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THE ROLE OF DISINTEGRANTS IN SOLID ORAL DOSAGE MANUFACTURING

Anisur R. Khan*

Group Leader in Square Pharmaceutical Ltd, Dhaka.

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***Corresponding Author**
Anisur R. Khan
Group Leader in Square Pharmaceutical Ltd, Dhaka.

ABSTRACT

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 thereby increasing the available surface area and promoting a more rapid release of the drug substance. In the other way Disintegrant are formulated to cause a rapid break-up of solids dosage forms when they come into contact with moisture.[6] Disintegrants are added to oral solid dosage forms to aid in their deaggregation. Disintegration is typically viewed as the first step in the dissolution process and promote the drug release by increasing the water wicking into the plug, and they promote deaggregation of the plug particles. For Immediate Release tablets disintegrant are essential, but for capsules, they are less important because the plug is less of a barrier to the drug release than a compressed tablet.

KEYWORDS: Disintegrants, drug release, wicking, diaggregation.

INTRODUCTION

Disintegrants are added to oral solid dosage forms to aid in their deaggregation. Disintegration is typically viewed as the first step in the dissolution process and promotes the drug release by increasing the water wicking into the plug, and they promote deaggregation of the plug particles.

There are two classes of disintegrants:

1. Traditional disintegrants,
2. Super disintegrants,

1. TRADITIONAL DISINTEGRANT

Until fairly recently, starch was the only excipients used as a disintegrant. To be effective, corn starch has to be used in concentrations of between 5-10%. Below 5%, there is insufficient "channels" available for wicking (and subsequent swelling) to take place. Above 10%, the incompressibility of starch makes it difficult to compress tablets of sufficient hardness.

Pregelatinized starch is a directly compressible form of starch consisting of intact and partially hydrolyzed ruptured starch grains. Pregelatinized starch has multiple uses in formulations as a binder, filler and disintegrant. As a disintegrant, its effective use concentration is between 5-10%. It's major mechanism of action as a disintegrant is thought to be through swelling.

Like Pregelatinized starch, microcrystalline cellulose is widely used in formulations because of its excellent flow and binding properties. It is also an effective tablet disintegrant when used in a concentration of between 10-20%.

2. SUPER DISINTEGRANTS

Because of the increased demands for faster dissolution requirements, there are now available, a new generation of "Super Disintegrants" in addition to the disintegrants discussed earlier.

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:

1. *Modified Starches*- Sodium Carboxymethyl Starch, Chemically treated Potato Starch i.e. Sodium Starch Glycolate (Explotab, Primogel)

Mechanism of Action of *Modified Starches* is Rapid and extensive swelling with minimal gelling. Effective Concentration is 4-6%. Above 8%, disintegration times may actually increase due to gelling and its subsequent viscosity producing effects.

2. *Cross-linked polyvinyl pyrrolidone*- water insoluble and strongly hydrophilic. i.e. Crospovidone (Polyplasdone XL, Kollidon CL) Mechanism of Action of Cross-linkepolyvinyl pyrrolidone 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 and Mechanism of Action of Modified Cellulose is Wicking due to fibrous structure, swelling with minimal gelling and its Effective Concentrations: 1-3% (Direct Compression), 2-4% (Wet Granulation)

SELECTION OF SUPERDISINTEGRANT

Since superdisintegrants is used as an excipients 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. The ideal disintegrant should have.[2]

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. Although some are better than others, the currently marketed superdisintegrants exhibit an optimum combination of properties.

METHOD OF ADDITION OF SUPRADISINTEGRANTS

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

The procedure of adding disintegrant to a formulation can have a profound influence on its effectiveness. Disintegrants can be added:

- Intragranular – the disintegrant is added before the granulation process
- Extragranular – the disintegrant is added after granulation and before the compression process
- Disintegrant can also be added at both the intragranular and extra granular stages

When a wet granulation process is employed, the addition of disintegrant extra granular promotes more rapid disintegration than that added intragranular. Having said that, there appears to be a general view that adding some disintegrant in both steps provides the best results.

