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POLYMERS USED IN FLOATING DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

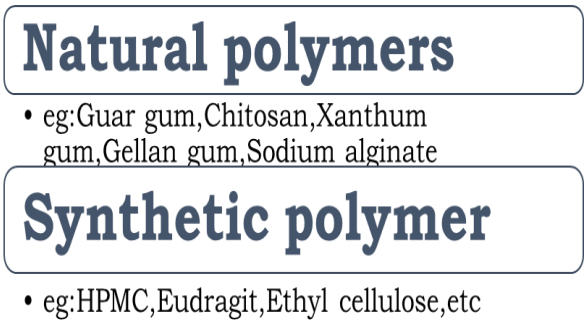
Oral drug delivery system is the most preferred route of administration for drug delivery. In the development of the drug delivery system many components play important role. Polymers are amongst those components which have evolved with the drug delivery system. Polymers are the macromolecule compound containing many monomer units joined to each other by bonds. Polymers used in the drug delivery system are of two types Natural and Synthetic based on their origin. Both types of the polymers have some advantages and disadvantages. This particular article gives information about the different types of natural and synthetic polymer used in the drug delivery system. This article also provide information about the different evolution stages of polymer in medical field. Natural polymers like guar gum, chitosan, Xanthan gum, Gellan gum and sodium alginate are mentioned in the article. Synthetic polymer mentioned are HPMC, Eudragit, and Ethylcellulose.

KEYWORDS: Polymers, HPMC, GRT, floating drug delivery system.

Oral drug delivery is the most preferred route of drug delivery due to ease of administration, patient compliance. Floating system are low density system that float over the gastric content and tending to keep afloat in the stomach without affecting gastric emptying rate for prolonged period of time. While the system floating on gastric content drug is released slowly from system at desired rate, after release of drug; system is emptied from the stomach. This results in increased in GRT and better control of fluctuation of plasma drug concentration.[1]

Polymer are used in floating system so as to target the drug delivery at specific region in the GI tract i.e. stomach. Both synthetic and natural polymers are used in the floating drug delivery. Natural polymer used in floating system are Guar gum, Chitosan, Xanthan gum, Gellan gum, Sodium alginate, etc. Synthetic polymer used for the floating drug delivery are HPMC, Eudragit, ethyl cellulose, etc. This articles gives information on different polymer used in floating drug delivery system.[2]

polymer have been used in medical field is not a novelty. They have been used in herbal medicines. First drug polymer conjugates appeared in 1955. e.g. Mescaline-N-vinyl pyrolidine conjugates. Ten years after than Frank Davis and Abraham Abuchowski develop a technique PEGylation. In 1994 first synthetic polymer-drug conjugates was tested. In 2000 Two polymer protein conjugates. e.g. PEG-interferon α and PEG-GCSF.[19]



EVOLUTION OF POLYMER IN MEDICAL APPLICATION[28]

Sr no.	Year	
1.	1930	PMMA in tooth fillings
2.	1940s	PMMA, PE, PA, PU, PVC in vascular devices
3.	1950s	PDMS, PMMA, PVC, PA in pumps, valves, shunts
4.	1960s	PE, PDMS, PTFE, PU in blood pumps, biodegradable suturs
5.	1970s	PU, PDMS, EG in drug delivery, artificial skin
6.	1980s	PDMS, FR-PS in contact lences
7.	1990s	PEG, PLA, PU and collagen in bone repair, blood pumps
8.	Recent development	PU, PC, ZINC polymer in smart watches, flexible batteries

Natural polymers

Natural gums (obtained from plants) are hydrophilic carbohydrate polymer of high molecular weight. They are generally insoluble in organic solvent like hydrocarbon, ether. Gums either water soluble or absorb water and swell up or disperse in cold water to give a viscous solution or jelly. List of natural gum given below:

List Of Natural Polymer Used In Floating Drug Delivery System[12]

Sr no.	Polymer	Source
1.	Guar gum	Endosperm of seed of *Cynopsis tetragonolobus*
2.	Chitosan	Shell of marine invertibrates
3.	Xanthan gum	Fermentation of glucose by *Xanthomonas compestris*
4.	Gellan gum	*Pseudomonas elodea*
5.	Sodium alginate	*Laminaria hyperboria*

