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Research Article

FORMULATION AND EVALUATION OF CEFIXIME FLOATING BEADS

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ABSTRACT

A suitably designed controlled release drug delivery system can improve the therapeutic efficacy and safety of a drug by spatial placement in the body thereby reducing the frequency of dosage form. Polymeric gel beads are used for controlled release of various therapeutic agents. Cefixime is a third generation cephalosporin antibiotic which is highly effective against various infections. For this purpose calcium ions were used as cross linking agents in formulation of alginate and alginate pectin beads by ionotropic gelation method. Next, characterization of the beads, drug entrapment within the beads and the drug release kinetic were investigated. Results showed that as the concentration of alginate was increased in the formulation the spherical shape of the beads was maintained and also more sustained action was observed. But when pectin was used along with sodium alginate the shape of beads turned somewhat irregular or disc like. Also the sustained action was reduced.

Keywords: Controlled release, Cefixime, Ionotropic gelation, Bead formulation.

INTRODUCTION

An appropriately designed controlled release drug delivery system can improve the therapeutic efficacy and safety of a drug by precise temporal and spatial placement in the body, thereby reducing both the size and number of doses required[1] .One approach for controlled release formulation of different therapeutic agents is the production of polymeric gel beads. The beads are discrete spherical microcapsules that serve as the solid substrate on which the drug is coated or encapsulated in the core of the beads. Beads can provide sustained release properties and amore uniform distribution of drugs include, within the gastrointestinal tract. Furthermore, bioavailability of drugs formulated in beads has been enhanced .Numerous studies have been reported, concerning the use of alginate beads as a controlled release carrier. Alginate, is a linear unbranched polysaccharide composed of varying proportion of 1,4- linked beta-D mannuronic acid (M) and alpha- L guluronic acid (G) residues. Alginate has a unique gel- forming property in the presence of multivalent cations, such as calcium ions in an aqueous medium, which takes place mainly at junctions in the G-G sequence rich chain region known as egg box junctions. When divalent metal ions such as calcium, barium diffuse into an alginate solution, the rapid ion binding and formation of a polymeric network produces an inwardly moving gelling zone. In fact alginate moves from the gel core towards this gelling zone, leading to the deletion of the alginate within the core. Therefore, alginate is used as an immobilization matrix for cells and as pharmaceutical adjuvant[2]. Varying proportions of pectin were used in few of the formulations along with alginate as the main polymer. Pectin is a heterogeneous anionic polysaccharide present in the cell wall of most plants. It is non toxic, almost totally degraded by colonic bacteria and is not digested by gastric enzymes .Pectin forms water insoluble complexes with several drugs and may be

useful additive for sustained release preparations[3]. Natural biodegradable polysachharides such as pectin, guar gum, chitosan and sodium alginate have been used in controlled drug delivery[4]. The low methoxy polysaccharide, pectin with the degree of esterification less than 50% can form rigid gels by the action of calcium ions which cross link the galacturonic acid chains of pectin to yield hydrogels that are stable at low ph[5]. Pectin is an inexpensive nontoxic polysaccharide extracted from citrus peels and apple pomaces and is used as a thickening and gelling agent[6].The classification of pectins depends upon the degree of esterification and degree of amidation which are both expressed as a percentage of carboxyl groups[7].Sodium alginate has been used as a food additive, an antacid adjuvant, cell immobilizer and viscosifier[8]. Cefixime Trihydrate was taken as a model drug. Cefixime is an orally active third generation semisynthetic cephalosporin type of beta lactam antibiotic. Chemically, Cefixime is 5-Thialazabicyclo[4,2,0]oct-2-ene-2-carboxylic acid, 7 –[[2 amino 4 thizolyl) (carboxy methoxy) imino]acetyl]amino]-3-ehenyle-8oxo,trihydrate.It is soluble in methanol and 0.1 M NaOH insoluble water and 0.1 M HCl[9].

