

## SUPERDISINTEGRANTS

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### Abstract

Oral route is mostly considered the best route for administration of solid dosage form. About 85% of solid dosage form administered orally. In improving the drug action Disintegration shows main role . Disintegrants are ingredients added to the drug preparation that enhances the disintegration of the tablet or capsule into reduced particles in aqueous environment that dissolve more quickly than in the nonexistence of disintegrants. Nowadays several newer agents have been highly-developed identified as Superdisintegrants. Superdisintegrants are the ingredients, which facilitate the quicker disintegration with lesser quantity in compare to disintegrants. These have two type's natural and synthetic superdisintegrants. Superdisintegrants are mostly used at a low level in the solid dosage form, usually 1- 10 % by weight relative to the complete weight of the dosage unit. These are used to increase the effectiveness of solid dosage form. Examples of superdisintegrants are primogel, crosprovidone, Gellan gum etc.

Keyword: Disintegrants, Disintegration, Superdisintegrating agent

### Introduction

Oral route for the drug delivery is the most attractive route for the delivery of drugs. Different kinds of dosage forms administered orally, the tablet is the most desired dosage forms among them for of its ease of preparation, ease in administration, correct dosing, and stability related with oral liquids and because it is more tamper proof than capsules. The bioavailability of drug relays on several factors as like in vivo disintegration, dissolution, and many physiological factors. Disintegrants are ingredients or mixture of ingredients added to the drug formulations, which help dispersion or breakdown of tablets and contents of capsules into reduced particles for rapid dissolution when it comes in interaction with water in the GIT. They might function by drawing water into the tablet, swelling and causing the tablet to break into small particles. Such tablet fragmentation may be critical to the consequent dissolution of drug and to completion of reasonable of drug bioavailability. Starch USP and many starch derivatives are the most common disintegrating agents. Several pregelatinized starches are also used as disintegrants, typically in 5% conc.

## Selection Of SuperDisintegrants:

There are many factors which are Considered in selection of Superdisintegrants.

- Quantity of disintegrates present in preparation.
- Tablet hardness.
- Kind of addition and mixing.
- Drug nature.
- Good flow ability.
- Occurrence of surface active agents.
- Compactable to formulate less friable tablets.
- good mouth feel produce to the to the patient

## IDEAL PROPERTIES OF SUPER-DISINTEGRANTS

### Good Compressibility and Flow Properties

When the powders have 12-16% compressibility, they are considered as a good flow powders. Crospovidones are considerably more compressible relative to other superdisintegrants.

### Poor Solubility

The solubility of the key component in a tablet preparation can affect both the rate and the mechanism of action of tablet disintegration. Water soluble materials likely to be dissolved somewhat than disintegrate, while insoluble materials usually produce fast disintegrating tablets.

### Poor Gel Formation Capacity

Gels can slow down the dissolution because the drug need first diffuse through the gel layer before being released into the body. Primogel is utilizes as superdisintegrant in tablet preparation at a concentration of 4-6%.

### Good Hydration Capacity

Drugs and other excipients, which are hydrophobic and can be adsorbed on disintegrate surfaces, influence the degree of hydration and the efficacy of these disintegrates. Addition of rapid disintegrates of high hydration capacity is stated to decrease this problem, and therefore, increase dissolution.

### Complexation

Anionic disintegrants similar to croscarmellose sodium and primogel form complex with cationic drug actives and may cause slow dissolution. Crospovidone a non-ionic polymer does not interact with cationic drug actives to hinder drug release. The effects of superdisintegrating agent as like croscarmellose sodium, primogel and polyplasdone XL on the dissolution actions of numerous cationic drugs with changing water solubility reports that polyplasdone XL had a more fast dissolution rate for the model cationic drugs, regardless of their aqueous solubilities.

## METHODS OF INCORPORATING DISINTEGRANTS INTO TABLETS.

### Internal Addition (Intragranular)

In Internal addition process, before wetting the powder mixtures with the granulating fluid the disintegrate is mixed with other powders. Thus the disintegrate is merged within the granules. In dry

granulation technique, the disintegrant is added to other excipients before pressing the powder among the rollers. .

### **External Addition (Extragranular)**

In external addition technique, the disintegrant is added to the sized granulation with mixing previous to compression. .

