ejpmr, 2015,2(3), 390-400

SJIF Impact Factor 2.026

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A REVIEW ON ROLE OF NOVEL SUPERDISINTEGRANTS IN PHARMACY

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Article Received on 13/03/2015 **Article Revised on 05/04/2015** **Article Accepted on 28/04/2015**

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ABSTRACT

Immediate release oral dosage forms, i.e., tablets and capsules, are most widely used drug delivery systems available because of its convenience of self administration, compactness and easy manufacturing. These products are designed to disintegrate in the stomach followed by their dissolution in the fluids of the gastrointestinal tract.Immediate drug release dosage forms disintegrate rapidly after administration with enhanced rate of dissolution. Superdisintegrants are used to improve the efficacy of solid dosage forms. This is achieved by decreasing the disintegration time which in turn enhances the drug dissolution rate. 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. The basic approach used in development tablets is the use of superdisintegrants like Cross linked Polyvinylpyrrolidone or crospovidone (Polyplasdone), Sodium starch glycolate (Primogel, Explotab), carboxymethylcellulose (Croscarmellose) etc. These superdisintegrants provide instantaneous disintegration of tablet after administration in stomach. The present review comprises the various kinds of Superdisintegrants like natural and synthetic which are being used in the formulation to provide the safer, effective drug delivery with patient's compliance. The various sources of superdisintegrants and their modification to improve disintegration property are also high-lighted.

KEYWORDS: Superdisintegrants, Crospovidone

INTRODUCTION

Many patients especially children and elderly have difficulty in swallowing tablets and capsules and consequently unable to take medicine as prescribed. Almost 40-50% of the population is affected by such problem, resulting in the high incidence of non compliance and

ineffective therapy. Despite increasing interest in controlled release drug delivery systems, the most common tablets are those intended to be swallowed whole and to disintegrate and release their medicaments rapidly in the gastrointestinal tract (GIT) still remains the dosage form of choice. As disintegration plays a crucial role, so for development of solid orals, formulators are fascinating towards selection of proper disintegrants / superdisintegrants in dosage systems.

Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. The emphasis on the availability of drug highlights the importance of the relatively rapid disintegration of a tablet as a criterion for ensuring uninhibited drug dissolution behavior.

Superdisintegrants are the 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 there by increasing the available surface area and promoting a more rapid release of the drug substance. They promote moisture penetration and dispersion of the tablet matrix.[1,2,3]

The disintegration of dosage forms are depends upon various physical factors of superdisintegrants.[4,5]

They are as follow:

1. Percentage of disintegrants present in the formulation.
2. Proportion of disintegrants used.
3. Compatibility with other excipients.
4. Presence of surfactants.
5. Hardness of the tablets.
6. Nature of Drug substances.
7. Mixing and types of addition.

A disintegrate 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 disintegrate 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 disintegrate.

Since a compaction process does not involve its exposure to wetting and drying, the disintegrate used intragranularly tends to retain good disintegration activity.

And hence the proper choice of a disintegrant or a superdisintegrants and its consist performance are of critical importance to the formulation development of such immediate release tablets.[6]

They all should possess the following characteristics:

1. Poor water solubility with good hydration capacity,
2. Poor gel formation,
4. Good flow properties,
5. Good compressibility,
6. Inert,
7. Non-toxic,
8. Requirement of least quantity.

Method of Incorporation

The incorporation of superdisintegrants in the dosage forms are mainly of three types

A. Intragranular or during granulation -

In this process the superdisintegrants are blend with other powders and granulation is carried out. Thus the superdisintegrants are incorporated within the granules.

B. Extragranular or prior to compression –

In this process, the superdisintegrants are mixed with prepared granules before compression.

C. Incorporation of superdisintegrants at intra and extra granulation steps-

In this process part of superdisintegrants are added to intragranular and a part to extragranules. This method usually produces better results and more complete disintegration than type I and type II.[7]

Mechanism of Disintegrations by Superdisintegrants[8,9]

Swelling

Although not all effective disintegrants swell in contact with water, swelling is believed to be a mechanism in which certain disintegrating agents (such as starch) impart the disintegrating effect. By swelling in contact with water, the adhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart.

