A Review on: Importance of Superdisintegrants on Immediate Release Tablets

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Abstract: Among the different routes of administration, the oral route of administration continues to be the most preferred route due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance. The different dosage forms include tablets and capsules. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer and lead to better patient compliance. They are also a tool for expanding markets, extending product life cycles and generating opportunities.

Immediate drug release dosage forms disintegrate rapidly after administration with enhanced rate of dissolution. The basic approach used in development tablets is the use of superdisintegrants like Cross linked Polyvinylpyrrolidone or crospovidone (Polyplasdone), Sodium starch glycolate (Primogel, Explotab), carboxymethylcellulose (Crosarmellose) etc. These superdisintegrants provide instantaneous disintegration of tablet after administration in stomach.

Keywords: Immediate release tablets, Superdisintegrants, Polyvinylpyrrolidone, Sodium starch glycolate, carboxymethylcellulose.

I. INTRODUCTION

At present novel drug delivery systems are developed for expanding markets/indications, extending product life cycles and generating opportunities. Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly patient compliance. In these solid formulations do not require sterile conditions and are therefore, less expensive to manufacture. [1]

The oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, manufacturing and ease of administration lead to high levels of patient compliance. Many patients require quick onset of action in particular therapeutic condition and consequently immediate release of medication is required. It is estimated that 50% of the population is affected by this problem, which results in a high incidence of ineffective therapy.[2]

Immediate release drug delivery system are based on single or multiple-unit reservoir or matrix system, which are designed to provide immediate drug levels in short period of time.

Immediate release drug delivery is desirable for drugs having long biological half life, high bioavailability, lower clearance and lower elimination half life. But main criterion for immediate release dosage form is poor solubility of the drug and need the immediate action of drug to treat unwanted defect or disease. [3]

Immediate release solid oral dosage forms are classified as either having rapid or slow dissolution rates. Immediate release dosage forms are those for which ≥85% of labelled amount dissolves within 30 min. For immediate release tablets, the only barrier to drug release is simple disintegration or erosion stage, which is generally accomplished in less than one hour. To enhance dissolution and hence bioavailability of any drug from immediate release tablets, disintegration is one of the important process. Few Super-disintegrants are available commercially as Crosarmellose sodium, Crospovidone and SSG. [4]

II. DISINTEGRANTS

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. 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. Diverse categories of Superdisintegrants such as synthetic, semi-synthetic, natural and co-processed blends etc. have been employed to develop effective immediate release tablets and to overcome the limitations of conventional tablet dosage form. [5]

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 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. 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. [6]

III. MECHANISM OF DISINTEGRATION BY SUPERDISINTEGRANTS

There are five major mechanisms for tablet disintegration as follows:-

1) Swelling
2) Porosity and Capillary Action (Wicking)
3) Deformation
4) Due to disintegrating particle/particle repulsive forces
5) Enzymatic reaction

1) Swelling: 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. E.g Sodium starch Glycolate. [7]

2) 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. E.g. Crospovidone, Crosscarmillose [8]

3) 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 [9]

4) 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 nonswellling 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. 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.
5) By Enzymatic Reaction: Enzymes present in the body also act as disintegrants. These enzymes enhance 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 [10].

When it comes to immediate-release tablet formulations, the choice of disintegrant can have a significant effect on the rate and extent of drug dissolution. Once a tablet disintegrates, the characteristics of the API, either alone or assisted by other formulation ingredients, determine the dissolution rate and extent of the API. Thus, the choice of superdisintegrant is important, especially with poorly soluble APIs.

IV. NOT ALL SUPERDISINTEGRANTS ARE THE SAME

The three most common classes of superdisintegrants are: crospovidone, croscarmellose sodium and sodium starch glycolate. In general, all of these provide rapid disintegration at low use levels in both wet and dry granulations and direct compression tablet processes; however, the classes of disintegrants differ in chemistry and particle morphology. Crospovidone possesses unique pyrrolidone chemistry and a highly porous particle morphology that results in high surface area. The high surface area combined with unique chemistry results in high-interfacial activity that serves to enhance the dissolution of poorly soluble drugs in a way that is not possible with other disintegrant technologies. Indeed, studies have shown that tablets containing a poorly soluble API and crospovidone, Type B, have significantly faster dissolution rates compared with tablets formulated with other superdisintegrants.

It has been widely reported that more than 60% of drugs in development and over 40% of recently launched drugs have issues related to poor solubility, leading to long development times or cancellations. Before evaluating advanced techniques, such as amorphous solid dispersions, more traditional approaches such as the influence of superdisintegrants on dissolution are now being considered. The selection of a superdisintegrant and the use level plays a key role in determining the drug release of finished formulations.

