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A Comprehensive Review of Disintegrants: Backbone of disintegration

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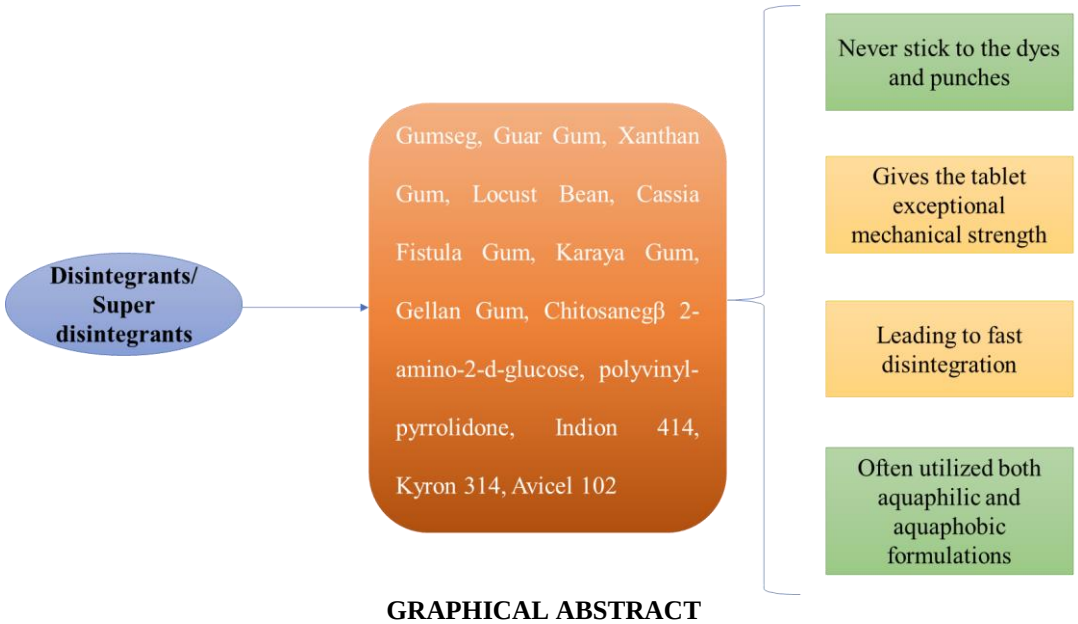
Abstract:
Strong attractive bonding forces works among the particles of solid dosage forms such as mechanical, solid and intermolecular and bioavailability of solid dosage form is preferentially dependent on in vivo disintegration then dissolution. This review is focused for disintegrating agents, their categories, mechanisms of action, associated pros and cons. Furthermore, more emphasis is on natural superdisintegrants, those perform disintegration at fastest rate with limited side effects. So, they are in frequent use to create number of preparations like fast dissolving tablet, pulsatile and tablet dispersible tablet etc. Despite of various disintegrants, superdisintegrants co-processed form of them are thoroughly investigated along with novel techniques of production such as Melt Extrusion, Crystallization, Spray Drying, Solvent Evaporation, Granulation/ Agglomeration.

Keywords: Disintegrants Superdisintegrants, Melt Extrusion, Crystallization, Spray Drying, Solvent Evaporation, Granulation/ Agglomeration



GRAPHICAL ABSTRACT

Introduction

The Although, a variety of dosage forms are available but still oral dosage forms are more preferred by humankind. As solid dosage forms are compact in structure that make them more acceptable dosage form. Different bonding forces among solid particles work during the preparation of solid dosage forms, particularly granules and tablets, to transform them into appropriate dosage forms. The mechanism followed by dominating bond additionally, surface area across which these bonds are active could be regarded as the two main criteria for the compactability of powders. These aspects have not been thoroughly assessed for medicinal materials due

to significant experimental challenges. Instead, studies and relationships with tablet strength typically focus on more auxiliary, indirect aspects. Such auxiliary elements as particle form, plastic deformation, surface roughness, particle size and particle fragmentation, Elastic deformation and have all been examined as important volume reduction methods [1-4].

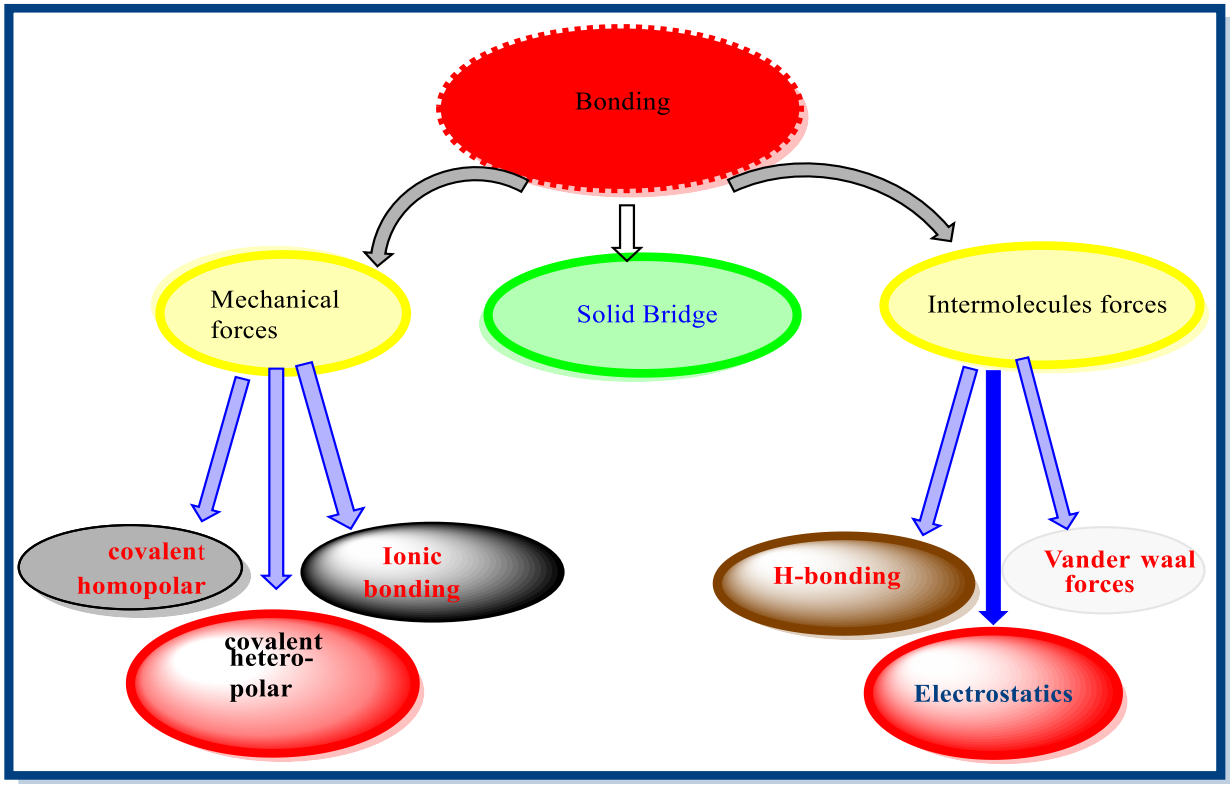


Figure 1 Different bonding between particles

The bonding mechanisms that have been discussed include mechanical interlocking, that represents the bond kind which dependent on twisting and hooking of uneven particles in shape, solid bridges, which represent uninterrupted solid bridges between tablet and granules particles, intermolecular forces, which represent infirm attraction forces active over the distances. Computation of dense strength have been made in media that are acknowledged to diminish intermolecular forces bonding in order to describe the dominant bond mechanisms. Liquids with various dielectric constants and films made of magnesium stearate served as the media. The findings show that the intermolecular forces are the primary type of bonding in medicinal materials. Bonding with solid bridges can only improve compact strength of particles having coarse nature, plastically deforming materials that could melt during compaction. Only for coarse plastically deforming materials that can melt during compaction can bonding with solid bridges help to the compact strength. All bonding shown in (Figure 1).

Only a proportionate connection between the bonding surface area and compact surface area may be feasible for all materials joining with intermolecular interactions [2]. If the particle surface area in the tablet is big, a huge bonding surface area for such materials will be obtained. This could be done by using materials that are heavily fragmented or qualities with noticeable surface roughness or by using very refined particles materials. It is indicated that the majority of the supposed plastically deforming pharmaceutical materials frequently lack the flexibility necessary to produce sizable zones that could participate in the attraction of different particles by different molecules.

