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Open Access Review Article

Superdisintegrant: crucial elements for mouth dissolving tablets

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ABSTRACT

Mouth dissolving tablets have gained more popularity among solid oral dosage forms. They perform better than conventional tablets because of its ease of administration and patient's compliance. It facilitates water less administration and rapid onset of action. It also helps in improving oral bioavailability. The fast disintegration followed by dissolution leads to quick therapeutic activity makes these tablets superior over available tablets and capsules. Disintegration is an important key step for any solid dosage forms to show its pharmacologic effect as any solid dosage forms should disperse into its fine particles from which it is prepared. In mouth dissolving tablets superdisintegrants are incorporated in right amount for quick disintegration with improved bioavailability. Based on the source various types of superdisintegrants are available. They are synthetic, semi-synthetic, natural, and co-processed. In this review, main emphasis is given on different types of superdisintegrants used in mouth dissolving tablets, their mechanisms and applications.

Keywords: Superdisintegrants, Mouth dissolving, Disintegration, Bioavailability

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1. INTRODUCTION

Mouth dissolving tablets are novel drug delivery systems having fast disintegration capabilities and recently gained its popularity by overcoming the disadvantages of conventional tablets. It can be defined as a solid unit dosage form containing active ingredient having the property to disintegrate quickly as soon as it comes in contact with saliva without water or chewing.[1] Disintegration is a key step for any solid unit dosage forms like tablets or capsules to show its action. In this regard, disintegrating agents are added in the solid dosage forms. Disintegrants are the agents which help in breakdown of tablets into its small particles or fragments as they come in contact with aqueous environment. In case of mouth dissolving tablets fast disintegration is an essential step for faster drug release and quick action, thus superdisintegrants are added to facilitate faster disintegration. They are used in less concentration of 1-10% by weight relative to total weight of dosage units.[2] Different types of superdisintegrants are available and are used based on their source and mechanism of action while formulating mouth dissolving tablets. Disintegration of tablets depends on various factors of superdisintegrants like [3];

a) Amount of superdisintegrant added.
b) Proportion of superdisintegrant used.
c) Method of addition of superdisintegrant
d) Compatibility with other excipients
e) Nature of drug substance added.

Selection criteria for superdisintegrants[4,5]:

- Particle size should be small.
- Should be non-toxic
- Compatible with other excipients and drug.
- Good hydration capacity.
- Good flow property
- Good mouthfeel
- Effective in less quantity

As the superdisintegrants can be easily available, less expensive and direct compressible, use of superdisintegrant is more suggestible and profitable method to prepare fast dissolving tablets as compared to other patented technologies. Particles of superdisintegrants are small and porous which facilitate rapid disintegration of tablets without giving objectionable mouthfeel. The ideal superdisintegrants should give good flowability, compressibility, compatibility without affecting mechanical strength of tablets.

Advantages of superdisintegrants[6]:

Required in less concentration.
Compatible with large number of drug and excipients
Does not affect compressibility and flowability.

Disadvantages of superdisintegrants

Sensitive to moisture leading to instability.

2. SUPERDISINTEGRANTS

2.1 Modes of addition of superdisintegrant

There are different methods for addition of superdisintegrants in the formulation of mouth dissolving tablets

1. Internal addition (Intragranular)
2. External addition (Extragranular)
3. Partially internal and external

In table 1, different modes of superdisintegrant addition are given.

Table 1: Methods of superdisintegrant addition[7, 8]

S. No.	Method	Inferences	Advantage
1	Intragranular/Internal addition/During granulation	Superdisintegrants are granulated along with other excipients means they are added during granulation. Addition during wet granulation leads to decrease in activity of superdisintegrant.	Easy to add and suitable for direct compression method.
2	Extragranular/External addition/Prior to compression	Superdisintegrants are added to already prepare granules before compression.	Suitable for wet granulation process
3	Partially internal and external	Some amount of superdisintegrant is added during granulation (internally) and part are added after granulation.	More effective method and gives immediate disintegration of tablet.

