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SUPERDISINTEGRANTS IN FAST DISINTEGRATING DRUG DELIVERY SYSTEMS: A BRIEF REVIEW

Vimal V.V[1*], Aarathi T.S[1], Anuja[1], Soumya Baby John[2]

[1]Bipha Drug Laboratories, Kottayam, Kerala, India
[2]JDT College of Pharmacy, Vellimadukunnu, Calicut, Kerala, India

***Corresponding authors e-mail:** vimalvv24786@gmail.com

ABSTRACT

Disintegration plays a major role in facilitating drug action in oral solid dosage forms. Disintegrants (substances or mixture of substances) when added to the drug formulation facilitates the breakup or disintegration of tablet or capsule content into smaller particles that dissolve more rapidly. The inclusion of right disintegrant is a prerequisite requirement to get an optimum bioavailability in tablets and capsules which need rapid disintegration. Super-disintegrants are used to improve the efficacy of solid dosage forms. This is achieved by decreasing the disintegration time which in turn enhances drug dissolution rate. Super-disintegrants are generally effective in a low concentration, and generally at higher concentrations they hinder disintegration. Examples of Super-disintegrants are crosscarmelose, crosspovidone, sodium starch glycolate which represents crosslinked cellulose, crosslinked polymer and a crosslinked starch, respectively. The development of fast dissolving or disintegrating tablets provides an opportunity to take an account of tablet disintegrants. The disintegrants have the major function to act against the efficiency of the tablet binder and the physical forces that act under compression to form the tablet. The stronger the binder, the more effective must be the disintegrating agents in order for the tablet to release its medication. . The present review describes super-disintegrants, their types, selection criteria and various methods of incorporating disintegrants and mechanism of tablet disintegration.

Keywords: Superdisintegrants, Classification, Mechanisms of action, selection criteria

INTRODUCTION

Tablets are the most favored oral solid dosage form, mainly because of several advantages like,

1. Ease of administration
2. Good chemical and microbiological stability
3. Ease of swallowing
4. Lowest cost among all other solid dosage forms
5. Dose precision and least content variability
6. Ease of packing e.t.c.

Infact, it is the most popular dosage form and almost 70% of medicines are dispensed in tablet form. In addition to active ingredients, tablets contains a number of excipients like diluents, binders, disintegrants, lubricants, glidants, colouring agents, flavouring agents and sweetening agents. Disintegrants are added to a tablet formulation to facilitate its breaking or disintegration when it contact in water in the GIT.

An oral solid dosage form should ideally disperse into the primary particles from which it was prepared. For tablets and capsules which need rapid disintegration, the inclusion of the right disintegrant is a prerequisite for optimal bioavailability. Super-disintegrants are used to improve the efficacy of solid dosage forms. This is achieved by decreasing the disintegration time which in turn enhances drug dissolution rate [1]. In more recent years, increasing attention has been paid to formulating not only fast dissolving and/or disintegrating tablets that are swallowed, but also orally disintegrating tablets that are intended to dissolve and/or disintegrate rapidly in the mouth. The task of developing rapidly disintegrating tablets is accomplished by using a suitable super-disintegrants.[2] In recent years several

newer agents have been developed known as "Super-disintegrants". These newer substances are more effective in lower concentrations with greater disintegrating efficiency and mechanical strength. Super-disintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of super-disintegrants, the wetted surface of the carrier increases, which promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution.[3] The ability to interact strongly with water is essential to disintegrant function. Combinations of swelling and/or wicking and/or deformation are the mechanisms of disintegrant action. The disintegrants have the major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablet.[4]

TYPES OF SUPERDISINTEGRANTS

The Super-disintegrants can be classified into two categories

1. Natural Super-disintegrants
2. Synthetic Super-disintegrants

Natural super-disintegrants: They are natural in origin and are preferred over synthetic substances because they are comparatively cheaper, abundantly available, non irritating and non toxic 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 mucilages are available which have super-disintegratingavtivity .[5]

***Plantago Ovata Seed Mucilage (Isapgula)*:** Isapghula consists of dried seeds of the plant plantago ovata and it contains mucilage which is present in epidermis of the seeds. The seeds of *Plantago ovata* are soaked in distilled water for 48 hrs and then boiled for few minutes for complete release of mucilage into water. The material squeezed through muslin cloth for filtering and separating out the marc. Then, an equal volume of acetone added to the filtrate so as to precipitate the mucilage. The separated mucilage is dried in oven at temperature less than 60°C .[6] The mucilage of *plantago ovata* is a recent innovation for its superdisintegration property when compared with Crospovidone.[7] It shows faster disintegration time than the superdisintegrant,Crosspovidone.

