



REVIEW ARTICLE

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A summarized review about natural polymers role in floating drug delivery system and *in-vivo* evaluation studies

Muhammad Umar Javaid¹, *Qurat-ul-Ain^{1,2}, Umer Tahir^{1,2} and Safwan Shahid¹

¹Faculty of Pharmacy, The University of Lahore, Lahore, Pakistan

²Foundation for Young Researchers, Lahore, Pakistan

ABSTRACT

The approach of eco-friendly and safe environmental materials for various industrial applications like medicine, agriculture and similar areas is growing rapidly. The advantages of biologically degradable and non-toxic materials like the natural polymers are evident by the mounting level of its use in pharmaceutical field particularly. The various natural polymers have been aiding the drug delivery systems for long time as the drug transporters with the objective of improving the efficacy and efficiency. The floating drug delivery systems are required to possess proper floating capability in gastric systems and use of natural polymers in such delivery systems has been very beneficial. The physical characteristics of natural polymers facilitate them to be brilliant drug carriers for such type of drug delivery systems. The aim of this review is to provide the overview of role of natural polymers in floating drug delivery system, its characteristic effects, ongoing research and trend of future developments and applications in the field.

Key Words: Natural Polymers, Advantages, Efficiency, Floating Drug Delivery system, Applications, Transporters.

INTRODUCTION

In the development of novel drug delivery system, natural polymers and their semi synthetic derivatives broaden admiration. Advantages of natural polymers are their compatibility with other agents and degradability, readily availability and ability for chemical modification. Natural excipients are given preference because synthetic excipients cause unwanted effects in human. Herbal products are safer so now patients looking for the natural herbal constituents. Natural polymers release reformed form of drugs. Studies showed that natural polymers containing formulations release activities of drug influenced by the physiochemical properties, morphology, and release pattern of polymer, shape of dosage form and particle size. (Kumar *et al.*, 2012a). In drug delivery system natural gums have diverse applications as binders, suspending agents, disintegrant and emulsifying agents. They are also useful in preparation of sustained release and immediate release formulations (Goswami and Naik, 2014). Floating system are of two types, effervescent and non-effervescent system, without effecting on gastric emptying rate it remains buoyant or bouncy in stomach for longer time because this system consists of bulk density that is less than gastric fluids. At the time when system floats in gastric substances the drug is released deliberately in certain amount from this system. The best events of these systems are well regulated fluctuations in plasma drug concentration and augmented gastric retention time (Bangalore *et al.*, 2012; Bhowmik *et al.*, 2009).

Advantages of Gastro Retentive Drug Delivery System

GRDDS is suitable for all those drugs which absorbed through stomach and show local action in it, i.e., antacids etc. Due to vigorous intestinal movement poor drug absorption may occur in diarrhea, it can be prevented by

using this system to retain drug and its better response. It increases the patient compliance and lowers the dosing frequency. Therapeutic effect can be improved of drugs having short half-life. In this system the continuous drug release sustains a desired plasma drug concentration. Formulations which are unstable in intestinal pH can also be used. Dose dumping cannot occur. Sustained and uniform release of drug can prevent the gastric irritation. By the administration of prolonged release gastro retentive dosage forms dissolution in gastric fluid can be maintained as well as in alkaline pH of small intestine (Kanavaje *et al.*, 2014; Reddy *et al.*, 2013).

Disadvantages of Gastro Retentive Drug Delivery System

This system is not suitable for those drug which are acid insoluble or unstable in acidic medium, e.g., phenytoin and erythromycin respectively. It can't be used for those drugs which produces gastric lesions on slow release, e.g., non-steroidal anti-inflammatory drugs. This system is not compatible with those drugs which absorb specifically in colon, e.g., corticosteroids. Drug delivery systems with increased size may contain the high risk of preservation in stomach for long time and may pose a life threatening effect on further use of this system. For bio adhesive system the most difficult for is the high turnover proportion of gastric mucus. For efficient result and effect, this floating system needs high fluid level in stomach so it can float (Nayak, 2012; Kajale and Chandewar, 2013).

