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Review Article

ROLE OF XANTHAN GUM (*XANTHOMONAS COMPESTRIS*) IN GASTRORETENTIVE DRUG DELIVERY SYSTEM: AN OVERVIEW

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ABSTRACT

Floating drug delivery system is the form of gastro-retentive drug delivery system. That controls kinetic release rate of drug to a specific site for its pharmacological action. These are achieved by use of various polymeric substances including natural polymer such as xanthan gum. This delivery system prolongs the retention time of the drug in the stomach as compared to conventional dosage form. The present article highlights the use of xanthan gum for the formulation of the gastro-retentive drug delivery system especially with natural polymer (xanthan gum). The main goal of any drug delivery system is to achieve desired concentration of the drug in blood or tissue, which is therapeutically effective and non toxic for a prolonged period. Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation etc. From immediate release to cite specific delivery, oral dosage forms have really progressed.

Key words: Natural gum, floating system, fermentation process.

INTRODUCTION

Gastric floating drug delivery system (GFDDS) is particularly useful for drugs that are primarily absorbed in the duodenum and upper jejunum segments. The GFDDS is able to prolong the retention time of a dosage form in the stomach, thereby improving the oral bioavailability of the drug. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients[1].

Advantages of Gastro Retentive Drug Delivery System

- In the treatment of peptic ulcer disease.
- Use for the delivery of drugs with narrow absorption window in the small intestine.
- Reduced dosing frequency.
- Improved bioavailability of the drug.
- Use for drugs which are unstable in intestinal fluids.
- Use to sustain the delivery of drug.
- Use for maintaining the systemic drug concentration within the therapeutic window.
- Site specific drug delivery is also possible.

Disadvantages of Gastro Retentive Drug Delivery System

- These require sufficiently high levels of stomach fluids, for the system to float and to work efficiently.
- Not suitable for drugs with stability or solubility problem in stomach.
- Drugs which undergo extensive first pass metabolism are not suitable candidates.
- Drugs with irritant effect also limit the applicability[2].

Table: List of Drugs Formulated as Single and Multiple Unit Forms of Floating Drug Delivery Systems[3]

Dosage forms	Drugs
Tablet	Chlorpheniramine maleate, Theophylline, Furosemide, Ciprofloxacin, Pentoxyfillin, Captopril, Acetylsalicylic acid, Nimodipine, Amoxycillin trihydrate, Verapamil HCl, Isosorbide di nitrate, Sotalol, Atenolol, Isosorbide mono nitrate, Acetaminophen, Ampicillin, Cinnarazine, Diltiazem, Fluorouracil, Piretanide, Prednisolone, Riboflavin- 5′ Phosphate
Capsules	Nicardipine, L- Dopa and benserazide, chlordiazepoxide HCl, Furosemide Misoprostal, Diazepam, Propranlol, Urodeoxycholic acid
Microspheres	Verapamils, Aspirin, griseofulvin, and p-nitro aniline, Ketoprofen, Tranilast Ibuprofen, Terfenadine
Granules	Indomathacin, Diclofenac sodium, Prednisolone
Powders	Cinnarizine
Films	Several basic drugs

Natural polymer used in Gastro Retentive Drug Delivery System

The aim of this work is tried to give to the role of natural polymer in the development of floating drug delivery system. The use of natural polymer is valuable based on proven biocompatibility and safety. Polymers are generally employed in floating drug delivery system so as to target the delivery of drug to a specific region in the gastrointestinal tract i.e., stomach moreover these polymers are safe, nontoxic and capable of chemical modification and gel forming nature[4].

These are advantages of natural polymer

- Biodegradable is the naturally available. They are produced by all living organism.
- Basically all of these plant materials are repeating sugar polysaccharides.
- Cheaper to use as natural sources, the production cost is less compared to synthetic material.
- There less chance for side and adverse effect with natural material compared with synthetic one[5].

Xanthan Gum

Xanthan is extracellular hetropoly-saccharides produced by pure culture aerobic fermentation of carbohydrate with bacterium *xanthomonas compestris*. Xanthan is a well known biopolymer. It is an ionic polysaccharides, whose primary structure depend on bacterial strain and fermentation condition, xanthan gum is a natural, biosynthetic, edible gum and an extracellular polysaccharides, xanthan gum is consists of glucose, mannose and glucuronic acid, and it is used in different foods as thickener and stabilizer[6].

