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REVIEW : OF SUPERDISINTEGRANT INGREDIENTS IN FAST DISINTEGRANT TABLET TABLET PREPARATIONS

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ABSTRACT

This study aimed to evaluate the potential of synthetic and natural disintegrating agents in fast-disintegrating tablet (FDT) formulations. The methodology used includes a comprehensive literature review on the definition, characteristics, working mechanisms, and applications of super disintegrants in the manufacture of FDTs. The results of the study showed that super disintegrants play an important role in facilitating rapid disintegration of tablets. Synthetic super disintegrants such as crospovidone, croscarmellose sodium, and sodium starch glycolate have the advantage of lower concentrations and better intragranular effectiveness. On the other hand, natural superdisintegrants such as mucilages, gums, and polysaccharides from plants have easy availability, affordable prices, non-toxic properties, and biologically acceptable characteristics. In conclusion, the selection of an appropriate super disintegrant, whether synthetic or natural, is a key factor in effective FDT formulation and providing rapid disintegration. The combination of using super disintegrants at the granulation stage (intragranular) and before compression (extragranular) can produce better performance compared to a single method.

Keywords: FDT, Super disintegrant, Synthetic, Natural

INTRODUCTION

Oral administration of medications remains the standard choice in the pharmaceutical industry as it is considered a safe, practical, and economical method for ensuring patient compliance. However, despite the widespread use of tablets and capsules, there is a general disadvantage associated with swallowing difficulties, especially in individuals who have difficulty swallowing, which can reduce patient compliance rates, especially in elderly patients (Handayani & Abdasah, 2013).

FDT (Fast Disintegrating Tablets) is the latest innovation in drug delivery, aiming to ensure safety and effectiveness with a formulation that is comfortable when given to patients, especially special patients such as children, geriatrics, as well as patients with mental disorders including those who suffer from hangovers. or a sudden allergy attack. Non-compliance and ineffective therapy often occur in these cases. ODT dosage forms, which disintegrate rapidly when taken into the mouth, are considered a better alternative to oral medications in an effort to improve patient's quality of life and compliance with their treatment (Sa'adah, 2015).

The use of super disintegrants, such as cross-linked cellulose (croscarmellose), carboxymethyl cellulose starch glycolate (primogel, explotab), cross-linked polyvinylpyrrolidone (crospovidone), etc., is the basic method for making easily soluble tablets (FDT). (croscarmellose), sodium starch glycolate (primogel, explotab), cross-linked polyvinylpyrrolidone (crospovidone), etc., are the basic methods for making easily soluble tablets (FDT). The cause of this is that the tablet dissolves as soon as it is placed on the tongue, so that the drug is released into the saliva during this process. As soon as it is placed on the tongue, the drug is released into the saliva during this process. Consequences for the

absorption of the drug in the oral cavity and absorption of drugs from the oral cavity saliva which contains drugs that are distributed and descend into the stomach can increase the bioavailability of some drugs. Absorption of drugs from pre-gastric saliva-containing drugs that are distributed and descend into the stomach, can increase the bioavailability of some drugs. In addition, when compared to traditional pills, the number of drugs that go through first-pass metabolism is less. There are fewer drugs that go through first-pass metabolism. (Sharma *et al.,* 2012), which only contains a crusher or disintegrant whose function is to break down the tablet into smaller parts or powder by increasing the dissolution of the active substance. Crushing agents or disintegrants work against the action of the binder of the tablet and against the pressure during compression of the tablet. This material will destroy the tablet if it comes into contact with water or digestive tract fluids (Azhary *et al*., 2017).

Tablets containing super disintegrants disintegrate quickly in the mouth within a very short time, approximately 20-30 seconds after being exposed to saliva, causing the drug to immediately react pharmacologically (Ikasari. *et al*., 2022). The bioavailability of this drug is much higher than traditional tablet dosage forms. Dosage forms Dissolvable oral dosage forms are preferred and increasingly widely known among academics and industry because of their benefits. (Sharma *et al*., 2012).

