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COMPARATIVE REVIEW OF FUNCTIONALITY AND PERFORMANCE OF THE NATURAL AND SYNTHETIC SUPERDISINTEGRANTS

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ABSTRACT

Immediate release oral solid dosage forms such as orally disintegrating tablets are usually formulated in order to provide safer, immediate and effective drug delivery to the patient. There is a need for proper selection of disintegrants or superdisintegrants and to know their performance when added in the formulation of orally disintegrating tablets. Superdisintegrants are usually added to the formulation of fast dissolving tablets in order to improve the efficacy of the dosage form and to obtain optimum bioavailability by reducing the disintegration time. Superdisintegrants are usually used in low concentration (1-10%w/w) in the solid dosage form. The objective of this review is to compare the functionality and the performance of different types of natural and synthetic commercially available superdisintegrants. This review may provide insight in to the selection of superdisintegrants according to the class of drug selected for the formulation of orally disintegrating tablets.

Keywords: *Superdisintegrants; polysaccharides; asaliyo; co-processed blends; resins.*

INTRODUCTION

Disintegrants are the excipients which are added in the tablet and capsule formulations which help in penetration of moisture and rapid dispersion of tablets into small particles. The resulting small particles will have more surface area resulting in rapid dissolution and release of the drug[1].

Superdisintegrants are the excipients which are added to the formulations which require fast release of the active components or the drug. These help in faster disintegration of the tablets resulting in smaller particles which dissolve faster and provide good dissolution and absorption[2]. Superdisintegrants are superior in activity when compared to disintegrants, so they are effective in low concentrations, with greater disintegrating capacity and are more effective intragranularly[3].

Advantages of superdisintegrants

- They help in rapid disintegration
- They provide higher tablet breaking force and lower friability.
- Rapid disintegration is by swelling without gelling and provides good texture.
- They are available in two particle sizes of which smaller particles provide smoother mouth feel[4].

The faster disintegration of superdisintegrants is due to combined mechanism of swelling and water absorption by the formulation. When these superdisintegrants swell their wet surface area increases leading to increase in wettability and dispersibility of the system, thus promoting disintegration and dissolution. Based on the critical concentration of the disintegrants the optimum concentration of superdisintegrants can be selected which means that below the critical concentration, the tablet disintegration time is inversely proportional to the concentration of superdisintegrant and when higher than critical concentration the disintegration time remains almost constant or even increases[5].

In the formulation of fast dissolving tablets, disintegration of the tablet is an essential step which requires attention for obtaining rapid drug release. There are a number of factors which affect the disintegration of the tablets. The disintegrants which are added should have stronger physical force compared with strong binder for release of the active pharmaceutical ingredient from the medication. There are different mechanisms of disintegration like swelling or wicking etc. Therefore in case of fast dissolving tablets, usually super disintegrants are added which help in disintegration of tablets usually within 60 seconds.

There are different ways or methods in which the disintegrants are added into the formulation. They are intra and extra granular additions or partly internal and partly external addition. Disintegrant, which is usually added both intra and extra granularly, is more effective thereby resulting in the release of the drug from the granules into the aqueous environment. The disintegration activity of disintegrants is not lost or retained when added extra granularly (i.e. by the addition of disintegrants before compression) when

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compared to the intra granular addition. This is because when disintegrants are added intra granularly i.e. during the wet granulation process, the disintegrants are exposed to aqueous environment as well as drying step resulting in decrease in the disintegrants activity[1].

DISINTEGRATION MECHANISMS OF TABLETS

The disintegration mechanisms of tablets is

By Capillary action

The first step in tablet disintegration is absorption of aqueous medium by capillary action and this aqueous medium weakens the intermolecular bonds present between the particles. This weakening of bonds is due to the replacement of adsorbed air by the aqueous medium resulting in breaking of the tablet into fine particles. For the disintegration of hydrophilic drug/ excipient the disintegrants should have porous structure and less interfacial tension towards the aqueous medium, which creates a hydrophilic network around the drug/excipient particles resulting in the disintegration of the tablet when put into the aqueous medium.

By swelling action

Swelling action is the most common type of mechanism of disintegration. The tablet with low porosity shows good disintegration compared to the tablet with high porosity as well as high packing fraction. This is because the tablet with low porosity will have sufficient swelling force acting on it resulting in the disintegration whereas in case of high packing fraction the disintegration of the tablet is slow because of the inability of penetration of water into the tablet.

By particle repulsive forces/ disintegrating particle

According to Guyot-Hermann particle repulsion theory, the disintegration of the tablet is also possible by non-swelling particles, apart from the swelling action mentioned above. The mechanism involved in the disintegration is due to electric repulsive forces between the particles, for which water is required. It is also observed that repulsion is the secondary mechanism of wicking.

By deformation

According to Hess, the disintegration during the tablet compression process, get deformed and come back to their normal structure when they are in contact with aqueous environment. Recently this mechanism was studied for starch, in which the swelling capacity of the starch granules improved when they were extremely deformed during the compression process.

By release of gases

In the formulation of fast disintegrating tablets there is a need for the tablet to disintegrate in less time. This is possible by the addition of effervescent mixture which releases carbon dioxide due to the interaction between bicarbonate and carbonate with citric acid or tartaric acid. In this mechanism the disintegration of the tablet is seen because of pressure generated within the tablet. In these formulations, small changes in temperature and humidity should be controlled. Therefore usually these effervescent mixtures are added prior to compression or in two separate fraction of formulations.

By air expansion

There are a few types of disintegrants which exhibited exothermic properties. Due to this property the disintegrants when wetted, localized stress is released because of capillary air expansion, resulting in the disintegration of the tablet.

