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A REVIEW ON SUPERDISINTEGRANTS

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Abstract: The most common route for administration of solid dosage form is the oral route. Disintegrants are substances or mixture of substances added to the drug formulation that facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Superdisintegrants are the substances, which facilitate the faster disintegration with smaller quantity in contrast to disintegrants. These are used to improve the efficacy of solid dosage form. The present review comprises the various types of Superdisintegrants like natural and synthetic, Mechanism of action of superdisintegrants, method of incorporation and applications of Superdisintegrants. Examples of superdisintegrants are Gellan gum, Locust bean gum, alginates, microcrystalline cellulose.

Keywords: Superdisintegrants, Disintegration, Natural, Synthetic

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INTRODUCTION

The most appealing route for the delivery of drugs is the oral route. Different dosage forms are administered orally, one of the most preferred dosage forms amongst them is the tablet because of its accurate dosing, ease of manufacturing, stability & convenience in administration, as compared with the oral liquids & because it is more tamperproof than the capsules. The drugs bioavailability is dependent on the various physiological factors, in vivo disintegration & dissolution. As an essential step in obtaining the fast release of drug the tablet disintegration has received considerable attention. The emphasis on the drug availability highlights the importance of the relatively rapid disintegration of the tablet as the criterion for ensuring the uninhibited drug dissolution behaviour. The disintegrants are the agents that are added to the tablet [& some of encapsulated] formulations to promote the breakup of tablet [& capsule "slugs"] into the smaller fragments in the aqueous environment thereby increasing the surface area that is available & promoting the more rapid release of a drug substance. It promotes the dispersion & moisture penetration of the tablet matrix. In the granulated formulation processes the disintegrant used can be more effective if used both "extragranularly" & "intragranularly" & thereby acting to break a tablet up into the granules & having the granules further disintegrate to release a drug substance into the solution. The most common tablets that are those intended to be swallowed whole & to disintegrate & release their medicaments rapidly into the GIT [Gastrointestinal tract]. The proper choice of the disintegrant & its performance consistency are of critical importance for the development of formulation of such tablets. [1-3]

In recent years, the increasing attention has been paid to formulating not only fast dissolving &/or disintegrating tablets that are swallowed but also the orally disintegrating tablets that are intended to dissolve &/or disintegrate rapidly into the mouth. By using a suitable superdisintegrants the task of developing the rapidly disintegrating tablets is accomplished. Several newer agents have been developed in recent years known as "Superdisintegrants". At lower concentrations these newer substances are more effective with greater disintegrating efficiency & mechanical strength. The water penetration rate & the rate of disintegration force development are generally positively related to the disintegrant efficiency in the nonsoluble matrices. Such a positive correlation however is not always observed between the tablet dissolution rate of drug & disintegration time. Due to the combined effect of swelling and water absorption by the formulation the superdisintegrants provide quick disintegration. Because of the swelling of the superdisintegrants the wetted surface of the carrier increases which promotes the dispersibility & wettability of the system thus enhancing the dissolution & disintegration. The effective superdisintegrants provide the improved compatibility, compressibility & have no negative impact on the mechanical strength of the formulations

containing the high-dose drugs. There are number of factors which affect the disintegration behaviour of the tablets. The optimum concentration of the superdisintegrant can be selected according to the critical concentration of the disintegrants. The ability to interact strongly with the water is essential to the disintegrant function. The combinations of swelling &/or wicking &/or deformation are the mechanisms of the disintegrant action. The disintegrants have a major function to oppose the efficiency of a tablet binder & the physical forces that act under the compression to form a tablet. [4-7]

IDEAL PROPERTIES OF SUPERDISINTEGRANTS

a. Poor gel formation.

b. It should be non toxic.

c. It should have a good mouth feel.

d. The flow properties must be good.

e. It should have good hydration capacity.

f. It should be Inert.

g. No tendency to form the complexes with the drugs.

h. It should have poor solubility. [8-9]

THE SELECTION OF SUPER DISINTEGRANTS

The various factors which are considered in selection of the superdisintegrants are:

