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FORMULATION AND EVALUATION OF LORNOXICAM AS MUCOADHESIVE MICROCAPSULES

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ABSTRACT

The microencapsulation has a major role in solving the problems regarding targeting of drug to a specific organ tissue and controlling the rate of drug delivery to the target site. Microencapsulated drug delivery system plays a major role in developing oral controlled release systems. The objective of this work was to discuss how the efficiency of drug delivery can be increased and also how the release of drug and drug targeting can be improved. This work provides the thorough literature review of different techniques involved in microencapsulation and evaluation parameters of microencapsulation process. Various formulations were developed by using release rate controlling and gel forming polymers like HPMC-5 and HPMC-15. From among all the developed formulations, F3 formulation with HPMC-5 sustained the drug release for longer period of time as compared to other formulations. So, F3 formulation with HPMC-5 was selected as the best formulation. It was concluded that the release followed Zero order kinetics. Thus, best formulation satisfied physicochemical parameters and *in vitro* drug release profile requirements for a sustained drug delivery system.

Keywords: Microencapsulation, Core Material, Coating Material

INTRODUCTION

Mucoadhesive drug delivery system are delivery system which utilizes the property of bioadhesion of certain polymers which become adhesive on hydration and can be used for targeting a drug to a particular region of the body for extended periods of time. [1, 2] The term "mucoadhesion" was coined for the adhesion of the polymers with the surface of the mucosal layer. Bioadhesion is a phenomenon in which two materials at least one of which is biological and are held together by means of interfacial forces. The attachment could be between an artificial material and biological substrate such as adhesion between polymer and a biological membrane in case of polymer attached to the mucin layer of mucosal tissue. The term mucoadhesion is used when the mucosal layer lines a number of regions of body including a gastrointestinal tract, urogenital tract, the airways, the ears, nose and eye. These represent potential sites for attachment of bioadhesive system and hence the mucoadhesive drug delivery system could be designed for buccal, oral, vaginal, rectal, nasal and ocular route of administration.

Lornoxicam (chlortenoxicam), a new nonsteroidal anti-inflammatory drug (NSAID) of the oxicam class with analgesic, anti-inflammatory and antipyretic properties, is available in oral and parenteral formulations. It is distinguished from established oxicams by a relatively short elimination half-life (3 to 5 hours), which may be advantageous from a tolerability standpoint. Data from preliminary clinical trials suggest that lornoxicam is as effective as the opioid analgesics morphine, pethidine (meperidine) and tramadol in relieving postoperative pain following gynecological or orthopedic surgery, and as effective as other NSAIDs after oral surgery. Lornoxicam was also as effective as other NSAIDs in relieving symptoms of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, acute sciatica and low back pain. Lornoxicam has a tolerability profile characteristic of an NSAID, with gastrointestinal

disturbances being the most common adverse events. Limited clinical experience to date suggests that, as with a number of other NSAIDs, lornoxicam may provide a better-tolerated alternative or adjuvant to opioid analgesics for the management of moderate to severe pain. It has also demonstrated potential as an alternative to other NSAIDs for the management of arthritis and other painful and inflammatory conditions.

MATERIALS AND METHODS

Ionic Gelation Method: Sodium Alginate, drug and HPMC were weighed. Sodium Alginate and HPMC are dissolved in water. Then drug is added till smooth and viscous dispersion is formed. Calcium Chloride solution is being prepared. The viscous dispersion is added drop wise by syringe 22 size. After 15 min the microcapsules were separated and cleaned and washed with water. The microcapsules are kept for drying at 45^{o}c for 12 hours.

UV Spectrum analysis of Lornoxicam: The solution was scanned in the range of 200 to 400nm to fix the maximum wavelength and UV spectrum was obtained by using UV Spectrophotometer

Preparation of 0.1N NaOH: Dissolve about 4.2mg of HCl in 1000ml water.

Preparation of Standard Graph in 0.1N NaOH: Take 10 mg of Lornoxicam and add 10 ml of 0.1N NaoH. Sonicate it for 10 minutes and makeup the volume up to 100 ml with 0.1N NaoH. From this prepare various solutions in the range of 200 – 800 µg/ml and take the absorbance at 378 nm. And prepare calibration curve.

