NOVEL NATURAL POLYMERS FOR FAST DISSOLVING TABLET

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ABSTRACT
Fast dissolving tablets are very popular now a day as they get dissolved and disintegrated in mouth with in few second of administration without water. Fast dissolving tablets are beneficial for pediatric, geriatric and mentally ill patients who have difficulty in swallowing tablet and capsules. Natural polymers like lepedium sativum, chitosan, Gum Arabic, plantago ovata, gum karaya, gellan gum, ocimum mucilage, cordia mucilage, terminalia gum, isapghula mucilage, albizia gum, almond gum, improve the properties of tablets and used as binder, diluent, superdisintegrant, enhance the solubility of poorly water soluble drug. Natural polymers are obtained from the natural sources. They are non-toxic, cost effective, biodegradable, ecofriendly, devoid of any side effect, renewable and provide nutritional supplement. It is proved from the studies that natural polymers are more safe and efficacious than the synthetic polymers. Thus the present article reviews some new natural polymers used the formulation of FDTs.

KEYWORD: fast dissolving tablet, Natural polymers, chitosan, gellan gum, aegle marmelos.

INTRODUCTION
Fast dissolving tablets (FDTs) are the novel dosage form. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. The faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. This dosage form mostly preferred by geriatric and pediatric patients with poor physiological and physical abilities and also by the travelling patients suffered from motion sickness FDTs are very effective in such situation as it dissolved rapidly in mouth and have quick action.1 Fast disintegrating tablets are very popular these days as they get dissolved or easily disintegrated in mouth with in few seconds of administration without the need of water.2

Of all the dosage forms administered orally, the tablet is one of the most preferred dosage forms. Disintegrants are agents integrated to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule “slugs” into more small fragments in an aqueous environment thereby incrementing the available surface area and promoting a more rapid release of the drug substance. They promote moisture penetration and dispersion of the tablet matrix. Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. The accentuation on the availability of drug highlights the importance of the relatively rapid disintegration of a tablet as a criterion for ascertaining uninhibited drug dissolution behavior. Number of factors affects the disintegration replace of tablets. The disintegrants have the major function to oppose the efficacy of the tablet binder and the physical forces that act under compression to compose the tablet. The more strong the binder, the more efficacious must be the disintegrating agents in order for the tablet to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but additionally into powder particles from which the granulation was yare. Disintegrants are an essential component to tablet formulations. The ability to interact strongly with water is essential to disintegrate function. Combination of swelling and/or wicking and/or deformation is the mechanisms of disintegrant action. A disintegrant utilized in granulated formulation processes can be more efficacious if utilized both “intragranelarly” and “extragranelarly” thereby acting to break the tablet up into granules and having the granules further disintegrate to release the drug substance into solution. However, the portion of disintegrant integrated intragranelarly (in wet
granulation processes) is conventionally not as efficacious as that integrated extragranularly due to the fact that it is exposed to wetting and drying (as a component of the granulation process), which reduces the activity of the disintegrant. Since a compaction process does not involve its exposure to wetting and drying, the disintegrant used intragranularly inclines to retain good disintegration activity.[3][4]

The aim of this review is to study different novel natural polymers and their pharmaceutical uses which are used in fast dissolving tablets.

Characteristics of Fdts
- Administered without water, anywhere, any time
- Fast dissolving tablet should not require water to dissolve.
- Fdt should be quickly disintegrated with in seconds when placed in mouth.
- Being a unit dosage form it should provide accurate dosing.
- Quick dissolution and absorption in the oral cavity.
- Easy to convey.
- Less sensitive to enviromnental condition like humidity and temperature.
- Tablets are manufactured with conventional equipment with in low cost.
- It should less fragile and should maintain its hardness.[5]

Advantages of Fdts
- Ease of administration for those patients who have difficulty in swallowing tablet.
- No need of water to swallow the dosage form.
- Useful for pediatric, geriatric and psychiatric patients.
- Have acceptable taste masking property.
- They should be less fragile and should maintain its hardness
- It is easily portable as it is a solid dosage form and less sensitive to environmental condition
- Achieve increased bioavailability through pre-gastric absorption of drugs from mouth, pharynx and esophagus as saliva passes down.
- Have a pleasant mouth feel and leave minimal or no residue in the mouth after drug administration.
- Have rapid dissolution and absorption of the drug which will produce quick onset of action.
- It combines advantages of solid dosage form in terms of stability and liquid dosage form in term of bioavailability
- FDTs are very safe and easy to swallow because there is no risk of suffocation in the airways due to physical obstruction during swallowing.
- FDTs are less sensitive to environmental condition hence they are very stable.