Porosity and Capillary Action (Wicking)

Effective disintegrants that do not swell are believed to impart their disintegrating action through porosity and capillary action. Tablet porosity provides pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness & compressibility) themselves act to enhance porosity and provide these pathways into the tablet. Liquid is drawn up or "wicked" into these pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart.

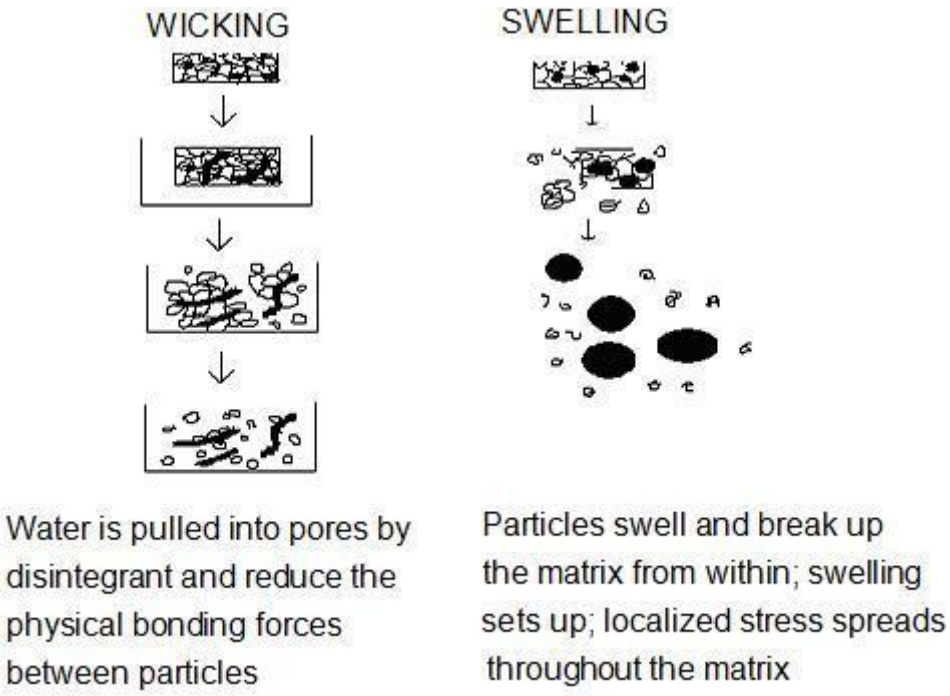

Figure 1. Disintegration of Tablet by Wicking and Swelling

Deformation

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.

Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'nonswellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

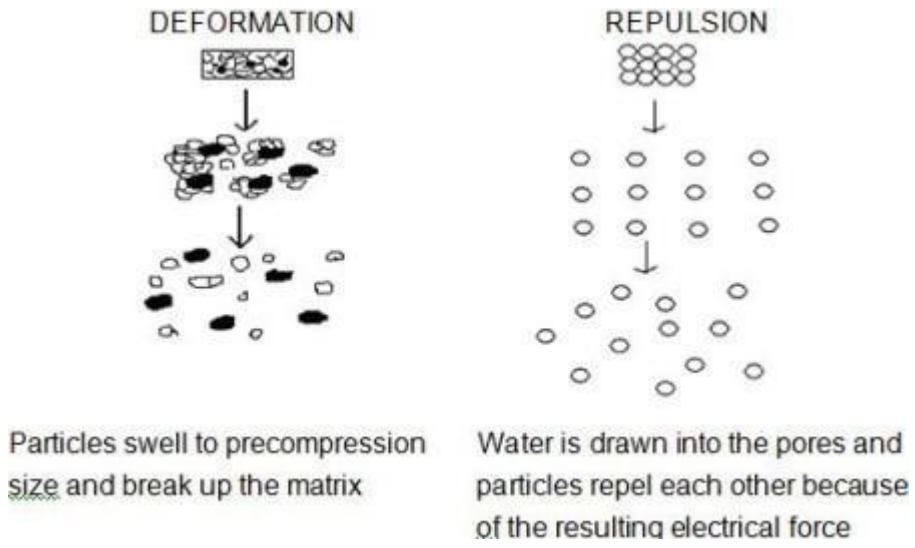

Figure 2. Disintegration by Deformation and Repulsion

Super-Disintegrants Used In Dosage Forms[10-14]

