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A DETAILED STUDY ON DISINTEGRANTS AND SUPERDISINTEGRANTS

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ABSTRACT

Oral route is the most common route for administration of solid dosage form, about 85% of solid dosage administered by oral route. Disintegration plays major role in improving the drug activity. Disintegrants are substances added to the drug formulation that increase the breakup of the tablet or capsule into smaller particles in aqueous environment that dissolve more rapidly than in the absence of disintegrants. Nowadays some newer agents have been developed known as Superdisintegrants. Superdisintegrants are the substances, which facilitate the faster disintegration with smaller quantity in contrast to disintegrants. These are of two type's natural and synthetic superdisintegrants. 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. These are used to improve the efficacy of solid dosage form. Examples of superdisintegrants are sodium starch glycolate, crospovidone, Gellan gum etc.

KEYWORDS

Disintegration, Disintegrants and Superdisintegrants.

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INTRODUCTON

The orally administered compacted tablet is the most common and prefered solid unit dosage form for delivering medicaments to patience. Not all the excipient types may be included in a formulation except when expressly needed. Disintegrants bring about tablet matrix breakup in an aqueous medium and are commonly further classified. Nowadays some newer agents have been developed as superdisintegrants. The growing demand for faster and more rapid disintegrating formulations has stimulated pharmacists to develop what the industry is calling "superdisintegrants". These derivatives are developed to have greater effectiveness even at low concentrations. Superdisintegrants function principally by swelling on absorbing water.

Types and List of Tablet Disintegrants

Starch (Amylum)

The mechanism of action of starch is wicking and restoration of deformed starch particles on contact with aqueous fluid and in doing so release of certain amount of stress which is responsible for disruption of hydrogen bonding formed during compression.

The conditions best suited for rapid tablet disintegration are sufficient number of starch agglomerates, low compressive pressure and the presence of water. The concentration of starch used is also very crucial part. If it is below the optimum concentration then there are insufficient channels for capillary action and if it is above optimum concentration then it will be difficult to compress the tablet.

Pregelatinized starch (Starch 1500)

Pregelatinized starch is produced by the hydrolyzing and rupturing of the starch grain. It is a directly compressible disintegrants and its optimum concentration is 5-10%. The main mechanism of action of Pregelatinized starch is through swelling.

Modified starch - Sodium starch glycolate (primogel, explotab)

To have a high swelling properties and faster disintegration, starch is modified by carboxy methylation followed by cross linking. Mechanism of action of this modified starches are rapid and extensive swelling with minimum gelling. Optimum concentration is 4-6 %. If it goes beyond its limit, then it produces viscous and gelatinous mass which increases the disintegration time by resisting the breakup of tablet. They are highly efficient at low concentration because of their greater swelling capacity.

Cellulose and its derivatives

Sodium carboxy methylcellulose (NaCMC and carmellose sodium) has highly hydrophilic structure and is soluble in water. But when it is modified by internally crosslinking we get modified crosslinked cellulose i.e. Crosscarmellose sodium which is nearly water insoluble due to cross linking. It rapidly swells to 4-8 times its original volume when it comes in contact with water.

Microcrystalline cellulose (MCC)

MCC is insoluble and act by wicking action. The moisture breaks the hydrogen bonding between adjacent bundles of MCC. It also serves as an excellent binder and has a tendency to develop static charges in the presence of excessive moisture content. Therefore, sometimes it causes separation in granulation. This can be partially overcome by drying the cellulose to remove the moisture.

Alginates (alginic acid and Na-alginate)

Alginates are hydrophilic colloidal substances which has high sorption capacity. Alginic acid is insoluble in water, slightly acidic in reaction.It should be used in only acidic or neutral granulation. Alginates do not retard flow and can be successfully used with ascorbic acid, multivitamin formulations and acid salts of organic bases.

Ion-exchange resin

Ion exchange resin (Ambrelite IPR-88) has highest water uptake capacity than other disintegrating. It has tendency to adsorb certain drugs.

Miscellaneous

This miscellaneous category includes disintegrants like surfactants, gas producing disintegrants and hydrous aluminium silicate. Gas producing disintegrating agents is used in soluble tablet, dispersible tablet and effervescent tablet.

