SUPERDISINTEGRANTS: AN EMERGING PARADIGM IN ORODISPERSIBLE TABLETS

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ABSTRACT

The oral route is the most convenient route for administration of solid dosage form, about 85% of solid dosage administered by oral route because of 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. In recent years, several newer agents have been developed known as superdisintegrants. Diverse categories of superdisintegrants such as synthetic, semi-synthetic, natural, co-processed blends, multifunctional superdisintegrants, etc. have been employed to develop effectual orodispersible tablets and to overcome the limitations of conventional tablet dosage forms. The objective of the present article is to highlight the various kinds of superdisintegrants along with their role in tablet disintegration and drug release, which are being used in the formulation to provide the safer, effective drug delivery with patient compliance.

Key words: Disintegrants, Superdisintegrants, Natural, Synthetic, Multifunctional Superdisintegrants.

INTRODUCTION

Oral route of drug administration is perhaps most useful and important route for drug delivery. Tablets are the most favored oral solid dosage form mainly because of several advantages like,
- Ease of administration
- Good chemical and microbiological stability
- Easy to swallowing
- Lowest cost among all other solid dosage form
- Dose precision and least content variability
- Ease of packing
- Self-medication
- Patient compliance

In fact, it is more popular dosage form and almost 70% of medicines are dispensed in tablet form (Pahwa R & Gupta N, 2011; Vimal V et al., 2013). 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 important role in development of solid oral, formulator give special emphasis on selection of disintegrant / Superdisintegrant in dosage system. Disintegrants are substance or mixture of substances added to the drug formulations, which facilitate dispersion or breakup of tablet content of capsule in to smaller particles for quick dissolution. Superdisintegrant, are those substance, which facilitate the faster disintegration with smaller quantity in contrast to disintegration.

The disintegration of dosage form are depends upon various physical factors of disintegrant/superdisintegrant. They are as follows (Shihora H & Panda S, 2011).
1. Percentage of disintegrant present in formulation.
2. Proportion of disintegrant used.
3. Compatibility with other excipients.
4. Presence of surfactant.
5. Hardness of the tablet.
7. Mixing and types of addition.

**Ideal characteristic of Superdisintegrants:** (Shihora H & Panda S, 2011; Pahwa R & Gupta N, 2011; Sharma V et al., 2010)

- Poor water solubility with good hydration capacity
  - Poor gel formation
  - Good compressibility
  - Inert
  - Non-toxic
  - Good flow properties
  - Requirement of least quantity
  - Good mouth feel
  - Particle size

Different Superdisintegrants and their effective concentration used in formulation as described in table 1 (Shihora H. Panda S, 2011; Bhowmik D et al., 2010). Method of incorporation of superdisintegrants as shown in table 2.

**Disadvantage**

Superdisintegrant having great affinity for water that can impact the stability of moisture sensitive material under accelerated stability storage condition (Charles R & Laura K, 1999).

**Mechanism of Superdisintegrants**

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. The optimum concentration of the superdisintegrant can be selected according to critical concentration of disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if concentration of superdisintegrant is above critical concentration, the disintegration time remains almost constant or even increases (Kaur T et al., 2011).

a) Swelling action
b) Capillary action (Wicking)
c) Combination action
d) Deformation recovery
e) Heat of wetting
f) Chemical reaction (acid base reaction)
g) Particle repulsive forces/ due to disintegrating particle
h) Enzyme reaction

**Swelling action**

Swelling is widely accepted mechanism for tablet disintegration. Although water penetration is a necessary first step for disintegration. Particles of disintegrants swell on coming in contact with suitable medium the adhesiveness of the other ingredient in tablet is overcome causing the tablet to fall apart. Tablets with high porosity show poor disintegration 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 is again slows down.

**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. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug/excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles (Pahwa R & Gupta N, 2011).

**Combination action**

In this mechanism, the combination of both wicking and swelling action facilitate disintegration.