Applications of Gastro Retentive Drug Delivery

GFDDS stays in stomach for extensive period of time to enhance GRT while sustained drug delivery system shows limited effect due to short retention time in stomach. It can't pass through pylorus because of increased size and low density than their gastric fluids. (Mishra and Gupta, 2012) Those drugs which metabolized in upper GIT, their bioavailability and absorption can be enhanced by using this system. (Makwana *et al.*, 2012) Those drugs that absorbed from the stomach and proximal part of intestine have advantage of this system. It provides sufficient therapeutic level and effect and decreases the systemic exposure

*Corresponding Author:
Qurat-ul-Ain
Faculty of Pharmacy
The University of Lahore
Lahore, Pakistan
E-mail: ammieshah51214@hotmail.com
Contact No.: 0345-4945291



to the drug and reduced side effects due to slow delivery of drug from this system. It can also reduce the dosing frequency of certain drugs due to prolonged gastric availability, e.g., Feurosemide. (Goyal *et al.*, 2011). This system can decrease the counter action of the body may lead to higher efficiency and productivity of drug. (Kajale and Chandewar, 2013) Unwanted actions or activities of drug in colon can be avoided due to retention of drug in GRDF. Beta lactam antibiotics that absorbed from the small intestine and their presence in the colon may cause microorganism's resistance (Kumar *et al.*, 2012a).

Advantages of Natural Polymers

Biodegradable or natural polymers can be produced by living organism and are naturally available. They show no adverse reaction on human or on environmental health. Most of the natural polymers are nontoxic and biocompatible because these plant materials are carbohydrates in nature. Natural sources are easily collected in different seasons in large quantities and have low cost. Now in developing countries their productions have been promoted because of its wide use in industries (Tekade and Chaudhari, 2013).

Disadvantages of Herbal Polymers

They are disclosed to external environment so they may contain microbial contamination. Production of natural polymers depends on environment and various physical factors while synthetic manufacturing is controlled method with fixed amounts of ingredients. The percentage of content and constituents in natural materials may vary due to differences in their collection from different region, and at different times. They may have slow rate of production (Kulkarni *et al.*, 2012).

NATURAL POLYMERS USED IN FLOATING DRUG DELIVERY

Guar Gum

Guar gum belongs to family *Leguminosae* and derived from *Cyamopsis tetragonolobus* kernels. It is also known as Guarana, cluster bean, *Cyamopsis*, Calcutta lucern and Guarina (Chatrchyan *et al.*, 2014). It is a whitish yellow powder and has taste or odor. It is water soluble and are not soluble in organic solvents (Sahoo *et al.*, 2013). It has increased viscosity and used in solid dosage forms as a disintegrant and binder in pharmaceutical industries (Gomber and Parihar, 2013).

Xanthan Gum

Bacterium *Xanthomonas campestris* produced xanthum gum naturally. (Gomber and Parihar, 2013) This gum appears as odorless, free flowing fine powder or cream. Polysaccharide B-1459, Keltrol, Rhodigel, Merezan and Corn sugar gum are soluble in warm or cold water and are insoluble in ethanol and ether. This gum is stable material and is polysaccharide in nature with D-glucose backbone like cellulose. Their aqueous solutions are durable in existence of enzymes, bases, salts, acids and stable at pH range 3-12 and temperature between 10-60°C. It is nontoxic and nonirritant and used in cosmetics and food products, in topical and oral pharmaceutical formulations and preparations. It is also used as stabilizing agent, gelling agent, viscosity-increasing agent, suspending agent, emulsifying agent and thickening agent (Kola and Kumar, 2013; Sai Rekha *et al.*, 2015).

Chitosan

It is composed of glucosamine and Nacetylglucosamine and is linear cationic polysaccharide. Chitosan is prepared by the deacetylation of chitin that is obtained from crustacean shells. (Singh *et al.*, 2011). It is biodegradable, biocompatible and nontoxic (Shah *et al.*, 2013). It is odorless creamy or white flakes or powder and partially insoluble in 95% ethanol and soluble in water. It is used as viscosity enhancer, mucoadhesive, film forming agent, tablet binder, coating agent and disintegrant (Sai Rekha *et al.*, 2015).

Pectin

Pectin is nontoxic and economic polysaccharide extracted from apple pomaces and citrus peels. On the base of both extraction process and source pectin is a complex structure. Actually it's a-D-galacturonic acid polymer with 1-4 linkages. It is used as bulking agent, food additive and a gelling agent (Thirawong *et al.*, 2007) due to the pectin ability to form gel based on degree of esterification and molecular size, it's an alluring candidate for pharmaceutical care, e.g. as drug carrier for controlled released applications (Raj, 2012).

