



## SUPERDISINTEGRANTS: AN OVERVIEW

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### ABSTRACT

An oral solid dosage form should ideally disperse into the primary particles from which it was prepared. Tablets and capsules which need rapid disintegration, the inclusion of the right disintegrant is a prerequisite for optimal bioavailability. Superdisintegrants are used to improve the efficacy of solid dosage forms. This is achieved by decreasing the disintegration time which in turn enhances drug dissolution rate. Disintegrants are substances or mixture of substances added to the drug formulation that facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Superdisintegrants are generally used at a low level in the solid dosage form, typically 1- 10 % by weight relative to the total weight of the dosage unit. The present study comprises the various kinds of superdisintegrants which are being used in the formulation to provide the safer, effective drug delivery with patient's compliance.

**Keywords:** superdisintegrants, dissolution rate, polymers, ion exchange resins.

### INTRODUCTION

Disintegrants are agents added to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule "slugs" into smaller fragments in an aqueous environment there by increasing the available surface area and promoting a more rapid release of the drug substance. They promote moisture penetration and dispersion of the tablet matrix. Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. The emphasis on the availability of drug highlights the importance of the relatively rapid disintegration of a tablet as a criterion for ensuring uninhibited drug dissolution behavior. Number of factors affects the disintegration behavior of tablets. The disintegrants have the major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablet. The stronger the binder, the more effective must be the disintegrating agents in order for the tablet to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but also into powder particles from which the granulation was prepared. Disintegrants are an essential component to tablet formulations. The ability to interact strongly with water is essential to disintegrant function. Combinations of swelling and/or wicking and/or deformation are the mechanisms of disintegrant action. A disintegrant used in granulated formulation processes can be more effective if used both "intragranularly" and "extragranularly" 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 disintegrant 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 disintegrant. Since a compaction process does not involve its exposure to wetting and drying, the disintegrant 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. In a direct compression process, drug is blended with a variety of excipients, subsequently lubricated and directly compressed into a tablet. A disintegrant used in this type of formulation, simply has to break the tablet apart to expose the drug substance for dissolution<sup>1,2</sup>.

Most common tablets are those intended to be swallowed whole and to disintegrate and release their medicaments rapidly in the gastrointestinal tract (GIT). The proper choice of disintegrant and its consistency of performance are of critical importance to the formulation development of such tablets. In more recent years, increasing attention has been paid to formulating not only fast dissolving and/or disintegrating tablets that are swallowed, but also orally disintegrating tablets that are intended to dissolve and/or disintegrate rapidly in the mouth. Most prior studies have focused on the function-related properties of superdisintegrants with special emphasis on correlating these functional properties to disintegrant efficiency and drug release rate. Water penetration rate and rate of disintegration force development are generally positively related to disintegrant efficiency in nonsoluble matrices. However, such a positive correlation is not always observed between tablet disintegration time and drug dissolution rate.



## MECHANISM OF TABLET DISINTEGRATION

**A. Swelling:** Although not all effective disintegrants swell in contact with water, swelling is believed to be a mechanism in which certain disintegrating agents (such as starch) impart the disintegrating effect. By swelling in contact with water, the adhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart.

**B. Porosity and Capillary Action (Wicking):** Effective disintegrants that do not swell are believed to impart their disintegrating action through porosity and capillary action. Tablet porosity provides pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness & compressibility) themselves act to 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.

**C. Deformation:** Starch grains are generally thought to be “elastic” in nature meaning that grains that are deformed under pressure will return to their original shape when that pressure is removed. But, with the compression forces involved in tableting, these grains are believed to be deformed more 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.

**D. Due to disintegrating particle/particle repulsive forces:** Another mechanism of disintegration attempts to explain the swelling of tablet made with ‘nonswellable’ disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking<sup>3</sup>.

In recent years, several newer agents have been developed known as “Superdisintegrants”. These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs. Super disintegrants offer significant improvements over starch. But hygroscopicity may be a problem in some formulations. As day’s passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrants i.e. Superdisintegrants which are effective at low concentration and have greater

disintegrating efficiency and they are more effective intragranularly. And this superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration. Three major groups of compounds have been developed which swell to many times their original size when placed in water while producing minimal viscosity effects. Different commonly used superdisintegrants are

### 1. Modified Starches- Sodium Carboxymethyl Starch (Sodium Starch Glycolate)

It is possible to synthesize sodium starch glycolate from a wide range of native starches, but in practice potato starch is used as it gives the product with the best disintegrating properties. After selection of the appropriate starch source the second step is the cross-linking of the potato starch. This is typically carried out using an FDA approved starch esterifying agent such as sodium trimetaphosphate or phosphorus oxychloride in alkaline suspension. The effect of introduction of the large hydrophilic carboxymethyl groups is to disrupt the hydrogen bonding within the polymer structure. This allows water to penetrate the molecule and the polymer becomes cold water soluble. The effect of the cross-linking is to 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.

