.75 % w/v) where did act like a viscous improving entity. Compatability studies of opoid components have been done utilizing fourier transform infrared studies. An optimized formulation have been characterized such as precision, Gelation studies, ph drug loading, *In vitro* release study. *In vitro* release studies demonstrated that such F8 formulation containing 0.3% w/v of sodium but also hydroxypropyl methylcellulose (10cps & 15cps) with 0.5% w/v each shows sustained release of drug up to 8hrs & nearly tries to follow zero order kinetics of super case II transmit process. A clearness, ph but also pure drug of an optimized formulation have been discovered of being satisfying. A designed system is indeed an alternative to the conventional ophthalmologic falls, patient compliance, commercially focussed as well as economical.

*Corresponding Author

Name: Sravya B
Phone: +91 9000461480
Email: dureddysravya@gmail.com

eISSN: 2583-5254 pISSN:

DOI: https://doi.org/10.26452/ijebr.v1i2.376

Production and Hosted by

Pharmasprings.com
© 2022 | All rights reserved.

INTRODUCTION

Opoid administered through initial installation should permeate the eyes but do so mainly through to the cornea retinal permeation is often more efficient just like sclera as well as conjunctival permeation, wherein withdrawal through blood vessels into the global circulation did occur. Numerous ophthalmologic opoids were also weak acids and thus are meant to apply to a retinal even through aqueous medium like about there sulphates. A freebase and also the sulphates would be in a kind steady state it will rely upon its ph and also the individual characteristics of a molecules [1]. To assist through trying to maintain storage stability as well as solubilisation, a medicine could be acidified in the meanwhile like initial installation even though, generally, a neutralizing activity of a lacrimal liquid might transform this quickly to a neutral ph. Range (~ pH 7.4) where at there'll be enough free base current to start permeation of corneal epithelium. While inside an epithelium (lipid rich) undisso-

ciated free base disintegrates instantaneously to such a degree. A disconnected moiety will then are likely to permeate a stroma even through it is water-soluble. Just at junction of a stroma (lipid poor) but also endothelial surface (lipid rich), the same process that will take position so at outermost layer of an epithelial layer should eventuate once more. Ultimately, a completely detached opioid leaves an endothelial surface for such aqueous humour [2]. Thus it could freely dispersed to a retinal as well as the choroidal, the location of all its biological activity. A topical application like ophthalmically effective substances to a cornea is most recommended path like administering again for treatment of a variety of conjunctival illnesses. It's indeed commonly accepted that its intro-ocular bioactivity like topical application substances is incredibly impoverished. On such initial installation of just an ophthalmologic option; almost all of the integrated amount has been excluded from pre-corneal region. Such destruction is especially because of irrigation of excessive fluid even by lacrimal conduit as well as eradication like the answer through split turnaround, that will leading to poor conjunctival bioactivity [3].

MATERIALS AND METHODS

The drug Ketorolac used in the present study was gathered from BMR Chemicals, Hyderabad and the polymers sodium alginate, HPMC 10cps,HPMC 15cps, Benzalkonium chloride and sodium chloride used are procured from S.D.Fine Chem. Ltd.

Preparation of pH Induced In-Situ Gelling System

In situ forming fluids have been able to prepare utilising various concentration of another HPMC 10cps but also HPMC 15cps with combination like HPMC 10cps & HPMC 15cps. Ketorolac (0.5 w/v) was did weigh individually but also disintegrated within deionized water HPMC 15cps & HPMC 10cps concentrations of various formulations (0.25%, 0.5%, and 0.75%) were prepared through distributing an amount required through deionized water as for consistent trying to stir till the dissolved completely Ketorolac, clear answer has been acquired [4]. Further, to weird these mix different concentrations of HPMC 15cps & HPMC 10cps have been got to add. Sodium benzoate chloride (0.02% w/v) has been got to add as just food preservation to previous remedies. Proper amount like sodium hypochlorite has been added into the solution to preserve isotonicity. Ultimately, the quantity has been adapted as for deionised water as much as 100ml [Table 1]. Slightly diluted pluronic remedies have been deposited up overnight inside a fridge there as 4^0C such as moisture but also agitated periodically till the clarify relatively homogeneous remedies have been acquired. 9 batches like preparation have been able to prepare through using various concentration like HPMC 15cps but also HPMC 10cps.

