ABSTRACT
Disintegrants are substances or mixture of substances added to the drug formulation that facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Superdisintegrants are generally used at a low level in the solid dosage form. Examples of Superdisintegrants are crosscarmelose, crosspovidone, sodium starch glycolate which represent example of a crosslinked cellulose, crosslinked polymer and a crosslinked starch respectively. There are various natural substances like gum karaya, modified starch and agar have been used in the formulation of FDT’s. Mucilage of natural origin is preferred over semi synthetic and synthetic substances because they are comparatively cheaper, abundantly available, non irritating and nontoxic in nature. The present study comprises the various kinds of natural superdisintegrants which are being used in the formulation to provide the safer, effective drug delivery with patient’s compliance.

Keywords: Natural polymers, Gums and mucilages, Superdisintegrants, Fast disintegrating tablet.

INTRODUCTION
Disintegrants are substances or group of substances added to the formulations that facilitate the breakup or disintegration of tablets into smaller particles that dissolve more rapidly than in the absence of disintegrants. Disintegrant have the major function to oppose the efficiency of tablet binder and physical forces that act under compression to form the tablets. Tablet disintegration has been considered as the rate limiting step in faster drug release. Disintegrants are substances that are added to formulations to dissolve more rapidly in aqueous environment\[1, 2\]. Mucilages have been used as disintegrants due to their swelling properties. They can display good binding property; both of these properties depend upon the concentration of mucilage in formulation. Generally in the 1 to 10% concentration of total tablet weight mucilages can act as disintegrant. This is an important parameter to determine the application of mucilage in particular formulation.
Mucilages are used as disintegrant in solid pharmaceutical formulations. Many of them are already evaluated for its disintegrant properties and others are in process.

Disintegrants are an essential component to tablet formulations. The ability to interact strongly with water is essential to disintegrant function. Combinations of swelling and/or wicking and/or deformation are the mechanisms of disintegrant action. In a direct compression process, drug is blended with a variety of excipients, subsequently lubricated and directly compressed into a tablet. A disintegrant used in this type of formulation, simply has to break the tablet apart to expose the drug substance for dissolution\cite{3, 4}. Most common tablets are those intended to be swallowed whole and to disintegrate and release their medicaments rapidly in the gastrointestinal tract (GIT).

The proper choice of disintegrant and its consistency of performance are of critical importance to the formulation development of such tablets. In more recent years, increasing attention has been paid to formulating not only fast dissolving and/or disintegrating tablets that are swallowed, but also orally disintegrating tablets that are intended to dissolve and/or disintegrate rapidly in the mouth. Most prior studies have focused on the function related properties of superdisintegrants with special emphasis on correlating these functional properties to disintegrant efficiency and drug release rate. Water penetration rate and rate of disintegration force development are generally positively related to disintegrant efficiency in nonsoluble matrices.

**NATURAL SUPERDISINTEGRANTS**

Disintegrating agents are substances routinely included in the tablet formulations to aid in the breakup of the compacted mass when it is put into a fluid environment. They promote moisture penetration and dispersion of the tablet matrix. In recent years, several newer agents have been developed known as “Superdisintegrants”. These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs. The natural superdisintegrants involve various natural substances like gums, mucilages, and other substances of natural origin which are more effective at lower concentrations with
greater disintegrating efficiency and mechanical strength. Some natural substances like gum karaya, modified starch and agar have been used in the formulation of FDT’s. Mucilage of natural origin is preferred over semi synthetic and synthetic substances because they are comparatively cheaper, abundantly available, non irritating and nontoxic in nature.

Some natural polymer provides the fast disintegration as synthetic superdisintegrants. Recently some gums and mucilages have been investigated to improve the disintegration processes.

**Plantago ovata seed mucilage**

Psyllium or Ispaghula is the common name used for several members of the plant genus Plantago whose seeds are used commercially for the production of mucilage. Mucilage of *Plantago ovata* has various characteristics like binding, disintegrating and sustaining properties[5].

In an investigation fast disintegrating tablets of Amlodipine Besylate was prepared by direct compression method using different concentrations of *Plantago ovata* mucilage as a natural superdisintegrant. All formulations were evaluated for weight variation, hardness, friability, disintegration time, drug content and dissolution. The optimized formulation shows less in vitro disintegration time 11.69sec with rapid in vitro dissolution within 16 mins. In vitro disintegration time decreases with increase in concentration of natural superdisintegrant. The conclusion is clear that the dried isabgol mucilage as a superdisintergrant in the tablet is suitable for the formulation of fast disintegrating tablet[6].