1. The occurrence of surface active agents.

2. Good flow ability.

3. Tablet hardness.

4. The quantity of disintegrates present in the preparation.

5. The nature of Drug.

6. The good mouth feel produce to the to the patient

7. Compactable to formulate the less friable tablets.

8. The kind of mixing & addition. [10-12]

4. TYPES OF SUPERDISINTEGRANTS

A. Natural Superdisintegrants

B. Synthetic Superdisintegrants

Natural Superdisintegrants

The Gellan Gum

From the Pseudomonas elodea the gellan gum is obtained. It is the linear anionic polysaccharide biodegradable polymer which contains the linear tetra saccharide repeat structure & is used as the food stabilizer. The gellan gum as the superdisintegrating agent & the efficacy of the gum is compared with the other conventional disintegrating agents such as the corn starch which is dried, exploitable, advice [pH 102], Ac- di-sol. The tablet disintegration might be due to the instant swelling features of the gellan gum when it comes into the contact with the water due to its hydrophilic nature which is high. Within 4 minutes the observation of the complete disintegration of tablet is carried out, with gellan gum concentration of 4 % w/w & 90 % of the drug dissolved within 23 minutes. The Ac-di-sol shows very similar pattern of the disintegration & the in vitro dissolution rates. The tablet with the same concentration with the explotab shows 36 minutes for the 90% of the release of drug & with starch shows 220 minutes. The gellan gum has been proved itself as the superdisintegrating agent by this result.

The Locust Bean gum

The other name of the locust bean gum is the carob bean gum. It extracts from the endosperm of a seeds of a carob tree Ceretoniasiliqua which produces in the mediterranean states. The starch & cellulose & some other polysaccharides which contains long chains of the sugar glucose. The ratio of the mannose to galactose is greater than the in guar gum in the locust bean gum, which gives it characteristics that is slightly different & allows the 2 gums to interact synergistically & together they make the thicker gel. The locust bean gum shows as the binder & as the disintegrating agent property at various concentrations. In food industry as a thickening and gelling agent the locust bean gum has been broadly used. The locust bean gum has also been stated to have the solubility enhancement & bio adhesive properties.

The Isapghula Husk Mucilage [Plantago ovate]

The isapghula husk contains the certain amount of the dried seeds of the plant which is known as the plantago ovata. In the epidermis of the seeds the plant holds the mucilage. The Mucilage of the plantago ovata has different features like disintegrating, sustaining & binding properties. The mucilage is the superdisintegrating agent which is used to formulate the fast dissolving

tablets because the swelling index percentage is very high [around 89 ± 2.2% v/v] as compared to other superdisintegrants. Due to the swelling of super disintegrating agents the rapid disintegration of the fast dissolving tablets takes place to produce sufficient hydrodynamic pressure for complete & quick disintegration of the tablet. The rate at which the swelling occur & significant force of the swelling also defines its efficiency of disintegrating.

Synthetic superdisintegrants

Indion 414

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

Microcrystalline Cellulose [Avicel]

Less than 10 percent concentration of Avicel shows the enhanced disintegration. This mechanism depends on the entry of the water in the tablet matrix through the capillary pores, which break or disrupt the hydrogen bonding between the nearby bundles of the cellulose microcrystals. Particularly in the oral disintegrating tablet with high concentration due to the fast capillary absorption & quicker dehydration of the tablet surface it shows an affinity to stick to the tongue. The Avicel has the rapid wicking rate for the water hence this is in the combination with starch & gives an excellent & quick disintegration in the OTD preparations.

The Chitin

From the waste shell of shrimp, crab, squid & krill, naturally chitin is taken out & used for the manufacture of the chitosan by the deacetylation reaction in the alkaline media. From the relative study of the other superdisintegrating agents with the Chitin-silica co precipitate has showed better function.