V. CHOOSING AN OPTIMAL SUPERDISINTEGRANT

It is important to consider the impact of the superdisintegrant with respect to the performance of the final dosage form. As drug dissolution is essential for absorption by the body, formulators no longer select disintegrants based on the lowest disintegration time because it is important to also consider the effect of the superdisintegrant on dissolution. Additionally, the ionic nature of both the API and the superdisintegrants must also be considered. Anionic superdisintegrants, such as croscarmellose sodium and sodium starch glycolate, can interact with cationic APIs and retard dissolution. Thus, nonionic superdisintegrants are preferred when working with cationic APIs. Formulators also consider the impact of the superdisintegrant on physical tablet characteristics, such as tablet breaking force and friability. In today’s high-speed tablet presses, superdisintegrants that provide tablets with high breaking force and low friability, while maintaining fast disintegration, are particularly important. [11]

VI. SELECTION OF SUPERDISINTEGRANT

Since superdisintegrant is used as an excipient in the tablet formulation, it has to meet certain criteria other than its swelling properties. The requirement placed on the tablet disintegrant should be clearly defined. Th ideal disintegrants should have

1. Poor solubility
2. Poor gel formation
3. Good hydration capacity
4. Good moulding and flow properties
5. No tendency to form complexes with the drugs
6. Good mouth feel.
7. It should also be compatible with the other excipients and have desirable tableting properties. [12]

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 (Chemically treated Potato Starch) i.e. Sodium Starch Glycolate (Explotab, Primogel).

Mechanism of Action: Rapid and extensive swelling with minimal gelling.

Effective Concentration: 4-6%. Above 8%, disintegration times may actually increase due to gelling and its subsequent viscosity producing effects.

2) *Cross-linked polyvinylpyrrolidone*- water insoluble and strongly hydrophilic. i.e. crospovidone (Polyplasdone XL, Kollidon CL)

Mechanism of Action: Water wicking, swelling and possibly some deformation recovery.

Effective Concentration: 2-4%

3) *Modified Cellulose*- Internally cross-linked form of Sodium carboxymethyl cellulose. i.e. Ac-Di-Sol (Accelerates Dissolution), Nymcel

Mechanism of Action: Wicking due to fibrous structure, swelling with minimal gelling.

Effective Concentrations: 1-3% (Direct Compression), 2-4% (Wet Granulation) [13]

**VII. METHOD OF ADDITION OF SUPERDISINTEGRANTS**

There are three methods of incorporating disintegrating agents into the tablet.

1) **Internal Addition**

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

2) **External Addition**

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

3) **Internal and External Addition**

In this method, disintegrant is divided into two portions. One portion is added before granule formation (intra) and remaining portion is added to granules (extra) with mixing prior to compression. This method can be more effective. If both intragranular and extragranular methods are used, extra-granular portion break the tablet into granules and the granules further disintegrate by intra-granular portion to release the drug substance into solution. However, the portion of intra-granular disintegrant (in wet granulation processes) is usually not as effective as that of extra-granular 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 intragranular disintegrant tends to retain good disintegration activity. [12]

<table>
<thead>
<tr>
<th>Name of excipients</th>
<th>Category</th>
<th>Concentration</th>
<th>Stability criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alginic acid</td>
<td>Disintegrants</td>
<td>1-5%</td>
<td>Hydrolyzes slowly at room temperature</td>
</tr>
<tr>
<td>Colloidal Silicon Dioxide</td>
<td>Disintegrants</td>
<td>5-10%</td>
<td>Hygroscopic, but do not liquefy upon absorption of water</td>
</tr>
<tr>
<td>Cross-povidone</td>
<td>Superdisintegrants</td>
<td>2-5%</td>
<td>As hygroscopic in nature, stored in an air-tight container, in a cool and dry place.</td>
</tr>
<tr>
<td>Methyl cellulose</td>
<td>Disintegrants</td>
<td>2-10%</td>
<td>Slightly hygroscopic, but stable</td>
</tr>
<tr>
<td>Micro-crystalline cellulose</td>
<td>Superdisintegrants</td>
<td>5-15%</td>
<td>Stable at dry and air tight condition</td>
</tr>
<tr>
<td>Starch</td>
<td>Superdisintegrants</td>
<td>5-10%</td>
<td>Stable at dry and air tight condition</td>
</tr>
</tbody>
</table>

Table-1 List of Common Disintegrants and Superdisintegrants

**VIII. ADVANTAGES OF SUPERDISINTEGRANTS**

The uses of superdisintegrants are extended in the applications of immediate release tablets, oral disintegration tablets, fast-dispersible tablets, capsules, mouth-dissolving films, etc

- 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.[14]

IX. CONCLUSION
Overviews of role of various types of superdisintegrants with their method of disintegration have been discussed. The ease of availability of these agents and the simplicity of their use in both wet granulation and in the direct compression process suggest that their use would be a more economic alternative in the preparation of drugs showing immediate release action, than the sophisticated and patented techniques.

REFERENCES

[12]. www.pharmtutor.org/articles/overview-superdisintegrants