2.2 Mechanism of superdisintegrants

Mechanism through which superdisintegrants facilitate quick breakdown of tablets into small fragments which results in faster dissolution and rapid onset of action are:

1) Swelling
2) Wicking (Porosity and capillary action)
3) Heat of wetting
4) Chemical reaction
5) Particle repulsive force
6) Deformation recovery
7) Enzymatic reaction
8) Combination action (Swelling and wicking)

2.2.1 Swelling

Swelling is the most common mechanism of both natural and synthetic superdisintegrants to cause tablet disintegration.[9] As the tablet comes in contact with suitable medium, penetration of water is the prime necessary step for this mechanism followed by swelling of the disintegrant particle which leads to development of swelling force result in breakdown of tablet as shown in figure 1.

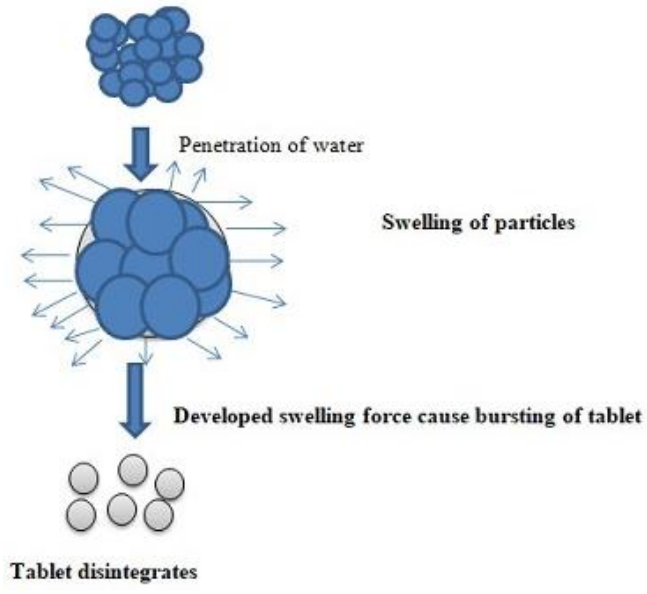

Figure 1 Swelling mechanism of tablet disintegration

2.2.2 Wicking (Porosity and capillary action)

Disintegration of tablet occurs by penetration of medium into the tablet and replacing the adsorbed air on the particles results in weakening of intermolecular bond and breakdown of tablets into its fine particles. Figure 2 is shows the details of wicking mechanism of tablet disintegration. Here, hydrophilic property of the drug and excipient along with tableting conditions determines the water uptake of tablet. For creating a hydrophilic network across drug particles, maintenance of porous structure and low interfacial tension towards aqueous fluid is very important [10].

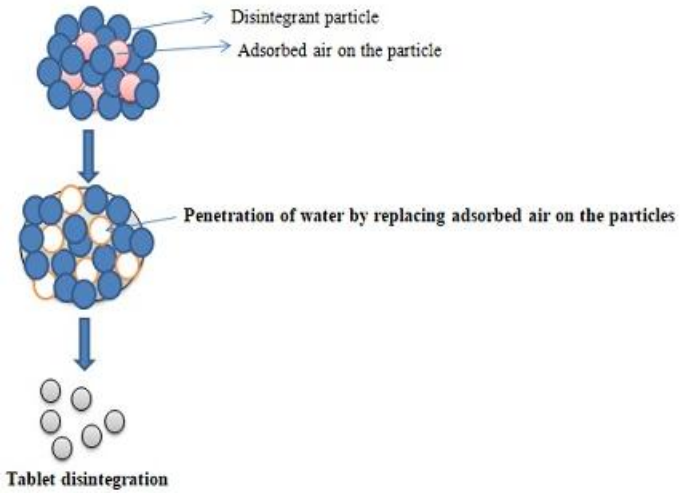

Figure 2 Wicking mechanism of tablet disintegration

2.2.3 Heat of wetting

This mechanism is applicable for the disintegrant having exothermic property. When these disintegrant comes in contact with suitable media and get wetted, there is a capillary air expansion leads to localized stress which cause disintegration of tablet [11].