1. Sodium Starch Glycolate (Explotab® and Primogel®)

The oldest and probably the most widely used disintegrant, the starch is modified with a dramatic disintegrating properties and are available as Explotab® and Primogel®. These are low substituted carboxy methyl starches in granular forms. The mechanism involves rapid absorption of water leading to an enormous increase in volume of granules result fast and uniform disintegration. When these superdisintegrants are used in formulations they show the disintegration of solid dosage form within two minutes. The higher dissolution rates observed with superdisintegrants may be due to rapid disintegration and fine dispersion of particles formed after disintegration.

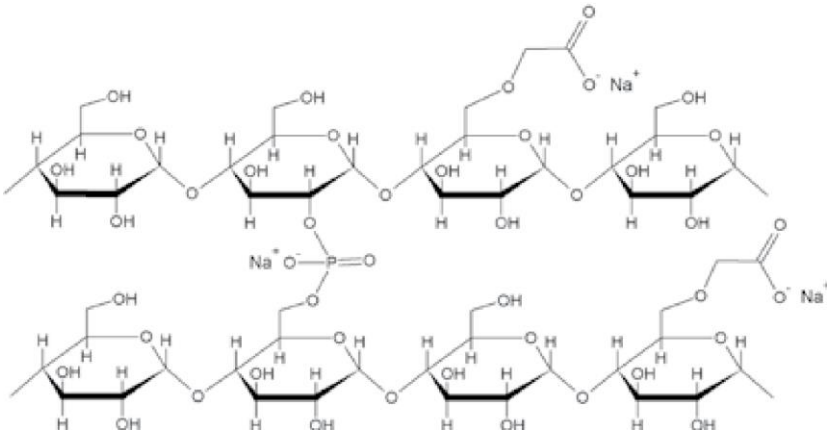

Figure 3. Basic Structure of Sodium Starch Glycolate

2. Cross-linked poly-vinyl Pyrrolidone (Cross Povidone)

In case of mouth-dissolving formulations, Crospovidone quickly wicks saliva into them to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth. Unlike other superdisintegrants, it relies on both swelling and wicking principally for disintegration. When examined under a scanning electron microscope, crospovidone particles appear to be granular and highly porous. This unique, porous nature facilitates wicking of liquid into the dosage systems and causes rapid disintegration. Due to high crosslink density of crospovidone, it swells rapidly in water without gel formation than others.

In contrast to other superdisintegrants like sodium starch glycolate and croscarmellose sodium, Crospovidone exhibit virtually no tendency toward gel formation, even at high ratio. As disintegrants that result gel formation is not appreciable in orally disintegrating tablets (ODTs) and chewable products.

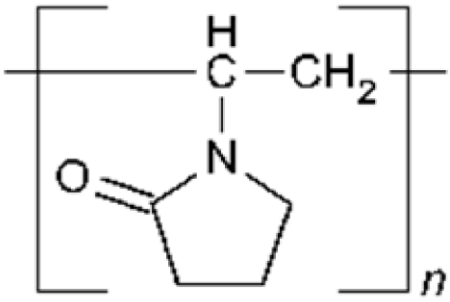

Figure 4. Basic Structure of Crospovidone

3. Cellulose Derivatives (Ac-Di-Sol®)

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. 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.