Compatibility Studies

Fully ready in-situ silicone compositions have been evaluated again for integrity like opioid within various formulations through it going to compare as for containing drug. Those were all taken to ensure that, a pharmaceutically important substance really hasn't undertaken whatever transition after it's been forced to submit of about processing methods throughout preparedness like in-situ gelation processes [5]. Such studies have been performed through trying to take IR pectroscopy utilising potassium bromide technique.

Evaluation of Formulation

Visual Appearance and Clarity

Visual appearance and clarity has been performed below fluorescent lights against such a blacks and whites background story such as appearance of every fine particulate [6].

pH

A pH that able to prepare in-situ gelation process now since addition of any of the components has been evaluated utilising pH meter [7].

Drug Content Analysis

Drug loading evaluation like fully ready in-situ gelation processes has been done utilizing spectrophotometry. An analyte of such compositions has been done through pipetting 0.1ml among all 4 optimisation compositions. But that was solubilised up to 100 ml like designed to stimulate tear liquid (pH 7.4). Absorbance was recorded about as 293 nanometers utilising UV-Visible spectrophotometrically.

In-Vitro Gelation

Gelation capabilities of formulations containing various ratios like HPMC 10cps but also HPMC 15cps has been analysed. This was accomplished through trying to place one fall-like polymeric solution through tubes containing 1ml like simulation model tear liquid, freshly cooked as well as evenly balanced there as 34^0C, but also visibly reviewed a gel created as well as duration as a gelling along with time it takes for the gel formed to dissolve [8].

Measurement of Gelation Temperature

At room temperature, ten milliliters of cold sample solution (pluronic containing formula) were put into

Table 1: Formulation of Ketorolac Ocular *In situ* Gels

Ingredients (%w/v)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ketorolac	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	100ml	100ml	100ml	100ml	100ml	100ml	100ml	100ml	100ml

a beaker (25 mL) but also positioned inside a low heat steam bath. One thermometer has been submerged into the standard solution such as strong monitoring. A solution has been subjected to heat as for trying to stir there as 200 rpm that used a magnetostrictive bar (9 $\times$ 25 mm). A temp where the magnetostrictive bar moved slowly because of gelling has been mentioned even as gelling temp (T_{gel}). Every test has been evaluated through triplicate [9].

Rheological Studies

It is also an influential point to find out its holding time like substance within cornea through going to consider its viscous of such ingrained composition. Prepared solutions have been permitted to gel about as biological temp and afterwards the viscous calculation was carried out using the Brookfield viscosity was measured (Brookfield DV+Pro, Brookfield Engineering research labs, Middleboro, MA, USA). Through intending diagram like shear rate vs shear stress, a different flow has been inspected [10].

In-Vitro Release Studies

In vitro drug permeability studies were conducted out through placing those in situ gelling preparation through Millipore membrane filtration (0.15 mm) here between donation as well as neurotransmitter storage area of such an all-glass reconfigured Franz diffusion organelle. To replicate a retinal epithelial boundary, a Millipore membrane filtration has been used, just like excluded colored part of the eye would not stay intact further than 4 hours work. A neurotransmitter storage area of such an all-glass reconfigured Franz dispersion organelle has been stuffed with 10 ml freshly made to stimulate tear liquid (pH 7.0), but all bubbles have been ejected out from storage area [11]. A kind equal volume (1 mL) like sample solution has been positioned upon that Millipore membrane filtration, and also the beginning of a donation organelle has been enclosed with such a cover glass glide, a neurotransmitter liquid has been maintained there as 37 $\pm$ 0.5°C as for constant stirring using just a Teflon-coated magnetic shake particles. Permeability research has been prolonged such as 10 hr. But also specimens have been forced to withdraw through the neurotransmitter as well as evaluated such as Ketorolac information through monitoring absorption there as 293nm in such a spectrophotometrically.

Drug Release Kinetic Studies

Within present research, information with the in vitro release have been equipped of about different formulas as well as kinetic model that explains the kinetic release model like representative Linagliptin out from buccal tablet devices. Kinetic designs were mostly zero order equation, 1^{st} order, higuchi release as well as Korsmeyer-Peppas model type [12].

Kinetic Studies: Mathematical Models

Different release kinetic formulae (zero-order, first-order, Higuchi's equation and Korsmeyer-peppas equation) have been implemented of about perceive the discharge rate of a substance through the matrix processes again for prepared formulations. The simplest suitable as for significant correlation (r^2) has been determined by calculating.