By enzymatic action

Enzymes also help in disintegration of the tablet by destroying the binding action of the binders used in the formulation.

Actually disintegration of the tablet occurs by swelling because pressure is created towards the outer direction of the tablet. This results in the tablet to burst. Disintegration may also be possible due to enormous increase in the volume of granules because of accelerated absorption of water [6-8].

SELECTION OF SUPERDISINTEGRANTS

Apart from the superdisintegrants activity, at high concentration levels superdisintegrants affect the friability and hardness of tablets and mouth feel. There are several factors that must be taken into consideration for the selection of superdisintegrants like

Compatibility

In the formulation of oral disintegrating tablets it is desirable to select suitable disintegrants which are more compatible and produce stronger and less friable tablets. The oral dispersible tablets should have acceptable hardness in order to get robust tablets and to avoid the use of special packaging while maximizing production speed.

Disintegration

The selected disintegrants should have the ability to quickly wick the saliva into the tablet in order to produce hydrostatic pressure and volume of expansion required for the rapid disintegration in the mouth.

Flow

Usually in case of direct compression tablet formulations, flow property and content uniformity is required. In normal formulations the concentration of superdisintegrants used is 2-5%, whereas in case of oral disintegrating tablet formulations their concentration may be increased. The flow properties of disintegrants at those high concentrations may contribute to the flow characteristics of the blend.

Mouth Feel

The oral dispersible tablets should have patient compliance. In order to obtain good palatable experience to the patient, small particles are usually preferred rather than large particles because of the gritty feeling they produce in the mouth. Consumers

object usually if the tablet forms gel like consistency when they come in contact with water because they form a gummy texture [9].

NATURAL SUPERDISINTEGRANTS

Natural superdisintegrants obtained from plant products are usually used as an alternative to the commercially available superdisintegrants because of many advantages like biodegradability, biocompatibility, lower cost, friendly to the environment and availability for local accessibility, nontoxic and nonirritant compared to the synthetic superdisintegrants[10].

Isabgol

Isabgol mucilage

Isabgol mucilage is obtained from the plant Plantago ovata. Dried mucilage of the plant acts as hydrophilic superdisintegrant[11]. Apart from the superdisintegrant activity and high swelling index it shows other characteristics like binding, suspending, emulsifying and sustaining properties[12-15].

In the formulation of rapidly disintegrating tablet of Diclofenac Sodium prepared by either direct or wet granulation process 2-5% of dried isabgol mucilage was said to be the optimum concentration for the formulation. When the concentration is above that the tablets were shown to be fragile[16].

In the formulation of fast dissolving tablets of Aceclofenac as a model drug, Plantago ovata mucilage was compared with synthetic superdisintegrants like sodium starch glycolate and crosscarmellose sodium. It was observed that the formulation with mucilage showed highest swelling index and found to have better disintegrating property than the synthetic superdisintegrants[17].

In the formulation of fast dissolving tablets of Carbamazepine, Plantago ovata seed powder and mucilage powder were compared. Increasing concentration of mucilage showed decrease in disintegration time.

The best formulation was 25% mucilage powder. Among both powders mucilage powder showed disintegration within 1min, therefore mucilage powder is suitable for the formulation of fast dissolving tablets[18]. In the formulation of fast disintegrating tablets of Prochlorperazine maleate 8% mucilage and 8% crosspovidone were compared which also showed that the mucilage had superior disintegrating property compared to crospovidone[19] .

Isabgol husk

Husk is the covering of seeds of the genus Plantago. The husk obtained from Plantago psyllium is found to possess disintegration property. When Metformin tablets prepared with husk and crosspovidone were compared, it was found that husk showed less disintegration time than crosspovidone[20].

In the formulation of fast dissolving tablets of Aspirin Plantago ovata husk was used as superdisintegrant and compared with synthetic superdisintegrants like Ac-Di-Sol, crosspovidone, sodium starch glycolate. 6, 8, 10 % concentrations of the above disintegrants were formulated. All the formulations of above three percentages showed disintegration within 30sec. Among the three percentages 10 % of all the three superdisintegrants showed better disintegrant activity. The order of disintegration time of the superdisintegrants was observed as follows. Plantago ovata (8sec) < Ac-Di-Sol (11sec) < crosspovidone (14sec) < sodium starch glycolate (22sec) [21].

Ocimum

Ocimum gratissimum belongs to the family Labatiae. The oil obtained from it is used as local anesthetic, antibacterial and as a mosquito repellent[22].

In the formulation of Metformin HCl dispersible tablets Ocimum gratissimum seed powder and mucilage powder were used as disintegrants. The formulations of different concentration percentages of 5,10,15,20 were prepared and evaluated for the disintegrant property. It was observed from the study that both seed powder and mucilage powder had good disintegrating property in low concentrations (5%). It was also inferred that mucilage powder had faster disintegration activity compared to seed powder and also good binding efficiency, therefore it also acts as a strong binder for tablets[23].

Glycine

It is an amino acid which is suitable in the formulation of rapid disintegrating tablets because of its good wetting nature[24]. In the formulation of rapidly disintegrating tablets using Ethenzamide and Ascorbic acid as a model drugs, the disintegrant activity of glycine was tested. Its disintegrant activity was observed in combination with one of the best superdisintegrant. The best superdisintegrant was selected by comparing different superdisintegrants disintegration times. The different superdisintegrants which were compared are carmellose (NS-300), carmellose calcium (ECG-505), croscarmellose sodium (Ac-Di-Sol), low substituted hydroxypropyl cellulose (L-HPC, LH21), crosspovidone (Polyplasdone, XL-10). Among them the best superdisintegrant was NS-300, which disintegrated the tablets in 30 sec. The tablets formulated with combination of NS-300 and glycine disintegrated in 5sec when compared to only tablets with NS-300[25].

