



Review Article

A CONCISE REVIEW ON NOVEL ASPECTS OF SUPERDISINTEGRANTS

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Abstract: Disintegrants (substances or mixture of substances) when added to the drug formulation it facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly. The inclusion of right disintegrant is a prerequisite requirement to get an optimum bioavailability in tablets and capsules which need rapid disintegration. The efficacy of solid dosage forms can also be improved by superdisintegrants which is achieved by decreasing the disintegration time and in turn enhances the drug dissolution rate. Superdisintegrants are croscarmellose, crospovidone and sodium starch glycolate which represent crosslinked cellulose, crosslinked polymer and a crosslinked starch respectively. The objective of this review was to provide a closer look at the functionality of superdisintegrants in promoting tablet disintegration. In recent years, more attention is to formulate 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 present review describes superdisintegrants, their types, ideal properties and various methods of incorporating disintegrants, mechanism of tablet disintegration. This review comprises superdisintegrants, which provide safe and effective drug delivery with patient's compliance.

Key words: Disintegrants, Superdisintegrants, Types, Ideal Properties, Methods and Mechanism of superdisintegrants

Introduction:

Disintegrates are substances or mixture of substances added to tablet formulations to promote the break-up of the tablet (and capsule "slugs") into smaller fragments in an aqueous environment thereby increasing the available surface area and promoting a more rapid release of the drug substance¹. The advantages of rapidly disintegrating tablets are increasingly being recognized in both industry and academia. Their growing importance was underlined recently when European Pharmacopoeia² adopted the term "orodispersible tablet" as a tablet to be placed in the mouth where it disperses rapidly before swallowing.

The fast disintegration and dissolution effect of oral disintegrating tablets mainly depends on the type of superdisintegrants used in the tablet formulation. Most commonly used superdisintegrants include sodium starch glycolate, croscarmellose sodium (cross-linked carboxymethylcellulose), crospovidone (cross linked povidone)³. Use of these superdisintegrants in combination mainly reduces the disintegration and dissolution time of ODT. Natural superdisintegrants shows less disintegration time compared to synthetic super disintegrant. With increase in concentration of superdisintegrants, disintegration time decreases⁴.

In tablets and capsules, disintegrants and superdisintegrants are used to ensure that these compacts are rapidly broken down into the primary particles to facilitate the dissolution or release of the active ingredients. The superdisintegrants are a particulate agglomerate of coprocessed starch or cellulose and a sufficient amount of an augmenting agent to increase the compatibility of the superdisintegrant. The augmented superdisintegrant provides a fast disintegration of a solid dosage form when incorporated in sufficient quality therein, without untowardly affecting the compatibility of the solid dosage form.

Some superdisintegrants and their properties are:

1. Croscarmellose sodium (AC-Di-Sol)
High swelling capacity, effective at low concentration (0.5-2.0 can be used up to 5.0%).
2. Crospovidone: (Polyplasdone XL, poly plasdone XL 10)
Rapidly disperses and swells in water, but does not form gel even after prolonged exposure, completely insoluble in water. Greatest rate of swelling compared to other disintegrants. In comparison to other disintegrants, greater surface-area to volume ratio. Recommended concentration 1 to 3%. Available in

micromised grades if needed to improve uniform dispersion in the powder blend.

3. L-HPC: (Low substituted hydroxy propyl cellulose)
Insoluble in water, rapidly swells in water. Greatest degree of swelling exhibited by Grades LH-11 & LH-21. Certain grades while retaining disintegration capacity can also provide some binding properties. Recommended concentration 1-5%.
4. Sodium starch glycolate: (Primojel)
As it absorbs water rapidly so it results in swelling which leads to rapid disintegration of tablets and granules. Recommended concentration 1.0-4% but may need to use upto 6.0%. Gelling and loss of disintegration occur at high concentration.

Ideal Properties:

Poor solubility

Among the physical properties of accompanying particles that affect the effectiveness of a disintegrant, the solubility is considered of great importance. The solubility of the major component in a tablet formulation can affect both the rate and the mechanism of tablet disintegration. Insoluble materials generally produce rapidly disintegrating tablets while water-soluble materials tend to dissolve rather than disintegrate. Due to the presence of porous morphology, liquid is drawn up or "wicked" into these pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart.

Poor gel formation

Disintegrants form gels when fully hydrated, particularly at high use levels required in some formulations to achieve desired tablet disintegration or drug dissolution. Gels can delay dissolution as the drug must first diffuse through the gel layer before being released into the body. Sodium starch glycolate is used as superdisintegrant in tablet formulation at a concentration of 4-6%. Above 8%, disintegration times may actually increase due to gelling and its subsequent viscosity producing effects. Because crospovidone does not form gel upon wetting, it maintains high disintegration efficiency, even after undergoing several wetting and drying cycles⁵.