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.

***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 powders show poor bulk density, thus results in poor flowability and compressibility.[8] To overcome such weakness they may be coprecipitated with colloidal silicon dioxide to improve their physical properties.

***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 higheramount of mucilage, dimeric imidazole alkaloids lepidine B, C, D, E and F and two new monomeric imidazole alkaloids semilepidinosideA and B. Mucilage of Lepidiumsativumhas various characteristic like binding,disintegrating, gelling[9]

***Hibiscus rosa-sinensis Linn. Mucilage*:** *Hibiscus rosa-sinensis Linn* of the *Malvaceae* family is also known as the shoe flower plant, China rose, and Chinese hibiscus. The plant is available in India in large quantities and its mucilage has been found to act as a superdisintegrant. Theplant contains cyclopropanoids, methyl sterculate, methyl-2-hydroxysterculate, 2-hydroxysterculatemalvateand rosasterol. The leaves contain carotene (7.34 mg/100g of fresh material) moisture, protein, fat, carbohydrate,fibers, calcium, and phosphorus. Mucilage of *Hibiscusrosa-sinensis* contains L_rhamnose, D_galactose,D_galactouronic acid, andD_glucuronic acid.[10]

Cucurbita maxima pulp powder: Study revealed that *Cucurbita maxima* pulp powder have comparable dissolution behavior to that of sodium starch glycolate. It also has comparable hardness and friability thus the naturally obtained *Cucurbita maxima* pulp powder stands as a good candidate to act as disintegrant and it is possible to design promising Fast disintegrating tablet using this polymer.[11]

Gellan gum: Gellan gum is a linear anionic polysaccharide, biodegradable polymer produced by the microbe *Pseudomonos elodea* consisting of a linear tetrasaccharide repeat structure and used as a

tablet disintegrant. Gellan polymer consists of monosaccharide _-L-rhamnose, _-D-glucuronic acid and _-D-glucose in molar ratio of 1:1:2 linked together to form a linear primary structure. The disintegration of tablet might be due to the instantaneous swelling characteristics of gellan gum when it comes into contact with water and owing to its high hydrophilic nature.

***Guar Gums*:** Guar gum is naturally occurring guar seed extract, containing about 80% of galactomannan(guaran), 10% moisture, 5-7% protein and trace amounts of heavy metals and ash. It is free flowing, completely soluble, neutral polymer and is approved for use in food. It is not

sensitive to pH, moisture contents or solubility of the tablet matrix. It is not always pure white and sometimes varies in color from off-white to tan tends to discolour with time in alkaline tablets. As a disintegrant, guar gum has been found to be superior to some common disintegrants such as corn starch, celluloses, alginates and magnesium aluminium silicate. Particle size can affect disintegration, with finer particle sizes having greater disintegrating capabilities. It is available in the market under the trade name jaguar.

Synthetic super-disintegrants

Modified starch (sodium starch glycolate,Primojel): It is possible to synthesize sodium starch glycolate from a wide range of native starches, but in practice potato starch is used as it gives the product with the best disintegrating properties. After selection of the appropriate starch source the second step is the cross linking of the potato starch. This is typically carried out using an FDA approved starch esterifying agent such as sodium trimetaphosphate or phosphorus oxychloride in alkaline suspension. The effect of introduction of the large hydrophilic carboxymethyl groups is to disrupt the hydrogen bonding within the polymer structure. This allows water to penetrate the molecule and the polymer becomes cold water soluble. The effect of the cross linking is to reduce both the water soluble fraction of the polymer and the viscosity of dispersion in water. The optimum balance between the degree of substitution and the extent of cross-linking allows for rapid water uptake by the polymer without the formation of a viscous gel that might impede dissolution.

Crosslinked polyvinlypyrrolidone (crospovidone, Polyplasdone XL): 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.

Unlike other Superdisintegrants which are either poorly compressible or non-compressible, Crospovidone disintegrants are highly compressible materials as a result of their unique particle morphology. In contrast to sodium starch glycolate and croscarmellose sodium, Crospovidone Superdisintegrants exhibit virtually no tendency toward gel formation, even at high use levels. Disintegrants that gel can result in ODT and chewable products with an unpleasant, gummy texture.Crospovidone Superdisintegrants provide the best overall sensory experience as well as rapid disintegration and robust tablets.

