DESIGN, FORMULATION AND CHARACTERIZATION OF MICROCAPSULES OF NSAID DRUG

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ABSTRACT:
Microencapsulation is a technology that involves the production of small, spherical particles called microcapsules that are designed to enclose a material or substance within a protective shell. This technology has gained popularity in recent years due to its numerous applications in different fields. Pharmaceutical, cosmetic, agriculture and other fields are using microencapsulation as new approach to improve the stability, shelf-life, and bioavailability of different substances. This paper showed formulation of microencapsulation, their advantages and disadvantages, and the various applications of microencapsulation. Beside conventional microcapsules, it also encompasses self assembling structure and other particulate requiring preparative manipulation. This paper provides an overview of encapsulation materials, the mechanism of release through the capsule wall and preparation techniques, and the numerous applications to which microcapsules can be applied. NSAIDs are pain relieving drugs which are used to treat arthritis pain and also for body aches, swelling, stiffness. When core materials are surrounded by Microcapsules of Etoricoxib were prepared by solvent evaporation method by using different drug-polymer ratio with different solvent. Prepared microcapsules were evaluated for the particle size, percentage yield, incorporation efficiency, flow property and in vitro drug release. From the result we can conclude that as the concentration of polymer increases, it affects the particle size, percentage yield and drug release of microcapsules. And different shape of microcapsules had seen with different solvent (Chloroform, Dichloromethane, Acetone) and polymer (HPMC, 2-Hydroxypropyle-beta cyclodextrin, Polyvinyl alcohol). The excellent flow properties, particle size, percentage yield (93.24%), incorporation efficiency (95.69%) and percentage drug release (96.88%) showed by F6 for a period of 15 hrs. Results of the present study indicate that Etoricoxib microcapsules can be successfully designed to offer protection and enhance the bioavailability.

Keywords: Microencapsulation, 2-Hydroxy propyle-beta-cyclodextrin, NSAIDs, Core material, Coating material, Chloroform.

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INTRODUCTION

Microencapsulation could be a method wherever an eternal film of chemical compound material through coating fenced in terribly little droplets or particles of liquid or solid material that is termed core material. Introduction or coating of core material or active substance protects the active substance (core material) from adverse changes within the close atmosphere. Microencapsulation is freakishly differentiated macro coating techniques, in this the sooner involves the coating of particles move dimensionally from many tenths of metric linear unit to 5000 microns in size. Microencapsulation provides the suggests that of changing liquids to solids, neutering mixture and surface properties, providing environmental protection, and dominant the discharge characteristics or accessibility of coated materials. Many of those properties are often earned by small packaging techniques; but, the individuality of microencapsulation is that the littleness of the coated particles and their consequent use and adaptation to a large form of dose forms and not has been technically satisfactory a pair of. Microencapsulation involves the protection of active ingredients by packing them into diminutive or little capsules. These capsules having a variety from one metric linear unit to seven millimeters, unleash their contents at a later time by suggests that applicable to the appliance. This new technology doesn't exclude issues areas like no single microencapsulation method is all-mains to any or all core materials and difficulties like incomplete or discontinuous coating, the time period of sensitive prescribed drugs, and economic limitations area nit typically encountered within the arrange to apply specific microencapsulation to a selected task. Microencapsulation is receiving respectable attention, basically, developmentally, and commercially. {1,2,3}

Mechanism of releasing core material from microcapsule: There are four typical mechanisms by which the core material is released from a microcapsule:

1) Mechanical rupture of the capsule wall
2) Melting of the wall
3) Diffusion through the wall.
4) Dissolution of the wall

Applications:

- Microencapsulation is aim to delivers a dose of active substance or medicaments (core material) over an extended period of time, that will work slowly and for a longer time.
- The applications of microencapsulation include masking taste of chewable tablets, suspensions and powders.
- Single-layer tablets containing chemically incompatible ingredients, as well as innovative formulation concepts for creams, ointments, aerosols, and suppositories, are examples of microencapsulation applications.
- The applications of microencapsulation consist three imperative areas, where first one is stabilization of core materials, second one is controlled delivery or availability of core materials and last one is taking apart of tablet and powder mixture and chemically reactive ingredients.{4,5,6}

Formulation considerations: Microcapsules have some basic general properties such as nature of the core and coating material, compatibility of core and coating material with each other, releasing mechanism of active ingredients, and the microencapsulation method.