Zero-Order Model

Solubilization through the pharmaceutical formulations which do not disaggregate but also discharge a substance [13] gradually could be represented by a formula.

$Qt = Q0 + K0t$

Within which Qt has been the amount of substance diluted through time t, Q0 were just the initial amount of substance such as the solution (most times, Q0 = 0) as well as K0 is indeed the zero-order release consistent expressed as the number like concentration/time. To review the discharge kinetic rate, data obtained from in vitro research have been obtained by plotting just like combined total like substance set to release versus time.

Implementation

Has been used to define a drug dissolution among

several kinds of controlled–release pharmaceutical formulations aspects, like in the instance of certain subcutaneous processes, and also capsules as for poorly soluble substances through absolutely covered aspects, osmolarity processes, etc.

First Order Model

A first order equation explains the discharge through the processes where ts dissolution rate depends upon accumulation of solubilising organisms [14]. Release behavior patterns usually follows the subsequent 1^{st} order equation:

Log C= Log C_o-kt/2.303

Where C is the amount of drug dissolved at time t,

C_o is the amount of drug dissolved at t=0 and

k is the first order rate constant.

A graph of log cumulative of % drug remaining vs time yields a straight line. A pharmaceutical formulations aspects going to follow such a dissociation characterization, particularly ones comprising water-soluble substances through amorphous lattice, discharge opioids in such a manner which is compared to the quantity like substance leftover through its interior, in certain manner, that such number of drug ejected through time unit declines.

Higuchi Model

A first exemplar of such a mathematical formula designed to investigate release of drug from such a system has been posited through higuchi such as 1961. Initially designed as a planar processes, it had been maintained to different geometric patterns as well as erodible system design [15]. Such a model relies upon that hypothesis a certain. Initial substance concentration within has been much greater than solubility of drug; drug dispersion did take place mostly in each parallel universe (edge impact has to be negligible); drugs particulate are so much shorter just like process depth; Effusion but also dissociation have been negligible; Drug diffusion coefficient has been consistent; but also perfect sink situations always are achieved within secretion environmental. In a general way, a Higuchi model is just demonstrated through following equation

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

Where, K_H is the Higuchi dissolution constant.

The information acquired have been schemed just like cumulative drug discharge vs square root of time. Application: Such a connection could be used to define a dissolution rate of several kinds of controlled–release pharmaceutical formulations aspects like in the instance of certain transdermal processes as well as tablet devices of highly soluble in water substances.

Korsmeyer-Peppas Model

It inferred an easy relationship which characterized release of drug from such a polymeric process equation [16]. To find out of the control system like release of drug, first 60% release of drug information have been equipped through Korsmeyer-Peppas concept,

Mt / M∞ = Kt^n

where Mt / M∞ is indeed a couple of percent like substance set to release about as time t, k has been the release rate consistent but also n seems to be the discharge exponent. An n value is being used to categorize different access such as cylinder–shaped matrix. In this model, the value of characterizes the release mechanism of drug. The outcome from *in vitro* release secretion features acquired again for BDDS compositions have been equipped into the four styles of information diagnosis just like continues to follow:

1. Cumulative percent drug released versus time (zero-order kinetic model).

2. Log cumulative percent drug remaining versus time (first-order kinetic model).

3. Cumulative percent drug released versus square root of time (Higuchi's model).

4. Log cumulative percent drug released versus log time (Korsmeyer - Peppas equation)

RESULTS AND DISCUSSION

FTIR Studies

A fully ready in-situ gelation system design have been analyzed as a association studies to make sure that there's no interplay did occur between those substance as well as polymeric materials. For all of this conformation of about stabilisation like substance within optimized formulation an IR spectroscopy have been determined by comparison with those of the containing drug. The results of such research reveals that there have been no certainty varies acquired within bands like substance for pure drug [Figure 1 & Figure 2]. For such final confirmation of integrity of an opioid through compositions, the whole formulations have been exposed to IR research as well as in comparison with IR absorption spectra like containing drug. Researches revealed that there has been no certainty varies through bands seem to be recognized for containing drug. It was complied certain preparations didn't get any opioid-polymer interplay.

