Available online on 15.04.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Review Article

A review on natural and synthetic polymers employed in the formulation of oral disintegrating tablets

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ABSTRACT

The oral route is the most popular route of administration for numerous drugs because it is considered as a safest, most preferred and less economical. Disintegrating agents are the substances that disperse or dissolve within a matter of seconds. This disintegrating mechanism helps in dysphagia, pediatric and geriatric patients. Synthetic disintegrating agents are available as a highly economical and less effective when compared to natural disintegrating agents. Therefore natural disintegrants serve as the best alternative to overcome the problems of these synthetic substances. Due to their numerous advantages over synthetic products they are widely used in the pharmaceutical field as a binder, disintegrants, gums, and mucilages.

Keywords: Disintegrants, dysphagia, synthetic substances.

Article Info: Received 23 Feb 2019; Review Completed 30 March 2019; Accepted 05 April 2019; Available online 15 April 2019

Cite this article as:

Madhulika G.S.S.V., Ramya Kuber B., A review on natural and synthetic polymers employed in the formulation of oral disintegrating tablets, Journal of Drug Delivery and Therapeutics. 2019; 9(2-s):652-658

http://dx.doi.org/10.22270/jddt.v9i2-s.2553

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INTRODUCTION

Disintegrants are the substances that are intended to break-up the tablet matrix into small fragments in the presence of an aqueous environment thereby increasing the surface area and providing a more rapid drug release of the drug substance. They provide moisture penetration and dispersion of the tablet matrix. Tablet disintegration is considered as a rate-limiting step in the faster drug release. There are a number of factors that affect the disintegration replace tablets. The disintegrants have several functions to oppose the efficiency of the tablet binder and the external forces like compression of the tablet. The more strength of the binder, the more effective must be the disintegrating agent's in-order to release drug from the tablet matrix. Disintegrants are the main component in the tablet formulations. It should cause the tablets to disperse, not only into the granules when it was compressed but also into powder particles from which the granulation was prepared. The mechanism of tablet disintegration action includes swelling, wicking, and deformation.

There are 3 methods to incorporate disintegrating agents into the tablet formulation:

A) Internal addition (Intragranular)

B) External addition (Extragranular)

C) Partly internal and external

Disintegrants that are incorporated in the granulated formulation process are most effective if utilized both "Intragranular and Extragranularly" thereby promoting the tablet to break-up into small granules and further disintegrate to release the drug into solution. However, the disintegrant added in the wet granulation process is not as effective as that of dry granulation process results in reduced activity of the disintegrate. Hence, A compaction process does not involve its exposure to wetting and drying, the disintegrate using intragranularly is considered to be good disintegration activity [1-2].

The oral route is preferred as the most accepted route for the delivery of drugs. Different kinds of dosage form administered orally among them solid dosage forms are popular because of its:

- Ease of preparation
- Ease in administration
- Accurate Dosing
- Self-medication

- Stability related to oral liquids
- Safest and economical route
- Compaction
- Patient compliance

Patient compliance is one of the most important topics in pharmacy practice. Now- days, In pharma industry development of new drug delivery system to ensure the delivery of the drugs to the patients efficiently and with fewer side effects. A solid dosage form allows difficulty in swallowing for pediatric, geriatric, mentally retarded and for traveling patients who do not have immediate access to water. Therefore, recent advances in novel drug delivery system have shown a better result in the convenient dosage form for administration and to achieve better patient compliance known as fast dissolving tablets or orally disintegrating tablets or mouth melting tablets or mouth dissolving tablets.

Fast dissolving tablets is a solid dosage form containing medicinal substances that disintegrate rapidly in saliva, within a matter of seconds in the absence of water. When compared to the conventional dosage form this disintegrating tablet has greater drug dissolution and absorption. When these oral disintegrating tablets placed in the oral cavity, saliva easily enters into the pores and causes rapid tablet disintegration. The small volume of saliva is sufficient for the tablet disintegration in the oral cavity (Jyoti V et al., 2017). Saliva containing medication is absorbed partially or entirely into the systemic circulation through blood vessels or it can be directly swallowed as a solution in the gastrointestinal tract. Addition of disintegrants in oral disintegrating tablets leads to faster disintegration of tablets leads to good dissolution.

