Superdisintegrants and Their Inevitable Role in Orodispersible Tablet

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ABSTRACT

Oral drug delivery systems provide wide varieties of advantages in recent and current periods. And it is a widely acceptable route by all type of patients. Orodispersible tablets are those solid dosage forms which contain drugs that disintegrate completely in the oral cavity within one minute. In the pharmaceutical industries also they are widely using. The orodispersible tablets get rapidly disintegrate in the oral cavity, they don’t need any requirement of chewing and water. The major component present in the orodispersible tablets are the superdisintegrants. The superdisintegrants are those agents which help to improve the disintegration of the tablet. There are multiple categories of superdisintegrants used in the fast disintegrating or oral disintegrating tablets. They are of synthetic, semi-synthetic, natural, co-processed blends, multifunctional superdisintegrants, etc. This review highlights the different types of superdisintegrants, their mechanism, their properties and ideal characters.

Keywords:- Superdisintegrants, Disintegrants, Natural & Synthetic, Co-processed

INTRODUCTION

One of the important drug delivery route for the drug administration is the oral route.1 Hence through this route the oral tablets can be administered. Solid dosage forms are well known because of their accurate dosing, better patient compliance, self-medications and also ease of administration.2 The orally disintegrating tablets can be effectively used. They can provide a better performance than the conventional tablets. Orodispersible tablets get disintegrate on the buccal mucosa of patient. So the orodispersible tablet is a novel drug delivery system which providing a better patient compliance or acceptance. It can also be used as a better alternative for other oral medications.3

In recent times the orodispersible tablets becoming very popular. It is because they can be disintegrate within few seconds on the mouth of patient after administration.3 So the disintegration having a major role in orodispersible tablets. And the selection of disintegrant or the superdisintegrants should provide with a special emphasis.

Disintegrants are those agents, which helps the tablet to breakup into small fragments and they also promote more rapid drug release. They help in moisture penetration and also dispersion of the tablet. In order to achieve a fast drug release the disintegration is considered as the essential and important step.4 Various factors of superdisintegrants influencing the disintegration of tablets, they are;

a) Amount of superdisintegrant
b) Percentage of disintegrant in the formulation
c) Method for the addition of superdisintegrant
d) Compatibility with other excipients
e) Nature of added drug substance
f) Manner of mixing

**Superdisintegrants:** Superdisintegrants are those agents which facilitates the disintegration in a faster manner. The superdisintegrants are used in very small concentration of 1-10% by weight relative to total weight of dosage units. These agents are having absorbance property other than a swelling property. They not at all absorb significant amounts of water but they swells very fast. Superdisintegrants can be considered as a structural weakener which helps in disintegration of solid dosage forms. When the dosage form get exposed to the wet environment, they get physically dispersed within the dosage form and will expand. These particles are also compressible which helps to improve tablet hardness and friability. The superdisintegrants provide compressibility, compatibility in an improved manner and they show no negative impact on the mechanical strength of formulations containing high dose drugs. \[2,5\]

**IDEAL CHARACTERISTICS OF SUPERDISINTEGRANTS:**

Since superdisintegrant is one of the inevitable excipient in the oral disintegrating tablet. So an ideal superdisintegrant should meet certain criterias other than the swelling property. The ideal characteristics of superdisintegrants involve the following:

- **Good hydration capacity**
The drugs or other excipients which have a hydrophobic nature, and could be adsorbed on the disintegrant surfaces, may influence the extent of hydration and also the effects of disintegrants. When fast disintegrants, which are having high hydration capacity were added, this problem can be reduced and thus enhance the dissolution. \[7\]

- **Poor Solubility**
The solubility is an important physical property accompanying by the particles which affect the effectiveness of the disintegrant. In a tablet formulation, solubility of the major component may affect both the rate and mechanism of tablet disintegration. Water soluble materials are more susceptible to dissolve than disintegration, while insoluble materials generally produce rapidly disintegrating tablets. And because of the presence of porous structure liquid may drawn up into these pathways via capillary action and results in the breakage of interparticulate bonds cause the tablet to break.

