

# [Biopolymers in drug delivery biology essay](https://assignbuster.com/biopolymers-in-drug-delivery-biology-essay/)

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## INTRODUCTION

Polysaccharides are the most important organic compounds obtained from the plant sources. They are long complex carbohydrate molecules containing monosaccharide units joined together by glycosidic bonds into linear or branched chains, and are classified on the basis of their main building units, i. e. monosaccharide units, type of linkages involved and its anomeric configuration. The main function of polysaccharide is either structure or storage related and plays a crucial role in living organisms. They can be divided into several groups according to their functions i. e. structural polysaccharide (cellulose), protective polysaccharides (pectin, chitin, hemicelluloses) and storage polysaccharide (starch, glycogen). Polysaccharides can also form glycoconjugates with proteins and lipids. Among all polysaccharides, starch is considered as one of the most widely used polysaccharide for industrial purposes such as in the food industry, in pharmaceutical, medicinal, paper and pulp industries, printing and textile industries, etc. due to its low cost, ease in availability, biodegradability, biocompatibility and simple chemical modification.

## Biopolymers in Drug Delivery

Biopolymers may be defined as the naturally occurring polymers synthesized in the living organisms either internally in an organism’s structure or externally in an appropriate conditions: Most of the polymers formed in nature during the life cycles of green plants, animals, bacteria and fungi. Biopolymers include the polysaccharides such as cellulose, starch, the carbohydrate polymers produced by bacteria and fungi and animal protein based biopolymers such as wool, silk, gelatin and collagen etc. The development of biodegradable polymers as drug carriers for an effective drug, protein and DNA delivery has been increasing during the last decade. They are being used to encapsulate proteins and peptides. Apart from the synthetic biodegradable polymers developed for biomedical applications, the use of natural biodegradable polymers remains attractive because of their easy availability, enhanced biocompatibility, biodegradability, simple chemical modification, flexibility in obtaining a desirable drug release profile, cost effectiveness, broad range of physicochemical properties and regulatory acceptance. Natural polysaccharide based biodegradable matrices are of great interest because the degradation of natural products like starch occurs naturally in the human body. Some of the biopolymers used in drug development and delivery are listed below:

## Starch:

Starch is the most abundant polysaccharide produce by all the green plants and acts as a reserve food material for growth, dormancy and germination. It is a heterogeneous mixture of linear amylose (containing α-1→4 glycosidic linkage) and branched amylopectin (containing α-1→6 glycosidic linkages), which are synthesized by plant enzymes and simultaneously packed into dense water-insoluble granules. Starch granules vary in size and shape, which are characteristic of their specific plant origin. Starch granules when dissolve in hot water then they absorb water and swell in size, causing the mixture to thicken. With continued heating the mixture becomes less thick, and the amylose and amylopectin become soluble in the hot mixture. This process of swelling and fragmenting of granules is known as gelatinization. Once gelatinized the granules cannot be recreated and the starch merely behaves as a mixture of amylose and amylopectin. Because of the larger size of the swollen granules compared to the size of amylose and amylopectin, the viscosity of the swollen granule mixture is much higher than the viscosity (the resistance to flow or a liquid or semi-liquid mixture) of the amylose/amylopectin mixture. Starch is used as an additive for food processing and as thickeners and stabilizers in food such as puddings, custard, sauces, soups, noodles, etc. In the pharmaceutical industry, starch is also used as an excipient, as tablet disintegrant or as binder. The estimated world production of starch amounts to 58 million tonnes, extracted from maize (46 million), wheat (4. 6 million), potatoes (3. 5 million), and the rest comes from rice and cassava roots. The main commercial refined starches found are corn starch, tapioca, wheat and potato starch. It is an established and widely used biodegradable polymer because of its low cost, availability, and production from renewable resources. However, it has some limitations like low moisture resistance, poor processability (high viscosity), and incompatibility with some hydrophobic polymers. G: Potato\_Starch. jpgPotato starch