Chemistry of xanthan gum

Xanthan is long chain polysaccharides with large number of trisaccharide side chain. It consists of a b-(1, 4)-D-glucose backbone, which is the same as for cellulose. The side chains are composed of two mannose unit and one glucuronic acid unit. The mannose closest to the backbone can carry an acetyl group and terminal mannose a pruvate group. This gum develops a weak structure in water. This creates high viscosity at low concentration[7].

Properties of xanthan gum

Xanthan is a highly soluble in cold and hot water and this behavior is related to polyelectrolyte nature of the xanthan molecule. Xanthan gum is mainly considered to be non-gelling and used for viscosity. It hydrates rapidly in cold water without lumping to give reliable viscosity encouraging its use as thickener stabilizer, emulsifier and foaming agent. Xanthan gum is highly viscous even at low concentration. This property use ful in industrial application, especially in the food and cosmetic industries. Anionic character of this polymer is due to presence of both glucuronic acid and pyruvic acid groups in the side chain[8].

Characteristics of Natural polymer

- High stabilizing property
- High viscosity at low concentration
- Soluble in hot and cold water
- Very resistant to temperature variations
- Compatible with all commercial thickeners and stabilizers[9]

Manufacture

Xanthan gum production

For the gum production, 10ml of the inoculums was added to 90ml of the production medium in a 500ml Erlenmeyer flask. The flasks were kept for fermentation for 96 hrs at 28c and 200 rpm in rotary shaker. After 96hrs, final broths were heated at 80c for 30 minutes. Then, diluted with five volumes of water and broths were centrifuged at 8000g for 40minutes. Suspended cell mass was removed while supernatant was used for xanthan gum isolation. Three volumes of chilled 96% alcohol were added to the supernatant solution. After sometime, Xanthan gum was precipitated and settled down. This precipitated gum was left in an oven at 50c. Finally the constant weight of gum powder was taken[10].

Other procedure

The bacterium *Xanthomonas campestris* produces the polysaccharide at the cell wall surface during its normal life cycle by a complex enzymatic process. In nature the bacteria are found on the leaves of the *Brassica* vegetables such as cabbage. Commercially, xanthan gum is produced from a pure culture of the bacterium by an aerobic, submerged fermentation process. The bacteria are cultured in a well-aerated medium containing glucose, a nitrogen source and various trace elements. To provide seed for the final fermentation stage, the process of inoculums build-up is carried out in several stages. When the final fermentation has finished the broth is pasteurized to kill the bacteria and the xanthan gum is recovered by precipitation with isopropyl alcohol. Finally, the product is dried, milled and packaged[11].

Advantages of Xanthan Gum in Gastro Retentive Drug Delivery System

It is used as a tablet excipient to increase or decrease the drug release but not much has been reported concerning its use for sustained drug release. Xanthan has the potential advantage of drug release with zero order release kinetics. However its major drawback is that the drug release is influenced by the pH and the presence of ions in the medium.

Literature Review

Patel et al investigated gastro retentive tablet of verapamil hydrochloride using different hydrocolloid polymers including carbopols, hydroxyl propyl methyl cellulose, and xanthan gum by direct compression technique. Selected tablet containing xanthan gum along with citric acid showed buoyancy more than 24hrs[12].

Dave et al developed gastro retentive delivery system of ranitidine HCl. Guar gum, xanthan gum and HPMC were used as gel forming agents. Sodium carbonate was incorporated as a gas-generating agent. The effects of citric acids and xanthan gum on drug release profile and floating properties were investigated[13].

Renuka et al prepared of floating controlled release tablets of carvedilol. The gastro retentive floating drug delivery is a promising approach to achieve *in vitro* buoyancy and there by longer gastric retention time by using natural polymers like xanthan and guar gum and gas generating agent sodium bicarbonate. The *in vitro* evaluation of drug delivery system showed that floating tablets containing natural polymers like both xanthan and guar gum exhibited more controlled release than xanthan gum alone[14].