- **Poor Gel Formation**
When fully hydrated, disintegrants forms gel. For certain formulations they are required in a high level inorder to achieve desired tablet disintegration or drug dissolution. As the drug must first diffuse through the gel layer before being released into the body and gel delay dissolution. Sodium starch glycolate is one of the important superdisintegrant used in tablet formulation, at a concentration of 4-6%.Disintegration time may increase due to gelling and its subsequent viscosity producing effect, when the concentration become above 8% . \[6\]

- **Good Compressibility and Flow Properties**
The powders in the formula for tablet preparation, must attain a consistent particle size distribution and density to achieve proper flow. If the powders have a compressibility of 12-16%, then they are said to be good flow powders. Crospovidone is significantly more compressible than other Superdisintegrants and provides significantly higher breaking force. \[8,9\]

- **Complexation**
The potential interaction between drug actives and excipients is an important formulation consideration. Croscarmellose sodium and sodium starch glycolate are the anionic disintegrants. They may form complex with cationic drug actives and slow dissolution. \[10\]

**MODES OF ADDITION OF SUPERDISINTEGRANTS**
The methods for the addition of superdisintegrants to the tablet formulation
are of three types. The superdisintegrants can be incorporated into the formulation by following methods \[^{[11,13]}\].

1. **Internal Addition (Intragranular)**
2. **External Addition (Extragranular)**
3. **Partly Internal and External**

**1. Internal Addition (Intragranular):** In internal addition method, the superdisintegrants mixed with other excipient powders and they are added during the granulation. As a result superdisintegrants can be incorporated within the granules. The major advantage of this method is the easy addition and suitable for direct compression method.

**2. External Addition (Extragranular):** In external addition method, the superdisintegrants are added to the prepared granules along with mixing before compression. It is suitable for wet granulation process.

**3. Partially Internal and External:** In this method, part of disintegrant can be added internally or during granulation and part are added externally or after granulation. This method is more effective and result in immediate disintegration of tablet. \[^{[13]}\]

**Advantages of Superdisintegrants** \[^{[14,15]}\]

- Required in less concentration.
- They are compatible with large number of drug and excipients.
- Does not affect compressibility and flowability.

**Disadvantages of Superdisintegrants**

- Sensitive to moisture leading to instability.

**MECHANISM OF SUPERDISINTEGRANTS** \[^{[2,11,16,17]}\]

Superdisintegrants are used to enhance the efficacy of solid dosage forms. Due to the combined effect of swelling and water absorption of the formulation, the superdisintegrants may provide a rapid disintegration of the solid dosage form. The wetted surface of carrier get increases due to the swelling of the Superdisintegrants and this promotes the wettability and dispersibility of the system which in turn, enhance the disintegration and dissolution of the system. Superdisintegrants facilitate the rapid breakdown of tablets into small fragments and then forms a homogenous suspension which results in the faster dissolution and rapid onset of action. This can be achieved by various mechanisms:

- Swelling
- Wicking (Porosity and capillary action)
- Heat of wetting
- Chemical reaction
- Particle repulsive force
- Deformation recovery
- Enzymatic reaction
- Combination action (Swelling and wicking)

**1. Swelling**

Swelling is the most widely used general mechanism of action for tablet disintegration. A necessary first step for the tablet disintegration is the water penetration. Particles of disintegrants get swells and comes in contact with suitable medium the adhesiveness of the other ingredient in tablet is overcome causing the tablet to fall apart as shown in fig. 1. \[^{[18]}\] Due to lack of adequate swelling force, the tablets with high porosity show poor disintegration. And in the tablet with low porosity, sufficient swelling force should be exerted. Fluid is unable to penetrate in the tablet if the packing fraction is high also the disintegration slows down again.

![Figure 1: Swelling](image-url)
2. **Wicking (Porosity & capillary action)**
The penetration of medium tablet may lead to the disintegration of the tablet by the replacement of adsorbed air on the particles results in weakening of intermolecular bond and breakdown of tablets into its fine particles as shown in fig 2.\(^{18}\) The effective disintegrants which do not swell shows their disintegrating action through porosity and capillary action. The water uptake by the tablet mainly depends upon the hydrophilicity of drug or excipients based on the tabletting conditions. It is very important to maintain a porous structure and low interfacial tension towards the aqueous fluid for creating a hydrophilic network across drug particles.

![Figure 2: Wicking](image)

Disintegrant pulls water into the pores and reduce the physical bonding force between particles.

3. **Heat of Wetting**
For this mechanism to be happen disintegrants should have exothermic properties. When the disintegrant comes in contact with the aqueous medium or get wetted, a capillary air expansion may occur which leads to localized stress this in turn leads to the disintegration of tablet.

4. **Chemical reaction**
Tablet rapidly disintegrates due to the liberation of carbon dioxide internally in water, it occurs when tartaric acid or citric acid reacts with alkali bicarbonates or carbonates with water. The tablets disintegrate due to the formation of pressure within the tablet. The dissolution of active pharmaceutical ingredient in water as well as taste masking effect get enhanced due to the liberation of carbon dioxide gas. These disintegrants are highly sensitive to small changes of temperature and humidity.

