REVIEW ARTICLE

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CONFLICT OF INTEREST NONE DECLARED

Starch: A Mucoadhesive Polymer in Novel Drug Delivery System.

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Abstract
Mucoadhesive drug delivery system is a popular novel drug delivery system because mucus membranes are relatively permeable allowing for the rapid uptake of a drug into the systemic circulation and avoiding such a major problem of first pass metabolism.
Mucoadhesive drug delivery systems are gaining popularity day by day in the global pharma industry and in the area of research and development. Mucoadhesive polymer plays an important role in this drug delivery system, for which in the last few years much more attention has been focused on the development of novel mucoadhesive polymers. This current review provides a good insight on starch as a mucoadhesive polymer having capability of delivering the drug at a specific delivery site for long period of time.
Keywords: Starch, Mucoadhesion, Novel Drug Delivery System

Introduction
The goal of any drug delivery system is to provide a therapeutic amount of drug to proper site in the body to achieve and maintain the optimum drug concentration, this is why the drug delivery system deliver drug at a place where needed by the body over a specific period of treatment.
This focuses on the two important aspect of any drug delivery system these are:

- Targetting a drug to specific organ or tissue
- Control the rate of drug delivery to target tissue

Now a day' scientists are trying to improve the bioavailability of the drug by tailoring properties of delivery system rather designing new drug. Mucoadhesive drug deliverysystems are being studied from different angles including development of novel mucoadhesive system, design of the device, mechanism of mucoadhesion and permeation enhancement.
Mucoadhesive drug delivery should include the following:

- Gastrointestinal drug delivery system
- Nasal drug delivery system
- Ocular drug delivery system
- Buckle drug delivery system
- Vaginal drug delivery system
- Rectal drug delivery system.[1]

Starch
Synonyms: Amylum
Biological Source:
Starch consist of polysaccharide granules obtained from the grains of maize (zea mays linn); rice (oryza sativa linn.); or wheat (triticumaestivumlinn.); belonging to family graminae or from the tubers of potato (solanumtuberosumlinn.), family solanaceae.
Description
Starch occurs as a fine powder and or angular, irregular masses readily reducible to powder.Colour of rice starch grains are white, while wheat is cream coloured and potatoes slightly yellowish, odor of starch is odourless and taste is mucilaginous. Size and shape ofstarch grains are very depending upon the types. [2]
Standards
For pharmaceutical purpose, starch should have following standards:

1) Loss on drying: not more than 15 percent for rice, wheat, and maize starches. And not more than 20 percent for potato starch.
2) Ash: not more than 0.3 percent for potato, wheat and maize starches.

Not more than 0.6 percent in case of rice starch.
Chemical Constituents
Starch contains chemically two different polysaccharides: amylase (B-amylose) and amylopectin (α-amylose), in the proportion of 1:2 amylose is water soluble and amylopectin is water insoluble, but swell in water and is responsible for the gelatinizing property of the starch.
Identification
Boil 1g of starch with 15 ml of water and cool. The translucent viscous jelly is produced.Thejelly turns deep blue by the addition of solution of iodine, the blue coloursdisappearson warming and reappears on cooling.
Starch in Pharma Industry
Starch is most easily and widely available natural polymer i.e polysacchrides. It has various applications in normal today life. The starch used pharmaceautically obtained from various sources such as:maize, corn, potato, cassava and sago etc are widely used for various purposes. Sodium starch glycolate the derivatives of starch which is the well known excipients in pharma-industry. Due to its unique physicochemical and functional characteristics starch found as a potential biomaterial for pharmaceutical application. [3-4]

It is a biopolymer, which is easily available from nature and it is renewable means it is not expensive. In addition to this, starch based materials are biodegradable which offer a great advantage over the synthetic polymer that are non-biodegradable.[5]Starch is produced within the plant cells as an energy storage mechanism which is in the form of spherical granules. Granules fall in the size range of <1µm upto 100 µm. granules size, amount, and composition of the granules vary between plant species. [6-7]

Starch species	Granule size(µm)	Average size(µm)
Corn	5-25	14.3
Cassava	3-38	14
Arrow root	9-40	23
Sago	15-50	33
Potato	10-70	36
Sorghum	3-27	16
Wheat	3-34	6.5-19.5
Sweet potato	4-40	18.5
Canna	22-85	
Waxy rice	2-13	5.5
High amylase corn	4-22	9.8

Table 1-Granule distribution of various starches

It is the major carbohydrate in plants in many different plant organs where it is used as a source of energy during the dormancy and regrowth period. The plant organ includes seeds, fruits, tubers, and roots. The examples of starch storing are the grains of maize, the grains of rice, the tubers of cassava and potatoes are the major foodstuffs in the daily human diet.

