Abstract

Oral drug delivery system offers several advantages because of flexibility in design of dosage forms and patient compliance. The colon is the specific site where, local and systemic delivery takes place and also local delivery allows topical treatment of inflammatory bowel disease. Hydrogel beads are one of the successful multi particulate system by which drug can be targeting to specific site. This article mainly focus on potential of hydrogel beads as target release system to stomach and technologies used in preparation methods. Also therapeutic uses of hydrogel beads.

Key words: Multi particulate, Ionotrop gelation.
INTRODUCTION

The basic rationale of controlled drug delivery system is to optimize the pharmacokinetic, pharmacodynamic and biopharmaceutical properties of drug administered. This offers the therapeutic maintainance of drug target site and decrease the frequency of drug administration, reduced side effects with desirable therapeutic concentration and increase patient compliance [1]. The recent efforts have been made to design novel drug dosage formulation so that more and more effectiveness can be achieved relative to the conventional dosage forms. Hydrogel beads and other multiparticulate systems of polymers have been formulated using either systemic or natural polymeric material. Therapeutic molecules complexed by polymers capable of forming a gel may also released by diffusion hence, drug delivery system by a polymeric matrix that is non–toxic, biocompatible and biodegradable.

DRUG SUITABLE FOR CONTROLLED OR EXTENDED RELEASE DOSAGE FORMS

Drugs having absorption window in stomach

Drugs causing irritation and unsafe in the lower GI region.

Highly active in stomach.

Design of multi particulate drug delivery system is intended for oral, topical and parenteral formulation. Several multiparticulate includes pellets, granules, micro particles, lipoparticles, beads etc. These system consists of thousands of particles in which dosage form is substantially divided and embedded in which sub unit with selective diameter range. To achieve the desired therapeutic dose these sub units are encapsulated and compressed into tablet form. One of the multi particulate drug delivery system is hydrogel beads formulated from hydro collide polymers whose size ranges from 0.2 to 0.3mm and mostly spherical in shape.

ADVANTAGES

- Increased therapeutic efficiency as more drug reaches to target site.
- Avoid risk of toxicity.
- Plasma concentration of drug is maintained for prolonged period.
- Better absorption as surface area is increased.
- Patient compliance will be increased because of taste masking Improved stability.

DISADVANTAGES

- The main disadvantage are high cost and sensation felt by movement of the meggots.
- Hydrogels are non adherent, they made need to secured by a secondary dressing.
Incorporation of suitable concentrations of active ingredients for therapeutic uses in hydrogel beads are generally carried out by two methods.
- Incorporation of active ingredients during the process of preparation of hydrogel beads.
- Adsorption of a solution or suspension of active ingredients in previously cross linked hydrogel beads, when active ingredients are incompatible with dehydration solvents.
- More preferable and more drug entrapment efficiently can be achieved by first process.

**Preparation of hydrogel beads by using different techniques:**
- Ionotropic gelation technique
- Emulsion internal Ionotropic gelation.
- Ionotropic gelation under a high voltage electrostatic field.
- Ionotropic gelation followed by coacervation.
- Multi polyelectrolyte hydrogel beads.
- Ionotropic gelation followed by compression.

**POLYMERS**

**Sodium alginate [2,3]**
Sodium alginate is salt of alginic acid, bio-compatible, non-toxic, natural polysaccharide found in all species of brown algae. Alginate beads advantages are non toxic orally, high biocompatibility, inability to re-swell in acidic environment and easily re-swell in an alkaline environment there by protecting the acid sensitive drugs from gastric environment. The higher sodium alginate concentration improves the gelling capacity and lower sodium alginate concentration sustain the drug release for an extended period.

**Chitosan [4]**
Chitosan obtained by alkaline the deacetylation of chitin. Chitosan is non toxic, biodegradable, natural, linear polymer resembling the structure of cellulose. The more effective beads for drug delivery can be formed by using combination of both alginate and chitosan. Chitosan because of its anti-ulcer and antacid properties decreases stomach irritatation.

**Carboxy Methyl Cellulose [5,6]**
Cellulose is a plant product in these product on carboxy methylation process it can be modified as carboxy methyl cellulose. The carboxy methyl cellulose can be cross linked with aluminium salt to get bio degradable hydrogel beads.
Gellan [7]
Gellan gum as an excellent flavor release, stability and high gel strength, process flexibility and thermo reversible capacity obtained from fermented Sphingomonas Eloda. The chain undergoes arrangement and rearrangement when temperature changes occurs, resulting in a conformational change in structure and entrap the drug.

Pectin [8]
Pectin is a non toxic polysaccharide extracted from citrus peal and it has been used as a gelling agent.