- Fast dissolving tablets are formulated mainly by 2 techniques:

1. By the addition of disintegrants.
2. The maximizing pore structure of the tablets by freeze drying and vacuum drying.

Ideal properties of disintegrants:

- Low solubility
- Low gel formulation
- Improved hydration capacity
- Good compressibility
- Good flow properties
- Should not form complexes with the drugs [3-5].

ADVANTAGES OF ORAL DISINTEGRATING TABLETS

1. Improved compliance/added convenient new business opportunities, product differentiation, line extension, lifecycle management, exclusivity of product production and patent life extension.
2. No need of water and chewing.
3. Suitable for controlling/ sustained release activities
4. Ability to provide advantages of liquid medication in the form of solid preparation.
5. Improved stability
6. Adaptable and amendable to existing processing and packaging materials.
7. Cost effective.
8. Rapid drug therapy intervention.
9. Best for patients with esophageal problems.
10. High drug dosing is possible.
11. Have an acceptable taste and pleasant mouth feeling.
12. No specific packaging is necessary.

LIMITATIONS OF ORAL DISINTEGRATING TABLETS

1. Drugs with relatively larger doses difficult to formulate ODT.
2. Tablets which have insufficient mechanical strength.
3. They are sensitive to humidity and temperature.
4. Drugs with a shorter half-life and frequent dosing are unsuitable to formulate ODT.
5. Patients who frequently take anti-cholinergic medication may not be good candidates for these tablet formulations [1, 4].

MECHANISM OF DISINTEGRATION [3-6]

Swelling:

Swelling is considered as the most accepted mechanism in tablet disintegration. By swelling in contact with the particles enlarge Omni-directionally to push apart the adjoining component in tablet results in the break-up of the tablet matrix. The swelling capacity of a disintegrant depends on several factors like chemical structure and degree of cross-linking. A porous tablet matrix with large void spaces increases the efficiency of tablet disintegration whereas low porosity tablet matrix decreases the efficiency of tablet disintegration. Hence, porosity plays a major part in disintegration phenomena. The amount of disintegrant and swelling capacity plays an important role in formulating a tablet dosage form. The swelling capacity of some disintegrants is affected by p^H conditions.

Wicking:

It is defined as the process of liquid enters into the tablet matrix through capillary action to displace the air. Porosity helps to penetrate fluid into a tablet matrix and replaces the air adsorbed on the particles, therefore, weakens the intermolecular bond and break the tablet into small pieces. Effective disintegrants with low cohesiveness and compressibility enhance the porosity of the tablets. Some superdisintegrants like crospovidone and pyrrolidone quickly wicks saliva into the tablet to provide rapid disintegration. Recent investigations proved that the water sorption properties of several tablet disintegrants are efficacy with high rates of water uptake. **(Fig. 1)** shows the mechanism of action of wicking and swelling in disintegrating tablets.

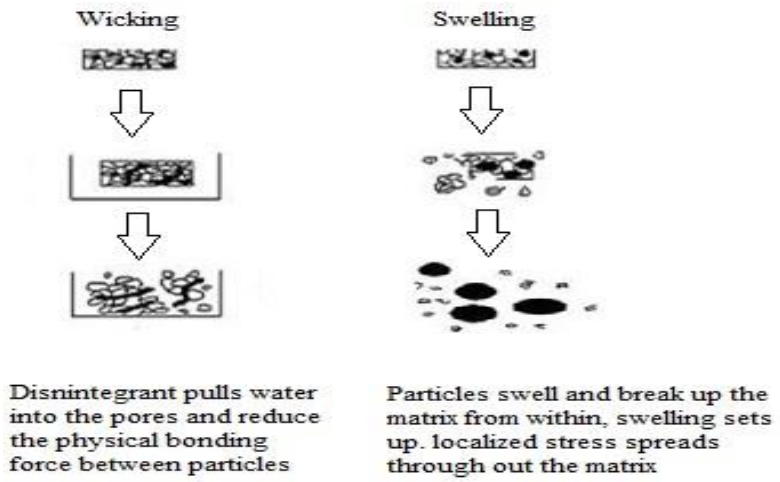

Figure 1: Disintegration of tablets by Wicking and Swelling mechanism

Particle-particle repulsive forces:

This mechanism explains the swelling properties of non-swellable disintegrants. Guyot-Hermann has proposed a theory known as particle repulsion based on this theory non-swellable particles also cause disintegration of the tablet matrix. Mechanism of disintegration depends upon the electric repulsive forces between the particles and water is the main requirement in this phenomena. According to this theory, the water enters into a tablet through hydrophilic pores and a continuous starch network is created that can cause of entry of water from one particle to the neat, providing significant hydrostatic pressure. The water that penetrates between the particles causes the breaking of hydrogen bonds and other forces that holding the tablet.

