Review Article

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Superdisintegrants, Utility in Dosage Forms: A Quick Review

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ABSTRACT:

In dosage forms, solid orals gain maximum popularities, about 85%, because of many advantages over others. The therapeutic activity of these formulations is obtained through a typical manner like disintegration followed by dissolution. Hence disintegration has major role for facilitating drug activity and thus gain popularity among other dosage forms. In this review article, more emphasis is given on application and usage of various superdisintegrants comparing with other disintegrants in reference to available scientific studies. The various sources of superdisintegrants and their modification to improve disintegration property are also high-lighted.

Keywords: Disintegrants, Orally disintegrating tablet, Superdisintegrants.

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Introduction:

Controlled drug delivery systems are starting their pace in today's pharmaceutical market, but the solid orals particularly tablets are most common and favorable approach with patient compliance as on date. These conventional tablets are intended to be swallowed whole and desired to disintegrate, release the medicaments for dissolution and providing therapeutic efficacy rapidly in the gastrointestinal tract. As disintegration plays a crucial role, so for development of solid orals, formulators are fascinating towards selection of proper disintegrats / superdisintegrants in dosage systems. [1, 2]

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. Superdisintegrants, are those substances, which facilitate the faster disintegration with smaller quantity in contrast to disintegrants.

The disintegration of dosage forms are depends upon various physical factors of disintegrants/superdisintegrants. [3,4] They are as follow:

1. Percentage of disintegrants present in the formulation.
2. Proportion of disintegrants used.
3. Compatibility with other excipients.
4. Presence of surfactants.
5. Hardness of the tablets.
6. Nature of Drug substances.
7. Mixing and types of addition.

Table 1. List of Common Disintegrants and Superdisintegrants:-

Sr. no	Name of excipients	Category	Conc.	Stability criteria
1	Alginic acid	Disintegrants	1-5%	Hydrolyzes slowly at room temperature
2	Colloidal Silicon Dioxide	Disintegrants	5-10%	Hydroscopic , but do not liquefy upon absorption of water
3	Cross-povidone	Superdisintegrants	2-5 %	As hygroscopic in nature, stored in an air-tight container, in a cool and dry place.
4	Methyl cellulose	Disintegrants	2-10%	Slightly hygroscopic, but stable
5	Micro-crystalline cellulose	Superdisintegrants	5-15%	Stable at dry and air tight condition
6	Starch	Superdisintegrants	5-10%	Stable at dry and air tight condition

They all should possess the following characteristics:

1. Poor water solubility with good hydration capacity,
2. Poor gel formation,
4. Good flow properties,
5. Good compressibility,
6. Inert,
7. Non-toxic,
8. Requirement of least quantity.

METHOD OF INCORPORATION:

The incorporation of superdisintegrants in the dosage forms are mainly of three types

I. Intragranular 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.

II. Extragranular or prior to compression - In this process, the superdisintegrants are mixed with prepared granules before compression.

III. Incorporation of superdisintegrants at intra and extra granulation steps- In this process part of superdisintegrants are added to intragranular and a part to extragranules. This method usually produces better results and more complete disintegration than type I and type II.

Mechanism of Action:

The following mechanisms are responsible for the breaking of tablets and bulk contents of capsules into small pieces. They are of four types such as –

1. By Swelling action: - In this mechanism, superdisintegrants swell when they come in contact with water (e.g. starch).

2. By capillary (wiking) action -In this mechanism, the disintegrants that do not swell facilitate disintegration by their physical nature of low cohesiveness and low compressibility. Thus they provide porosity and capillary action for the penetration of liquid into the bulk, rupture intra particulate bonds and cause the disintegration.

3. Combination action: - In this mechanism, the combination of both wicking and swelling action facilitate disintegration. E.g. Crosspovidone

4. Deformation: - In case of starch (such as potato starch and corn starch) are believed to be elastic in nature, but due to high compaction force in case of tableting the elasticity deformed to plasticity with energy rich potential. When these tablets are exposed to aqueous environment, the energy potential of deformed starch grain will be triggered to cause disintegration.

SUPER-DISINTEGRANTS USED IN DOSAGE FORMS

1. Sodium Starch Glycolate (Explotab® and Primogel®)

The oldest and probably the most widely used disintegrant, the starch is modified with a dramatic disintegrating properties and are available as Explotab® and Primogel®. These are low substituted carboxy methyl starches in granular forms. The mechanism involves rapid absorption of water leading to an enormous increase in volume of granules result fast and uniform disintegration. (Figure 1)

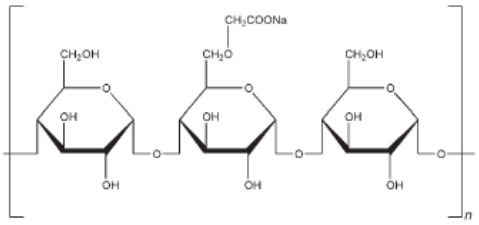

Figure 1. Structure of Sodium Starch glycolate

When these superdisintegrants are used in formulations they show the disintegration of solid dosage form within two minutes. The higher dissolution rates observed with superdisintegrants may be due to rapid disintegration and fine dispersion of particles formed after disintegration.