Polysaccharides

In the formulation of novel fast disintegrating tablets saccharides which were used performed as superdisintegrants. There are two types of saccharides low and high compressibility categories. The low compressibility group had very less disintegration time when compared to the high compressibility ones but

with less hardness. Therefore in order to increase the compressibility and to maintain fast disintegration, particles of low compressibility saccharides were modified by coating and granulating with high compressibility saccharides.

For example mannitol and 1% maltose seed powder was granulated with maltose solution resulting in sufficient hardness and disintegrated in 10 sec[26].

Soy polysaccharide

Synonym: Emcosoy.

It is a natural superdisintegrant. It does not contain starch or sugar. It has good application in nutritional products because it is a dietary fiber[27].

In the formulation of hydrochlorthiazide tablets soy polysaccharide was used in the formulation and evaluated for its disintegrant activity. It was observed that it was more effective than starch and less than carboxy methyl cellulose when used in equal concentrations. As the concentration of soy polysaccharide is increased there was less friability of the tablets. The mechanism of disintegration is by rapid swelling in aqueous medium or wicking action[28].

Modified Polysaccharides

In the formulation of orodispersible tablets of Roxithromycin modified polysaccharides such as co grinded treated agar (C-TAG), co grinded treated guar gum (C-TGG) were used as superdisintegrants. With help of factorial design[29] four formulations of each modified polysaccharides were prepared in combination with microcrystalline cellulose. The ratio of modified polysaccharide and microcrystalline cellulose taken were 1:2, 1:1, 1:3, and 2:3. All the formulations showed good disintegration property within 60 sec but the best ratio selected for the formulation was 1:3 ratios for C-TAG and MCC and 1:2 ratios for C-TGG and MCC. The mechanism of disintegration was swelling of polysaccharides due to their porous nature resulting in absorption of water without the formation of gelatinous mass in water leading to excellent disintegration[30].

Asaliyo

It is known as Lepidium sativum belonging to the family Cruciferae. It is used as herbal medicine as well as pharmaceutical excipient as superdisintegrant. Its mucilage has various characteristics like binding, gelling, disintegrating activity and is available in higher amounts in the seeds. In the formulation of fast dissolving tablets of Nimesulide Lepidium sativum mucilage was used as superdisintegrant and was compared with the conventional synthetic superdisintegrants like sodium starch glycolate, Ac-Di-Sol. 5% of mucilage and 5% sodium starch glycolate was compared for disintegrating activity and was found that mucilage was best one. The mucilage concentration which acted as the best superdisintegrant was optimized by comparing different percentages of mucilage superdisintegrants like 2%, 4%, 6%, 8%, 10%, 12%, 14%, from which 10% was observed as the best concentration of mucilage to act as superdisintegrant. 10% mucilage, 5% sodium starch glycolate, 4% Ac-Di-Sol was compared and mucilage gave the best superdisintegrant activity compared to other two. The order of disintegration time observed was mucilage (17sec), Ac-Di-Sol (36sec), SSG (39sec) [31].

Mango Peel Pectin

Mango peel pectin is obtained from the plant Mangifera indica. From the previous study it is found to act as a rich source of pectin along with a high degree of esterification and phenolic compounds, such as flavonol *O*- and xanthone *C*-glycosides[32].

In the formulation of fast dispersible tablets of Diclofenac as a model drug mango peel pectin was compared to synthetic superdisintegrant like sodium starch glycolate. Mango peel pectin was extracted by wet granulation method. It was observed that mango peel pectin acted as a good superdisintegrant because of its good solubility and swelling index, but not as good as sodium starch glycolate[33].

Sodium Alginate

Synonyms: Algin, Alginic acid, Sodium salt, E401, Kelcosol, Protanal, Sodium polymannuronate.

It appears as white to pale yellowish brown powder and is odorless and tasteless. It is practically insoluble in chloroform, ethanol (95%), ether and mixture of ethanol and water where ethanol content is more than 30%, aqueous acidic solutions where pH is less than 3 and other organic solvents. It is slowly soluble in water and forms viscous colloidal solution[34].

It is used as a binder as well as disintegrant in the formulation of tablets, whereas in capsule formulations it is used as a diluent. It is used in formulation of sustained release dosage forms because it delays the dissolution of drug from aqueous suspensions, tablets and capsules. The concentration ranges of sodium alginate are 5-10% in pastes and creams, 1-3% as stabilizing agent in emulsions, 1-5% as suspending agent, 1-3% as tablet binder and 2.5-10% as a tablet disintegrant[35-41].

Locust Bean Gum

Locust bean gum is a vegetable gum obtained by the extraction of Carob tree (Ceretonia siliqua), which is usually seen in the Mediterranean regions and therefore it is also called as Carob Bean Gum. It is a galactomannan derivative which is widely used as gelling and thickening agent in food industry. It also has solubility enhancement and bioadhesive properties[42-44]. The mechanism of its superdisintegrant activity is by concentration dependent wicking action by which the tablet disintegrates within few seconds due to the porous nature formation of the gum.

In the formulation of orodispersible tablets of Nimesulide its superdisintegrant activity was compared

with crosscarmellose sodium and it was observed that 10% locust bean gum prepared tablets showed faster disintegration time (13sec) compared to 10% crosscarmellose sodium (25sec) [45].

