A Review on Superdisintegrants

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ABSTRACT
The therapeutic activity of the formulations is obtained by disintegration followed by dissolution. The inclusion of right disintegrant is a prerequisite to get optimal bioavailability in tablets and capsules. Disintegrants are the substances that causes rapid disintegration of the capsules or tablets into smaller particles that dissolves more rapidly than in the absence of the disintegrants. On the other hand, superdisintegrants, as it name suggests superior to disintegrants are the substances which facilitates or increases the disintegration time even at low level, typically 1-10% by weight relative to the total weight of the dosage unit. These are used to increase the effectiveness of solid dosage form. This review article focus on the classification, ideal characteristics, advantages, disadvantages, selection and mechanism of action of superdisintegrants which are being used in the formulation to provide the safer, effective drug delivery with patient’s compliance.

Keywords: Bioavailability, Disintegrants, Patient compliance, Superdisintegrants, Tablets.

INTRODUCTION

Oral delivery of the drug is most preferred route of administration which have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. Among the dosage forms administered orally, the tablet is the most desired dosage forms for its ease of preparation, ease in administration, correct dosing and stability related with oral liquids and more tamper proof than capsules. Immediate release may be provided by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption. Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for the pediatric and geriatric patient. United States Food and Drug Administration (FDA) defined fast dissolving tablet (FDT) as “a solid dosage form containing medicinal element or active ingredient which disintegrate or dissolve rapidly within seconds when placed upon the tongue.” Fast dissolving tablets are also known as mouth-dissolving tablets, rapid dissolving, melt-in-mouth tablets, or dispersible tablets, melts, porous tablets, quick dissolving, quick melt and quick disintegrating tablets. Fast dissolving tablets are novel drug delivery system that dissolves, disintegrate or disperse the Active Pharmaceutical Ingredients in saliva within few seconds with or without intake of water. The faster the dissolution of drug into the solution, quicker is the absorption and onset of clinical effect. The bioavailability of some drugs may increase due to absorption of drugs in oral cavity or also due to pregastric absorption of drug from saliva that pass down into the stomach. Natural and synthetic superdisintegrants like mucilage, cross linked carboxymethyl cellulose (croscarmellose) sodium starch glycolate, poly vinyl pyrollidone are used to provide immediate disintegration of tablets and facilitate the design of delivery system with desirable characteristics. These types of formulations are widely recommended for the drugs used in emergency. Disintegrants are substances or mixture of substances added to the drug formulations, which facilitate dispersion or breakup of tablets and contents of capsules into smaller particles for quick dissolution when it comes in contact with water. The may function by drawing water into the tablet, swelling and causing the tablet to burst apart. Superdisintegrants provide quick disintegration due to combined effect of swelling and water absorption. Superdisintegrants promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution. 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. The superdisintegrants are more effective at low concentration than disintegrants.
with greater disintegrating efficiency and mechanical strength. It is used in low amount in tablet typically 1-10% by weight relative to the total weight of the dosage unit. One gram of superdisintegrants absorb 10-40 gm of water or aqueous medium. After absorption it creates stress and cause the whole tablet structure to break apart.\textsuperscript{13,14}

**Advantages of Superdisintegrants**\textsuperscript{15, 16, 17}

- Remarkable tendency on wetting causing rapid disintegration.
- No lump formation on disintegration.
- Compatible with commonly used therapeutic agents and excipients.
- Does not stick to the punches and dyes.
- Effective in lower concentrations.
- Less effect on compressibility and flow ability.
- More effective intragrannularly.
- Some are anionic and may cause some slight in vitro binding with cationic drugs.
- Biodegradable.

**Disadvantages of Superdisintegrants**\textsuperscript{18}

- Expensive.
- Time consuming and fragile.
- More sensitive and hygroscopic in nature.

**IDEAL PROPERTIES OF SUPERDISINTEGRANTS**\textsuperscript{17, 19, 20, 21}

- It should produce rapid disintegration.
- It should produce good moulding and flow property.
- It should have good particle size, good hydration capacity and compressibility index.
- It should have poor water solubility.
- It should produce compactable less friable tablets.
- Effective at very low concentration and should have greater disintegrating efficiency.
- Nontoxic and should have good mouth feel.
- It should have no tendency to form complexes with the drugs.
- It should be compatible with the other excipients and should have desirable tableting properties.

**TYPES OF SUPERDISINTEGRANTS**

1. Natural Superdisintegrants
2. Synthetic Superdisintegrants

1. Natural Superdisintegrants

**Ispaghula Husk Mucilage (Plantago ovata)**

Ispaghula husk consists of dried seeds of the plant which is known as *Plantago ovata* and it contains mucilage which is present in the epidermis of the seeds. The seeds of *Plantago ovata* were soaked in distilled water for 48 hours and then boiled for few minutes for complete release of mucilage into water. The mucilage of plantago ovata has different features like binding, disintegrating and sustaining properties. Mucilage is a super disintegrating agent which is used to formulate fast dissolving tablets.