### **Partly Internal and External**

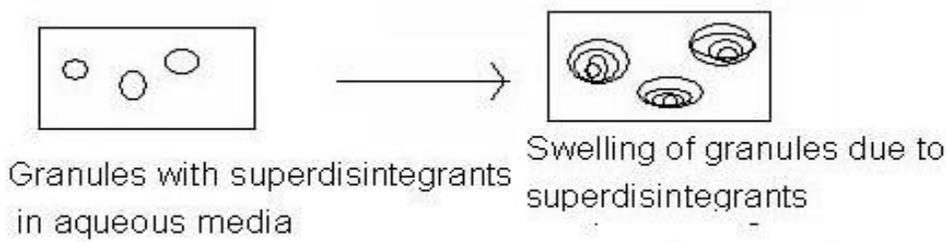
In this technique, part of disintegrant can be part externally and added internally . This effects in instantaneous break down of the tablet into previously compressed granules while the disintegrant in the granules produces additional erosion of the granules to the original powder particles. This process can be more operative. If both intra granular and extra granular procedures are used, extra granular portion breakdown the tablet into granules and the granules more disintegrate by intra granular portion to discharge the drug substance into solution. However, the portion of intra granular disintegrant (in wet granulation methods) is generally not as operative as that of further granules due to the fact that it is exposed to wetting and drying (as part of the granulation method) which decreases the activity of the disintegrant. The intra granular disintegrant have a tendency to keep good disintegration activity in case of compaction process as it does not contain its exposure to wetting and drying.

## **Mechanism of action of SuperDisintegrants**

1. By Swelling.
2. Capillary action (wicking).
3. Due to heat of wetting.
4. Enzymatic reaction.
5. Due to release of gases.
6. Deformation.
7. Combination action.
8. Chemical reaction.
9. Electrostatic repulsion.

### **1. By Swelling**

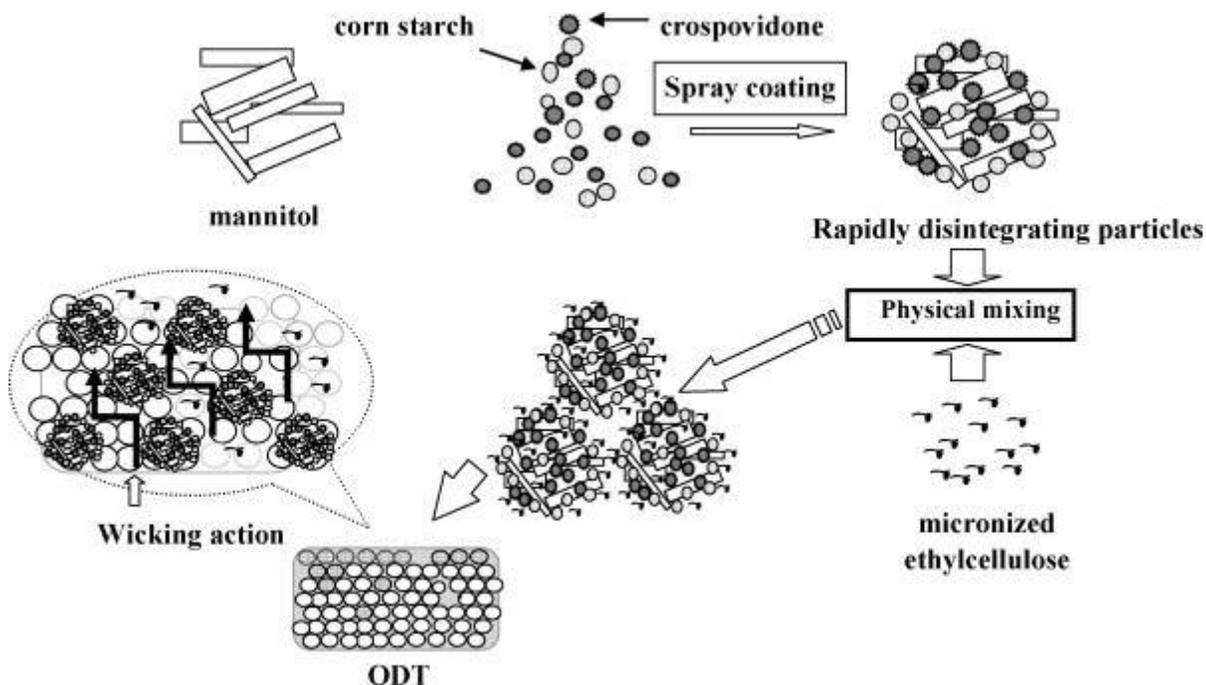
It is a process in which definite disintegrating agents (such as starch) generate the disintegrating effect. It swells when it come up to in contact with water , the adhesiveness of other pharmaceutical ingredients which is present in a tablet can be overcome which causes the tablet breaks. as in figure 1eg: Sodium starch glycolate