This research evaluating the potential of natural superdisintegrants, such as mucilages, gums, and polysaccharides from plant sources, is still limited. Several studies have shown that these natural ingredients can be used as promising alternatives as super disintegrants in FDT formulations. The advantages of natural superdisintegrants include easy availability, affordable prices, non-toxic properties, and biologically acceptable characteristics. This study positions itself to comprehensively evaluate and compare the potential use of synthetic and natural super disintegrants in FDT formulations. This aims to identify key factors that influence the rapid disintegration of tablets, as well as provide a better understanding regarding the selection of appropriate super disintegrants in the development of effective FDT. The novelty of this research lies in a more comprehensive approach to evaluating and comparing synthetic and natural super disintegrants, as well as exploring their combined use to achieve optimal tablet disintegration. It is hoped that the research results will provide valuable insights for the development of FDT formulations in the future.

RESEARCH METHODS

Tools and materials

This research was conducted through a comprehensive literature review using various reference sources, including textbooks, scientific journals, and relevant online databases such as PubMed, Scopus, Scholar, and Sinta. The tools used in this research are computer devices, Microsoft Word word processing software, and Mendeley reference management software.

Article Selection Criteria

The articles selected in this study meet the following criteria :

1. Discuss the definition, characteristics, mechanism of action, and application of Super disintegrants in fast-disintegrating tablet (FDT) formulations.
2. Includes information about synthetic and natural super disintegrants.
3. Published within the last 10-15 years and available in Indonesian or English.

Research procedure

This research procedure consists of several steps, namely :

1. Identify and collect relevant articles through searches in various online databases such as Scopus, Scholar, and Sinta.
2. Select articles based on predetermined criteria.
3. carry out analysis and synthesis of information obtained from selected articles.
4. organize and compile the results of the literature review into appropriate sub-chapters

Data analysis

Analysis is carried out by studying, comparing, and interpreting information obtained from the articles that have been collected.

Article Selection Criteria

Inclusion Criteria:

1. Article discussing the definition, characteristics, mechanism of action and application of super disintegrants in fast disintegrating tablet (FDT) formulations.
2. Articles that include information about super disintegrants from both synthetic and natural sources.
3. Articles published in the last 10-15 years.
4. Articles are available in Indonesian or English.

Exclusion Criteria :

1. Articles that do not focus on super disintegrants in FDT formulations.
2. Articles that only discuss super disintegrants in pharmaceutical dosage forms other than FDT.
3. Articles published before 2013.
4. Articles that cannot be accessed in full-text form.
5. Articles published in languages other than Indonesian or English.

Article Selection Process

Article searches were conducted using several relevant online databases, including PubMed, Google Scholar, Scopus, and Sinta. The search utilized keywords such as "super disintegrant," "fast disintegrating tablet," "synthetic super disintegrant," and "natural super disintegrant." Following this, articles were selected based on predetermined inclusion and exclusion criteria. The chosen articles were then thoroughly analyzed to extract the necessary information for this literature review.

Research Procedure

This research was conducted through a comprehensive literature review by following these steps:

- Article Search

The article search process begins by identifying and collecting various relevant references through searches in online databases such as PubMed, Google Scholar, and Scopus. Keywords used in the search included super disintegrant, fast disintegrating tablet, "synthetic super disintegrant", and "natural super disintegrant".

- Article Selection

After gathering a number of articles, a selection process was conducted based on predetermined inclusion and exclusion criteria. Articles that met the inclusion criteria were considered for further analysis.

- Data Extraction

The selected articles extracted relevant data and information, including definitions, characteristics, working mechanisms, and applications of super disintegrants in fast-disintegrating tablet (FDT) formulations. Information on synthetic, and natural super disintegrants is also extracted comprehensively.

- Analysis and synthesis

The extracted data and information were then analyzed and synthesized to obtain an in-depth understanding of the role of super disintegrants in FDT formulation. A comparison between synthetic and natural super disintegrants was carried out to identify the advantages, disadvantages, and potential applications of each.

- Preparation of Review Results

The results of the analysis and synthesis from this literature review are then arranged systematically into appropriate sub-chapters, including background, research objectives, methods, results and discussion, and conclusions. The presentation is carried out using clear and structured language.

