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FORMULATION AND DEVELOPMENT OF LORNOXICAM MICROSPHERES FOR ENHANCED DRUG DELIVERY AND THERAPEUTIC EFFICACY

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Abstract

The aim of this study was to develop lornoxicam microspheres to overcome its low solubility and subsequently improve its bioavailability. The microspheres were prepared using the solvent evaporation method. Two polymers, Eudragit and Ethyl cellulose, were utilized in different ratios with the drug. In formulation F1, a ratio of 1:3 of drug to Ethyl cellulose was used, while in F2 and F3, the ratios of drug to both polymers were 1:2:1 and 2:5:2, respectively. The formulations underwent evaluation for particle size analysis, drug content, and dissolution rate. The results showed that as the concentration of the polymers increased, the drug encapsulation in the microspheres also increased. Among the formulations, F3 exhibited the best performance. Thus, this study highlights the efficacy of solid dispersion in enhancing the solubility and dissolution rate of poorly soluble drugs like lornoxicam.

Keywords: Lornoxicam, Solid dispersion, enhance solubility, microsphere.

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Introduction:

In the realm of pharmaceutical research, the formulation and development of drug delivery systems with improved therapeutic efficacy and enhanced patient compliance are constant pursuits. Microsphere-based drug delivery systems have emerged as a promising approach, offering controlled release, increased bioavailability, and targeted delivery of therapeutic agents. Lornoxicam, a potent non-steroidal anti-inflammatory drug (NSAID), has shown immense potential in the management of pain and inflammation associated with various medical conditions. However, its limited aqueous solubility and rapid elimination pose challenges to achieving optimal therapeutic outcomes. (1)

This study focuses on the formulation and development of lornoxicam microspheres, which serve as an innovative drug delivery system for overcoming the limitations associated with conventional dosage forms. The goal is to improve drug solubility, prolong drug release, and enhance therapeutic efficacy through the utilization of microencapsulation techniques.

Microspheres are small, spherical particles ranging in size from a few micrometers to several hundred micrometers. They can be formulated using various materials, such as biodegradable polymers, which provide a matrix for drug entrapment. These microspheres offer numerous advantages, including sustained release characteristics, protection of the drug from degradation, reduced frequency of administration, and improved patient compliance.(2)

The development of lornoxicam microspheres involves the selection of suitable polymers, optimization of formulation parameters, and evaluation of physicochemical properties, drug release kinetics, and therapeutic effectiveness. Various techniques, such as emulsion-solvent evaporation, spray drying, and solvent extraction, can be employed for the preparation of lornoxicam-loaded microspheres. These techniques enable the encapsulation of lornoxicam within the polymeric matrix, resulting in controlled release and improved drug stability.(3)

The enhanced drug delivery and therapeutic efficacy achieved through lornoxicam microspheres can be attributed to several factors. Firstly, the microspheres protect the drug from degradation in the harsh gastrointestinal environment, allowing for improved absorption. Secondly, the sustained release profile ensures a constant and prolonged drug concentration at the target site, reducing the frequency of dosing and improving patient compliance. Finally, the controlled release mechanism facilitates the maintenance of effective drug concentrations, leading to enhanced therapeutic outcomes and minimized adverse effects.(4)

This research endeavor aims to contribute to the existing body of knowledge by providing valuable insights into the formulation and development of lornoxicam microspheres for enhanced drug delivery and therapeutic efficacy. The utilization of microsphere-based drug delivery systems holds immense potential in addressing the challenges associated with lornoxicam's limited solubility and short half-life. By optimizing formulation parameters and evaluating the performance of lornoxicam microspheres, this study aims to pave the way for improved treatment options in pain management and inflammatory disorders. (5)

Methods of Preparation of Mucoadhesives

Liquid or gases in one or more polymeric coatings of microspheres incorporation of solid dispersion is done by various technique. The various methods of preparations are:-

1) **Phase Separation Coacervation Technique (6)**

The Coacervation technique involves reducing the solubility of a polymer in an organic phase, leading to the formation of a polymer-rich phase known as coacervates.

In this technique, drugs are dispersed within a polymer solution, and an incompatible polymer is introduced to the system, causing the initial polymer to undergo phase separation and encapsulate the drug particles. Various process variables influence the rate at which coacervates are formed, which in turn affects the distribution of polymer film, particle size, and the tendency for particle agglomeration. To prevent agglomeration, the suspension is stirred at an appropriate speed, as the formation of microspheres begins, and the polymerized globules tend to adhere and form agglomerates. Therefore, careful control of the kinetics of particle formation is necessary, as there is no fixed state of equilibrium achieved in this process.