2.2.4 Chemical reaction (Acid-base reaction)/Due to release of gases

Tablet disintegrates mainly due to generation of pressure within tablet because of liberation of carbon dioxide from

water, which forms when tartaric acid or citric acid reacts with alkali bicarbonates or carbonates (acid reacts with bases). Dissolution of active ingredient and taste masking is also getting enhanced due to liberation of carbon dioxide gas. Environmental conditions should be strictly controlled as these disintegrant are highly sensitive to small change in temperature and humidity. Here, effervescent blends are added either prior to compression.[12]

2.2.5 Particle repulsive force

Non swellable disintegrant particles causes tablet breakdown by this method which is based on particle repulsive theory proposed by Guyot-Hermann. Tablet disintegration occurs due to electric repulsion between the particles and water is required for it. It was found by researcher that repulsion is secondary to wicking. Guyot-Hermann repulsion theory proposed that, "Tablet in contact with suitable medium, water penetrates into the tablet through hydrophilic pores leading to the formation of continuous starch like network which helps in transfer of water from one particle to another and creates hydrostatic pressure." Thus, results in breaking of hydrogen bonds and other forces which hold tablet particles together.[13]

2.2.6 Deformation recovery

Deformation recovery mainly based on the principle that, some disintegrant particles structure get distorted or change while compression and after compression when it comes in contact with aqueous media, it returns to their pre-compression structure leading to the disintegration of the tablet as shown in figure 3. For example, starch has shown increased swelling capacity after the granules are compressed. High elastic nature of starch (like potato starch and corn starch) deformed to plasticity due to high compaction force while compression with energy rich potential. When these deformed starch particles comes in contact with water, tablet disintegration occurs as it triggers the energy rich potential of the deformed starch [14].

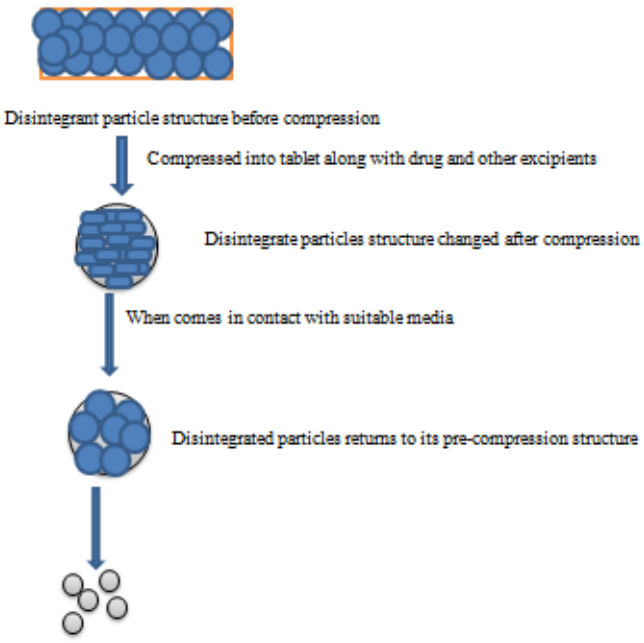

Figure 3: Tablet disintegration due to deformation recovery

2.2.7 Enzymatic reaction

Tablet disintegration occurs by some enzymes present in our body which acts as disintegrant by decreasing the binding ability of the binder. Swelling cause pressure in the outer direction makes tablet to burst or more water absorption results in excessive granular volume promotes in disintegration of tablet. Our body enzymes which help in disintegration of tablets are given in the table 2.

Table 2: Examples of enzymes acts as a disintegrant[15]

S. No.	Enzymes
1	Amylase
2	Protease
3	Cellulase
4	Invertase

2.2.8 Combination action

Here, disintegrant cause breakdown of tablet by combination of both swelling and wicking mechanism. Example: Crospovidone acts by combination of swelling and wicking.

2.3 Classification of superdisintegrants

Based on their source of origin, superdisintegrants can be categorized as

a) Natural

b) Synthetic

c) Co-processed

2.3.1 Natural superdisintegrant

Natural superdisintegrants are commonly used in tablet formulation which facilitates disintegration of tablet. Examples of natural superdisintegrants are given in table 3.

Advantages

- Local accessible
- Eco-friendly and Bio-acceptable
- Low price as compared to synthetic and renewable source.

2.3.2 Synthetic superdisintegrant

Synthetic superdisintegrants are commonly used in tablet formulation which facilitates disintegration of tablet. Examples of synthetic superdisintegrants are given in table 4.