The experimental work conducted by choudhary *et al*[5] shows better dissolutions profile of sparfloxacin tablets with addition of primogel and other disintegrants such as cross carmellose sodium, cross povidone and potato starch.

The sodium starch glycolate was incorporated in the beads of the enteric coated antigen micro spheres as a superdisintegrant by Zhang *et al*[(6)], shows significantly faster antigen release rate and reduction in breaking time of the film due to the swelling force generated by incorporation of this superdisintegrant .

2. Cross-linked poly-vinyl Pyrrolidone (Cross Povidone)

In case of mouth-dissolving formulations, Crospovidone quickly wicks saliva into them to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth. Unlike other superdisintegrants, it relies on both swelling and wicking principally for disintegration.

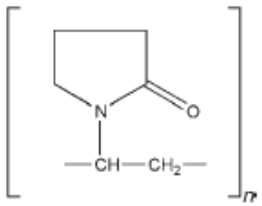

Figure 2. Structure of Cross-povidone

When examined under a scanning electron microscope, crospovidone particles appear to be granular and highly porous. This unique, porous nature facilitates wicking of liquid into the dosage systems and causes rapid disintegration. Due to high crosslink density of crospovidone, it swells rapidly in water without gel formation than others [(7)].

In contrast to other superdisintegrants like sodium starch glycolate and croscarmellose sodium, Crospovidone exhibit virtually no tendency toward gel formation, even at high ratio. As disintegrants that result gel formation is not appreciable in orally disintegrating tablets (ODTs) and chewable products.

3. Alginates

These are hydrophilic colloidal substances extracted naturally from certain species of Kelp or chemically modified from natural sources like alginic acid or salt of alginic acid. They are having higher affinity for water absorption and capable for an excellent disintegrants. They can be successfully used with ascorbic acid, multivitamins formulation.

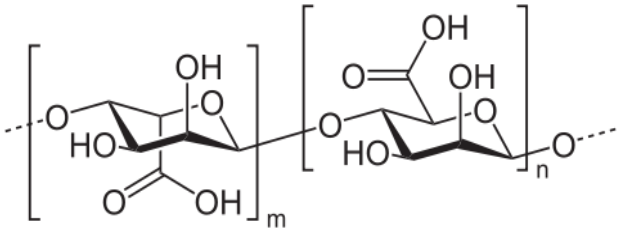

Figure 3:- Structure of alginic acid

4. Cellulose Derivatives (Ac-Di-Sol®**)**

Croscarmellose sodium is described as a cross-linked polymer of carboxy methyl cellulose (CMC). This polymer is different in synthesis and structure as compare to Sodium starch glycolate. Most importantly, the degree of substitution using Williamson's ether synthesis of croscarmellose sodium is higher than that of sodium starch glycolate, and the mechanism of crosslinking is also different. The chemistry of SSG is different that of cross carmellose sodium

As some of the carboxymethyl groups themselves are used to cross-link the cellulose chains. For example, the cross-linking in Primogel are phosphate ester rather than carboxyl ester links as compare to Cross carmellose sodium.

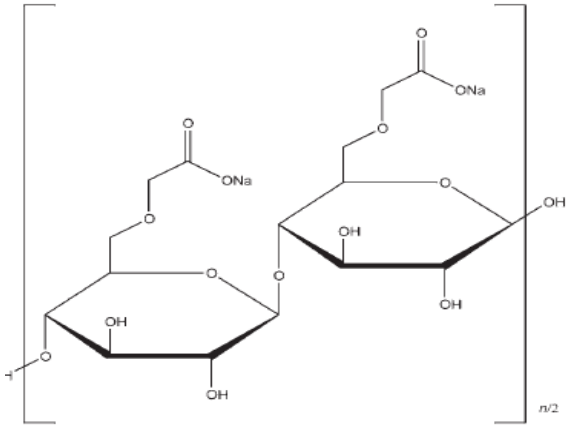

Figure 4: Structure of Crosscarmellose sodium

Augsburger *et al* [(8)] has designed to examine the dissolution profile of Hydrochlorthiazide direct compressible tablet at different pH with various disintegrants like Ac-Di-Sol, primogel®, polyplasdone –XL-10 and corn starch for their rapid liquid absorption and swelling nature. Among all Ac-Di-Sol shows better drug dissolution with minimum disintegrant concentration with no significant variation.