Basic Requirement For Fast Dissolution Of Solid Dosage Form

According to all theories and researches; for rapid dissolution, particle size plays vital role. A tablet's mechanical disintegration into fine particles or granules, or the breakdown of the inter-particle connections

produced during compression process of granulated particles that contains therapeutic agent and excipients, is known as disintegration [5].

Disintegration typically occurs in two stages once the liquid come in contact with tablet's surface and enters its capillaries: first, the tablet breaks down into small grains, and then, the granules break down [6]. For the speed of the tablet's initial medication release, the first step is crucial. However, the gelling of a disintegrant slows down this procedure. If there was no disintegration, only the API at the close's surface would disintegrate. A faster rate of dissolution is produced by the increased surface area compared to the entire tablet.

However, different novel dosages forms are available still, the oral route is the best way to provide therapeutic drugs since it is simple to administer, has cheap manufacturing costs, and results in high patient compliance. For a given therapeutic situation, many patients require an immediate commencement of effect, necessitating an instantaneous release of the medication. This issue, which is thought to impact 50% of the population, leads to a high rate of ineffective therapy [7, 8]. A single or multiple-unit reservoir or matrix system is the foundation of an immediate release drug delivery system, which is intended to deliver immediate drug levels quickly. For medications with lengthy biological half-lives, high bioavailability, lesser clearance, and shorter elimination half-lives, immediate release drug delivery is preferred. However, the primary requirement for an instant release dosage form is a drug's weak solubility and the necessity for a drug's quick action to treat an undesired defect or disease [9]. With immediate effect there are two types of solid oral dosage forms: those that dissolve quickly and those that dissolve slowly. A dose form is considered to be immediate release if less than 85% of the specified quantity dissolves in 30 minutes. For tablets with a quick release, the sole hurdle to drug release is the straightforward breakdown or erosion stage, which often happens in less than an hour. Disintegration is a crucial mechanism that can improve any drug's bioavailability and dissolution from immediate release tablets [5]. Disintegrants could be added to the formulation to augument the disintegration of dosage form's when they come in contact with a fluid [10]. The incorporation of more than one disintegrants into the formulation of product is often done to enhance the product's surface area and soften the binding substance that binds the solid components of the product together. The end result is that a tablet that is subjected to aqueous fluid breaks down into fine particles after first breaking down into granules. When the tablets or capsules are reduced to fine particles, the dissolution rate in the media accelerates as the particle's size decreases and is at its highest. Rapid dissolving speeds up the pace at which the active substance is absorbed by the body, leading to the intended therapeutic effect [11]. All a forementioned matter comprised in (Figure 2).

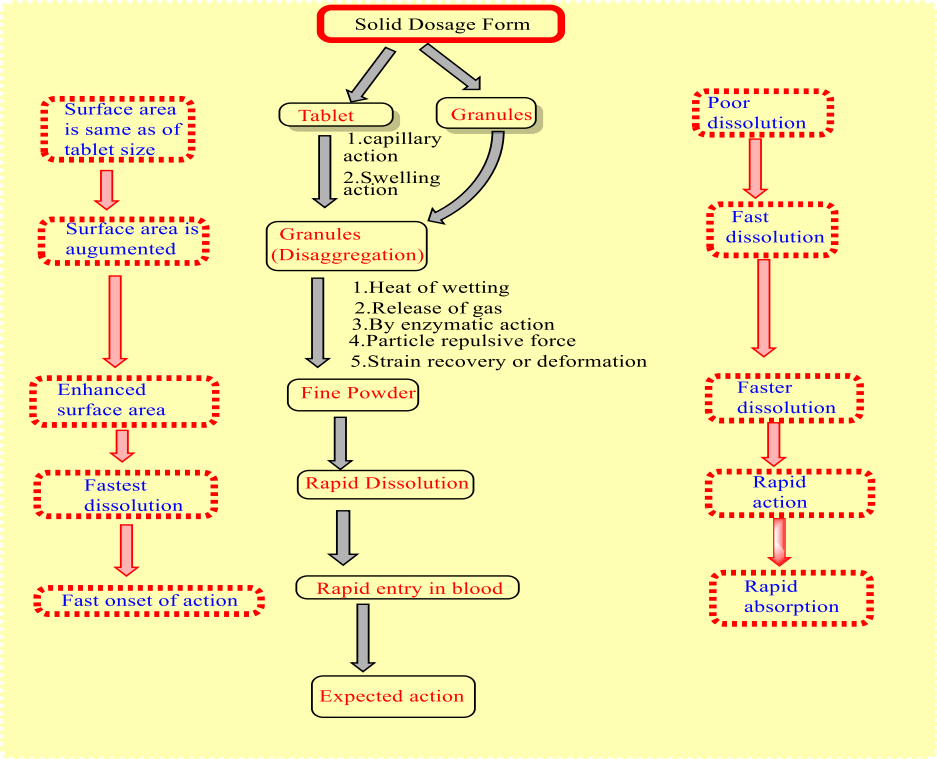


Figure 2 Disintegration of solid dosage form

Disintegration Influenced By Following Factors

Nature of Lubricants: Water is repelled by the majority of lubricants, or hydrophobic substances. To safeguard the tablet surface while it is created in the tablet press, lubricants are frequently mixed to formulations. The tablet's susceptibility to disintegration can frequently be increased by such addition. The use of lubricants can negatively impair the uptake of water. The inclusion of lubricants typically has little effect on the disintegration time when a powerful disintegrant is already in the formulation. For instance, the presence of hydrophobic lubricants has no effect on the performance of sodium starch glycolate [12].

Proportion of Diluents or Filler used: The amount of bulking agent has an impact on the rate and nature of disintegration. The viscosity of the absorbed fluid may rise as a result of water-soluble additives. This has the result of weakening the disintegrating agents' effectiveness. If sufficient amounts of disintegrants are added, diluents that are water insoluble could promote breakdown [13].

Use of Surfactants: According to HLB scale a wide range of surfactants are added to solid dosage forms to reduce the hydrophobicity of drugs because due to high hydrophobicity, dosage forms consume longer time to disintegrate. Concentration of surface acting agents in each formulation is effective in various ranges. A variety of surfactants are available having different nature, additionally follow specific behavior. For illustration, with or without the addition of nonionic surfactants, the disintegration time of water-soluble tablets stays essentially the same; nevertheless, when surfactants are added, the rate of water penetration generally rises, especially for granules that are manufactured with somewhat soluble ingredients. Another example is sodium lauryl sulphate, which is frequently included as a surfactant in medicine formulations and can alter both the liquid penetration for tablets and the rate at which starch is absorbed by water.

Time of Adding disintegrant to the product formulation: There are primarily three stages at which disintegrants are incorporated into dosage forms.

While granulation: Disintegrants are blended with other powders in this process, which occurs intragranular or during granulation. Consequently, the granules have the superdisintegrants embedded into them [13].

Prior to Compression: In this method, before compression process the disintegrants are combined with ready-to-use granules [14].

Addition of super disintegrants at intra and extra granulation steps: A portion of disintegrants are introduced to intragranular and a part to extra granular during process. Compared to method nd b, this procedure higher up the outcomes and more

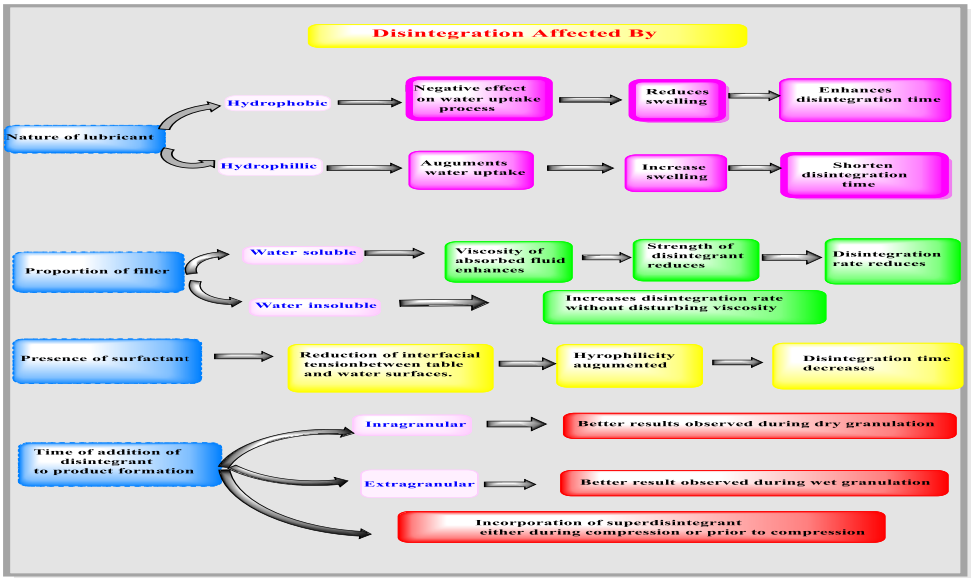


Figure 3 Different f actors affects disintegration

thorough disintegration [15]. The incorporation of disintegrant extragranular enhances more fast disintegration than that of the added intragranular when a wet granulation method is used. Despite this, it seems that most people agree that the best results are obtained by including some disintegrant in both steps [16, 17]. Effect of each above factor shown in (Figure 3).