Natural polymer has advantages over synthetic polymer. They are as follows:

1. Biodegradable.
2. Biocompatible and non-toxic.
3. Low cost.
4. Environment friendly.
5. Local availability.

Natural polymer has some disadvantages. They are as follows:

1. Microbial contamination.
2. Batch to batch variation.
3. Uncontrolled rate of hydration.
4. Reduced viscosity on storage.[12]

1. Guar gum

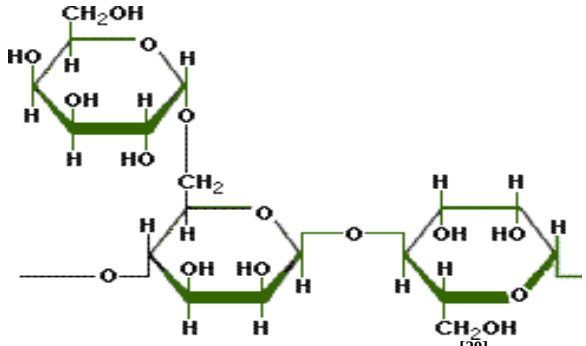
Guar gum is naturally occurring galactomannan polysaccharide. Guar gum hydrates and swells in cold water forming viscous colloidal dispersions or sols. This gelling property retard the drug release and make it a flexible carrier for extended release Dosage forms.[2] In pharmaceutical guar gum is used as disintegrants and as a polymer in floating drug delivery system.

- **Properties of guar gum**

1. It is soluble in water but insoluble in organic solvents. 2. Strong hydrogen bond property. 3. Excellent thickening, emulsion, film forming property. 4. Ability to control rheology.

- **Advantages of guar gum in floating drug delivery system**

It has been reported that polymer swelling play an important role in the pattern and amount of drug release. It was found that guar gum formulation were relatively insensitive to stirring speed during in vitro drug dissolution testing and dissolution profile were not affected significantly[1]



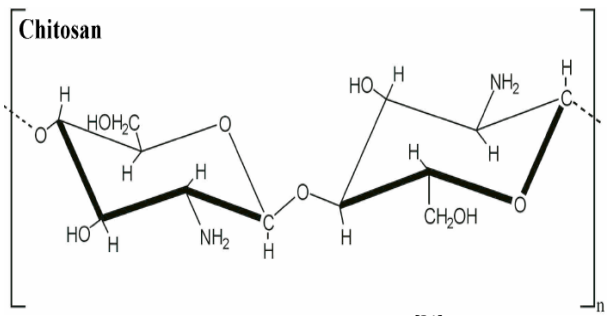
Guar Gum: Structure Diagram[20]

2. Chitosan

Chitosan is natural polymer obtainer by deacetylation of chitin. It has favorable biological properties such as non-toxic, biodegrable, biocompatible. It is a bioadhesive polymer and have anti-bacterial properties thus make it suitable for site specific delivery. Chitosan is high molecular weight polycationic weak base with pka value of 6.2-7. On addition to acidic pH of 1.2 or neutral media it become buoyant in nature and provide control release.[2] By increasing thickness of chitosan film release rate can be decreased.[1]

- **Advantages of chitosan**

1. It forms film that reduces effect of gastrointestinal transit time. 2. Hallow microcapsule tend to float on gastric fluid for about 12hrs. 3. Release rate of drug followed zero order kinetics.[1]



Structure of Chitosan[21]

3. Xanthan gum

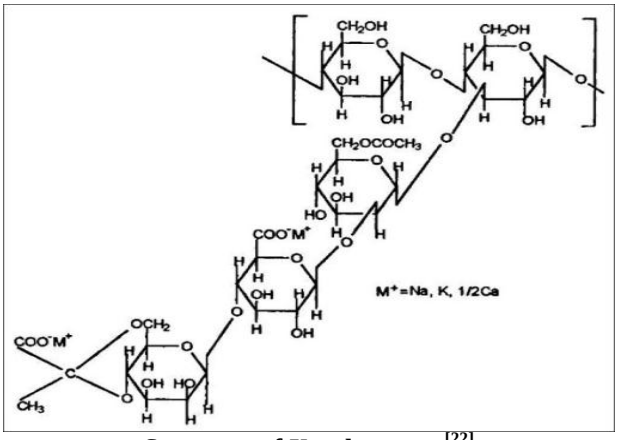
Xanthan gum is a high molecular weight extracellular polysaccharide produced by pure culture aerobic fermentation of carbohydrate. Xanthan is a longchained

polysaccharide with large number of trisaccharide side chains. Gum also has an excellent solubility and stability under acidic and alkaline conditions and in the presence of salts and resists common enzymes.