Strain recovery/ Due to deformation:

During tablet manufacturing, tablet constituents are subjected to high compaction pressure. Due to compaction, particles deform and return to their pre-compression shape upon wetting, thereby this increase in the size of a deformed particle causes the tablet to break into small pieces. Strain recovery is the reversible process of deformation. This phenomenon is an important part of tablet disintegration such as crospovidone and starch exhibits little or no swelling. **(Fig.2)** shows the mechanism of action of deformation and repulsion in disintegrating tablets.

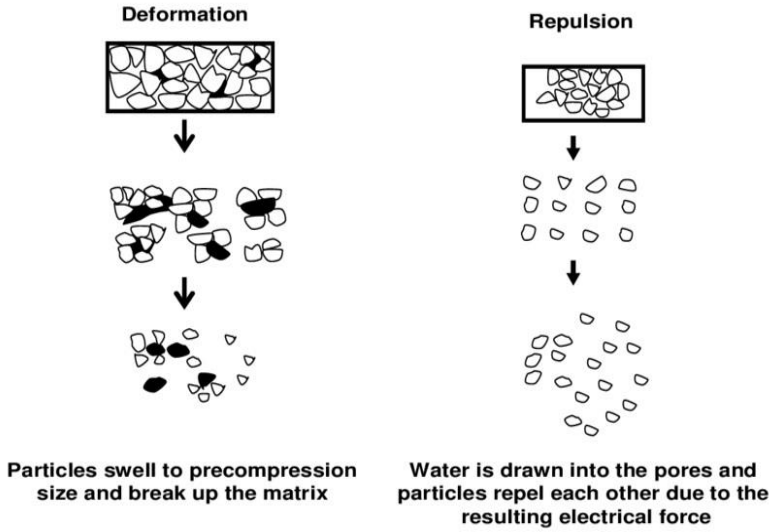

Figure 2: Disintegration of tablets by Deformation and Repulsion

Heat of interaction / Heat of wetting:

When disintegrants with exothermic properties interact with the aqueous medium, localized stress is created due to capillary air expansion, which causes disintegration of the tablet matrix. If heat generation was an important mechanism of disintegration then break-up would have occurred during compaction. Increase in temperature of the aqueous medium causes no change in the disintegration process. This mechanism is limited to a few types of disintegrants.

Chemical reaction/ Due to release of gases:

The tablet disintegration is caused due to pressure within the tablets. In case of effervescent tablets carbon dioxide released within tablets on wetting due to the interaction between bicarbonate and carbonate with citric acid or tartaric acid. As these disintegrants are highly sensitive to

humidity level strict control of the environment is required during the manufacturing of tablets.

Enzymatic reactions:

Some enzymes present in our body acts as a disintegrant. These enzymes decrease the binding action of binder and help in disintegration. In swelling, the pressure is exerted in outer region that causes the tablet to burst and promotes disintegration. List of enzymes used as a disintegrating agent are specified in **(Table 1)**.

Table 1: Examples of enzymes as disintegrating agents

Enzyme	Binder
Amylase	Starch
Protease	Gelatin
Cellulose	Cellulose and its Derivatives
Invertase	Sucrose

DESCRIPTION ON SYNTHETIC POLYMERS

These are most commonly used disintegrants in oral disintegrating tablets to improve the rate and extent of tablet disintegration, therefore, increases tablet dissolution.