Disintegraton Occur By Following Different Path

Different paths of disintegration mechanism are shown in (Figure 4).

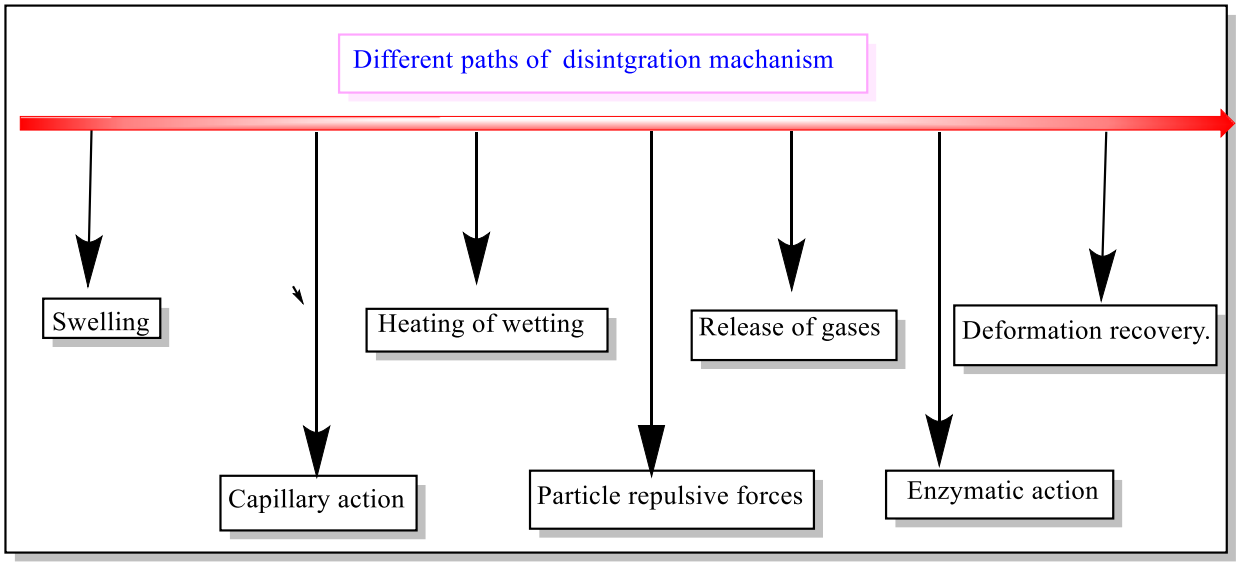


Figure 4 Different paths of disintegration mechanism

4.1 Swelling: One of the most popular disintegration methods [18].When particles swell in all directions, they push apart other elements and destroy the matrix. The inclusion of a disintegrant is one of the most used strategies for encouraging tablet disintegration. The chemical make-up and degree of crosslinking of a disintegrant determine how much it swells. The compact porosity is another element that affects the disintegrant performance. On the one hand, a matrix with high porosity and lots of empty spaces may be less effective since the force of the disintegrant swelling is reduced. Low porosity and strong compression force, on the other hand, can obstruct liquid penetration into the matrix and prolong disintegration time. Gel-forming substances that cause swelling are ineffective.

Materials that gel when they swell are ineffective disintegrants because the gel's viscosity delays liquid penetration and lengthens disintegration time. As a result, disintegrants like tragacanth, agar, karaya, and made from swelling gums are not very effective.

4.2 Capillary action: These are efficient disintegrants that function by way of capillary and porosity action and do not cause swelling. The presence of pores creates a conduit for liquid to enter, diminish the strength of intermolecular link and leading the tablet to crumble into minute pieces also break intra-particle connections, which leads to disintegration. A few types of disintegrants must maintain a porous structure and low interfacial tension toward aqueous fluid in order to disintegrate by forming a hydrophilic network surrounding the drug particles.

Water will be drawn in by the material, creating a capillary network that will allow liquid to permeate the tablet. After then, water will cause soluble particles to dissolve or disintegrate.

4.3 Deformity or Strain recovery: Breaking up the compact matrix by the form recovery procedure. The reversible viscoelastic process of deformation is a less common description of this mechanism. The substance inside the tablet is bent during the compression process, but it is likely to regain its original shape and volume once the disintegrant interacts with the water. The disintegration medium can also encourage the disintegrant's polymer chains to select the configuration that is most energetically advantageous. More research has been done

on the motions and volume expansion than on swelling and wicking [5, 10, 19, 20]. The compact matrix may disintegrate due to the motions and volume expansion caused by the form recovery process. Compared to swelling and wicking, this mechanism is less understood.

4.4 Particle repulsive forces: This mechanism is presented as a compact that is comprised of a non-swellable disintegrant. Through hydrophilic pores, water enters compacts and dissolves forces such as hydrogen bonds.

4.5 Enzyme Participation: The product may contain small levels of enzymes. On the other hand, the body's own enzymes may destroy excipients like starch or other binder ingredients, leading to disintegration. For examples amylase disintegrates starch, Protease able to break gelatin bonding and invertase is suitable for sucrose dissociation.

4.6 Release of gases: Citric and tartaric acids interact with alkali metal carbonates or bicarbonates (bases), releasing CO2 into the water as a result. This creates pressure inside the tablet and speeds up tablet disintegration. Due to the extreme sensitivity of these disintegrants, stringent temperature and humidity control is needed for making the tablets. Effervescent tablets are created in a way that causes them to quickly dissolve when they come into touch with water and release CO_2 [21] . An interaction between an acid and carbonate or bicarbonate causes this.