**Fig:Swelling mechanism**

## 2. Capillary Action

Disintegrating agents which does not swell they act by the mechanism of porosity and capillary action. Porosity of the tablet gives pathways for the fluid penetration into tablets. The disintegrating particles which have low cohesiveness and compressibility by their own increases porosity and gives these pathways into the tablet. Liquid is drawn up or “wicked” into these paths ways through capillary action and break the bonding of inter particles which causes the tablet to break apart . like Crospovidone, Crosscarmillose as described in pic.2.



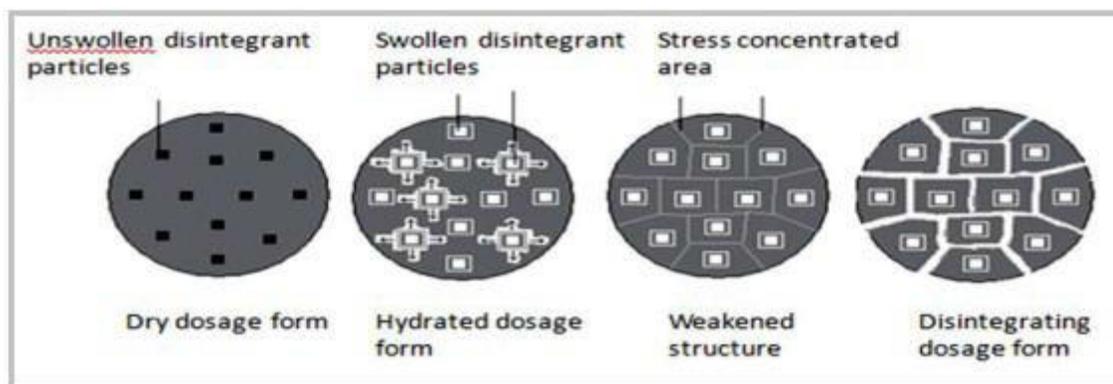
**Fig: Capillary action**

## 3. Due to heat of wetting

When disintegrating agents with their exothermic properties becomes wetted, capillary air expansion generates localized stress. It helps in tablet disintegration. This mechanism of action explains the action of some types of disintegrants and cannot explain the action of modern disintegrants.

#### 4. Enzymatic reaction

Few enzymes which are present in our body also act as disintegrating agents. Binding ability of binders that are decrease by these enzymes helps in disintegration process. Swelling exerts the pressure towards the outer direction, which causes the tablet to break and helps in enhancing the water absorption that provides a huge volume of granules for better disintegration process.