Starch is versatile and useful polymer not only because it is cheap and natural, easily available but also because of its various physicochemical properties can be altered through chemical or enzyme modification or physical treatment. [8]

Properties of Starch

Pure starch is a white, tasteless and odourless powder that is insoluble in cold water or alcohol.It consists of two types of molecule:

- Linear and helical amylase.
- Amylopectin.

Depending upon the source that is the type of plant, starch generally contains 20 to 25 % amylase and 75 to 80 % percent amylopectin by weight. [3, 9, 10, 11]

Amylase:

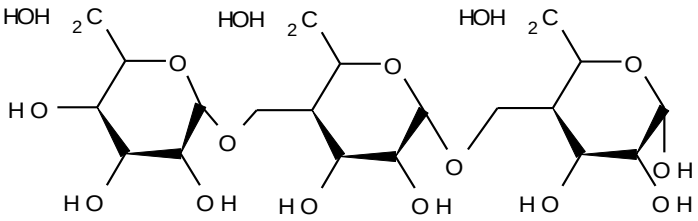

Figure 1- Structure of amylase

Amylopectin:

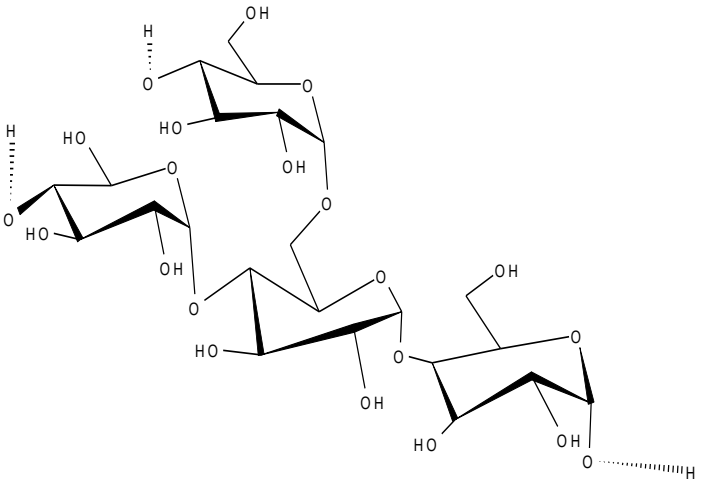

Fig-2 Structure of amylopectin

Starch (source):	% Amylose
Waxy starch	0
High amylase corn	70
Corn	28
Cassava	17
Waxy soreghum	0
Wheat	26
Sweet potato	18
Arrow root	21
Sago	26

Table 2- Amylose content of various starches [3,12]

Effect of Temperature on Various Properties of Starch

Ricardo tadeu evaluated the effect of various temp on the physiological, pasting, thermal, crystallinity and morphological properties of maize and stored for 12 months.

When the maize grains stored at 35^{0}c which causes the reduction of 22.1% in the extraction yield and starch showing yellowish color hence it is appear less attractive for application where the paste clarity is an important. When starch from maize isolated and stored for 12 months showed lower crystallinity than that of the starch harvested grains. Hence it is resulted in a more organized rearrangement of starch chains within the granule and promoted interaction with other constituents in the starch stored at 35^{0}c for 12 month. [13]

Figure 3- Application of native and modified starches in food industry

The wide range of food products uses the starch unlimited in many forms but the utility of these

starches is almost entirely depend upon the natural or synthetic functional characteristics. There can be a doubt that the particular physical and chemical properties of the starches are the keys to their success.

Starch as a Pharmaceutical Excipient

Starch can be mainly obtained from two sources i.e fruits and vegetables. It is the most common source of glucose in the body. Its cost is very low and it is being used for the benefits of human being. Starch is one of the safest excipient and it is concluded in the Generally Regarded as Safe (GRAS) list of the WHO. Starch obtained from various sources and used for various reasons in pharmaceutical industry.

Native starches are used as a binder and disintegrant in solid dosage form but due to their poor flowability their utilization is restricted. Pregelatinised i.e modified starch which is marketed under the name of starch 1500 is the most preferred directly compressible excipient in pharma industry. Recently modified rice starch, starch acetate and hydrolyzed dioscorea starches are the multifunctional excipients in pharmaceutical industry.