Advantages

- Effective in low concentrations
- More effective intragranularly
- Less effect on compressibility and flowability

Limitations

✓ Sensitive to moisture

Sodium starch glycolate

It is also known as carboxymethyl starch sodium salt, explotab, primojel, and Viva-star P. it is white to white-off, freely flowing and practically tasteless, odorless powder. It consists of an oval or spherical granules 30-100µm in diameter. It is sparingly soluble in ethanol and practically insoluble in water and settles in the form of a highly hydrated layer. Tablets which are prepared by using sodium starch glycolate have good storage life. It is stable and should be stored in a closed container to protect it from wide variation in humidity and temperature to avoid caking. The physical properties of Sodium starch glycolate remain unchanged up to 4 years if stored at a moderate temperature and humidity conditions. It is widely used in oral pharmaceuticals as a disintegrant in tablet and capsule formulations. It is mostly used in tablets prepared by either direct compression or wet granulation process. The usual concentration employed in a formulation is 2-8%.

Low-substituted hydroxypropyl cellulose

It is white to slightly yellow powder. It is insoluble in water or practical organic solvents and soluble in 10% NaOH as a viscous and turbid solution. It is used as a disintegrant with low chemical side reactivity, for direct compression and pelletization (fast disintegrating pellets).

Crospovidone

It is also known as crosslinked povidone, polyvinyl pyrrolidone and polyplasdone. It is freely soluble on acids, chloroform, ethanol (95%), ketones, methanol, and water. It is a white to creamy white in color, with a free-flowing property, tasteless, odorless and hygroscopic in nature. It may be stored under ordinary conditions without undergoing decomposition or degradation. Due to its property of being hygroscopicity, it should be stored in an airtight container in a cool, dry place. It is widely used in a variety of pharmaceutical formulations. It is generally regarded as a non-toxic and non-irritating excipient [7].

Croscarmellose sodium

It has a high swelling capacity and effective at low concentration. It is a crosslinked polymer of carboxymethyl cellulose. In tablet formulation, it may be used in both direct compression and wet granulation. It should be added in both intra and granularly so that wicking and swelling properties may be increased. The disintegration action of croscarmellose sodium is higher than that of sodium starch glycolate and the mechanism of cross-linking is different [2-3].

Microcrystalline cellulose

It is also known as Avicel. It's mechanism of action generally involves entry of water by means of capillary pores results in the breakdown of hydrogen bonds present between adjacent bundles of cellulose microcrystals and exhibits effective disintegration. It is partially depolymerized cellulose prepared from alpha cellulose. In tablet formulation, it may be used in direct compression method. It acts as a disintegrant in the concentration range of 5-15% [2]. List of synthetic superdisintegrants employed in oral disintegrating tablets is specified in **(Table 2).**

Table 2: Synthetic superdisintegrants employed in oral disintegrating tablets

Synthetic polymers	Properties	Effective concentration for disintegration
Crospovidone	It is completely insoluble in water. It has a high swelling index when compared to other disintegrating agents	It is used in the range of 1-3% w/w
Croscarmellos sodium	It is insoluble in water and swells up to 4-8 times its in original volume in contact with water	It is used in the range of 5% w/w
Sodium starch glycolate	Absorbs water rapidly, resulting in swelling up to 6% concentration	It is used in the range of 4-6%

DESCRIPTION ON NATURAL POLYMERS

These are various plant-based materials. Plant-based materials serve as an alternative to synthetic products because of the following reasons:

- Local availability
- Having a renewable source
- Low cost
- Biodegradable
- Eco-friendly

Agar and treated agar:

It is the dried gelatinous substances obtained from *gelidium amansii* (gelidanceae) and several other species of red algae

like *Gracilaria* and *Pterocladia*. Agar is a yellowish gray or white with mucilaginous taste and is available in the form of divests, sheet flakes, or coarse powder. Agar consists of two polysaccharides agarose and agaropectin. Agarose is

Guar gum:

It is a high molecular weight polysaccharide extracted from the seeds of *Cyamopsis tetragonaloba* which has thickening and stabilizing properties used in the food and industrial application. It is available in marketed form as jaguar [8]. Guar gum of natural origin is preferred over synthetic or semi-synthetic substances because it is relatively cheaper, easily available, non-irritating, and non-toxic. In pharmaceutical application, it is widely used as binder and disintegrant and also been investigated in the preparation of sustained release matrix tablets in the place of cellulose derivatives such as methylcellulose [9].