5. **Particle Repulsive Force**
This mechanism of disintegrants explaining the swelling of tablet, made with non-swellable disintegrants. From Guyot-Hermann’s particle-particle repulsion theory, through hydrophilic pores the water may enter into the tablet and leads to the formation of a complete starch network and it transfer water form one particle to another, this leads to develop a hydrostatic pressure. When the water penetrates between the starch grains there cause an affinity of the starch surfaces, there leads to the breaking of hydrogen bonds and other forces holding the tablet together as shown in fig 3.\(^{19}\)

![Figure 3: Repulsion](image)

Water is drawn into the pores and particles repel each other due to the resulting electrical force.

6. **Deformation Recovery**
According to the deformation recovery theory, the shape of disintegrant particles change during compression and upon wetting, the particles return to their pre-compression shape thus this increase in shape of the deformed particles cause the tablet to break apart as shown in fig 4.\(^{19}\)

This type of phenomenon is the very important aspect of the mechanism of action of non swellable disintegrants like cross povidone and starch. Due to high compaction force while compression with energy rich potential, the high elastic nature of starch deformed to plasticity. Tablet disintegration occurs and triggers the energy rich potential of the deformed starch, when
these starch particles comes in contact with water.

Particles swell to precompression size and break up the matrix. 

**Figure 4:-Deformation**

7. Enzymatic reaction
Tablet disintegration occurs by some enzymes present in our body. They act as disintegrants by decreasing the binding ability of the binder. Swelling exerts pressure in the outer direction which makes the tablet to burst or by high amount of water absorption results in excessive granular volume which promotes the disintegration of tablet. Some disintegrating enzymes used are Amylase, Protease, Cellulase, Invertase etc.

8. Combination action (Swelling and wicking)
In this, the disintegrant cause breakdown of tablet by the combination of swelling and wicking mechanism. Crospovidone acts by combination of swelling and wicking is an example.

**TYPES OF SUPERDISINTEGRANTS**
Based on the source of origin and availability, superdisintegrants can be classified as;

a. Natural Superdisintegrants
b. Synthetic Superdisintegrants
c. Co-processed Superdisintegrants

**a. Natural Superdisintegrants**
These are the class of Superdisintegrants which are of natural origin. They are cheaper comparatively, abundantly available, non-irritating and nontoxic in nature. Because of easy availability, cost effectiveness, emollient, non-irritant nature, non-toxicity, capable of multitude of chemical modifications, potentially degradable and compatibility some natural materials like gums and mucilages have been widely used in the field of drug delivery. Several gums and mucilages which are having superdisintegrant actions are extensively used.[21-24]

Mucilages are the secondary plant metabolites. They are having high water binding capacity due to high concentration of hydroxyl groups in polysaccharide. So they can be widely used in pharmaceutical industries as thickeners, water retention agents, suspending agents and Superdisintegrants.[22, 23]

Some gums and mucilages have superdisintegrant activity are available which are given in table 1, some of them are;

**Isapgula (Plantago ovata seed mucilage):**
It mainly consist of the dried seeds of Plantago ovata which contain mucilage present in the epidermis of seeds. The seeds were soaked with distilled water for 48 hours and for complete mucilage release they are boiled for few minutes. Filtering and separation of marc were then done by squeezing the material through muslin cloth. The separated mucilage was then dried in an oven in less than 60ºc. This mucilage is having better superdisintegrant property compared to cross povidone.[24-26]

**Lepidium sativum Seed Mucilage:**
It is also known as asaliyo, they are widely used as herbal medicine and for different pharmaceutical applications. Seeds contain higher portion of mucilage, dimeric imidazole alkaloids etc. The extracted mucilage can be used for the development of fast dissolving tablets. They are having a characteristic odour and it is a brownish white powder which decomposes above 200ºc.