**Fig: Enzymatic reaction**

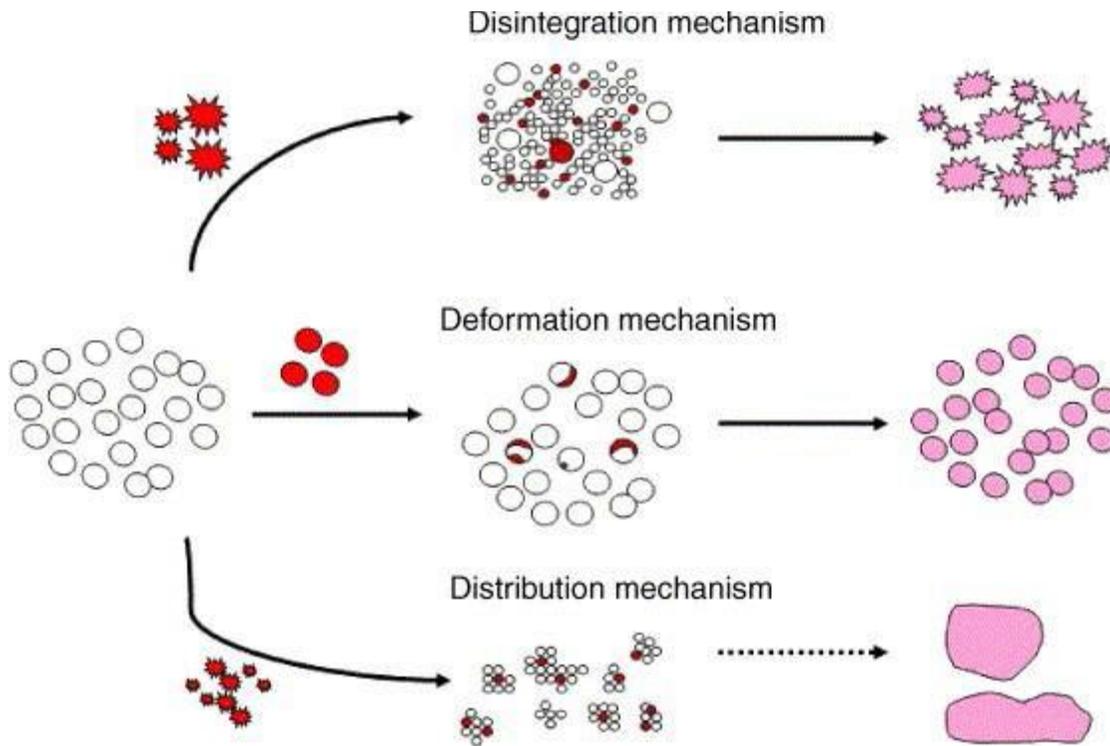
#### 5. Due to release of gases

When carbonates and bicarbonate interact with the citric acid or tartaric acid, carbon dioxide is released in tablets due to wetting. Disintegration of the tablets is caused because of pressure generation in the tablet. When pharmacist wants to formulate very fast dissolving tablets or fast disintegrating tablet this effervescent mixture helps. These disintegrating agents

highly sensitive to minor changes in Humidity level and Temperature. During manufacturing of the tablets, strict control of environment is required. The effervescent mixture is either added rapidly before compression or can be mixed in to two separate fraction of formulation.

#### 6. Deformation

Grains of starch are usually "elastic" in nature means that grains which are de-shaped under Pressure. That grain comes to their usual shape when that pressure is removed. But, when the Compression forces which are involved in tablet formation applied to these grains than they are deformed permanently and are said to be "energy rich" with this energy being free over exposure to water. In other words, the capability of starch to swell is higher in "energy rich" starch grains than it is for starch grains that have not been de-shaped under pressure. It is supposed that not a single mechanism is responsible for the action of most disintegrating agents. But relatively, it is more possible the result of inter-relationships in these major mechanisms.



**Fig: Deformation mechanism**

### 7. Combination reaction

In this mechanism of action, the disintegrating agents utilize the combination of both wicking and swelling action e.g. Croscopolymers.