The Modified starch [primo gel, sodium starch glycolate]

From an extensive range of natural starches it is likely to synthesize the sodium starch glycolate, but potato starch is used in the preparation which gives a product that has the best disintegrating characteristics. The second step is the cross linking of the potato starch when an

appropriate starch source is selected. This step is usually carried out by using the Federal Drug Administration selected starch esterifying agent such as the phosphorus oxychloride or sodium trimetaphosphate in the alkaline suspension. The large hydrophilic carboxymethyl groups are introduced because they have the effect to break the hydrogen bonding within the structure of polymer. That process allows the water to enter the molecule & the polymer becomes cold water soluble. The influence of a cross linking is to reduce both the water soluble fraction of the polymer & the viscosity of the dispersion in water. The optimal equilibrium between the degree of the substitution & the degree of the cross-linking permits for the fast water uptake by a polymer without a development of the viscous gel that might inhibit the dissolution.

The Alginates

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

The modified cellulose

The croscarmellose sodium should be defined as the cross-linked polymer of the carboxymethyl cellulose. There are various differences between the starch & the cellulose polymer & the important includes the differences between the synthetic processes that are used to modify the polymer. Most notably, the DS of the croscarmellose sodium is greater than that of the sodium starch glycolate & the process of the cross linking is changed. The substitution is implemented by the Williamsons ether synthesis to give a sodium salt of the carboxymethyl cellulose. The significant change from the chemistry of the SSG is that certain of the carboxymethyl groups themselves are utilized to cross-link the cellulose chains the procedure being accomplished by the dehydration. Hence, the crosslinks are carboxyl ester links relatively than the phosphate ester links as in the primo gel. [13]

MECHANISM OF ACTION OF SUPERDISINTEGRANTS

a. By Swelling.

b. Capillary action [wicking].

c. Enzymatic reaction.

d. Due to heat of wetting.

e. Due to release of gases.

f. Electrostatic repulsion.

g. Combination action.

h. Chemical reaction.

i. Deformation.

a. By swelling

In this mechanism certain disintegrating agents [like starch] impart the disintegrating effect. It swells when it comes in contact with water the adhesiveness of the other ingredients in the tablet is overcomed by causing the tablet fall apart.

b. The capillary action

The disintegrants that do not swell, they act through the porosity & capillary action. For the penetration of the fluid into the tablets, the porosity of tablet provides the pathways. The disintegrant particles [with low compressibility & cohesiveness] themselves enhance the porosity & provide these pathways into the tablet. Through the capillary action the liquid is drawn up or "wicked" into these pathways & rupture the interparticulate bonds thus causing the tablet to break apart.

Example: Crosscarmillose, Crospovidone.[10-11,14]

c. The Enzymatic reaction

Some enzymes that are present in the body also act as disintegrants. These enzymes reduce the binding ability of the binder & helps in the disintegration. The pressure is exerted in the outer direction due to the swelling which causes the tablet to burst or to enhance absorption of water that leads to an enormous increase in the volume of the granules to improve the disintegration

d. Due to the heat of wetting

When the disintegrants with exothermic properties get wetted the localized stress is generated due to the capillary air expansion which helps in the tablet disintegration. To only a few types of disintegrants this explanation is however limited & it cannot describe the action of most of the modern disintegrating agents.

e. Due to the release of gases

The carbon dioxide is released within the tablets on wetting due to the interaction between the carbonate & bicarbonate with the tartaric acid or citric acid. Due to the generation of pressure within the tablet the tablet disintegrates. When the pharmacist needs to formulate fast disintegrating tablet or very rapidly dissolving tablets this effervescent mixture is used. Strict control of the environment is required during manufacturing of the tablets as these disintegrants are highly sensitive to small changes in the temperature & humidity level. The effervescent blend is either added in to two separate fraction of formulation or added immediately prior to compression. [12, 15-16]

f. Electrostatic repulsion

A particle repulsion theory has been proposed by Guyot - Hermann on the basis of his theory he had observed that the particle that have no swelling action also causes the disintegration of tablets. The mechanism of disintegration is based on the electric repulsive forces between the particles & water is required for it. Researchers found that the repulsion is secondary to the wicking.

g. The Combination reaction

The disintegrants act through the combination of both the wicking and swelling action in this mechanism.

