REVIEW ARTICLE ISSN: 2249-3387

AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

TABLET DISINTEGRANTS: AN OVERVIEW

Mahendra Singh[1*], Dr. S. K. Prajapati[1],Akanksha Singh[1], VinayKumar[1], Vinod Kumar Kanaujia[1]

1. Institute of Pharmacy, Bundelkhand University, Jhansi (U.P.), India.

ABSTRACT

Fast dissolving, fast melting, chewable and orally dissolving or disintegrating tablets are solid dosage forms that disintegrate rapidly and dissolve in the mouth withoutwater. The principle challenge with orally disintegrating tablets (ODTs) is to develop tablet formulations for standard direct compression processes that deliver rapid disintegration, pleasant mouth feel and high breaking force for tablet robustness. Superdisintegrant affect a range of formulation parameters, including the rate of disintegration, tablet breaking force, and mouth feel. 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. Number of factors affects the disintegration behavior of tablets. The development of fast dissolving or disintegrating tablets provides an opportunity to take an account of tablet disintegrants. 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.

Key words: Tablet Disintegrants, Superdisintegrants, Kyron T-314.

*Corresponding Author Email: mahendra.pharma88@gmail.com

Received 23 November 2011, Accepted 10 December 2011

Please cite this article in press as: Singh M *et al.*, Tablet Disintegrants: An Overview. American Journal of PharmTech Research 2012.

INTRODUCTION:

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.

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.[1, 2,4, 6.]

Mechanism

There are three major mechanisms and factors affecting tablet disintegration as follows**:**

- Swelling
- Porosity and Capillary Action (Wicking)
- Deformation
- Due to disintegrating particle/particle repulsive forces

A. 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.

B. 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 inter particulate bonds causing the tablet to break apart.

C. 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.

D. Due to disintegrating particle/particle repulsive forces:

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non-swelling 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.[3, 17.]

Until fairly recently, starch was the only excipient 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.

Although the connection between bioavailability of drug and tablet disintegration took some time to become appreciated, it is now accepted that the role of the disintegrant is extremely important.

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)

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. 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 granules}.[1, 3, 11]

In addition to starch, the following are some of the disintegrants which were available prior to the use of the "super-disintegrants" to be discussed later:

Pre-gelatinized Starch (Starch 1500)

Pre-gelatinized starch is a directly compressible form of starch consisting of intact and partially hydrolyzed ruptured starch grains. Pre-gelatinized starch has multiple uses in formulations as a binder, filler and disintegrant. As a disintegrant, its effective use concentration is between 5-10%. Its major mechanism of action as a disintegrant is thought to be through swelling.[9]

Microcrystalline Cellulose (Avicel)

Like pre-gelatinized 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%.[7]

Others

Sodium Bicarbonate in combination with citric or tartaric acids is used as an "effervescent" disintegrant.

Alginic Acid at a concentration of between 5-10% is an effective, but very expensive disintegrant.

Ion Exchange Resins (Amberlite 88) has disintegrant properties at a concentration of between 1-5%. But this type ofdisintegrant is rarely used.[13, 14. 15]

SUPERDISINTEGRANTS:

Recently new materials termed as superdisintegrants have been developed to improve the disintegration processes. Selecting appropriate formulation excipients and manufacturing technology can obtain the design feature of fast disintegrating tablet. 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. The stronger the binder, the more effective must be the disintegrating agents in order for the tablet to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but also into powder particles from which the granulation was prepared.[3, 6, 8]

Four 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)

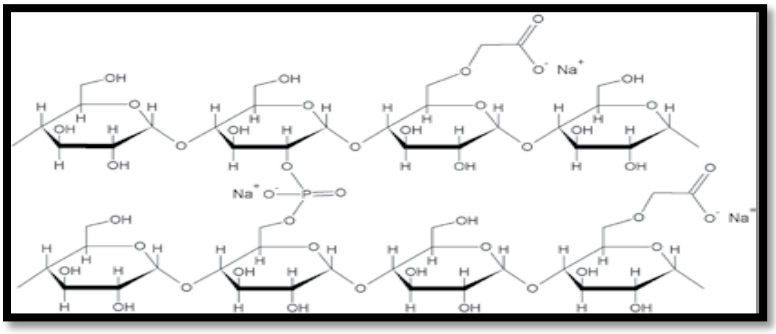

Figure 1: Basic Structure of Sodium Starch Glycolate.