**Fenugreek seed mucilage:**
It is commonly known as fenugreek and it is a herbaceous plant. These seeds contain a high amount of mucilage and this can be used as a disintegrating agent in mouth dissolving
tablet formulations. Mucilage is an amorphous powder and it is off-white cream yellow coloured. The mucilage dissolves in warm water to form viscous colloidal solution. [23]

**Chitosan:** Chitosan is a natural polymer which is the second most abundant polysaccharide. Superdisintegrant property of chitosan can be utilized in the formulation of fast mouth dissolving tablets. When they come in contact with aqueous media, they engulf water and burst due to the pressure exerted by capillary action. So this leads to a fast disintegration. [28]

**Agar:** Agar is a dried gelatinous substance which is yellowish grey or white to nearly colourless. It is odourless with mucilaginous taste. Agar consist of two polysaccharides agarose and agarpectin. The agarpectin is responsible for the viscosity of agar solution. [29]

**Starch:** It is one of the most widely used disintegrant. This disintegrant acts in such a way that, it will form pathways throughout the tablet matrix which leads to draw water inside the structure due to capillary action, this results in disruption of tablet.

### Table 1. Some Natural Superdisintegrants with their source and mechanism[19,20]

<table>
<thead>
<tr>
<th>Sl. no</th>
<th>Natural Superdisintegrants</th>
<th>Source</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lepidium Sativum Mucilage was obtained from the seeds of Lepidus sativum</td>
<td>Swelling</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Locust bean gum Extracted from the seeds of carob tree.</td>
<td>Swelling and capillary action</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Guar gum Isolated from the endosperm seed of the gua gum</td>
<td>High strength gelling property.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Agar and treated agar Dried gelatinous substance obtained from Gelidium amansui and several other species of red algae.</td>
<td>Swelling</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Chitin and chitosan Chitin obtained from natural polysaccharide obtained from crab and shrimp shells.</td>
<td>Swelling</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Xanthum gum Derived from Xanthomonas compestris</td>
<td>Swelling property</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Soy polysaccharide High molecular weight polysaccharides obtained from soy beans.</td>
<td>Swelling</td>
<td></td>
</tr>
</tbody>
</table>

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### Advantages
- Local accessible
- Bio-acceptable and Eco-friendly.
- As compared to synthetic and renewable source they are of low price.

### b. Synthetic superdisintegrant

Synthetic Superdisintegrants are widely used in tablet formulation to facilitate or to improve the rate and extent of disintegration of tablet thereby increase the rate of drug dissolution.
Crosподовидон (cross-linked polyvinyl pyrrolidone): This superdisintegrant acts in combination of swelling and wicking mechanism. Because of its high cross linking density nature, crosподовидон swells rapidly without forming gel. Crosподовидон particles are granular and highly porous and this facilitates the wicking of liquid into the tablet and this leads to generate disintegration. Crosподовидон has solubility enhancing action also. [30]

Croscarmellose sodium: This is an internally cross linked polymer of carboxymethyl cellulose sodium. And it has high swelling capacity with minimal gelling which results in rapid disintegration. Croscarmellose also shows wicking action due to their fibrous nature. In tablet formulations, croscarmellose sodium can be used in both direct compression as well as in wet granulation processes. [30]

When croscarmellose sodium is used in wet granulation, it should be added in both wet and dry stages of the process. So the wicking and swelling ability of the disintegrant can be utilized well. [31,32]

Sodium Starch Glycolate: It is the sodium salt of a carboxymethyl ether of starch. These are also modified starches which are made by crosslinking of potato starch. The degree of crosslinking and substitution are the major factors which helps to consider it’s superdisintegrant effects. The effect of crosslinking is to reduce the water soluble fraction of the polymer and the viscosity of dispersion in water. [33] The mechanism of swelling of the starch takes place by the rapid absorption of water which leads to a great increase in the volume of granules results in rapid disintegration. [34]

Advantages [14]
- As compared to starch, effective in low concentration.
- Low effect on compressibility and flowability.
- Intragraνually more effective.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Synthetic Superdisintegrant</th>
<th>Mechanism</th>
<th>Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sodium starch Glycolate/sodium carboxymethyl starch</td>
<td>Absorb water quickly results in swelling, Swells in 3 dimension and high level acts as sustained release matrix.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Crosподovideн</td>
<td>Combination of swelling and wicking</td>
<td>Water insoluble, spongy in nature</td>
</tr>
<tr>
<td>3</td>
<td>Croscarmellose Sodium</td>
<td>Swelling and Wicking</td>
<td>Swells in 2 dimension</td>
</tr>
<tr>
<td>4</td>
<td>Cross linked Alginic acid</td>
<td>Rapid swelling or wicking</td>
<td>Promotes disintegration in both dry and wet granulation</td>
</tr>
<tr>
<td>5</td>
<td>Calcium silicate</td>
<td>Wicking action</td>
<td>Highly porous and have light weight</td>
</tr>
</tbody>
</table>

c. Co-processed Superdisintegrants

These are the new and improved Superdisintegrants continue to be developed to meet the needs of advanced tablet manufacturing. The major requirement for this is the development of various added functionality excipients. They are used to achieve formulations with desired and appropriate end effects. And now these are available as blends of excipients which can provide with disintegration property given in table 3. Co-processing excipients provides superior property compared to physical mixture of individual excipient mixture.