Advantages of synthetic superdisintegrants

- Effective in low concentration as compared to starch.
- Have low effect on compressibility and flow ability.
- More effective intragranually.

Limitations

- Hygroscopic in nature and may cause problems with water sensitive drugs.

Table 3: List of natural superdisintegrants along with their source and mechanism of action [16, 17, 18]

S. No.	Superdisintegrant name	Source	Mechanism
1	Mucilage of Lepidus sativum (asaliyo)	Mucilage was obtained from the seeds of Lepidus sativum	Swelling
2	Locust bean gum(carob bean gum)	Extracted from the seeds of carob tree.	Swelling and capillary action
3.	Isapghula husk(Plantago ovata)	From the seeds of Plantago ovata	Swelling
4	Hibiscus rosa sinesis linn.	Mucilage of hisbiscus rosa sinesis	Swelling
5.	Fenugreek seed mucilage	Mucilage of Fenugreek seed	
6.	Gellan gum	Obtained from Pseudomonas elodea.	Swelling
7.	Xanthum gum	Derived from Xanthomonas compestris	Swelling property
8	Soy polysaccharide	High molecular weight polysaccharides obtained from soy beans.	Swelling
9	Mango peel pectin	Extracted from mango peel which constitutes 20-25% of the mango processing waste.	Swelling, have good solubility and high swelling index.
10	Agar and treated agar	Dried gelatinous substance obtained from Gelidium amansii (Gelidanceae) and several other species of red algae.	High strength gelling property.
11	Guar gum	Isolated from the endosperm seed of the guar gum, Cyamopsis tetragonaloba.	Swelling
12	Chitin and chitosan	Chitin obtained from natural polysaccharide obtained from crab and shrimp shells. Chitosan structural element in the exoskeleton of crustaceans (such as crabs and shrimp) and cell walls of fungi.	Swelling

Table 4: List of synthetic superdisintegrants along with their source and mechanism of action[19, 20]

S. No.	superdisintegrant name	Nature	Brands available	Mechanism	Properties
1	Sodium starch Glycolate/sodium carboxymethyl starch	Modified starch /Cross-linked starch	Explotab Primogel Tablo Vivastar	Absorb water quickly results in swelling, swells 7-12 folds in less than 30 seconds	Swells in 3 dimension and high level acts as sustained release matrix
2	Crospovidone	Cross-linked PVP	M Kollidon Polyplasdone	Combination of swelling and wicking	Water insoluble, spongy in nature
3.	Croscarmellose Sodium	Modified cellulose	Ac-Di-Sol Nymce ZSX Primellose Solutab Vivasol L-HPC	Swelling and wicking within 10 seconds, swells upto 4-8 folds	Swells in 2 dimension
4	Croslinked Alginic acid	-	Alginic acid NF	Rapid swelling or wicking	Promotes disintegration in both dry and wet granulation
5.	Calcium silicate	-	-	Wicking action	Highly porous and have light weight
6.	MCC and L-HPC				
7.	Ion exchange resins	Crosslinked polyacrylic	Indion 414 Tulsion 339 Amberlite IRP 88	Swelling	Has high water uptake capacity and high purity pharmaceutical grade weak acid cation resin supplied in dry form.
8	Chitin and Chitosan	-	-	Swelling	-

2.3.3 Co-processed superdisintegrants

Co-processing excipients provides superior property compared to physical mixture of individual excipient mixture. Examples of commercially available co-processed superdisintegrants are given in table 5.

Table 5: List of co-processed superdisintegrants

S.No.	Co-processed superdisintegrants	Consists of
1.	Ludipress	(Lactose monohydrate, polyvinylpyrrolidone and crospovidone)
2	Starlac	Lactose and maize starch
3.	Starcap 1500	Corn starch and Pregelatinized starch)
4.	Ran-Explo-C	(Microcrystalline cellulose, silica and crospovidone)
5.	Ran-Explo-S	Microcrystalline cellulose, silica and sodium starch glycolate)
6.	Pan Excea MH300G	(Microcrystalline cellulose, hydroxyl-propyl-methyl cellulose and crospovidone
7.	Ludiflast	(Mannitol, crospovidone and polyvinyl acetate)

3. CONCLUSION

Superdisintegrants plays a critical role in the formulation of mouth dissolving tablets. These agents help and facilitate tablets to disperse into its smaller fragments. Selection criteria, methodology and mechanism of different types of superdisintegrants have been studied and incorporated. It has been found that superdisintegrants addition method by direct compression gained popularity among researchers. The ease of availability and compactability makes formulation of mouth dissolving tablets less complex than other patented technologies.