RESULTS AND DISCUSSION

A. Definition and characteristics of Super Disintegrant in FDT Tablet Preparations

Superdisintegrant is a key component in the formulation of Fragile Tablets (FDT). The addition of super disintegrant aims to facilitate the process of breaking or disintegrating the tablet when exposed to water, which in turn will increase the surface area of the tablet fragments and facilitate the release of the drug from the tablet. Superdisintegrant has the ability to expand quickly and high so that it can be pushed out quickly, which causes the tablet to disintegrate quickly. The use of super disintegrants is only needed in small quantities (Sulaiman, 2007).

Superdisintegrants are categorized into two types: natural and synthetic. Synthetic super disintegrants are typically used to enhance the speed and extent of tablet disintegration, thereby accelerating drug dissolution. Examples include SSG, crospovidone, croscarmellose sodium, and resins. In contrast, natural super disintegrants are frequently used in drug disintegration due to their availability, affordability, non-toxicity, and other benefits. Examples of natural super disintegrants are *Plantago ovata*, *Lepidium sativum* (*asaliyo* seed mucilage), fenugreek seed mucilage, gellan gum, and guar gum. Commonly used super disintegrants include crospovidone, croscarmellose sodium, and sodium starch glycolate (SSG). These three types of super disintegrants show very fast disintegration characteristics in making tablets using both wet granulation and dry granulation (Anggrawati, 2023).

The use of super disintegrants in pharmaceutical formulations must meet a number of criteria, and characteristics include the super disintegrant's ability to have low solubility, not have the gel-forming ability, have optimal hydration capacity, show good flow properties and can be molded easily, do not tend to form complexes with the active substance of the drug, and must also be compatible with other excipients in the formulation (Pahwa & Gupta, 2011).

B. Advantages and disadvantages of super disintegrants in FDT preparations

The disintegration process of this dosage form depends on several physical factors of the super disintegrant. These factors include the percentage of disintegrants used in the formulation, the proportion of disintegrants applied, the compatibility of the excipients with each other, the level of tablet hardness, the mixing technique, the method of adding the ingredients, and the presence of natural medicinal ingredients in the formulation. (Anggrawati, 2023). For this reason, super disintegrant materials have several advantages and disadvantages when formulating or making FDT tablets.

Advantages of Superdisintegrant:

- Exceptional wetting ability results in rapid disintegration.
- Does not form lumps when crushed.
- Compatible with commonly used therapeutic agents and excipients.
- Does not adhere to punches and dies.
- Effective at lower concentrations.
- Minimal impact on compatibility and flowability.
- More effective when used intragranularly.
- Some are anionic and may cause minor in vitro binding to cationic drugs.
- Biodegradable.

Disadvantages of Super disintegrant:

- Costly

- Time-consuming and delicate
- Highly sensitive and hygroscopic

(Shobana *et al.*, 2020).

The criteria for a good super disintegrant are

- Should have a small particle size.
- Must be non-toxic.
- Compatible with other excipients and drugs.
- Exhibits good hydration capacity.
- Possesses good flow properties.
- Provides a pleasant mouth feel.
- Effective in small quantities.

Superdisintegrants can be obtained easily, are more economical, and can be directly compressed by the user, so they are recommended over other technologies because they are more profitable. The small and porous super disintegrant particles facilitate tablets to disintegrate quickly without causing discomfort in the mouth. An ideal super disintegrant should have good flowability, compressibility, and compatibility without compromising the mechanical strength of the tablet (Bhatti & Kaushik, 2022).

C. Superdisintegrant Mixing Technique

The incorporation of super disintegrants in dosage forms mainly consists of three types of processes for using super disintegrants in making tablets as follows:

1. During granulation (intragranular), the super disintegrant is mixed with other powders and then granulated, ensuring that the super disintegrant is distributed throughout the granules.
2. Before compression (extragranular) in this process, the super disintegrant is mixed with granules that have been prepared before the compression process.
3. Combining the use of super disintegrants at both the granulation stage (intragranular) and before compression (extragranular): In this process, part of the super disintegrant is added during granulation, and the rest is mixed with the granules before compression. This method typically results in improved performance and more efficient disintegration compared to using either method alone. (Bhatti & Kaushik, 2022).