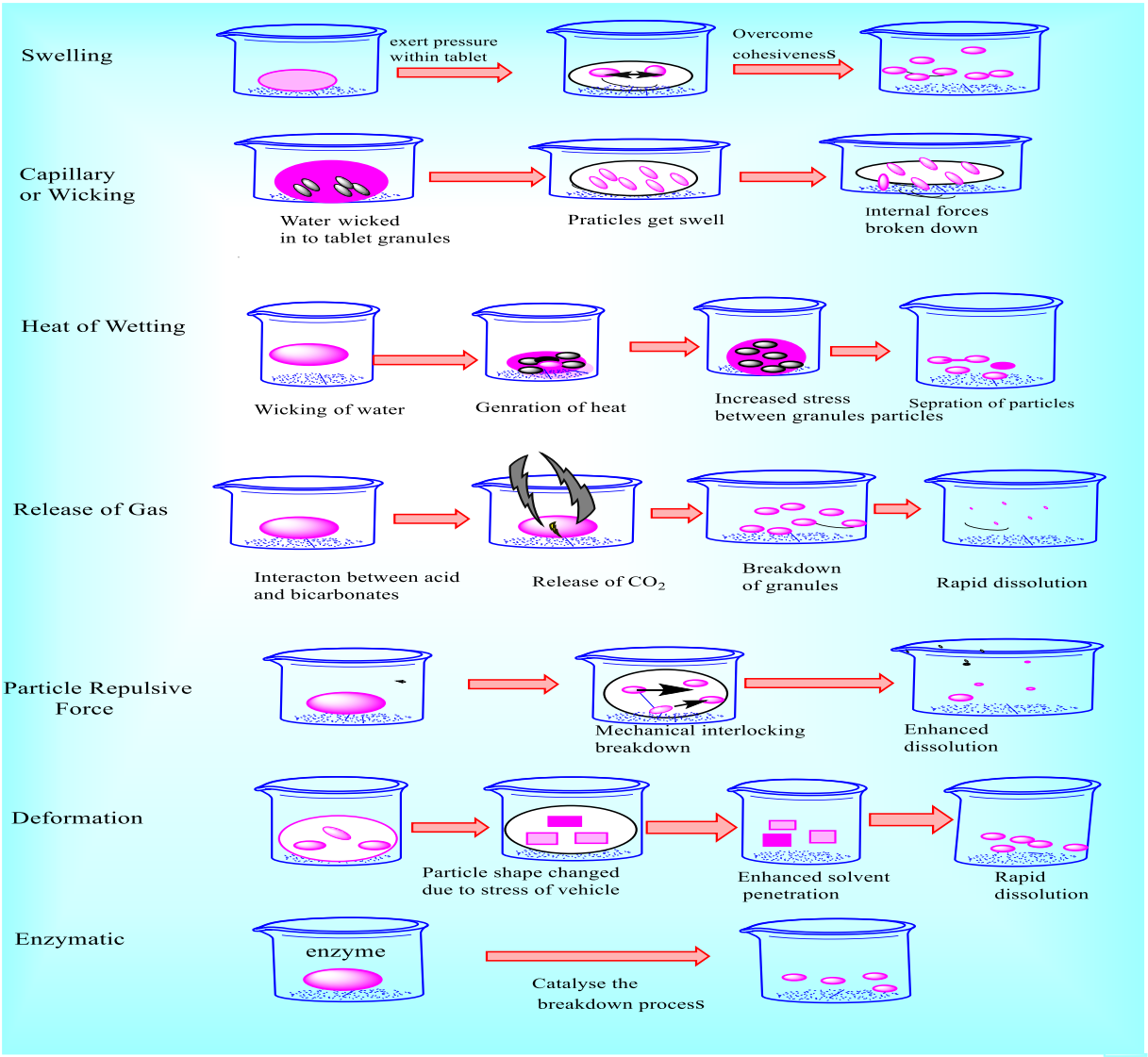


Figure 5 Various mechanism of disintegration

4.7 Heat release while wetting: Materials exhibit exothermic or endothermic interactions when they come into contact with water [20, 22] When disintegrants and aqueous media mix, exothermic characteristics are seen [23].

The exension of air held in the closed -pack can theoretically be aided in compact disintegration by the heat generated, which can lead to localised stress [24]. This mechanism is the subject of intense debate. However, other researchers hypothesised that the heat produced by soaking may not be significant enough to effectively induce the compact's entrapped air to expand, leading to the compact's breakup [25]. It further argued that if heat creation were a key factor in tablet disintegration, it would have happened during comparession or ejection because compression generates a lot of heat. It was noted that in some tablet formulations, the disintegration process was not always accelerated by raising the temperature of the aqueous medium [18]. Some of the disintegrants also show endothermic characteristics [25]. In order to determine the amount of its impact and determine whether a thermodynamic model could be created to describe its function in the pill breakdown process. According to some writers, exothermic reactions between materials and water produce heat that can cause localised stress, which in turn causes the air trapped inside the compact to expand, leading to the matrix's disintegration. Other researchers contend that the heat produced by soaking process is insufficient for expansion of the trapped air. If so, breaking up of the dense would happen during production, either when ejecting Or compacting the tablet. Exothermic disintigrants are wetted locally under stress caused by capillary air expansion, which contributes in the disintegration of the dosage form. All mechanisms shown in (Figure 5).

AN INFORMATORY NOTE ON DISINTEGRANTS

In order to facilitate the disintegration of tablets or capsules when they come into contact with fluid matter or liquid, disintegrants are excipients that are added into the formulation of granules, tablets or capsules. Disintegrants come in a variety of varieties that can be differentiated based on how they work and have been used often for many years. The incorporation of one or more than one disintegrants into the formulation of product is often done to enhance the product's surface area and soften the binding substance that binds the solid components of the product together. The end result is that a tablet that is subjected to aqueous fluid breaks down into fine particles after first breaking down into granules. When the tablets or capsules are reduced to fine particles, the dissolution rate in the required media accelerates as the of particle decreases and is at its highest. Rapid dissolving accelerates the rate of active pharmaceutical ingredient absorption by the body, resulting in the desired therapeutic effect. Be aware that chewable tablets often do not need a disintegrant to be included in the formulation [6, 12].

A LIST OF PROPERTIES SHOULD BE CONSIDER WHILE SELECTION OF DISINTEGRANT

It ought to have good compressibility.
It should be the least amount necessary.
It should have a positive mouth feel effect.
It ought to have good flow qualities.
There should be no propensity for the drugs to form complexes.
It ought to be inert and non-toxic.
Poor water solubility is what it should be.
Poor gel formation should be the result.
It should have a good capacity for hydration.

A NOVEL CONCEPT OF SUPERDISINTEGRANT

One more kind of super-absorbing substance with specialised swelling capabilities is called a superdisintegrant. These more recent compounds have increased mechanical strength and disintegration efficiency, making them more effective at lower concentrations [7]. Superdisintegrants are primarily employed in solid dosage forms at modest concentrations, approximately 1–10% of the total weight of the dosage unit [26]. These materials are not intended to suck up a lot of water or other fluids that are aqueous in nature; instead, they are intended to swell quickly. Superdisintegrants are preferred to decrease the disintegrable solid dosage forms' structural integrity. To fulfill the purpose of disintegration, they scattered (physically) throughout the matrix of the dosage form, and they will expand when exposed to a moist environment [27]. They typically have small, porous particles, which enable quick tablet dissolution in the mouth without an unpleasant mouth-feel from either gelling or large particles. Additionally, the compressible particles, enhancing the tablet's friability and hardness [28]. Effective superdisintegrants improve the compressibility and compatibility of high-dose medication formulations while having no adverse effects on their mechanical strength.

Aqueous media or water can typically be absorbed by one gramme of superdisintegrant, between 10 and 40 grammes. After absorption, isotropic swelling, swelling pressure and of the superdisintegrants particles create stress-concentrated areas where a gradient of mechanical properties will exist, resulting in the collapse of the entire structure [29].

REASONS BEHIND FREQUENT USE OF SUPERDISINTEGRANT

The applications of superdisintegrants are expanded to include mouth-dissolving films, oral disintegration tablets, fast-dispersible tablets, instant release tablets, and capsules, among others because

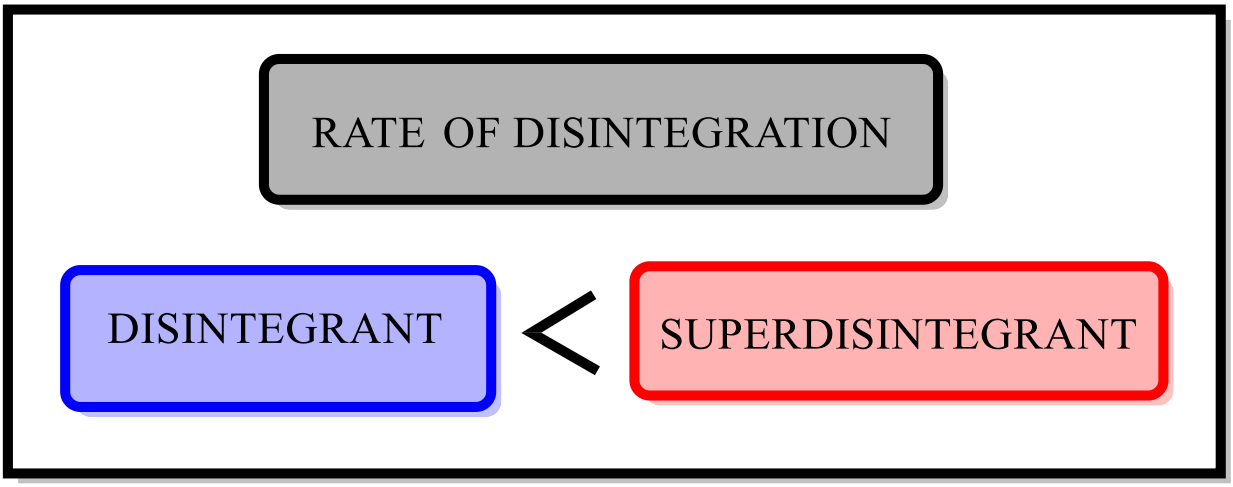


Figure 6 Comparison between disintegrant and super disintegrant on behalf of disintegration rate

Never stick to the dyes and punches.
Gives the tablet exceptional mechanical strength, making packing and transit simple
Exceptional tendency to wet, leading to fast disintegration
On disintegration, no lumps formed
Compatibility with excipients and medicinal medications that are often utilized both aquaphilic and aquaphobic formulations are equally effective.
Comparison between disintegrant and superdisintegrant on behalf of rate of disintegration shown in (Figure 6).