Mechanism of Action: Rapid and extensive swelling with minimal gelling.

Effective Concentration: 4-6%. Above 8%, disintegration times may actually increase due to gelling and its subsequent viscosity producing effects.[3, 15.]

2. Cross-linked polyvinylpyrollidone- water insoluble and strongly hydrophilic.

I.e. crospovidone (Polyplasdone XL, Kollidon CL)

Mechanism of Action: Water wicking, swelling and possibly some deformation recovery.

Effective Concentration: 2-4%.[3, 15.]

3. Modified Cellulose- Internally cross-linked form of **Sodium carboxymethyl cellulose**.

i.e. Ac-Di-Sol (Accelerates Dissolution), Nymcel.

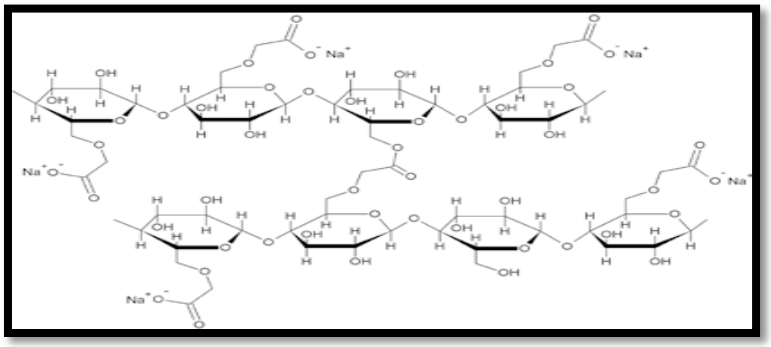

Figure 2: Basic Structure of Croscarmellose Sodium

Croscarmellose sodium is described as a cross-linked polymer of carboxymethylcellulose.

Mechanism of Action: Wicking due to fibrous structure, swelling with minimal gelling.

Effective Concentrations: 1-3% (Direct Compression), 2-4% (Wet Granulation).[3, 15.]

4. Crosslinked polymer of Polycarboxylic acids.

Kyron T-314 is derived from crosslinked polymer of Polycarboxylic acids as per USP/NF & has the K^+ ionic form. It is a very high purity polymer used in pharmaceutical formulations as a super-fast disintegrant as well as dissolution improver in solid dosage forms like tablets, capsules, pellets etc. It is available in white free flowing powder hence it is suitable for the both wet granulation as well as direct compression system for tablet formulations.

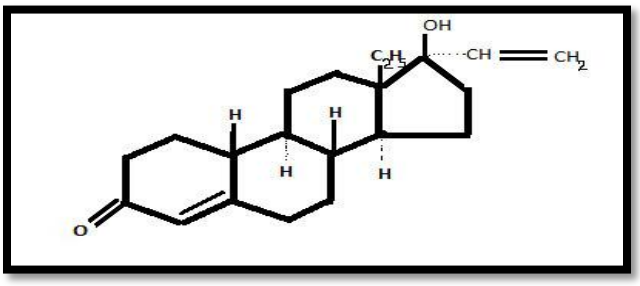

Figure 2: Basic Structure of Kyron

Advantage of Kyron

- Rapid disintegrating agent
- Elimination of lump formation
- Compatible with all therapeutic agents and excipients
- Imparts excellent strength to the tablets
- Elimination of the sticking problems to the dies and punch
- Improves bioavailability of the drug
- Uniformly mix with low dose tablets blend or formulations
- Smooth surface after storage
- Provide smooth cream-like mouth feel, so more suitable for ODT
- Suitable for both direct compression and wet granulation methods
- Cost effective
- White in color
- Directly compressible grade
- Dissolution improver
- Effective at very low concentration (0.5 to 4.0%).