### 2. Cross-linked polyvinylpyrrolidone (crospovidone)

Crospovidone quickly wicks saliva into the tablet to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth. Unlike other superdisintegrants, which rely principally on swelling for disintegration, Crospovidone superdisintegrants use a combination of swelling and wicking. When examined under a scanning electron microscope, crospovidone particles appear granular and highly porous. This unique, porous particle morphology facilitates wicking of liquid into the tablet and particles to generate rapid disintegration. Due to its high crosslink density, crospovidone swells rapidly in water without gelling. Other superdisintegrants have a lower crosslink density and, as a result, form gels when fully hydrated, particularly at the higher use levels in ODT formulations. Unlike other superdisintegrants which are either poorly compressible or non-compressible, Crospovidone disintegrants are highly compressible materials as a result of their unique particle morphology. In contrast to sodium starch glycolate and croscarmellose sodium, Crospovidone superdisintegrants exhibit virtually no tendency toward gel formation, even at high use levels. Disintegrants that gel can result in ODT and chewable products with an unpleasant, gummy texture.



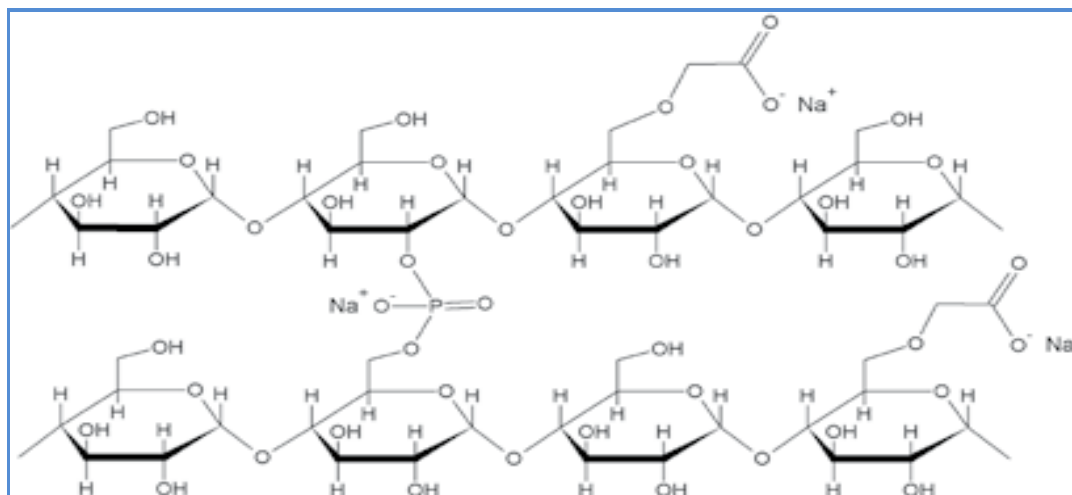
Crospovidone superdisintegrants provide the best overall sensory experience as well as rapid disintegration and robust tablets.

### 3. Modified Cellulose (croscarmellose sodium)

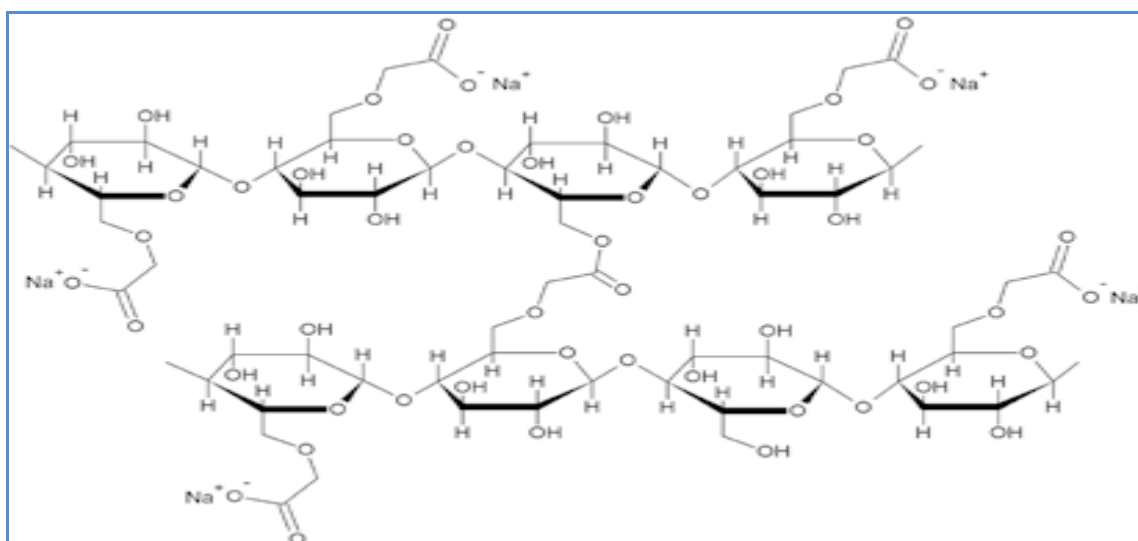
Croscarmellose sodium is described as a cross-linked polymer of carboxymethylcellulose. Apart from the differences between the starch and cellulose polymer backbones, there are Differences between the synthetic processes used to modify the polymer. Most importantly,

the DS of croscarmellose sodium is higher than that of sodium starch glycolate, and the mechanism of cross-linking 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<sup>4-9</sup>.