***Cucurbita maxima* pulp powder:**

It is commonly known as pumpkin, belongs to the family Cucurbitaceae. The study revealed that Cucurbita maxima pulp powders have comparable dissolution behavior to that of sodium starch glycolate. It also has the same hardness and friability thus it stands as a disintegrant and polymer in fast dissolving tablets [3].

Gum karaya or Tragacanth:

It is also known as gum sterculia or Indian gum tragacanth is a vegetable gum obtained from the trees of the genus *Sterculia.* Chemically, gum karaya is an acid polysaccharide composed of the sugar galactose, rhamnose, and galacturonic acid. Due to its viscous nature, it is used as a binder and disintegrant in the development of conventional dosage form [8]. Studies revealed that modified gum karaya produces rapid disintegration and utilized as a super disintegrant due to its low cost, biocompatibility with other plant hydrocolloids as well as proteins and carbohydrates [5].

Soy polysaccharide:

It is a fibrous carbohydrate material obtained from the cell wall structural components of soybeans that include soy flakes primarily cell wall material of the soybean cotyledon [12]. This natural super disintegrant does not contain any starch or sugar so it can be used in nutritional purpose. High molecular weight polysaccharide obtained from soybean used as a disintegrant in tablets [5]. Soy polysaccharide includes mainly cellulose, arabinogalactan, arabinan and an acidic polysaccharide complex [11].

Chitin and chitosan:

Chitin is naturally obtained from the crabs and shrimp shells. It contains amino group covalently linked to the acetyl group as compared to a free amino group in chitosan. Chitosan is produced by deacetylation of chitin, which is a structural element in the exoskeleton of crustacean (crabs and shrimps) and cell wall of fungi. Chitin was included in the conventional tablets, the tablet disintegration time was found to be 5 to 10 minutes irrespective of solubility of the drug [13]. Studieshad shown that Callinectes chitosan is suitable for use as a super disintegrant in tablets, it appears to be superior to cornstarch as a disintegrating agent [14].

Gellan gum:

Gellan gum is high molecular weight water-soluble anionic polysaccharides of linear tetrasaccharides derived from *Pseudomonas elodea* having good super disintegrant property similar to the modified starch and cellulose [15]. The disintegrating action of gellan gum is due to its swelling nature when it comes to contact with water and owing to its high hydrophilic nature [8].

responsible for gel vigor and agaropectin is responsible for the viscosity of agar solutions. High gel vigor of agar makes it a potential candidate as a disintegrant [8].

Xanthum gum:

It is produced by the bacteria *Xanthomonas campestris* is official in USP with high hydrophilicity and low gelling tendency. It has low water solubility and extensive swelling properties for faster disintegration. It is a heteropolysaccharide consisting of repeated pentasaccharide units formed by 2 glucose units, 2 mannose units, and one glucuronic acid units [15].

***Cassia fistula* gum:**

Cassia fistula is commonly known as the golden rain tree belongs to the family Fabaceae. The gum obtained from the seeds of *Cassia fistula* containing β-(1,4) linked d-mannopyranose units with a random distribution of α-(1,6) linked d-galactopyranose units as side chain having mannose galactose ratio of 3.0 [5]. Carboxymethylation of *cassia fistula* seed showed better swelling properties than that of crude gums. It is further used as a disintegrant, diluent and drug release controlling agent in the pharmaceutical industry [16].

Fenugreek seed mucilage:

Trigonella foenum graceum commonly known as fenugreek belongs to the family Leguminosae. A fenugreek seed contains a high percentage of mucilage functions as a disintegrant, food preservatives [3]. Mucilage is an off-white cream yellow color amorphous powder that quickly dissolves in warm water to form viscous colloidal solution[3]. Studies revealed that this natural disintegrant showed better disintegrating property than synthetic superdisintegrants like Ac-di-sol in the formulation of oral disintegrating tablets [8].

***Portulaca oleraceae* mucilage:**

It is commonly known as red root and pursely. It belongs to the family portulaceae. The leaf contains omega-3-fatty acids and dietary minerals. It is used as a natural disintegrant in the formulation of fast dissolving tablets; studies revealed that the results obtained from the *portulaca oleraceae* mucilage are better than those of conventional commercial formulations [18].