Disadvantage of Fdts
- Fragile and brittle.
- It needs special package for protection during storage and transportation.
- Difficult to swallow in case of children and unconscious patient.
- Some drug resists compression into dense compact owing to amorphous nature, low density character.

Classification of polymers used in fast dissolving tablet
1. Natural Polymers
Natural polymers are obtained from natural sources. These polymers are found in plants and animals. Examples are proteins, cellulose, starch, resins and rubber.

2. Semi-synthetic Polymers
Semi-synthetic polymers are obtained from natural polymers by subjecting them to some chemical process. Cellulose derivatives as cellulose acetate (rayon) and cellulose nitrate, etc. are the usual examples of this sub category.

3. Synthetic Polymers
A synthetic polymer is a man-made macromolecule that is made of thousands of repeating units. Sometimes these polymer are straight chained like paper clip chain and consist of one long chain of monomers bonded end to end. synthetic polymer are light weight, hard to break and last a long time. A variety of synthetic polymers as plastic (polythene), synthetic fibers (nylon 6, 6) and synthetic rubbers (Buna - S) are examples of man-made polymers.

Natural polymers improve the tablet properties in the fast dissolving tablets like disintegration time the tablet get disintegrated fastly within few seconds because of the use of superdisintegrant as natural polymer like Lallemandia reylene seed mucilage, mangifera indica gum, dehydrated banana powder etc., they increase the porosity of the granules so that the tablet formed is easily get dissolved in the mouth without the use of water, the drug get rapidly released from the tablet by the action of natural polymer, natural polymer like Modified Aegle Marmelos gum can increase the solubility of poorly water soluble drug like Aceclofenac, Natural polymers have appreciable effects on hardness and friability.
macrophage functioning, it cause significant deviation in the GSH (glutathione) concentration in liver, kidney, stomach and intestine.[6]

Lallemantia reylenne seeds
The seeds of Lallemantia reylenne seed are mucilaginous and have medicinal properties. It is an annual herb. It is cultivated in northern India it is also known as Tukhmalanga in India, it belongs to Lamiaceae family. It has extensive swelling properties. It is used to cure boil pain and bursting of boil. The seed due to the presence of high mucilage content quickly adsorb water when soaked and produce a sticky, turbid and tasteless liquid.[7]

Locust bean gum
It is a galactomannan vegetable gum extracted from the seeds of carob tree (Ceretonia Siliqu) found in mediterranean region. It is also known as Carob ben gum. Locust bean gum is used as gelling and thickening agent in food industry and used as bioadhesive and enhance the solubility. The gum is white to yellowish white odourless powder. It is insoluble in most organic solvent including ethanol. It is partially soluble in water at ambient temperature and soluble in hot water and need heating to above 850 for 10 min for complete solubility.[8]

Ficus indica fruit mucilage
Ficus indica is a large tree up to 3 meter and very fast growing with spready branches and arial roots. The mucilage of ficus indica fruit is used as superdisintegrant which is obtained from the pulp of fruit ficus indica. The fruits of ficus indica are of the size of cherry. It has nutritional as well as medicinal value.[9]

Mangifera indica gum (MIG)
Mango is the Common name of mangifera indica is belongig to Anacardicae family. It is non-toxic and used as disintegrant, binder, suspending agent, emulsifying agent in different formulations. The gum is white to off white in colour to cream colour powder, the powder was soluble in water and practically insoluble in acetone chloroform, ether, methanol and ethanol It is easily available and gum is devoid of toxicity and each and every part of the tree has pharmacological activity like diuretic, astringent, diabetes, asthma, diarhoea, urethritis and scabies.[10]