- **Advantages of Xanthan gum**

1. It is used to increase or decrease rate of release of drug from formulation. 2. Soluble in water. 3. High viscosity at low concentration. 4. It has potential advantage of drug release at zero order kinetics.

Some tablet containing Xanthan gum and citric acid show buoyancy for more than 24hrs.



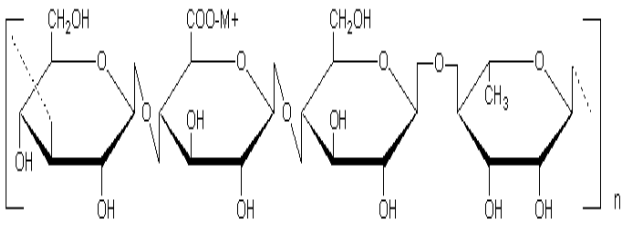
Structure of Xanthan gum[22]

4. Gellan gum

Gellan gum is an anionic, high molecular weight, deacetylated extracellular, linear polysaccharide. This gum has an outstanding flavor release, high gel strength, an excellent stability, process flexibility, high clarity, good film former and thermally reversible gel characteristics.[2] Gellan gum is produced as a fermentation product from *spingomonas elodea*.

- **Advantages of Gellan gum**

1. It has excellent flavor release, high gel strength, and excellent stability. 2. It forms gel when positively charged ions are added. 3. It is used in food product as thickening agent or stabilizing agent.[1]



Structure of Gellan gum[23]

5. Sodium alginate

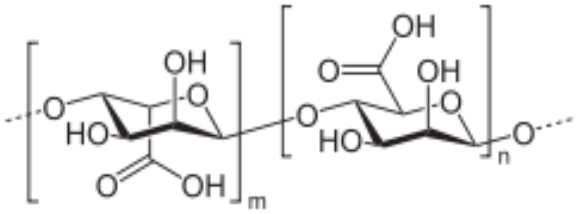
Sodium alginate consists chiefly of the sodium salt of alginic acid, which is a mixture of polyuronic acids composed of residues of D maunnuric acid and L-guluronic acid. The block structure and molecular weight of sodium alginate Samples have been investigated.

- **Typical Properties**

Acidity/alkalinity pH _ 7.2 (1% w/v aqueous solution).

Solubility: Practically insoluble in ethanol (95%), ether, chloroform, and ethanol/water mixtures in which the ethanol content is greater than 30%. Also, practically insoluble in other organic Solvents and aqueous acidic solutions in which the pH is less than 3. Slowly soluble in water, forming a viscous colloidal Solution.

Viscosity (dynamic): Various grades of sodium alginate are commercially available that yield aqueous solutions of varying Viscosity. Typically, a 1% w/v aqueous solution, at 208C, will have a viscosity of 20–400mpa s (20–400cp). Viscosity may vary depending upon concentration, ph, temperature, or the Presence of metal ions. Above pH 10, viscosity decreases.[4]



Structure of sodium alginate [24]

Synthetic polymers

Synthetic polymer are becoming increasingly important in pharmaceuticals. Use of synthetic polymer ranges from binder, film coating agent, etc. Polymer are macromolecule having very large, contain a variety of functional group. Synthetic polymers are either purely synthetic or they are modified form of natural polymer know as semi-synthetic.

List of synthetic polymer used is as follows:
1. Hydroxy propyl methyl cellulose.
2. Eudragit.
3. Ethyl cellulose.