In another investigation N. G. Raghavendra Rao et al studied that fast dissolving tablets of poorly soluble drug, carbamazepine showing enhanced dissolution, will lead to improved bioavailability, improved effectiveness and hence better patient compliance by using natural superdisintegrant like *Plantago ovata* mucilage. In their study fast dissolving tablets of the carbamazepine was developed by wet granulation method, using different concentrations of natural superdisintegrating agent like *Plantago ovata* seed powder and mucilage. Prepared formulations were evaluated for hardness, friability, in vitro disintegration time, wetting time and dissolution test. The formulations prepared with mucilage of *Plantago ovata* were showed disintegration time between the ranges of
84.58 to 24.74 sec and drug release showed between the ranges of 14 – 16 min. However the formulations prepared with seed powder did not disintegrate in specified limit of time for fast dissolving tablet. The optimized formulations showed 99.71 % drug release within 16 min[7].

In another approach fast dissolving tablets of Granisetron hydrochloride was prepared using plantago ovata mucilage and sodium starch glycolate as super disintegrants (2.5 to 10 % w/w) following by direct compression method. Formulations were evaluated for precompressional parameters such as angle of repose, carr’s compressibility index and hausner’s ratio. The tablets were evaluated for uniformity of weight, thickness, hardness, friability, drug content, wetting time, and in-vitro dispersion time and in-vitro dissolution study. The prepared tablets were characterized by FTIR studies. No chemical interaction between drug and excipients was confirmed by FTIR studies. The formulations GPO4 and GSG4 shows drug release within 5 & 8 min. Compare to sodium starch glycolate formulations, plantago ovata formulations shows faster release of drug, this is due to more swelling property of plantago ovata mucilage. In case of formulation GPO4, the 50% and 90% of drug release was found within 0.43 and 2.51min[8].

Lepidium sativum mucilage

Lepidium sativum (family: Cruciferae) is known as asaliyo and is widely used as herbal medicine in India. It is widely available in market and has very low cost. Parts used are leaves, root, oil, seeds etc. Seeds contain higher amount of mucilage, dimeric imidazole alkaloids lepidine B, C, D, E and F and two new monomeric imidazole alkaloids semilepidinoside A and B. Mucilage of Lepidium sativum has various characteristic like binding, disintegrating, gelling etc. The mucilage is extracted from seeds of Lepidium sativum.

Recently a study was performed on disintegrating property of Lepidium sativum mucilage. Kalpesh K. Mehta et al developed fast dissolving tablets of Nimesulide containing natural Lepidium sativum mucilage. The disintegration property of extracted mucilage in FDTs was compared with widely used superfdisintegrants like Sodium starch glycolate (SSG), Kyron T314, Ac Di Sol. The prepared FDTs were evaluated for Uniformity of weight, Hardness, Tablet thickness, Percentage friability, Wetting time, In
In vitro disintegration time and in vitro dissolution. From the study, it was concluded that higher dissolution of tablet could be obtained when mucilage concentration is 10% and also the mannitol concentration was 10%. Promising optimized batch exhibited better drug dissolution (79.9%) after 30 min than the other tablets. The disintegration and mean dissolution time for this batch was 17 sec and 5.27 sec respectively is better than other tablet prepared from other synthetic disintegrating agent [9].

Gum karaya

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 [10]. The high viscosity nature of gum limits its uses as binder and disintegrant in the development of conventional dosage form. Gum karaya gum has been investigated for its potential as a tablet disintegrant. The results showed that modified gum karaya produce rapid disintegration of tablets. The optimized formulation showed acceptable physical characteristics. The optimized batch produced complete drug release within 6 minutes. The incorporation of clove oil provided additional properties such as symptomatic relief from nausea and vomiting, good mouth feel and taste masking. Kinetic analysis showed that drug release from optimized formulation was adequately described by first order release kinetics. Gum karaya can be used as an alternative superdisintegrants to commonly available synthetic and semisynthetic superdisintegrants due to their low cost, biocompatibility as well as easily availability [11].

Fenugreek seed mucilage

Trigonella Foenum-graceum, commonly known as Fenugreek, is an herbaceous plant of the leguminous family. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). Although 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 [12].

Ravi Kumar et al in a study was investigated Trigonella foenum-graceum as disintegrant for use in mouth dissolving tablet formulations containing metformin hydrochloride. Mucilage extracted from fenugreek seeds were subjected to toxicity
studies, it showed that extracted mucilage is devoid of toxicity. Fast disintegrating tablet (FDT) of metformin HCl was formulated using different concentration (2, 4, 6 8 and 10% w/w) of natural disintegrant viz; isolated mucilage of fenugreek seed and synthetic superdisintegrants like croscarmellose sodium and were compared. Disintegration time and drug release were taken as the basis to optimize the rapidly disintegrating tablet. Prepared tablets were evaluated for thickness, hardness, friability, uniformity of weight, disintegration time, wetting time and dissolution study. The formulated tablets had good appearance and better drug release properties as compared to the marketed conventional tablets. Fenugreek mucilage in the concentration of 4 % gives shorter disintegration in 15 sec. and shows 100% drug release within 18 min.