METHODS
Ionotropic gelation technique
Ionotropic gelation technique is based on ability of polyelectrolyte to cross link in presence of counter ions by using this technique drugs and bio molecules can be encapsulated inspite of having the release rate retarding nature. The natural polymers also have some anions the chemical structure. These anions triggers the gelation and form insoluble mesh work like structure by combining with counter acting cations. The hydrogel beads are formed by adding drop wisely drug loaded polymeric soluble into aqueous solu

NOVALITY IN IONOTROPIC GELATION TECHNIQUES
Emulsion Internal Ionotropic Gelation Technique
It is an advanced method. In this the beads containing oil phase is gently homogenized with polymer containing aqueous phase and then extruded into calcium chloride solution. In these technique initially polymer was dissolved in aqueous phase, to this oil was added and stirred continuously to form emulsion, to which drug was added. Finally this mixture was extruded into the calcium chloride solution with gentle agitation at room temperature [11,12,13].

Polyelectrolyte Complexation Technique [14]
The quality of hydrogel beads like mechanical strength and permeability barrier can be improved by addition of oppositely charged another polyelectrolyte to ionotropically gelated hydrogel beads.
Coacervation Technique [15,16]

Ionotropic gelation followed coacervation to improve the stability and physic chemical properties of hydrogel beads. The hydrogel beads formed by gelation via calcium cross-linking and alginate – chitosan complex coacervation.

EVALUATION OF HYDROGEL BEADS

Particle size analysis

Particle size of the bead formulation were measured by an optical microscope. In this microscope fitted with an ocular and stage micrometer and particle distribution was calculated [16]

Fourier transform infrared spectroscopy (FTIR) studies

FTIR spetra of hydrogel beads are recorded using the FTIR spectrophotometer. And it is used to determine their structure and intramolecular interactions [17].

Scanning electron microscopy(SEM)

The shape and surface characteristic of the hydrogel beads was investigated by using scanning electron microscope(SEM). The vacuum dried particle were coated to 200 A thickness with gold palladium using prior to microscopy. The coated beads were observed under scanning electron microscopy instrument at the required magnification at the room temperature [18].

Swelling studies

Swelling of hydrogel beads were determined in various pH range. The release of the entapped drug from hydrogel depends on the swelling behavior, because of swelling is directly propotional to drug release. The hydrogel beads swell slightly in stomach, but swelling gradually increases intestinal pH and maximum in the colon. Swelling ratio was studied by measuring the percentage water uptake by the beads [19]. The beads were removed at definite time intervals from their respective swelling media and weighed after drying the surface water using filter paper. Swelling (%) is calculated according to the following formula

Swelling index= (S-T) T/100

Where,

S = The weight of the hydrogel beads after swelling.
T = The initial weight of the hydrogel beads.

Drug entrapping efficiency

Drug entrapment efficiency of the water soluble drugs is less as the medium used is mostly aqueous and the drug will be lost more in the medium, longer the curring time., lesser the extent
of entrapment [20]. The water insoluble drugs having good entrapment efficiency [21]. The more concentration of the drug, more will be the entrapment. The increase in coating polymer concentration also increases the drug entrapping efficiency [22].

**Estimation of Drug content**

To ensure the consistency of dosage units, each unit in a batch should have active substance content within a narrow range around the label claim. Dosage units are defined as dosage forms containing a single dose or a part of a dose of an active substance in each dosage form. Beads from each formulation were powdered. Equivalent weight of beads was weighed and dissolved in 5ml of water in 50ml standard flask. Shake them and make up with phosphate buffer and then centrifuge it. From that take 5ml of solution in 50ml standard flask make up with phosphate buffer. Generally, the drug content in any formulation should fall within the limit of 90 – 110%.

**In vitro release studies of Hydrogel beads**

Dissolution is considered as one of the most important quality control tests performed on pharmaceutical dosage forms and is now developing into a tool for predicting bioavailability, and in some cases, replacing clinical studies to determine bioequivalence. In vitro release studies of prepared Hydrogel beads were carried out using USP Type I dissolution apparatus (basket) at 100 rpm [23]. Dissolution was carried out for a total period of 8 hours using 0.1 N HCl (pH 1.2) for first 2 hours, phosphate buffer (pH 6.8) for the next 3 hours and 7.4 pH for the rest of the period maintained at a temperature of 37±0.5°C, 37±1°C and 37°C [24,25]. At periodic time intervals, the samples are withdrawn at specific time interval and assayed spectrophotometrically at the wavelength of maximum absorbance. And cumulative percent drug release was calculated. The study was performed in triplicate. Five milliliters of fresh dissolution media was added each time to maintain the sink conditions [26].

**CONCLUSION**

The modified technique of multiparticulate system can be successfully encapsulated into hydrogel mesh works ensuring the constant release rate once a desired period by retaining their structural integrity. These hydrogel beads can also be used as a reservoirs for bioactive carrier molecules on their surface. The recent studies on multiparticulate system provides an tremendous opportunities and desiging new controlled and delayed release oral formulation, thus extending for future pharmaceutical development, encapsulating small hydrophilic molecule.
REFERENCES


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