Disadvantagesof synthetic polymer are as follows:
1. High cost toxicity environmental pollution.
2. Acute and chronic adverse effect.
3. Poor biocompatible.
4. Inflammatory response and local reaction.[12]

1. Hydroxy propyl methyl cellulose

Hydroxypropyl methylcellulose ethers belong to an extensive family of white to off-white, odorless, water soluble polymers that bind, retain water, thicken, form films, lubricate. It is a semi synthetic, inert, viscoelastic polymer, used as an excipient and controlled-delivery component in oral medicaments, found in a variety of commercial products. Synonym for hydroxypropyl methylcellulose (HPMC) is Hypromellose.

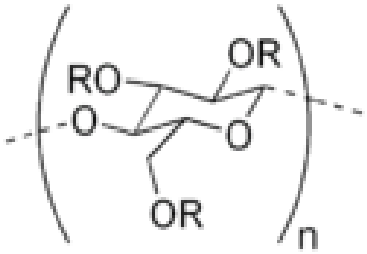
Properties

General properties common to the Hypremellose are listed below. Individual type exhibits these properties to varying degrees and may have additional properties that are desirable for specific applications.

1) Apparent density: 0.25~0.70g/cm 3.
2) The refractive index=1.336.
3) Surface tension: 42 to 56mn/m.
4) Solubility**:** dissolve in water and some solvent.

Advantages

1. Water soluble and most abundant polymer in nature. 2. Used as a thickener, film former and water retension agent. 3. Hydrophilic matrix is the simplest sustained release technology for oral dosage form.[6]



$R = H \text{ or } CH_3 \text{ or } CH_2CH(OH)CH_3$

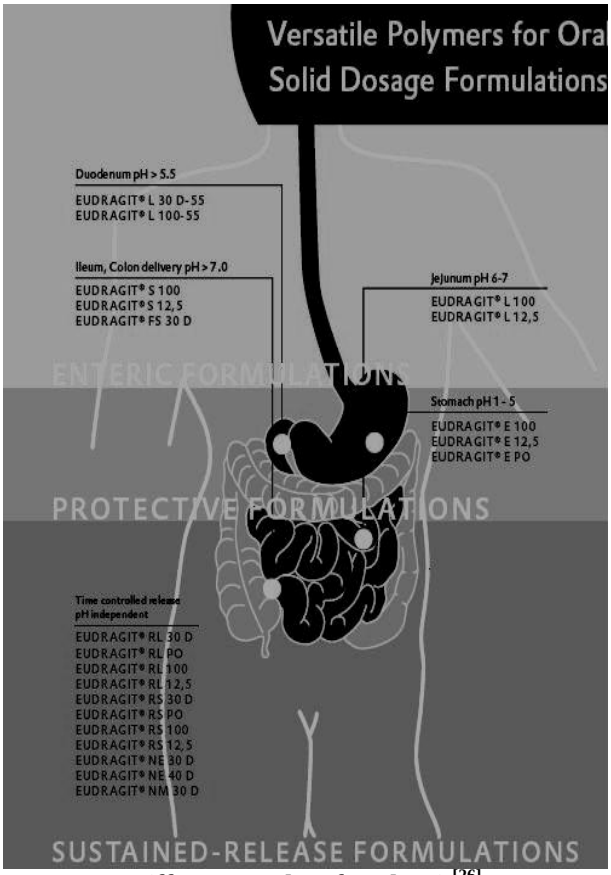
Structure of HPMC[25]

1. Eudragit

Polymethacrylates (Eudragit) are primarily used in oral capsule and tablet formulation s as film-coating agents. Depending on the type of polymer used, films of different solubility characteristics can be produced. Soluble in gastric fluid below pH 5. In contrast, Eudragit L, S and FS types are used as enteric coating agents because they are resistant to gastric fluid. Different types of enteric coatings are soluble at different pH values: e.g. Eudragit L is soluble at pH >6 whereas Eudragit S and FS are soluble at pH >7. The S grade is generally used for coating tablets, while the flexible FS 30 D dispersion is preferred for coating particles.