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 experiment, the study show the effect of incorporating a disintegrant, croscarmellose 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 dissolve at a faster rate when the super disintegrant is included intragranularly. Tablet friability is not affected by the method of disintegrant incorporation.

External Addition

In both wet and dry granulation method, the superdisintegrants is added to the granules during dry mixing prior to compression. The effect of mode of incorporation of superdisintegrants (croscarmellose sodium, sodium starch glycolate and crospovidone) on dissolution of three model drugs with varying aqueous solubility (carbamazepine, acetaminophen and cetrizine 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.[9]

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 extra granular 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.

Mechanism of disintegrations by superdisintegrants

There are five major mechanisms for tablet disintegration as follows:[1,3]

1. Swelling
2. Porosity and Capillary Action (Wicking)
3. Deformation
4. Due to disintegrating particle/particle repulsive forces
5. Heat of wetting
6. Due to release of gases
7. Enzymatic reaction
8. Combination action

TYPES OF SUPERDISINTEGRANTS

The Superdisintegrants can be classified into two categories on the basis of their availability[6]:

1. Natural Superdisintegrants.
2. Synthetic Superdisintegrants.

1. Natural Superdisintegrants: -These superdisinegrating 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 mucilages 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 are available which have super-disintegrating activity.

i. Lepidiumsativum Mucilage

Lepidiumsativum (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, Eand F and two new monomeric imidazole alkaloids Semilepid inoside A and B. Mucilage of Lepidium sativum has various characteristic like binding, disintegrating, gelling.[20]

ii. Plantago Ovata Seed Mucilage (Isapgula)

Isapghula consists of dried seeds of the plant plantagoovata and it contains mucilage which is present in the epidermis of the seeds. The seeds of Plantagoovata 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 plant ago ovatais a recent innovation for its super disintegration property when compared with Crospovidone. It shows faster disintegration time than the superdisintegrant crospovodone.

iii. 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 Urenstree (Family-Sterculiaceae). Its synonyms are Karaya, sterculia, Indiantragacanth, Bassoratragacanth, kadaya, Kadira, katila. Gum Karaya is compatible with other plant hydrocolloids as well as proteins and carbohydrates.

iv. 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, Cyamopsistetragonaloba (L) Taub. (Synonym-Cyamopsispsoraloides). It is used as thickener, stabilizer and emulsifier, and approved in most areas of the world (e.g. EU, USA, Japan, and Australia).[2,5] 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.

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vii. 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-graceumare used as vegetables. Fenugreek has been used in treating colic flatulence, dysentery, diarrhoea, 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.[28,29]

viii. Locust Bean gum

Locust bean gum is extracted from the endosperm of the seeds of the carob Tree Ceretoniasiliqua, which grows in Mediterranean countries. It is also called Carob bean gum. Some other familiar polysacharides 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.

2. Synthetic Superdisintegrants

A group of superdisintegrants including croscamellose sodium (Ac-Di-Sol) sodium starch glycolate (Primojeland Explotab) and crospovidone (Polyplasdone XL) alleviate most of these problems. Use of the superdisintegrants in fast dispersible tablet is possible as tablet shows optimum physical properties.

Advantages of Synthetic Superdisintegrants

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

i. Sodium Starch Glycolate[3,4] (Explotab, Primogel) Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsule and tablet formulations. It is recommended to use in tablets prepared by either direct-compression or wet-granulation processes. The recommended concentration in a formulation is 2-8%, with the optimum concentration about 4% although in many cases 2% is sufficient.[8] Disintegration occurs by rapid uptake of water followed by rapid and enormous swelling. The disintegrant efficiency of sodium starch glycolate is unimpaired in the presence of hydrophobic excipients, such as lubricants unlike many other disintegrants. Increasing the tablet compression pressure also

appears to have no effect on disintegration time. These are modified starches with dramatic disintegrating properties and are available as explotab and primogel which are low substituted carboxy methyl starches. Explotab consisting of granules that absorb water rapidly and swell. The mechanism by which this action takes place involves rapid absorption of water leading to an enormous increase in volume of granules result in rapid and uniform disintegration. The natural pre dried starches swell in water to the extent of 10-20 percent and the modified starches increase in volume by 200-300 percent in water.

