Indian Journal of Novel Drug Delivery

IJNDD

An Official Publication of Karnataka Education and Scientific Society

Research Article

Formulation, Characterization and Evaluation of Aceclofenac- Alginate /Potato Starch Micro Beads

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ARTICLE DETAILS

Article history:
Received on 01 February 2012
Modified on 10 June 2012
Accepted on 15 June 2012

Keywords:
Microencapsulation,
Aceclofenac,
Potato Starch,
Alginates,
SEM

ABSTRACT

Microencapsulation is a process by which very tiny droplets or particles of liquid or solid material are surrounded or coated with a continuous film of polymeric material. It means of converting liquids to solids, of altering colloidal and surface properties. The capsule protects the active ingredient from its surrounding environment until an appropriate time and material escapes through the capsule wall either by rupture, dissolution, melting or diffusion. In the view of converting the active pharmaceutical ingredients into dosage forms suitable for administration, the present study is an attempt to formulate a hydrogel bead of micron size by ionotrophic gelation technique using potato starch as a release retardant and thereby increasing the release time of the encapsulated drug and providing a delayed/controlled release formulation. It was observed that increase in polymer concentration, the drug release and particle size was gradually decreased. The formulation were investigated for various parameters life particle size, micrometric properties, surface morphology by SEM, incorporate efficiency and *invitro* release study. With the obtained results of mentioned parameter it reveals that microbeads with high potato starch concentration (F1 & F2) show delayed release of aceclofenac. Decrease in concentration of alginate results in reduced size of the microbeads along with high efficiency, thus satisfied the need of formulation of delayed release aceclofenac microbeads.

INTRODUCTION

In recent years extensive efforts are being made in various pharmaceutical research laboratories for the development of novel and targeted drug delivery system with an aim of improved patient convenience, better therapeutic efficacy, less side effects, reduced dosage regimen, targeted drug delivery with less toxicity for the treatment of cancer and other serious infective diseases. Conventional oral drug delivery administration does not usually provide rate controlled release or target specificity. In many cases conventional drug delivery provides sharp increase of drug concentration of potentially toxic levels, drug concentration eventually decreases until re-administration.

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Today new methods of drug delivery are possible, desired drug release can be provided by rate controlling membranes or by implanted bio degradable polymers containing dispersed medications.[1,2] Controlled release systems include any drug delivery system that releases the drug over an extended period of time. If the system is successful in maintaining a constant drug level in the blood or target tissue, it is considered as controlled release system. If it is unsuccessful in this but only extends the duration of actions, it is considered as prolonged release system. Oral route is the most convenient and common mode of administration of controlled release system. Oral controlled release system include coated pellets, matrix tablets, microcapsules, mixed release granules, poorly soluble drug a complexes, ion exchange resins, complexes, osmotic pumps etc.,

Micro encapsulation is at present most common and rapidly expanding technology for controlled drug delivery system."Microencapsulation is process by which thin coating can be applied

reproducibly to small particles of solids or droplets of liquid dispersions or even gases are encapsulated into micro sonic particles".

Particle size range dimensionally from 1 µm to 1000 µm . Microspheres may assume various shapes as globules, spherical, kidney shaped, rice grains like flocculate and massive wall may contain one or many substances. Contents of the capsules are contained within wall until released by some means that serve to break, crush, melt, dissolve, rupture or remove the shell or the internal phase caused to diffuse out through the capsule wall.[3-6]

Ionotropic Gelation method is used for preparation of beads by exchange of ions like Na+ or Ca++ in this process Hydrogels (or) wet gels can be formulated.