### 8. Acid base reaction (Chemical reaction)

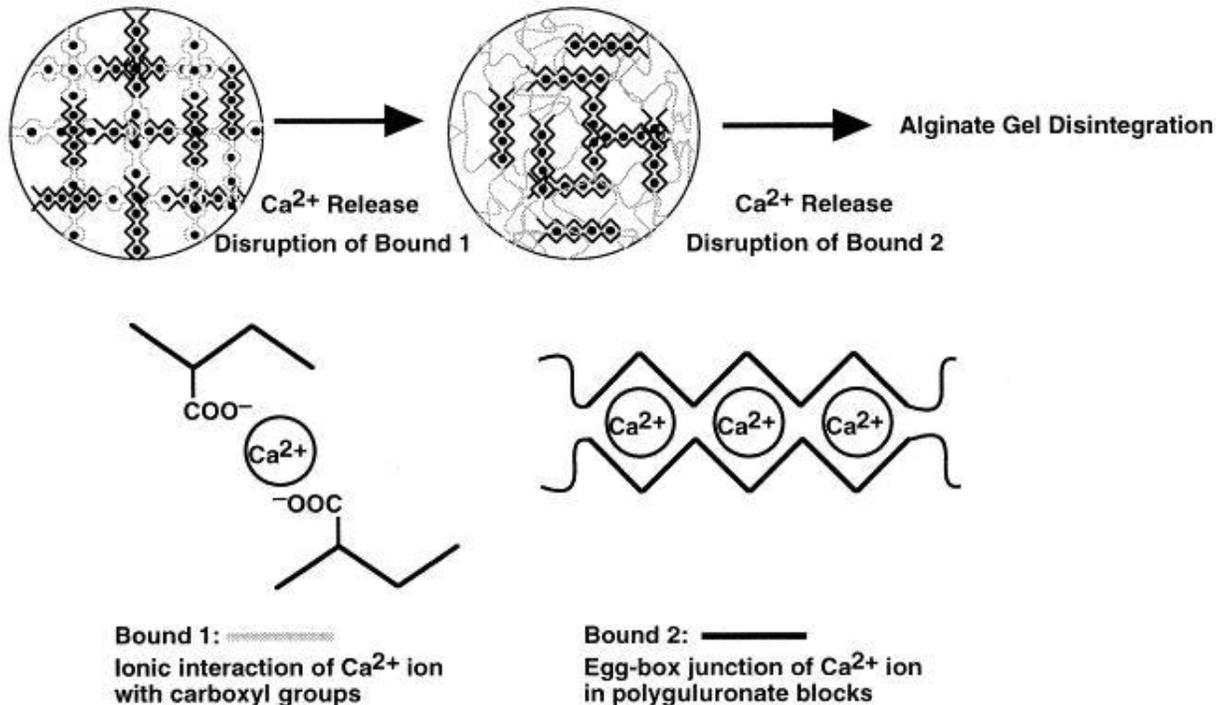
By internal release of CO<sub>2</sub> in water because of interaction in citric acid and tartaric acid (Acids) with alkali metal bicarbonates or carbonates (Bases) in existence of water tablet quickly fragments. The tablet disintegrates due to pressure generation in the tablet.

Due to release of Carbon dioxide gas, the dissolution of APIs in water and taste masking effect is increased. As these disintegrating agents are very sensitive to minor changes in Temperature and Humidity level, environmental control is necessary for the preparation of the tablets. The effervescent mixture is either rapidly before to compression and can be added in two separate fractions of formulation.

### 9. Electrostatic repulsion

The particles which have no swelling action also cause disintegration of tablets. The process of disintegration is based on electric repulsive forces among particles and water is required for this as in figure. Scientists found that repulsion is secondary to

wicking



**Fig:Electrostatic repulsion.**

### Types of SuperDisintegrants:

1. Natural SuperDisintegrants.
2. Synthetic SuperDisintegrants

### Natural SuperDisintegrants

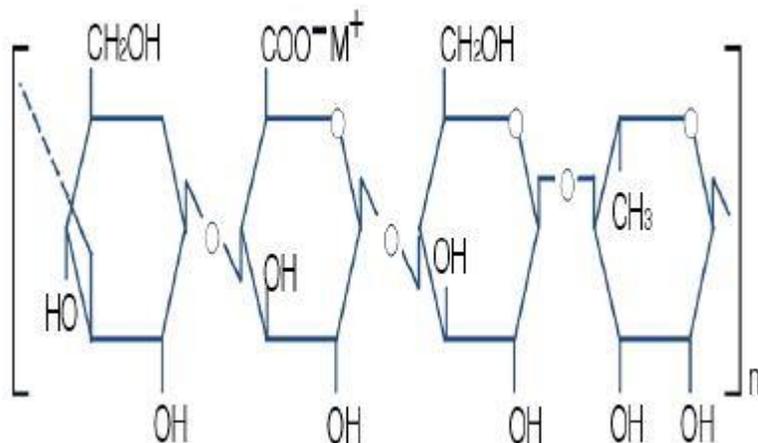
#### Isapghula Husk Mucilage (*Plantago ovata*)

Isapghula Husk contains the certain amount of dried seeds of the plant which is known as *plantago ovata*. The plant holds mucilage in the epidermis of the seeds. The Mucilage of *plantago ovata* has different features like binding, disintegrating and sustaining properties. Mucilage is a superdisintegrating agent which is used to formulate fast dissolving tablets because the percentage of swelling index is very high (around  $89 \pm 2.2\% \text{ v/v}$ ) as compared to the other superdisintegrants. The rapid disintegration of the fast dissolving tablets are due to the swelling of Super disintegrating agents to produce sufficient hydrodynamic pressure for quick and complete disintegration of the tablet. The rate at which swelling occur and significant force of swelling also define its disintegrating efficiency.