## Guar Gum:

Guar gum, also called as guaran is extracted from the seeds of the leguminous shrub Cyamopsis tetragonoloba. Seeds usually comprise 9-10% moisture, 22-23% crude protein, 11-13% pentosan and 35-42% endosperm gum. The seeds are light to dark brown in colour, medium sized and dicotyledenous. Chemically, guar gum is a galactomannan type of polysaccharide having very high molecular weight. The macromolecular structure of guar lies between a spherocolloid (like amylopectin) and a linear hydrocolloid (e. g. cellulose). Structurally, it is a polysaccharide composed of the sugar units-galactose and mannose having main chain of (β 1→4) glycosidic-linked mannose units, on which branches of single galactose units are attached through (1→6) linkage. Guaran is a creamish amorphous powder, dispersible in cold or hot water to form a nearly clear colloidal solution. It produces very high viscosity even at low concentration (3500-6000 cPs in 1% solution). It is non-ionic and maintains a high viscosity over a broad range of pH(3-9) and is compatible with a variety of inorganic and organic substances, including certain dyes and various constituents of food. It bears excellent thickening, suspending, emulsifying, stabilizing and film forming properties. At very low concentrations, it has excellent settling (flocculation) property, and acts as a filter aid. It has strong hydrogen bonding properties due to the cis-pair of --OH groups in main mannan chains. Galactose to mannose ratio of guaran is found to be about 1: 2. Guar gum has almost eight times more water thickening potency than corn starch. G: Guar-Gum-Powder. jpgG: guar-gum-seed. jpgGuar gum seedGuar gum powderGuar gum is one of the prominent vegetable hydrocolloids used extensively in different industries like paper, textile, pharmaceutical, mining, petroleum well-drilling, food etc. in various forms. A brief description of its applications is as follows:

## Industry

## Uses

TechnicalPrinting, paper, mining, tobacco, explosion, water treatment, fire fighting, fracturing aid etc. Food, Human & AnimalsFrozen foods, bakery, dairy products, canned foods, dressings, instant mixes, beverages, animal feedings, etc. Pharmaceutical & CosmeticsLaxative, binder, disintegrant, slimming aids, diabetic treatment, tablet preparation, etc. India produces 10. 0 - 12. 5 lakh tonnes (1 - 1. 25 million tonnes) of guar annually, making it the largest producer of guar accounting approximatly 80% of world production. In India, Rajasthan, Gujarat and Haryana are the main producing regions, and Jodhpur, Sri GangaNagar and Hanumangarh in Rajasthan are the major Guar trading markets. The world production for guar gum and its derivatives is about 7. 0 lakh tons (700, 000 tonnes).

## Pectin:

Pectin, a structural heteropolysaccharide, found in the cell wall of plants is a biopolymer of D-Galactouronic acid residing in an α(1→4 ) chain. It is also present in the junctional zone between the cells of the secondary cell wall. It allows primary cell wall extension and plant growth. During fruit ripening, it is broken down by the enzymes, pectinase and pectinesterase. It is a soluble dietary fiber which binds to cholesterol in the gastrointestinal tract and slows absorption of glucose by trapping carbohydrates. Fruits like guava, apple, oranges, gooseberries, etc. contain large amount of pectin whereas fruits like grapes, strawberries, cherries, etc. contains small amount of pectin. Pectin is used as an excipient, as gelling agent, as thickening agent and as a stabilizer in food , for eg., to stabilize acidic protein drinks, as a food additive, etc. People use pectin to control the levels of cholesterol, triglycerides and to prevent colon and prostate cancer. G: Pectin-Powder. jpgPectin

## Chitin:

Chitin is a naturally occuring polysaccharide found in the outer skeleton of insects, crabs, shrimps and lobsters as well as in yeast and fungi. It resembles cellulose in structure but it has an acetamido group instead of hydroxyl group at the C-2 position of the backbone polymer chain. It is composed of 2-acetamido-2-deoxy β-D-glucose attached with β((1→4 ) linkages and is degraded by chitinase. It is biocompatible, biodegradable, non-toxic and have good adsorption properties, which make them suitable for various drug delivery applications. It is used as an additive to thicken and stabilize food and as a binder in dyes, adhesives, etc. C: UsersshrotriyaDesktopavdeep1 march ecent picsChitin. jpgChitin

## Alginate:

Alginate or alginic acid is a linear, unbranched polysaccharide found in brown sea weed and marine algae and is composed of linear block copolymers of 1→4 linked β-D-mannuronic acid and α-L-gluronic acid. Alginates have high molecular weight of 20 to 600 kDa and can be used as stabilizers in emulsions, suspending agents, tablet binders and tablet disintegrants. G: sodium alginate. jpgAlginate