D. Types of Super disintegrants

Two types of super disintegrant materials are often used in tablet formulations, namely natural and synthetic.

Synthetic Super disintegrant: It is effective in lower concentrations than starch, besides that natural super disintegrants have less effect on compressibility and flow ability, and are effective intragranular. However, in terms of use, synthetic super disintegrants have a number of limitations that need to be considered when applying them in formulations, namely :

- More hygroscopic, which may be problematic for moisture-sensitive drugs.
- Some are anionic, potentially causing slight in-vitro binding with cationic drugs (though not an issue in vivo).
- Acidic media significantly reduce the fluid absorption rate and capacity of sodium starch glycolate and croscarmellose sodium but do not affect crospovidone. The swelling degree of Primojel and Polyplasdone XL10/crospovidone is reduced after wet granulation due to the presence of ionic strength, which negatively impacts their swelling capacity. (Pahwa & Gupta, 2011).

The following are some examples of synthetic super disintegrants that are commonly used:

1. Sodium Starch Glycolate (SSG)

SSG, an abbreviation of Sodium Starch Glycolate, is a white or slightly white powder that has good flow properties and tends to be hygroscopic. European Pharmacopoeia 6.0 explains that when SSG is observed under a microscope, it can be seen that SSG consists of granules that have an irregular shape, such as an egg or pear with a size of around 30-100 µm, or a round shape with a size of around 10-35 µm. Due to its hygroscopic nature, SSG needs to be stored in an airtight container to prevent the effects of temperature and humidity which can cause clumping (Rowe, 2009). SSG can be produced from various types of starch, but the synthesis of SSG from potato starch produces optimal disintegration properties. The synthesis process involves converting starch with an esterification agent such as sodium trimetaphosphate or phosphorus oxychloride in an alkaline environment. Significant amounts of hydrophilic carboxymethyl groups are added to disrupt hydrogen bonds in the starch structure. This allows the polymer to absorb more water without forming a gel that can inhibit dissolution (Mohanachandran PS, 2011).

2. Crospovidone

Crospovidone can rapidly absorb saliva into the tablet, causing volume expansion and hydrostatic pressure necessary for rapid disintegration in the mouth. When examined under a scanning electron microscope, crospovidone particles appear granular and highly porous. This unique porous property facilitates fluid absorption into the dosing system and induces rapid disintegration. In contrast to other super disintegrants such as sodium starch glycolate and croscarmellose sodium, crospovidone shows almost no tendency to gel formation, even at high concentrations. Crospovidone is a material that is very easy to compress due to its unique particle morphology. Crospovidone is used as a super disintegrant at low concentrations (2-5%) in direct compression, wet granulation and dry processes (Jain & Savanth, 2023).

3. Croscarmellose

Croscarmellose sodium is a substance that has a fibrous, fibrous structure and does not have cavities. It is a cross-linked polymer of carboxymethylcellulose and is available as a white or greyish-white powder. Croscarmellose sodium can expand up to 4-8 times its weight and has excellent water absorption capacity. As one of the super disintegrants commonly used in Rapid Disintegrating Tablet (FDT) formulations, Croscarmellose sodium is often used in a concentration range of 0.5%-5%. The pH range of Croscarmellose sodium is 5.0-7.0 (Rowe, 2009).

4. Alginat

Alginate is a hydrophilic colloidal material that is obtained naturally from certain types of seaweed or can be chemically modified from natural sources such as alginic acid or alginic acid salts. Alginic acid is a polymer derived from seaweed, consisting of D-mannuronic and L-guluronic units. Its properties of having a high affinity for water absorption and a large absorption capacity make it a superior super disintegrant. Alginic acid is generally used as a disintegrating agent in concentrations of 1-5%, while sodium alginate is used in concentrations of 2.5-10%. This ingredient is also effective in formulations containing ascorbic acid and multivitamins (Shobhana K, 2020).