#### Gellan Gum

Gellan gum is obtained from *Pseudomonas elodea*. It is a linear anionic polysaccharide biodegradable polymer which containing a linear tetrasaccharide repeat structure and is used as a food stabilizer. Gellan gum as a superdisintegrating agent and the efficacy of gum is compared with other conventional disintegrating agents such as dried corn starch, exploitable, advice (pH 10.2), Ac-di-sol. The disintegration of tablet might be due to the instant swelling features of gellan gum when it comes into contact with water due to its high hydrophilic nature. Observation of the complete disintegration of tablet is carried out within 4 minutes with gellan

gum concentration of 4 percent w/w and 90 percent of drug dissolved within 23 minutes. Ac-di-sol shows very similar pattern of disintegration and in vitro dissolution rates. The tablet with the same concentration with explotab show 36 minutes for 90% of drug release and with starch show 220 minutes. with this result gellan gum has been proved itself as a superdisintegrating agent.



### Locust Bean gum

Locust bean gum is the other name of Carob bean gum. It extracts from the endosperm of the seeds of the carob tree *Ceretoniasiliqua*, which produces in Mediterranean states. Starch and cellulose some other polysaccharides, which contains the long chains of the sugar glucose. In Locust Bean Gum, the ratio of mannose to galactose is greater than in Guar Gum, which gives it slightly different characteristics, and allows the two gums to interact synergistically and together they make a thicker gel. Locust bean gum shows as a binder and as a disintegrating agent property at different concentration. Locust bean gum has been broadly used in food industry as a thickening and gelling agent. Locust bean gum has also been stated to have bioadhesive and solubility enhancement properties.

### Synthetic super-disintegrants

Modified starch (sodium starch glycolate , Primojel ):

It is likely to synthesize sodium starch glycolate from an extensive range of natural starches, but in preparation potato starch is used which gives the product that has the best disintegrating characteristics. When an appropriate starch source is selected the second step is the cross linking of the potato starch. This step is usually carried out using a Federal Drug Administration selected starch esterifying agent such as sodium trimetaphosphate or phosphorus oxychloride in alkaline suspension. Large hydrophilic carboxymethyl groups are introduced because they have the effect to break the hydrogen bonding within the polymer structure. That process allows water to enter the molecule and the polymer becomes cold water soluble. The influence of the cross linking is to reduce both the water soluble fraction of the polymer and the viscosity of dispersion in water. The optimal equilibrium between the degree of substitution and the degree of cross-linking permits for fast water uptake by the polymer without the development of a viscous gel that might inhibit dissolution.

### **Modified cellulose:**

Croscarmellose sodium should be defined as a cross-linked polymer of carboxymethylcellulose. There are many differences between the starch and cellulose polymer and the important includes Differences between the synthetic processes that is used to modify the polymer. Most notably, the DS of croscarmellose sodium is greater than that of sodium starch glycolate, and the process of cross linking is changed. The substitution is implemented by Williamsons ether synthesis to give the sodium salt of carboxymethylcellulose. A significant change from the chemistry of SSG is that certain of the carboxymethyl groups themselves are utilise to cross-link the cellulose chains, the procedure being accomplished by dehydration. Thus the crosslinks are carboxyl ester links relatively than phosphate ester links as in Primojel.

### **Chitin**

Naturally Chitin is taken out from the waste shell of shrimp, crab, krill, and squid and used for the manufacture of chitosan by a deacetylation reaction in alkaline media. The relative study of other superdisintegrating agents with Chitin–silica co precipitate has showed better function.