Practical Drug content: Lornoxicam content in the microcapsules was estimated by UV spectrophotometrically method at 378nm in phosphate buffer of pH 7.4. Microcapsules containing equivalent to 100mg of Lornoxicam were crushed as fine powder. The fine powder was added to 10ml of phosphate buffer pH 7.4. 1ml of the sample was taken and made up to 10ml with phosphate buffer pH 7.4 and the absorbance was measured at 378nm.

***In vitro* drug release studies of microcapsules:** *In vitro* drug release studies of microcapsules were carried out using six-station dissolution rate test apparatus Type-II with a basket stirrer at 100 rpm in 900 ml 0.1N HCl for 1^{st} 2 h then in phosphate buffer of pH 7.4 at 50 rpm at temperature $37+0.5^{0}$C. Microcapsules equivalent to 100 mg of Lornoxicam were filled and kept in the basket. 5 ml samples of dissolution fluid were withdrawn at regular intervals and replaced with fresh quantity of dissolution fluid. The samples were filtered, diluted and analyzed by using UV Visible-Spectrophotometer at 378nm.

***In Vitro* wash-off test for mucoadhesive microcapsules:** The mucoadhesive property of the microcapsules was evaluated by an *in vitro* adhesion testing method known as wash-off method. A piece of goat intestinal mucous (2x2 cm) was mounted on to glass slides of (3x1 inch) with elastic bands. Glass slide was connected with a suitable support. About 50 microcapsules were spread on to each wet intestinal mucosa and there after the support was hanging on to the USP tablet disintegrating test machine. The disintegration machine containing intestinal mucosa was adjusted, regular up and down moment in a 6.8 pH phosphate buffer at 37^{o}C taken in a beaker. At the end of 1hour and later at hourly intervals up to 8 hours, the machine was stopped and the number of microcapsules still adhering on to the tissue was counted.

RESULTS AND DISCUSSIONS

The microencapsulation efficiency and mucoadhesive efficiency was found greater with HPMC-5 than HPMC-15. The drug release from the microcapsules was sustained over prolong period of time. The study states the release depended on the core material: coating material ratio which got retarded as the coat material percentage increased. Microcapsules prepared using HPMC-5 showed better sustained action and formulation containing Drug: SA: HPMC-5 in the ratio 1:3:1 is confirmed as best formulation as it released maximum drug with in 24hrs.

The mucoadhesive microencapsulation by following orifice Ionic Gelation Technique could be adaptable in laboratory as well as in industry. HPMC-5 and HPMC-15 microcapsules could be used for better mucoadhesive action and Sod. Alginate for better sustained action and for prolonged period of time. Lornoxicam is a non-steroidal anti-inflammatory drug with analgesic property which is used for the better treatment of arthritis. Moreover, the site of absorption of Lornoxicam is in the intestine and has a short half life of 3 to 4 h. The present study was concerned with the development of the sustained release mucoadhesive microcapsules which after oral administration were designed to prolong the duration of action. The higher viscosity polymer had been seen to inhibit the initial burst release of Lornoxicam. Various formulations were developed by using release rate controlling and gel forming polymers like

HPMC-5 and HPMC-15. From among all the developed formulations, F3 formulation with HPMC-5 sustained the drug release for longer period of time as compared to other formulations. So, F3 formulation with HPMC-5 was selected as the best formulation. It was concluded that the release followed Zero order kinetics. Thus, best formulation satisfied physicochemical parameters and *in vitro* drug release profile requirements for a sustained drug delivery system.