**Deformation recovery**

Hess had proved that during tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression.

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 (Shihora H & Panda S, 2011; Vimal V et al., 2013).

**Heat of wetting**

When disintegrants with exothermic properties get wetted, localized stress is created due to capillary air expansion, which aids 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.
Chemical reaction (acid base reaction)

The tablet is quickly broken apart 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. 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 enhanced. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is 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 prior to compression or can be added into two separate fraction of formulation.

Particle repulsive forces/ due to disintegrating particle

This is another mechanism of disintegration that attempts to explain the swelling of tablet made with non-swellable disintegrants. According to Guyot-Hermann’s particle-particle repulsion theory, water penetrates into tablet through hydrophilic pores and a continuous starch network is created that can convey water from one particle to the next, imparting a significant hydrostatic pressure. The water then penetrates between starch grains because of its affinity for starch surfaces, thereby breaking hydrogen bonds and other forces holding the tablet together. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researcher found that particle repulsion force is secondary to wicking (Pahwa R & Gupta N, 2011; Mangal M et al., 2012; Vimal V et al., 2013).

Enzyme reaction

Enzymes present in the body also act as disintegrants. These enzymes earth the binding action of binder and helps in disintegration. Due to swelling, pressure is exerted in the outer direction that causes the tablet to burst or the accelerated absorption of water leads to an enormous increase in the volume of granules to promote disintegration (Pahwa R, Gupta N, 2011). Various Superdisintegrant along with their mechanism of action and brand names as depicted in table 3 (Vimal V et al., 2013; Mohanachandran PS & Sindhumol PG, 2011; Bele MH & Derle DV, 2008; Velmurugan S & Vinushitha S, 2011).

Type of Superdisintegrant and their example

Two types of Superdisintegrant:
A) Synthetic superdisintegrant
B) Natural superdisintegrant

A) Synthetic Superdisintegrant

Synthetic super-disintegrants are frequently used in tablet formulations to improve the rate and extent of tablet disintegration thereby increasing the rate of drug dissolution. The most widely used synthetic superdisintegrants are illustrated below.

Sodium Starch Glycolate (Explotab® and Primogel®)

Sodium Starch Glycolate is the sodium salt of a carboxymethyl ether of starch. These are modified starches made by crosslinking of potato starch as it gives the product with the best disintegrating properties. The degree of cross-linking and substitution are important factors in determining the effectiveness of these materials as superdisintegrants. The effect of the crosslinking is to reduce both the water soluble fraction of the polymer and the viscosity of dispersion in water. The natural predried starches swell in water to the extent of 10-20 percent and the modified starches increase in volume by 200-300 percent in water. The mechanism by which this action takes place involves rapid absorption of water leading to an enormous increase in volume of granules that result in rapid and uniform disintegration. These are available as explotab and primogel which are low substituted carboxymethyl starches. 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.

Cross-linked poly-vinyl Pyrrollidone (Crosspovidone)

Unlike other superdisintegrants, which rely principally on swelling for disintegration, crosspovidone use a combination of swelling and wicking. Due to its high crosslink density, crosspovidone swells rapidly in water without gelling. Crosspovidone particles are found to be granular and highly porous which facilitates wicking of liquid into the tablet and particles to generate rapid disintegration. Larger particles provide a faster disintegration than smaller particles. Crosspovidone disintegrants are highly compressible materials as a result of their unique particle morphology. Crosspovidone can also be used as solubility enhancer. It is available in two particle sizes in the form of Polypasdone XL and Polypasdone XL-10.

Modified Cellulose (crosscarmellose sodium, Ac-Di-Sol)

It is an internally cross linked polymer of carboxymethyl cellulose sodium. It has high swelling capacity with minimal gelling resulting in rapid disintegration. Due to fibrous structure, crosscarmellose particles also show wicking action. In tablet formulations, crosscarmellose sodium may be used in both direct compression and wet-granulation processes. When used in wet-granulation, the crosscarmellose sodium should be added in both the wet and dry stages of
the process (intra- and extra-granularly) so that the wicking and swelling ability of the disintegrant is best utilized.

