Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 05, 2021

FORMULATION AND ASSESSMENT OF ALBUMIN MICROSPHERES LOADED WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

NIRANJAN BABU MUDDULURU[*1], SIVA JYOTHI PALAMAKULA[2], SIREESHA MUDE[2]

[1]Department of Pharmacognosy, Seven Hills College of Pharmacy, Tirupati, A.P., India
[2]Department of Pharmacology, Seven Hills College of Pharmacy, Tirupati, A.P., India

Corresponding Author:Dr. M. Niranjan Babu
Professor
Department of Pharmacognosy
Seven Hills College of Pharmacy,
Tirupati, A.P., India – 517561
Contact: 7702484513
Email: principal.cq@jntua.ac.in

ABSTRACT:
This study focuses on the formulation and evaluation of albumin microspheres encapsulating non-steroidal anti-inflammatory drugs (NSAIDs). The goal is to enhance the therapeutic efficacy and reduce the side effects associated with NSAIDs. Albumin, a natural protein, was chosen for its biocompatibility, biodegradability, and non-immunogenic properties, making it an ideal carrier for drug delivery systems. The microspheres were prepared using an emulsion solvent evaporation technique, optimizing various parameters such as polymer concentration, drug-to-polymer ratio, and emulsifier type and concentration. Characterization of the microspheres included particle size analysis, surface morphology, drug loading efficiency, and in vitro drug release studies. DSC, CDR & UV Spectral analysis was used to assess the surface and shape of the microspheres, revealing a spherical structure with a smooth surface. The drug loading efficiency was determined using spectrophotometric methods, demonstrating high encapsulation efficiency. In vitro release studies were conducted in simulated gastrointestinal fluids to mimic the drug release profile in the human body. The release kinetics were analyzed using various mathematical models to understand the mechanism of drug release. The formulated albumin microspheres showed a controlled and sustained release of NSAIDs, reducing the frequency of dosing and potentially improving patient compliance. Cytotoxicity studies indicated that the microspheres were non-toxic and safe for use. This research highlights the potential of albumin microspheres as an effective drug delivery system for NSAIDs, offering a promising approach to improving the therapeutic outcomes and minimizing the adverse effects associated with these drugs.

KEYWORDS: DSC, CDR, Keteprofen, Microspher, UV analysis

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 05, 2021

INTRODUCTION

Sustained release systems encompass drug delivery systems designed to release drugs slowly and steadily over an extended period. Specifically, sustained drug delivery aims to maintain a constant and effective drug level in the body while minimizing undesirable side effects.

In sustained release dosage forms, an initial dose of the drug is administered to achieve a desired pharmacological response. The remaining portion of the drug is released gradually at intervals to sustain the peak pharmacological activity over a prolonged period beyond what is typically achieved with a single dose. This sustained release is achieved through the continuous replenishment of drug molecules (see Fig 1.1).