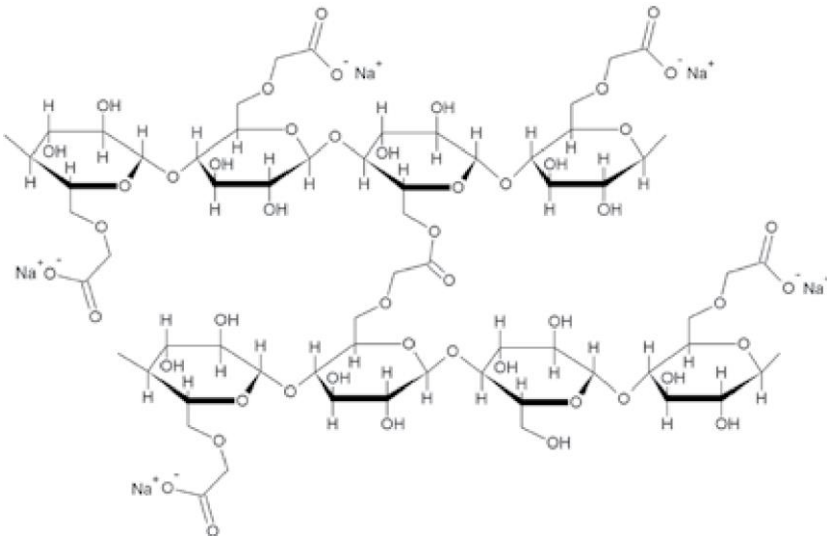

Figure 5. Basic Structure of Croscarmellose sodium

4. Microcrystalline Cellulose (Avicel)

Avicel concentration of less than 10%, exhibits better disintegration. This mechanism is depending on entry of water to the tablet matrix through capillary pores, which breaks the hydrogen bonding between adjacent bundles of cellulose microcrystals. With more concentration, particularly in oral disintegrating tablet, it shows a tendency to stick to the tongue due to rapid capillary absorption and faster dehydration of the tablet surface. As Avicel has a fast wicking rate for water, hence this in combination with starch makes an excellent and rapid disintegration in OTD formulations.

5. 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+. 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 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.

6. Natural Superdisintegrants

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 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 polysscharide, karaya gum is modified using distilled water to achieve superdisintegration property in dispersible tablet development. This modified karaya gum(MKG) is easy to prepare, cheap, easily available, biodegradable and stable compared to available synthetic super disintegrants in market.

Mucilage of plantago ovate seed husk (Isapghula) is also used as superdisintegrants. The mucilage of plantago ovata is a recent innovation for its super disintegration property when compared with Crospovidon. It shows faster disintegration time than the superdisintegrants, Crosspovidone.

Table 1: Various Superdisintegrants and Their Properties[15-17]

Superdisintegrants	Commercially available grades	Mechanism of action	Special comment
Crosslinked cellulose	Crosscarmellose® Ac-Di-Sol®, Nymce ZSX® Primellose®, Solutab®, Vivasol®, L-HPC.	Swells 4-8 folds in < 10 seconds. Swelling and wicking both.	Swells in two dimensions. Direct compression or Granulation Starch free.
Crosslinked PVP	Crosspovidon M® Kollidon® Polyplasdone®	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.
Crosslinked starch	Explotab® Primogel®	Swells 7-12 folds in < 30 seconds.	Swells in three dimensions and high level serve as sustain

			release matrix.
Crosslinked alginic acid	Alginic acid NF	Rapid swelling in aqueous medium or wicking action.	Promote disintegration in both dry or wet granulation.
Soy polysaccharides	Emcosoy®		Does not contain any starch or Sugar. Used in nutritional products.
Calcium silicate		Wicking action	Highly porous, Light weight.

Superdisintegrants Used in Immediate release formulations

Drug	Superdisintegrants	Method	Formulation	Reference
Gliclazide	Crodpovidone Ac-Di-Sol Sodium Starch glycolate	Direct Compression	Fast Dissolving Tablet	[18]
Disulfiram	Sodium Starch Glycolate (Glycolis Type A)	Dry granulation, Slugging	Immediate Release Tablet	[19]
Ibuprofen	kollidon CL(K) Explotab(E)	Wet Granulation	Fast Dissolving Tablets	[20]
Losartan Potassium	Crodpovidone Ac-Di-Sol Sodium Starch glycolate	Direct Compression	Taste Masked Fast Dissolving Tablets	[21]
Granisetron HCl	PlantagoOvata husk Direct	Direct Compression	Fast Dissolving Tablets	[22]

CONCLUSION

Overviews of various superdisintegrants which are available have been discussed. The ease of availability of these agents and the simplicity in the direct compression process suggest that their use would be a more economic alternative in the preparation of Immediate Release Tablets than the sophisticated techniques. The uses of superdisintegrants are extended in the applications of oral disintegration tablets, fast-dispersibletablets, capsules, mouth-dissolving films, etc.