Co-processed blends of Excipients

Ludiflash: It is an unique co-processed blend of Mannitol (95%), crosподovideн(5%) and polyvinyl acetate(5%) which is manufactured under a validated patented process. It rapidly disintegrates within seconds into soft and creamy consistency. It specially designed to use in direct compression on standard high speed tablet machine for hard tablet and it gives extremely fast release rate. [32, 35]

F-melt: It is a spray dried excipient which is used in orally disintegrating tablets. F-melt consists of saccharides, disintegrating agents and inorganic excipients. It also exhibits excellent tabletting properties. And
to achieve a fast disintegration time, it facilitates rapid water penetration.

**Modified chitosan and silicon dioxide:** It is a new type and based on the co-precipitation of chitosan and silica. The chitosan and silica forms physical interaction and create an insoluble, hydrophilic highly absorbent material resulting in superiority in water intake, water saturation for gelling formation. \[^{36}\]

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Co-processed superdisintegrants</th>
<th>Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ludipress</td>
<td>Lactose monohydrate, polyvinylpyrrolidone and cross povidone</td>
</tr>
<tr>
<td>2</td>
<td>Starlac</td>
<td>Lactose and maize starch</td>
</tr>
<tr>
<td>3</td>
<td>Starcap 1500</td>
<td>Corn starch and Pregelatinized starch</td>
</tr>
<tr>
<td>4</td>
<td>Ludiflast</td>
<td>Mannitol, cross povidone and polyvinyl acetate</td>
</tr>
<tr>
<td>5</td>
<td>Ran-Explo-C</td>
<td>Microcrystalline cellulose, silica and crospovidone</td>
</tr>
<tr>
<td>6</td>
<td>Ran-Explo-S</td>
<td>Microcrystalline cellulose, silica and sodium starch glycolate</td>
</tr>
</tbody>
</table>

**Modified mannitols:**

**Pearlitol 200 SD:** These are the granulated mannitol which are of white, odourless, has a slight sweet taste and crystalline powder. They are having, great organoleptic property, non-carcinogenic and sugar free properties also exceptional physical and chemical stability. This can be used in wet or dry granulation, direct compression, compaction or freeze drying. It also has properties like flowable, excellent compressibility, non-hygroscopic, excellent chemical stability. Because of the porous crystalline particle Pearlitol SD dissolves rapidly. \[^{35}\]

**Mannogem EZ:** It is the spray dried mannitol and specially designed for direct compression tablet. It is having certain advantages like high compatibility, non-hygroscopic, chemically inert, narrow particle size distribution and mainly rapidly disintegrating property which benefits for quick dissolve application.

**Modified Resins:**

**Polacrilin Potassium:** It is a crosslinked polymer of methacrylic acid and divinyl benzene. It is a weak acidic cationic exchange resin. The resin swells by approximately 150% on wetting, thereby causing the tablet to disintegrate. The tablet disintegration property is due to their extremely large swelling capacity in aqueous solutions. Water can exert low force between particles within tablet pores. It is biocompatible and also non-toxic.

**Modified sugars:**

**Glucidex IT:** This is obtained by moderate hydrolysis of starch. It is the micro granulated form which enables instantaneous dispersal and dissolution in water. All the co-processed and modified excipients play very important role in the development of easy dosage forms which are resistant to atmosphere. \[^{37}\]

**CONCLUSION**

The orodispersible drug delivery system has become one of the most acceptable forms in novel drug delivery. Although, by the use of different types of Superdisintegrants in the orodispersible formulation, better and fast disintegration can be achieved. For those tablets and capsules which need rapid disintegration, the inclusion of the right disintegrant is a prerequisite for optimal bioavailability. The superdisintegrants are used to improve the efficacy of solid dosage forms. This can be achieved by decreasing the disintegration time, which in turn enhances drug dissolution rate. So this review comprises with various kinds of superdisintegrants which provide the safer and effective drug delivery with patient's compliance. And from this, it was concluded that Natural and synthetic superdisintegrants both have better effects on orodispersible tablets. Natural superdisintegrants are preferred over synthetic superdisintegrants as they are nontoxic, easily available at low cost, used in low concentration and they are naturally.
extracted, also provide nutritional supplement.

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REFERENCE


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