2) Emulsion Cross Linking Method (7)

In this technique, the drug is combined with an aqueous gelatin solution and heated to 40°C for 1 hour. The resulting solution is then added drop by drop into liquid paraffin while stirring at 1500 rpm at 35°C for 10 minutes, forming a water-in-oil (w/o) emulsion. The emulsion is further stirred for 10 minutes at 15°C. The microspheres formed in this process are subsequently washed three times with acetone and isopropyl alcohol, air dried, and then dispersed in 5ml of an aqueous solution of glutaraldehyde saturated with toluene at room temperature for 3 hours. An example of this technique is the preparation of Gelatin A microspheres.

3) Solvent Evaporation (8)

This process involves utilizing a liquid vehicle, where the microcapsule coating is mixed with a volatile solvent that is immiscible with the liquid vehicle phase. The microencapsule is then dissolved or dispersed in a coating polymer solution, and through agitation with the core material, the mixture is dispersed in the liquid vehicle phase to achieve a uniform microcapsule size. If necessary, the mixture may be heated to facilitate the evaporation of the solvent, allowing the polymer to shrink around the core material. This process leads to the formation of matrix-type microcapsules, where the core material is dispersed within the coating polymer solution. The solvent evaporation method involves the formation of an emulsion between an immiscible continuous phase and a polymer solution, which can be either aqueous (o/w) or non-aqueous, and can be compared to the production of mucoadhesive microspheres.

4) Ionic Gelation (9)

For Diclofenac sodium release, alginate or chitosan system was prepared by this technique. Drug is mixed with sodium alginate aqueous solution and stirring is continued then added drop wise to Ca^{2+} /Al^{3+} solution. Formed microspheres are keep in original solution for 24 hr and followed by filtration for separation. The release is done at pH 6.4-7.2 and drug will not release in acidic pH.

5) Spray Drying (10)

To begin the process, a polymer is dissolved in a suitable volatile organic solvent, such as dichloromethane or acetone, for spray drying. The drug, in solid form, is then dispersed within the polymer solution and mixed using high-speed homogenization. The mixture is subsequently atomized in hot air. This atomization step generates small droplets and a fine mist, allowing the solvent to evaporate rapidly. As a result, microspheres with a size range of 1-100 μm are formed. The micro particles are separated from the hot air using a cyclone separator, and any remaining traces of solvent are removed through vacuum drying. One notable advantage of this process is its ability to be performed under aseptic conditions. This process can be repeated to produce porous micro particles.

6) Multiple Emulsion Polymerization Technique (11)

In this method, an oil-in-water (o/w) emulsion, also referred to as a non-aqueous

drug solution, is formed by combining a drug solution in a polymer solution. This o/w emulsion is then added to an external oily phase, resulting in the formation of an o/w/o emulsion. A cross-linking agent, such as glutaraldehyde, is introduced to facilitate the cross-linking process. Subsequently, the organic solvent is evaporated. This technique allows for the incorporation of poorly water-soluble drugs, thereby enhancing their bioavailability. The microspheres formed using the multiple emulsion technique provide a means to improve the bioavailability of poorly water-soluble drugs like ketorolac tromethamine **(13-33).**

MATERIAL AND METHOD

Lornoxicam and other ingredient were provided by our collage. All agents are pharmaceutical grade. Distilled water used for all the experiments.

Preparation of Lornoxicam Microspheres (12)

Microsphere containing Lornoxicam were prepared by solvent evaporation method. Drug loaded microsphere of lornoxicam prepared individually by using single emulsion solvent evaporation method. Drug and polymers in different proportion were weight and co-dissolved at room temperature in to a mixture of Ethanol and Dichloromethene with magnetic stirring. This was slowly poured into the dispersion medium consisting of few ml of different % of Polyvenyalchol (PVA) and 1.5 (w/v) spans 80. This solution prepared by probe sonicator for 2H. System was put in magnetic stirrer over night for complete evaporation of organic solvent. Prepare suspensions was centrifuged at 1500 rpm. Suspension was filtered and dries the filtered and collected (Table 1).

Table 1. Composition of Microspheres Formulation

S.no.	Ingredient	F1	F2	F3
1	Drug (mg)	100	100	200
2	Ethyal cellulose (mg)	300	200	500
3	Eudragit (mg)	_	100	200
4	PVA (%)	3	2	3
5	Ethanol (ml)	20	30	40
6	Span 80(1.5%µl)	100	100	100
7	DCM (ml)	5	7	10

Evaluation of Microsphere

Particle Size Analysis

Particle size analyses of microsphere were analyzed by optical microscope. Size of partical of various formulations is given in table 2, 3 and 4.