Enhanced *in-situ* hydrogel have been confined as a

Table 2: Evaluation of pH Induced In-Situ Gelling System

Formulation	Gelation Temperature	pH	Drug Content	Gelling Capacity
F1	26.92±0.15	7.5±0.01	96.14±0.22	+
F2	26.52±0.45	6.9±0.07	93.27±0.56	++
F3	25.15±0.22	6.9±0.06	98.39±0.01	++
F4	29.92±0.50	7.2±0.09	99.78±1.86	+
F5	31.18±0.33	6.9±0.04	96.65±0.52	++
F6	30.46±0.48	7.2±0.03	97.19±0.48	++
F7	38.36±0.12	7.0±0.20	96.45±1.89	++
F8	37.68±0.28	7.1±0.15	95.36±2.46	++
F9	35.43±0.72	7.3±0.05	98.52±0.66	+++

Table 3: Rheological Studies of All the Formulations

Shear Rate (F	Viscosity (cps) of Formulations								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
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

Table 4: *In-Vitro* Release Profile of Ketorolac Ocular *In situ* Gels (F1-F6)

Time(hr)	F1	F2	F3	F4	F5	F6
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
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
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
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
5	-	98.34±0.31	83.96±0.26	98.96±0.56	76.48±0.22	66.08±0.95
6	-	-	97.34±0.16	-	89.38±0.46	86.34±0.42
7	-	-	-	-	95.61±0.29	98.68±0.54
8	-		-	-	–	-

Table 5: *In-Vitro* Release Profile of Ketorolac Ocular *In situ* Gels (F7-F9)

Time(hr)	F7	F8	F9
0	0	0	0
1	22.64±0.46	19.06±0.12	16.85±0.20
2	36.53±0.23	22.63±0.26	26.37±0.62
3	46.25±0.52	39.38±0.48	37.31±0.23
4	59.76±0.89	49.85±0.84	46.38±0.15
5	72.84±0.66	66.07±0.62	55.82±0.01
6	86.84±0.34	70.49±0.31	59.31±0.62
7	96.81±0.21	83.94±0.20	63.68±0.23
8	-	98.52±0.46	79.64±0.15

Table 6: Drug Release Kinetics

Formulation	r^2 Values Zero-order	First-order	Higuchi	Korsmeyer - Peppas	n values Korsmeyer-Peppas (n)
F8	0.991	0.725	0.921	0.698	1.490

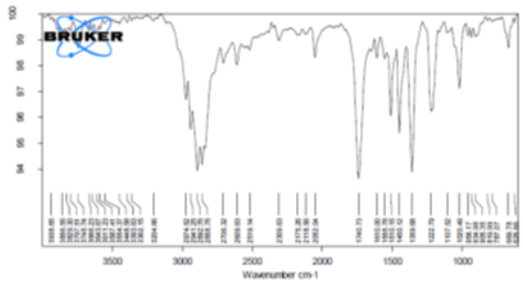

Figure 1: IR Spectra of Pure Drug

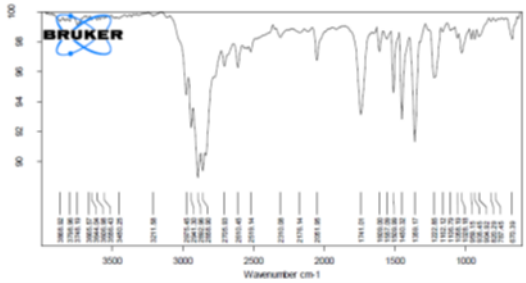

Figure 2: IR Spectra of Optimized Formulation

preliminary assessment such like, visual look, clearness, pH but also pure drug. The whole preparations that have been discovered were clear and transparent. pH of preparations is well within rules limiting. Drug content has been noticed inside of 93.27 % to 99.78% overall enhanced in–situ gelatinization system design [Table 2].

In-Vitro Gelatinization

Fully ready in-situ gelation system design have been analyzed as an in-vitro gellation capabilities. All of the preparations got positive outcomes.

Rheological Studies

Throughout blinking a shearing force upon that preparedness would be huge amount. If a viscous about as increased shear rate is just too greater, it will lead to irritation.

Alternatively, if a viscous is just too lesser, this would give effect of about enhanced drains. So, a composition must have optimised viscous for simple initial installation through into cornea just like fluid, which would undertake a quick sol-to-gel transfer, therefore the pleasant gelatinization capabilities [Table 3].