The international joint conference on excipients declared that starch is one of the top ten pharmaceutical ingredients. [14, 15]

PHARMACEAUTICALAPPLICATIONS OF STARCH

The various pharmaceutical applications of starches are as follows:

- Disintegrating agent
- Binder
- Film forming material
- Microspheres
- Colon targeting of drug
- Nanoparticle.

Pharmaceutically starch found as a new potential biomaterial because of its unique physicochemical and functional characteristics. Starch used as a pharmaceutical excipient, as a tablet disintegrant, sustained and controlled release polymer for drug and hormones, as a plasma volume expander, in bone tissue engineering, in red cells, in nanotechnology. [16]

Mucoadhesion

Mucoadhesion is defined as a state in which two materials, at least one is biological in nature are held together for an extended period of time by interfacial forces.

It is also defined as the ability of a material (synthetic or biological) to adhere to a biological tissue for an extended period of time.

In case of mucoadhesion, the biological tissue is the mucus membrane and for the process of mucoadhesion a succession of phenomena is required. Mucoadhesion has two steps:

- First stage involves an intimate contact between a mucoadhesion polymer and a membrane either from good wetting of the mucoadhesivesurface or from the swelling of the mucoadhesive materials..
- In the second stage,penetration of mucoadhesive into the cervice of tissue surface.[1,17]

Mechanism of Mucoadhesion

The mechanism of mucoadhesion is divided into two stages:

- Contact stage
- Consolidation stage

The contact stage involves contact between the mucoadhesive and the mucus membrane with spreading and swelling of the formulation, which initiate deep contact with mucus layer.

In the consolidation stage, the mucoadhesive materials are activated by the presence of moisture. Moisture helps mucoadhesive molecules to break up free and link up by weak vanderwaals and hydrogen bond. [17]

Theories of Mucoadhesion

There are following theories related to the process of mucoadhesion:

- Absorption theory
- Diffusion theory
- Electronic theory
- Mechanical theory
- Wetting theory

Absorption Theory

This theory describes the initial contact between two surfaces. The material adheres because of various forces involved in it.

In the absorption theory, intermolecular forces are involved. These forces are of two types:

First is a primary force which include covalent bond and secondary force includes hydrogen bonding, hydrophobic bonds and vander wall force.

Diffusion Theory

This theory involves the penetration of polymer in the mucus; this penetration depends on the diffusion coefficient and the contact time. This theory describes the polymeric chains from the bioadhesive interpenetrate into the glycoprotein mucin chain and reach a sufficient depth within the opposite matrix and lead to the formation of semi permeable bond. The concentration gradient plays an important role in this theory.

Electronic Theory

This theory involves, transfer of electrons among the surface of membrane and mucoadhesive materials which produce electrical double layer so that attractive forces produced.

Mechanical Theory:

In this theory, interlocked structure formed between polymer and the membrane.

Wetting Theory:

This theory is only applicable to the liquid bioadhesive materials. When lower the contact angle of mucoadhesive substances with membrane then it shows higher affinity towards substrate. It is the very oldest theory of adhesion this theory is best applied to liquid or low viscosity bioadhesive. It explains adhesion as bedding, whereby adhesive agents penetrate into the

surface of the substrate; this theory helps to calculate the contact angle and thermodynamic work of adhesion. (18, 19, 48)

Factor Important to Mucoadhesion

The bioadhesive power of the polymer is depend upon the nature of both, the polymer and surrounding media. The factors important to mucoadhesion are as follows:

A) Polymer related factor:

1. Molecular weight
2. Concentration of active polymer
3. Flexibility of polymer chains
4. Spatial confirmation

B) Environmental factor:

1. Applied strength
2. pH
3. Initial contact time
4. Swelling

C) Physiological variables:

1. Mucin turnover
2. Disease status

Molecular weight

The bioadhesive property of the polymer depends upon the molecular weight of the polymer, if molecular weight is 100,000 and more then only the bioadhesion is successful. e.g, polyehyleneglycol with a molecular weight of 20,000 has little adhesive character whereas polyethylene glycol with 200000 molecular weight has improved and also PEG with 400,000 has superior adhesive properties. The bioadhesive nature of the polymer improved with increasing molecular weight of polymer.

Concentration of active polymer

Bioadhesive property of the polymer is related with concentration of the polymer. If there is optimum concentration of bioadhesive polymer then produce maximum bioadhesion.

In case of highly concentrated polymer, if the concentration is beyond the optimum level then adhesive strength ultimately drops significantly because the coiled molecules become separated from the medium so that the chains which is required for interpenetration is limited.