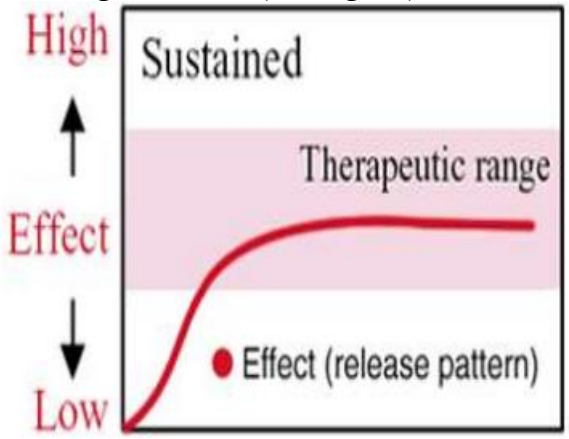

Fig 1.1 Sustained drug release effect

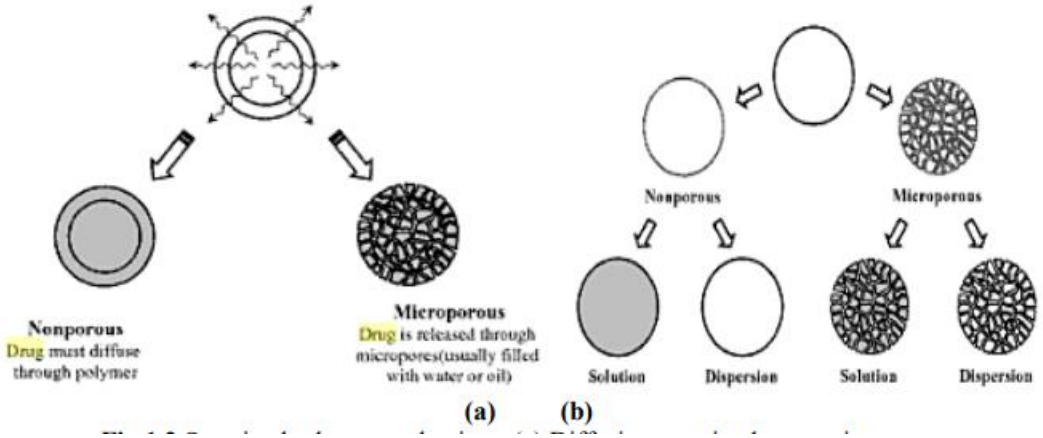

Fig 1.2 Sustained release mechanisms (a) Diffusion sustained reservoir systems.

1.2 MICROENCAPSULATION

Microencapsulation involves enclosing solids, liquids, or gases within microscopic particles by forming thin coatings of wall material around these substances. Various methods exist for delivering therapeutic substances in a sustained release manner, with microspheres serving as carriers for drugs.

1.2.1 Microspheres

Microspheres are solid, nearly spherical particles ranging in size from 1 to 1000 μm. They are composed of biodegradable synthetic polymers such as polymeric waxes or other protective materials, as well as modified natural products like starches, gums, proteins, fats, and waxes. Natural polymers include albumin and gelatin, while synthetic polymers include polylactic acid and polyglycolic acid. Solvents chosen for dissolving these polymeric materials depend on polymer and drug solubility and stability, process safety, and economic considerations. Microspheres are small with a large surface-to-volume ratio, and at the lower end of their size range, they exhibit colloidal properties. The interfacial properties of microspheres are crucial, often influencing their activity.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 05, 2021

1.3 NATURAL POLYMERS

Despite the emergence of synthetic biodegradable polymers, research into the use of natural biodegradable polymers for drug delivery remains active. Natural polymers are attractive due to their origin from living organisms, ready availability, relative affordability, and ability to undergo various chemical modifications. Proteins (e.g., collagen, gelatin, albumin) and polysaccharides (e.g., starch, dextran) have been extensively studied as matrices in drug delivery systems. Many protein-based delivery systems involve solid cross-linked microspheres where the drug is dispersed throughout the polymer matrix.

In addition to their compatibility with natural origin, easy availability, cost-effectiveness, eco-friendliness, and potential degradability, natural gums such as agar, guar gum, chitosan, gelatin, carboxymethyl cellulose, xanthan gum, sodium alginate, and lotus bean gum have been studied for their potential applications in pharmaceutical and biomedical fields.

1.3.1 Technologies for Albumin Microspheres Preparation

Novel drug delivery systems represent a highly interdisciplinary field that advances drug delivery and healthcare. The techniques used for preparation must meet specific criteria, including the ability to incorporate high drug concentrations and sustain particle size by adjusting parameters such as:

1. Type and concentration of albumin
2. Speed of agitation
3. Chemical cross-linking or heat denaturation
4. Cross-linking agent concentration or temperature
5. Addition or absence of surfactants
6. Type of oil used
7. Mixing conditions (with or without baffles)

Particle size analysis is typically conducted using laser diffraction techniques to determine the optimal size for specific routes of administration and desired duration of drug action. For parenteral products, minimizing particle size is crucial to avoid irritation at the injection site. Additionally, stability and shelf life are essential considerations for ensuring the longevity of albumin microspheres.

Methods of Microsphere Manufacturing:

Wax Coating and Hot Melt: Wax is used to coat core particles, encapsulating the drug by dissolving or dispersing it in molten wax. The waxy solution or suspension is dispersed into a cold liquid paraffin through high-speed mixing. After agitation, the external phase (liquid paraffin) is decanted, and microspheres are suspended in a non-miscible solvent and air-dried. Wax-coated microspheres, though cost-effective, release drugs more rapidly compared to polymeric microspheres. Materials like carnauba wax and beeswax can be blended to achieve desired characteristics.

Spray Coating and Pan Coating: This method involves heat-jacketed coating pans where solid drug core particles rotate while the coating material is sprayed onto them. The particles range in size from micrometers to a few millimeters, and the coating material is sprayed at an angle into the pan until an even coating is achieved. Coating numerous particles ensures a consistent release pattern superior to coated tablets. Multiple batches of microspheres with varying coating thicknesses can be mixed to achieve specific sustained release patterns.