5. Explotab

It was chosen because it is a super disintegrant that is effective in making tablets both through granulation and direct molding processes and has good flow properties. Usually, the concentration of Explotab used in making tablets is around 4-6%. However,

when the concentration exceeds 8%, the tablet disintegration time tends to increase (Soemarie *et al*., 2018).

6. Alginic Acid

Alginic acid has good absorption ability in aqueous and HCl solutions and has good swelling ability in buffers. This causes chaos due to the interaction between the swelling and shape recovery systems. The effectiveness of alginic acid in dissolving is not influenced by the characteristics of the media. When used sparingly in tablet formulations, alginic acid, sodium starch glycolate, and crospovidone can cause very rapid disintegration. Even in more hydrophobic formulations, the disintegration activity of alginic acid is only slightly lower than that of other super disintegrants. In the supplement and nutraceutical industry, where the use of natural additives is a routine requirement, alginic acid is recommended as a super disintegrating agent for tablets, especially in simple water formulations made from natural ingredients (Chen, 1997).

7. Sodium Alginate

Alginate is a natural polymer that has been researched for its potential in the fields of food and medicine. However, information about its potential use as a tablet super disintegrant is still limited. In phosphate buffer, the swelling-driven absorption of sodium alginate and alginic acid in the liquid appears more obvious, whereas, in corrosive acid and water, the wick-driven absorption of the liquid is more pronounced. Alginic acid and sodium alginate work through swelling and shape recovery mechanisms. Due to its gel formation, sodium alginate is not generally used as a tablet disintegrator (Osman Nur, A., 2014).

Each super disintegrant material has its working mechanism. The following is a table of the working mechanism of this synthetic super disintegrant material :

Table I. Mechanism of action of synthetic superdisintegrants

Superdisintegrant	Superdisintegrant mechanism of action
Sodium starch Glycolate	Absorbs water quickly, causing swelling 12 times in less than 30 seconds when the drug tablet reacts and swells in 3 dimensions. This high level of swelling acts as a sustained release matrix. (Santosh Kumar & Kumari, 2019).
Crospovidone	Carrying out a swelling mechanism by wicking (Santosh Kumar & Kumari, 2019).
Croscarmellose Sodium	Swelling and wicking in 10 seconds causes swelling up to 4-8 times, swelling in 2 dimensions (Santosh Kumar & Kumari, 2019).
Alginat	The same as alginic acid because it is a derivative (Santosh Kumar & Kumari, 2019).
Explotab	Works quickly, absorbs water, and expands in water by 200 - 300%, causing rapid hydrophilicity, swelling and breaking down (Sharma D, 2013).
Alginic acid	Performs a fast swelling or wicking mechanism (Santosh Kumar & Kumari, 2019).
Sodium Alginate	Sodium alginate operates by triggering swelling and restoration of shape. Due to its ability to form gels, the use of sodium alginate as a tablet disintegrating agent is not common. (Osman Nur, A., 2014).

Natural superdisintegrant:

Currently, many pharmaceutical excipients are derived from plant materials, and researchers have explored various potential uses for these naturally derived pharmaceutical super disintegrants. These plant-based ingredients are considered alternatives to synthetic products for several reasons, including local availability, environmental friendliness, biological compatibility, renewable nature, and lower cost compared to many synthetic products.

The majority of research related to disintegration activity in natural polymers focuses on polysaccharides and proteins, due to their ability to produce various materials and properties based on their molecular structure. Polysaccharide hydrocolloid structures such as mucus, gum, and glucan are abundant in nature and are generally found in various higher plants. Mucilage, as one of the secondary metabolites of plants, has a high concentration of hydroxyl groups in polysaccharides, which results in a high capacity to bind water. Because of this, research on the role of mucus in plant interactions with water has become a topic of interest. It has been proposed that mucilage's ability to hydrate may provide a protective mechanism for plants against desiccation. Therefore, natural sap and mucilage have been widely explored as disintegrating agents (Pahwa & Gupta, 2011).