Ionotropic gelation is based on the ability of polyelectrolytes to cross link in the presence of counter ions to form hydrogels. Since, the use of alginates, gellan gum, chitosan, and carboxymethyl cellulose for the encapsulation of drug and even cells, ionotropic gelation technique has been widely used for this purpose [7] The natural polyelectrolytes inspite, having a property of coating on the drug core and acts as release rate retardants contains certain anions on their chemical structure. These anions forms meshwork structure by combining with the polyvalent cations and induce gelation by binding mainly to the anion blocks. The hydrogel beads are produced by dropping a drug-loaded polymeric solution into the aqueous solution of polyvalent cations. The cations diffuses into the drug-loaded polymeric drops, forming a three dimensional lattice of ionically crossed linked moiety. Biomolecules can also be loaded into these hydrogel beads under mild conditions to retain their three dimensional structure.

Alginate is a non-toxic, biodegradable, naturally occurring polysaccharide obtained from marine brown algae, certain species of bacteria. Sodium alginate is a sodium salt of alginic acid a natural polysaccharide and a linear polymer composed of 1,4-linked β-D-Mannuronic acid (M) and α-D-gluronic acid (G) residues in varying proportions and arrangements. The homopolymer regions composed of M-blocks and G-blocks are interspersed with M G heteropolymeric regions known as “egg box junction” [8, 9].

MATERIALS AND METHODOLOGY

The following chemicals were procured from: aceclofenac (Rds Laboratory), Sodium alginate (Marine chemicals), Potato starch (SSP Pvt Limited), Potassium dihyrogen phosphate (Vishnu Priya Chemicals Pvt Ltd), Sodium hydroxide (Sakthy Sunder Acids Pvt Ltd) and calcium chloride (Halocarbon Products Corporation)

Extraction of potato starch

Potatoes (1 kg) were washed carefully in tap water, dried and processed through a juice presser (Moulinex). The residual is filtrated through a sieve (mesh 125 lm) with addition of 1 L tap water removing cell wall material. To the residual starch slurry (final volume 2 L) is added 2 mL 38–40% sodium bisulphate solution and the slurry stands to settle for 1/2 hour. The pellet of starch is washed two times in 1 L tap water and allowed to stand for 1/2 hour. Finally the starch is dried at room temperature on filter paper over night.

Testing properties of potato starch from different scales of isolations—A ringtest Bente Wischmann, Tina Ahmt, Ole Bandsholm *et.al* Journal of Food Engineering 79 (2007) 970–978

Procedure for preparation of Aceclofenac micro beads [10-12]

Accurately weighed drug was dissolved in acetone (solution 1). Sodium alginate and potato starch was dissolved in water (solution 2). Then solutions 1 was mixed with solution 2 (Table 1). The mixture was placed in a beaker with constant stirring using magnetic stirring until homogenous solution is obtained. It is then taken in a glass syringe and injected into calcium chloride solution (5%) to form micro beads. Glutaraldehyde (3-4ml) is added to $CaCl_2$ solution as a cross linking agent. Micro beads were filled and dried in a low temperature (40 ^{0}C).

Table 1: Formulation of Microbeads

S.No	Ingredients	F1	F2	F3	F4
1	Aceclofenac	1	1	1	1
2	Sodium alginate	1	2	3	4
3	Potato starch	4	3	2	1
4	Calcium chloride	5%	5%	5%	5%
5	Glutaraldehyde	2 ml	2 ml	2 ml	2 ml
6	Curing time	30 min	30 min	30 min	30 min

Evaluation

Production yield

The percent yield of each batch of microspheres was obtained on weight basis with respect to the weight of starting material and the result obtained is shown in Table 2.

Incorporate efficiency

100 mg of dried microbeads were taken and extracted in 100 ml of phosphate buffer (pH 6.8) for 4 hours. Then the dispersion of micro spheres was sonicated at 125 w for 30 min (imeco sonicator, imeco ultronics. India) and the solution were filtered through a 0.45 µm filter. Finally, the polymeric debris was washed twice with fresh solvent (phosphate buffer) to extract any adhering drug. The drug content of filtrate and washing was determined spectrophotometrically at 273 nm. Each determination was made in triplicate and the values are represented in Fig. 1.

