ABSTRACT

Oral route is the most common route for administration of solid dosage form, about 85% of solid dosage administered by oral route. Disintegration plays major role in improving the drug activity. Disintegrants are substances added to the drug formulation that increase the breakup of the tablet or capsule into smaller particles in aqueous environment that dissolve more rapidly than in the absence of disintegrants. Nowadays some newer agents have been developed known as Superdisintegrants. Superdisintegrants are the substances, which facilitate the faster disintegration with smaller quantity in contrast to disintegrants. These are of two type’s natural and synthetic superdisintegrants. Superdisintegrants are generally used at a low level in the solid dosage form, typically 1- 10 % by weight relative to the total weight of the dosage unit. These are used to improve the efficacy of solid dosage form. Examples of superdisintegrants are sodium starch glycolate, crospovidone, Gellan gum etc.

Keyword: Disintegration, Disintegrants, Superdisintegrants.

INTRODUCTION

Oral route of drug delivery is the most appealing route for the delivery of drugs. Different types of dosage forms administered orally, the tablet is one of the most preferred dosage forms amongst them because of its ease of manufacturing, convenience in administration, accurate dosing, and stability compared with oral liquids and because it is more tamperproof than capsules. The bioavailability of drug is dependent on various factors like in vivo
Disintegration, dissolution, and various physiological factors. 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 fragments for quick dissolution. The task of developing rapidly disintegrating tablets is accomplished by using a suitable superdisintegrants. In recent years several newer agents have been developed known as “Superdisintegrants”. These are the substances, which facilitate the faster disintegration with smaller quantity in contrast to disintegrants. Superdisintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases, this promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution.

There are various factors considered during selection of Superdisintegrants:

- Amount of disintegrants present in formulation.
- Hardness of tablets.
- Type of addition and mixing.
- Nature of drug.
- It should have good flow ability.
- Presence of surface active agents.
- Compactable to produce less friable tablets.
- Produce good mouth feel to the patient.

A superdisintegrants used in granulated formulation processes can be more effective if used both “intragranularly” and “extra granularly” 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 superdisintegrant added intragranularly (in wet granulation processes) is usually not as effective as that added extragranularly due to the fact that it is exposed to wetting and drying (as part of the granulation process) which reduces the activity of the superdisintegrant. Since a compaction process does not involve its exposure to wetting and drying, the superdisintegrant used intragranularly tends to retain good disintegration activity. There are three methods of incorporating disintegrating agents into the tablet: A. Internal Addition (Intragranular) B. External Addition (Extragranular) C. Partly Internal and External. The proper choice of a disintegrant or a superdisintegrant and its consist performance are of critical importance to the formulation development of capsule and tablets.
Ideal properties of Superdisintegrants\textsuperscript{7,8}

1. It should have poor solubility.
2. Poor gel formation.
3. Have good hydration capacity.
4. It must have good flow properties.
5. No tendency to form complexes with the drugs.
6. It should have good mouth feel.
7. Inert.
8. Non toxic.

Types of Superdisintegrants-

1. Natural Superdisintegrants.
2. Synthetic Superdisintegrants

1. Natural Superdisintegrants

Isapghula Husk Mucilage (\textit{Plantago ovata})

Isapghula Husk consists of dried seeds of the plant known as plantago ovata. The plant contains mucilage in the epidermis of the seeds. Mucilage of plantago ovate has different characteristics like binding, disintegrating and sustaining properties. Mucilage can be used as superdisintegrant to formulate fast dissolving tablets because it has very high percentage of swelling index (around 89±2.2%v/v) as compared to the other superdisintegrating agents. The rapid disintegration of the FDTs are due to the swelling of Superdisintegrants to create enough hydrodynamic pressure for quick and complete disintegration of the tablet. The rate at which swelling develops and significant force of swelling also determine its disintegrating efficiency\textsuperscript{9,10}.