### **Indion 414**

Indion 414 is an ion exchange resin and when used as superdisintegrating agent, swells on getting hydrated without dissolution and lacking of adhesive tendency gives reason of uniform tablet disintegration. Model drugs which are belonging to various classes were taste masked and prepared into palatable tablets. Experiments were carried out to assess the disintegrating property of Indion 414 in fast disintegrating dosage form like mouth dissolving tablets because they offer enhanced hardness to the tablets on compression. Effectiveness of Indion 414 is more in hydrophobic formulations, as compared to the conventional disintegrants.

### **Microcrystalline Cellulose (Avicel)**

Avicel concentration of less than 10%, shows enhanced disintegration. This mechanism depends on entry of water in the tablet matrix through capillary pores, which disrupt or break the hydrogen bonding between nearby bundles of cellulose microcrystals. With high concentration, particularly in oral disintegrating tablet,

it shows an affinity to stick to the tongue due to fast capillary absorption and quicker dehydration of the tablet surface. Avicel has a rapid wicking rate for water, Hence this is in combination with starch gives an excellent and quick disintegration in OTD preparations.

### **Alginates**

These are hydrophilic colloidal ingredients that are extracted naturally from certain types of Kelp or chemically improved from natural sources like agonic acid or agonic acid salts. They are having greater affinity for water absorption and capable for an outstanding disintegrates. They can be effectively used with ascorbic acid, multivitamins preparation.

### **Others**

Though we know about several super disintegrating agents, which provides superior disintegration, the research for newer disintegrating agents is continuing and researchers are testing with modified natural products, similar to formalin casein, chitin, chitosan, polymerized agar acrylamide, xylem, cross-linked carboxymethylguar and modified tapioca starch. Studies have proposed that the water insoluble superdisintegrating agents show improved disintegration property than the to some extent water soluble agents, since they do not have an affinity to swell. Superdisintegrating agents that have a tendency to swell show minor retardation of the disintegration property due to formation of sticky barrier. There is no certain upper limit regarding the amount of superdisintegrating agent as long as the mechanical properties of the tablet are well-matched with its intended use. The super disintegrating agent may be used alone or in combination with other superdisintegrating agent.

## **SOME APPLICATIONS OF SUPER- DISINTEGRANTS**

### **Formulation of Oral Disintegrating Tablet**

One of the most important streams of application of superdisintegrating agents are in the preparation of oral disintegrating tablets/mouth dissolving tablets. An ODT is a solid dosage form that disintegrates and dissolves in the mouth, either on or under the tongue or in the buccal cavity without water, within 60 s or lesser. The tablets comprise silicified microcrystalline cellulose. They are particularly appropriate for antibiotics.

### **Pharmaceutical Superdisintegrants**

Superdisintegrating agents which offer enhanced compressibility related to prior art super disintegrants. The super disintegrants contain a particulate agglomerate of co processed starch or cellulose and enough quantity of an augmenting agent to increase the compatibility of tablets.

### **Mouth Dissolving Tablets**

MDTs are dosage forms, which when retained in the mouth, disintegrate in the saliva in a minute without the assistance of water or chewing. Indion 414 is a high-purified pharmaceutical grade weak acid cation exchange resin presented as a dry powder in potassium form. It is manufactured in an Federal drug administration suggested manufacturing facility. The benefits of ion exchange resins as such superdisintegrating agents related to conventional ones that they swell on getting hydrated but do not dissolve or have an adhesive affinity. Thus the tablet disintegrates equally. Ion exchange resins are effective at considerable lesser levels than suggested for conventional disintegrants.

## CONCLUSION

With the progress in the formulation of Rapid disintegrating tablets, now it is possible to formulate these tablets with reduced quantity of superdisintegrants. Rapidly disintegrating dosage forms have been effectively commercialized by using numerous types of superdisintegrating agents. By the use of many and different types of superdisintegrating agents patient compliance, commercial and therapeutic benefits has enhanced. At a time when researchers are faced with increasing amounts of poorly soluble drugs, it is very important to select superdisintegrating agents that maximize drug dissolution. Due to fast acceptance of RDTs by patients and pharmaceutical companies, the market of this dosage form is growing and the product pipeline quickly, but without the field of superdisintegrating agents it would not have been possible.

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