Flexibility of polymer chains:

The effective length of the chain that penetrates into the mucus layer decreases with decrease in polymer chain which leads to reduced the bioadhesive strength. It is important for interpenetration and entanglement.

Spatial confirmation:

Along with molecular weight and chain length, spatial confirmation factor is an important factor. Dextran having molecular weight of 19,500,000 but they show similar adhesive strength as that of the PEG with molecular weight of 200,000. The helical confirmation of dextran may shield many adhesively active groups, primarily responsible for adhesion unlike polyethylene glycol polymer which having linear confirmation.

Applied strength:

If polymer do not have attractive interaction with mucin even though they become mucoadhesive, if high pressure is applied for sufficiently long period of time. The adhesive strength increases with the applied strength or with the duration of its application, hence it is necessary to apply defined strength whatever the polymer.

pH:

Bioadhesioncan be well influenced by the difference in pHof the medium. pH of the medium is responsible for the degree of hydration.

Initial Contact Time:

The extent of swelling and interpenetration of the bioadhesive polymer chains depends upon the contact time between the bioadhesive and mucus layer. Bioadhesive strength of polymer is directly propotional to the initial contact time.

Swelling:

Swelling of the polymer depends on the polymer concentration, ionic concentration, as well as presence of water over hydration results in the formation of slippery mucilage without adhesion.

Physiological Variables:

The physiological properties of the mucus are known to change during the disease condition such as common cold, gastric ulcers, ulcerative colitis, cystic fibrosis, bacterial and fungal infection of the female respiratory tract. (19, 20)

Characterstics of Mucoadhesive Polymer

- It should be non irritant to mucus membrane
- It should be inert and compatible with environment
- Polymer should be easily available in the market and economical
- The cost of polymer should not be so high so that prepared dosage form remains competitive
- It should adhere quickly to most tissue and should possess some site specificity.
- Polymer and its degradation product should be non toxic and should be no absorbable from the gastrointestinal tract.
- Unaffected by the hydrodynamic conditions, food and pH changes.
- Easy to incorporate in various dosage form.
- Possess peel, tensile and shear strength at the bioadhesive range.
- Shows bioadhesive properties in both dry and liquid state.Minimum impact on drug release.
- Optimum molecular weight.
- Possess adhesively active groups.
- Possess required spatial confirmation.
- It should form a non-covalent bond with membrane surface.(15,19)

Classification of Mucoadhesive Polymer

1) Natural Polymer:

a) Protein based polymer: Collagen, albumin, gelatin.
b) Polysaccharides: Alginates, cyclodextrins, chitosan, dextran, agarose, starch, cellulose.

2) Synthetic polymer

A) Biodegradable polymer:

Polyester: polylactic acid,polyglycolic acid, polyhydroxybutyrate,polycaprolactone,polydoxanones.
Polyunhydride: polyadipic acid, polyterphthalic acid
Polyamide:polyimonocarbonates, polyaminoacid
Phosphours based polymer:polyphosphates, polyphosphazenes
Others: polycyanoacrylates,polyurethanes, polyorthoesters

B) Non Biodegradable Polymer:

1) Cellulose derivatives: Carboxy methyl cellulose,Ethyl cellulose acetate 2)Colloidal silica:polydimethylsiloxanes, polymethcrylates. [15, 21, 22]

Natural Mucoadhesive Polysaccharides

Natural polymers are widely used in the Ayurveda from the ancient time because of their various qualities like biocompatible and non toxic nature. Natural mucoadhesive polysaccharides having less chance of biological toxicity because they are biodegradable in nature and can be easily metabolized. They can be easily obtained from natural sources which is environmental friendly processing with low cost. They show better patient tolerance. There are some examples of natural mucoadhesive polysaccharides which includes potato starch, rice starch, maize starch, wheat starch. Polysaccharides are polymeric carbohydrates and forms by the joining of mono or disaccharides, these units are joining to one another by glycoside bond**.** [8, 13, 20, 23, 24]

Polysaccharides are classified on the basis of their source: plant, animal, microbial origin. Polysaccharides obtained from plant origin are starch and cellulose, polysaccharides obtained from animal origin are chitin, and polysaccharides obtained from microbial origin are dextran, xanthan. Also there are storage polysaccharides like Potato, Rice, Maize, Wheat and various Homopolysaccharides like starch, cellulose, glycogen, insulin**.** [25, 26, 27]

Sources of Starch

- Grains of maize, rice, wheat, tubers of Potato, rice
- Dioscoreadumeterium,tacca.
- Involucrate,mung starch
- Tapioca starch
- Maize starch
- Sago starch
- Corn starch
- Hydroxyl propyl starch
- Enseleventricosum.[28]

Geographical Occurrence

Starch is commercially produced in many countries. In India and USA, maize is used for the manufacture of starch.