## Cellulose:

Cellulose is the principal constituent of the plant cell wall and constitutes the most abundant, renewable polymer resource available today. It is a linear homopolymer consisting of D-glucose units linked by β(1→4)-glycosidic bonds. It is insoluble in water because of extensive intra and inter-molecular hydrogen bonding, and is a highly crystalline polymer. Large scale commercial cellulose ethers include carboxymethyl cellulose (CMC), methyl cellulose (MC), hydroxyethyl cellulose (HEC), hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), ethyl hydroxyethyl cellulose (EHEC), and methyl hydroxyethyl cellulose (MHEC). Cellulose is a straight chain polymer: unlike starch, no coiling or branching occurs, and the molecule adopts an extended and rather stiff rod-like conformation, aided by the equatorial conformation of the glucose residues. Starch undergoes a crystalline to amorphous transition when heated beyond 60–70 °C in water (as in cooking), whereas cellulose requires a temperature of 320 °C and pressure of 25 MPa to become amorphous in water. C: UsersshrotriyaDesktopavdeep1 march ecent picsHpmc. jpgHydroxy propyl methylcellulose

## BIODEGRADABLE CAPSULES - AN OVERVIEW

The whole world is turning towards natural sources and slowly yet steadily synthetic is taking a backseat. Medicine or health care systems require carriers through which they can provide medication to different diseases. Capsules are the solid dosage forms enclosing a dose of medication within the shell (encapsulation). The medication may be a powder, a liquid or a semisolid mass. Various synthetic, ayurvedic capsules are available in the market having specific role in drug delivery. Synthetic capsules cause one of the biggest threats to the environment today. So to subdue this threat, the most promising solution is the discovery of biodegradable capsules which plays an important role having improved efficacy and safety over injectables. Biodegradable capsules are those which can be degraded from the action of naturally occurring micro-organisms such as bacteria, fungi and algae. In the 21st century, various biodegradable capsules are available which are either gelatin based or contains HPMC with high tensile strength. HPMC capsules ensures full compatibility compared to gelatin. Cellulose containing biodegradable capsules are also available comprising of methylcellulose solution. Biodegradable capsules have certain advantages over synthetic capsules. Firstly, they are made from renewable raw materials- so called " bio-capsules" or " organic capsules" and thus do not face the problem of exhaustion. Secondly, they are biodegradable, which implies that they are degraded by microbes and ultimately turn into compost after a certain period. Our research work is focussed on the preparation of natural polysaccharides based novel biodegradable capsules which might be a better alternative for synthetic and gelatin based capsules. Since the gelatin is still the material choice for the production of capsules due to excellent film forming properties and rapid dissolution in gastric fluid but the pharmaceutical companies, however, have been forced to develop gelatin-free capsules due to numerous reasons including a rise in vegetarianism i. e., religious and cultural objections and instability with drugs that are hygroscopic or contains reactive aldehyde groups. The major drawback associated with gelatin is that it is a protein derived from collagenous connective tissue of animal skin and bone. Gelatin may be obtained from bovine and swine animals although fish and birds have also been indicated in the literature as alternative. Large groups around the world choose not to ingest any animal based product of pigs (e. g., vegetarians, Hebrews, and Muslims) or the products of beef (e. g., vegetarians and Hindus). As medication and/or diet supplements are provided in gelatin capsules without any indication of the source of the gelatin, the use of capsules is restricted in many areas. In the gelatin based capsules there is a risk of encountering Bovine Spongiform Encephalopathy " BSE" or " Mad Cow Disease", which affects the central nervous system of bovine and is commonly believed to be a potential danger to humans. So the use of uncontrolled animal by-products has lost some level of commercial acceptance. In short, there is a need for the replacement of gelatin based capsules with those that are not derived from animal sources. Biodegradable capsules are those medicated dosage forms which contains a multi-molecular matrix type network forming tiny holes in their walls, making them permeable to nutrient exchange and allowing molecules produced by the encapsulated cells to escape from the capsule and enter the bloodstream or surrounding