Resins (Ion Exchange Resin)

The INDION 414 and KYRON 314 have been used as a superdisintegrant for ODT. It is chemically cross-linked polyacrylic potassium (Polacrillin potassium), with a functional group of – COO – and the standard ionic form is K+. 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 extend 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.

L-HPC (Low substituted hydroxyl-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%. The main advantages of synthetic super disintegrants are their efficacy in lower concentrations than starch, less interference with compressibility and flow ability. They are also more effective intragranularly (Mohanachandran PS & Sindhumol PG, 2011; Bhowmik D et al., 2010). Various Synthetic Superdisintegrant along with different drugs and method adopted for their preparation as described in table 4.

Advantages of Synthetic Superdisintegrant
- Effective in lower concentrations than starch.
- Less effect on compressibility and flow ability.
- More effective intragranularly.

Limitation Synthetic Superdisintegrant
- More hygroscopic (may be a problem with moisture sensitive drugs).
- Some are anionic and may cause some slight in-vitro binding with cationic drugs (not a problem in-vivo).
- An acidic medium significantly reduces the liquid uptake rate and capacity of sodium starch glycolate and crosscarmellose sodium, but not crospovidone.
- The degree of swelling of Primojel (sodium starch glycolate) and Polyplasdone XL101 (crospovidone) is minimized following wet granulation formulation. Finally, the medium ionic strength was found to have an adverse effect on the swelling capacity of crosscarmellose (Pahwa R & Gupta N, 2011; Mangal M et al., 2012; Vimal V et al., 2013).

Natural Superdisintegrant

These superdisintegrant-ting agents are natural in origin and are preferred over synthetic substances because they are comparatively cheaper, abundantly available, non-irritating and nontoxic in nature. The natural materials like gums and mucilage’s have been extensively used in the field of drug delivery for their easy availability, cost effectiveness, Eco friendliness, emollient and non-irritant nature, non-toxicity, capable of multitude of chemical modifications, potentially degradable and compatible due to natural origin. There are several gums and mucilage’s are available which have super-disintegrating activity.

Plantago ovata Seed Mucilage (Isapgula)

Isapghula consists of dried seeds of the plant Plantago ovata and it contains mucilage which is present in the epidermis of the seeds. The seeds of Plantago ovata were soaked in distilled water for 48 hrs and then boiled for few minutes for complete release of mucilage into water. The material was squeezed through muslin cloth for filtering and separating out the marc. Then, an equal volume of acetone was added to the filtrate so as to precipitate the mucilage. The separated mucilage was dried in oven at temperature less than 60°C. The mucilage of Plantago ovata is a recent innovation for its superdisintegration property when compared with Crosspovidone. It shows faster disintegration time than the superdisintegrant, Crosspovidone.

Lepidium sativum Mucilage

Lepidium sativum (family: Cruciferae) is known as asaliyo and is widely used as herbal medicine in India. It is widely available in market and has very low cost. Parts used are leaves, root, oil, seeds etc. Seeds contain higher amount of mucilage, dimeric imidazole alkaloids lepidine B, C, D, E and F and two new monomeric imidazole alkaloids semilepidinoside A and B. Mucilage of Lepidium sativum has various characteristic like binding, disintegrating, gelling.

Gum Karaya

Gum Karaya is a negative colloid and a complex polysaccharide of high molecular weight. On hydrolysis it yields galactose, rhamnose and galacturonic acid. Gum Karaya occurs as a partially acetylated derivative. It is a dried exudation of Sterculia Uren tree (Family-Sterculiaceae). Its synonyms are Karaya, sterculia, Indian tragacanth, Bassora tragacanth, kadaya, Kadira, katila. Gum Karaya is compatible with other plant hydrocolloids as well as proteins and carbohydrates.