Polyplasdone XL and Polyplasdone XL10 act by wicking, swelling and possibly some deformation recovery. Polyplasdone ®XL do not reduce tablet hardness, provide rapid disintegration and improved dissolution. Polyplasdone ® as disintegrating agent has small particle size distribution that impart a smooth mouth feel to dissolve quickly.

An Overview of Disintegrants

The ability of the active ingredient in a drug to be absorbed by the body depends on its bioavailability. This, in turn, is a function of the solubility of the active ingredient in the gastrointestinal fluids as the drug passes through the intestines. The ability to dissolve depends on the physical form and chemical composition of the drug. Nonetheless, the rate at which drugs dissolve in the biofluids of the body is influenced by the tablet's disintegration. For most tablets, it is necessary to overcome the cohesive forces that bind together the particles within the tablet that were introduced as a result of the tablet pressing process. This is made difficult in some cases through the introduction of materials that are added before the tabletting process with the aim of binding the particles together. For some tablets disintegration is even more difficult as the active

ingredients are capped inside a non-disintegrating shell. The shell protects the bulk of the materials from being exposed to the gastric fluids. To ensure that tablets disintegrate at a sufficiently fast rate within the body,

Formal disintegration tests can be routinely carried out on each batch that is manufactured. A disintegrant is an excipient that is incorporated into the formulation of tablets or capsules to promote their disintegration when they come into contact with liquid or fluid matter. Several types of disintegrant have been routinely used for many years and may be distinguished according to their mode of action: (a) those that enhance the action of capillary forces that promote the absorption of water (by wicking) (b) those that swell on contact with water and (c) those that release gases leading directly to disintegration of the tablet. The general purpose of incorporating one or more disintegrants in the product formulation is to increase the surface area of the product and soften the binding matter that holds together the solid particles that make up the product. The net effect is that a tablet when exposed to aqueous media disintegrates first into granules, and then into fine particles. The rate of dissolution in the media increases as the particle size reduces and is greatest when the tablets or capsules reduced to fine particles, as shown schematically in Rapid dissolution increases the rate of absorption of the active ingredient by the body, producing the desired therapeutic action. Note that tablets that are labelled as chewable generally do not require a disintegrant to be incorporated in the formulation with water exothermically by generating heat within the pores of the solid on account of a reaction between the absorbed water and the solid material. The heat generated can produce a rapid increase in internal temperature and expansion of the air entrapped within the pores which can start the disintegration process.

Disintegrating Forces

A further method of disintegration is observed in the case of non-swellable starch-based disintegrants. The theory of "Particle repulsion" 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.

Deformation of tablet

Hess Research has shown that during tablet compression, particles of starch disintegrant are deformed under stress and will return to their normal structure when the material is brought in contact with any liquid. Hess proved that the swelling capacity of starch material is greatly increased when the particles are deformed during compression process.

Release of Gas Materials

Effervescent tablets that release carbon dioxide when introduced into water are the basis for another type of disintegrant. The disintegration is caused by a mixture of solid chemical compounds such as citric or tartaric acid and a carbonate or bicarbonate. Gas is released when water is absorbed by the tablet leads to rapid disintegration of the tablet. This gas-producing disintegration is suitable when a rapid dissolving tablet or a fast-disintegrating tablet is required. The problem of using such materials is that they are very much sensitive to environmental conditions like temperature and humidity. For this reason gas-producing disintegrants should be in strictly controlled environment, and are introduced into the product mixture usually immediately prior to compression in the tablet manufacturing process.

By Enzymatic Action

Small amounts of enzymes may be added to the product. Simultaneously the enzymes present inside the body may attack excipients such as starch or other binder materials, thereby increasing process of disintegration.

Adding disintegrant to the product formulation

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 extragranular stages.

When a wet granulation process is employed, the addition of extragranular disintegrant promotes rapid disintegration. Than that added intragranular.

Starch

Starch (polysaccharide) is a polymer of high molecular weight. The starch molecules arrange themesleves into crystalline agglomerates or granules of different sizes that are visible under an optical microscope. Lowenthal and Wood, suggests that large agglomerates are required for starch to be an effective disintegrant. Starches performs best if low compression force is employed for the making of tablet. The concentration of starch in the formulation is also important. If the starch concentration is low it will create an number of channels for wicking of water or body fluid. Similarly, if the concentration is too high, the material will be difficult for compression into a tablet.