Table 1: Material used for the study

Material	Use	Supplier
Lornoxicam	NSAID	Glenmark pharmaceutical ltd.
Hydroxy Propyl Methyl Cellulose-5,15	Semi synthetic polymer	SDFCL
Sodium alginate	Coating agent	SDFCL
n-hexane	Cleaning agent	SDFCL
Calcium chloride	Chelating agent	SDFCL
Water	Solvent	-

Table 2: Equipments used

Equipment	Manufacturer
Electronic Weighing Balance	CONTECH
UV- Spectrophotometer	UV- 1800 Shimadzu
Digital Melting Point Apparatus	MAX
Magnetic Stirrer	Kapla Scientific Works
Mechanical Stirrer	INCO
FTIR Spectrophotometer	IR Prestige-21,Shimadzu
Millipore	Kapla Scientific Works

Table 3: Formula for Preparation of Microspheres of Lornoxicam

Ingredients	F1	F2	F3	F1	F2	F3
Drug (mg)	**250**	**250**	**250**	**250**	**250**	**250**
Sodium Alginate(mg)	**250**	**500**	**750**	**250**	**500**	**750**
HPMC-5(mg)	**250**	**250**	**250**	**-**	**-**	**-**
HPMC-15 (mg)	**-**	**-**	**-**	**250**	**250**	**250**
Water (ml)	**50**	**50**	**50**	**50**	**50**	**50**
Drug: Sodium Alginate: Polymer	**1:1:1**	**1:2:1**	**1:3:1**	**1:1:1**	**1:2:1**	**1:3:1**

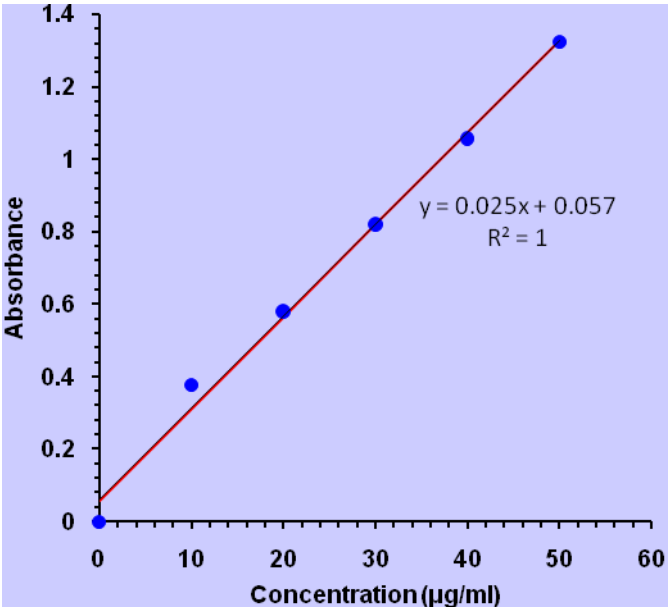

Figure 1: Calibration curve of Lornoxicam

Table 4: Practical drug content

Formulations	Absorbance	Concentration (µg/ml)	Conc. of drug in 100ml	Conc. of drug in mg	Conc. 0f drug in 100ml (Conc. X d.f d.f =10)
F1	0.732	22.5	2250	2.25	22.5
F2	0.623	20.1	2010	2.01	20.1
F3	0.497	18.4	1840	1.84	18.4
F4	0.432	10.1	1010	1.01	10.1
F5	0.293	6.25	6250	.625	6.25
F6	0.409	10.0	1000	1	10.0

Table 5: Encapsulation Efficiency

Formulation	Theoretical drug content (mg)	Practical drug content (mg)	% encapsulation efficiency
F1	33.33	22.5	67.5
F2	25	20.1	80.4
F3	20	18.4	92.0
F4	33.33	10.1	30.30
F5	25	6.25	25.0
F6	20	10.0	50