In the experiment of wicking and disintegrating property of primogel® and cornstarch, compared with Ac-Di-Sol in encapsulation of these superdisintegrants into hard gelatin capsule by Botzolakis[(9)] et al shows higher in Ac-Di-Sol.

5. Microcrystalline Cellulose (Avicel)

Avicel concentration of less than 10%, exhibits better disintegration. This mechanism is depending on entry of water to the tablet matrix through capillary pores, which breaks the hydrogen bonding between adjacent bundles of cellulose microcrystals. With more concentration, particularly in oral disintegrating tablet, it shows a tendency to stick to the tongue due to rapid capillary absorption and faster dehydration of the tablet surface. As Avicel has a fast wicking rate for water, hence this in combination with starch makes an excellent and rapid disintegration in OTD formulations [(10-12)].

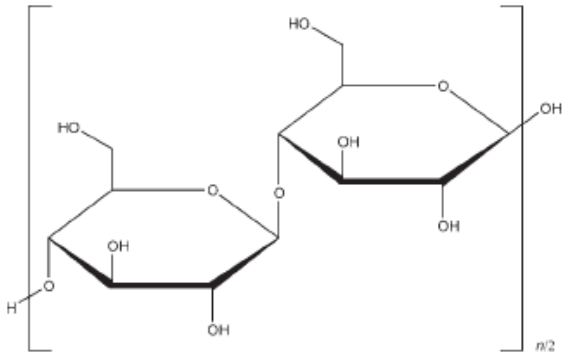

Figure 5: Structure of Microcrystalline cellulose

In a study, MCC was used as disintegrating agent in the formulation of fast releasing compressed propranol hydrochloride suppositories as reported.

Watanabe [13, 14] used microcrystalline cellulose as disintegrant along with low substituted hydroxy propyl cellulose (L-HPC) to prepare rapidly disintegrating tablets.

6) Chitin/Chitosan–Silicon Dioxide Coprecipitate

Chitin is one of the recent and most interesting category of superdintegrant. It is the second most abundant polysaccharide found in nature after cellulose

Naturally Chitin is extracted from the shell wastes of shrimp, crab, lobster, krill, and squid and used for the production of chitosan by a deacetylation reaction in alkaline medium. However, in large-scale handling of pharmaceutical blends both chitin and chitosan powders show poor bulk density, thus results in poor flowability and compressibility [15]. To overcome such weakness they may be coprecipitated with colloidal silicon dioxide to improve their physical properties.

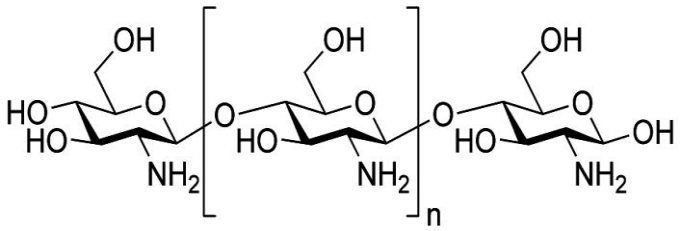

Figure 6: Structure of chitosan

The comparative study of other superdisintegrants with Chitin–silica coprecipitate has proved better disintegration and dissolution functionality.

The particle rearrangement and plastic deformation ability of chitin–silica undergoes in the same extent compared with Avicel. The good compressibility and the good compactability properties of chitin–silica may allow it to be used in direct compression applications [14, 16].

The high hygroscopicity and high water capillary penetration of chitin-silica provides the driving force for disintegration. The ability of chitin–silica used as filler in solid dosage form with no concentration limits of the superdisintegrant, can impart further benefit in pharmaceutical applications.

7) Indion 414

It is safe for oral consumption, economical and easily available polymer. By nature, it is ion exchange resin and if used as superdisintegrants as compared to conventional ones, swell on getting hydrated without dissolution and devoid of adhesive tendency, cause uniform tablet disintegration. [16 ,17]

They do not form lumps, do not stick to tablet press components and are compatible with commonly used active pharmaceutical ingredients as well as other pharmaceutical necessities.

They offer better hardness to the tablets on compression. Indion 414 is more effective in hydrophobic formulations, as compared to the conventional disintegrants [18,19].

For effective disintegration ability in the tablets, concentration of Indion 414 is used in range from 0.5 to 2%.