Coacervation: Coacervation involves separating a macromolecular solution into two immiscible liquid phases: a dense coacervate phase concentrated in macromolecules and a dilute equilibrium phase. Simple coacervation occurs with a single macromolecule and is induced by factors like temperature changes or the addition of non-solvents, promoting polymer interactions over solvent interactions. Complex coacervation involves multiple macromolecules of opposite charges, influenced by parameters such as pH, ionic strength,

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 05, 2021

macromolecule concentration, ratio, and molecular weight to produce microspheres with tailored properties.

Table 4.1: List of chemicals used with grade and supplier

Sl. no.	Materials used	Grade			Manufacturer
1.	Ketoprofen	Pharma Grade			Acharya chemicals, Maharashtra, India
2.	Bovine serum albumin	Pharma Grade			S D fine-chem limited, Mumbai
3.	Petroleum ether	LR			S D fine-chem limited, Mumbai
4.	Sunflower oil	LR			S D fine-chem limited, Mumbai
5.	Paraffin liquid light	LR			S D fine-chem limited, Mumbai
6.	Paraffin liquid heavy	LR			S D fine-chem limited, Mumbai
7.	Ethanol	LR			S D fine-chem limited, Mumbai
8.	Acetone	LR			S D fine-chem limited, Mumbai
9.	Tween 80	LR			Central drug house (p) Ltd, Bombay
10.	Sodium hydroxide pellets	LR			Qualigens fine chemicals, Bombay
12.	Hydrochloric acid	LR			S D fine-chem limited, Mumbai
12.	Potassium dihydrogen phosphate	LR			Qualigens fine chemicals, Bombay
13.	Potassium chloride	LR			Qualigens fine chemicals, Bombay