7.2 SUPERDISNTEGRANT'S CATEGORIES

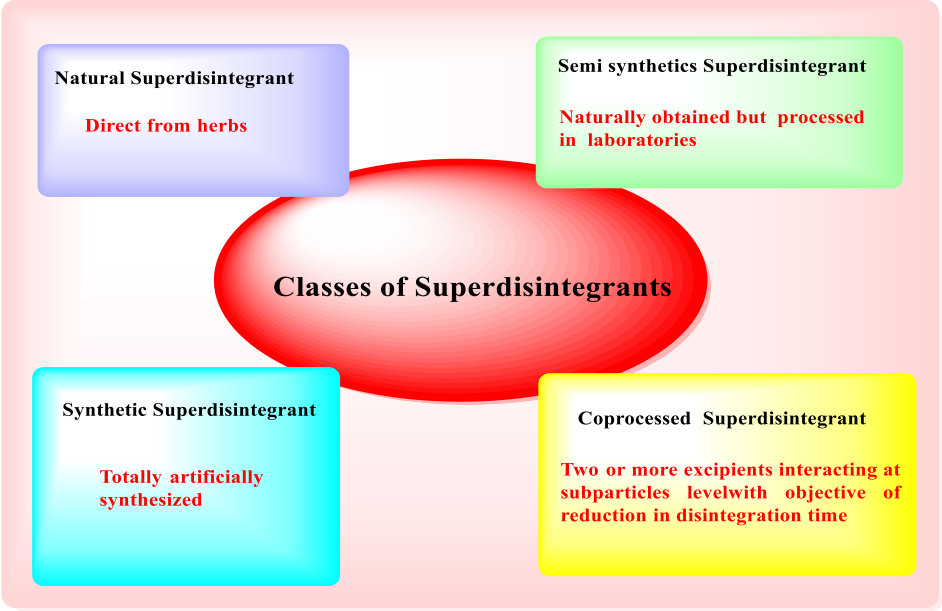


Figure 7 Classification of super disintegration

7.2.1 Superdisintegrants Obtained from Nature
Gumseg. Guar Gum, Xanthan Gum, Locust Bean, Cassia Fistula Gum, Karaya Gum, Gellan Gum.
Agar eg. Gelidiumamansii
Chitosanegβ 2-amino-2-d-glucose
Soy polysaccharide Emcosoy

Superdisintegrants Made Synthetically
Modified starches eg. Sodium Starch Glycolate
Modified cellulose eg. Croscarmellose
Cross-linked poly-vinyl pyrrolidone eg. Crospovidone, polyvinyl-pyrrolidone
Modified Resin eg. Indion 414, Kyron 314
Microcrystalline Cellulose eg. Avicel 102
Cross-linked alginic acid eg. Alginic acid NF
L-substituted Hydroxypropyl derivatives.

Co-processed superdisintegrants
EgStarlac (maize starch and lactose).
Starcap 1500 (pregelatinized starch and corn starch).
Ran Explo-C (silica, microcrystalline cellulose, and crospovidone).
Ludipress (crospovidone, lactose monohydrate and polyvinylpyrrolidone).
PanExcea MH300G (microcrystalline cellulose, crosspovidone and hydroxyl- propyl- methyl cellulose).
Ran Explo-S (microcrystalline cellulose, sodium starch glycolate and silica).

7.2.1 SUPERDISINTEGRNT OBTAINED FROM NATURE
Many nature-based pharmaceutical excipients are currently available, and numerous researchers have looked into the potential of some of plant-based materials used as pharmaceutical disintegrants [30]. These natural disintegrating agents are preferred to processed ones because they are plentiful, relatively less expensive, soft, and non-toxic by behavior. Due to their simplicity, environmental friendliness, low cost of chemical modifications, potential for degradability, and compatibility due to their natural origin, materials obtained from nature like mucilage and gums have been widely used in the drug delivery field. There are many gums and mucilage products that are available and have a high disintegration rate [31].

7.2.1.1 PROS OF NATURAL DISINTEGRANTS
Low cost: They are more affordable to use as natural resources. In comparison to synthetic material, the production cost is lower. India and many other emerging nations depend heavily on agriculture, and significant sums of money are invested in it.
Biodegradable: Since they are produced by all living things and are naturally occurring, they are biodegradable.
Public acceptance as well as patient tolerance: Danger of adverse consequences and negative outcomes than m: Natural materials have a lower manufactured ones [23].
Biocompatiblity and harmless: All of them having components of are essentially repeating sugar polysaccharide.
Environmental friendly processing: Due to the straightforward production methods used, a variety of natural chemicals produced from various plant sources are extensively used in the pharmaceutical sector and are amassed in enormously vast numbers.
Local availability: Governments in India and other similar developing nations actively promote the use of plants as medicinal excipients and also offer the infrastructure for large-scale manufacturing of products like gum and mucilage, which have numerous industrial uses. All advantages are summarized in (Figure 7), (Figure 8).

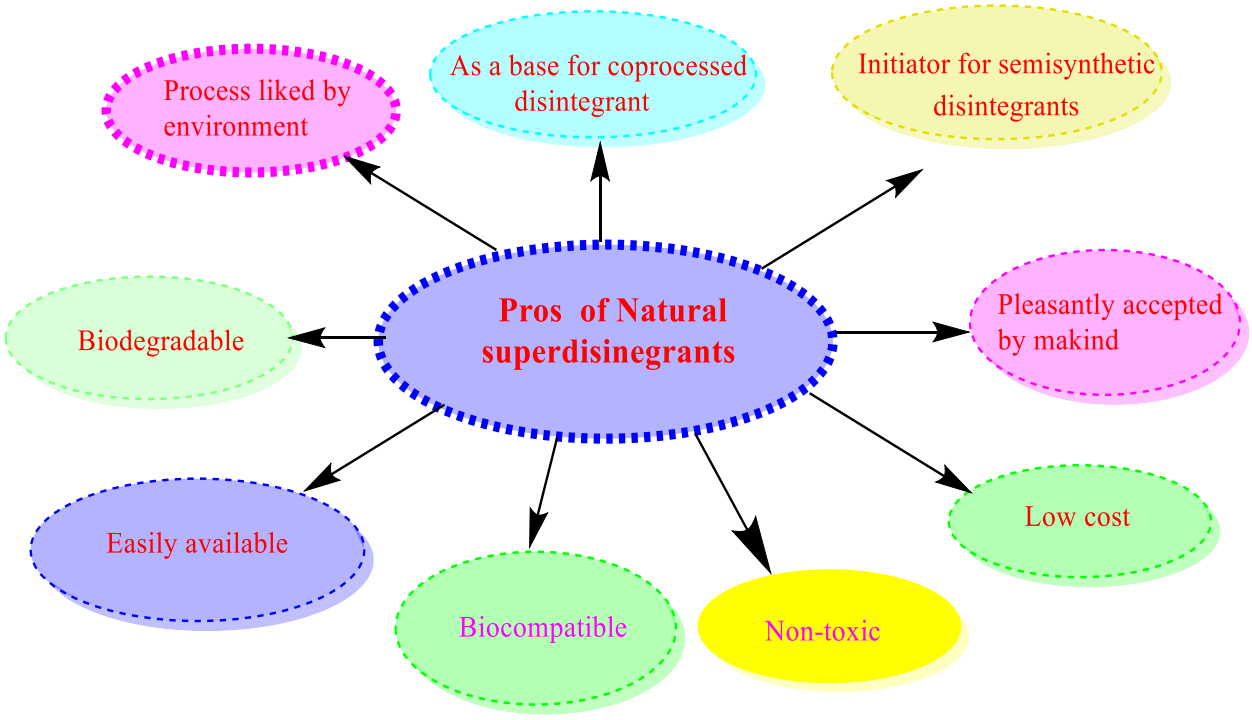


Figure 8 Advantages of superdisintegrants

7.2.1.2 EXAMPLES OF NATURAL DISINTEGRANT

Guar gum: It is a neutral polymer made of free-flowing sugar units, which are fully soluble. Additionally, permitted for use in food. It is made from the endosperm of the seed of the guar plant, Cyamopsis tetragonoloba (L) Taub, and consists primarily 50,000–8,000,000 molecular weight. It is insensitive to solubility of the tablet matrix, moisture content or pH. It is not always perfectly white and can occasionally be off-white or tan, and it tends to discolor over time in alkaline environments. It is legal in most parts of the world and used as an emulsifier, stabilizer, and thickener (e.g., EU, USA, Japan, and Australia). It is gum that naturally occurs (Jaguar as trade name).