Fanugreek Seed Mucilage

Trigonella Foenum-graceum, commonly known as Fenugreek, is an herbaceous plant of the leguminous family. 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-graecum are used as vegetables. Fenugreek has been used in treating colic flatulence, dysentery, diarrhea, dyspepsia with loss of appetite, chronic cough, dropsy, enlargement of liver and spleen, rickets, 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. 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.

Guar gum
Guar gum is a galactomannan, commonly used in cosmetics, food products and in pharmaceutical formulations. Guar gum is mainly consisting of the high molecular weight (approximately 50,000-8,000,000) polysaccharides composed of galactomannans and is obtained from the endosperm of the seed of the guar plant, Cyamopsis tetragonoloba (L) Taub (Synonym-Cymopspispsoridaloeins). It is used as thickener, stabilizer and emulsifier, and approved in most areas of the world (e.g. EU, USA, Japan, and Australia). Its synonyms are Galactosol; guar flour; jaguar gum; meprogat; meyprodor. It has also been investigated in the preparation of sustained release matrix tablets in the place of cellulose derivatives such as methylcellulose. In pharmaceuticals, guar gum is used in solid-dosage forms as a binder and disintegrant, and in oral and topical products as a suspending, thickening, and stabilizing agent, and also as a controlled-release carrier. Guar gum has also been examined for use in colonic drug delivery.

Cassia fistula gum
Seeds of Cassia fistula gum obtained from Cassia fistula tree. Gum obtained from the seeds of Cassia fistula comprises β-(1→4) linked d-mannopyranose units with random distribution of α (1→6) linked d-galactopyranose units as side chain. Carboxymethylation as well as carbamoylthlelation of Cassia gum is reported to improve cold water solubility, improve viscosity and increase microbial resistance as compared to native gum Therefore, an attempt was made to incorporate calcium or sodium salts of carboxymethylated or carbamoylthlelated C. fistula gum as superdisintegrant in the formulation development of FDT.

Locust Bean gum
Locust bean gum is extracted from the endosperm of the seeds of the carob tree Ceretonia siliqua, which grows in Mediterranean countries. It is also called Carob bean gum. Some other familiar polysaccharides 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. Pharmaceutical application of locust bean gum in various novel drug delivery systems. 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. There are various reports that Locust bean gum can be used in pharmaceutical and biotechnological purpose.

Hibiscus rosa-sinensis Linn. Mucilage
Hibiscus rosa-sinensis Linn of the Malvaceae family is also known as the shoe-flower plant, China rose, and Chinese hibiscus. The plant is available in India in large quantities and its mucilage has been found to act as a superdisintegrant. The plant contains cyclopropanoids, methyl sterculate, methyl-2-hydroxysterculate, 2-hydroxysterculate malvate and β-rosasterol. The leaves contain carotene (7.34 mg/100 g of fresh material) moisture, protein, fat, carbohydrate, fibers, calcium, and phosphorus. Mucilage of Hibiscus rosa-sinensis contains L-rhamnose, D-galactose, D-galactouronic acid, and D-glucuronic acid.

Mango Peel Pectin
Dried mango peel powder is used for extracting pectin. Rather mango peel pectin cannot be used for promising the behavior of superdisintegrants, but due to its good swelling index and good solubility in biological fluids it can be used to prepare fast dispersible tablets (Shihora H & Panda S, 2011; Mangal M et al., 2012). Various Natural Superdisintegrant along with different drugs and method adopted for their preparation as described in table 5.

Co-processed Superdisintegrant
New and improved superdisintegrants continue to be developed to meet the needs of advanced tablet manufacturing. It requires the development of various added functionality excipients, which are used to achieve formulations with desired end effects. Until now only superdisintegrants are available to prepare the dosage forms, but now days different blend of excipients are available which can give disintegration property. Some
co-processed excipients blends are designed to satisfy the need of more than one excipient.

**Co-processed blends of excipients**

It involves the mixture blend of more than two excipients to satisfy the required quality using different technique like spray drying and freeze drying etc.