tissues. For instance, capsules containing insulin-producing cells(beta cells) from the pancreas, implanted in patients with type I diabetes, would produce insulin that could travel out of the capsules into the bloodstream of the patient to all the body organ that require insulin. Another important feature of biodegradable capsules is that they protect cells from being attacked by the recipient’s immune system by hiding them within capsules so immune cells and antibodies cannot enter the capsules to destroy these cells. Although not a permanent cure, biodegradable capsules can provide lasting release of molecules into the body. This approach would likely require that biodegradable capsules be changed every few months; so in case of diabetes, this might be a better alternative than daily injections of insulin. Biodegradable capsules can be synthesized and characterized for control release of drugs. Various techniques were adopted to synthesize biodegradable capsules like phase separation technique, ionotrophic gelation technique, layer-by-layer deposition method, by complex coacervation, etc. For e. g., Alginate biodegradable capsules coated with mucoadhesive polymer chitosan were prepared by ionotropic gelation technique utilizing calcium chloride as a cross linking agent, to take the advantage of swelling and mucoadhesive property of alginate beads for improving the oral delivery of gliclazide, a drug used in diabetes mellitus. In this formulation, depending upon the variability in the concentration of alginate, percentage of cross linking agent, time of curing, the factors like particle size, incorporation efficiency and release rate of biodegradable capsules varies. In medical areas, biodegradable and biocompatible capsules have been designed for controlled release of drug molecules, targeted drug delivery, reduced side effects, and improved therapeutic effects. Drugs encapsulated in biodegradable capsules can release either by diffusion through the polymer barrier, by erosion of the polymer material, or by a combination of both mechanisms. Our research work relates to the method for the preparation of gelatin free biodegradable capsules having equal tensile strength than that of gelatin capsules. This invention includes a composition of polysaccharides comprising guar gum, pectin, chitin, glucose and polyethylene glycol as an additives, glycerol and sorbitol as plasticizer, potato starch, etc. These polysaccharides are pseudoplastic or exhibit " shear thinning" behaviour in solution and exhibit excellent synergy. Their thickness can be varied and due to their multimolecular forming nature the release of the drug inside the capsule can be controlled accordingly. These capsules are free of cracking, completely natural, low in moisture content and resist brittleness. The method for preparing these capsule comprises the steps in which biphasic blend of two phase is used. The first phase comprises polysaccharide and the second phase consists of galactomannan which acts a filler for the first phase blended together at 65° C with water as solvent. After this, the moulding pins are dipped into the blend and put into an oven maintained at 65° C. The hot air blown helps to blow the water away from the outer surface of the dipped pins. The remaining water can be blocked with the numerous hydroxyl group present in the polysaccharide. As the water is bonded and locked due to the generation of hydrogen bonding from the water molecule and OH groups present in the polysaccharide, these capsules show antimicrobial activity. The natural colouring agents can also be added to the biphasic mixture of these capsules. Glycerol is often used as plasticizer because of its hydrophilic properties, making it miscible with water. It reduces the interaction between protein molecules and increases the flexibility and extensibility of the final product. It also reduces the intermolecular forces and increasing the mobility of the biopolymer chains. Besides, glycerol also reduces the extent of edge-edge interactions (i. e. H-bonding interactions), hence making it possible to achieve a better dispersion. Plasticizer increases the plasticity or fluidity of the material. Polyethylene glycol, glucose, etc. are often used as an additives. PEG is used to induce complete fusion and binds water. Glucose is used as a sweetening agent. Sorbitol ( or glucitol), a sugar alcohol obtained by reduction of glucose, is used as plasticizer and its direct plasticizing capability is very much reduced in comparison with glycerol. It helps in increasing the cross-linking between the polysaccharide molecules. The prepared natural polysaccharide based gelatin-free biodegradable capsules were then subjected to several quality control parameters.