**Figure 1: Basic Structure of Sodium Starch Glycolate**



**Figure 2: Basic Structure of Croscarmellose Sodium**



**4. Soy polysaccharide**-It is a natural super disintegrant that does not contain any starch or sugar so can be used in nutritional products.

**5. Cross-linked alginate acid** -It is insoluble in water and disintegrates by swelling or wicking action. It is a hydrophilic colloidal substance, which has high sorption capacity. It is also available as salts of sodium and potassium.

**6. Gellan gum** -It is an anionic polysaccharide of linear tetrasaccharides, derived from *Pseudomonas elodea* having good superdisintegrant property similar to the modified starch and celluloses.

**7. Xanthan gum** -Xanthan Gum derived from *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.

**8. Calcium Silicate** -It is a highly porous, lightweight superdisintegrant, which acts by wicking action.

**Ion exchange resins** -The INDION 414 has been used as a superdisintegrant for ODT. It is chemically cross-linked polyacrylic, with a functional group of – COO – and the standard ionic form is K<sup>+</sup>. It has a high water uptake capacity. It is a high purity pharmaceutical grade weak acid cation exchange resin supplied as a dry powder. It is an extremely effective tablet disintegrant which provides the necessary hardness and chemical stability to the tablet. The product swells up to a very great extent when in contact with water or gastrointestinal fluids causing rapid disintegration without the formation of lumps. It is a high molecular weight polymer, therefore it is not absorbed by the human tissues and totally safe for human consumption. It has several advantages<sup>10-15</sup>.

#### Advantages

Remarkable tendency on wetting causing rapid disintegration

No lump formation on disintegration

Compatible with commonly used therapeutical agents and excipients.

Work equally effective in hydrophilic and hydrophobic formulations.

Provides good mechanical strength to the tablet facilitating easy packing and transportation.

Does not stick to the punches and dyes.

Although there are many superdisintegrants, which show superior disintegration, the search for newer disintegrants is ongoing and researchers are experimenting with modified natural products, like formalin casein, chitin, chitosan, polymerized agar acrylamide, xylan, smecta, key jo-clay, crosslinked carboxymethyl guar and modified tapioca starch. Studies have suggested that the water insoluble superdisintegrants show better disintegration property than the slightly water soluble agents, since they do not have a tendency to swell. Superdisintegrants that tend to swell show slight retardation of the disintegration property due to formation of viscous barrier. There is no particular upper limit regarding the amount of superdisintegrant as long as the mechanical properties of the tablet are compatible with its intended use. The superdisintegrant may be used alone or in combination with other superdisintegrants. Commercially available superdisintegrants are listed in the table given below<sup>16-18</sup>.

**Table 1:** Various Superdisintegrants and Their Properties

Superdisintegrants	Commercially available grades	Mechanism of action	Special comment
Crosslinked cellulose	Crosscarmellose <sup>®</sup> Ac-Di-Sol <sup>®</sup> , Nymce ZSX <sup>®</sup> Primellose <sup>®</sup> , Solutab <sup>®</sup> , Vivasol <sup>®</sup> , L-HPC.	Swells 4-8 folds in < 10 seconds. Swelling and wicking both.	Swells in two dimensions. Direct compression or Granulation Starch free.
Crosslinked PVP	Crosspovidon M <sup>®</sup> Kollidon <sup>®</sup> Polyplasdone <sup>®</sup>	Swells very little and returns to original size after compression but act by capillary action.	Water insoluble and spongy in nature so get porous tablet.
Crosslinked starch	Explotab <sup>®</sup> Primogel <sup>®</sup>	Swells 7-12 folds in < 30 seconds.	Swells in three dimensions and high level serve as sustain release matrix.
Crosslinked alginic acid	Alginic acid NF	Rapid swelling in aqueous medium or wicking action.	Promote disintegration in both dry or wet granulation.
Soy polysaccharides	Emcosoy <sup>®</sup>		Does not contain any starch or Sugar. Used in nutritional products.
Calcium silicate		Wicking action.	Highly porous, Light weight,

#### CONCLUSION

Overviews of various types of superdisintegrants which are available have been discussed. The ease of availability of these agents and the simplicity in the direct compression process suggest that their use would be a more economic alternative in the preparation of ODT than the sophisticated and patented techniques

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