CORE MATERIALS:

The core material, which refers to the specific substance to be coated, might be either liquid or solid. The liquid core can be distributed or dissolved components; hence the composition of the core material can vary. Active ingredients, stabilizers, diluents, excipients, and release-rate retardants or accelerators make up the solid core. The ability to change the composition of the core material gives you a lot of versatility, and you can use that flexibility to create and build the microcapsule features you want.

COATING MATERIALS:

The coating material and also the core material ought to be practiced with one another and make certain that coating material ought to be with chemicals compatible and nonreactive with the core material; and supply the required coating properties, like strength, flexibility, solidity, optical properties, and stability. The coating materials utilized in microencapsulation ways area unit amenable, to some extent, to in place modification.

The selection of a given coating typically are often power-assisted by the review of existing literature and by the study of free or solid films, though sensible use of free-film info typically is obstructed for the subsequent reasons:

1. Traditional casting procedures create a cast or free films that are significantly thicker than those produced by microencapsulation of tiny particles; hence, results gained from cast films may not be extrapolated to thin microcapsule coatings.
2. The exact microencapsulation approach used to apply a coating creates unique and intrinsic features that are difficult to replicate using current film-casting techniques
3. Coating characteristics may be influenced by the coating substrate of the core material. As a result, while choosing a coating material, both free-film data and applied outcomes must be taken into account.[7,8,9]

COATING MATERIAL PROPERTIES

1. Stabilization of core material.
2. Inert toward active ingredients.
3. Controlled release under specific conditions.
4. Film-forming, pliable, tasteless, stable.
5. Non-hygroscopic, no high viscosity, economical.
6. Soluble in an aqueous media or solvent, or melting.
7. The coating can be flexible, brittle, hard, thin etc.

Examples of coating materials:

1. Water soluble resins –Gelatin, Gum Arabic, Starch, Polyvinylpyrrolidone, Carboxy-methylcellulose, Hydroxyethyl-cellulose, Methylcellulose, Arabinogalactan, Polyvinyl alcohol, Polyacrylic acid.

2. Water insoluble resins–Ethylcellulose, Polyethylene, Polymethacrylate, Polyamide (Nylon), Poly (Ethylene Vinyl acetate), and Cellulose nitrate, Silicones, Poly (lactideco-glycolide).

3. Waxes and lipids –Paraffin, Carnauba, Spermaceti, Beeswax, Stearic acid, Stearyl alcohol, Glyceryl stearates. 4. Enteric resins – Shellac, Cellulose acetate phthalate.[10,11,12]

TECHNIQUESTO MANUFACTURE MICROCAPSULES:

Encapsulation of core materials include various methods or technologies. Broadly the methods are divided into three types. Different types of microencapsulation techniques are listed in table 1.

1. Chemical methods
2. Physico-chemical methods
3. Physico-mechanical methods.

Table 1. Different techniques used for microencapsulation (Ghosh 2006).

Chemical processes	Physico-mechanical methods.
Interfacial polymerization	Spray drying and congealing
In situ polymerization	Fluid bed coating
Poly condensation	Pan coating
	Solvent evaporation

The above-mentioned techniques are widely used for microencapsulation of several pharmaceuticals. The most commonly used methods for microencapsulation of several pharmaceuticals are solvent evaporation, pan coating, air suspension method, spraydrying and spray-congealing.[13,14]

Table 2 illustrates microencapsulation processes and their applicabilities.