ii. Cross-linked polyvinyl-pyrrolidone[10]

(Crospovidone, PolyplasdoneXL, XL10) Crospovidone quickly wicks saliva into the tablet to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth. Unlike other superdisintegrants, which rely principally on swelling for disintegration, Crospovidone superdisintegrants use a combination of swelling and wicking. When examined under a scanning electron microscope, crospovidone particles appear granular and highly porous.

This unique, porous particle morphology facilitates wicking of liquid into the tablet and particles to generate rapid disintegration. Due to its high crosslink density, crospovidone swells rapidly in water without gelling. Other superdisintegrants have a lower crosslink density and, as a result, form gels when fully hydrated, particularly at the higher use levels in ODT formulations. Swells very little and returns to original size after compression but act by capillary action.

iii. Cellulose Derivatives (Ac-Di-Sol®)[3,4]

Croscarmellose sodium is described as a cross-linked polymer of carboxy methyl cellulose (CMC). This polymer is different in synthesis and structure as compare to Sodium starch glycolate. Most importantly, the degree of substitution using Williamson's ether synthesis of croscarmellose sodium is higher than that of sodium starch glycolate, and the mechanism of crosslinking is also different.[8] The chemistry of SSG is different that of cross carmellose sodium As some of the carboxymethyl groups themselves are used to cross-link the cellulose chains. For example, the cross-linking in Primogel are phosphate ester rather than carboxyl ester links as compare to Cross carmellose sodium.

iv. Alginates

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

v. Chitin/Chitosan–Silicon Dioxide Coprecipitate

Chitin is one of the recent and most interesting category of superdintegrant. It is the second most abundant polysaccharide found in nature after cellulose Naturally Chitin is extracted from the shell wastes of shrimp, crab, lobster, krill, and squid and used for the production of chitosan by a deacetylation reaction in alkaline medium. However, in large-scale handling of pharmaceutical blends both chitin and chitosan n powders show poor bulk density, thus results in poor flowability and compressibility.[8]

The comparative study of other superdisintegrants with chitin–silica coprecipitate has proved better disintegration and dissolution functionality. The particle rearrangement and plastic deformation ability of chitin–silica undergoes in the same extent compared with Avicel. The good compressibility and the good compactability properties of chitin–silica may allow it to be used in direct compression applications.

vi. Ion Exchange Resins

The INDION 414 has been used as a superdisintegrant for ODT. It is chemically cross-linked polyacrylic, with a functional group of – COO – and the standard ionic form is K+ and is a weak acid cationic exchange resin. 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 superdisintegrant 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.

vii. Modified Polysaccharides

Agar (AG) and guar gum (GG), natural polysaccharides are treated with water and co grinded further with mannitol which exhibit superdisintegration property. These modified

polysaccharides may call C-TAG (co grinded treated agar) and C-TGG (co grinded treated guar gum) respectively.

They are biodegradable, directly compressible, having desirable swelling dynamics. The above modified polyschharides were further used as superdisintegrants in Roxithromycin fast dispersible tablets and compared with conventional tablets containing MCC. The C-TAG and C-TGG have shown better disintegration for their porous nature, better water intake ability and free flowing property than others. Another natural polysschariide, karaya gum is modified using distilled water to achieve superdisintegration property in dispersible tablet development.[7] This modified karaya gum (MKG) is easy to prepare, cheap, easily available, biodegradable and stable compared to available synthetic super disintegrants in market.