Carrageenan

Carrageenans, naturally occurring repeating units of galactose and 3, 6 anhydrogalactose high molecular weight anionic gel-forming polysaccharides extracted from red seaweeds species as *Euchema*, *Chondrus crispus*, *Iridaea*. And *Gigartina stellate*. Depending on degree of sulfation, are classified into different types: λ -carrageenan (three-sulfate), κ -(di-sulfate) and ι -(mono-sulfate). Highly sulphated λ -carrageenan is a thickener agent and does not form gel while κ - and ι -carrageenan forms gel, which influence their release kinetics. (Singh *et al.*, 2011) Carrageenans are mostly utilized because of their superb physical functional properties in food industries, such as bulking agent, thickening, stabilizing abilities and gelling. Because of the high robustness, good compatibility and persistent viscoelasticity of the tablet during granulation and compression, it proved to be useful as tablet excipient agents. Hence for sustained-release formulations carrageenans are suitable excipients (Campo *et al.*, 2009).

Gum Karaya

Gum Karaya is known as *Sterculia* gum obtained from *Sterculiaurens* Roxburgh and other species of *Sterculia* (Family – *Sterculiaceae*). After acid hydrolysis, Gum Karaya commonly produces D-galactose, D-galacturonic acid, L-rhamnose and small proportions of D-glucuronic acid. Sparingly soluble in water; poorly soluble in 0.1N HCl and simulated gastric fluid; slightly insoluble in ethanol (95%), other similar organic solvents, and alkali solutions at pH above approximately 6.5 (Sarathchandiran and Suresh, 2014). As the gum karaya swells in water, thus in different formulations it is used as release rate controlling polymer. It possessed higher erosion and very low hydration capacity. Under investigation, zero order drug release is observed along with erosion of matrices (Kuppast and Vasanthkumar Pai, 2014).

Okra Gum

Okra gum collected from the pods of *Hibiscus esculentus*, Yields high viscosity mucilage at low concentrations. Okra gum, one of the advantageous polysaccharides and hydrophilic polymer currently being studied in the pharmaceutical industry as a pharmaceutical dosage forms. Okra gum contains different coil polysaccharides consisting of rhamnose, galactose and galacturonic acid are

used as a tablet binding agent and to produce tablets with good friability, hardness and drug release profiles. Due to its chemically inert, safe, biodegradable, nonirritant, eco-friendly and biocompatible properties it has advantage over most commercial synthetic polymers because it is widely harvested and don't require toxicology studies. Okra gum is beneficial as a retarding polymer in the formulation of sustained release tablets as extraction in water give highly viscous solution with slimy appearance (Zaharuddin *et al.*, 2014).

Locust Bean Gum

Locust bean gum known as Carob bean gum is derived from the seeds of the leguminous plant *Ceratonia siliqua* Linn, consists basically of neutral galactomannan polymer made up of 1, 4-linked D-mannopyranosyl units with every fourth or fifth chain unit is substituted on C6 with a D-galactopyranosyl unit. There is variation in ratio of D-galactose to D-mannose based on varying origins of the gum source materials and growth effecting conditions of the plant during production (Beneke *et al.*, 2009). LBG is more effective to use as a gelling, stabilizer and thickening agent (Kivrak *et al.*, 2015) and shows a wide variety of application in preparation and development of various novel drug delivery systems (Dey *et al.*, 2012).

Psyllium Husk

Psyllium comes from the plant *Plantago psyllium*, the husk and seed of *Plantago ovata* is referred to as psyllium. Psyllium is classified as a mucilaginous fiber due to its powerful gel forming ability in water (Patil *et al.*, 2014). Psyllium husk is biocompatible, inert, swellable, biocompatible, inexpensive and easily available and environment friendly polymeric substance. The seed contains sterols, unsaturated fatty acids ranging 5-10% lipids, traces of cyclopentano pyridine-type alkaloids, proteins (15-18%), aucubi, trisaccharide, carbohydrates-planteose, and 10-12% mucilage of the heteroxylan type. Psyllium husk serve as reliable means for gastro retentive drug delivery system as it shows release retardant properties Researchers have also focused on prolonged retention of dosage form use in the GIT; stomach (Ishida and Kumar, 2013).