Lepidium sativum Seed Mucilage

It is also known as asaliyo. Natural \textit{Lepidium sativum} (family: Cruciferae), has wide application in pharmaceutical field as disintegrating agent and as herbal medicine. Seeds contain a major proportion of mucilage, dimeric imidazole alkaloidslepidine B, C, D, E and F and two new monomericimidazole alkaloids semilepidinoside A and B. Themucilage can be extracted from seeds by differentprocedures and its yield varies from 14% to 22%. Mucilage of \textit{Lepidium sativum} has various characteristic like binding,disintegrating, gelling etc. The extracted mucilage is used to develop fast dissolving tablets. Mucilage is found to be abrownish white powder which decomposes above 200oCand have characteristic odour. On
evaluating its various physicochemical characteristics, the values of swelling index, angle of repose, bulk density and tapped density are estimated as following 18, 32°C, 0.58g/cc and 0.69g/cc respectively\textsuperscript{11}.

**Fanugreek Seed Mucilage**

*Trigonella Foenum-graceum* (leguminous family). It is an herbaceous plant. It has found wide applications as a food, a food additive, and as a traditional medicine. The leaves and both the ripe and unripe seeds of *Trigonella Foenum-graceum* are used as vegetables. Fenugreek has been used in treating dyspepsia with loss of appetite, chronic cough, dropsy, enlargement of liver and spleen, rickets, colic flatulence, dysentery, diarrhoea, gout, and diabetes. It is also used as gastro protective, antiurolithiatic, diuretic, antidandruff agent, Anti-inflammatory agent and as antioxidant. The seed is stated to be a tonic\textsuperscript{12}. It also is used in post-natal care and to increase lactation in nursing mothers. 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. The resulting soft mass is not absorbed by the body, but instead passes through the intestines and triggers intestinal muscle contractions\textsuperscript{13}.

**Gellan Gum**

Gellan gum is obtained from *Pseudomonos elodea*. It is a linear anionic polysaccharide biodegradable polymer consisting of a linear tetrasaccharide repeat structure as shown in Fig and is used as a food additive. Gellan gum as a superdisintegrant and the efficiency of gum is compared with other conventional disintegrants such as dried corn starch, explotab, avicel (pH 102), Ac di-sol and Kollidon CL studied by Antony et al\textsuperscript{14}. 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 is 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 shows very similar pattern of disintegration and in vitro dissolution rates. With the same concentration tablet with explotab show 36 minutes for 90% of drug release and with starch show 220 minutes. From this result gellan gum has been proved itself as a superdisintegrant.
Locust Bean gum

Locust bean gum also called Carob bean gum. It is extracted from the endosperm of the seeds of the carob tree Ceretonia siliqua, which grows in Mediterranean countries. Some other familiar polysacharides are starch and cellulose, which are made of long chains of the sugar glucose. In locust bean gum, the ratio of mannose to galactose is higher than in guar gum, giving it slightly different properties, and allowing the two gums to interact synergistically so that together they make a thicker gel than either one alone. It shows as a binder and as a disintegrant property at different concentration. Locust bean gum has been widely used in food industry as a thickening and gelling agent. Locust bean gum has also been reported to have bioadhesive and solubility enhancement properties\textsuperscript{15, 16}.

2. Synthetic Superdisintegrants.

Sodium starch glycolate

It is also called as sodium carboxy methyl starch. It is a modified starch. It is a cross linked polymer of carboxymethyl starch. Generally potato starch is used to synthesize sodium starch glycolate it gives the product with the best disintegrating properties. After selection of the appropriate starch source the next step is the crosslinking of the potato starch by using an FDA approved starch esterifying agent such as sodium trimetaphosphate or phosphorus oxychloride in alkaline suspension. Introduction of the large hydrophilic carboxymethyl groups is to disrupt the hydrogen bonding within the polymer structure. It allows water to penetrate the molecule and the polymer becomes cold water soluble. Cross-linking reduce both the water soluble fraction of the polymer and the viscosity of dispersion in water. The optimum balance between the degree of substitution and the extent of cross-linking allows for rapid water uptake by the polymer without the formation of a viscous gel that might impede dissolution\textsuperscript{17}.
Crosspovidone

These are synthetic, insoluble, cross linked homopolymers of N-vinyl-2- pyrrolidone. Under scanning electron microscope, Crosspovidone particles appear as granular and are highly porous. It does not form complexes with drugs because of their nonionic nature. Crosspovidone act by combination of mechanisms to provide rapid disintegration. Although Crosspovidone polymers swell by 95% to 120% upon contact with water, swelling is not the only mechanism for tablet disintegration. Their porous particle morphology rapidly absorbs water (wicking) via capillary action. In addition, during tablet compaction, the highly compressible Crosspovidone particles become extremely deformed. When the deformed Crosspovidone particles come in contact with water that is wicked into the tablet, the Crosspovidone particles recover their normal structure and then swell, resulting in rapid volume expansion and high hydrostatic pressures that cause tablet disintegration. Due to its high crosslink density, Crosspovidone swells rapidly in water without gelling. Crosspovidone are highly compressible materials as a result of their unique particle morphology. At low concentration levels (2-5%) crosspovidone is used as superdisintegrant in direct compression, wet and dry granulation processes.17
Modified Cellulose (Croscarmellose sodium)