The incorporate efficiency was calculated by the formula:

Incorporate efficiency=

(Practical drug content / Theoretical drug content) x 100

Table 2: Production yield & incorporate efficiency

Formulations	Production yield %	Incorporate Efficiency %
F1	96.7±3.09	89.32±4.06
F2	93.8±3.09	82.19±2.01
F3	89.1±2.97	73.86±1.90
F4	86.3±2.72	61.42±1.55

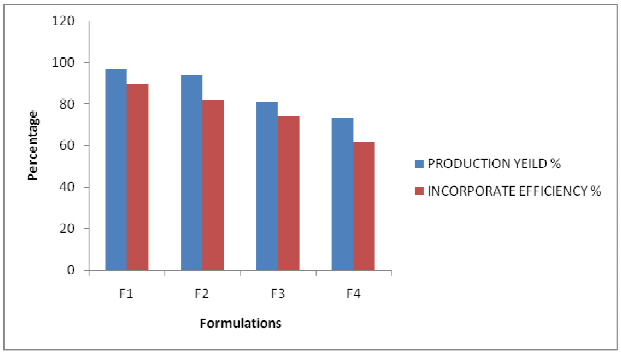

Figure 1: Plot showing percentage Yield and incorporate efficiency

Determination of micromeritic properties

Particle size analysis [19]

The particle sizes of both placebo and drug loaded formulations were measured by an optical microscope fitted with an ocular and stage micrometer and particle size distribution was calculated. The Olympus model (SZX-12) having resolution of 30 xs was used for this purpose. The instrument was calibrated at 1 unit of eyepiece micrometer was equal to 1/30mm (33.33µm). In all measurements at least 100 particles in five different fields were examined.

Flow rate

Flow rate of pure drug and microbeads formulation were determined as the ratio of mass (g) with respect to time (seconds). The flow rate was determined using a steel funnel with orifice diameter of 10 mm. Each experiment was conducted in triplicate. The obtained results were shown in the Table 3.

Angle of repose

The flow properties were investigated by measuring the angle of repose of drug loaded microbeads using fixed base cone method. Microbeads were allowed to fall freely through a funnel fixed at 1cm above the horizontal flat surface until the apex of the conical pile just touches to the tip of the funnel. The angle of repose was determined by tan -1(h/r): h=cone height, r=radius of circular base formed by the microbeads on the ground.

Density Parameters

The bulk density, tap density carr's index was measured in a 10ml graduated cylinder as a measure of pack ability of the microbeads. Each experiment was carried out in triplicate. The results were depicted in the Table 3.

Size morphology [7-9]

A texture of surface for prepared microbeads was done by SEM photograph (IIT - Chennai) (Fig. 2)

In Vitro release studies [13-20]

An *in vitro* study was carried out in USP dissolution apparatus (basket type) at 37± 0.5 C and speed of 50 rpm using phosphate buffer (pH6.8) as dissolution medium. 5ml of sample were withdrawn at fixed time intervals and equal volume of fresh phosphate buffer was replaced. The samples were suitably diluted and aceclofenac content in phosphate buffer was estimated. Values obtained are plotted against time and the results were given in the Table 4.

Table 3: Micrometric Evaluation of Prepared Microbeads

S.No	Formulation	bulk density g/ml	Tap density g/ml	Carr's index	Angle of repose	
					values	Comments
1	Pure drug	0.96±0.77	0.61±0.071	36.4	$39^0$21±2.01	Poor flow
2	F1	1.43±0.74	1.04±0.97	27.27	$22^0$40±1.99	Good flow
3	F2	1.59±0.04	1.33±0.79	16.98	$23^0$28±1.03	Good flow
4	F3	1.25±0.09	0.94±0.08	24.8	$21^0$47±3.09	Good flow
5	F4	0.93±0.07	0.71±0.08	23.65	$20^0$25±2.61	Good flow