Pregelatinized starch is produced by rupturing and hydrolyzing of starch grains and It can be widely used as a disintegrant in tablets as well as capsules, at concentrations between 5 to 10% by weight. It is highly compressible in nature and gets easily digested in the gut.

Starches can be chemically modified by carboxymethylation to enhance cross-linking between the molecules. Such modified type of starches produces a higher degree of swelling when it absorbs water, leading to faster disintegration of the tablet. Sodium starch glycolate is such a starch derivative that can absorb 20 times its weight in water. It is commonly manufactured from potato starch, and can compare favourably with other modified starches and it is widely used as a disintegrant under the brand names Primojel and Explotab.

Modified starches and starch derivatives extensively swells with minimal gelling capacity, and optimum concentration levels of 4-6% by weight. When fully hydrated the starch becomes sticky and gelatinous matter that helps in the disintegration process as it helps to hold keep the tablet particles together. Due to high swelling capacities, modified starches are highly efficient even in low concentrations.

Cellulose and derivatives

Sodium carboxy-methylcellulose and crosscarmellose sodium are two highly hydrophilic and water-soluble compounds. These compounds can be modified to increase cross-linking between the cellulose molecules thereby reducing their solubility in water. Crosslinking of cellulose increases the volume of water absorbed by as much as 4-8 times, and an example of a widely used cross-linked cellulose is crosscarmellose sodium.

Microcrystalline Cellulose

Microcrystalline cellulose (MCC) is one of the refined form of natural cellulose found in most plant materials. It is used as dehydrated form and is used as both disintegrant and binder in pharmaceutical products.

Hydrophilic Colloidal Substance – Alginates

Alginates are examples for hydrophilic colloidal substances with high water absorbing capacities. When Alginates dissolved in water forms acidic solutions which renders them useful only for neutral or acidic granulation. Unlike Microcrystalline cellulose or starch derivatives, alginates therefore can be used with multivitamins, ascorbic acid and with formulations containing organic acids.

Ion-Exchange Resins

Ion-exchange resins are well-characterized molecular structures having a higher water absorption capacity than most other readily available disintegrants. They are also used in pharmaceutical products as taste-masking agents.

They are high molecular weight water insoluble polymers containing positively or negatively charged functional groups in their matrix, which have an affinity for oppositely charged counter ions. They can exchange with surrounding medium reversibly and Stochiometrically.

Ion exchange resins are Styrene (Di Vinyl Benzene) copolymer containing

Acidic groups like Carboxylic or sulphonic for Cation E.R.

Basic groups like Quaternary Ammonium for Anion E.R

Based on the nature of the ionic species being interchanged, the IE process is known as either cation exchange (CE) or anion exchange (AE). The IE process is competitive in nature. In general, drug in an ionic form (usually solution) is mixed with the appropriate Ion exchange resin to form a complex, known as 'resinate'.

There are numerous functional groups that have charge, only a few are commonly used for man-made IER. They are as follows:

- COOH, that is weakly ionized to -COO^- ,
- SO3H, that is strongly ionized to -$SO3^-$,
- NH2, that weakly attracts protons to form NH3 + ,
- Secondary and tertiary amines that also attract protons weakly,
- NR3 +, that has a strong, permanent charge (R stands for some organic group).

Types of Ion-exchange Resins

There are two major classes of ion-exchange polymers

(a) Cation and (b) anion exchange resins.

Cation exchange resins are negatively charged functional groups and exchanges positively charged ions. There will be prepared by copolymerization of styrene and divinyl benzene and have sulfonic acid groups (-SO3H) introduced into most of the benzene rings.

The mechanism of cation exchange process can be represented by the following reaction in Eq. (1): R- - ex+ + C+ →R- - C+ +ex+ (1)

where, R is a resin polymer with SO3-sites available for bonding with exchangeable cation (ex+), and C+ indicates a cation in the surrounding solution getting exchanged.

Cation exchange resins can be further classified as:

(a) strong acid cation exchange resins and (b) weak acid cation exchange resins.