Good hydration capacity

Drugs or other excipients, which are hydrophobic and could be adsorbed on disintegrant surfaces, advertently influence the extent of hydration and the effectiveness of these disintegrants. Addition of fast disintegrants of high hydration capacity is reported to minimize this problem, and therefore, enhance dissolution⁶.

Good compressibility and flow properties

If the powders have 12-16% compressibility, they are said to be good flow powders. To achieve consistent tablet weights, the formula must be designed to flow consistently and to fill volumetrically. Thus, in order to attain proper flow and achieve volume of fill, the powders in the formula must possess a consistent particle-size distribution and density⁷. Crospovidones are significantly more compressible than other superdisintegrants, allowing for tablets with high breaking force and low friability. The breaking force of pure compacts of several disintegrants is tested at various compaction forces. The results report that Crospovidone provides significantly higher breaking force⁸.

Complexation

The potential interaction between drug actives and excipients are an important formulation consideration. Anionic disintegrants like croscarmellose sodium and sodium starch glycolate may complex with cationic drug actives and slow dissolution. Crospovidone, a non-ionic polymer does not interact with cationic drug actives to retard drug release⁹. The effects of superdisintegrants like croscarmellose sodium, sodium starch glycolate and polyplasdone XL (crospovidone) on the dissolution behavior of several cationic drugs with varying water solubility reports that polyplasdone XL had a more rapid dissolution rate for the model cationic drugs, irrespective of their aqueous solubilities¹⁰.

Desired criteria for oral disintegrating tablets:

- Requires no water for oral administration, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking agent.
- Be portable without friability concern.
- Have a pleasing mouth feel.
- After oral administration, leave minimal or no residue in the mouth.
- Exhibit less sensitivity to environmental conditions such as temperature and humidity.
- Allow high drug loading.
- Allow the manufacturing of tablets using conventional processing and packaging equipments at low cost.

Salient features of oral disintegrating tablets¹¹:

- a) Ease of administration to patient, such as pediatric, geriatric and psychiatric patients who refuses to swallow tablets.
- b) No water is required for swallowing the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.

c) Quick onset of action is produced due to rapid dissolution and absorption of drug.

d) Bioavailability of drugs is increased as some drugs are absorbed from the mouth, pharynx and esophagus when the saliva passes down into the stomach.

e) Pregastric absorption can result in improved bioavailability and clinical performance through a reduction of unwanted effects as a result of reduced dosage.

Methods of tablet compression:

Tablets are manufactured by three methods-

Wet Granulation Process

In wet granulation process, the drug substance is blended with other excipients, followed by the addition of binder solution to a blended powder and mixing for a pre-determined period of time at a given mechanical speed. Once the process is complete, the wet mass is milled and dried to produce the granules. The wet mass usually is passed through a low-shear mill and then dried for 8-24 h. A drying process that is too short will produce granules that have entrapped moisture. But if the drying process is too long then the granules become very dry and friable. Prior to being compressed into a tablet, the resulting granules are then blended with additional excipients¹².

Dry Granulation Process

Granules are formed by dry granulation process without using a liquid solution because the product may be sensitive to moisture, heat or both. There are two techniques to produce dry granules.

- **Slugging**

When the initial blend of powders is forced into the dies of a large capacity tablet press and is compacted by means of flat faced punches, the compacted masses are called slugs and the process is referred to as "slugging". The slugs are then screened or milled to produce granules.

- **Roller compaction**

On a large scale, a specially designed machine called roller compactor is used to perform the compression granulation. Powder material is fed between the rollers by a screw conveyor system. After passing through the rollers, the compacted mass resembles a thin wide ribbon that has fallen apart into large segments. Then segments are screened or milled for the production of granules. Prior to being compressed into a tablet, the resulting granules are then blended with additional excipients.

Direct Compression

In direct compression process, drug is first blended with a variety of excipients, subsequently lubricated and then directly compressed into a tablet. A disintegrant simply has to break the tablet apart to expose the drug substance for dissolution.

Lamotrigine orally disintegrating tablets prepared by direct compression technique using three different superdisintegrants like Sodium starch glycolate, Croscarmellose sodium and Crospovidone XL-10 in combination to achieve optimum release profile, disintegration time and hardness. The results show that the tablets dispersed rapidly in mouth within 8 secs and are concluded¹³ that addition of superdisintegrants is a useful method for preparing orally disintegrating tablets by direct compression method.

Methods of addition of disintegrants:

Three methods are used for incorporating disintegrating agents into the tablet.