Mean, n=3

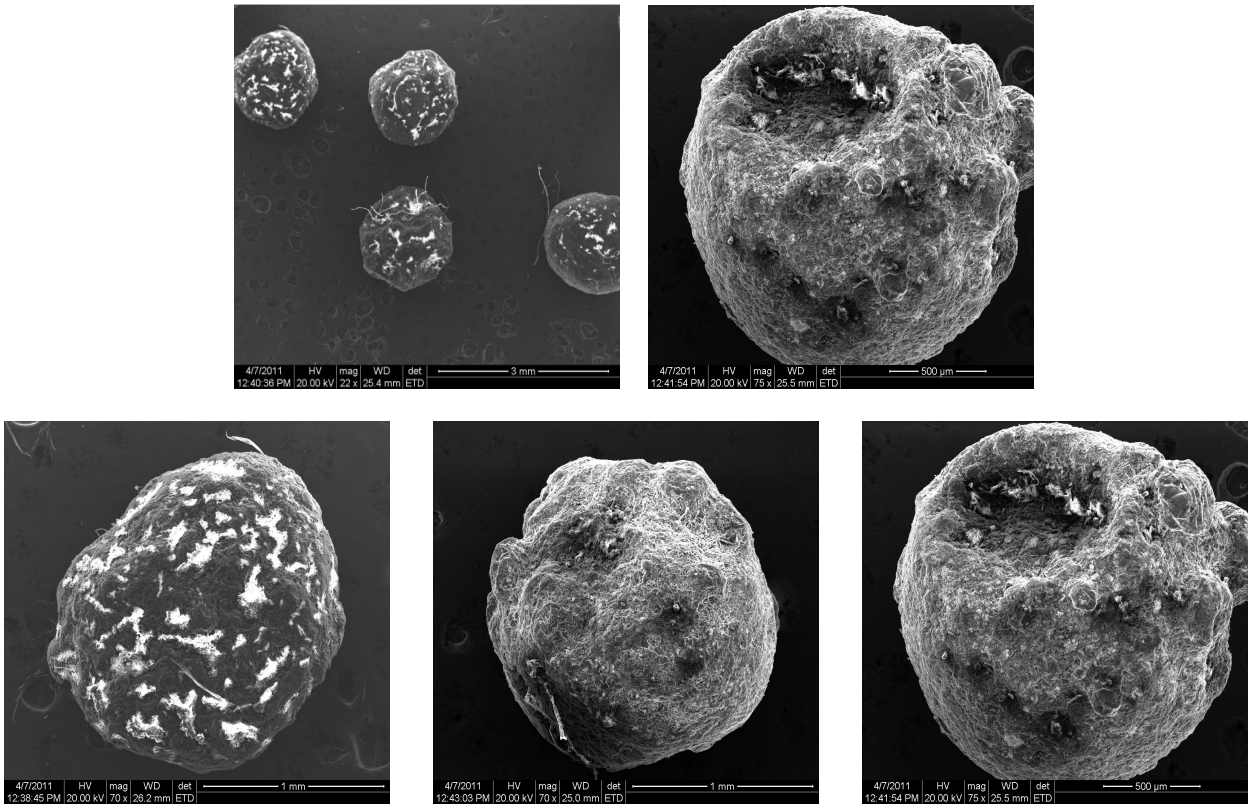

Figure 2: Scanning Electron Microscopy of F1 Formulation

Table 4: *In-Vitro* Release Studies

S.No	Time (h)	Percentage of drug release			
		F1	F2	F3	F4
1	1	33.23±1.033	35.64±2.561	42.22±0.990	46.23±1.529
2	2	47.34±1.732	51.45±1.512	58.34±3.011	59.11±1.0789
3	3	58.36±2.092	63.33±1.821	69.67±0.011	64.29±0.514
4	4	63.42±0.912	79.65±3.073	83.72±3.017	86.03±4.072
5	5	77.65±0.002	82.12±1.154	89.43±1.671	94.54±2.819
6	6	79.38±1.77	85.32±1.004	92.34±1.975	96.43±2.052