Fig 5.1 IR Spectrum of Ketoprofen

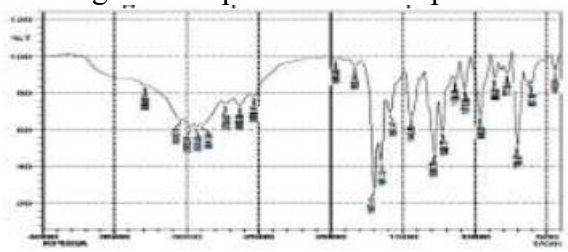

Fig 5.2 IR Spectrum of physical mixture of Ketoprofen and Bovine serum albumin

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 05, 2021

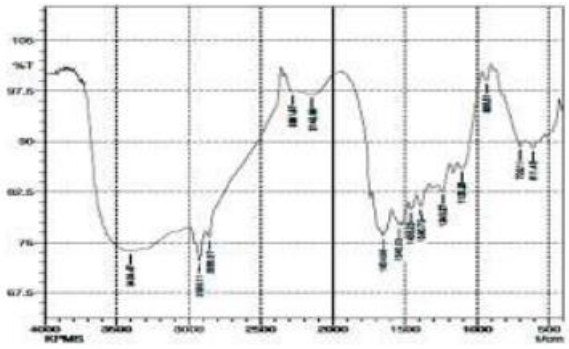

Fig 5.3 IR Spectrum of Ketoprofen microspheres using Bovine serum albumin

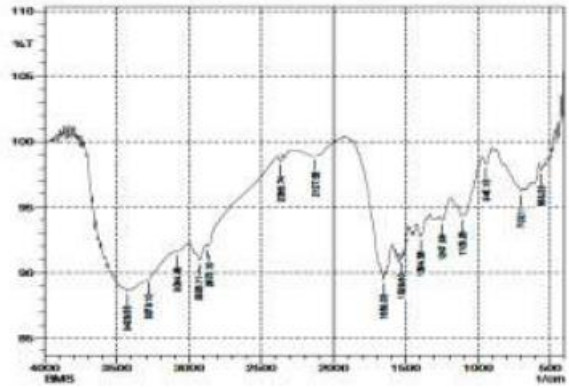

Fig 5.4 IR Spectrum of blank microspheres using Bovine serum albumin

Table 5.1 IR Spectrum data

Sl.no	IR Spectrum	Peaks(cm^{-1})	Groups	Stretching /Deformation
1	Ketoprofen	2885.6	C-H(alkyl)	Stretching
		1699.34	C=O(aromatic ketone)	Stretching
		1651.12	COOH(unsaturated carboxylic acid)	Stretching
		3043.77	O-H(Carboxylic acid)	Stretching
2	Physical mixture of Ketoprofen and Bovine serum albumin	2891.39	C-H(alkyl)	Stretching
		1697.41	C=O(aromatic ketone)	Stretching
		1651.12	COOH(unsaturated carboxylic acid)	Stretching
		3045.7	O-H(Carboxylic acid)	Stretching
3	Ketoprofen microspheres of Bovine serum albumin	2856.67	C-H(alkyl)	Stretching
		1654.98	C=O(aromatic ketone)	Stretching
		1645.03	COOH(unsaturated carboxylic acid)	Stretching
		2926.11	O-H(Carboxylic acid)	Stretching
4	Blank microspheres of Bovine serum albumin	2872.1	C-H(alkyl)	Stretching
		1653.05	C=O(aromatic ketone)	Stretching
		1629.6	COOH(unsaturated carboxylic acid)	Stretching
		3084.28	O-H(Carboxylic acid)	Stretching

DISCUSSION

This study introduces a novel approach to fabricate microspheres containing the NSAID KP, utilizing bovine serum albumin (BSA) as a natural polymer carrier to enhance treatment efficacy for conditions like rheumatoid arthritis, pain, and inflammation. Microspheres

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 05, 2021

loaded with KP were produced via the solvent evaporation method employing BSA. Various evaluation parameters were meticulously assessed to achieve sustained release of KP.

In this study, six formulations were meticulously prepared, and their detailed compositions are outlined in Table 4.3. The fabricated KP microspheres underwent comprehensive characterization including FTIR spectroscopy, SEM imaging, particle size and distribution analysis, percentage yield determination, drug content assessment, drug entrapment efficiency evaluation, in vitro dissolution studies, release kinetics analysis, as well as DSC and XRD analyses.

REFERENCES

1. Remington. The science and practice of pharmacy 21st edition, vol. 1, 939.
2. http://www.pharmaceuticaltechnology.com/contrators/drug_delivery/avera/ avera2.html, Nov 2010.
3. Eroglu H, Suheyla KASH, Oner L, Sargon M, Hincal AA. Preparation of bovine serum albumin microspheres containing Dexamethasone Sodium Phosphate and the in vitro evaluation. Turk J Med Sci 2000; 30:125–8.
4. Hong W, Kinam P. Oral controlled formulation design and drug delivery: Theory to practice 1st edition, 6.
5. http://www.doyouknow.in/Articles/Pharmaceutical/Controlled-Release-DrugDelivery-System-Cdds.aspx, Nov 2010.
6. Venkatesan.P, Manavalan.R, Valliappan.K. Microencapsulation: a vital technique in novel drug delivery system. J harm Sci & Res 2009; 1(4):26-35.
7. Gunja C, Prakash. B, Saha.RN. Microspheres technology and its applications. (PDF). http://docstoc.com/docs/38166355/reviewon-microspheres, Nov 2010.
8. Jain NK. Biodegradable polymers Controlled and Novel Drug Delivery 1stedition, 81-239.
9. Murali Mohan Babu GV, Himasankar K, Churuvu PS Narayan , Ramana Murthy KV. Controlled release of diclofenac sodium by gum karaya-chitosan complex coacervate: In vivo evaluation. Ind J Pharm Sci 2001; 63(5):408-12.
10. Sinha VR, Singla AK, Wadhawan S, Kaushik R, Kumria R, Bansal K, Dhawan S. Chitosan microspheres as a potential carrier for drugs. Int J Pharm Sci 2004; 274: 1-33.
11. Tuncay M. In vitro and in vivo evaluation of Diclofenac Sodium loaded albumin microspheres. J Microencapsulation 2000; 17(2):145-55.
12. Felix k. Albumin as a drug carrier: Design of prodrugs, drug conjugates and nanoparticles. Journal of Controlled Release 2008; 132:171–83
13. Thakkar H, Sharma RK, Mishra AK, Chuttani K, Murthy RR. Albumin Microspheres as Carriers for the Antiarthritic Drug Celecoxib. AAPS PharmSciTech 2005; 6(1):65-73
14. Torrado JJ, Illum L, Davis SS. Particle size and size distribution of albumin microspheres produced by heat and chemical stabilization.I J Pharm 1989; 51(1): 85-93
15. http://en.wikipedia.org/wiki/Sciatica, Nov 2010.