Application of Kyron T-314

- **As Disintegrating agent:** Kyron T-314 has a very high swelling tendency of hydration either in contact with water or G.I. fluids causing fast disintegration without the

formation of lumps and thus acts as an effective tablet super disintegrant. Required quantity is from 0.5% to 4.0% to get fast disintegration.

- **As Dissolution Improver:** Kyron T-314 breaks the tablets into very smaller particles, thus it increases the effective surface area for the absorption of the active substances and thus it increases the dissolution and bioavailability of the active substances. Required quantity is from 2.0% to 6.0% for dissolution improvement.

Toxicity

Kyron T-314 is high molecular weight polymer, so doesn't get absorbed by body tissue and is safe for human consumption. It has no physiological action at recommended dosage and it is non-toxic.

Storage

Store in tightly closed container, keep away from moisture. If moisture is absorbed then dry at 90°C to 100°C to remove moisture content and make it below 10%.

Packing

5 kg, 10 kg, 20 kg, net in laminated corrugated box with polyethylene liner.

5. Soy polysaccharide-It is a natural super disintegrants that does not contain any starch or sugar so can be used in nutritional products.

6. Cross-linked alginic acid -It is insoluble in water and disintegrates by swelling or wicking action. It is a hydrophilic colloidal substance, which has high sorption capacity. It is also available as salts of sodium and potassium.

7. Gellan gum -It is an anionic polysaccharide of linear tetra saccharides, derived from Pseudomonas elodea having good Superdisintegrants property similar to the modified starch and celluloses.

8. Xanthan gum -Xanthan Gum derived from Xanthomonascampestris is official in USP with high hydrophilicity and low gelling tendency. It has low water solubility and extensive swelling properties for faster disintegration.

9. Calcium Silicate -It is a highly porous, lightweight superdisintegrant, which acts by wicking action.

Advantages of disintegrants

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

- Remarkable tendency on wetting causing rapid disintegration
- No lump formation on disintegration
- Compatible with commonly used therapeutically agents and excipients.
- Work equally effective in hydrophilic and hydrophobic formulations.
- Provides good mechanical strength to the tablet facilitating easy packing and transportation.
- Does not stick to the punches and dyes. [10, 12.]

Table 1: Various Superdisintegrant and Their Properties[1, 3, 5]

Superdisintegrants	Commercially available grades	Mechanism of action	Special comment
Crosslinked cellulose	Croscarmellose®,Ac-Di-Sol®, NymceZSX®, Primellose®, Solutab®,Vivasol®,L-HPC.	Swells 4-8 folds in <10seconds Swelling and wicking both.	Swells in two dimensions Direct compression or Granulation Starch free.
Crosslinked PVP	CrosspovidonM® Kollidon® Polyplasdone	Swells very little And returns to original size aftercompression 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 serves as sustain release matrix.
Crosslinked alginicacid	Alginic acid NF	Rapid swelling in aqueous medium or wicking action.	Promote disintegration in both dry or wet granulation
Soy polysaccharides (Natural super-disintegrants)	Emcosoy®	Rapid Dissolving	Does not contain any starch or Sugar. Used in nutritional products.
Calcium silicate		Wicking action.	Highly porous, Light Weight.
Crosslinked polymer of Polycarboxylic acids	Kyron T-314	High swelling tendency of Hydration. Swelling Index 12 (Cross PVP and Crosscarmellose are of Swelling Index 7 and 9 respectively.)	Elimination of lump formation. It is suitable for the both wet granulation as well as direct compression
Ion exchange resin	Indion 414, Indion 234, Tulsion 234, Tulsion 344, Amberlite IPR 88	Swelling	…..
Gas evolving disintegrants	citric acid, tartaric acid, sodium bicarbonate	Effervescence substance	Evolution of CO_2 after contact with fluid

Disadvantages of disintegrants

- More hygroscopic (may be a problem with moisture sensitive drugs)
- Some are anionic and may cause some slight in-vitro binding with cationic drugs (not a problem in-vivo.) [10, 12]