Fenugreek

Trigonella Foenum-graceum usually called as Fenugreek, is an herb belonging to leguminous family. It has a number of applications like it is used as an additive in food products, and as traditional medicine. Ripe and unripe seeds and its leaves are used as vegetables. The other applications are it is used as diuretic, gastro protective, antioxidant, antiurolithiatic, antidandruff, cosmetic agent and anti-inflammatory agent. It is used in the treatment of many diseases and also taken as a tonic. A natural gummy material in the form of mucilage is obtained from the seed coatings[46-50]. In the formulation of Metformin Hcl fast dissolving tablets fenugreek was used as superdisintegrant and compared with Ac-Di-Sol. Fenugreek mucilage and Ac-Di-Sol of different concentrations (2, 4, 6, 8, 10%w/w) were taken and formulated as fast dissolving tablets. The mucilage obtained is a polysaccharide. From the formulations prepared and evaluated it was found that 4% of the mucilage was the optimum concentration and was compared with 8% optimized concentration of carmellose sodium. It was found that the tablet with fenugreek mucilage disintegrated within 15 sec compared to the disintegration time (28sec) of crosscarmellose sodium. The concentration of mucilage above 4% and 8% of crosscarmellose sodium increased the disintegration time of the tablets. The mechanism of disintegration is by swelling of mucilage creating the required hydrodynamic pressure resulting in complete and rapid disintegration of the tablet[51].

Bamboomanna and Chitosan

Bamboomanna (Phylostachys nigra) is the inner sap of bamboo. It is called as zhu li in in traditional Chinese medicine and is similarly used to clear inflammation and phlegm from the lungs[52].

There are number of applications of bamboo manna like it is used as an astringent, acrid affect, sweetener, cooling effect, cardio tonic, haemostatic, aphrodisiac and diuretic, anti-inflammatory agent[53-54].

Chitosan has some medical and non-medical applications like:

Non-medical use: Binding agent, mucoadhesive, biocompatible, biodegradable, non-toxic polymer.

Medicinal uses: Antifungal, antibacterial, antiprotozoal, anticancer, antiplaque, antitartar, haemostatic, wound healing, potentially anti-inflammatory response, inhibits growth of carcinogenic bacteria, immunopotentiation, antihypertensive, serum cholesterol lowering, absorption enhancer, increases salivary secretion (antixerostomial) and formation of bone substitute materials[55-60].

In the formulation of orodispersible tablets of Metronidazole three different superdisintegrants like sodium starch glycolate, bamboo manna, chitosan and combinations of these three were used and evaluated for the superdisintegrant activity. Individually prepared formulations containing bamboo manna did not show disintegration below 1 min. Chitosan formulation showed disintegration in 24 sec, but combinations of sodium starch glycolate: bamboo manna and sodium starch glycollate : chitosan in 1:1 ratio showed best superdisintegrant activity i.e., disintegration in 5 sec and 9 sec respectively[61].

SYNTHETIC SUPERDISINTEGRANTS

There are different superdisintegrants available for the formulation of different dosage forms, but now different blends of excipients are available which show the disintegration activity. Some novel disintegrants, modified sugar, modified sweeteners and co processed blend of excipients are developed which facilitates the need of more than one excipient[62].

Co-processed blend of excipients

This consists of mixture of more than two excipients prepared using different techniques like spray drying and freeze drying etc to satisfy the required quality[63].

a) Ludiflash

It is a coprocessed blend of 90% mannitol, 5% kollidon CL-SF (crosspovidone), 5% kollicoat SR 30D (polyvinyl acetate). It is a novel excipient which disintegrates rapidly within seconds and provides soft, creamy consistency, designed for fast dissolving drug delivery systems. It has no segregation of the active ingredients, has good flowability, less water absorption and therefore can be processed easily. It produces hard tablet with low friability on a standard high speed tablet compression machine which is designed for direct compression. Ludiflash reduces the cost of excipients because of multifunction like filler, binder and disintegrant and facilitates faster product development. The release rate is very fast and is a sugar free composition with pleasant taste[64].

b) Pharmaburst

Pharmaburst is smooth and creamy, offers low adhesion to punches, masks taste and grittiness of active ingredients. The benefits of pharmaburst are that it is of low cost, helps in rapid disintegration and it is highly compatible[65].

c) F-melt

This is a fast dissolving excipient system developed by spray drying technique. It is co processed blend of carbohydrates, disintegrant and inorganic ingredients. The commercially available ones are Type C and Type M. It is used in the formulation of fast dissolving tablets by direct compression method. It helps in rapid disintegration by faster penetration of water and also shows good tabletting properties. The benefits of

F-melt are rapid disintegration within 30 sec, economical and time saving, less sticking or capping, free low of spherical dense particles, neutral pH, high loads of API, useful for nutritional supplements and pharmaceutical medication, pleasant mouth feel, good tablet hardness with low friability[66].

d) Modified chitosan with silicon dioxide:

It is prepared by co precipitation of chitosan and silica and has the properties of superdisintegrant and filler. This new excipient involves physical interaction between silica and chitosan resulting in the formation of an insoluble, hydrophilic and highly absorbent material which shows higher water uptake and water saturation for gel formation. It has swelling and capillary action, compaction properties and acts as superdisintegrant with improved flow[67-68].

e) Modified mannitol

It is usually used as a sweetener with good mouth feel in orally disintegrating tablets and in sublimation techniques. Therefore at present these are modified so that they can function as more than one excipient.

(i) Orocell

It is spheronized mannitol used in the formulation of oral dispersible tablets because of its different properties like as a binder, filler and a carrier. Orocell has outstanding processing features because of its spherical technology. The benefits of Orocell are its superior strength, excellent flow, leaves the taste in the mouth with cooling sensation. It is available in two forms, Orocell 200 with 90% mannitol having particle size less than 315µm and Orocell 400 with 90% mannitol having particle size less than 500 µm[69].