Croscarmellose sodium is a modified cellulose and is described as a cross-linked polymer of carboxymethylcellulose. Apart from the differences between the starch and cellulose polymer backbones, there are differences between the synthetic processes used to modify the polymer. Most importantly, the disintegration rate of Croscarmellose sodium is higher than that of sodium starchglycolate and the mechanism of crosslinking is different. The substitution is performed using Williamson’s ether synthesis to give the sodium salt of carboxymethylcellulose. A key difference from the chemistry of SSG is that some of the carboxymethyl groups themselves are used to cross-link the cellulose chains, the process being accomplished by dehydration.

Thus the cross-links are carboxyl ester links rather than phosphate ester links as in Primojel. Croscarmellose sodium is a crosslinked polymer of carboxymethyl cellulose sodium. Crosslinking makes it insoluble, hydrophilic, highly absorbent material, resulting in excellent swelling properties and its unique fibrous nature gives it excellent water wicking capabilities. It also provides superior drug dissolution and disintegration characteristics, thus improving bioavailability. It is used in oral pharmaceutical formulations as a superdisintegrant for capsules, tablets and granules.

![Basic structure of Croscarmellose Sodium](image)

Fig. 4 Basic structure of Croscarmellose Sodium

Resin

Resins although insoluble, have great affinity for water and hence, act as a disintegrant. Moreover, because of their smaller particle size the rate of swelling is high making them a superdisintegrant. Like conventional disintegrant, they don’t lump but additionally
impert strength to the tablets. The use of ion exchange resins into drug delivery systems have been encouraged because of their physicochemical stability, inert nature, uniform size, spherical shape assisting coating and equilibrium driven reproducible drug release in ionic environment. Ion exchange resins are insoluble polymers that contain acidic or basic functional groups and have the ability to exchange counter-ions within aqueous solutions surrounding them. Drug, molecules attached to the resins are released by appropriate charged ions in the gastrointestinal tract, followed by diffusion of free drug molecules out of the resins\textsuperscript{18}.

Table. I Synthetic Superdisintegrants with their mechanism of action and Properties

<table>
<thead>
<tr>
<th>Superdisintegrants</th>
<th>Mechanism of action</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross linked cellulose</td>
<td>Swelling and Wicking</td>
<td>Swelling in two dimension</td>
</tr>
<tr>
<td>Cross linked PVP</td>
<td>Capillary action</td>
<td>Water insoluble and spongy in nature so get porous tablet</td>
</tr>
<tr>
<td>Cross linked starch</td>
<td>Swelling</td>
<td>Swells in 3 dimensions and high level serve as sustain release matrix</td>
</tr>
<tr>
<td>Cross linked alginic acid</td>
<td>Swelling and wicking</td>
<td>Promote disintegration in both dry and wet granulation</td>
</tr>
<tr>
<td>Calcium silicate</td>
<td>Wicking</td>
<td>Highly porous and have light weight</td>
</tr>
</tbody>
</table>

**Mechanism of action of Superdisintegrants**

1. By Swelling.
2. Capillary action (wicking).
3. Due to heat of wetting.
4. Enzymatic reaction.
5. Due to release of gases.
6. Deformation.
7. Combination action.
8. Chemical reaction.

1. **By Swelling**

It is a mechanism in which certain disintegrating agents (such as starch) impart the disintegrating effect. When it comes in contact with water it swell, the adhesiveness of other
ingredients in a tablet is overcome causing the tablet fall apart as in figure 1. e.g: Sodium starch glycolate.

2. Capillary Action
Disintegrants that do not swell they act through porosity and capillary action. Tablet porosity provides pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness & compressibility) themselves enhance porosity and provide these pathways into the tablet. Liquid is drawn up or “wicked” into these pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart. E.g. Crospovidone, Crosscarmillose as shown in Fig.2.