Some examples of plants used as super disintegrants are:

1. Jackfruit seeds

The starch derived from jackfruit is characterized by its crisp texture, slight granularity, free-flowing nature, and stability. Evaluation of pre-compression parameters indicated that the granules exhibited desirable qualities. In vitro dissolution studies were conducted on all matrix tablets prepared according to USP standards. The dissolution study results revealed that the type and proportion of jackfruit seed starch used as a super disintegrant significantly impacted dissolution parameters. Various formulations of starch derived from jackfruit seeds show promise as super disintegrants. Recent studies have demonstrated that jackfruit seed starch exhibits swelling capabilities and water absorption profiles similar to those of croscarmellose and sodium starch glycolate. (Suryadevara *et al*., 2017).

2. Chitosan

Chitosan has a high swelling capacity when exposed to water, and due to the pressure caused by its capillary action, it will disintegrate (Sulistriyani *et al*., 2022), Chitosan is a biopolymer compound produced from the deacetylation of chitin isolated from the shells of hard-skinned animals (Crustacea), such as crabs, clams, shrimp and crab. The production volume in Indonesia reaches 300,000 tonnes, making the chitosan industry begin to develop to the point where it can produce 1-1.5 tonnes per month. The chitosan produced has been used as a raw material for the chemical, food, and pharmaceutical industries (Dewi Astuti *et al*., 2022).

3. Gum Karaya

Gum Karaya is a natural exudate obtained from trees belonging to the Sterculia genus. Chemically, it comprises an acidic polysaccharide composed of galactose, rhamnose, and galacturonic acid. Its high viscosity has traditionally limited its application as a binder and disintegrant in conventional dosage forms. Nevertheless, research indicates the potential of gum karaya as a tablet disintegrator. Several studies have demonstrated that modified karaya gum can facilitate rapid tablet disintegration. Therefore, gum karaya presents itself as an alternative super disintegrant to synthetic and semi-synthetic materials, offering affordability, biocompatibility, and easy accessibility. (A. Shirwaikar, 2008).

4. Guar Gum

Guar gum, derived from Cyamopsis tetragonolobus seeds, finds frequent application across the cosmetic, food, and pharmaceutical sectors. Primarily employed in solid oral dosage forms, it serves as both a binder and a tablet disintegrator. Additionally, guar gum

functions as a suspending agent, thickener, and stabilizer in numerous topical products. Furthermore, it has gained popularity as a drug carrier within release-controlled-release systems. (Nur *et al.*, 2014). Guar gum primarily comprises high molecular weight polysaccharides, typically ranging from approximately 50,000 to 8,000,000, containing galactomannan. It serves as a thickening, stabilizing, and emulsifying agent. This compound has been approved for use in numerous countries worldwide, including the European Union, the United States, Japan, and Australia. Guar gum exhibits stability in tablet formulations against variations in pH, water content, or matrix solubility. However, resulting tablet colors may vary from grayish-white to brown, and there can be color changes over time, particularly in alkaline tablets. (P. Batham,1986).

5. Gellan Gum

Gellan Gum, also referred to as Gelrite, is a water-soluble polysaccharide derived from the bacterium Pseudomonas elodea. It is a deacetylated, anionic, exocellular polysaccharide with a high molecular weight, produced via fermentation by pure cultures of Pseudomonas elodea. Its molecular structure comprises a repeating tetrasaccharide unit consisting of one L-rhamnose, one D-glucuronic acid, and two D-glucose residues. Gellan gum demonstrates effective disintegrating properties compared to conventional agents like dry corn starch, Explotab, Avicel (pH 10.2), Ac-di-sol, and Kollidon CL. The tablet disintegration mechanism may involve sustained release. Modified xanthan gum, which is biodegradable and compressible, exhibits favorable swelling characteristics, making it suitable as a hydrophilic excipient in rapid disintegration tablets. Rapid disintegration roxithromycin tablets were formulated using lower levels of modified gellan gum. (Sharma V, 2013).