Strong acid cation exchange resins: These resins are highly ionized in both the acid (R-SO3H) and salt (RSO3Na) form of the sulfonic acid group (-SO3H). They will convert a metal salt to the corresponding acid by the reaction in

Eq. (2): 2(R-SO3H) + NiCl2 → (R-SO4) Ni + 2HCl (2).

On the other hand, the exchange capacity of strong acid resins is independent of the solution. These resins behave similarly as weak organic acids that are weakly dissociated.

weak acid resin has the ionisable group of carboxylic acid (COOH) as opposed to the sulfonic acid group (SO3H) used in strong acid resins.

Anion exchange resins have positively charged functional groups and thereby exchanges negatively charged ions.

The mechanism of anion exchange process can be represented by the following reaction in Eq. (3): R+ - ex - + A- → R+ - A- + ex- (3)

Where, R+ indicates a resin polymer with number of sites available for bonding with exchangeable anion (ex-), and A- denotes cations in the surrounding solution getting exchanged.

Anion exchange resins can be further classified as follows: Strong base anion exchange resins Strong base resins are highly ionized.

These resins are used in the hydroxide (OH) form for water deionization. They will react with anions in solution and can convert an acid solution

Eq. (4): R-NH3OH + HCl → R-NH3Cl + H2O (4)

Weak base resins are like weak acid resins and the degree of ionization is strongly influenced by pH.

The weak base resin does not have an OH ion form as that of strong base resin

Eq. (5): R-NH2 + HCl → R-NH3Cl (5)

Others

In addition to the above listed disintegrants are those that function be releasing gases; examples include hydrous aluminium silicate and various surfactants. These are widely used in effervescent tablets as they are soluble and dispersable.

Most recent polymer materials includes products such as different grades of cross-linked Polyplasdone (e.g., Polyplasdone XL10 and Polyplasdone XL) which, like starches, promote the disintegrantion process through swelling, deformation and wicking mechanisms. Cross-linked polymers increases the rate of disintegration and dissolution not affecting the hardness of the tablet. Polyplasdone can produced in the form of small particle size giving it a smooth feeling in the mouth.

Super Disintegrants

The growing demand for faster and more rapid disintegrating formulations are “superdisintegrants”. They are developed to have greater effectiveness even at low concentrations. They are effective intragranularly and most superdisintegrants are hygroscopic in nature and readily absorbs moisture, which generally rules them out for drugs that are moisture-sensitive.

Superdisintegrants function principally by swelling on absorbing water.

Table No.1: List of Disintegrants

S.No	Disintegrants	Concentration In Granules (%W/W)	Special Comments
1	Starch	5-20	Higher amount is required, poorly compressible
2	Starch 1500	5-15	-
3	Avicel®(PH 101, PH 102)	10-20	Lubricant properties and directly compressible
4	Solkafloc®	5-15	Purified wood cellulose
5	Alginic acid	1-5	Acts by swelling
6	Na alginate	2.5-10	Acts by swelling
7	Explotab®	2-8	Sodium Starch Glycolate, superdisintegrant.
8	Polyplasdone®(XL)	0.5-5	Crosslinked PVP
9	Amberlite® (IPR 88)	0.5-5	Ion exchange resin
10	Methyl cellulose, Na CMC, HPMC	5-10	-
11	AC-Di-Sol®	1-3 2-4	Directcompression Wet granulation
12	Carbon dioxide	-	Created insitu in effervescent tablet

Table No.2: Disintegrating Enzymes

S.No	Enzymes	Binder
1	Amylase	Starch
2	Protease	Gelatin
3	Cellulase	Cellulose and it's derivative
4	Invertase	Sucrose

Table No.3: List of Disintegrants

S.No	Disintegrants	Concentration in Granules (%W/W)	Special Comments
1	Starch USP	5-20	Higher amount is required, poorly compressible
2	Starch 1500	5-15	
3	Avicel$_{(r)}$(PH 101, PH 102)	10-20	Lubricant properties and directly compressible
4	Solkafloc$_{(r)}$	5-15	Purified wood cellulose
5	Alginic acid	1-5	Acts by swelling
6	Alginic acid	1-5	Acts by swelling
7	Na alginate	2.5-10	Acts by swelling
8	Explotab$_{(r)}$	2-8	Sodium starch glycolate, superdisintegrant.
9	Polyplasdone$_{(r)}$(XL)	0.5-5	Crosslinked PVP
10	Amberlite$_{(r)}$ (IPR 88)	0.5-5	Ion exchange resin
11	Methyl cellulose, Na CMC, HPMC	5-10	
12	AC-Di-Sol$_{(r)}$	1-3 2-4	Direct compression Wet granulation
Carbon dioxide			Created insitu in effervescent tablet