Soy Polysaccharide: It is a naturally obtained superdisintegrant that is free of starch and sugar and can be used in food items. In tablets manufactured by direct compression using lactose and dicalcium phosphate dihydrate as diluent, soy polysaccharide is high molecular weight polysaccharides obtained from soy beans [16]. Corn starch and across-linked sodium carboxymethyl cellulose were used as control disintegrants. With results that are comparable to cross-linked CMC, soy polysaccharide works well as a disintegrating agent in direct compression formulations [32, 33].

Chitin and Chitosan: is a pure polysaccharide that could be found in the crab and shrimp's shells. As opposed to the liberated amino group in chitosan, it has an amino group that is covalently bound to an acetyl group. Chitin, the structural component of crustacean exoskeletons (such those of crabs and shrimp), and the cell walls of fungi are used to make chitosan for commercial use. In spite of the drug's solubility, Bruscato and Danti (1978) found that when chitin was added to traditional tablets, the tablets dissolved in 5 to 10 minutes. Surface free energy can be used to examine both the wetting time and the disintegration time in the oral cavity. Chitosan is the most well-known natural polysaccharide used in the pharmaceutical sector for its wide range of uses [24].

Gum Karaya: This is a type of vegetable gum that is secreted by Sterculia tree species. The sugars galactose, rhamnose, and galacturonic acid make up the acid polysaccharide gum karaya in terms of chemistry. Gum's high viscosity restricts its application as a binder and disintegrant in the creation of conventional dosage forms. The complex polysaccharide gum karaya has a negative colloid and a high molecular weight. Its hydrolysis results in the production of galactose, rhamnose, and galacturonic acid. An acetylated derivative of gum karaya is found naturally. It is the dried exudate of the Sterculia Uren tree (Family-Sterculiaceae). The terms kadaya, kadira, katila, Indian tragacanth, sterculia, and Bassora tragacanth are few synonyms for this organism. Various

findings indicated that modified gum karaya causes pills to dissolve quickly. Due to its low cost, biocompatibility, and ease of availability, gum karaya can be used as a substitute superdisintegrant to commercially available processed and semiprocessed superdisintegrants [18].

Fenugreek Seed Mucilage: The research indicated that this natural disintegrant, fenugreek mucilage, outperformed the most popular man-made superdisintegrants, such as Ac-di-sol, in the FDT formulations in terms of predominant disintegration property. According to studies, the extracted mucilage works well as a pharmacological assistant and specifically as a disintegrating agent [34]. A significant amount of a gummy substance is present in fenugreek seeds (present in seeds coatings). Mucilage generates a thick, sticky substance when it comes into contact with liquids but does not dissolve in water. Fenugreek seeds swell and when exposed to liquids become slippery, just as other materials that contain mucilage. Trigonella foenum-graceum kenned as fenugreek, is belonging to leguminous family.

Gellan Gum: The effectiveness of the gum was compared with other common disintegrants such dry corn starch, Explotab, Avicel (pH 10.2), Ac-di-sol, and Kollidon CL in Antony and Sanghavi's 1997 study on the gellan gum as a disintegrant [35]. An immediate swelling properties and high hydrophilic nature when it comes into contact with water are responsible for its disintegration quality. The tablet's complete disintegration has established itself as a superior disintegrant [33]. Gellan gum produced by a bacterium called Pseudomonas elodea in form of water-soluble polymer. A pure culture of Pseudomonas elodea produces gellan gum, which is an anionic, deacetylated exocellular polysaccharide gum, having high molecular weight, as a fermentation product cantaining a tetra saccharide repeating unit of one -D-glucuronic acid, one -L-rhamnose, and two -D-glucose residues.

Lepidium sativum Mucilage: Lepidium sativum, known as Asaliyo, its family is cruciferae and is a commonly used herbal remedy in India. Oil, seeds, roots, leaves, and other ingredients are used [36]. The amount of mucilage in seeds is larger, as well as the dimeric imidazole alkaloids lepidine B, C, D, E, and F, as well as two nascent monomeric imidazole alkaloids, which have various properties such as binding, dissolving, and gelling. It is inexpensive and generally accessible in the market.

Aegle marmelos Gum: It is made through a heat-treating process. It makes medications that aren't very more soluble [37]. In diabetic individuals, it lowers plasma insulin, raises blood sugar levels, reduces lipid peroxidation and glycosylated haemoglobin, and liver glycogen, stimulates macrophage activity, and significantly alters glutathione (growth stimulating harmone) concentration in the intestine, liver, kidney and stomach. L-Rhamnose (6.5%), L-arabinose (12.5%), and bael gum acid (7%), all purified [38-43]. It is produced from the fruits of Aegle marmelos, which dissolve more quickly and uniformly compare to ascroscarmellose sodium. Reddish-colored with a mucilaginous and astringent flavour, the ripened fruit pulp is also pulpy. The pulp has nutrients such as Omethyl fordinol and isopentyl halfordinol, as well as carbs, proteins, vitamins C and A, angelenine, marmeline, and dictamine.

Ficus Indica Fruit Mucilage: The Ficus indica tree grows quite rapidly, touching heights of up to 3 metres, and has spread-out branches along with aerial roots. Cherry-sized fruits are produced by the ficus indica. It has both therapeutic and nutritional value. It is used to treat systemic issues, wound rejuvenation, fever, discomfort, inflammation, and urinary issues [44-47]. Since it is made from the fruit pulp of the ficus indica, the mucilage is used as a superdisintegrant.

Hibiscus Rosa Sinensis Mucilage and Treated Agar: The plant is easily available, and the leaves mucilage contains the sugars L-rhamnose, D-galactose, D-glucuronic acid, and D-galacturonic acid. Agar is prepared into yare by soaking it in water for one day [14]. It also goes by the names, China rose, Chinese hibiscus, shoe flower plant and is one member of the Malvaceae family. Thickening, suspending, water retention, and disintegrant functions are all carried out by mucilage [48].

Mangifera indica Gum: The gum powder was almost insoluble in, methanol, acetone, chloroform, ether, and ethanol but soluble in water and ranged in colour from white to off-white [49]. Each, every part of the tree has pharmacological activity, such as astringent, diuretic, urethritis, diabetic, asthma, and scabies, and the gum is easily accessible and toxic-free [50]. Mangifera indica, which is a belongs to family Anacardiaceae and is often known as mango, it is harmless and used in a various kind of preparations as an emulsifying agent, suspending agent in biphasic dosage forms, disintegrant, binder (solid dosage forms).

Dehydrated Banana Powder: Plantain is another name for banana. DBP is a member of the Musaceae family and is a kind of banana known as Ethan and nenthran (nenthra vazha) [51]. It is used to treat diarrhoea and ulcers in stomach since it includes vitamin A. Vitamin B6, that aids in lowering anxiety and tension, is present in it all. Due to the rich content of carbohydrate and potassium level, essential for better functioning of the brain, it is a very good source of energy [38]. The outcomes of various researches indicate material tablet properties and physicochemical of the corn starches and banana are considerably varied. While used as disintegrant in tablet formulations, starch of banana had longer disintegration times than those containing corn starch [2].

Locust Bean Gum: It is a type of vegetable gum called galactomannan that is made from the seeds of the Mediterranean region's carob tree, Ceretonia siliqua [52]. The solubility is improved by gum of locust bean, which is also preferred as a bio glue, thickening agent, gelling in the food industry. The gum comes as an odourless, white to yellow-white powder. Organic solvents, along with ethanol, cannot dissolve it. When heated to a temperature over 850 for 10 minutes, it becomes completely soluble in water. It is only slightly soluble in hot water and in water at room temperature [53].