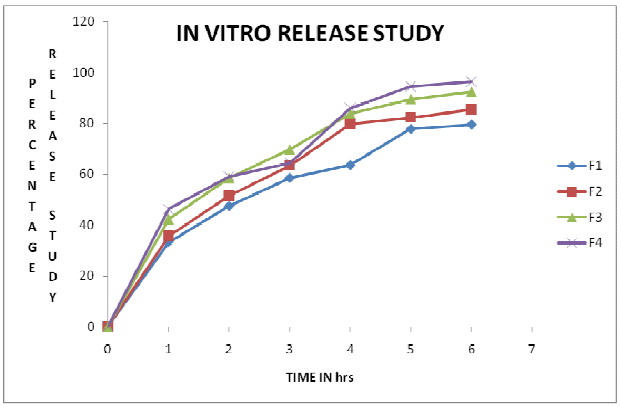

Figure 3: *In-Vitro* Release Studies of Aceclofenac Beads

RESULTS AND DISCUSSION

Particle size analysis

The particle size analysis of four batches of aceclofenac microbeads were performed by optical microscope and the results are given under the Table 5 and the same was showed in the graphical representation, Fig. 4.

Table 5: Particle size analysis

S.No	Batch.	Average size (mm)
1	F1	1.8±0.16
2	F2	2.0±0.71
3	F3	2.5±0.11
4	F4	2.7±0.24

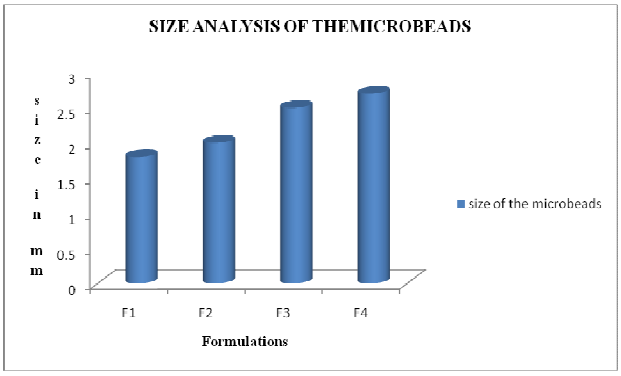

Figure 4: Particle size analysis

Size morphology

The morphology of the prepared micro beads were studied with the help of scanning electron microscopy which itself has the size analysis measurement which is show in the following Fig. 2.

DISCUSSION

Aceclofenac microbeads were prepared by ionotrophic gelation technique of various concentration of alginate/potato starch had narrow paricle size distribution,the formulation [F1,F2] with reduced concentration of alginate shows reduction in particle size and range from 1.8-2 mm. Shape and Morphology of prepared beads show rough surface and presence of drug particles on the surface evidence by SEM photograph. Micromeritics property of the beads reflects good flow property and packing ability. *Invitro* release study reveals that microbeads with high potato starch concentration (F1 & F2) shows delayed release of Aceclofenac with good entrapment efficiency and production yield, thus satisfied the need of formulation of delayed release aceclofenac microbeads.

CONCLUSION

The above study had showed that the Ionotrophic Gelation Technique was a simple technique used in the preparation of sustained release microbeads of aceclofenac using potato starch as release retardants. And the prepared beads showed good flow property comparing with the pure drug reflects good packing ability along with entrapment efficiency and production yield. Major factor to be noticed is that the size of the microbeads was decreased with low concentration of alginate at the same time the entrapment efficiency was increased.

ACKNOWLEDGEMENT

I hereby feel my heartful thanks to my institution which helped me a lot to perform this research in S.Chavaan's College of Pharmacy and extend my thanks to the students who worked parallel with me and those who provided the gift samples to end up this research in well designed way.

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