Tamarind Gum

Tamarind xyloglucan also called as Tamarind Kernel Powder (TKP) is collected from seed of the tamarind tree, *Tamarindus indica*, a member of the evergreen family. Tamarind gum; a polysaccharide composed of galactosyl: xylosyl: glucosyl in the ratio of 1:2:3. Higher plant primary cell walls has major structural polysaccharide called Xyloglucan and used as binder, gelling agent, stabilizer and thickener in pharmaceutical and food industries (Mali *et al.*, 2012). Tamarind gum used in formulating matrix tablets are evaluated for its drug release characteristics by wet granulation technique. Different concentrations of polymers are used in tablets preparation. Decrease in drug release is observed with increase in polymer content (Choudhary and Pawar, 2014).

Tara Gum

Tara gum is obtained from family Leguminosae or Fabaceae from the endosperm of seed of *Caesalpinia spinosa*. Tara gum is odorless and white powder. Like, guar and locust bean gums, major component is galactomannan polymers consist of a linear main chain of (1-4)- β -D-mannopyranose units with α -D-galactopyranose units attached by (1-6) linkages. The ratio of galactose to mannose is 1:3, produce highly viscous thick solutions, at 1% concentration

(Krishna *et al.*, 2011). Tara gum is used in formulation of gastro retentive controlled release tablets and emulsions for drugs in pharmaceutical industries like nifedipine, metformin hydrochloride, carvedilol, clozapine and ciprofloxacin hydrochloride nimodipine has been claimed in patents. Good gastro retentive property is observed using tara gum in combination increases floating time of the dosage form. Tara gum also used in formulation of emulsions (MH and Mathew, 2015).

IN-VIVO EVALUATION

Radiology

For internal body systems examinations X-rays are widely used. One most widely used Radio Opaque Marker is Barium Sulphate so widely used in Dosage forms and GR imaging is done by X-rays at intervals (Pandey *et al.*, 2012). Now a days X-Ray is used in floating dosage forms for assessment parameters. One can conclude and correlate the route of dosage form and gastric emptying time in the GIT. As the result for the solid dosage form radio opaque material visual is done by X-Rays (Neetika and Manish, 2012).

Gamma Scintigraphy

γ -camera or scinti scanner is used for the indirect observation of a formulation by the involvement of a γ emitting radio nucleotide. In γ -scintigraphy, the γ -rays emitted by the nucleotide are directed on a camera, which aids to focus and view to locate the location of the dosage form in the gastrointestinal tract (Chhetri and Thapa, 2014; Kumar *et al.*, 2011).

Gastroscopy

Peroral endoscopy is also known as gastroscopy used with video systems or fiber optics and used to observe visually the evaluation of GRDDS and effect of prolongation in stomach (Kumar *et al.*, 2012b).

Magnetic Marker Monitoring

In this method, iron powder is magnetically used as marker inside the dosage form and images are resulted by highly sensitive bio-magnetic measuring equipment. It is more beneficial as it has no radiations making it safer. Structures are elegantly checked by the help of iron powder and pictures are taken in accurate and delicate bio-attractive way (Waghmare Sneha *et al.*, 2015).

Ultrasonography

They are used occasionally as it does not show results in intestine. Imaging of some abdominal organs is obtained in the interface on the reflection of substantially different acoustic impedances. As fine acoustic results on interference with physiological milieu are not achieved by the DFs therefore it is not used on regular bases for conclusion of FDDS. The characterization included solvent penetration in the gel, interactions among gastric wall and FDDS during peristalsis and assessment of intra gastric location of the hydrogels (Neetika and Manish, 2012; Khan, 2013).

¹³C Octanoic Acid Breath Test

In GRDDS due to stomach chemical reactions octanoic acid releases CO₂ gas through the breath so ¹³C Octanoic Acid is incorporated in it. Major thing observed in this reaction is the formation of ¹³C isotope instead of the CO₂ gas. Dosage form gastric retention time is observed with the passage of time in release of ¹³CO₂ gas. This method is cheaper and as the dosage form reaches the intestine there no CO₂ gas is observed (Chauhan *et al.*, 2013).

DISCUSSION

The objective of this review is to provide the overview of role of natural polymers in floating drug delivery system, its characteristic effects, ongoing research and trend of future developments and applications in the field. The physical characteristics of natural polymers facilitate them to be brilliant drug carriers for such type of drug delivery systems.

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