## Disintegration test:

Disintegration refers to the process of breaking large molecule into its constituent fragments. This test determines whether dosage forms such as tablets, capsules, boluses pessaries and suppositories disintegrate within a prescribed time when placed in a liquid medium under prescribed experimental conditions or not. Disintegration is defined as that state in which no unit residue under test remains on the screen of the test apparatus or, if a residue remains, it consists of fragments of disintegrated parts of tablets components or of capsule shells. If disc have been used with capsules, any residue remaining on the lower surfaces of the discs consists only of fragments of shells. Disintegration apparatusThe apparatus consists of a circular basket-rack assembly, a 1-litre beaker, a thermostatic arrangement for heating the fluid and a mechanical device for raising and lowering the basket-rack in the immersion fluid at a constant frequency rate of 28-32 cycles/min through a distance of 50-60 mm. The basket-rack assembly is rigid and consists of six open-ended cylindrical glass tubes, 77. 5 ± 2. 5 mm long, 21. 5 mm in internal diameter and with a wall thickness of about 2 mm. The tubes are held vertically by two superimposed transparent plastic plates, circular in shape and each about 90 ± 2 mm in diameter and 6. 75 ± 1. 75 mm thick, perforated by six holes having same diameter as the tubes. The holes are equidistant from the centre of the plate and are equally spaced one from another. A piece of woven gauze, made of stainless steel wire about 0. 635 mm in diameter, with a mesh aperture of 2. 0 mm is attached to the underside of the lower plate. The upper plastic plate is covered with a stainless steel disc perforated by six holes, each about 24 ± 2 mm in diameter, which fits over the tubes and holds them between the plastic plates. The holes coincide with those of the upper plastic plate and the upper ends of the glass tubes. The plates are held rigidly in position and 77. 5 mm apart by vertical metal rods at the periphery and a metal rod is also fixed to the centre of the upper plate. This enables the assembly to be attached to a suitable mechanical device so that it may be lowered and raised. A cylindrical disc 20. 7 ± 0. 15 mm in diameter and 9. 5 ± 0. 15 mm thick, made of transparent plastic with a relative density of 1. 18 to 1. 20 and pierced with five holes, each 2 mm in diameter, one in the centre and the other four spaced equally on a circle of radius 6 mm from the centre of the disc. Four equally spaced grooves are cut on the lateral surface of the disc in such a way that at the upper surface of the disc they are 9. 5 mm wide and 2. 55 mm deep and, at the lower surface, 1. 6 mm square.

## UV-Visible spectrophotometry:

UV-Visible spectrophotometry is one of the most frequently employed technique in pharmaceutical analysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance in solution. Instrument which measure the ratio of the intensity of two beams of light in the UV-Visible region are called Ultraviolet-Visible spectrophotometers. In qualitative analysis, organic compounds can be identified by use of spectrophotometer, if any recorded data is available, and quantitative spectrophotometric analysis is used to ascertain the quantity of molecular species absorbing the radiation. Spectrophotometric technique is simple, rapid, moderately specific and applicable to small quantities of compounds. The fundamental law that governs the quantitative spectrophotometric analysis is the Beer -Lambert law. Absorption measurement could be used to determine the concentration of the substance, assay of certain chemical reactions and identification of structural component in a biomolecule. Quantification of medicinal substance using spectrophotometer may carried out by preparing solution in transparent solvent and measuring it’s absorbance at suitable wavelength. The wavelength normally selected is wavelength of maximum absorption (λmax). UV-Vis spectrophotmetry is routinely carried out for the quantitative determination of different analytes, such as transition metal ions, highly conjugated organic compounds, and biological macromolecules. Organic compounds, especially those with a high degree of conjugation (e. g. DNA, RNA, protein), also absorb light in the UV or visible regions of the electromagnetic spectrum.