Hence, the study revealed that this natural disintegrant (fenugreek mucilage) showed better disintegrating property than the most widely used synthetic superdisintegrants like Ac-di-sol in the formulations of FDTs. Studies indicated that the extracted mucilage is a good pharmaceutical adjuvant, specifically a disintegrating agent. Optimized formulation was subjected to stability studies as per ICH guidelines at 250 and 65% RH, 40° and 75% RH showed insignificant change in hardness, disintegration time and in vitro drug release at the end of three months.[13]

Mango peel pectin

Mango peel which constitutes 20–25% of the mango processing waste was found to be a good source for the extraction of pectin of good quality, suitable for the preparation of fiim and acceptable jelly. Pectin is a complex hetero-polysacharides which is a hydrophilic colloid[14]. Rishabha Malviya et al investigated that mango peel pectin stand as a good candidate as superdisintegrant though, not as stronger as synthetic superdisintegrant but due to its good solubility and higher swelling index, it may be used in the formulation of fast dispersible tablets[15].

Agar and treated agar

Agar is the dried gelatinous substance obtained from Gelidium Amansii (Gelidaceae) and several other species of red algae like, Gracilaria (Gracilariaceae) and Pterocadia (Gelidaceae).

Agar is yellowish gray or white to nearly colorless, odorless with mucilaginous taste and is available in the form of strips, sheet flakes or coarse powder. Agar consists of
two polysaccharides as agarose and agaropectin. Agarose is responsible for gel strength and Agaropectin is responsible for the viscosity of agar solutions. High gel strength of agar makes it a potential candidate as a disintegrant. The treated agar mucilage is prepared by dissolving 5-10 gm powder in 100ml of distilled water. Agitation was done continuously by a stirrer for one day to swell the contents. The swollen contents were dried on a tray for 3 days at room temperature. The dried powders were grinded by mortar and pestle\textsuperscript{[16]}. Then grinded powder was passed through sieve no.100.

Prabhu Halakatti et al developed Mouth dissolving tablets or fast dissolving tablets of cinnarazine by direct compression method. Addition of superdisintegrants and natural polymers were used each containing different concentration each group with five formulations. Pre-compression parameters and post-compression parameters were evaluated for all the ten formulations. I.R. study revealed that all polymers and excipients used were compatible with the drug. The time required for complete wetting of all the formulations was found between 22 and 43 seconds. Water absorption ratio was found in the range of 82 - 85. The time taken for the \textit{in vitro} disintegration and \textit{in vitro} dispersion were found in the range of 9 - 13 sec, 20 - 28 sec, respectively. All formulations showed good palatable mouth feel. \textit{In vitro} drug release showed almost 90% of the drug was released from all formulations within 15 minutes. Thus crospovidine and treated agar proved best disintegrants. it may be concluded that the mouth dissolving tablets can be prepared by treated agar are more palatable and less expensive\textsuperscript{[17]}. Guar gum

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 endosperm of the seed of the guar plant, \textit{Cyamopsis tetragonoloba} (L) Taub. (syn. \textit{Cyamopsis psoraloides}). It is used as thickener, stabilizer and emulsifier, and approved in most areas of the world (e.g. EU, USA, Japan, and Australia)\textsuperscript{[18]}. It is naturally occurring gum (marketed under the trade name jaguar). It is free flowing, completely soluble, neutral polymer composed of sugar units and is approved for use in food. It is not sensitive to pH, moisture contents or solubility of the tablet matrix. It is not always pure white and sometimes varies in color from off-white to tan tends to discolor with time in alkaline tablets\textsuperscript{[19]}. 

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Vijay Sharma et al developed a dosage form that was easy to administer and provides rapid release of the drug roxithromycin, using modified polysaccharides as rapidly disintegrating excipients. Modified polysaccharides co-grinded treated agar (C-TAG) and co-grinded treated guar gum (C-TGG) were prepared by subjecting pure polysaccharides namely agar and guar gum respectively to sequential processes of wetting, drying and co-grinding with mannitol (1:1). The modified polysaccharides were characterized by Scanning Electron Microscopy and Diffuse Reflectance Spectroscopy and evaluated for particle size distribution, derived properties, swelling index and biodegradability. Optimization studies based on 22 factorial designs, with friability and disintegration time as response parameters were used to formulate orodispersible tablets of roxithromycin and evaluated for wetting time, water absorption ratio and in vitro drug release at salivary pH 6.4 and physiological pH 7.4. Results indicated that lower levels of modified polysaccharides namely C-TAG in F3 and C-TGG in F7 and higher levels of microcrystalline cellulose, exhibited least disintegration times without friability concerns. In vitro release of optimized formulations F3 and F7, both at salivary pH and physiological pH was found to be more than 90% within 30 min as compared to 27.82% at the same time point of conventional formulation. Stability studies carried out as per ICH Q1A guidelines suggested the formulations to be stable for a period of 6 months. Thus the approach of using modified polysaccharides as fast disintegrating excipient can be used to formulate a stable orodispersible formulation.[20]