**Ludiflash**

Ludiflash is an innovative, unique co-processed blend of Mannitol (95%), crosspovidone (5%) and polyvinyl acetate (5%) manufactured in a validated patented process. It disintegrates rapidly within seconds with soft, creamy consistency. It is specially designed for direct compression on standard high speed tablet machine for hard tablet with very low friability. It gives extremely fast release rate.

**F-melt**

F-MELT® is a spray-dried excipient used in orally disintegrating tablets that contain saccharides, disintegrating agent, and inorganic excipient. F-MELT exhibits excellent tableting properties and facilitates rapid water-penetration for a fast disintegration time.

**Pharmaburst**

Pharmaburst is a Quick Dissolving delivery system in which there is addition of active drug in a dry blend with Pharmaburst excipients and compress by tablet machine. Pharmaburst is a co-processed excipient system with specific excipients, which allows rapid disintegration and low adhesion to punches.

**Modified Chitosan with silicon dioxide**

This is the new excipients based on co-precipitation of Chitosan and silica. The physical interaction between Chitosan and silica create an insoluble, hydrophilic highly absorbent material, resulting in superiority in water uptake, water saturation for gelling formation. Studies have shown that Chitosan–silica delivers superior performance in wet granulation formulations and is the only disintegrant that is effective at all concentrations in tablet formulation.

**Modified Mannitol**

**Pearitol 200 SD**

These are the granulated Mannitol white, odorless, slightly sweet tasting, crystalline powder. It has a unique blend of exceptional physical and chemical stability, with great organoleptic, non-carcinogenic, sugar-free properties. Together with its versatile powder properties, it can be used in different processes wet or dry granulation, direct compression and compaction or freeze-drying. It has properties like flowability, excellent compressibility, non-hygroscopic and excellent chemical stability. Pearitol SD dissolves very rapidly because of its porous crystalline particles.

**Mannogem EZ**

Mannogem EZ is spraying dried Mannitol, specially designed for direct compression tablet. It has advantages of highly compatible, non hygroscopic, chemically inert, narrow particle size distribution and mainly rapid disintegration property benefits quick dissolve application. It is highly stable and inert to many of the chemical reactions which are problematic with lactose, microcrystalline cellulose, or starch.

**Modified Resins**

**Polacrilin Potassium (Tulsion 339)**

It is a crosslinked polymer of methacrylic acid and divinylbenzene supplied as the potassium salt. Polacrilin potassium is weakly acidic cation exchange resin. On wetting, the resin swells by approximately 150 %, thereby causing the tablet to disintegrate. Tablet disintegration property is due to its extremely large swelling capacity in aqueous solutions. Water can exert force between particles within tablet pores, but this force is low. This is used effectively at 1-2% of solid dosage forms. It is bio compatible and non-toxic. It is available in various grades i.e., tulsion-335, tulsion-344, tulsion-345 and tulsion-412.

**Modified sugars**

**Glucidex IT**

Glucidex IT is obtained by moderate hydrolysis of starch. It is micro granulated form enables almost instantaneous dispersal and dissolution in water. Different range of Glucidex IT products is available.

All co-processed and modified excipients are playing a vital role in the development of easy dosage forms which are resistant to atmosphere. The improved physical, chemical and mechanical properties of such excipients as compared to existing excipients, have helped in solving formulation problems such as flowability, compressibility, hygroscopicity, palatability, dissolution, disintegration, sticking, and dust generation (Pahwa R. Gupta N, 2011). Various Multifunctional Superdisintegrants as shown in table 6.