## Fourier transform infrared spectroscopy (FTIR):

FTIR spectrophotometry is a technique used to obtain an infrared spectrum of absorption, emission, photoconductivity or Raman scattering of a solid, liquid or gas. It is the preferred method for infrared detection of chromatographically separated species. It is based on the principle of absorption just like UV-Vis but the difference is that it involves infrared transitions between vibrational level of the ground state of the molecule, resulting in absorption of light in the infrared region whereas UV-Vis absorption produces transition in electronic energy level. It is also a wonderful tool for detecting functional groups but cannot necessarily be used to elucidate the complete structure of an unknown molecule. It is unlikely that any two compound give same infrared spectrum. Infrared radiation of frequencies lesser than about 100 cm-1(wavelength longer than 100µm) is absorbed and converted by an organic molecule into energy of molecular rotation. This absorption is quantized: thus a molecular rotation spectrum consists of discrete lines. The two important areas for a preliminary examination of an infrared spectrum are the region 4000 – 1300 cm-1 and the 909 – 650 cm-1. The high frequency portion of the spectrum is called the functional group region. The characteristic stretching frequencies for important functional groups such as OH, NH and C= O occur in this portion of the spectrum. The intermediate region of the spectrum , 1300 – 909 cm-1 , is usually referred to as the " fingerprint" region. This fingerprint region is studied in great detail with a compound just like a fingerprint to confirm identity. The lack of strong absorption bands in the 909 – 650 cm-1 region generally indicates a non-aromatic structure. Besides identification of the functional groups, IR spectroscopy is best used to ascertain the presence of hydrogen bonding in a molecule. It has also been used to distinguish between geometrical isomers, to identify enantiomers in solid state and as a valuable tool for conformational analysis.

## Viscosity:

The most common way of characterizing a liquid or fluid material is by measurement of its viscosity, which is actually a measure of fluid friction. The force of friction can be considered as the energy rerequired to move an object that rubs on another, i. e., viscosity is the measure of the internal friction resisting the movement of each layer of fluid as it moves apart an adjacent layer of fluid. A highly viscous material is one possessing great deal of internal friction, it will not pour or spread as easily as a material of lesser viscosity. Viscosity of the solution can be determind by passing the solution through a capillary using a capillary viscometer. The degree of viscosity depends upon the characteristics of galactomannans particularly their man/gal ratio and branching pattern of a particular galactomannan. The viscosity of a polysaccharide depends upon the following factors which include size of the particles, concentration of the solution, temperature of the solution, shear rate, time factors, etc. Viscosity behaviour of a gum is one of the important aspect which determines its industrial utility. The utility of a particular gum mainly depends upon its viscosity behaviour. The guar gum is dispersible in water at room temperature and vigorous stirring is required to prepare homogeneous solutionThe desired concentration solution was prepared by stirring it to get homogeneous solution. Then viscosity study was carried out using viscometer at appropriate rpm using suitable spindles.

## Biodegradability test:

Biodegradability test, an important parameter for the evaluation of the ecological behaviour of substances, is used to determine the rate of the biodegradation process under in-vitro or natural environmental conditions. Under in-vitro conditions, defined media are used and inoculated with either a mixed microbial population or individual microbial strains which have been especially screened for a particular polymer, which may be optimized for the activity of the particular micro-organisms used, polymers often exhibit much higher degradation rate than under natural environmental conditions. Under natural environmental conditions, the samples are to be buried in the soil. There is several disadvantages associated with this type of biodegradation test. One is that environmental conditions such as temperature, pH, humidity, etc. cannot be controlled well and the analytical opportunities are limited to monitor the degradation process.

## Effect of temperature and time:

Temperature causes greater influence on an organoleptic properties of the biodegradable capsules. Variations in the temperature with increase in time period may cause changes in the colour, texture, weight, microbial growth, etc. It effects physical and biological stability of the biodegradable capsules.

## Encapsulation efficiency:

Encapsulation efficiency refers to the ratio of the estimated concentration of the entrapped substance to its theoretical initial concentration. The higher the molecular weight of the encapsulant, the higher is the encapsulation efficiency and vice versa. Encapsulation Efficiency was calculated using an equation: Encapsulation Efficiency(% EE)= ( Initial drug added – free drug / initial drug added) \* 100It can also be expressed as absolute encapsulation efficiency, which is the ratio of the moles of bound drug to the moles of initial drug added.

## Dissolution test:

Dissolution test (intended for capsule or tablet) is used to determine compliance with the dissolution requirements for solid dosage forms administered orally. Dissolution test is an in vitro test which measures the amount of time required for a given percentage of drug substance in a capsule to go into solution under specified conditions. Dissolution is a standardised method for measuring the rate of drug release from a dosage form. The principle function of the dissolution test may be summarised as follows: Optimisation of therapeutic effectiveness during product development and stability assessment. Routine assessment of production quality to ensure uniformity between production lots. Assessment of ‘ bioequivalence’, that is to say, production of the same biological availability from discrete batches of products from one or different manufacturers. Prediction of in-vivo availability, i. e. bioavailability (where applicable).