List of Superdisintegrants

Super disintegrant	Mechanism of Action	Special Comment
Crosscarmellose Ac-Di-Sol(r) Nymce ZSX(r) Primellose(r) Solutab(r) Vivasol(r) Cross linked cellulose	Swells 4-8 folds in < 10 seconds. -Swelling and wicking both.	Swells in two dimensions. -Direct compression or granulation -Starch free
Crosspovidone Crosspovidon $M_{(r)}$ $Kollidon_{(r)}$ $Polyplasdone_{(r)}$	Swells very little and returns to original size after compression but act by capillary action	Water insoluble and spongy in nature so get porous tablet
Sodium starch glycolate, Explotab(r)Primogel(r)	Swells 7-12 folds inSwells in three dimensions and high level serve as sustain release matrix	Sodium starch glycolate Explotab(r) Primogel(r)
Alginic acid NF $Satialgine_{(r)}$	Rapid swelling in aqueous medium or wicking action	Promote disintegration in both dry or wet granulation
Soy polysaccharides, $Emcosoy_{(r)}$		Does not contain any starch or sugar. Used in nutritional products.
Calcium silicate	Wicking action	-Highly porous -Light weight -Optimum concentration is between 20-40%

Mechanism of Disintegration

Tablets disintegrate by[1,3,5]

1. Swelling or distension
2. Porosity and Capillary Action (Wicking)
3. Deformation of the tablet
4. Due to disintegrating particle/particle repulsive forces

5. Heat of wetting
6. Disintegrating forces
7. Due to release of gaseous materials
8. Combination action
9. being triggered by enzymatic action

Each of these mechanisms and examples of disintegrant materials is described below.[6]

1. *Swelling or distension*: The most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets may swell as a consequence of liquid becoming absorbed in the pores of the solid material through capillary action and wicking. If absorption of liquid is low, the rate of swelling will be low.[7] If liquid is absorbed, it can exert considerable forces within the pores, especially within small hydrophilic pores, causing particles of either active agent or excipient to swell and fracture. Forces may be great enough in solids of high packing density for stresses to penetrate throughout the material causing severe disintegration.

The incorporation of a disintegrant that will swell on contact with water is one of the most practiced methods of promoting disintegration in tablets Swelling is believed to be a mechanism in which certain disintegrating agents (such as starch) impart the disintegrating effect.[11] By swelling in contact with water, the adhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart. Tablets with high porosity show poor disintegration due to lack of adequate swelling force.[11] 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.

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, PlatagoOvata.

2: *Porosity and Capillary Action (Wicking):* There is a general consensus that water uptake into the tablet by capillary action is the necessary first step in the disintegration process.[7] When a porous tablet is placed in an aqueous liquid, the liquid will quickly penetrate the pores of the solid by capillary forces. The pores act as a wick that draws liquid into the solid. Such liquid absorption can lead to breakage of the solid matter of the tablet by weakening the forces that hold together the solid particles.

The amount of aqueous liquid that is absorbed depends on the 'hydrophilicity' of the solid material, sometimes referred to as its 'wettability'. Typically between 5 and 20% by weight is incorporated into the material before tabletting. Such levels do not significantly change the pore structure of the material[5]. Absorption of water also depends on the pore size distribution of the solid material which in turn is dependent on the particle size distribution in the tablet starting material, and on the manner in which the disintegrant is added (e.g., whether it is added before or after the solid granulation process). It is also possible that the tabletting conditions can affect the water uptake, since the density and porosity may to some extent depend on the force used to compress the tablet. Water will be drawn into large pores more slowly than small pores, and to increase the rate of disintegration an disintegrant may be incorporated into a table that promotes a low surface tension of the liquid (i.e., increases the hydrophilicity of the solid), thereby encouraging liquid to be absorbed around the particles of drug matter.

3. *Deformation:* 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.[5] Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet.[9]

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.

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.

The classical example of the earliest known disintegrant is Starch. Corn Starch or Potato Starch was recognized as being the ingredient in tablet formulations responsible for disintegration as early as 1906 (even though tablet disintegration was itself not given much importance in tablet formulations until much later).

4. *Due to disintegrating particle/particle repulsive forces*

A further method of disintegration is observed in the case of non-swellable starch-based disintegrants. The "particle repulsion theory" proposed by Guyot-Hermann is based on the notion there are electrical repulsive forces between similarly charged particles, and that these effect particle disintegration. The fact that water needs to be present to achieve the breakup suggest that such repulsive forces are only secondary to water absorption or wicking in terms of promoting material disintegration.