E.g: Crosspovidone.

h. The Acid base reaction [Chemical reaction]

Due to the internal liberation of the carbon dioxide in the water due to the interaction between the citric acid & tartaric acid [acids] with the alkali metal carbonates or the bicarbonates [bases] in presence of the water the tablet quickly broken apart. Due to the generation of pressure within the tablet, the tablet disintegrates. Because of the liberation in carbon dioxide gas the taste masking effect & the dissolution of the active pharmaceutical ingredients in water is increased. Control of environment must be required during preparation of the tablets as these disintegrants are highly sensitive to small changes in the humidity & temperature level. The effervescent blend is either added in two separate fraction of formulation or can be added immediately prior to compression.

i. The Deformation

Generally the starch grains are “elastic” in nature means that grains that are deformed under pressure will return to their original shape when that pressure has been removed. But, when the compression forces involved in the tableting applied then these grains are deformed permanently & are said to be rich in energy with this energy being released upon the exposure to the water, in other words the ability of the starch to swell is higher in “energy rich” starch grains than it is for the starch grains that have not been deformed under pressure. No single mechanism is responsible for the action of most disintegrants. But it is more likely the result of the inter-relationships between these mechanisms which are major. [15, 17-20]

THE METHODS OF INCORPORATION OF SUPERDISINTEGRANTS:

The incorporation of superdisintegrants in the dosage forms are mainly of 3 types:-

3.1 During granulation or Intragranular: In this method the superdisintegrants are blended with other powders & the granulation is carried out. Thus the superdisintegrants are incorporated within the granules.

3.2 Prior to compression or Extragranular: In this method, before compression the superdisintegrants are mixed with prepared granules.

3.3 Incorporation of the superdisintegrants at intra and extra granulation steps: In this method the part of the superdisintegrants are added to the intragranular & a part to the extragranules. This method usually produces better results & more complete disintegration than the type I & type- II [18].

APPLICATION OF SUPERDISINTEGRANTS

Superdisintegrants are used in different types of formulation. These are as follows

1. Rapidly disintegrating tablet: Sandeep B. Patil et al prepared the Olanzapine quick dispersing tablets by the direct compression method. The effect of the super disintegrant crospovidone on the disintegration time, wetting time, in vitro release & drug content have been studied

2. Mouth dissolving tablet: Khalidindi et al 1982 evaluated the soy polysaccharide [a group of high mol. weight polysaccharides obtained from the soy beans] as the disintegrant in tablets are made by the direct compression using dicalcium phosphate dehydrate & lactose as fillers

3. Fast disintegrating tablet: Shirsand et al carried out the preparation & evaluation of the fast dissolving tablets of the metaclopramide by using novel co-processed superdisintegrant. In the present study the novel co-processed superdisintegrants were developed by the method of

solvent evaporation by using crospovidone & sodium starch glycolate in the various ratios (1:1, 1:2 & 1:3) for use in a fast dissolving tablet formulations. [21-23]

Table- 1: List of Common Disintegrants and Superdisintegrants [19]

Sr. no	Name of excipients	Concentration	Stability criteria	Category
1	Cross-povidone	2-5 %	As hygroscopic in nature, stored in an air-tight container, in a cool and dry place.	Superdisintegrants
2	Micro-crystalline cellulose	5-15%	Stable at dry and air tight condition	Superdisintegrants
3	Alginic acid	1-5%	Hydrolyzes slowly at room temperature	Disintegrants
4	Starch	5-10%	Stable at dry and air tight condition	Superdisintegrants
5	Colloidal Silicon Dioxide	5-10%	Hydroscopic , but do not liquefy upon absorption of water	Disintegrants
6	Methyl cellulose	2-10%	Slightly hygroscopic, but stable	Disintegrants

CONCLUSION

Different types of Superdisintegrants have been discussed in this article. The rapidly disintegrating dosage forms have been commercialized effectively by using numerous types of super disintegrating agents. The easy of availability of these superdisintegrants & the simplicity of its use in compression process [direct compression] suggest that its use would be alternative and it is economic in the preparation of drugs showing immediate release action.