Preparation:

Maize starch:

Maize grains are soaked in water for 3 to 4 days in presence of sulfur dioxide. (SO2) prevents fermentation).Now, water is added to the soaked grains. The embryo which floats is separated. This contains minerals and soluble proteins. This water is used as a culture medium for the production of antibiotics. The starch material left behind is washed repeatedly with water and dried.

Rice starch:

Broken pieces of rice are soaked in 0.5 percent caustic soda solution, which causes softening and dissolution of the gluten. After that the soaked pieces are crushed and starch is prepared.

Potato starch:

The potatoes are washed to remove earthy matter.They are crushed or cut and converted into slurry then this slurry is filtered to remove earthy matter. After the filtration, the milk slurry containing starch purified by centrifugation and washing. Then it is dried.

Wheat starch:

Wheat is being the major article of food and is rarely used for preparation of starch. In this process, the wheat flour is converted into dough and kept for a while. The gluten in the dough swells and the masses are taken to grooved rollers, wherein water is poured over them with constant shaking the starchy liquid coming out of the rollers and is processed to take out the starch, which is then dried. **[29, 30]**

Process for Obtaining Mucoadhesive Starches

Bioadhesive starches are obtained by two processes:
Spray drying or drum drying reported by Bottenberg, p et.al. prepared formulations from polymer like drum dried waxy maize and spray dried waxy maize. This article concludes that bioadhesive polymer such as thermally modified corn starch with 5% polyacrylic acid or polyethylene glycol can be used as slow release device for fluoride.

We have surprisingly found that bioadhesive starches obtained by grinding or milling.

Grinding and milling are the very simple and cheap processes, that do not require any expensive instrument, equipment and do not require any complicated procedure as compared to drum drying, spray drying, and extrusion process.

The process for obtaining bioadhesive starches comprising of high energy grinding or high energy milling of non bioadhesive starch. Native starches are starches extracted from vegetables such as graminaceous or leguminous alike wheat starch, maize starch, rice starch and tuberous starch such as manioc starch, potato starch. Nonbioadhesive starches may be for eg. Native starches have different amylase and amylopectin ratio, when the amylopectin content is 100% then the starches are defined as waxy starch.

Evaluation of Mucoadhesion Properties

Cocoyam Starch

Odeniyiet.al evaluated the bioadhesive properties of native and modified Cocoyam (xanthosomasagittifolium) starches. The methods used are pregelatinisation and acetylation. The starches

were evaluated for the properties like particle size, swelling ability, mucoadhesion and viscosity.

The mucoadhesive evaluations of starches were performed by rotating cylinder method. The evaluation studies were done in 0.1m Hcl and phosphate buffer (pH-6.8) to stimulate the stomach and small intestine respectively. Friability and crushing strength are used to determine the mechanical properties of the compacted starches. The particle so prepared has irregular shape and size in the range of 9.38 to 10.67 nm.In 0.1 m Hcl the mucoadhesion time was in the order of acetylated starch> native starch>pregelatinised starch. In 6.8 buffer the mucoadhesion time in the order of pregelatinised starch> native starch> acetylated starch. Any other severe signs such as appearance of epithelial necrosis, sloughing of epithelial cells were not observed in ileum sections. Hence such study concludes that modified cocoyam starches could be useful in targeted mucoadhesive drug delivery. [28, 30]

Banana starch

The same study i.e evaluation of bioadhesive properties of starches was carried on banana (musa-paradisica) natural and modified starches (pregelatinised and acetylated). The study was carried in 0.1 m Hcl and 6.8 p^H phosphate buffer to stimulate the stomach and small intestine using rotating cylinder method.

Starches were evaluated for the characteristics like particle size, swelling capacity, bulk density, particle density, angle of repose, viscosity, and FTIR spectroscopy. Mechanical properties are also evaluated using the crushing strength. The bioadhesive property of starches are not related to the viscosity as the pregelatinised starch was the least viscous having long time detachment in both media. Mixture of starches with polyvinylpyrrolidone showed significantly increased adhesion time. Hence, such study concludes that pregelatinised starch could be useful in formulation of drug targeted to the stomach which when mixed with polyvinylpyrrolidone significantly increases adhesion time. [30, 31]

Assam Bora Rice Starch

Nikhil.et.al study was carried on the Assam Bora rice starch to evaluate its pharmaceutical utility as bioadhesive polymeric excipient in drug delivery. In this study microbead prepared using ionotropic gelation method, which is industrially feasible conventional method using pregelatinised Bora rice starch along with sodium alginate as per SUPAC-MR guidelines.