Eudragit RL, RS, NE 30D, NE 40D, and NM30D are used to form water-insoluble film coats for sustained-release products. Eudragit RL films are more permeable than those of Eudragit RS, and films of varying permeability can be obtained by mixing the two types together. Polymethacrylates are also used as binders in both aqueous and organic wet-granulation processes. Larger quantities (5–20%) of dry polymer are used to control the release of an active substance from a tablet matrix. Solid polymers may be used in direct compression processes in quantities of 10–50%. Polymethacrylates polymers may additionally be used to form the matrix layers of transdermal delivery systems and have also been used to prepare novel gel formulations for rectal administration.[4]

The optimized formulation exhibited improved drug Permeation through the rat skin and improved antifungal efficacy as evidenced from higher zone of inhibition. Dominguez et al, prepared triclosan nanoparticles suspension by the Emulsification-diffusion by solvent displacement method, using Eudragit® E 100 as polymer. Triclosan was molecularly dispersed in the nanoparticle batches containing triclosan. Nanoparticles exhibited higher permeation compared to solutions and creams. Patil et al explored the application of Eudragit E 100 as taste masking agent in orally disintegrating tablet of tramadol hydrochloride. The results demonstrated successful masking of bitter taste[18]



Different grades of Eudragit[26]

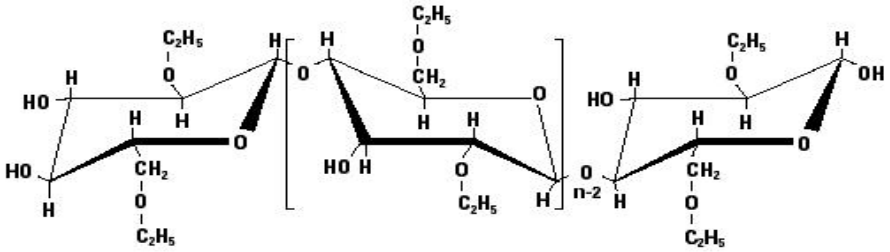
2. Ethyl cellulose

Ethocel (Ethylcellulose polymers) has been widely used in the pharmaceutical industry for over 50 years. Ethylcellulose has been used for choice in pharmaceutical formulations for various purposes, such as taste-masking of bitter actives, moisture protection, stabilizer, extended release multiparticulate coating, micro-encapsulation of actives, extended release binder in inert matrix systems, solvent and extrusion granulation. The application of EC in wet extrusion processes is limited, since the polymer has considerable elastic properties, but can be successfully used as matrix former in combination with some plasticizing agents. Mallipeddi et al. used the potential of coarse Ethylcellulose (CPEC) and fine particle Ethylcellulose (FPEC) as diluent with high molecular weight

polyethylene oxide (PEO), which was used as an extrusion aid and a binder. Their results have shown that water is sufficient to prepare a wet granulation product when using FPEC. MCC was included in their formulations to contribute its plasticity to the wetted mass during extrusion and to the extrudate during spheronization. Ethylcellulose is a water insoluble cellulose ether, which is prepared from cellulose, it is a partly O-ethylated cellulose, its ethoxy content (-OC2H5) is between 44-51 %. Ethylcellulose is an ideal polymer for the formation of products allowing modified drugrelease. It is insoluble at any pH that occurs in organism, but in the presence of the gastric Juice it undergoes swelling. It is then permeable for water and permits extended modified drug release. This makes it suitable for improved patient compliance. A small number of Ethylcellulose polymers have been approved for general pharmaceutical application and are used in extended release solid dosage formulations. Several types of such Ethylcellulose exist, e.g. Ethocel 4, Ethocel 10 and Ethocel 45, which differ in the length of the polymer chains,

The rate of dissolution, and the viscosity of their solution. Ethylcellulose is suitable to prepare MR coatings.[7]

Chemical structure of ethylcellulose



Structure of ethyl cellulose[27]

CONCLUSION

From the year 1930 polymer are being used in the field of medical application. In 1955 Frank Davis and Abraham Abuchowaski develop the concept of PEGylation and from then many development has been taken place in the field of polymer. Polymers are used for the purpose of the controlled release of drug from dosage form. Polymer are the substances which are being used in the formulations for many reasons like gelling agents, emulsifying agents, viscosity increasing agents etc. Therefore knowledge of the polymer in field of the drug delivery plays an important role.

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