6. Hibiscus Rosa Sinensis Slime and Processed Agar

This plant, known by various names such as hibiscus, Chinese rose, and Chinese hibiscus, is a member of the Malvaceae family. Its mucilage serves several purposes including thickening, emulsifying, water retention, and as a disintegrant. It is readily available and its leaves contain mucilage composed of L-rhamnose, D-galactose, D-galacturonic acid, and D-glucuronic acid. The resulting gelatin is obtained by soaking it in water for a day. (K. Prabhu, 2010). The leaves of Hibiscus rosa sinensis are rich in mucilage, making them a supplementary ingredient in pharmaceutical tablet formulations. These formulations underwent evaluation on several parameters before and after compression, including tablet hardness, thickness, friability percentage, and wetting time, all of which fell within acceptable limits. Tablets containing 6% mucilage exhibited an in vitro disintegration time of approximately 24 seconds. In contrast, Gellan gum rapidly swells upon contact with water, owing to its highly hydrophilic properties. (P. J. Antony, 1997).

7. *Xanthan gum*

Xanthan gum, derived from the bacterium *Xanthomonas campestris*, is a polysaccharide. It is recognized in the United States Pharmacopoeia (USP) for its high hydrophilicity and its capacity to form a minimal gel. *Xanthan gum* exhibits low solubility in water and possesses significant swelling properties, which facilitate rapid disintegration (Mohanachandran PS, 2011). *Xanthan Gum* is generated via fermentation involving the bacterium *Xanthomonas campestris*. It exhibits high hydrophilicity and has a tendency to form a gel with low viscosity. The fundamental structure of *xanthan gum* comprises a chain of β-(1→4)-D-glucose units, with each glucose unit linked to a trisaccharide composed of mannose, glucuronic acid, and mannose. The negatively charged carboxylate group of glucuronic acid facilitates the formation of a highly viscous liquid at a suitable pH. Despite being classified as a non-gelling agent, *xanthan gum* yields a thick medium due to weak associations. Although it readily swells, *xanthan gum*

delays drug release in tablet formulations containing 4% crospovidone by approximately 42 seconds. (Rowe RC, 2003).

8. The *Lepidium sativum* slime

The mucilage extracted from the *Lepidium sativum* plant, a member of the Cruciferae family, is commonly referred to as Asaliyo and is frequently utilized as a herbal remedy in India. This plant is readily available in the market and is cost-effective. Various parts of the plant, including leaves, roots, oil, seeds, and other components, are used for medicinal purposes. The seeds, in particular, contain significant amounts of mucilage, along with dimeric imidazole alkaloids like lepidin B, C, D, E, and F, as well as two recently discovered monomeric imidazole alkaloids, semilepidinoside A and B. The mucilage derived from *Lepidium sativum* possesses distinctive characteristics, including binding ability, disintegration properties, and gel formation, among others (K. K. Mehta, 2010).

9. Fenugreek Seed Mucus

The mucilage extracted from Fenugreek seeds, derived from the Trigonella *foenum-graceum* plant, is commonly referred to as Fenugreek. This plant, belonging to the legume family, finds various applications in food, food additives, and traditional medicine. Both ripe and raw Fenugreek leaves and seeds are frequently used as vegetables. Fenugreek has a long history of use in treating diverse digestive disorders such as stomach colic, bloating, dysentery, diarrhea, and loss of appetite. Additionally, it is employed to address chronic coughs, sore throats, liver and spleen swelling, rickets, gout, and diabetes. The plant possesses gastroprotective, anti-urolithic, diuretic, anti-dandruff, anti-inflammatory, and antioxidant properties. Fenugreek seeds are considered a tonic and are utilized in postnatal care and to enhance breast milk production in lactating mothers. The high mucilage content in Fenugreek seeds, a natural gummy substance found in the seed coating, forms a thick, sticky mass upon contact with liquid.. (Gandhi & Akhtar, 2019). While mucilage itself does not dissolve in water, upon contact with liquid, it transforms into a dense, adhesive substance. Similar to other mucilage-rich substances, fenugreek seeds exhibit swelling and become slick when in contact with liquid. This study demonstrated that fenugreek mucilage, serving as a natural disintegrant, exhibited superior disintegration capabilities compared to commonly utilized synthetic super disintegrants like Ac-di-sol in Fast Dissolving Tablet (FDT) formulations. The findings of the research confirmed that mucilage extracted from fenugreek serves as a valuable pharmaceutical additive and can effectively function as a disintegrating agent (R. Kumar, 2009).