Lepedium Sativum
Lepedium sativum is also called Asaliyo and belonging to the family Cruciferae. It is widely available in market and has very low cost. Components used are leaves, root, oil, seeds and so forth. Seeds contain higher amount of mucilage, dimeric imidazole alkaloids lepidine B, C, D, E and F and two incipient monomeric imidazole alkaloids, semilepidinoside A and B. Mucilage is extracted from the seeds of lepedium sativum which is used as binder, disintegrant and gelling agent. It is used in India as herbal medicine. The mucilage is brownish white powder which have characteristic odour and decomposes above 2000C.[11]

Hibiscus Rosa sinensis mucilage
The plant is easily available and its leaves contain mucilage and in mucilage L-rhamnose, D-galactose, D-galactouronic acid and D-glucuronic acid is present. It is also called shoe flower plant, China rose, Chinese hibiscus belonging to family Malvaceae. Mucilages are used as thickeners, suspending agent, water retention agent, disintegrants.[12]

Dehydrated banana powder (DBP)
Banana is also called Plantain belonging to the family Musaceae. DBP is prepared from the variety of banana called Ethan and nenhtran (nenthra vazha). It contains vitamin A so used in the treatment of gastric ulcer and diarhoea. It also contains vitamin B6, which help in reducing the stress and anxiety. It is a very good source of energy due to high carbohydrate content and it contain pottasium which is responsible for better brain functioning.[13]

Chitosan
Chitosan is a linear polysaccharide produced by the deacetylation of chitin, a naturally occurring polymer. Chitosan is widely used in a range of diverse fields, including waste management, medicine, food and agriculture. Chitosan has unique biological properties such as biocompatibility, antimicrobial, biodegradable, mucoadhesion, anticholesterolemic and permeation enhancement effects. Chitosan is produced commercially by deacetylation of chitin, which is the structural element in the exoskeleton of crustaceans (such as crabs and shrimp) and cell walls of fungi.[14]

Gum Arabic
Gum Arabic is a natural polysaccharide derived from exudates of Acacia Senegal and Acacia Senegal trees Gum arabic (GA) or acacia gum is the exudate from the Acacia senegal and Acacia seyal trees, belonging to Leguminosae family. It’s a complex, branched heteropolysaccharide, either neutral or slightly acidic and composed of 1, 3-linked β-D-galactopyranosyl units. L-arabinose, L-rhamnose, and D-glucuronic acid have also been detected as constituents of this polymer.[15]

Plantago ovata
Isaphghula also known as Psyllium seed husks, isabgol, or simply as psyllium, are portions of the seeds of the plant Plantago ovata, (genus plantago), a native of India and Pakistan.They are soluble in water, expanding and becoming mucilaginous when wet. Seeds are used commercially for the production of mucilage. Plantago ovata mucilage is used as natural superdisintegrant. The mucilage also has various properties like binding, disintegrating and sustaining property. The dried seeds of Isaphghula husk of a plant called as plantago ovata. The swelling index of the tablets is around 89+2.2%v/v. FDTs are rapidly disintegrated due to the presence of
mucilage which create hydrodyanamic pressure. The mucilage is clear, colourless gel; it is obtained from the seed coat of psyllium. Milled seed mucilage is white fibrous material which is hydrophilic in nature. [16]

Guar Gum
It is naturally occurring gum (marketed under the trade name Jaguar). It is free flowing, consummately soluble, neutral polymer composed of sugar units and is approved for use in food. Guar gum is mainly consisting of the high molecular weight (approximately 50,000–8,000,000) polysaccharides composed of galactomannans and is obtained from the endosperrn of the seed of the guar plant, Cyamopsis tetragonoloba (L) Taub. (Syn. Cyamopsis psoraloides). It is utilized as thickener, stabilizer, and emulsifier and approved in most areas of the world (e.g. EU, USA, Japan, and Australia). It is not sensitive to pH, moisture contents, or solubility of the tablet matrix. It is not always pristine white and sometimes varies in color from off-white to tan and inclines to discolor with time in alkaline tablets. [17]