**Chitin/Chitosan-Silicon di oxide**

Naturally chitin is extracted from the shell wastes of shrimp, crab, lobster, krill and squid used for the production of chitosan by a deacetylation reaction in alkaline medium. The comparative study of other superdisintegrants with chitin-silica co precipitate has proved better function.\textsuperscript{28} Bruscato et. al. 1978 reported that when chitin was included in the conventional tablets, the tablets disintegrated within 5 to 10 minutes irrespective of the solubility of drug. Chitosan is the best known natural polysaccharide used for its versatile applications in pharmaceutical industry.\textsuperscript{29}

**Locust Bean Gum**

Locust bean gum is the other name of Carob bean gum. It is extracted from the endosperm of the seeds of the carob tree ceretonia siliqua. Locust bean gum can be used as a binder and as a disintegrating agent in different applications in pharmaceutical industry.
concentrations. Locust bean gum has also been reported to have bio adhesive and solubility enhancement properties. There are various reports that Locust bean gum can be used in pharmaceutical and biotechnological purpose.

Mango Peel Pectin

Dried mango peel powder is used for extracting pectin. Mango peel pectin due to its good swelling index and good solubility in biological fluids can be used to prepare fast dispersible tablets. 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 film and acceptable jelly.

Soy Polysaccharide

It is a natural superdisintegrant that does not contain any starch or sugar and can be used in nutritional products. A cross linked sodium carboxy-methyl cellulose and corn starch were used as control disintegrants. Soy polysaccharide performs well as a disintegrating agent in direct compression formulations with results paralleling those of cross-linked CMC.

2. Synthetic Superdisintegrants

Modified Starch (Sodium starch glycolate, Primojel)

Sodium starch glycolate is the sodium salt of a carboxymethyl ether of starch. These are modified starches made by crosslinking of potato starch as it gives the product with the best disintegrating properties. The degree of cross-linking and substitution are important factors in determining the effectiveness of these materials as superdisintegrants. The effect of the crosslinking is to reduce both the water soluble fraction of the polymer and the viscosity of dispersion in water. The natural pre dried starches swell in water to an extent of 10-20 percent and the modified starches increase in volume by 200-300 percent in water. The mechanism by which this action takes place involves rapid absorption of water leading to an enormous increase in volume of granules that result in rapid and uniform disintegration. The tablets formulated by using these superdisintegrants may disintegrate in less than two minutes.

Cross-linked Polyvinyl Pyrrolidone (Crospovidone)

Crospovidone quickly wicks saliva into the tablet to generate the volume expansion and hydrostatic pressure necessary to provide rapid disintegration in the mouth. When examined under a scanning electron microscope, crospovidone particles appears to be granular and highly porous. This unique, porous nature facilitates wicking of liquid into the dosage systems and causes rapid disintegration. In contrast to other superdisintegrants such as sodium starch glycolate and croscarmellose sodium, crospovidone exhibit virtually no tendency towards gel formation, even at a high ratio. Crospovidones are highly compressible materials as a result of their unique particle morphology. Crospovidone is used as a superdisintegrant at low concentration levels (2-5%) in direct compression, wet and dry granulation processes.

The polymer has a small particle size distribution that imparts a smooth mouth feel to dissolve quickly. Varieties of grades are available commercially as per their particle size in order to achieve a uniform dispersion for direct compression with the formulation.

Modified Celluloses (Croscarmellose Sodium)

It is insoluble in water, although it rapidly swells to 4-8 times its original volume on contact with water. It specific surface area is 0.81-0.83 m²/g and swelling index is 65±1.7% v/v. Cross-linked sodium carboxymethylcellulose is a white, free flowing powder with high absorption capacity. It has a high swelling capacity and thus provides rapid disintegration and drug dissolution at lower levels. It also has an outstanding water wicking capability and its cross-linked chemical structure creates an insoluble hydrophilic, highly absorbent material resulting in excellent swelling properties. Its recommended concentration is 0.5-2.0%35. Croscarmellose sodium should be defined as a cross-linked polymer of carboxymethylcellulose. There are many differences between the starch and cellulose polymer and the important one included difference between the synthetic processes that is used to modify the polymer. In tablet formulations, croscarmellose sodium may be used in both direct compression and wet-granulation processes. When used in wet-granulation, the croscarmellose sodium should be added in both the wet and dry stages of the process (intra- and extra-granularly) so that the wicking and swelling ability of the disintegrant is best utilized,

Microcrystalline Cellulose (Avicel)

Microcrystalline cellulose is a purified, partially depolymerized cellulose that occurs as a white, odorless, tasteless, crystalline powder composed of porous particles. Avicel concentration of less than 10%, shows enhanced disintegration. This mechanism depends on entry of water in the tablet matrix through capillary pores, which disrupt or break the hydrogen bonding between nearby bundles of cellulose microcrystals. With high concentration, particularly in oral disintegrating tablet it shows an affinity to stick to the tongue due to fast capillary absorption and quicker dehydration of the tablet surface. It has a fast wicking rate for water, hence this and starch makes an excellent combination for effective and rapid disintegration in tablet formulation. It is commercially available in different particle sizes and moisture grades that have different properties and applications. Eg: Avicel pH-101, pH-102 and pH-1058, 35.