Table 2. Size of Particle of Various Formulations

Formulation	Average particle size(µm)
F1	54.408
F2	63.76
F3	46.88

Table 3. Percentage Practical yield

Formulation	% Practical Yield
F1	77.41
F2	84.47
F3	85.46

Table 4. Drug Content

Formulation	% Drug content
F1	66.6
F2	75.8
F3	73.0

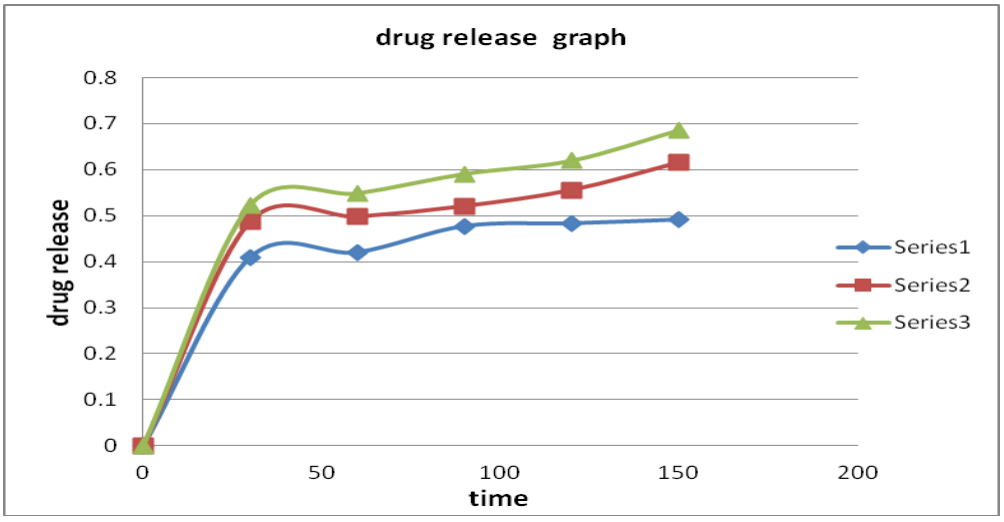
In Vitro Drug Release Study

100 mg of lornoxicam microsphere were taken and filled in capsules and subjected for dissolution test in dissolution test apparatus using basket method. Dissolution media was 900 ml of phosphate buffer pH 6.8 maintained at 37 ± 2C and rotated at 100 rpm. Sample were withdrawn at specified time intervals and replaced with the same volume of fresh medium, filtered and analyzed at 275 nm (Table 5).

Table 5. Table Drug Release from Microsphere

Time (min)	F1		F2		F3	
	Absorbance	% Drug Release	Absorbance	% Drug Release	Absorbance	% Drug Release
30	0.240	40.96 %	0.266	48.72 %	0.445	52.32%
60	0.246	42.04 %	0.271	49.74 %	0.462	54.83%
90	0.250	47.74 %	0.283	52.03 %	0.496	59.07%
120	0.244	48.33 %	0.300	55.51 %	0.519	61.93%
150	0.258	49.13 %	0.330	61.47 %	0.572	68.52%

Fig. 1. Drug Release Graph



Conclusion: The formulation and development of lornoxicam microspheres for enhanced drug delivery and therapeutic efficacy represent a significant advancement in the field of pharmaceutical research. This innovative drug delivery system holds tremendous potential for improving the treatment of pain and inflammation associated with various medical conditions.

The utilization of microspheres provides several advantages, including controlled release, increased drug solubility, and targeted delivery. Through the encapsulation of lornoxicam within biodegradable polymers, the microspheres offer sustained drug release, protecting the drug from degradation and ensuring a constant and prolonged drug concentration at the target site. This sustained release profile not only reduces the frequency of administration but also improves patient compliance.

The formulation and optimization of lornoxicam microspheres involve careful selection of suitable polymers, as well as evaluation of physicochemical properties, drug release kinetics, and therapeutic effectiveness. Various microencapsulation techniques, such as emulsion-solvent evaporation, spray drying, and solvent extraction, can be employed for their preparation, allowing for tailored drug release profiles and improved stability.

The enhanced drug delivery and therapeutic efficacy achieved through lornoxicam microspheres can lead to improved treatment outcomes. By maintaining effective drug concentrations and minimizing adverse effects, these microspheres have the potential to enhance patient comfort and quality of life.

In conclusion, the formulation and development of lornoxicam microspheres offer a promising solution for overcoming the limitations of conventional dosage forms. The sustained release and targeted drug delivery achieved through these microspheres have the potential to revolutionize pain management and inflammatory disorder treatments. Further research and optimization efforts in this field will likely contribute to the development of advanced drug delivery systems and improve therapeutic outcomes for patients.

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