Gum Karaya
Gum karaya can be utilized as an alternative superdisintegrant to commonly available synthetic and semisynthetic superdisintegrants due to its low cost, biocompatibility as well as facile availability Gum karaya is a vegetable gum produced as an exudate by trees of the genus Sterculia. Chemically, gum karaya is an acid polysaccharide composed of the sugars galactose, rhamnose, and galacturonic acid. The high viscosity nature of gum limits its uses as binder and disintegrant in the development of conventional dosage form. Gum karaya has been investigated for its potential as a tablet disintegrant. Different results showed that modified gum karaya produces rapid disintegration of tablets. [18]

Agar and Treated Agar
Agar is yellowish-gray or white to proximately colorless, inodorate with mucilaginous taste and is available in the form of dives, sheet flakes, or coarse powder. Agar consists of two polysaccharides, agarose and agar pectin. It is the dried gelatinous substance obtained from Gelidium amansii (Gelidaceae) and several other species of red algae like Gracilaria (Gracilariaeaceae) and Pterocladia (Gelidaceae). Agarose is responsible for gel vigor and agar pectin is responsible for the viscosity of agar solutions. High gel vigor of agar makes potential candidate as a disintegrants. [19]

Fenugreek Seed Mucilage
Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). Trigononola foenum-graceum commonly knenned as fenugreek, is an herbaceous plant of the leguminous family. Albeit it does not dissolve in water, mucilage forms a viscous tacky mass when exposed to fluids. Like other mucilage-containing substances, fenugreek seeds swell up and become slick when they are exposed to fluids. Hence, the study revealed that this natural disintegrant (fenugreek mucilage) showed more preponderant disintegrating property than the most widely used synthetic superdisintegrants like Ac-di-sol in the formulations of FDTs. Studies betokened that the extracted mucilage is a good pharmaceutical adjuvant and concretely a disintegrating agent. [20]

Soy Polysaccharide
It is a natural superdisintegrants that does not contain any starch or sugar so can be utilized in nutritional products. Evaluated soy polysaccharide (a group of high molecular weight polysaccharides obtained from soy beans) as a disintegrant in tablets made by direct compression utilizing lactose and dicalcium phosphate dihydrate as fillers. Cross-linked sodium carboxymethyl cellulose and corn starches were utilized as control disintegrants. Soy polysaccharide performs well as a disintegrating agent in direct compression formulations with results paralleling those of cross-linked CMC. [20][21]

Gellan Gum
Gellan gum is an anionic, high molecular weight, deacetylated exocellular polysaccharide gum produced as a fermentation product by a pristine culture of Pseudomonas elodea with a tetra saccharide reiterating unit of one α-L-rhamnose, one β-D-glucuronic acid and two β-D-glucose residues. Gellan gum is a water-soluble polysaccharide produced by Pseudomonas elodea, a bacterium. Antony and Sanghavi 1997 studied the gellan gum as a disintegrant and the efficiency of gum was compared with other conventional disintegrants such as dried corn starch, Explotab, Avicel (pH 10.2), Ac-di-sol, and Kollidon CL. The disintegration of tablet might be due to the instantaneous swelling characteristics of Gellan gum when it comes in contact with water and owing to its high hydrophilic nature. The consummate disintegration of tablet was has proved itself as superior disintegrant. [22]

Aloe mucilage
Aloe mucilage is obtained from the leaves of aloe barbadensis Miller. Aloe vera leaves and the exudate arising from the cells adjacent to the vascular bundles. The bitter yellow exudate contains 1, 8 dihydroxy anthraquinone derivatives and their glycosides. [23] Many investigators have identified partially acetylated mannan as the primary polysaccharide of the gel, while others found pectic substance as the primary polysaccharide. Other polysaccharides such as arabinan, arabinorhamnogalactan, galactan, galactogalacturan, glucogalactomannan, galactoglucoarabinomannan and glucuronic acid containing polysaccharides have been isolated from the Aloe vera inner leaf gel part. [24] A controlled delivery system of glibenclamide using aloe mucilage was studied. [25]