Alginate

These are hydrophilic colloidal ingredients that are extracted naturally from certain types of kelp or chemically improved from natural sources like alginic acid or alginic acid salts. Alginic acid is a polymer derived from seaweeds comprising D-mannuronic and L-guluronic units. Its affinity for water absorption and high sorption capacity.
makes it an excellent disintegrant. Algic acid is used as disintegrant at 1-5 % concentration while sodium alginate at 2.5-10 % concentration. It can be successfully used with ascorbic acid and multivitamin formulations37, 38.

**MECHANISM OF ACTION OF SUPERDISINTTEGRANTS**

- Swelling.
- Porosity and capillary action (wicking).
- Combination action.
- Heat of wetting.
- Deformation.
- Enzymatic reaction.
- Electrostatic repulsion.
- Chemical reaction.

**Swelling**

Swelling is widely accepted mechanism and necessarily the first step for tablet disintegration. It is a process in which certain disintegrating agents (such as starch) generate the disintegrating effect. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. Particles of disintegrants swells when it comes in contact with water, the adhesiveness of other pharmaceutical ingredients present in a tablet can be overcome which causes the tablet to Break19, 39. The mechanism of disintegration through swelling is shown in figure: 1

**Porosity and Capillary Action (Wicking)**

Disintegrating agents which does not swell, act by the mechanism of porosity and capillary action. Porosity of the tablet produce pathways for the fluid penetration into tablets. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug/excipient and on tableting conditions. Liquid is drawn up or “wicked” into these pathway through capillary action and break the bonding of inter particles which causes the tablet to break apart. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

**Combination Action**

In this mechanism, the combination of both wicking and swelling action to disintegration19, 39. The mechanism of tablet disintegration by wicking shown in figure: 2

**Heat of wetting**

When disintegrating agents with exothermic properties becomes wetted, capillary air expansion generates localized stress, which helps in tablet disintegration. This mechanism of action explains the action of some types of disintegrants and cannot describe the action of most modern disintegrants41.

**Deformation**

The disintegrated particles gets deformed during tablet compression and these deformed particles regain their normal structure when they come in contact with water. The swelling capacity was improved during deformation which results in breakup of tablets. In case of starch (such as potato starch and corn starch) are believed to be elastic in nature, but due to high compaction force during tableting, the elasticity of grains that are deformed under pressure will return to their original shape, when that pressure is removed. When these tablets are exposed to aqueous environment, the energy potential of deformed starch grain will be triggered to cause disintegration40, 42. The mechanism of disintegration by deformation shown in figure 3:
Enzymatic action

Enzymes available in the body also act as disintegrants. These enzymes act on binding action of binder and helps in disintegration. Due to swelling, pressure is exerted in the outer direction that causes the tablet to breakup or burst. The accelerated absorption of water leads to an enormous increase in the volume of granules to promote disintegration i.e swelling exerts the pressure towards the outer direction, which causes the tablet to break and helps in enhancing the water absorption1, 43. Example some disintegrating enzymes with binders shown in table 1.

Table 1: Some Disintegrating Enzymes with Binders

<table>
<thead>
<tr>
<th>Enzymes</th>
<th>Binders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase</td>
<td>Starch</td>
</tr>
<tr>
<td>Protease</td>
<td>Gelatin</td>
</tr>
<tr>
<td>Cellulase</td>
<td>Cellulose and its derivatives</td>
</tr>
<tr>
<td>Invertase</td>
<td>Sucrose</td>
</tr>
</tbody>
</table>

Electrostatic Repulsion

This is another mechanism of disintegration that attempts to explain the swelling of tablet made with non-swellable disintegrants. Guyot-Hermann’s has proposed a particle – particle repulsion theory based on the observation that non swelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. The water penetrates between starch grains because of its affinity for starch surfaces, thereby breaking hydrogen bonds and other forces holding the tablet together44.

Chemical Reaction (Acid Base Reaction)

Liberation of carbon dioxide within tablets on wetting due to interaction between tartaric acid and citric acid (acids) with alkali metal carbonates or bicarbonates (bases) in presence of water causes breaking of tablets. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablets. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of these tablets. The effervescent blend is either added immediately prior to compression or can be added in two separate fractions during formulation18.

CONCLUSION

The article discussed the overviews of various types of superdisintegrants which are available at present. With the progress in the formulation of fast dissolving tablets, now it is possible to formulate these tablets with numerous types of superdisintegrants in reduced quantity. Approximately one-third of the patients need quick therapeutic action of the drug. Superdisintegrants used in fast dissolving tablet offers combined advantages of ease and convenience of dosing, release the medicaments with an enhanced rate, also provide safe, effective drug delivery with better patient compliance and enhanced therapeutic benefits.

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REFERENCES

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