Table 6: Recent literature on fast dissolving tablets prepared by addition of superdisintegrant

S. N.	Name of the Drug	Category	Reason for formulation into Fast Dissolving System	Superdisintegrants used	Result	Ref
1	Aceclofenac	Nonsteroidal anti-inflammatory drug	To evaluate Starch Xanthate, a new superdisintegrant in the formulation of fast dissolving tablets of poorly soluble drug.	Starch Xanthate (a novel superdisintegrants), croscarmellose sodium and sodium starch glycolate	Formulation containing 10% of starch xanthate in combination with 5 % of Croscarmellose sodium can be used in the formulation of fast dissolving tablets.	[21]
2	Amisulpride	Anti- psychotic	To increase patients compliance by giving rapid action via disintegration without difficulty in swallowing.	Crospovidone, croscarmellose Sodium	Formulation containing 9 % crospovidone and 9 % croscarmellose sodium in combination shows rapid disintegration gave fast onset of action.	[22]
3	Bauhinia Veriagata Linn	Anti –diabetic, Anti -ulcer, Anti-infective and anti-leprosy.	To Prepare fast dissolving tablets with sufficient mechanical integrity and fast disintegration without need of water.	Crospovidone and sodium starch glycolate and mixture of crospovidone and sodium starch glycolate	Formulation containing 3% crospovidone showed better results for herbal fast dissolving tablets qualifying all criteria and official limits.	[23]
4	Bambuterol Hydrochloride	Anti –asthamatic	To improve patient compliance by preparing fast dissolving tablet with enhanced dissolution rate.	Sodium starch glycolate, crospovidone, croscarmellose sodium, pregelatinized starch	Order of increase in dissolution rate With different superdisintegrant are: crospovidone > croscarmellose sodium> sodium starch glycolate> pregelatinized starch	[24]
5	Clove	Analgesic	To prepare fast dissolving neutraceutical analgesic tablet which gives rapid onset of action.	Crospovidone	The formulation containing superdisintegrant in more amount showed better dissolution profile compared to other formulations.	[25]
6	Cetirizine Hydrochloride	Antihistamine	To formulae and optimize cetirizine hydrochloride oral disintegrating tablets using central composite design with combined effect of natural or synthetic polymers.	Croscarmellose sodium (synthetic), hibiscus rosasinesis mucilage	This central composite design can be used in the formulation of fast dissolving tablets with qualifying all parameters.	[26]
7	Domperidone	Anti-emetic	To prepare fast dissolving tablets of Domperidone.	Sodium starch glycolate, crospovidone	Formulation containing 3.3% w/w of crospovidone shows better disintegration results than sodium starch glycolate.	[27]
8	Doxazosin mesylate	Used in hypertension	To formulate and fast dissolving tablet of Doxazosin mesylate	Crospovidone, croscarmellose sodium, Physical mixture of crospovidone and croscarmellose, Coprocessed superdisintegrants (mixture of crospovidone and croscarmellose sodium in concentration of 2% and 5%.)	Formulation having coprocessed mixture of crospovidone and croscarmellose sodium in concentration of 5% Helps in significantly reduced the disintegration time and enhanced the drug release.	[28]
9	Ergotamine Tartrate	Vasoconstrictor	To design fast dissolving tablets of ergotamine	Crospovidone and croscarmellose	Formulation containing 62.5% of crospovidone as a	[29]