Table 7 gives the data for different superdisintegrant used and number of patents. It is a combined data obtained from NIC and USPTO database. From the table it can be seen that Amylose is the most widely patented superdisintegrants. Very little numbers of patents are found on formulation containing superdisintegrants like Crosscarmellose sodium, Sodium starch glycolate and few ion exchange resins. This indicates that there is still a scope for exploring these superdisintegrants in pharmaceutical tablet formulation and patenting this research (Bele MH. Derle DV, 2008).
Table 1. List of superdisintegrants and their Concentration

<table>
<thead>
<tr>
<th>Superdisintegrants</th>
<th>Concentration ( % W/W)</th>
<th>Special Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch USP</td>
<td>5-20</td>
<td>Higher amount is required, poorly compressible</td>
</tr>
<tr>
<td>Starch 1500</td>
<td>5-50</td>
<td>-</td>
</tr>
<tr>
<td>MCC (Avicel)</td>
<td>10-20</td>
<td>Lubricant Properties and Directly Compressible</td>
</tr>
<tr>
<td>Alginic Acid</td>
<td>1-5</td>
<td>Swelling or Wicking</td>
</tr>
<tr>
<td>Sodium Alginate</td>
<td>2.5-10</td>
<td>Swelling or Wicking</td>
</tr>
<tr>
<td>Explotab</td>
<td>2-8</td>
<td>Sodium starch glycolate</td>
</tr>
<tr>
<td>Polyplasdone (XL)</td>
<td>0.5-5</td>
<td>Crosslinked PVP</td>
</tr>
<tr>
<td>Amberlite (IPR 88)</td>
<td>0.5-5</td>
<td>Ion Exchange resin</td>
</tr>
<tr>
<td>Ac-Di-Sol</td>
<td>1-3</td>
<td>Direct Compression</td>
</tr>
</tbody>
</table>

Table 2. Method of incorporation of Superdisintegrants

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Method</th>
<th>Special comments</th>
<th>Advantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Intragranular OR Internal Addition OR during granulation:</td>
<td>In this process the Superdisintegrants are blend with other powder and granulation is carried out. Thus the superdisintegrant are incorporated within the granules. (Mangal M et al., 2012). Addition of superdisintegrant into the wet granulation process, which may leads to decrease in activity of superdisintegrant.</td>
<td>-Easy to incorporate -Suitable for direct compression.</td>
</tr>
<tr>
<td>2</td>
<td>Extragranular OR External Addition OR prior to compression:</td>
<td>In this process, the superdisintegrant are mixed with prepare granules before compression. (Mangal M et al., 2012).</td>
<td>-Easy to incorporate - Suitable for wet granulation process</td>
</tr>
<tr>
<td>3</td>
<td>Partly internal and external:</td>
<td>In this method part of disintegrant can be added internally and part externally. This result in immediate distruption of the tablet in to previously compress granules while the disintegrating agents within the granules produce additional erosion of the granules to the original powder particles. (Pahwa R. Gupta N, 2011).</td>
<td>-More complete disintegration -Produce better result - Immediate distruption - More effective method</td>
</tr>
</tbody>
</table>

Table 3. Superdisintegrants with their Mechanism of Action and Brand Name

<table>
<thead>
<tr>
<th>Superdisintegrants</th>
<th>Brand names</th>
<th>Mechanism of action</th>
<th>Special comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crosslinked cellulose</td>
<td>Crosscarmelllose®, Ac-Di-Sol®, Nymce ZSX®, Primellose®, Solutab®, Vivasol®, L-HPC, Nymcel</td>
<td>Swelling and Wicking both</td>
<td>Swelling two dimensions, Direct compression or Granulation starch free.</td>
</tr>
<tr>
<td>Crosslinked PVP</td>
<td>Crosspovidone M®, Kololidone®, Polyplasdone®, polyplasdone XL®, Kololidone CL®</td>
<td>Capillary action</td>
<td>Water insoluble and spongy in nature so get porous tablet</td>
</tr>
<tr>
<td>Crosslinked Starch</td>
<td>Explotab®, Primogel®, Tablo®, Vivastar®</td>
<td>Swelling</td>
<td>Swells in three dimensions and high level serve as sustain release matrix</td>
</tr>
<tr>
<td>Crosslinked alginic acid</td>
<td>Alginic acid NF®, Staialgine®</td>
<td>Swelling or Wicking</td>
<td>Promote disintegration in both dry and wet granulation</td>
</tr>
<tr>
<td>Soy polysaccharides</td>
<td>Emcosoy®</td>
<td>-</td>
<td>Does not contain any starch or sugar. Used in nutritional products.</td>
</tr>
<tr>
<td>Gallen Gum</td>
<td>Kilcogel®</td>
<td>-</td>
<td>Natural superdisintegrant</td>
</tr>
<tr>
<td>Xanthum Gum</td>
<td>Grindsted®, Xanthum SM®</td>
<td>-</td>
<td>Natural superdisintegrant</td>
</tr>
<tr>
<td>Ion Exchange Resin</td>
<td>Indion 414®, Tusion 339®, Amberlite IRP 88®</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
### Table 4. A list of synthetic Superdisintegrant used in formulation