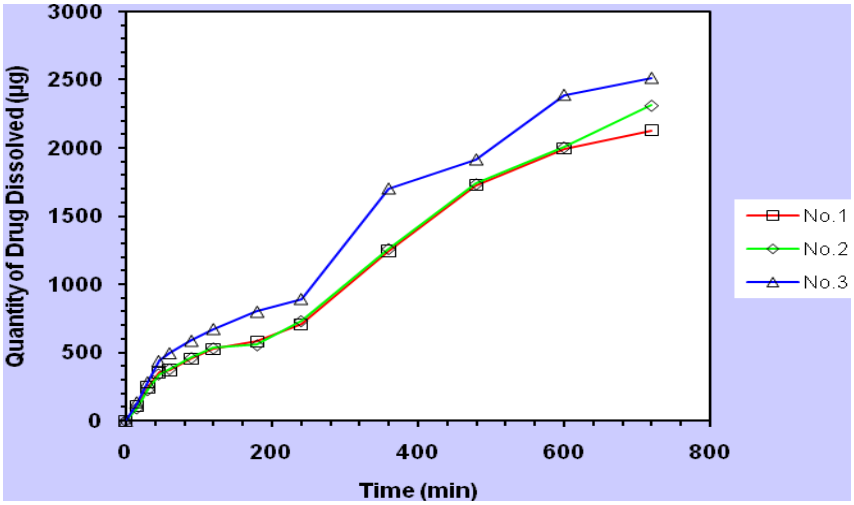

Figure 2: *In vitro* drug release studies of batch F1, F2 and F3 with HPMC-5

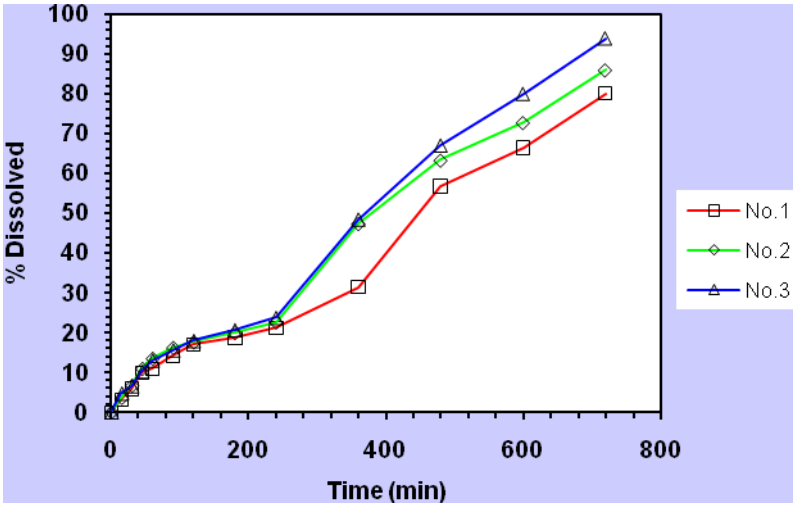

Figure 3: *In vitro* drug release studies of batch F1, F2 and F3 with HPMC-15

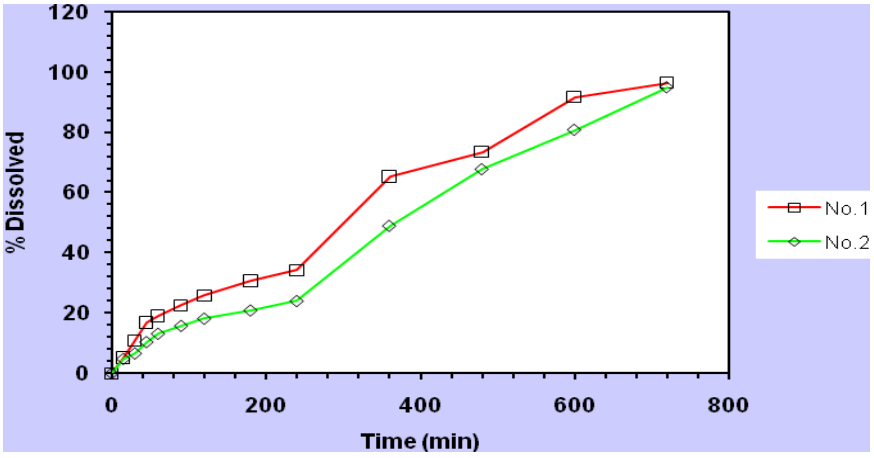

Figure 4: Comparison between Batch F3 of HPMC-5 and Batch F3 of HPMC-15

***Table 6: In vitro* Wash off test for formulation:**

formulation	% of microcapsules adhering to tissue at hrs in phosphate buffer pH 7.4			
	1 hr	2hrs	4hrs	8hrs
F1	22	19	15	10
F2	38	29	21	17
F3	43	31	25	31
F4	39	30	23	06
F5	24	20	17	08
F6	37	31	23	16

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