Mango peels pectin:

Mango peel contains 20-25% of mango processing waste used as a good source for the extraction of pectin of good quality used for the preparation of film and jelly. Pectin is a heteropolysaccharide which as hydrophilic colloid [5]. Naturally obtained mango peel pectin stands as a good candidate to act as a super disintegrant. Due to its good solubility and higher swelling index it may be used in the formulation of the fast disintegrating formulation [10].

***Lepidium sativum* mucilage:**

Lepidium sativum also known as saliyo belongs to the family Cruciferae. It has major scope in herbal medicine and as a disintegrating agent. The seed contains a high amount of mucilage, dimeric imidazole alkaloidslepidine B, C, D, E and F and two new monomericimidazole alkaloids semi lepidinoside A and B [5]. The mucilage can be extracted from the seeds by different procedures and its yield varies from 14% to 22%. Mucilage has various properties like binding, disintegrating, gelling etc. Extracted mucilage was used to develop fast dissolving tablets. Mucilage is found to be a

brownish white powder which decomposes above 200^{0}C and has a characteristic odor [3].

Ispaghula husk mucilage:

Ispaghula husk mucilage is obtained from the seeds of *Plantago ovate*. The plant contains mucilage in the epidermis of the seed[5]. This mucilage contains a variety of properties like binding, suspending and easily dispersible agent in the pharmaceutical industry. Extracted mucilage also used as a matrix for entrapment and delivery of various drugs, proteins, and cells [19]. Mucilage can be used as a super disintegrant to formulate quick release tablets because it has a high swelling index [5].

***Aegle marmelos* gum:**

It is commonly known as bael belongs to the family Rutaceae. The fruit pulp is red in color with a mucilaginous and astringent taste. The pulp contains carbohydrates, proteins, vitamin C, vitamin A, angelenine, marmeline, dictamine, O-methyl fordinol, and isopentyl halfordinol. It is prepared by heat treatment technique. It is used in the case of diabetic condition to increase glucose levels in diabetic patients [5]. It is widely used in pharmaceutical industries as a binder, disintegrant, and additive due to their low toxicity, biodegradable, availability and low cost [20].

Locust bean gum:

It is also known as carbogum, carob bean. It is a vegetable gum extracted from the seeds of the carob tree mostly found in the Mediterranean region. In the food industry, it is widely used as a thickening and gelling agent. It has also been reported to have bioadhesive and solubility enhancement properties. Swelling index was found to be 2000 which point towards good swelling competency of locust bean gum [21]. It shows as a binder and disintegrant at different concentrations [5].

***Ficus indica* fruit mucilage:**

Opuntia ficus indica mill belongs to the family Cactaceae. *Ficus indica* fruit mucilage was a natural polysaccharide that contains arabinose, rhamnose, galactose and xylose [22]. *Ficus indica* fruits are of the size of a cherry. Mucilage of *ficus indica* fruit is used as a super disintegrant. It is mainly used in the treatment of fever, pain, inflammation, wound rejuvenating and blood quandaries [5].

***Hibiscus Rosa Sinensis* mucilage:**

It is also known as shoe-flower plant belongs to the family Malvaceae. It is abundantly available in India and the leaves contain mucilage. This mucilage contains L-rhamnose, D-galactose, D-galacturonic acid and D-glucuronic acid [5]. Studies revealed that disintegrating property of this mucilage powder had shown better disintegrating property than the most widely used synthetic super disintegrant like Ac-di-sol in the fast release formulations [23].

***Ocimum americanum* seed mucilage:**

It is also known as American basil. It is an annual herb with a white or lavender flower. It contains a higher portion of mucilage. Studies revealed that the mucilage separated from *Ocimum americanum* linn could be used as a disintegrant in the tablet formulations as it shows very good disintegrating property [24].

***Mangifera Indian* gum:**

It is a dried gummy exudates polysaccharide obtained from the bark of *Mangifera indica* belongs to the family Anacardiaceae. It is mainly used as a tablet binder, disintegrant, suspending and emulsifying agent [25]. Disintegrating property of this gum was also studied. Tablets containing this gum should good appearance and better drug release [26]. The gum powder is white to off-white in color and the powder was soluble in water and virtually insoluble in acetone, chloroform, ether, methanol, and ethanol. Every component of the tree has a pharmacological activity like diuretic, astringent, diabetes and asthma [5].