(ii) Mannogem EZ

It is spray dried mannitol as sweet as sucrose. It is designed for tablets prepared by direct compression method. The advantages of Mannogem EZ are

It has a smooth mouth feel
It is chemically inert
Non hygroscopic
Free flowing
Non friable
Rapid disintegration
Reduced segregation due to narrow particle size distribution
Highly compatible
High binding capacity of API and flavors
Open crystalline structure resulting in excellent compressibility[70].

f) Crosspovidone and Sodium Starch Glycollate

In the formulation of fast dissolving tablets of Metaclopromide HCl novel co-processed superdisintegrants were used, which were developed by solvent evaporation technique. Crosspovidone and sodium starch glycolate in different ratios like 1:1, 1:2 and 1:3 were co processed and used in the formulation. Among the different formulations prepared, 4% co processed superdisintegrants (1:1 mixture of crosspovidone and sodium starch glycolate) was the best formulation[71].

Resins

Ion exchange resins are the newer pharmaceutical grades of excipients used as superdisintegrants in pharmaceutical dosage forms. The benefits of these resins in comparison to synthetic ones are that they swell when they absorb water but do not dissolve or have any adhesive tendency which is usually observed in gums. Thus there is even disintegration of the tablets when resins are used. These are usually used in lower percentages compared to the conventional superdisintegrants. They provide greater hardness to the tablets. Conventional superdisintegrants are usually ineffective with hydrophobic formulations whereas ion exchange resins are effective with hydrophilic as well as hydrophobic formulations.

Indion 414 is the commonly used weak acid cation exchange resins as superdisintegrant for pharmaceutical dosage forms. It appears as white to pale yellow colored powder, insoluble in water and in common solvents, free from foreign matter. It is usually available in dry potassium form with carboxylic acid and its matrix is made of crosslinked acrylic polymer. The optimum % of indion 414 to be used in formulations is 0.5-2%. The benefits of indion 414 as a disintegrant is its swelling nature on hydration resulting in rapid disintegration, no lump formation on disintegration, compatibility with commonly used excipients and therapeutic agents, does not stick to the tablet punches[72].

Polacrilin Potassium

Synonyms: Amberlite IRP-88, Methacrylic acid polymer with divinyl benzene, Potassium salt, Polacrillinum kalii. It appears as cream color, free flowing, tasteless and odorless powder. When dispersed in aqueous medium they have bitter taste. It is practically insoluble in water and most of the other liquids.

It is a potassium salt of a cross linked polymer derived from methacrylic acid and divinyl benzene and acts as a weakly acidic cation exchange resin. It is used as a tablet and capsule disintegrant. 2% w/w is usually sufficient for its action but usually used in the range 2-10% w/w. Other polacrillin resins are used as excipients for the formulation of sustained release dosage form, to modify or mask the taste of drugs, and for preparation of drug carriers. They are also used in the manufacture and analysis of food products and pharmaceuticals[73-76]. Tablet disintegrates upon hydration by swelling of resin. Water exerts low force between particles within tablet pores. It is used effectively at 1-2% in solid dosage forms. Due to hydrophilic nature, the resin absorbs water rapidly. Resins are effective as disintegrants compared to conventional ones due to their

nonadhesive nature whereas conventionally used cellulose disintegrants like cross carmellose sodium, sodium carboxy methyl cellulose have adhesive nature. So for disintegration the bonding between particles in tablets should be overcome for release of drug[77].

In the formulation of Metformin hydrochloride fast disintegrating tablets, different resins like indion 294, tulsion 349, doshion, amberlite 388 were compared for their superdisintegrant activity. The order of disintegration time obtained was amberlite388< doshion< tulsion349< indion 294, but the tablets with doshion as superdisintegrant was considered as the best because it showed good in vitro dispersion, wetting properties and dissolution profiles[78].

Kyron T-314:

It is a cat ion exchange resin used in the formulation of tablets as a superdisintegrant. It appears in the form of free flowing powder which is cream colored, tasteless and odorless.

In the formulation of orodispersible tablets of Aceclofenac, kyron T-314 was used as superdisintegrant in 10% and 12% concentration. The 12% concentration shows faster disintegration compared to 10% concentration. The mechanism of disintegration is by wicking action which results in rapid disintegration. This is because of porous structure which facilitates faster uptake of water[79].

Crosspovidone

Synonyms: Crosslinked povidone, E1202, Kollidon CL, Kollidon CL-M, Polyplasdone XL, Polyplasdone XL-10, Polyvinylpolypyrrolidone, PVPP, 1-vinyl-2-pyrrolidone homopolymer.

It appears as white to creamy white, hygroscopic, finely divided, free flowing, odorless and tasteless powder.

It is practically insoluble in most common organic solvents and water[34].

It is a water insoluble crosslinked homopolymer of N-vinyl-2-pyrrolidinone, used in 2-5% concentration and can be prepared by direct compression or wet or dry granulation. It shows high capillary and hydration capacity. Particle size of crosspovidone is important for disintegration activity especially for analgesic drugs. It is shown that larger particles show faster disintegration compare to smaller particles. By using co-evaporation technique, it can be used as solubility enhancer of poorly soluble drugs[80-86].

It may form molecular adducts with some of the materials when it is exposed to high amounts of water. It is compatible with most of the organic and inorganic pharmaceutical ingredients[34].