Internal Addition

In wet granulation method, the disintegrant is added to other excipients before wetting the powder with the granulating fluid. Thereby, the disintegrant is incorporated within the granules. In dry granulation method, the disintegrant is added to other excipients before compressing the powder between the rollers. In a computer optimized experiment, the study show the effect of incorporating a disintegrant, croscarmellose sodium, intra-granularly, extra-granularly or distributed equally between the two phases of a tablet in which a poorly soluble drug constituted at least 92.5% of the formulation. The results analyzed by means of a general quadratic response surface model suggest that, tablets with the same total concentration of croscarmellose sodium dissolve at a faster rate when the super disintegrant is included intragranularly. Tablet friability is not affected by the method of disintegrant incorporation¹⁴.

External Addition

In both wet and dry granulation method, the superdisintegrant is added to the granules during dry mixing prior to compression. The effect of mode of incorporation of superdisintegrants (croscarmellose sodium, sodium starch glycolate and crospovidone) on dissolution of three model drugs with varying aqueous solubility (carbamazepine, acetaminophen and cetirizine HCl) from their respective tablet formulations by wet granulation was studied. It is proved that crospovidone is effective in improving the dissolution of the drugs in extragranular mode of addition seems to be the best mode of incorporation, irrespective of the solubility of the main tablet component.

Internal and External Addition

In this method, disintegrant is divided into two portions. One portion is added before granule formation (intra) and remaining portion is added to granules (extra) with mixing prior to compression.

This method can be more effective. If both intragranular and extragranular methods are used, extragranular portion break the tablet into granules and the granules further disintegrate by intragranular portion to release the drug substance into solution. However, the portion of intragranular disintegrant (in wet granulation processes) is usually not as effective as that of extragranular due to the fact that it is exposed to wetting and drying (as part of the granulation process) which reduces the activity of the disintegrant. The intragranular disintegrant tends to retain good disintegration activity in case of compaction process as it does not involve its exposure to wetting and drying.

Mechanism of tablet disintegration:

The mechanism by which the tablets are broken into small pieces and then produces a homogeneous suspension is based on:

Swelling

Swelling is the most widely accepted general mechanism of action for tablet disintegration (Fig. 1). Poor disintegration is observed in case of tablets with high porosity due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration again slows down. The adhesiveness of other ingredients in a tablet is overcome by swelling in contact with water causing the tablet to fall apart. Pregelatinized starch is produced by hydrolyzing and rupturing of starch grain. It is a directly compressible disintegrant and its optimum concentration is 5-10%. Swelling is the main mechanism of action of pregelatinized starch. It¹⁵ is reported that pregelatinized starch is a modified starch which is prepared from potato starch and is used in piroxicam dispersible tablets. To prepare dispersion, different proportion of drug and disintegrants in the ratio 1: 1, 1: 3, 1: 9 are used. All the tablets disintegrated within three minutes. Due to superior swelling capacity of pregelatinised starch, the possible mechanism responsible for increased dissolution rate from this tablet is rapid disintegration.

Porosity and capillary action (Wicking)

Through porosity and capillary action, effective disintegrants that do not swell are believed to impart their disintegrating action. Tablet porosity is responsible for providing pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness and compressibility) themselves act to enhance porosity and provide these pathways into the tablet. Through capillary action, liquid is drawn up or "wicked" into these pathways and rupture the interparticulate bonds causing the tablet to break

apart (Fig. 1). Crospovidones are synthetic, insoluble, crosslinked homopolymers of N-vinyl-2-pyrrolidone. Crospovidone quickly wicks saliva into the tablet to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration. Unlike other superdisintegrants which depend principally on swelling for disintegration, crospovidones uses a combination of swelling, wicking and deformation¹⁶. Rajesh Y V et al.,¹⁷ formulated fast dissolving Efavirenz formulation by using three different superdisintegrants such as croscarmellose sodium (CCS), sodium starch glycolate (SSG) and crospovidone (CP). It is concluded that CP is able to release the drug faster than the other two disintegrants.

Deformation

Thoughtfully, starch grains are "elastic" in nature which means that the grains are deformed under pressure and will return to their original shape when that pressure is removed (Fig. 2). But, these grains are believed to be deformed more permanently with the compression forces involved in tableting and are said to be "energy rich" with this energy being released upon exposure to water. In "energy rich" starch grains, the ability for starch to swell is higher than it is for starch grains that have not been deformed under pressure. This mechanism of starch has only recently begun to be studied.

Electrostatic repulsion

Swelling of tablet made with 'nonswellable' disintegrants is another mechanism of disintegration. Guyot-Hermann et al.,¹⁸ has proposed a particle repulsion theory which is based on the observation that non-swelling particle also cause disintegration of tablets. The mechanism of disintegration is the electric repulsive forces between the particles and water is required for it (Fig. 3). It is observed that repulsion is secondary to wicking.