<table>
<thead>
<tr>
<th>Name of drug</th>
<th>Superdisintegrant</th>
<th>Method of compression</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solubutamol sulphate</td>
<td>Chitosan-alginate complex</td>
<td>Direct compression</td>
<td>(Kharade S. Bhutkar MA, 2013)</td>
</tr>
<tr>
<td>Metaclopramide HCl</td>
<td>Crosspovidone, Crosscarmellose sodium</td>
<td>Wet granulation</td>
<td>(Shirsand SB et al., 2010)</td>
</tr>
<tr>
<td>Lornoxicam</td>
<td>Crosspovidone, Banana powder, Soy polysaccharides</td>
<td>Direct compression</td>
<td>(Taksande JB et al., 2013)</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>Crosspovidone, Crosscarmellose sodium</td>
<td>Kneading techniques</td>
<td>(Kulkarni SV. Kumar RP, 2011)</td>
</tr>
<tr>
<td>Promethazine HCl</td>
<td>Crosspovidone, Crosscarmellose sodium, Sodium starch glycolate, pregelatinized starch, L-HPL</td>
<td>Direct compression</td>
<td>(Gudas GK et al., 2010)</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Crosspovidone, Crosscarmellose sodium, Sodium starch glycolate</td>
<td>Wet granulation</td>
<td>(Samal HB et al., 2010)</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Crosspovidone, Crosscarmellose sodium</td>
<td>Wet granulation</td>
<td>(Yelchuri VR et al., 2010)</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>Crosspovidone, Crosscarmellose sodium, Sodium starch glycolate</td>
<td>Direct compression</td>
<td>(Panigrahi R et al., 2012)</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Crosspovidone, Sodium starch glycolate, Cross linked CMC, Partially pregelatinized corn starch</td>
<td>Direct compression</td>
<td>(Charles R. Laura K, 1999; Zhao N. Augsburger LL, 2005)</td>
</tr>
<tr>
<td>Acetaminophen &amp; Codeine phosphate</td>
<td>Crosscarmellose sodium</td>
<td>Direct compression</td>
<td>(Popa G et al., 2010)</td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>Crosscarmellose, Sodium starch glycolate, Crosspovidone</td>
<td>Wet granulation</td>
<td>(Farhana M et al., 2013)</td>
</tr>
<tr>
<td>Famotidine</td>
<td>Crosspovidone, Crosscarmellose sodium, Sodium starch glycolate, Metacrylic copolymer with divinyl benzene</td>
<td>Direct compression</td>
<td>(Jagdale SC et al., 2010)</td>
</tr>
<tr>
<td>Nimesulide</td>
<td>Lipidium sativum (Cruciferae)</td>
<td>Direct compression</td>
<td>(Patil C. Das S, 2011)</td>
</tr>
<tr>
<td>Chlorpheneramine</td>
<td>Sodium starch glycolate</td>
<td>Direct compression</td>
<td>(Murtada AO et al., 2013)</td>
</tr>
<tr>
<td>Lomotrigine</td>
<td>Crosscarmellose, Sodium starch glycolate, Crosspovidone (XL10)</td>
<td>Direct compression</td>
<td>(Patil C. Das S, 2011)</td>
</tr>
<tr>
<td>Olopatadine HCl</td>
<td>Crosscarmellose, Sodium starch glycolate, Crosspovidone (XL10)</td>
<td>Fluidized bed granulation</td>
<td>(Rajendran NN et al., 2011)</td>
</tr>
</tbody>
</table>