In-Vitro Release Studies

Total nine compositions have been designed through utilising two different polymers but also gelling agent, among them F1 to F3 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 upto 6hrs. Further formulations were formulated using HPMC 15cps with same proportions. The F4 – F6 formulations were formulated using HPMC 15cps as viscosity enhancer. Among them HPMC 15cps with highest concentration shows maximum sustain release upto 7hrs. Further 3 formulations were designed with combination of HPMC 10cps & 15cps. The F7-F9 formulation was formulated using HPMC 10cps & HPMC 15cps in combination. F7 formulations shows maximum drug release of 96.81% up to 7hrs [Figure 3]. Whereas F8 compositions showed 98.52% of release of drug at then of 8th hour and F9 formulation shows 79.64% drug discharge at the end of 8^{th} hour due to higher proportion of polymer. So F8 formulation shows maximal release of substance like 8 hour hence it is chosen as enhanced formulations further release of drug kinetics studies have been conducted for F8 formulation [Table 4 & Table 5].

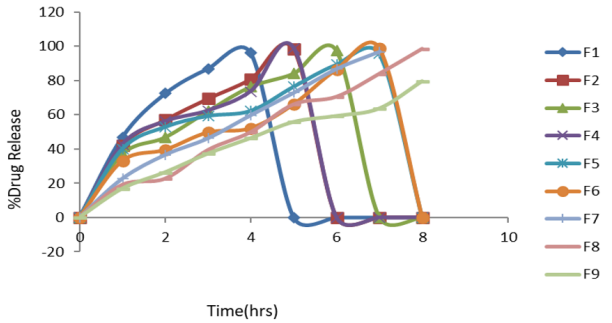

Figure 3: % Drug Release for All Formulations F1-F9

Release Order Kinetics

An *in vitro* drug release metrics as a finest composition F8 have been equipped in numerous kinetic model types i.e, zero-order, 1^{st} order, Higuchi as well as korsemeyer-peppas eqn. Prepared formulations F8 demonstrates value of R2 0.991. As this valu-

ation closer to a '1' this is complied since it tries to follow a zero-order release. A control system like release of drug is even further affirmed even by Korsmeyer as well as peppas plot, if n = 0.45 this is named Case I rather than Fickian diffusion, 0.45 < n < 0.89 is really for abnormal behaviour but rather non-Fickian transit, n = 0.89 such as case II transit as well as n > 0.89 as a Super case II transit. The 'n' value is 1.490 for the optimised formulation (F8) i.e., n value was n > 0.89 this indicates Super case II transport [Table 6].

Summary

The intention of such present study envisioned constructing a "pH Induced In-Situ gelation process like NSAID, Ketorolac" is for diagnosis like swelling and pain of eye, through supplying comfortness, complying to a sick people as well as enhanced therapeutic achievement of a substance over conventional eye solid dosage form. Optimisation in-situ gels have been exposed for preliminary assessment like, visual look, clearness, pH as well as drug content. A whole composition have been discovered clear and transparent. pH of compositions was still within rules limits. Drug content has been discovered 93.27 % to 99.78% throughout all enhanced in-situ gelation system design. To be able to analyze the Rheological properties, viscous of compositions has been analyzed utilising brook field viscometer. This have showed a certain viscous among all compositions decreased as the shear rate increased, where it have showed a personality like pseudo-plastic liquid. *In-vitro* discharge like Ketorolac out from chosen compositions must have been did study. Result illustrates a certain formulation (F8) displayed sustained release of a substance (above 95 %) as from HPMC as well as Sodium alginate as gelling agent network over 8 hours. All formulations have been exposed of about IR research as well as in comparison to IR absorption spectra like containing drug. Researches revealed that there has been no certainty varies through bands have been recognized for containing drug. So this was complied a certain compositions will not have any drug polymer connections. Results illustrates because no varies have been present in actual scenario, clarification as well as pH. Those certain compositions also were evaluated such as percentage substance residual.

CONCLUSION

Ketorolac has been effectively constructed as an in situ gel utilising HPMC as just a polymer. Sodium alginate as a gelation agent for use in combined effect of HPMC as either a viscous augmentation agent. A composition has been fluid as well as underwent a dramatic gelatinization on such making contact as for tear liquid. A f8 gel created in situ afforded sustained release across an 8-h duration. A composition have been potential therapeutic efficient. An optimized formulation is just a feasible alternative to standard eye drops because of the ability to improve bioactivity throughout its prolonged precorneal residence time and skill of about to sustain release of drug. As well essential seems to be the easiness like administering offered as well as lowered frequency like administering leading to better patient admittance.