Table 2. Microencapsulation processes and their applicability

Microencapsulation process	Nature of the core material	Approximate particle size (mm)
Air suspension	Solids	5–5000*
Phase separation and coacervation	Solids and liquids	2–5000*
Multi-orifice centrifugation pan coating	Solids and liquids	1–5000*
Spray drying and congealing	Solids	600–5000*
Solvent evaporation	Solids and liquids	Solids and liquids

MATERIALS AND METHODS:

METHOD:

In the solvent-evaporation process, polymer was dissolved in a water-immiscible volatile organic solvent such as dichloromethane and chloroform with different ratios, into which the core material (Etoricoxib) was dissolved or dispersed. The resulting solution was added drop wise to a stirring aqueous solution (50 ml) with a suitable stabilizer such as Span-80 to form small polymer droplets containing encapsulated material. The hardening process of the microcapsules is accomplished by the removal of the solvent from the polymer droplets either by solvent evaporation (by heat).[15]

Table 1: Formulation Table of Microcapsule Preparation:

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Etoricoxib	100g	100g	100g	100g	100g	100g	100g	100g	100g
2hydroxy propyle-beta cyclodextrin	100g	200g	300g	-	-	-	-	-	
Hydroxypropyle methyle cellulose	-	-	-	100 g	200g	300g	-	-	-
Polyvinyle alcohol	-	-	-	-	-	-	100 g	200g	300g
Dichloromethane	20ml	20ml	20ml	-	-	-	-	-	-
Chloroform	-	-	-	20ml	20ml	20ml	-	-	-
Acetone	-	-	-	-	-	--	20ml	20ml	20ml

Particle size analysis

Characterization of microcapsules

1. Particle size analysis: The particle size was measured by optical microscopy using Edmundsons equation.15 A drop of aqueous suspension of microcapsules was mounted on a slide and observed under microscope under 10X magnification. The ocular micrometer was first calibrated with stage micrometer. The mean particle size was calculated by measuring 100 particles with the help of a calibrated ocular micrometer.

Mean particle size.= ∑nd/ ∑n, Where n is no. of particle, D is diameter

15. Martin A, Bustamante P, Chun AHC. Physical Pharmacy, BI Waverly Pvt. Ltd, New Delhi. Edition 4. 1995; 557-58.

2. Percentage Yield[12]: The measured weight was divided by total amount of all non-volatile components which were used for the preparation of microcapsule.

% yield = (Actual weight of product / Total weight of excipient and drug)x100

Incorporation Efficiency: In100ml volumetric flask 25ml of microcapsules suspension were taken and dissolved with small quantity of ethanol the volume is made upto mark with pH 6.8 and stirred for 12hours. After stirring the solution was filtered through Whatman filter paper and from the filtrate appropriate dilutions were made and absorbance was measured at 206 nm by using UV-spectro photo meter 1800(Shimadzu).

3. Angleof Repose: Determination of angle of repose Trihexyphenidyl microcapsules were carried out by employing fixed funnel method.

Angleof repose $\theta=\tan^{-1}(H/R)$

Where,H= Height of the pile;R= Radius of the pile

Scanning Electron Microscopy: The samples for SEM analysis were prepared by following method. The shape and surface morphology of the microcapsules was studied by using scanning electron microscope. Microcapsules were mounted directly on to the SEM sample stub using double-sided sticking tape and coated with gold film (thickness200nm) under reduced pressure (0.001mmofHg).The micro capsules were viewed accelerating voltage of 10KV.

Drug Release: *Invitro* release studies: *Invitro* dissolution profile of each formulation was determined by employing g USP XXII type 2 basket method (900 ml o fpH6.8-phosphate buffer, 100rpm, 37±0.5^{O}C). Microcapsules loaded into the basket of the dissolution apparatus. Aliquot of 5mL was withdrawn from the dissolution media at suitable time interval s and the withdrawn volume was replenished with the same volume of dissolution medium in or derto keep the total volume constant. The absorbance of the samples was measured at λ_{max} 247 nm after suitable dilution if necessary, using phosphate buffer of pH 6.8 as blank. Results of in vitro drug release studies obtained from absorbance data were tabulated and shown graphically as Cumulative %drug released Vs Time.