Superdisintegrants

In recent years, several newer agents known as "Superdisintegrants" have been developed. These newer substances are having greater disintegrating efficiency, effective at lower concentrations and are more effective intragranularly. The superdisintegrants swell, hydrate, change volume or form on contact with water and produce a disruptive change in the tablet. Effective superdisintegrants have no negative impact on the mechanical strength of formulations thus provide improved compressibility and compatibility. Superdisintegrants offer significant improvements over starch. But hygroscopicity may be a problem in some formulations. With time, demand for faster disintegrating mechanisms in the formulation is

increased. Superdisintegrants act by swelling which causes tablet to burst or the accelerated absorption of water due to swelling pressure exerted in the outer direction or radial direction thus leading to an enormous increase in the volume of granules to promote disintegration. Three major groups of compounds (croscarmellose, crospovidone and sodium starch glycolate) have been developed which swell to many times their original size when placed in water while producing minimal viscosity effects.

Advantages

They are effective in lower concentrations than starch, have less effect on compressibility and flow ability and are more effective intragranularly.

Disadvantages

A few of them are more hygroscopic and some are anionic which may cause some slight in-vitro binding with cationic drugs.

Table no:-1 Commercially available superdisintegrants ¹

S.NO.	Superdisintegrants	Mechanism of Action	Properties	Commercial Available Grades
1	Cross linked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and wicking.	-Swells in two dimensions. -Direct compression or granulation. -Starch free.	Crosscarmellose Ac-Di-Sol [®] Nymce ZSX [®] Primellose [®] Solutab [®] Vivasol [®]
2	Cross linked PVP	Swells very little and returns to original size after compression but act by capillary action.	-Water insoluble and spongy in nature so get porous Table t.	Crospovidone Crosspovidon M [®] Kollidon [®] Polyplasdone [®]
3	Cross linked starch	-Swells 7-12 folds in < 30 seconds.	Swells in three dimensions and high level serve as sustain release matrix.	Sodium starch glycolate Explotab [®] Primogel [®]
4	Cross linked alginic acid	Rapid swelling in aqueous medium or Wicking action.	Promote disintegration in both dry and wet granulation.	Alginic acid NF Satialgine [®]
5	Soy polysaccharides		Does not contain any starch sugar. -Used in nutritonal products.	Emcosoy [®]
6	Calcium silicate	Wicking action	Highly porous light weight. Optimum concentration is between 20-40%.	

PVP – Polyvinylpyrrolidone

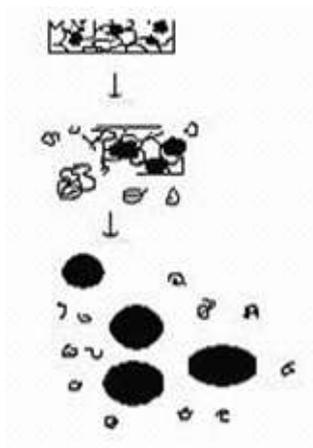


Figure 1: Particles swell and break the matrix form within tablet

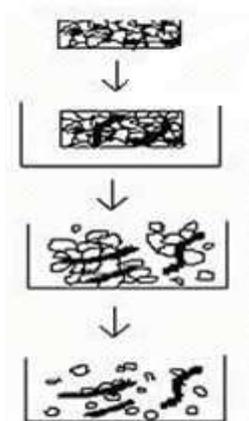


Figure 2: Wicking mechanism

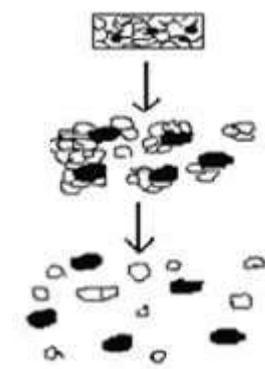


Figure 3: Particles swell to pre-compression size and break up matrix

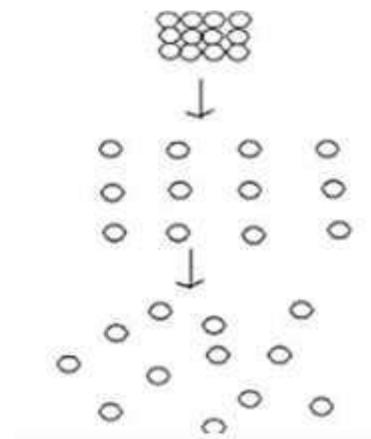


Figure 4: Electrostatic repulsion

Conclusion:

From the above review, it can be concluded that superdisintegrants are having greater disintegrating efficiency, effective at lower concentrations and are more effective intragranularly so 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. It is reported study wise that the water-insoluble superdisintegrants show better disintegration property than the slightly water-soluble agents, since they do not have a tendency to swell. The presence of a superdisintegrants produce sufficiently hard tablets that still disaggregate within seconds and can be considered as “fast dispersible”. Incorporation of superdisintegrant in solid dispersions also prevented crystallization of drug during dissolution in the presence of hydrophilic carriers. Tablets containing super disintegrants in combination show excellent in vitro dispersion time and drug release as compared to other formulations. 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.

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