5. *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.

6. *Due to release of gases*

Effervescent tablets that release carbon dioxide when introduced into water are the basis for another type of disintegrant. The simplest is a mixture of solid chemical compounds such as citric or tartaric acid and a carbonate or bicarbonate.[12] The release of gas when water is absorbed by the tablet leads to rapid disintegration within the tablet. Such gas-producing disintegration is favoured when a rapid dissolving tablet or a fast-disintegrating tablet is required. The problem with using such materials is that they are highly sensitive to environmental conditions such as temperature and humidity. For this reason gas-producing disintegrants are handled in a strictly controlled environment, and are introduced into the product mixture usually immediately prior to compression in the tablet manufacturing process.[5]

7. Combination action

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

8. Enzymatic Reaction

Small amounts of enzymes may be added to the product. Alternatively the enzymes found inside the body may attack excipients such as starch or other binder materials, thereby promoting disintegration These enzymes dearth 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. Some examples of disintegrating enzymes are presented in table 1 along with the binders against which these are active.

Factor Affecting Disintegration[5,6]

Other factors which affect the dissolution of Drugs from tablets are:

- Type and Concentration of Active Ingredient
- Type and Concentration of Binder Used
- Type and Concentration of Fillers Used (soluble vs. insoluble)
- Type and Concentration of Lubricant Used
- Type of Dissolution testing Used (Apparatus, Speed, Media)
- Manufacturing Process (wet granulation vs. compaction vs. direct compression)

Fillers : It affect the speed and the process of tablet disintegration. Water-soluble fillers can lead to an increase in viscosity of the absorbed fluid.[13] The effect of this is to reduce the strength of the disintegrating agents. Fillers that are insoluble in water can cause increased disintegration provided that a sufficient quantity of disintegrants is introduced.

Lubricants

Most lubricants are hydrophobic, i.e., they repel water. Lubricants are often added to formulations to protect the surface of the tablet as it is formed in the tablet press. Such addition can often render the tablet more susceptible to disintegration.[13]

If the tablet has little to no added disintegrants, the use of lubricants can have a negative influence especially on the uptake of water, and even affecting highly concentrated swelling disintegrants. In most cases, if a strong disintegrant is used in the formulation, the disintegration time is influenced little by the addition of lubricants.[9] The performance of sodium starch glycolate, for example, is unaffected by the presence of hydrophobic lubricants.

Surfactants

Surfactants are added to help reduce the hydrophobicity of drugs as high hydrophobicity leads to longer disintegration times. It should be noted that they are only effective within a certain range. Note that the chemical compound sodium lauryl sulphate, which is often added

as a surfactant in drug formulations, can increase water absorption of starch and also affect the liquid penetration for tablets.[9]

The disintegration time of water-soluble tablets remains almost the same with or without the introduction of nonionic surfactants; however when surfactants are added the rate of water penetration generally increases especially for granule.

Manufacturing Process

In a *direct compression process*, drug is blended with a variety of excipients, subsequently lubricated and directly compressed into a tablet. A disintegrant used in this type of formulation, simply has to break the tablet apart to expose the drug substance for dissolution.

In a *wet granulation process*, the drug substance is combined with other excipients and processed with the use of a solvent (aqueous or organic) with subsequent drying and milling to produce granules.[9] The resulting granules are then blended with additional excipients prior to being compressed into a tablet. {Dry compaction is similar. But compression and milling are used (rather than solvents) to make the granu.

A disintegrant used in granulated formulation processes can be more effective if used both "intragranularly" and "extragranularly" thereby acting to break the tablet up into granules and having the granules further disintegrate to release the drug substance into solution. However, the portion of disintegrant added intragranularly (in wet granulation processes) is usually not as effective as that added extragranularly 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 disintegrant used intragranularly tends to retain good disintegration activity.

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