### Table 5. A list of natural Superdisintegrants used in formulation

<table>
<thead>
<tr>
<th>Name of drug</th>
<th>superdisintegrants</th>
<th>Method of compression</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glimepride</td>
<td>Ocimum tenuiflorum</td>
<td>Direct compression</td>
<td>(Kamble MS et al., 2012)</td>
</tr>
<tr>
<td>Lisinopril</td>
<td><em>Plantago Ovata</em> mucilage, Alovera mucilage, Mucilage of hibiscus rosasinesis</td>
<td>Direct compression</td>
<td>(Panigrahi R et al., 2012)</td>
</tr>
<tr>
<td>Nimesulide</td>
<td>Lipidium sativum (Cruciferae)</td>
<td>Direct compression</td>
<td>(Patel HH et al., 2011)</td>
</tr>
<tr>
<td>Ondensetron HCl</td>
<td>Plantago ovate husk</td>
<td>Direct compression</td>
<td></td>
</tr>
<tr>
<td>Granisetron HCl</td>
<td>Plantago ovate husk</td>
<td>Direct compression</td>
<td></td>
</tr>
<tr>
<td>Fexofenadine HCl</td>
<td>Plantago ovate mucilage, Seed</td>
<td>Direct compression</td>
<td></td>
</tr>
</tbody>
</table>

Table 6. Multifunctional Superdisintegrants

<table>
<thead>
<tr>
<th>Superdisintegrant</th>
<th>Function</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyplasdone superdry/ Crosspovidone</td>
<td>superdisintegrant, Dissolution enhancer, chewable purpose</td>
<td>(Balasubramanian J. Bee T, 2009)</td>
</tr>
<tr>
<td>Kollidone CL-F, Kollidone CL-SF, Kollidone CL-M</td>
<td>superdisintegrant, Dissolution enhancer</td>
<td>(Mercado D et al., 2013)</td>
</tr>
<tr>
<td>Starch 1500</td>
<td>Binder, superdisintegrant</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 7. Different Superdisintegrants & number of patents

<table>
<thead>
<tr>
<th>Name of Superdisintegrants</th>
<th>Number of patents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylose</td>
<td>14</td>
</tr>
<tr>
<td>Co-processed starch</td>
<td>9</td>
</tr>
<tr>
<td>N-vinyl pyrolidone + sodium starch glycolate</td>
<td>15</td>
</tr>
<tr>
<td>Chitin</td>
<td>2</td>
</tr>
<tr>
<td>Co-processed cellulose</td>
<td>4</td>
</tr>
<tr>
<td>Granulated starch + veegum</td>
<td>1</td>
</tr>
<tr>
<td>Cellulose + methyl acrylic acid</td>
<td>4</td>
</tr>
<tr>
<td>Compressed gaur gum</td>
<td>3</td>
</tr>
</tbody>
</table>

CONCLUSION

With the ongoing demand of novel drug delivery, the fast dissolving drug delivery system has become one of the mile stone of present research. Although, there are many superdisintegrants, the search for newer disintegrating agent is going and researcher are experimenting with multifunctional superdisintegrants like polyplasdone superdry, kollidone CL, kollidone CL-F, kollidone CL-SF, kollidone CL-M, starch 1500, etc. Studies have suggested that ease of availability of these agents and the simplicity in the direct compression process developed more economic alternative in the preparation of orodispersible tablet than the sophisticated and patented techniques.

REFERENCES