Ocimum mucilage
The seeds of Ocimum americanum commonly called as Ocimum canum belongs to the Family: Lamiaceae (Labiates). Ocimum mucilage is obtained from the seeds
of Ocimum americanum. Seeds are having Nutlets with narrowly ellipsoid, punctulate black. Polysaccharides composed of xylose, arabinose, rhamnose and galacturonic acids. Pharmacognostic and phytochemical evaluation of Ocimum americanum was studied. Mucilage from the seeds of Ocimum americanum was explored as a tablet disintegrant.\textsuperscript{[27]}

**Cordia Mucilage**

Cordia Mucilage is obtained from raw fruits of Cordia Obliqua, willow family Boragiaceae. The mucilaginous substance of the fruit used as gum an expectorant and is effective in treating the disease of the lungs and the raw gum can be used beneficially in gonorrhoea. Efficacy of cordia obliqua fruit mucilage as pharmaceutical excipient as tablet binder.\textsuperscript{[28]}

**Terminalia gum**

The bark is smooth with beige to grey brown colour, with yellowish or beige slash while the stem is pubescent. Terminalia gum exudates obtained from the incised trunk of the tree Terminalia randii (Family Combretaceae). Extracts of the stem and bark of Terminalia randii. Gum exudates obtained from Terminalia randii has been evaluated as binding agent and compared with standard binders like polyvinylpyrrolidone (PVP) and corn starch.\textsuperscript{[29]}

**Cassia Tora Mucilage**

Cassia is used as tonic, carminative and stimulant. Cassia contains 1-2\% volatile cassia oil which is mainly responsible for the spicy aroma and taste. Cassia tora mucilage derived from the seeds of Cassia tora, belongs to Caesalpiniaeae is a wild crop and grows in most parts of India as a weed and locally known as charota.\textsuperscript{[30]} The primary chemical constituents of Cassia include cinnamaldehyde, gum, tannins, mannitol, coumarins and essential oils (aldehydes, eugenol and pinene); it also contains sugars, resins and mucilage among other constituents.\textsuperscript{[31]}

**Tara gum**

Tara gum is obtained from the endosperm of seed of Caesalpinia spinosa, commonly known as Tara. It is small tree of the family Leguminosae or Fabaceae. Tara gum is a white, nearly odorless powder. The major component of the gum is a galactomannan polymer similar to the main components of guar and locust bean gums, consist of a linear main chain of (1-4)-\(\beta\)-D mannopyranose units with \(\alpha\)-D-galactopyranose units attached by (1-6) linkages. The ratio of mannose to galactose in tara gum is 3:1, produce highly viscous solutions, even at 1\% concentration.\textsuperscript{[32]}

**Albizia Gum**

The genus Albizia containing some twenty-six species is a member of the Mimosaceae, a family which also includes the gum-bearing genera Acacia and Prosopis. only two species of Albizia, A. zygia and A. sassa, are however, known to produce gum.\textsuperscript{[33]} Albizia gum is obtained from the incised trunk of the tree Albizia zygia, family Leguminosae and is shaped like round elongated tears of variable colour ranging from yellow to dark brown. It consists of \(\beta\)-1– 3-linked D galactose units with some \(\beta\)-1-6-linked D-galactose units. Albizia gum is evaluated as a binding agent in tablet formulations in comparison with gelatin BP.\textsuperscript{[34]}

**Almond gum**

Almond gum is obtained from the tree Prunus communis which is a water soluble gum extrudes from the wounds on almond trees. The constitution of almond gum includes aldobionic acid, L-arabinose, L-galactose, D-mannose etc. It contains different components which have emulsifier, thickener, suspending pharmaceutical, adhesive, glazing agent and stabilizer. Gum obtained from Almond as a binder in tablet formulations was studied.\textsuperscript{[35]}

**CONCLUSION**

Natural polymers have better effects on fast dissolving tablets than Synthetic Polymers. Natural Polymers increases the drug release rate from the tablet by decreasing the dissolution and disintegration time. Natural polymers are preferred over synthetic polymers as they are nontoxic, easily available at low cost and used in low concentration. Thus these natural superdisintegrants exhibit faster drug dissolution and increased bioavailability and improve patient compliance and can be used for drug delivery.

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