REFERENCES

1. Gohel M, Parikh R, Brahmbhatt B, Shah A: Preparation and Assessment of Novel Coprocessed Superdisintegrant Consisting of Crospovidone and Sodium Starch Glycolate: A Technical Note: AAPS PharmSciTech: (2007) 8 (1): E1-E6.D.
2. Bhowmik, Chiranjib B, Krishnakanth, Pankaj, Chandira R: Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research: (2009): 1(1): 163-177.
3. Mohanachandran P, Sindhumol P, Kiran T: Superdisintegrants: An Overview: International Journal of Pharmaceutical Sciences Review and Research: (2011): 6: 105-109.
4. Chougule D, Ghodke D, Shah R, Ghaste R: Fast Dissolving Tablets: An Overview: (2010).
5. Deshmkh H, Chandrashekhara, Nagesh, Murade A, Usgaunkar S: Superdisintegrants: A Recent Investigation and Current Approach: Asian J. Pharm. Tech: (2012): 2: 19-25.
6. Kaur T, Gill B, Kumar S, Gupta G: Mouth Dissolving Tablets: A Novel Approach to Drug Delivery: International Journal of Current Pharmaceutical Research: (2010): 3: 1-7.
7. Kumar G, Nirmala R: Fundamental Aspects of Superdisintegrants: A Concise Review: Journal of Global Pharma Technology: (2012): 4: 1-12.
8. Omidian H, Park K: Swelling agents and devices in oral drug delivery: Journal of Drug Delivery Science and Technology: 2008: 18 (2): 93-83.
9. Iyad R, Mayyas A, Eftaiha A, Badwan A: Chitin-silicon dioxide coprecipitate as a novel superdisintegrant: Journal of Pharmaceutical Sciences: 2008: 97(11): 4969-55.
10. Singh I, Rehni A, Kalra R, Joshi G, Kumar M, Aboul-Enein H: Ion Exchange Resins: Drug Delivery and Therapeutic Applications: FABAD J. Pharm. Sci: (2007): 32: 91-100.
11. http: //www.anshulindia.com/pdfs/poly plasdone.
12. Pahwa R, Gupta N: Superdisintegrants in the Development of Orally Disintegrating Tablets: A Review: International Journal of Pharmaceutical Science and Research: 2011: (2): 2767-80.
13. Nasir A, Gohar UF, Ahmad B: A Review Article On: Superdisintegrants: International Research Journal of Pharmaceutical Sciences: 2017: 8: 001-011.
14. Grasono, Alesandro et al: US Patent 6,197,336 2001.
15. Khairnar D, Anantwar S, Chaudhari C, Shelke P: Superdisintegrants: An emerging Paradigm in orodispersible tablets: International Journal of Biopharmaceutics: 2014: 5(2): 119-28.
16. Kuchekar B, Bhise S, Arungam V: Design of Fast Dissolving Tablets: Indian J Pharm Edu. 2005: (35):150.
17. Reddy L, Ghosh B, Rajneesh: Fast dissolving drug delivery system: A review of Literature: Indian J Pharm Sci: 2002: 64(4):331-36.
18. Hermann G, Ringard J "Disintegration mechanisms of tablets contain starches. Hypothesis about the particle-particle repulsive force": Drug Dev Ind. Pharm.1981:7(2):155-77.
19. Shihora H, Panda S: Superdisintegrants, Utility in Dosage Forms: A Quick Review. Journal of Phamaceutical Science and Bioscientific Research (JPSBR): (2011): 1:148-153.

20. Shrivastava P, Sethi V: International Journal of Drug Research and Technology: 2013: 3(4):76-87.
21. Patil S, Shahi S, Udavant Y, Atram S ,Salunke R, Neb G: Formulation And Evaluation of Quick Dispersible Tablet of Olanzapine: International Journal of Pharma Research and Development: 2009.
22. Khalidindi S, Shangraw R: Evaluation of Soy polysaccharide as Disintegrating Agent. Drug Development and Industrial Pharmacy: 1982: 8:215-35.
23. Shirsand S, Ramani R, Swamy P: Novel Co-Processed Superdisintegrants in the Design of Fast Dissolving Tablets: International Journal of Pharma and Bio Sciences: 2010: 1(1):1-12.