In the formulation of fast dissolving tablets of Valsartan three superdisintegrants (crosspovidone, Ac-Di-Sol, sodium starch glycolate) were compared in which crosspovidone showed fastest disintegration. The order of disintegration time obtained was crospovidone <Ac-Di-Sol< sodium starch glycolate. The disintegration mechanism is by wicking through capillary action. Tablets prepared with crosspovidone showed fast capillary action, well hydrated and found to be soft in comparison to the other two superdisintegrants[87].

In the formulation of Carbamazepine fast dissolving tablets various superdisintegrants like Indion-414, crosspovidone, crosscarmellose sodium, sodium starch glycolate were compared with three different increasing concentrations. It was inferred that Indion 414, crosscarmellose, crosspovidone showed decrease in disintegration time with increase in concentration. Rapid disintegration in short time for crosspovidone and Indion 414 was due to easy swelling property and rapid capillary action compared to other two, but in case of sodium starch glycolate with increase in concentration the disintegration time also increased because of formation of viscous gel barrier which prevented the penetration of the disintegration medium[88].

Polyplasdone XL-10 has shown good performance in oral dispersible formulations. The mechanism of Polyplasdone crosspovidone in oral dispersible tablets was found that it quickly wicks saliva by capillary action into the formulation resulting in rapid disintegration by generating the required volume expansion and hydrostatic pressure in the mouth. Most of the superdisintegrants act by swelling action but Polyplasdone has both swelling and wicking action. The unique particle morphology i.e., their granular and highly porous nature help in capillary action resulting in rapid disintegration of the tablet and also acts as highly compressible material.

In the formulation of placebo oral dispersible tablets with 20% superdisintegrant, 78.7% mannitol and with low levels of lubricant and glidant, it was observed that Polyplasdone XL-10 crosspovidone showed highest tablet strength and lowest friability when different ranges of compaction forces were applied. The selected superdisintegrants particle size influences the texture of the formulation. Polyplasdone XL-10 crosspovidone has the smallest particle size in comparison to other superdisintegrants[4].

In the formulation of oral dispersible tablets using some anionic and cationic drugs as models, the effects of nonionic and anionic superdisintegrants were observed for the dissolution of cationic drugs. Among crosspovidone, sodium starch glycolate and crosscarmellose sodium; crosspovidone showed improved dissolution of poorly soluble cationic drugs because of its nonionic nature. There was no difference in the disintegration time of tablets using different superdisintegrants. The disintegration time for soluble cationic drugs was greater than poorly soluble cationic drugs[89].

Sodium Starch Glycolate

Synonyms: Carboxymethyl starch, sodium salt, Explosol, Explotab, Glycolys, Primojel, Starch carboxymethyl ether, sodium salt, Tablo, Vivastar P.
It appears as white to off white, free flowing, tasteless and odorless powder.

It is practically insoluble in water, sparingly soluble in ethanol (95%) and a 2% concentration disperses in cold water which settles in the form of highly hydrated layer.

It is usually used as a superdisintegrant in capsule and tablet preparations. It is usually used in tablets manufactured by either direct compression or wet granulation methods. The concentration range that can be used in the formulations is 2-8% where the optimum concentration is 4% and 2% is sufficient concentration that can be employed in the formulations. It is also used as a suspending vehicle. The mechanism of disintegration is rapid uptake of water followed by rapid swelling. It as the capacity of swelling up to 300 times its original volume. The disintegration time of sodium starch glycolate is affected by the solubility of the matrix formulation, the way in which it is added during wet granulation and also by highly soluble excipients where disintegration time is slowed down in tablets. It is observed that it shows incompatibility with ascorbic acid[34].

Carboxymethylcellulose Calcium

Synonyms: Calcium carboxymethylcellulose, Calcium CMC, ECG 505, Nymcel ZSC

It appears as white to yellowish white fine powder and is hygroscopic in nature. It is insoluble in water but swells to twice its original volume and forms a suspension. It is slightly soluble in 0.1 mol/lit sodium hydroxide, insoluble in 0.1 mol/lit hydrochloric acid. It is practically insoluble in chloroform, ether, ethanol (95%) and acetone.

It has different characteristics like as a suspending agent, stabilizing agent, water absorbing agent, viscosity increasing agent, tablet and capsule disintegrant. The importance of carboxy methyl cellulose calcium in tablet preparations is that it acts as a diluent, disintegrant, and a binder. It is usually insoluble in water but also acts as an effective disintegrant by swelling to several times its original volume when it comes in contact with water. It is used in the concentrations of 5-15% and 1-15% as a tablet binder and tablet disintegrant respectively; when the concentration exceeds 15% hardness of tablets is reduced[34].

In the formulation of mouth dissolving tablets of Rizatriptan benzoate different superdisintegrants like crosspovidone, carboxy methyl cellulose calcium, indion 414, indion 234 and their combinations were used and evaluated for their superdisintegrant activity. When the superdisintegrants were individually used in the formulations, the order of their superdisintegrant activity observed was indion 234>crosspovidone> carboxymethyl cellulose calcium>indion 414. Among the combinations crosspovidone and carboxy methyl cellulose calcium showed the fastest disintegration i.e., in 4sec[90].

Carboxymethylcellulose Sodium

Synonyms: Akucell, Aquasorb, Blanose, Cellulose gum, CMC sodium, E466, Finnifix, Nymcel, SCMC, Sodium carboxymethylcellulose, Sodium cellulose glycolate, Sodium CMC, Tylose CB
It appears as white, granular powder and is odorless. It is practically insoluble in ethanol (95%), toluene, acetone and ether. It easily disperses in water at all temperatures and forms clear, colloidal solutions. It forms a complex with collagen and complex co-acervates with gelatin and pectin.