Modified cellulose (crosscarmelose sodium,AC-Di-Sol): Croscarmellose sodium is described as a cross-linked polymer of carboxymethylcellulose. Apart from thedifferences between the starch and cellulose polymer backbones, there are Differences between the synthetic processes used to modify the polymer. Most importantly, the DS of croscarmellose sodium is higher than that of sodium starch glycolate, and the mechanism of cross linking is different. The substitution is performed using Williamson's ether synthesis to give the sodium salt of carboxymethylcellulose. A key difference from the chemistry of SSG is that some of the carboxymethyl groups themselves are used to cross-link the cellulose chains, the process being accomplished by dehydration. Thus the crosslinks are carboxyl ester links rather than phosphate ester links as in Primojel.

Ion Exchange Resin: The INDION 414 and KYRON 314 have been used as a superdisintegrant for ODT. It is chemically cross-linked polyacrylic potassium(Polacrillin potassium), with a functional group of – COO – and the standard ionic form is K+. 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 tablet disintegrant 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 withoutthe formation of lumps. It is a high molecular weight polymer,

therefore it is not absorbed by the human tissuesand totally safe for human consumption.

L-HPC: (Low substituted hydroxy propyl cellulose): Insoluble in water, rapidly swells in water. Greatest degree of swelling exhibited by Grades LH-11 & LH-21. Certain grades while retaining disintegration capacity can also provide some binding properties. Recommended concentration 1-5%. The main advantages of synthetic super disintegrants are their efficacy in lower concentrations than starch, less interference with compressibility and flow ability.They are also more effective intragranularly.

Limitations of synthetic super disintegrants

1)Hygroscopic (may be a problem with moisture sensitive drugs)

2)Some are anionic and may cause some slight *in-vitro* binding with cationic drugs (not a problem *in-vivo*).

3)An acidic medium significantly reduces the liquid uptake rate and capacity of sodium starch glycol ate and croscarmellose sodium, but not crospovidone.

4)The degree of swelling of primojel (sodium starch glycol ate) and polyplasdone xl(crospovidone) is minimized following wet granulation formulation. Finally, the medium ionic strength was found to have an adverse effect on swelling capacity of croscarmellose.[12,13]

MECHANISM OF ACTION OF DISINTEGRANTS:

1)By capillary action
2)By swelling
3)Because of heat of wetting
4)Due to release of gases
5)By enzymatic action
6)Due to disintegrating particle/particle repulsive forces
7)Due to deformation

Capillary action:

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants, maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.[14]

Swelling:

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling Tablets with high porosity show poor disintegration due to lack of adequate swelling force. 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.

Heat wetting:

When disintegrants with exothermic properties gets wetted, localized stress is generated due tocapillary air expansion, which helps 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.

Due to release of gases:

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants

are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

By enzymatic action:

Here, enzymes present in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration. Actually due to swelling, pressure exerted in the outerdirection or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

Due to 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. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression.[14]

· ***Disintegration of tablet by repulsion:***

Another mechanism of disintegration attempts to explain the welling of tablet made with 'non swellable' disintegrants. Guyot Hermann has proposed a particle repulsion theory based on the observation that no swelling particle also causes disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration andwater is required for it. Researchers found that repulsion is secondary to wicking.[14,15]

METHODS OF INCORPORATING DISINTEGRANTS INTO TABLETS:[16,17,18]

Internal Addition (Intragranular): In Internal addition method, the disintegrant is mixed with other powders before wetting the powder mixtures with the granulating fluid. Thus 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.

· **External Addition (Extragranular) :** In external addition method, the disintegrant is added to the sized granulation with mixing prior to compression.

· **Partly Internal and External:** In this method, part of disintegrant can be added internally and part externally. This results in immediate disruption of the tablet into previously compressed granules while the disintegrating agent within the granules produces additional erosion of the granules to the original powder particles. This method can be more effective. If both intragranular and extragranular methods are used, extragranular portion break the tablet into granules and the granules further disintegrate by intragranular portion to release the drug substance into solution. However, the portion of intragranular disintegrant (in wet granulation processes) is usually not as effective as that of extragranular 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. The intragranular disintegrant tends to retain good disintegration activity in case of compaction process as it does not involve its exposure to wetting and drying.