REFERENCES

1. Sood R et al. Immediate release antihypertensive valsartan oral tablet: A Review. Journal of Scientific Research in Pharmacy May 2012; 1(2): 20-26.
2. Swarbrick J. Encyclopedia of Pharmaceutical Technology, 3rd Ed, Informa Healthcare USA, Inc. New York.2000; 3641; 3657-59; 3612-13: 3928.

3. Howard C Ansel, Nicholas G Popvich, Loyd V Allen. Pharmaceutical Dosage Forms and Drug DeliverySystem, First Edition, 1998, pp 78.
4. Schimidt P C, and Brogramann B., Pharmaceutical Technology. 1988; (34): 22.
5. Cohen Y, and Lach J L, Journal of Pharmaceutical Sciences. 1963; (52): 122.
6. H. Shihora & S. Panda. Superdisintegrants, Utility in Dosage Forms: A Quick Review. Journal of Phamaceutical Science and Bio scientific Research (JPSBR), 2011; 1: 148-153.
7. Bhaskaran, S and Narmada, GV(2002), "Rapid Dissolving tablet A Novel dosage form", Indian Pharmacist,1: 912.
8. Kuchekar BS, Bhise SB and Arungam V. Design of Fast Dissolving Tablets. Indian J Pharm Edu 2005; 35: 150.
9. Reddy LH, Ghosh B and Rajneesh. Fast dissolving drug delivery system: A review of literature. Indian J Pharm Sci, 2002; 64 (4): 331-336.
10. List PH, Muazzamm UA .Swelling – A driving force in tablet disintegration, Pharm. Ind, 1979; 49: 1075 – 1077.
11. Caramella C, Novel methods for disintegrant characterization, Part 1, Pharm. Technol. Int, 1990; 2(9): 30 – 37.
12. Shangraw R, Wallace J, Bowers F, "Morphology and Functionality in Tablet Excipients for Direct Compression," Pharm. Technol. 1981; 5: 44–60.
13. Shangraw R, Mitrevej A, Shah M, "A New Era of Tablet Disintegrants," Pharm. Technol, 1980; 4: 48–57.
14. European Pharmacopeia, European Directorate for the Quality of Medicines, 2006; 5: 3151.
15. Cremer K. "Orally Disintegrating Dosage Forms Provide Life Cycle Management Opportunities," Pharm. Technol. Formulation and Solid Dosage, 2003; 22–28.
16. Parakh SR, Gothosakar AV, "A Review of Mouth Dissolving Tablet Technologies," Pharm. Technol. 2003; 27(11): 92–100.
17. Duriez X, Joshi AA, "Starches A Versatile Source," Pharma Form. Qual. 2004; 6(3): 48–50.
18. M. S. Chandra, S. P. Shinde, K. G. Parthiban, D. Krishnarajan& R. Manivannan. Extending the Drug Release of Fast Dissolving Tablets of Gliclazide. Imperial Journal of Pharmaceutics & Cosmetology. 2011; 1: 30-37.
19. N. Pathak, A. Kumar, V. Methkar, P. Pant & R. T. Rao. Formulation and Optimization of Immediate Release Tablet ofAnAntialcohlic Drug By Dry Granulation Method. International Journal of Comprehensive Pharmacy. 2011; 3: 1-4.

20. A. Fini, V. Bergamante, G. C. Ceschel, C. Ronchi& C. A. F. d. Moraes. Fast dispersible/slow releasing ibuprofen tablets. European Journal of Pharmaceutics and Biopharmaceutics. 2007; 69: 335-341.
21. S. Avulapati, A. K. Roy, K. R. Shashidhar& T. UgendarReddy. Formulation and Evaluation of Taste Masked And Fast Disintegrating Losartan Potassium Tablets. International Journal of Drug Development & Research. 2011; 3: 45-51.
22. B. S.Patil, N. G. R. Rao& K. D. Rao. Formulation and Evaluation Of Fast Dissolving Tablets Of Granisetron Hydrochloride. International Journal Of Applied Biology And Pharmaceutical Technology. 2011; 2: 22-28.