			tartrate with synthetic superdisintegrants.	sodium	disintegrant shown better disintegration drug release compared to others.	
10	Etoricoxib	Nonsteroidal anti-inflammatory	To prepare mouth dissolving tablets of Etoricoxib have enhanced patients compliance.	Crospovidone and croscarmellose sodium	Formulation containing solid dispersion of beta cyclodextrin and Etoricoxib in the ratio of 1:3 gives better results than other formulations.	[30]
11	Furosemide	Diuretics	To enhance patient's compliance and minimize the side effects	Pectin of mango peel (mangifera indica), crospovidone	Formulation containing 8%w/w Pectin of mango peel (Mangifera indica) is best formulation among all formulation with respect to disintegration time and drug release.	[31]
12	Glipizide	Anti-diabetic medicine	$A3^2$ full factorial design is applied for the optimization of the fast dissolving tablets of the Glipizide.	Sodium starch glycolate croscarmellose sodium	Formulation containing 7.14% sodium starch glycolate and Croscarmellose sodium showed least disintegration time with friability in limits.	[32]
13	Glimepiride	antidiabetic drug	To design and characterize fast dissolving tablets of Glimepiride.	Sodium starch glycolate croscarmellose Sodium crospovidone	Formulations containing 3% of croscarmellose sodium showed better dissolution compared to other formulations containing croscarmellose sodium as disintegrant and as compared to formulations containing crospovidone and sodium starch glycolate as superdisintegrants.	[33]
14	Hydrochlorothiazide and Atenolol Co-Crystals	antihypertensive	To develop a rapidly disintegrating fast dissolving tablet by using co-crystals of Hydrochlorothiazide and atenolol using solvent evaporation and solution co-crystallization methods and by applying 2^2 design to optimize the tablet formulations.	Crospovidone and sodium starch glycolate.	Formulations containing 4% of crospovidone and 4% of sodium starch glycolate shown better drug release compared to other formulations. Co-crystals have shown increased solubility, flow property and compressibility.	[34]
15	Irbesartan	Anti-hypertensive, diabetic nephropathy or kidney disease	To design and formulate fast dissolving tablets by using starch from jackfruit seeds as a novel superdisintegrant.	Jackfruit seed extract as a novel superdisintegrant (JFS1-Jackfruit starch extracted using water and JFS2: Jackfruit starch extracted using 0.1N NaOH, croscarmellose sodium.	Formulation containing JFS2 5%w/w and croscarmellose sodium showed similar and better drug release as compared to other formulation. Type of starch also determines its superdisintegrant property.	[35]
16	Irbesartan and Atorvastatin calcium	Anti-hypertensive and antihyperlipidemic	To enhance patients compliance by formulating a fast dissolving tablets of combined oral dosage of Irbesartan and Atorvastatin calcium.	Crospovidone, sodium starch glycolate and croscarmellose sodium.	Formulation containing 5% of crospovidone showed better drug release for both Irbesartan and Atorvastatin within 45 minutes and superior to all other superdisintegrants and in combination superdisintegrants.	[36]
17	Indomethacin	Nonsteroidal anti-inflammatory drug (NSAID)	To enhance the dissolution rate of indomethacin by preparing fast dissolving tablets using two different superdisintegrants and effervescent agents and also their combination.	Crospovidone, sodium starch glycolate and croscarmellose Sodium as superdisintegrants. Effervescent agents: sodium bicarbonate and citric acid combination.	Among formulations using superdisintegrants, formulation containing 3.42% of Croscarmellose showed more drug release compared to other formulation containing crospovidone and sodium starch glycolate. Overall,	[37]

					formulation containing combination of superdisintegrant croscarmellose 3.42% and effervescent agent gives best results because of synergistic effect of croscarmellose and effervescent agents.	
18	Ketorolac Tromethamine	Non-steroidal anti-inflammatory	To enhance the dissolution rate and absorption to improve the bioavailability of the drug and for rapid onset of action.	Crospovidone, sodium starch glycolate and croscarmellose sodium	Formulations containing 8% of crospovidone showed better drug release compared to all other formulations in 15 minutes. Its dissolution profile was found to be 3.5 fold enhanced compared to marketed conventional tablets.	[38]
19	Ketorolac Tromethamine	Non-steroidal anti-inflammatory	To enhance patients compliance.	Fenugreek mucilage, linseed mucilage crospovidone	The formulation containing 8% crospovidone as superdisintegrant show best result compared to all other formulations.	[39]
21	Lovastatin	Hyperlipoproteinemias (cholesterol-lowering agent)	To enhance dissolution rate.	Crospovidone, croscarmellose sodium, sodium starch glycolate.	The formulation containing 6% of crospovidone show best results compared to other formulations.	[40]

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