SELECTION CRITERIA FOR SUPERDISINTEGRANT

Although superdisintegrants primarily affect the rate of disintegration, but when used at high levels it can also affect mouth feel, tablet hardness and friability. Hence, various ideal factors to be considered while selecting an appropriate superdisintegrants for a particular formulation should:

1. Proceed for rapid disintegration, when tablet comes in contact with saliva in the mouth/oral cavity.
2. Be compactable enough to produce less friable tablets.
3. Produce good mouth feel to the patients. Thus, small particle size is preferred to achieve patient compliance.
4. Have good flow, since it improves the flow characteristics of total blend.[19]

CONCLUSION

Considerable research in developing Oral dispersible tablets have widened the scope of superdisintegrants ,and more research towards modification of starch and cellulose varieties to produce disintegrants with desirable properties have attracted the attention of researchers.Rapidly disintegrating dosage forms have been successfully commercialized by using various kinds of Superdisintegrants. This article aims to help starters to get acquaintance with the interesting world of superdisintegrants. It is reported study wise that the water-insoluble superdisintegrants show better disintegration property than the slightly watersoluble agents, since they do not have a tendency to swell. The presence of a superdisintegrants produce sufficiently hard tablets that still disaggregate within seconds and can be considered as fast dispersible. Incorporation of superdisintegrant in solid dispersions also prevented crystallization of drug during dissolution in the presence ofhydrophilic carriers. Tablets containing super disintegrants in combination show excellent in vitro dispersion time and drug release as compared to other formulations.

Table.1: A list of commercially available super disintegrants

Superdisintegrant	Commercially available grades
Cross linked Cellulose	AC-Di-Sol, Nymce ZSX,Primellose,Solutab,Vivasol
Crosslinked PVP	Crospovidone,kollidon,Polyplasdone, Polyplasdone XL
Crosslinked Starch	Explotab,Primojel,tablo,vivastar
Crosslinked alginic acid	Satialgine
Soy Polysaccharides	Emcosoy
Gellan gum	Kelcogel
Xanthan gum	Grindsted

REFERENCES

1. Bhowmik D, Chiranjib B, Yadav J, Chandira R M, Sampath Kumar KP. ,Der Pharm letter,2010;2(1): 495-504.
2. Kaur T,Gill B,Kumar S,Gupta GD.Int. j. Current. Pharm. Res,2010; 3(1):1-7.
3. Kumar GP,Nirmala R.J. Glob. pharm .Tech,2012;4(1):1-12.
4. Khinchi MP,Gupta MK,Bhandari A,Agarwal D,Sharma N.Int. j. Pharm. Sci.res,2011;(2):145-152.
5. Jyothi G,Lakshmi PK.Acta Pharm. Sciencia,2011:35-44
6. Shrishand S,Sarasija S.Indian .j Pharm. Sci.;72(1):41-43
7. Soares LL,Ortega GG,Petrovick PR,Schimdt PC.AAPS Pharmscitech, 2005;06:E367-E371.
8. Mehta KK,Patel HH,Patel ND,Vora CN,Patel NJ..Int. j. Pharm.pharm. Sci,2010;1:102-108.
9. Shah V,Patel R.Int. j appl Pharm,2010;2(1):18-21
10. Malviya R,Srivastava P,Bansal M,Sharma PK.Int. j. Pharm. Sci,2010;2(1):395-399.
11. Bussemer T,Peppas NA,Bodmeier R.Eu. j. Pharm. Biopharm,2003;56:261-270.
12. Zhao N,Augsburger LL.Pharm Dev Technol 2006;11:47-53.
13. Kuchekar BS,Bhise SB,Arungam V.Indian J Pharm Edu,2005;35:150.
14. Reddy LH,Ghosh ,Rajneesh.Indian j Pharm Sci 2002;64(4):331-336.
15. Bala R,Khanna S,Pawar P.Asian .j. Pharm. Cli. res,2012;5:8-14.
16. Bhaskaran S,Narmada GV.Indian.Pharma, 2002;1:9-12.
17. Parekh SR,Gothoskar AV.Pharm Tech, 2003;27(11):92-98
18. Sharma V,Arora V,Ray.Int.Bul .Drug Res;1(2):46-54
19. Kaushik D,Dureja H ,Saini TR.Indian drugs, 2004;41(4):187-192.
20. Deshmukh H, Chandrasekhara S, Nagesh C,Murade A, Usgaunkar S. Asian J. Pharm. Tech, 2012; 2(1): 19-25.