8) Modified Polysaccharides

Agar (AG) and guar gum (GG), natural polysaccharides are treated with water and co grinded further with mannitol which exhibit superdisintegration property. These modified polysaccharides may call C-TAG (co grinded treated agar) and C-TGG (co grinded treated guar gum) respectively. [20, 21]

They are biodegradable, directly compressible, having desirable swelling dynamics. The above modified polyschharides were further used as superdisintegrants in Roxithromycin fast dispersible tablets and compared with conventional tablets containing MCC. The C-TAG and C-TGG have shown better disintegration for their porous nature, better water intake ability and free flowing property than others. [22]

Another natural polysscharide, karaya gum is modified using distilled water to achieve superdisintegration property in dispersible tablet development. This modified karaya gum(MKG) is easy to prepare, cheap, easily available, biodegradable and stable compared to available synthetic super disintegrants in market.

9) Mucilage of *plantago ovate* seed husk (Isapghula)

The mucilage of *plantago ovata* is a recent innovation for its superdisintegration property when compared with Crospovidone [23]. It shows faster disintegration time than the superdisintegrant,Crosspovidone.

Applications of superdisintegrants

Table 2. Marketed Orally disintegrating formulations [24, 25]

Proprietry Name	Generic Name	Manufacturer
Caffeine fast dissolving film	Caffeine	Hughes medical corporation,U.S.A
Calritin Reditabs	Loratadine	Schering Plough,U.S.A
Diphemhydramine HCl fast dissolving films	Diphemhydramine HCl	Hughes medical corporation,U.S.A
Doneprezil rapid dissolving films	Doneprezil	Labtec Pharma, Germany
Folic Acid mouth dissolving film	Folic acid	Hughes medical corporation,U.S.A
Imodium lingual	Loperamide	R.P. Scherer Corp.,U.S.A
Maxalt	Rizatriptan Banzoate	Merk , USA
Methylcobalamin film	Methylcobalamine	Hughes medical corporation,U.S.A
Nimpain MD	Nimesulide	Prompt cure pharma, India
Nurofen Flashtab	Ibuprofen	Boots healthcare, China
Pepcidin Rapitab	Famotidine	Merck & Co.,U.S.A
Rapidfilm	Ondansatron	Labtec pharma,Germany
Zofran	Ondansatron	GlaxosmithKline , UK

The uses of superdisintegrants are extended in the applications of oral disintegration tablets, fast-dispersible tablets, capsules, mouth-dissolving films, etc. Particularly for ODTs and fast dispersible tablets, are optimized based on their disintegration time. ODTs need to be disintegrated in the presence of saliva in oral cavity within a minute. Thus these formulations achieve better patient compliance in all classes from pediatric to geriatric, bedridden and uncooperative patients including frequent travelers as it requires little or no access of water.

Few marketed formulations containing superdisintegrant(s) are high-lighted in the table no.2.

This review article inclined towards the approach of superdisintegrants in various formulations, the innovations, already patented in related field are listed as

1. **Pharmaceutical superdisintegrant** (US20050100600): Superdisintegrants which provide improved compressibility compared to prior art superdisintegrants. The superdisintegrants include a particulate agglomerate of coprocessed starch or cellulose and a sufficient amount of an augmenting agent to increase the compactibility of the superdisintegrant.

2. **Rapidly disintegrating enzyme-containing solid oral dosage compositions** (US20060013807): Invention relates to rapidly disintegrating solid oral dosage forms having an effective amount of an enzyme and a superdisintegrant. The enzyme lactase is claimed in this patent for solid oral formulations.

3. **Fast disintegrating tablets** (US20050169986): A fast disintegrating tablet comprising Nimesulide and one or more disintegrants. In this research superdisintegrants used are croscarmellose cellulose, crospovidone and sodium starch glycolate.

4. **Method of producing fast dissolving tablets** (US20100074948): A method of producing a fast-melt tablet. The process does not involve any granulation step, thereby making the process more energy efficient and cost effective. The fast dissolving sugar alcohol is selected from the group comprising: mannitol; sorbitol; erythritol; xylitol; lactose; dextrose; and sucrose. The active component is suitably provided in the form of microparticles or microcapsules having an average diameter of less than 125 microns.

5. **Disintegrating Loadable Tablets** (US20090186081): A disintegrating loadable tablet product in compressed form. A disintegrant or a mixture of disintegrants has a) porosity of 45% v/v or more, b) a hardness of at least 20 Newton, and c) a loading capacity of at least 30% of a liquid.

6. Rapidly disintegrating tablet (US20060115528): The study relates to rapidly disintegrating tablets intended to be used as orodispersible tablets or dispersible tablets. The tablets include silicified microsrystalline cellulose. They are especially suitable for antibiotics. Rapidly disintegrating tablets which contain amoxicillin and clavulanic acid are also described.

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