Plantago ovata Seed Mucilage: Plantago ovate's mucilage possesses a kind of capabilities, including dissolving, binding, and supporting qualities [54]. Using varied quantities of Plantago ovate mucilage as natural superdisintegrants, amlodipine besylate fast dissolving tablets were compressed using a direct compression method in a study. The disintegration time, drug content, weight variation, friability, hardness solubility of each formulation was all assessed. The improved formulation exhibits a quicker in vitro dissolution rate of 11.69 seconds and complete in vitro dissolution in 16 minutes. Natural superdisintegrant concentration increases with decreased in vitro disintegration time [55]. Another research also supports above lines for plantago ovate mucilage's disintegration quality. The Prochlorperazine Maleate (Dpm4) formulation was found to be promising and has shown water absorption ratio of 86%, a wetting time of 11 seconds, in vitro dispersion time of 8 seconds, and when compared to control formulation (DC0) which shows 244 seconds, 247 seconds, and 50% values respectively for the above parameters. According to the experimental data, crospovidone and Plantago ovata mucilage both produce results that are comparable to or slightly superior to each other [56].

7.2.2 SYNTHETIC SUPERDISINTEGRANT

In the formulation of tablets, synthetic superdisintegrants are frequently employed to speed up pill disintegration due to its more potency than a natural substance at low concentrations and have little impact on flow and compressibility [57]. Some examples are as follow:

7.2.2.1 Crospovidone: Crospovidone pills dissolve more quickly in the coarser grades [5]. In literature reports, different quantities of crospovidone were employed in tablet formulations. In tablets made using direct compression wet granulation techniques, crospovidone is often utilised in concentrations between 2% and 5% [58, 59]. There was no agreement among the several disintegrant action mechanisms that were initially postulated by researchers. Kornblum and Stoopak proposed that subsequent swelling would occur after wicking [60]. Crospovidone pills dissolve more quickly in the coarser grades [5]. In literature reports, different quantities of crospovidone were employed in tablet formulations. In tablets created using direct compression wet granulation techniques, crospovidone is often utilised in concentrations between 2% and 5% [58, 59]. There was no agreement among the several disintegrant action mechanisms that were initially postulated by researchers. According to Kornblum and Stoopak, wicking is followed by secondary edoema [60]. Kornblum and Stoopak put out the idea of wicking followed by subsequent swelling. Wicking was recommended by many researchers [61-63]. Some suggested that the disintegration process be good swelling efficiency or high swelling pressure [64, 65]. Later, the disintegration mechanism of crospovidone was also suggested and shown to involve strain recovery [66-68].

7.2.2.2 Starch derivatives: For disintegrants based on starch, swelling is the recognised mode of action. According to accurate measurements made by Krausbauer et al [69], the waxy corn starch, potato, corn, and tapioca starch grains all swelled to varying degrees. At 100% relative humidity (RH), swelling for corn,tapioca potato, and waxy corn starches was 9.1%, 12.7%, 28.4%, and 22.7%, respectively, after storing these starches at various humidity levels [70]. Researchers hypothesised that hydration at the network's connection points may cause the structure of the starch grain to expand, and that the total amount of hydration at junctions would determine how much swelling would occur. Because of their derivatizations, starch and its derivatives are versatile excipients that can be utilised in tablet formulations as, binders, diluents, glidants, disintegrants and thickening agents [71].

Starch's precise structure varies to some extent. According to the starch botanical source of the, the ratios of the two types of polysaccharides differ. For instance, amylose content of potato starch is stated to be 22%–25%, tapioca starch is said to be 17%–21% and 22%–30% of maize starch is believed to be [72]. Amylose is a linear a1- 4 linked polymer chain of glucose subunits cantained by starch which is soluble in nature. However, native starches may not have the standard characteristics for several of their alleged capabilities. For instance, for native starch to function effectively as a tablet disintegrant, a significant amount (10%–15%) may be needed. Additionally, starch is not very compressible. The characteristics of natural starches have been modified physically by gelatinization process and chemically [73]. The gelatinization process caused by heating the starch grains will cause the grain structures to break. Pregelatinized starches are the name for these processed starches. Different amounts of pregelatinization of starches will occur, depending on the temperature and exposure time. Pregelatinization significantly affects the preprocessed starch's physical characteristics as an excipient. The flowability and compressibility of starch are enhanced by partial pregelatinization although some disintegrant properties are still present. The excipient can be utilised as a binder after being fully pregelatinized, but it is no longer effective as a disintegrant [74]. In tablet formulations, sodium starch glycolate (chemically modified starch) concentrations can vary from 2% to 8% [75, 76]. Due to its extremely powerful swelling properties and spherical shape, sodium starch glycolate is categorised as a superdisintegrant and can enhance flow [77]. Between 2% and 8% of sodium starch glycolate can be found in tablet formulations [78].

7.2.2.3 Cellulose and Its Derivatives

Microcrystalline cellulose, a commonly used tablet excipient, is created when cellulose is subjected to acid hydrolysis, which breaks down the polymeric chains by dissolving the amorphous regions but largely preserves microcrystalline regions. After acid hydrolysis,the residue of insoluble cellulose is filtered, cleaned, and dried; after being re-suspended, drying is frequently done using a spray dryer to create dry, porous microcrystalline cellulose [79].

Microcrystalline cellulose aids in the creation of compacts at low compression forces and is utilised as a diluents, binder,or disintegrant, in tablet formulations [80]. At relatively low yield pressure it could undergo plastic deformation. Hydrogen bonds formed when adjacent particles are compacted are the commonly acknowledged mechanism for how microcrystalline cellulose works in consolidation. Nevertheless, Al-khattawi et al. showed that hydrogen bonding is not the only factor contributing to the densification of microcrystalline cellulose [81].

Cylindrical microcrystalline cellulose particles function as a disintegrant by acting as a capillary to draw fluids into dense structure for the separation of bound particles [20]. Microcrystalline cellulose's efficacy in promoting tablet disintegration isn't very high, though, and it might be necessary to use concentrations of up to 20%. Low-substituted hydroxypropyl cellulose is a low substituted version of cellulose ether and is a, water insoluble cellulose, modified hydrophilic that can be utilized as a tablet disintegrant in the range of 2% to 10% [57]. To effectively induce tablet disintegration, a concentration of up to 20% of microcrystalline cellulose may be required due to the low disintegration efficiency of this substance. The range of 2% to 10% can be employed as a tablet disintegrant when using low-substituted hydroxypropyl cellulose, a modified hydrophilic, water-insoluble cellulose. The crosslinked carboxymethyl cellulose sodium known as croscarmellose sodium is another modified cellulose excipient [82-84]. The fibrous, long, narrow, and curved particles of croscarmellose sodium are shaped in a particular way. It is suggested that this superdisintegrant has wicking, swelling, and strain recovery mechanisms [85]. In tablet formulations, it can use from 2% to 5% of the total weight [86].

7.2.2.4 Resin and Its Derivatives

The multifunctional excipient, in addition to serving as a disintegrant, enhances bioavailability due to the Donnan membrane phenomenon. Tablet disintegrants have also been made with ion exchange resins [87]. These cross-linked insoluble copolymers are made up of a primary polymer matrix that is mostly made of styrene that has been cross-linked with divinylbenzene and an ion-active functional component. The drug's progressive exchange for cations is made possible by its dual function as a cation exchange resin, which also permits a slower rate of dissolution. In order to create dosage forms with controlled release or disguised flavours, this behaviour has been studied. Drug interactions and potential enhancement of specific degradation mechanisms, like ester hydrolysis, have been linked to polacrilin potassium [88]. Polocrilin potassium is the most popular cation exchange resin that used as a disintegrant. It is produced by copolymerizing divinylbenzene and methacrylic acid, then neutralising the end result with potassium hydroxide [89]. Because of its high hydrophilicity and effective swelling properties, polacrilin potassium has a disintegrant effect [90]. Additionally mentioned as potential processes for this cation exchange resin are wicking and strain recovery [91]. Although

2% had been said to be sufficient, it is frequently used at doses of 2%–10% in tablet formulations [92]. The ability of several anion exchange resins to act as disintegrants was also studied. These included divinylbenzene and styrene cross-linked copolymers containing functional groups that are quaternary methyl amines. Anion exchange resins worked effectively as basic drug disintegrants to prevent ionic drug-resin binding [93]. The potential disintegrant properties of few anion exchange resins were also studied. These included cross-linked copolymers of styrene and divinylbenzene containing functional groups of quaternary methyl amine. In order to prevent ionic interaction between the resin and the drug, anion exchange resins worked effectively as a disintegrant for basic medicines [94]. A few synthetic disintegrants are summarized in (Table 1).