The prepared microbeads are evaluated for surface morphology, drug polymer compatibility, mucoadhesion and other pharmaceutical properties. This study concludes that Assam Bora rice starch has excellent mucoadhesive properties and being used as a drug release modulator in the drug carrier system. [31, 32]

Application of Starch In Mucoadhesive Drug Delivery

Moth Bean Starch

Acyclovir is an antiviral drug, most active against herpes simplex virus and herpes zoster. This drug is categorized as a Biopharmaceutical classification system (BCS) class-II drug. This drug is mainly absorbed from upper gastric region, hence to increase its bioavailability there is need to prepare mucoadhesive formulation by increasing its absorption at window site.

Akhilesh.et.al formulated and evaluated novel polymer mixer which were prepared by spray drying of an aqueous mixture of moth bean starch with carbopol 934p and HPMC k4m used for mucoadhesive drug delivery.

Using 3^2 factorial designevaluated the influence of different concentration of hydrophilic polymer i.e carbopol 934p and HPMC k4m with constant concentration of moth bean starch on drug release as well as in vitro adhesion time. All the formulations were studied for physical evaluation i.e hardness, friability, content uniformity, drug excipient compatibility, as well as stability study. From the evaluation it should be concluded that formulation exhibited desirable in vitro adhesion time greater than 8h and drug release is greater than 90% in controlled manner. [30, 33]

Starch

A,V.Yadav et.al prepared Domperidone microsphere for intranasal administration. The method used is emulsification cross linking techniques. Polymer used is starch which is biocompatible, biodegradable and bioadhesive in nature.illeum.et.al introduced the concept of using degradable starch microsphere for nasal delivery of drug in bioadhesive delivery system.

In the preparation of Domperidone microsphere epichlorhydrine is used as a cross linking agent. All the formulation were evaluated for particle size, morphological characteristics, bioadhesive strength, percentage mucoadhesion, swelling degree, percentage drug encapsulation, in vitro diffusion study using nasal cell. Spherical microsphere prepared in all the batches fall in the range of 22.8 to 102-63 micron meter. These domperidonemicrospheres showgood mucoadhesive property and swelling behavior. [34]

Cassava Starch Succinate

S.Surini.et.al studied application of pregelatinised cassava starch succinate, a physically and chemically modified starch for preparing mucoadhesive microsphere. Polymers used are Carbopol 934p and hydroxy propyl methyl cellulose. The method used for preparing mucoadhesive microsphere is spray drying technique. The prepared microspheres are evaluated for morphology, particle size distribution, entrapment efficiency, mucoadhesive strength of starch on intestine of rats.

In vitro drug release was performed in pH1.2 Hcl and 7.2 phosphate buffer. The drug Propranolol hydrochloride was introduced into the microspheres with an efficiency of 84-100%. All the types of

microspheres show good mucoadhesive properties on intestinal mucosa. The drug release from the microspheres produced extended release in pH 1.2 Hcl and 7.2 phosphate buffer. The release of Propranolol hydrochloride from the microspheres in pH7.2 was slower than that in pH1.2 Hcl. From this it should be concluded that microsphere having good mucoadhesive property on both gastric and intestinal mucosa, however the addition of HPMC and Carbopol 934p to the pregelatinised cassava starch succinatemicrosphere significantly extended the drug release. [3]

Assam Bora rice starch

Mohammad zaki ahmad et.al developed the novel colon targeted mucoadhesive microsphere for the delivery of 5-fluorouracil to the colon without the drug being released in the stomach or small intestine. Polymer used was the natural mucoadhesive Assam Bora rice starch. The method used for preparation of microsphere is double emulsion solvent evaporation method. The prepared microspheres are evaluated for the characteristics like shape, size, surface morphology, size distribution, incorporation efficiency, and drug release studies. After the evaluation the study confirmed that insignificant release of 5-fluorouracil was obtained from mucoadhesive microspheres. Nikhil .K. Sachan et.al studied that, in the field of, science and technology, the drug delivery technology is one of the areas of research. In drug delivery system considerable efforts have been made and are being continued to develop the new concepts in order to improve the therapeutic efficacy of drug. The microfabrication is one of the intelligent approaches for controlled drug delivery where the drug is coupled with a polymeric microcarrier which helps to modulate the release and absorption of the drug.