MATERIAL AND METHODS

Cefixime Trihydrate was a kind gift from Jackson Laboratories Pvt Ltd Amritsar. Sodium alginates, Pectin, Calcium chloride were provided by Teerthanker Mahaveer College of Pharmacy, Moradabad. All other chemicals were of analytical grade and used without further purification.

Preparation of the beads: Three different concentrations of the polymer were used in different formulations. The polymer was used in 2, 3 and 4 percent concentrations. Sodium alginate was dissolve in suitable quantity of deionized water. It was sonicated for 5 minutes. Then after required stirring cefixime was added to the solution. Then each of these drug suspensions was dropped (10 ml/min) through a syringe nozzle (#22) into calcium chloride solution (3 percent) made in distilled water. Whole of the procedure took place at room temperature. Different concentrations of sodium alginate and calcium chloride as well as varying curing times were examined .In some formulations suitable quantity of pectin was also added along with sodium alginate. The obtained beads were filtered using wattman filter papers washed twice by deionized water and dried at 37 degree celcius for 24 hours.

RESULT and DISCUSSION

The formulation compositions of the various batches of prepared beads are shown in the Table 1. The shape of beads varied from spherical to disc shape with changing concentration and ratio of polymers. In the case of beads prepared with the combination of sodium alginate and pectin, as the part of alginate was reduced , the spherical shape was lost and became disc like or irregular. The colour of pectin beads was darker than that of sodium alginate beads. Particle size determination: With the help of digital caliper the size or diameter of the beads was calculated and it was found that the average size was 1.20 mm.

Scan electron microscopy of the beads was performed and the surface morphology of the formulation was checked. It was found that with the increasing concentration of sodium alginate the beads were of smooth texture.

The drug entrapment of various batches varied from 65% to 79%.

The release of all the batches was studied in the 1.2ph buffer and 6.8ph buffer. It was found that with the increasing concentration of sodium alginate in the formulations better and long lasting release was observed. Formulation F3 was found to be the best of all. That might be due to the rich layer of the sodium alginate that binds the drug within the matrix for more time. The F3 formulation observed a first order release (Fig.1).

CONCLUSION

It was found that with increasing concentration of sodium alginate in the formulation the shape of the beads became spherical. As the concentration of pectin was increased in the formulation the shape of beads became irregular or disc like. Also, increased sustained action was observed with that formulation in which the concentration of sodium alginate was more.

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Table 1: Formulation chart

Ingredients	F1	F2	F3	F4	F5	F6
Cefixime	2 grams	2 grams	2 grams	2 grams	2 grams	2 grams
Sodium alginate	2 grams	2.5 grams	3 grams	2 grams	2 grams	2 grams
Pectin	0	0	0	0.5 gram	0.75 gram	1 gram
Calcium chloride	3%	3%	3%	3%	3%	3%

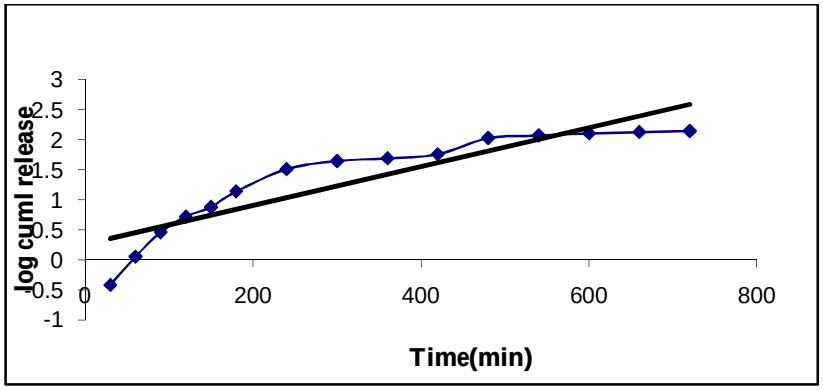

Fig. 1: The F3 Formulation observed a First Order Release.