Banana powder:

Banana powder is made from processed bananas and it is rich in dietary fiber. Studies showed that the disintegrant property of banana powder in the formulation of mouth dissolving tablet has shown the best results. The disintegration time obtained by tablets with banana powder was comparable to that obtained with other commonly used disintegrants; hence it can be used very effectively in the formulation of fast dissolving tablets. It is used as a potential pharmaceutical excipient in various solid dosage forms especially in fast dissolving tablets [27]. Literature review on applications of various polymers is specified in **(Table 3)**.

Table 3: A Literature review on applications of various polymers

S.N.	Polymer	Drug	Results	Ref
1.	Aegle marmelos gum	Ibuprofen	Tablets containing disintegrant concentration of 2% shows better disintegration time and with a high percentage of drug release	20
2.	Chitosan	Metronidazole	No adverse interaction between chitosan and metronidazole was observed. The disintegration time of tablets containing 2,4 and 8% chitosan were 12.2, 10.4 and 9.3 min respectively	14
3.	Cucurbita maxima pulp	Telmisartan	The results proved that a lesser amount of Cucurbita maxima starch is required as disintegrant (10%)w/w than corn starch to show the best disintegrating activity	28
4.	Fenugreek seed mucilage	Metformin	Fenugreek mucilage in the concentration of 4% gives shorter disintegration in 15 sec and shows 100% drug release within 18 minutes.	17
5.	Hibiscus rosa sinensis	Aceclofenac	The study revealed that hibiscus rosa sinensis mucilage powder was effective as a disintegrant in low concentrations of 4%. The mucilage was found to be a superior disintegrating agent than Ac-di-Sol.	23

CONCLUSION

This review has provided an overview of different natural and synthetic disintegrants and their application in the pharmaceutical industry. Natural disintegrants have a similar mechanism of action and disintegration phenomena compare to synthetic disintegrating agents. It is evident from the literature search that the disintegrating properties of husk powder, seed powder and mucilage powder of *Lepidium sativum, fenugreek* seed, and *Hibiscus Rosa Sinensis* mucilage etc., had been studied in comparison to artificial superdisintegrants. Thus natural disintegrants exhibit faster drug dissolution and improved bioavailability, thereby improving better patient compliance. Thus natural disintegrants can be effectively used as disintegrants in tablet formulations.