The main aim of his studies to evaluate the mucoadhesive and sustained release properties of bora rice starch of Assam and to explore its feasibility of its utilization in drug delivery system as a natural mucoadhesive polymer. The Bora rice was used in combination with sodium alginate for the preparation of drug loaded microbeads. The method used for preparation of microbeads is micro-orifice ionic gelation technique. After preparation the microbeads are evaluated for the characteristics like particle size, entrapment efficiency, size distribution, swelling, mucoadhesivity, chemical interaction and drug release properties. In vitro study concludes that Assam Bora rice starch polymer is having the potential for utilization not only to sustain the release of drug but it also exhibits excellent mucoadhesive properties. [31, 32, 34]

Starch Derivatives

Remon et.al prepared matrix mini tablets with the combination of microcrystalline waxes and starch derivatives and ibuprofen was the model drug. The production of mini tablets is preferred as compared to production of pellets because productions of pellets not involve any problematic error. The in vitro drug release rate varied using microcrystalline waxes with melting range between 68 and 72^{0}c. Slower drug releases were obtained ultimately with increasing wax concentration. Drug release pattern were also modified using different concentration and mixture of starches.

A Jain et.al studied the combination of starch Carbopol 934 and starch-polycarbophil. These are used as carriers to develop controlled bucoadhesive formulation. The tablet containing fixed amount of drug i.e carvediol. The method used for preparation is direct compression method using starch:carbopol 934 (f1 to f6) and starch:polycarbophil(e1 to e6) in the different ratios: (85:15,75:25,60:40,50:50,40:60,25:75.) The prepared tablet evaluated for thickness, hardness, mucoadhesive strength, drug release. According to in vivo study results, all the parameters are acceptable and within the limit. The maximum rate of release was observed in tablets of starch: carbopol 934 as compare to tablets of starch: polycarbophil. Hence the work concludes that formulated tablets of starch:carbopol 934 showed better matrix structure and better release profile as compared to tablets of starch: polycarbophil.[35]

Jackfruit Seed Starch

Amitkumar Nayak developed calcium pectinate-jackfruit (Artocarpusheterophyllus Lam). Seed starch (jackfruit seed starch) mucoadhesive beads containing metformin Hcl were developed through ionotropic-gelation method. The in–vitro drug release from these beads was followed controlled release pattern.

The pH of the medium was found critical for swelling and mucoadhesion. The optimized calcium pectinate-jackfruit seed starch beads are characterized by SEM and FTIR. These beads also exhibited good mucoadhesivity and significant hypoglycemic effect in Alloxan induced diabetic rats over the prolonged period of time.

Parichatphrukwiwattanaakul et al investigated the physicochemical properties of Starch from jackfruit seed and mung bean. Jackfruit seed starch had much higher resistant starch content (26.99%) than that of mung starch (4.04%), also the jackfruit seed starch had a higher gelatinization temp (t_0) that required more gelatinization energy compared to mung bean starch but the mung bean starch has higher amylose content and its granule were much larger than that of jackfruit seed.[36,37,44,51]

Taro starch

Karmaker R et al studied the native and modified starches isolated from conventional and non conventional sources and suggested that the physicochemical properties of taro starch more or less similar with other starches. Hexagonal shaped taro starch had higher amylose and carbohydrate leaching properties as compared to potato and corn starches. For the manufacture of food products the smaller stable granules and medium amylose content of taro starch are used.

The taro starch having higher viscosity of 7% possess greater retro degradation tendency. High amylose content of starch shows better gelling properties where the high amylopectin starch like taro used where viscosity is needed. It is a very cheap source for extraction of starch. [36, 38]

Non Food Application of Starches

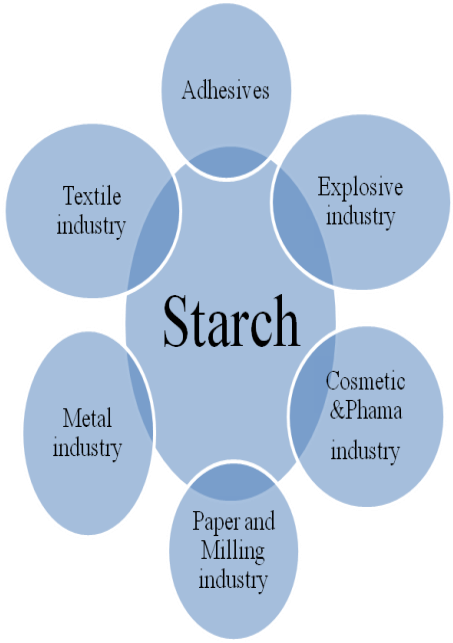

Figure 4-Non food applications of starches.