Superdisintegrant	Example	Mechanism of Action	Special Comment
Crosscarmellose(r) Ac-Di-Sol(r) Nymce ZSX(r) Primellose(r) Solutab(r) Vivasol(r)	Crosslinked 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)	Crosslinked PVP	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
Kollidon(r) Polyplasdone(r)			
Sodium starch glycolate Explotab(r) Primogel(r)	Crosslinked starch	Swells 7-12 folds inSwells in three dimensions and high level serve as sustain release matrix	
Alginic acid NF Satialgine(r)	Crosslinkedalginic acid	Rapid swelling in aqueous medium or wicking action	Promote disintegration in both dry or wet granulation
Soy polysaccharides Emcosoy(r)	Natural super disintegrant		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%

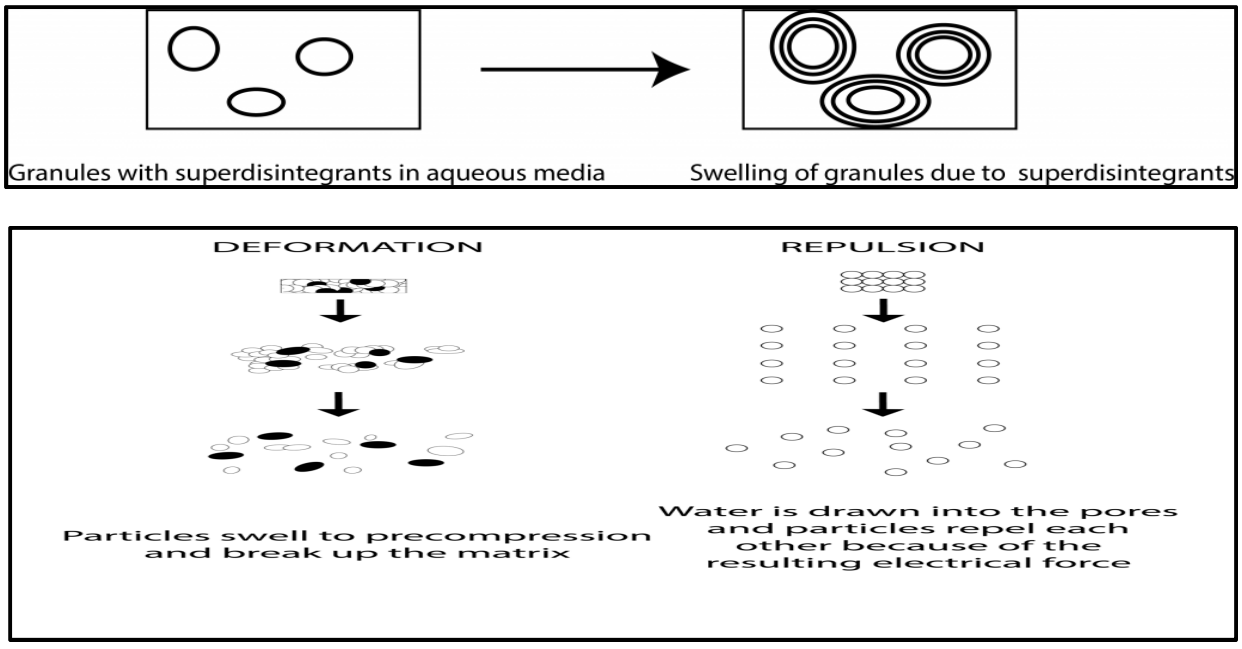

Figure No.1: Mechanism of Disintegration by Deformation and Repulsion

CONCLUSION

Overviews of various types of disintegrants and superdisintegrants that are available have been discussed in this article. The ease of availability of these disintegrating agents and their simplicity in the direct compression process suggests that their use would be a more economic alternative in the preparation of ODT than the sophisticated and patented techniques.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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