REFERENCES

1. Tausif A, Nayyar P, Pramod K.S. FDA- Approved natural polymers for fast dissolving tablets, Hindawi publishing corporation journal of pharmaceutics, 2014:1-6.
2. Rajini B, Sushil K, Pravin P. Polymers in the fast disintegrating tablets- A Review, Journal of pharmaceutical and clinical research, 2012; 5(2):8-14.
3. Rakesh P, Nisha G. Superdisintegrants in the development of orally disintegrating tablets- A Review, International journal of pharmaceutical science and research, 2011; 2(11):2767-2780.
4. Sparsh G, Rakesh R.M, Vashali G. Novel study in fast dissolving drug delivery system: a review, Indian journal of pharmaceutical and biological research, 2015; 3(1):93-107.
5. Jyoti V, Prajapati S.K, Irchhiaya R. An overview on superdisintegrants: A Review, European Journal of Pharmaceutical and Medical Research, 2017; 4(9):252-260.
6. Parind M.D, Celin V.L, Paul S.H. Review of disintegrants and the disintegration phenomena, Journal of pharmaceutical sciences, 2015; 1-11.
7. Rowe RC, Sheskey PJ, Weller PJ. Handbook of pharmaceutical excipients, 4th ed, London, Chicago: Pharmaceutical Press, American pharmaceutical association; 2003:37-643.
8. Vikas S, Vandana A, Chanda R. Use of natural superdisintegrants in mouth dissolving tablets- An emerging trend, International bulletin of drug research, 2012; 1(2):46-54.
9. Rambabu S, Deepak C, Anil B, Rajesh V, Ranawat M.S. A comparative study of novel super disintegrating agent, guar gum to existing super disintegrating agent, sodium starch glycolate on release rate of drug from fast dissolving tablet, Journal of pure applied science and technology, 2013; 3(2):16-24.
10. Rishabha M, Pranati S, Maynak B, Pramod K.S. Mango peel pectin as a super disintegrating agent, Journal of scientific and industrial research, 2010; 69:688-690.
11. Sievert D, Pomeranz Y, Abdelrahman A. Functional properties of soy polysaccharides and wheat bran in soft wheat products, Cereal chem., 1990; 67(1):10-13.
12. Khaled Mohamed H, Hisham Ahmed M, Ali Habiballah H. Soy polysaccharide as a novel superdisintegrant in sildenafil citrate sublingual tablet: preparation, characterization and in-vivo evaluation, Drug design development and therapy, 2015; 9:465-472.
13. Bruscato F.N, Danti A.G. Pharmaceutical tablets containing chitin and chitosan as a disintegrant, US Patent, 1978; (4):086-335.
14. Emmanuel O.O, Musiliu O.A, Ekaetel I.A. Evaluation of callinectes chitosan as a superdisintegrant in metronidazole tablet, International Journal of Pharmacy and Pharmaceutical Sciences, 2017; 9(10):111-118.
15. Mohanchandran P.S, Sindhumol P.G, Kiran T.S. Superdisintegrants an over review, International Journal of Pharmaceutical Sciences Review and Research, 2011; 6(1):105-109.
16. Kampanart H, Wancheng S. Developed and characterization of seed gums from *Tamarindus indica* and *Cassia fistula* as disintegrating agent for fast disintegration, Asian Journal of Pharmaceutical Sciences, 2017; 12(4):370-377.
17. Ravi K, Swati P, Patil M.B, Sachin R.P, Mahesh S.P. Isolation and evaluation of disintegrating property of *fenugreek* seed mucilage, International Journal of Pharm Tech Research, 2009; 1(4):982-996.
18. Shirsand S.B, Shivanand S, Keshavashetti G.G, Jonatham V. *Portulaca oleraceae* mucilage as a disintegrant in design of fast dissolving tablets, World journal of pharmacy and pharmaceutical sciences, 2016; 5(2):1508-1518.
19. Majmudar H, Mourya V, Devdhe S, Chandak R. Pharmaceutical applications of *ispaghula* husk mucilage, International journal of pharmaceutical sciences, 2013; 18(1):49-55.
20. Shabnam A, Qurratul A, Babita K. Investigation on novel bio-binder isolated from *aegle marmelos* used in ibuprofen tablets, International journal of Pharmacy and Pharmaceutical Sciences, 2015; 7(4):414-415.
21. Karan M, Inderbir S. Locust bean gum as a superdisintegrant-formulation and evaluation of nimesulide orodispersible tablets, Polimery w Medycynie, 2011; 41(1):17-28.
22. Betty M, Lusi E.L, Carmen S, Carlos C.U, Oriette Z. Chemical characterization of the mucilage from fruits of *Opuntia ficus indica*, Carbohydrate polymers, 2006; 63(2):263-267.
23. Viral S, Rucha P. Studies on mucilage from *Hibiscus Rosa sinensis* linn as oral disintegrant, International journal of applied pharmaceutics, 2010; 2(1):18-21.
24. Patel D.M, Prajapati D.G, Patel N.M. Seed mucilage from *Ocimum americanum linn* as disintegrant in tablets: separation and evaluation, Indian Journal of Pharmaceutical Sciences, 2007; 69(3):431-435.
25. Singh A.K, Selvam R.P, Sivakumar T. Isolation, characterization and formulation properties of a new plant gum obtained from *Mangifera indica*, International journal of pharmaceutical and biomedical research, 2010; 1(2):35-41.
26. Ravi K.N, Sachin R, Mirtyunjaya B. Evaluation of disintegrating properties of *Mangifera indica*, RGUHS Journal of pharmaceutical sciences, 2011; 1(1):11-20.
27. Olufunke C.B, Oluwatoyin A.O. Disintegrant properties of banana starch obtained from the unripe fruits of *Musa sapientum L*, Journal of applied pharmaceutical science, 2014; (09):083-088.
28. Sandra K.J, Nina V, Jayasankari M, Dhacshina S. Comparative study and evaluation of the disintegrating property of starch derived from *cucurbita maxima* pulp and official corn starch in telmisartan tablet, International journal of pharmacology and pharmaceutical sciences, 2016; 3(4):49-61.