Gellan gum

Gellan gum is a water-soluble polysaccharide produced by Pseudomonas elodea, a bacterium. Gellan gum is an anionic, high molecular weight, deacetylated exocellular polysaccharide gum produced as a fermentation product by a pure culture of Pseudomonas elodea[2], with a tetrasaccharide repeating unit of one α-L-rhamnose, one β-D-glucuronic acid and two β-D-glucose residues.[21, 22]

Antony et al 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 102), Ac-di-sol, and Kollidon CL. The disintegration of tablet might be due to the instantaneous swelling characteristics of gellan gum when it comes into contact with water and owing to its high hydrophilic nature. The complete disintegration of tablet was
observed within 4 minutes with gellan gum concentration of 4 percent w/w and 90 percent of drug dissolved within 23 minutes. Ac-di-sol and Kollidone CL showed very similar pattern of disintegration and in vitro dissolution rates. With the same concentration tablet made with starch showed 220 minutes. From this result gellan gum has proved itself as a superior disintegrant.[23]

Soy polysaccharide

It is a natural superdisintegrant that does not contain any starch or sugar so can be used in nutritional products.

Sanyasi R et al evaluated soy polysaccharide (a group of high molecular weight polysaccharides obtained from soy beans) as a disintegrant in tablets made by direct compression using lactose and dicalcium phosphate dihydrate as fillers. A cross-linked sodium carboxy-methyl cellulose and corn starch were used as control disintegrants. Parameters studied were compressibility, friability and disintegration times. Dissolution studies were conducted on tablets containing hydrochlorothiazide as a model drug of low water solubility. Soy polysaccharide performs well as a disintegrating agent in direct compression formulations with results paralleling those of cross-linked CMC at the 2% level and superior to corn starch at the 8% level. Dissolution rates of the drug from tablets were rapid, particularly at the 5% level and were not adversely affected by aging at room temperatures[24].

Chitin and chitosan

Chitin (β-(1→4)-N-acetyl-D-glucosamine) is a natural polysaccharide obtained from crab and shrimp shells. It possesses amino group covalently linked to acetyl group as compared to free amino group in chitosan[25, 26]. 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. Bruscato et al reported that when chitin was included in the conventional tablets, the tablets disintegrated with in 5n10 min irrespective of solubility of the drug. The disintegration time in the oral cavity as well as wetting time could be analyzed by surface free energy[27]. Chitosan is the best known natural polysaccharide used for its versatile applications in pharmaceutical industry.

Mitesh Nagar et al utilized superdisintegrant property of chitosan to develop a fast mouth dissolving tablet by utilizing a novel method of treatment which can replace
any other superdisintegrant. The properties of the rapidly dispersible tablet, such as porosity, hardness, disintegration time, wetting time and dissolution time, were investigated accordingly and the formulation was optimized as per 3 level full factorial design and analysed for response surface methodology to decide the best formulation which further evaluated for in-vitro performances. Fast mouth dissolving or OroDispersible tablets (ODTs) of Cinnarizine with acceptable compression parameters and pleasant mouth feel prepared within the optimum region hence Cinnarizine OroDispersible tablets (CODT) upon administration disperse in mouth as soon as in contact with saliva and release the drug content immediately which can be absorbed directly through oral mucosa or can be swallowed without the aid of water hence provide faster and better therapeutics\(^{[28]}\).

In another investigation the fast disintegrating tablets of ondansetron HCl was developed by using novel superdisintegrants, possessing sufficient mechanical strength and disintegration time comparable to those containing crospovidone or croscarmellose sodium. The FDTs were formulated using a novel superdisintegrant (chitosan-alginate (1:1) interpolymer complex and chitin) to achieve a sweet tasting disintegrating system. The results revealed that chitin (5\(n\)20\%) increased the porosity and decreased the DT of tablets. At higher concentrations chitin maintained tablet porosity even at 5.5 kg crushing strength. Ondansetron HCl was found to antagonize the wicking action of glycine. Further, evaluation of the mechanism of disintegration revealed that glycine transported the aqueous medium to different parts of the tablets while the chitosan-alginate complex swelled up due to transfer of moisture from glycine. This phenomenon resulted in breakage of the tablet within seconds. For preparing optimized FDTs, the reduced model equations generated from BoxnBehnken design (BBD) were solved after substituting the known disintegration time of FDTs containing superdisintegrants in the reduced model equations. The results suggested that excipient system under investigation not only improved the disintegration time but also made it possible to prepare FDTs with higher crushing strength as compared to tablets containing known superdisintegrants\(^{[29]}\).
REFERENCE


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