RESULTANDCONCLUSION:

When core materials are surrounded by Microcapsules of Etoricoxib were prepared by solvent evaporation method by using different drug-polymer ratio with different solvent. Prepared microcapsules were evaluated for the particle size, percentage yield, incorporation efficiency, flow property and in vitro drug release. From the result we can conclude that as the concentration of polymer increases, it affects the particle size, percentage yield and drug release of microcapsules. And different shape of microcapsules had seen with different solvent (Chloroform, Dichloromethane, Acetone) and polymer (HPMC, 2-Hydroxypropyle-beta cyclodextrin, Polyvinyl alcohol). The excellent flow properties, particle

size, percentage yield (93.24%), incorporation efficiency (95.69%) and percentage drug release (96.88%) showed by F6 for a period of 15 hrs. Results of the present study indicate that Etoricoxib microcapsules can be successfully designed to offer protection and enhance the bioavailability. During processing, it was observed that stirrer speeds of less than 500 rpm were not sufficient to produce microcapsules, and a huge coalesced mass was obtained. This is due in part to inadequate agitation of the media to disperse the inner phase in discreet droplets within the bulk phase. At stirring speeds above 1000 rpm, the turbulence caused frothing and adhesion of the microparticles to the container walls and propeller blade surfaces, resulting in high shear and a smaller size of the dispersed droplets. Spherical microspheres were obtained at a stirring rate of 500 rpm; therefore, this speed was used during manufacture of all microcapsules. As the solvent evaporated, the viscosity of the individual droplets increased, and highly viscous droplets were observed to coalesce at a faster rate than they could be separated. Polymer formed a thin film around the droplets and thereby reduced the extent of coalescence, before hardening of the capsules, on collision of the droplets. The resultant microcapsules were free-flowing, and the use of magnesium stearate was deemed effective. When 1:1 (w/w) drug/polymer concentrations were used the quality of microcapsules formed was poor. These were irregularly shaped, not flowing, and presented with lots of indentation. Microcapsules were only formed when the polymer concentration was increased to ratios of between 1:2 and 1:3 (w/w) with respect to the drug concentration. Etricoxib with Hydroxypropyle methyle cellulose (1:3) showed regular, spherical shape with good flow property (Fig: 1).

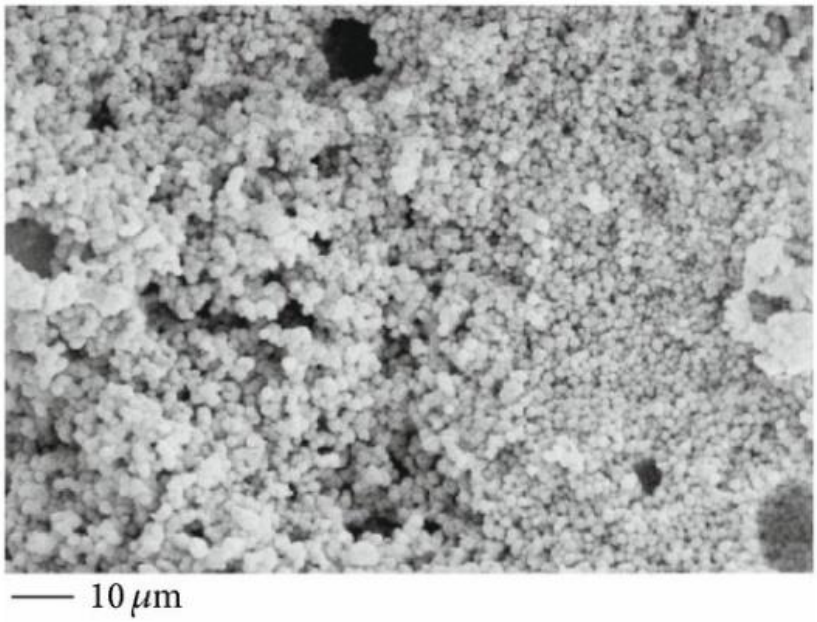

Fig 1: Etoricoxib: Hydroxypropyle methyle cellulose (1:3)

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