Functional Properties of Starches

1) Specific viscosity (hot and cold)
2) Thin boiling (faster canning heat transfer)
3) Viscosity resistance acid/ mechanical sheer
4) Freeze-thaw stability
5) Gel texture, body at various temp
6) Clarity, opacity
7) Processing condition tolerance
8) Oil retention, high or low
9) Resistance to setback (gel formation)
10) High shear
11) Flow properties
12) Emulsion stabilizing capacity
13) Mouth feel, lubricity, palate coating
14) Suspension characteristics
15) Adhesiveness
16) Crystallinity
17) Bland taste
18) Long shelf-life stability
19) Hygroscopicity
20) Colour
21) Anti-cacking
22) Cold water swelling
23) Swelling and resistance to swelling
24) Film forming property.[37,39]

Starches for Food Application

1) Native starches
2) Physically modified starches
3) Chemically modified starches.[36]

Chemically modified starches are used because they having various functional attributes in food application that native starches normally cannot provide:

- Heat resistance
- Acid resistance
- Shear resistance
- Improved freeze thaw solubility.

Chemically modified starches are used because they provide functional attributes but these attributes or properties depend upon:

- Raw material: Maize, potato, Wheat, Topioca, rice.
- Type of modification: Ether, Ester, Cross-linking.
- Degree of modification.[38]

Why Modification?

The modification of starch is very important to achieve many functional and additional properties:

1) Conferring rheology
2) Flow ability, elastic/viscous properties, texturing.
3) Thickening
4) Stabilizing, viscous control, long shelf life stability.
5) Increase of shear stability, Process tolerance
6) Improvement of pH-stability,acidic stability
7) Improvement of paste stability
8) Retrodegradation, gelling, amylase crystallization, freeze thaw-stability.
9) Flow properties
10) Elasticity, cohesion
11) Adhesiveness
12) Binding water
13) Flocculation
14) Starch for sensoric properties.

Examples of Cross-Linked Starches

- Acetylated distarchadipate
- Hydroxyl propyl distarch phosphate.[15,36]

Examples of Chemically Modified Starches

- Oxidised starch
- Monostarch phosphate/distarch phosphate
- Phosphateddistarch phosphate
- Acetylated starch
- Acetylated distarchadipate
- Hydroxy propyl starch
- Hydroxyl propyl distarch phosphate
- Starch sodium octenyl succinate
- Acetylated oxidized starch.[38]

Starch Based Derivatives

Starch is a natural polymer which has widespread application ranging from a simple filler or binder to a more functional ingredient in the formulation of capsule coating, subcutaneous implants and tablets.

In tablets starch mainly used as a binder, disintegrant, diluents and also as a sustained release agent in matrix system. It is synthesized from carbon dioxide and water by photosynthesis in plants. Its low cost, biodegradability, and renewability make it a suitable agent for sustaining the drug materials. Starch consist of two homopolymers of d- glucose: amylase, a mostly linear D (1, 4)-glucan and branched amylopectin having

the same backbone structure as amylase but with many linked branched points. Starch has many hydroxyl functional groups in its structure so for which it is hydrophilic in nature and this hydrophilicity can be used for improving the degradation rate of some biodegradable hydrophobic polymers. (39)

Mucoadhesive polymer	Mean adhesive force (%)Standard deviation
Polyacrylic acid	-185.0±10.3
Tragacanth	-154.4±7.5
Sodium alginate	-126.2±12.0
HPMC	-125.2±16.7
Karaya gum	-125±4.8
Polyethylene oxide	-128±2.4
Soluble starch	-117±31

Table 3-: Rank order of mucoadhesive force for various polymers (38, 40)

Conclusion

Polymer plays an important role in the novel drug delivery system that is polymer used to control the rate of drug release from the various formulations. The formulation scientists are trying to find newer ways of improving therapeutic efficacy of formulation by modifying formulation techniques or using various polymer systems. The use of novel polymer not only offers benefits but also can be harmful because of toxicity and incompatibility problems. When starch is studied from different angles as a mucoadhesive polymer, then it is cost effective, biocompatible multifunctional, less toxic. When the ideal mucoadhesive polymer taken into consideration then starch is proven or considered to be a novel natural mucoadhesive polymer.

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