3. Due to heat of wetting
When disintegrants with exothermic properties get wetted, localized stress is generated due to
capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents\textsuperscript{21}.

4. **Enzymatic reaction**

Some enzymes present in the body also act as disintegrants. These enzymes reduce the binding ability of binder and helps in disintegration. Due to swelling, pressure is exerted in the outer direction that causes the tablet to burst or enhance absorption of water leads to an enormous increase in the volume of granules to improve disintegration\textsuperscript{22} (Fig. 3).

![Enzymatic reaction](image_url)

**Fig.7. Enzymatic reaction**

5. **Due to release of gases**

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. 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 tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation\textsuperscript{23}.

6. **Deformation**

Starch grains are generally “elastic” in nature means that grains that are deformed under pressure will return to their original shape when that pressure is removed. But, when the compression forces involved in tableting applied, then these grains are deformed permanently and are said to be “energy rich” with this energy being released upon exposure to water. In
other words, the ability for starch to swell is higher in “energy rich” starch grains than it is for starch grains that have not been deformed under pressure. It is believed that no single mechanism is responsible for the action of most disintegrants. But rather, it is more likely the result of inter-relationships between these major mechanisms.\(^5\)

![Disintegration mechanism](image)

**Fig.8. Deformation mechanism**

7. **Combination reaction**
   In this mechanism, the disintegrants act through the combination of both wicking and swelling action\(^24\). E.g. Crosspovidone.

8. **Acid base reaction (Chemical reaction)**
   By internal liberation of CO2 in water due to interaction between tartaric acid and citric acid (acids) with alkali metal carbonates or bicarbonates (bases) in presence of water tablet quickly broken apart. The tablet disintegrates due to generation of pressure within the tablet. Due to liberation in CO2 gas, the dissolution of active pharmaceutical ingredients in water as well as taste masking effect is increased. As these disintegrants are highly sensitive to small changes in temperature and humidity level, control of environment must be required during preparation of the tablets. The effervescent blend is either added immediately prior to compression or can be added in two separate fraction of formulation. The effervescent blend is added immediately before compression or can be added into two separate fraction of formulation.\(^21\)

9. **Electrostatic repulsion**
   Guyot - Hermann has proposed a particle repulsion theory on the basis of his theory he
observed that the particle with no swelling action also causes disintegration of tablets. Mechanism of disintegration based on electric repulsive forces between particles and water is required for it as shown in figure. Researchers found that repulsion is secondary to wicking.

Method of incorporation

1. Intrgranular or during granulation-In this process the superdisintegrants are blend with other powders and granulation is carried out. Thus the superdisintegrants are incorporated within the granules.

Advantage-Easy to incorporate
Suitable for direct compression.

2. Extra granular or prior to compression-In this process, the superdisintegrants are mixed with prepared granules prior to compression.

Advantage-Easy to incorporate
Suitable for wet granulation process

3. Incorporation of superdisintegrants at intra and extra granulation steps-It is also called as internal and external mixing of disintegrants. In this part of superdisintegrants are added to intragranules and a part to extra granules. Superdisintegrants is divided into two portions. Half portion is added before granule formation (intra) and remaining is added to
granules (extra) with mixing prior to compression. This method can be more effective. If both Intragranular and extra granular methods are used, extra granular portion break the tablet into granules and the granules further disintegrate by Intragranular portion to release the drug substance into solution30, 31.

Advantage: More complete disintegration
Produce better result
Immediate disruption
More effective method

Application of Superdisintegrants
Superdisintegrants are used in different types of formulation. These are as follows

1. Mouth dissolving tablet; Khalidindiet al 1982 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 fillers32.

2. Fast disintegrating tablet; Shirsande et al carried out preparation and evaluation fast dissolving tablets of metaclopramide using novel co-processed superdisintegrant. In the present study, novel co-processed superdisintegrants were developed by solvent evaporation method using crospovidone and sodium starch glycolate in different ratios (1:1, 1:2 & 1:3) for use in the fast dissolving tablet formulations33.

3. Rapidly disintegrating tablet; Sandeep B. Patil et al prepared Olanzapine, quick dispersing tablets by direct compression method. Effect of super disintegrant crospovidone on wetting time, disintegration time, and drug content and in vitro release have been studied34.

REFERENCES