Shobhit Kumar et al the present review of the literature shows the release behavior of natural polymers, gums and mucilage. Therefore, in the years to come, these act as herbal excipients in drug delivery systems[15].

Anurag Verma et al prepared floating alginate beads in which, Incorporation of type B gelatin (M7) or XG (M8 and M9) into floating beads although extended the drug release up to 7-8 hours[16].

Mohammed Muqtader et al buoyant delivery systems are promising dosage forms which could be a better alternative to the conventional oral dosage forms in order to improve bioavailability by increasing the gastric retention time of the drug. Natural polymers such as xanthan gum and guar gum can be used to prepare floating drug delivery systems for drugs like famotidine which has higher absorption at low pH[17].

N. Narang et al floating drug delivery has become the most popular method for controlling the drug release. Stavudine floating tablets were prepared by blending the drug, polymers

(xanthan gum, guar gum, HPMC), gas generating agent, and diluents followed by slugging. These tablets swelled while coming in contact with the aqueous medium. The formulations containing xanthan gum and guar gum exhibited good drug retaining capabilities[18].

Puneeth K.P.et al in the present study Rosiglitazone maleate floating tablets by wet granulation method using natural gums like Xanthan gum and Guar gum was developed[19].

Phaechamud et al fabricated sustained-release matrix tablets containing chitosan combined with xanthum gum which prolonged the drug release more extensive as compared to that containing single polymer. By utilizing release retarding properties of xanthan gum, controlled release profile was achieved in delivery of pentoxifylline[20].

Gohel et al explored the use of blend containing xanthan gum and hydroxypropylmethyl cellulose for development of modified release drug delivery system of diltiazem HCl. The drug release kinetics for tablets followed Hixson-Crowell equation and showed drug release for 12 h[21].

Patel et al evaluate xanthan gum and guar gum for formulation of floating dosage form for dipyridamole. The prepared tablets had desired buoyancy characteristics. Hence xanthan gum could be use in floating drug delivery formulations[22].

Chaudhari et al formulate and evaluate floating drug delivery system containing theophylline as a model drug, because theophylline, a methyl xanthine derivative used in the treatment of chronic asthma as an adjunct to β2 agonist and corticosteroid therapy. It is rapidly absorbed after oral administration with a half-life of 4 – 8 hr's and no difference in the amount of absorption between the stomach, ileum & colon. Hence the floating form was developed. However, it is prepared by direct compression method. Direct compression method of theophylline tablet containing HPMC (K100M), xanthan gum, carbopol 934P, aerosol and sodium bicarbonate, PVP K30, lactose and MCC[23].

Iqwal Siddiqui Aslam et al *In vitro* study revealed that floating tablet of Diltiazem hydrochloride was adequately float on the medium and release the drug in sustained manner. The concentration of different grades of Hydroxyl Propyl Methyl Cellulose and Xanthan gum have great impact on the *in vitro* drug release of Diltiazem hydrochloride and Xanthan gum has more drug release retarding property than that of HPMC[24].

P Subhash et al prepared floating tablets of Diltiazem HCl using xanthan gum as carrier. The drug release from prepared tablets was found that the formulation with low amount of xanthan gum (40% w/w) showed a low release rate compared to formulation with higher concentration (60% w/w)[25].

Marella Radhakrishna et al designed to formulate and evaluate balanced floating drug delivery system as controlled release module, which prolongs the release rate of the drugs. And found that promising controlled release by gastro retentive floating tablet of Amoxicillin trihydrate using HPMC K4M, HPMC K15M, HPMC K100M and Xanthan gum by taking single polymer in the formulation in which gave better controlled release and floating properties comparsion to other formulation[26].

Thiruganesh Ramasamy et al developed a colon targeted drug delivery systems for Aceclofenac using xanthan gum as a carrier. The tablets prepared with high concentrations of xanthan gum showed a lower rate of erosion and a faster rate of swelling, as compared with the tablets containing lower concentrations of xanthan gum[27].

CONCLUSION

Natural polymers have been successfully used by many investigators for various approaches in floating drug delivery system. After through literature survey it have been concluded that natural polymer like xanthan gum play vital role in different formulation of floating drug delivery system along with better utilization and advantage over the synthetic polymer.

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