Table 1 Some synthetic disintegrants with characteristics

S.NO.	DISNTEGRANT	CHARACTERISTICS
1	Crospovidone	It cannot be dissolved at all in water. quickly spreads and expands in water. highest swelling rate, superior surface-to-volume ratio while compared to different disintegrants. If micronized grades are required to improve the dispersion condition in the powder blend, they are available. Index of swelling: 58.1% v/v [95].
2.	Croscarmellose sodium	when it comes in contact with water it quickly expands to a volume between 4 and 8 times its original size, insoluble in water. Surface area specific: 0.81 to 0.83 m2/g. 65-1.7% v/v swelling index. The fibrous, long, narrow, and curved particles of croscarmellose sodium are shaped in a particular way. It is suggested that this superdisintegrant has, wicking, swelling and strain recovery mechanisms it can range from 2% to 5% of the total weight in tablet formulations [96].
3	Sodium-starch glycolate	fast water absorption causes swelling of up to 6%. Gelling and loss of disintegration are brought on by high concentration. Index of swelling: 52-1.2% v/v. It is utilised between 4 and 6 percent. Due to its extremely powerful swelling properties and spherical shape, sodium starch glycolate is categorised as a superdisintegrant and can increase flow Between 2% and 8% of sodium starch glycolate can be found in tablet formulations [96].
4.	Croslinked Alginic acid	Promotes disintegration in dry as well as in wet granulation [97].
5.	Polacrilin potassium	It is produced by copolymerizing divinylbenzene and methacrylic acid, then neutralising the end result with potassium hydroxide. Potassium polacrilin has excellent swelling properties and is very hydrophilic. possesses a strong water absorption capability and pharmaceutical grade purity [98].

7.2.3 COPROCESSED SUPERDISINTEGRANTS

The co-processing approach is a brand-new and innovative idea that hides the unfavourable characteristics of a single excipient by interacting with multiple excipients at the sub-particle level [99]. Coprocessed excipients that have been created in this way have various advantages over the individual excipients or physical mixes of excipients, including better flow. Characteristics, compressibility, a better dissolving profile, and lower lubricant sensitivity [100]. There are a number of co-processed superdisintegrants that are marketed today. Some of these include Ludipress (lactose monohydrate, crospovidone and polyvinylpyrrolidone), Ran Explo-C (microcrystalline cellulose, crospovidone, and silica), Starlac (lactose and maize starch), Ludiflash (mannitol, polyvinyl acetate, and crospovidone). When excipients are co-processed, excipient granules are created that have better qualities than physical mixes of components or individual components [101]. The quantity of excipients used in tablet manufacturing has been significantly decreased because to these multipurpose excipients.

7.2.3.1 METHODS OF COPROCESSING

a. Melt Extrusion
b. Crystallization
c. Spray Drying
d. Solvent Evaporation
e. Granulation/Agglomeration

a. Melt extrusion
Melt extrusion is a method that turns molten substance that is extruded through an extruder into tiny beads and pellets [102]. It is preferable method because:
Complex and finely detailed shapes are feasible.
Less time is needed.
Some demerits also associated with this method
Expensive equipment and perish.
High minimum economic length.

b. Crystallization
Additionally, the process of crystallisation involves the mass transfer of a solute from a liquid solution to a pure solid crystalline phase [103].
Required conditions for crystallisaton: A solution needs to be supersaturated in order for crystallisation to happen from it. In order to maintain equilibrium, the solution must have more dissolved solute entities (molecules or ions) than it does now (saturated solution) is also required [104].
The most often employed techniques in industrial practise are
(1) mixing of a second solvent to decrease the solubility of solute this technique known as drown-out or antisolvent.
(2) solution cooling
(3) change in pH
(4) chemical reaction.

c. Spray Drying
Using this method, feed can be sprayed into a hot drying medium to change from a fluid condition to a dried particulate form [105]. It is an ongoing activity for drying and particle processing. The feed may take the form of a suspension, emulsion, solution or dispersion. According to the feed's physical and chemical characteristics, the dryer's design, and the required final powder attributes, the dried product may take the shape of powders, granules, or agglomerates [106].

d. Solvent Evaporation
A liquid manufacturing vehicle is used to carry out this procedure. The liquid production vehicle phase and the volatile solvent in which the coati ng excipient is dissolved are incompatible [107]. The coating polymer solution contains a core excipient ingredient that will be microencapsulated. Either water-soluble or water-insoluble materials can make up the core components. The core coating material combination is agitated in the liquid production vehicle phase to distribute it and create the proper size microcapsule. Then, if required, heat is applied to the mixture to help the solvent evaporate. The liquid vehicle temperature is lowered to ambient temperature (if necessary) with ongoing agitation once all of the solvent has evaporated. The microcapsules can now be employed in suspension, coated on surfaces, or alone [108].

e. Granulation/Agglomeration
The act or process of producing or crystallising into grains is known as granulation. Typically, granules range in size from 0.2 to 4.0 mm, depending on the application for which they will be used. "Agglomeration" alternative: Particle size enlargement methods, often known as agglomeration techniques, are excellent tools for changing a product's qualities. Powder aggregation is frequently utilised to enhance the product's wettability, flowability, bulk density, and attractiveness. Wet granulation and dry granulation are the two types of granulation technology used in the pharmaceutical sector. The coprocessing approach that is more popular is wet granulation [109].

Drying with co-spray
inclusion of ingredients in a dry and solid state during drying, accomplished by atomizing active ingredients in solution or as an emulsion.

Merits:
Increased tableting speed of the machine.
Consistent excipient physical characteristics for robust formulation.
Greater Uniformity than inactive granules.
Increases compressibility and hardness.
The removal of wet granulation production processes results in cost savings.

Productivity rises as machine speed rises.
There is no need to keep an inventory of different excipients.
Expenses can be reduced in cost.
Possibility to connect non-miscible goods in continuous operation
Possibility to fix and protect sensitive active compounds on neutral carrier
Possibility to mix and dry concurrently soluble and insoluble compounds

Demerits
There are some restrictions, such as a limited range of options for creating particles or structures with intricate morphologies and quick drug release rates that frequently have a burst effect [110, 111]. Some co-processed superdisintegrant with composition and preparation techniques summarized in [112, 113] (Table 2).

Table 2: **Some co-processed superdisintegrant with composition and preparation techniques**.

S.NO.	BRAND NAME	INGRADIENTS COMBINED	PREPARATION TECHNIQUES
1	(StarLac®)	Starch and lactose	Spray drying
2	Lycatab® or Sepistab®	Pregelatinized starch	Heating method followed by spray drying
3.	Vivapur 101®	Starch and microcrystalline cellulose	-
4	(StarCap 1500®)	Starch and pregelatinized starch	-
5.	Starch and acacia gum	a mixture of maize starch, acacia gum suspensions to partial pregelatinization of starch.	By drying process
6.	Starch and silicon dioxide	Rice starch with colloidal silicon dioxide.	Dispersion method
7.	Starch and magnesium silicate	Magnesium silicate with maize starch	Co precipitation
8	Ran Explo C	Microcrystalline cellulose, crospovidone silicon dioxide, and colloidal silicon dioxide microcrystalline cellulose, and sodium starch glycollate	Spray dried
9	Ludipress	Lactose monohydrate, crospovidone polyvinylpyrrolidone and	
10.	PanExcea MH300G	Microcrystalline cellulose, crospovidone hydroxyl- propyl-methyl cellulose	-
11	Ran Explo-S	Microcrystalline cellulose, sodium starch glycolate and silica	-

Conclusion

In this review, I have found that enormous attractive bonds exist among particles of solid dosage forms. But for absorption of drug, these bonding must be breakdown to enhance surface area as well as dissolution. However, numbers of disintegrating agents are available, such as natural, synthetic, semisynthetics and coprocessed, despite of them superdisintegrant are in frequent use, moreover each category follow different paths like swelling, capillary, heat of wetting, release of gas, particle repulsive force, deformation and enzymatic to achieve their targets, i.e. fastest onset of action still natural superdisintgrants are more prefered because of low toxicity, easy availability, biodegradablity, palatablity. Futhermore, different techniques have been used to enhance their activity by converting them in coprocessed form which is described in tabular form. Therefore, it is concluded that by using modern techniques, disintegration potential of natural agent could be enhanced which is responsible for absorption of active pharmaceutical agents.

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