It is used as a tablet and capsule disintegrant, suspending agent, coating agent, tablet binder, stabilizing agent for emulsions, water absorbing agent, and viscosity increasing agent in oral and topical formulations. It is one of the main ingredients of wound care, dermatological patches and self adhesive ostomy where it is used as a mucoadhesive and to absorb transdermal sweat and water or wound exudates. When encapsulated with carboxy methyl cellulose sodium helps in protection of drug and its delivery. It is also used in food products, surgical, personal hygiene, toiletries and cosmetics. The concentration ranges used in different formulations are 0.25-1% as emulsifying agent, 3-6% as gel forming agent, 0.05-0.75% in injections, 0.1-1% in oral solutions, 1-6% as a tablet binder[34].

Pregelatinized Starch

Synonyms: Compressible starch, Instastarch, Lycatab PGS, Merigel, National 78-1551, Pharma-Gel, Pregel, Sepistab ST 200, Spress B820, Starch 1500 G, Tablitz, Unipure LD, unipure WG220.
It appears as white to off white color, moderately coarse to fine powder. It has slight characteristic taste and is odorless. Depending upon the degree of pregelatinization it is slightly soluble to soluble in cold water.

It is a modified starch. It is used as a tablet and capsule diluent and disintegrant and as a binder for tablets prepared by dry granulation or direct compression methods, where it acts as a self lubricating agent. Usually stearic acid is added as a lubricant in combination with pregelatinized starch rather than magnesium stearate because concentrations greater than 0.25% affect the tablet strength and dissolution. It can also be used in wet granulation process. The concentration ranges of pregelatinized starch are 5-75% as diluents in hard gelatin capsules, 5-20% as a tablet binder for tablets prepared by direct compression and 5-10% for tablets prepared by wet granulation and 5-10% as tablet disintegrant[34].

Low Substituted Hydroxypropyl Cellulose

Synonyms: Hyprolose, Low-substituted, L-HPC.

It appears as white to yellowish white powder or granules. It is tasteless and slightly odorless. It is practically insoluble in ether, ethanol (95%), and water but swell in water. When tablet formulations containing alkaline substances are stored, disintegration may be prolonged[34].

It is usually used as a tablet and capsule disintegrant and as a binder for tablets prepared by wet granulation. It is used in the formulation of rapidly disintegrating tablets prepared by direct compression methods. It also has the capacity of delaying the drug release from matrix tablets. Different grades are available with different particle sizes and substitution levels. It is usually used in the concentration range of 5-25%.

LH-11-medium substitution level, largest particle size, used as disintegrant and anticapping agent for direct compression.

LH-21- used for tablets prepared by wet granulation method as a binder and disintegrant.

LH-31- small particle size, used to produce granules by extrusion process.

LH-22 and LH-32- low substitution grades, used for formulations which do not require high binding strength[91-93].

Camphor and Mannitol

In the formulation of Cetrizine dihydrochloride orodispersible tablets, combination of camphor and mannitol were used as superdisintegrants in different proportions like 1:1, 1:3, and 1:6. This study showed that 1:3 ratio of camphor and mannitol was the best formulation with less disintegration time i.e., 16sec. The order disintegration time of the three ratios was found to be as 1:3 (16sec), 1:6 (19sec), 1:1 (22sec) [94].

Microcrystalline Cellulose

Synonyms: Avicel PH; Celex, Cellulose gel, Celphere; Ceolus KG; Crystalline cellulose; E460; Emcocel; Ethispheres; Fibrocel; Pharmacel; Tabulose; Vivapur.

It appears as white, tasteless, odorless, crystalline powder which consists of porous particles. It is practically insoluble in dilute acids, water and most of the organic solvents.

Apart from disintegrant activity, it is also used as a suspending agent, adsorbent, tablet and capsule diluents. It is used for both direct compression and wet granulation process. It also has lubricant properties. It is also used in cosmetics and food products. Incompatibility is seen with strong oxidizing agents. There are different grades of microcrystalline cellulose which are available and differ in moisture content, particle size and flow properties and other physical properties[34].

In the formulation of fast dissolving tablets of Aloe vera gel different superdisintegrants were used in the formulation, compared and evaluated. The order of disintegrant activity observed was microcrystalline cellulose (36sec) < crosscarmellose sodium (41sec) < crosspovidone (45sec) < sodium starch glycolate (49sec). Among them microcrystalline cellulose showed the best disintegrant activity because of its better wicking and absorbing capacity compared to the other superdisintegrants. This is due to easy passage of water which breaks the hydrogen bonds resulting in instantaneous release of drug from the tablets. The other disintegrants showed high gelling tendency and slow water absorption resulting in delay in wetting as well as disintegration time[95].

Crosscarmellose Sodium

Synonyms: Ac-Di-Sol; crosslinked carboxy methyl cellulose, Explocel; modified cellulose gum; Nymcel Z XL; Primellose; Solutab, Vivasol.

It appears as white or grayish white odorless powder. It is practically insoluble in ethanol, acetone and toluene; insoluble in water even though it swells 4-8 times its original volume on contact with water.

It is used as a disintegrant in capsule and tablet formulations. It is used in both direct compression and wet granulation process. In wet granulation process crosscarmellose sodium is added in both wet and dry stages of the process because it has both wicking and swelling ability. Crosscarmellose sodium is used in 2%w/w concentration in direct compression, 3%w/w concentration in wet granulation process. The usual concentration that is used as tablet disintegrant is up to 5%w/w. It is not compatible with soluble salts of iron and other metals like mercury, zinc, aluminum and strong acids[34].