Summary of disintegrants:

- Disintegrants are an essential component to tablet formulations. While rapidly disintegrating tablets do not necessarily ensure fast bioavailability, slowly disintegrating tablets almost always assure slow bioavailability.
- 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.
- Super disintegrants offer significant improvements over starch. But hygroscopicity may be a problem in some formulations.[4, 15,16]

CONCLUSION:

Overviews of various types of superdisintegrants which are available have been discussed. Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. Disintegration remains a powerful influence and precursor for drug absorption. Disintegration of tablet or capsule is depending upon the type and quantity of disintegrants. The development of fast dissolving or disintegrating tablets provides an opportunity to take an account of tablet disintegrants. Therefore, there is a huge potential for the evaluation of new disintegrants or modification of an existing disintegrants into superdisintegrants, so as to formulate fast dissolving dosage form.

REFERANCE

1. Bhowmik Debjit, Chiranjib B, Krishnakanth P, Margret R.Chandira. Fast Dissolving Tablet: An Overview. J Chemical Pharma Res 2009 ;(1): 163-177.
2. Gupta A, Mishra A, Gupta V, Bansal P, Singh R, SinghA. Recent Trends of Fast Dissolving Tablet - An Overview of Formulation Technology. Int J Pharma & Biological 2010; (1):1 –10.
3. Mohanachandran PS, Sindhumol PG, Kiran TS. Superdisintegrants: An Overview. Int J Pharma Sciences Review Res 2011; (1): 105-108.
4. Swarbrick James, Boylan James C. Encyclopedia of Pharmaceutical Technology.Volume 20, New York: Marcel Dekker; 2001.

5. Mundada SA, Badgujar PB. The technologies used for developing orally disintegrating tablets: A review. Acta Pharm 2011; (61): 117–139
6. Jain NK, Sharma SN. A Text book of Professional Pharmacy. Fourth Edition, 1998: 16-25.
7. FMC BioPolymer Material Safety Data Sheet Avicel® PH Microcrystalline Cellulose,Philadelphia,PA,2008.
8. Liberman HA, Lachman L, Schawstr JB. The theory and Practice of Industrial Pharmacy. 3rd edition, 1987: 321-328.
9. Charles R. Cunningham, Laura K. Scattergood. Evaluation of a Partially Pre-gelatinized Starch in Comparison with Superdisintegrants in a Direct-Compression Hydrochlorothiazide Formulation. Poster Reprint, West Point PA, Colorcon, American Association of Pharmaceutical Scientists; 1999.
10. Gupta A, Mishra AK, Gupta V, Bansal P, Singh R, Singh AK. Recent Trends of Fast Dissolving Tablet - An Overview of Formulation Technology. Review article 2010; 1 – 10.
11. Johnson JR. Effect of Formulation Solubility and Hygroscopicity on Disintegrant Efficiency in Tablets Prepared by Wet Granulation, in Terms of Dissolution. J Pharm Sci 1991; 80: 469–471.
12. Pandit JK, Tripathi MK, Babu RJ. Effect of Tablet Disintegrants on the Dissolution Stability of Nalidixic Acid Tablets.Pharmazie 1997; (52): 538–540.
13. Sakr A, Bose M, Menon A. Comparative Effectiveness of Superdisintegrants on the Characteristics of Directly Compressed Triamterene Hydrochlorothiazide Tablets. Pharm Ind 1993; (55): 953–957.
14. Balasubramaniam J. Effect of Superdisintegrants on Dissolution of Cationic Drugs. Dissolution Technologies 2008; (15): 18–25.
15. John C Carter. The role of disintegrants in solid oral dosage manufacturing Carter Pharmaceutical Consulting, All Rights Reserved Carter Pharmaceutical Consulting Inc.2002 -2006.
16. http://www.corelpharmachem.com/kyron_t314.htm.
17. Mudgal Vinod, Sethi Pooja, Kheri Rajat, Saraogi GK, Singhai AK. Orally disintegranting tablets: a review. Int Res J Pharm 2011; 2(4): 16-22.