ACKNOWLEDGEMENT

I would like to thank Principal sir (Dr. Kamal Hassan), St. Mary's Group of Institutions, Deshmukhi (Village), Pochampally (Mandal), Yadadri Bhuvanagiri(Dist), Telangana-508284, India.

Conflict of Interest

The authors attest that they have no conflict of interest in this study.

Funding Support

The authors declare that there is no financial support for the current study.

REFERENCES

[1] Hill JM, et al. Ophthalmic drug delivery systems; 1993. p. 1–204. New York, Marcel Dekker Inc, ISBN: 9780824788063.

[2] Bourlais CL, et al. Ophthalmic drug delivery systems-Recent advances. Progress in Retinal and Eye Research. 1998;17(1):2–5.

[3] Chein YW. Novel drug delivery systems. Vol. 29; 1993. p. 269–300. 2nd ed. New York, Marcel Dekker Inc, ISBN: 9780824785208.

[4] Geeta MP, Madhubhai MP. Recent Advances and Challenges in Ocular Drug Delivery Systems. Pharma Times. 2007;39(1):21–25.

[5] Peppas NA, Bures P, Leobandung WS, et al. Hydrogels in pharmaceutical formulations. European journal of pharmaceutics and biopharmaceutics. 2000;50(1):27–46.

[6] El-Kamel A. In vitro and in vivo evaluation of Pluronic F127-based ocular delivery system for timolol maleate. International Journal of Pharmaceutics. 2002;241(1):47–55.

[7] Kulkami MC, Damle AV. Development of ophthalmic in situ gelling formulation of flurbiprofen sodium using gellan gum. Indian Drugs-Bombay. 2007;44(5):373–377.

[8] Kumar MT, et al. pH-induced in situ gelling

systems of indomethacin for sustained ocular delivery. Indian journal of pharmaceutical sciences. 2005;67(3):327.

[9] Rozier A, Mazuel C, Grove J, et al. Gelrite®: A novel, ion-activated, in-situ gelling polymer for ophthalmic vehicles. Effect on bioavailability of timolol. International Journal of Pharmaceutics. 1989;57(2):163–168.

[10] Lindell K, Engström S. In vitro release of timolol maleate from an in situ gelling polymer system. International Journal of Pharmaceutics. 1993;95(1-3):219–228.

[11] Kumar S, Haglund BO, Himmelstein KJ. In Situ -Forming Gels for Ophthalmic Drug Delivery. Journal of Ocular Pharmacology and Therapeutics. 1994;10(1):47–56.

[12] Vodithala S, Khatry S, Shastri N, et al. Formulation and evaluation of ion activated ocular gels of ketorolac tromethamine. Int J Curr Pharm Res. 2010;2(3):33–41.

[13] Ramesh Y, Sireesha V. Transdermal Patch of Ramipril Loaded Chitosan Nanoparticles Dispersed in Carbopol Gel. Journal of Drug Delivery and Therapeutics. 2017;7(6):56–65.

[14] Gupta SK, Arora P, Yadav R. Sustained Ophthalmic Delivery of Ketorolac Tromethamine from an ion activated In Situ gelling system. International journal of pharmacy and life sciences. 2014;5(12):4063–4073.

[15] Parthiban KG, Manivannan R, Kumar BS, et al. Formulation and evaluation of ketorolac ocular pH-triggered in-situ gel. International Journal of Drug Development and Research. 2010;2(2).

[16] Kumar S, Himmelstein KJ. Modification of in Situ Gelling Behavior of Carbopol Solutions by Hydroxypropyl Methylcellulose. Journal of Pharmaceutical Sciences. 1995; 84(3):344–348.

Copyright: This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Cite this article: Sravya B, Mandalapu Ruchitha, Kankala Soujanya, Nimmala Raveena, Syed Ahmed Hussaini, Modugula Jayaram. **Formulation and Evaluation of a pH Induced *In Situ* Occular Gelling System of Ketorolac**. Int. J.Exp. Biomed. Res. 2022; 1(2): 56-63.

© 2022 Pharma Springs Publication.