In the formulation of orodispersible tablets of Rabeprazole different superdisintegrants were tested to select the best one for Rabeprazole. Superdisintegrants like crosspovidone, crosscarmellose sodium, pregelatinized starch, agar treated powder, L-HPC in 5-10% concentrations were selected, formulated and evaluated. From disintegration results it was observed that 10 % superdisintegrants concentrations were more suitable. For Rabeprazole the best superdisintegrants selected were crosspovidone and crosscarmellose sodium because crosscarmellose sodium absorbs more amount of water and swells quickly. Because of its fibrous nature it is capable of absorbing large quantities of water at different concentration levels. Their fibrous natures help in both intra and inter particulate wicking property. Crosspovidone has the capacity of absorbing more quantity of water compared to crosscarmellose sodium because of good interactions between particles arranged in crosspovidone. Pregelatinised starch, L-HPC and TAG have less water absorption capacity compared to crosspovidone and crosscarmellose sodium[96].

In the formulation of oral dispersible tablets of Isoniazid and Rifampicin two superdisintegrants like Ac-Di-Sol and Polyplasdone XL were compared for disintegration property in which Ac-Di-Sol showed better disintegration compared to polyplasdone XL[97].

Table 1: *Comparison of natural and synthetic superdisintegrants*

Concentration of various Superdisintegrants	Drug	Inference	Reference
Plantago ovate seed powder, mucilage powder in 5,10,15, 20,25% concentrations	Carbamazepine	Among the concentrations 25% mucilage powder was found to be best.	18
Plantago ovate mucilage (8%), crospovidone	Prochlorperazine maleate	Mucilage powder showed superior disintegration than crospovidone	19
Ocimum gratissiumum seed powder, mucilage powder in 5, 10, 15 and 20% concentrations.	Metformin hydrochloride	5% of both seed powder and mucilage powder showed good disintegration property. Mucilage powder showed faster disintegration than seed powder.	23
Modified polysaccharides such as cogrinded treated agar (C-TAG), Cogrinded treated guargum (C-TGG). The ratio of modified polysaccharide to microcrystalline cellulose in 1:2, 1:1, 1:3, 2:3 were taken.	Roxithromycin	The best ratio selected for formulation is 1:3 for C-TAG and 1:2 for C-TGG.	29
Asaliyo mucilage 2, 4, 6, 8, 10, 12, 14 % were taken. 10% mucilage, 5% SSG, 4% Ac-Di-Sol were compared	Nimesulide	10% concentration was shown to be best. Among them mucilage gave best superdisintegrant activity	31
Mangopeel pectin, SSG were compared	Diclofenac	Mango peel pectin showed good superdisintegrant activity but not as good as SSG.	33
Indion 294, tulsion 349, doshion, amberllite 388 were compared.	Metformin hydrochloride	Order of disintegration was amberllite 388<doshion< tulshion349< indion294. Doshion was considered to be the best.	78
Crospovidone, Ac-Di-Sol, SSG	Valsartan	Order of disintegration time obtained was crospovidone< Ac-Di-Sol< SSG.	87
Indion 414, crospovidone, croscarmellose, SSG in 3 increasing concentrations	Carbamazepine	Indion 414, croscaremellose, crosspovidone showed decrease in disintegration time with increase in concentration. SSG showed increase in time with increase in concentration.	88
Combination of camphor and mannitol in 1:1, 1:3, 1:6 ratios.	Cetrizine	1:3 ratio of camphor and mannitol showed best formulation with least disintegration time.	94
Plantago ovate husk, crospovidone, SSG of each 6, 8 10% concentrations were compared.	Asprin	10% of 3 superdisintegrants showed disintegration within 30sec. the order of disintegration obtained was plantago ovate(8sec)<Ac-Di-Sol(11sec)<crosspovidone(14sec)<SSG(22sec)	21
10% locust bean, 10% croscarmellose sodium were compared.	Nimesulide	10% of locust bean showed faster disintegration (13sec) compared to 10% croscarmellose sodium (25sec).	45
4% fenugreek mucilage and 8% croscarmellose sodium were compared.	Metformin hydrochloride	Fenugreek mucilage disintegration was faster (15sec) compared to croscarmellose sodium (28sec)	51
SSG, bamboomannana, chitosan and their combinations were compared	Metronidazole	The best superdisintegrant activity was shown by combinations of SSG:bamboomannana and SSG: chitosan in 1:1 ratio in 5 and 9 secs respectively.	61
Novel co-processed combination of crosspovidone and SSG in 1:1, 1:2, and 1:3 ratios were compared.	Metaclopromide HCl	4% co-processed (1:1 mixture of crosspovidone and SSG) was found to be the best formulation.	71
Crosspovidone, carboxy methyl cellulose calcium, indion 414, 234 and combinations of them were compared.	Rizatriptan benzoate	When individually used the order of disintegration was indion 234> crosspovidone> carboxy methyl cellulose calcium> indion 414. Among the combinations crospovidone and carboxy methyl cellulose calcium showed best disintegration activity in 4 sec.	90
Microcrystalline cellulose, croscarmellose sodium, crospovidone, SSG was compared.	Aloe vera gel tablets	Micro crystalline cellulose showed the best superdisintegrant activity.	95

CONCLUSION

Superdisintegrants which are available in various overviews and research works have been discussed. The selection of superdisintegrants and mechanism of their disintegration is critical for the formulation of fast dissolving tablets. This review showed that the natural superdisintegrants are beneficial and more effective than the commercially available superdisintegrants. Apart from the frequently available commercial superdisintegrants, the other novel and co-processed superdisintegrants were also been discussed. This study helps in knowing the type and quantity of disintegrants required for the formulations. Therefore, there is a potential for the evaluation of new type of superdisintegrants or modification of the existing ones for the formulation of fast dissolving solid dosage forms.

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