10. The *Ficus Indica* Fruit Slime

The mucilage extracted from the pulp of *Ficus indica* fruit acts as a super disintegrant. Ficus indica, commonly referred to as the Indian fig tree, is a tall tree that can grow up to 3 meters in height. It is characterized by its rapid growth, spreading branches, and aerial roots. The fruit of Ficus indica, similar in size to a cherry, possesses both nutritional and medicinal properties. Dried and fresh *Ficus indica* fruit provides 230 kcal (963 KJ) of energy per 100 grams or 3.5 ounces. This fruit is utilized in treating various health conditions such as fever, pain, inflammation, wound healing, blood disorders, and urinary tract issues (H. Abdul Ahad, 2011).

11. The *Plantago ovata* slime

The findings indicated that Plantago ovata (PO) seeds were incorporated into the formulation of flurbiprofen fast-dissolving tablets (FDTs). Tablets containing PO demonstrated swift disintegration owing to their capacity to readily expand. Moreover, the study included details on the post-compression assessment of flurbiprofen FDTs and

the pre-compression evaluation of flurbiprofen FDT powder blends containing PO. Furthermore, data on the in vitro disintegration time and wetting time of flurbiprofen fast-dissolving tablets utilizing *Plantago ovata* were provided (Mohammed *et al.*, 2016). Tablets comprising 8% w/w *Plantago ovata* mucilage and 60% w/w microcrystalline cellulose have demonstrated encouraging outcomes. In the in vitro dispersion assessment, the tablet exhibited a dispersion time of 8 seconds, a wetting time of 11 seconds, and a favorable water absorption ratio (Shirsand *et al*., n.d.).

12. Agar and Processed Agar

It is a dried gelatin obtained from various species in the Gelidanceae family, such as Gelidium amansii, and several other species of red algae such as Gracilaria and Pterocladia. Agar is yellowish gray or white to almost colorless, has an unpleasant odor with a slimy taste, and is available in powder, sheet, or coarse flake form. Agar-agar consists of two types of polysaccharides, namely agarose which provides gel strength and agar pectin which is responsible for the viscosity of the agar solution. The high gel strength makes it a potential candidate as a super disintegrant (Bhardwaj P, 2018).

13. Mango Peel Pectin

Pectin extracted from mango peel, comprising approximately 20-25% of mango processing by-products, has been recognized as a valuable source of high-quality pectin suitable for producing functional films and jellies. This pectin is classified as a complex heteropolysaccharide, known for its hydrophilic properties. A study conducted by (Malviya R, 2011). Exploring the capabilities of pectin extracted from mango peel as a super disintegrant reveals its potential. While not as potent as synthetic super disintegrants, mango peel pectin exhibits commendable solubility and a greater swelling index, rendering it a feasible option for incorporatinginto fast-disintegrating tablet formulations. (Libermann HA, 1989).

14. Cassia Fistula gum

The seeds of Cassia Fistula are harvested from the Cassia Fistula tree. The sap derived from Cassia Fistula seeds comprises D-mannopyranose units linked to β-(1→4) polymers, with a random arrangement of D-galactopyranose units linked to α(1→6) as side chains. Carboxymethylation and carbamoyl ethylation processes applied to Cassia gum have been observed to enhance solubility in cold water, elevate viscosity, and increase resistance to microbes compared to the native gum. Consequently, endeavors have been undertaken to integrate calcium or sodium salts derived from Cassia Fistula gum subjected to carboxymethylation or carbamoyl ethylation as a super disintegrant in the development of Fast Dissolving Tablet (FDT) formulations (Gandhi & Akhtar, 2019).

15. Grasshopper Bean Gum

Locust Bean gum, also known as Carob bean gum, is extracted from the endosperm of the seeds of the carob tree Ceretonia siliqua, primarily found in the Mediterranean region. Similar to certain other polysaccharides like starch and cellulose, which consist of elongated glucose sugar chains, locust bean gum has a higher ratio of mannose to galactose compared to guar gum, resulting in slightly different properties. This disparity allows for synergistic interaction between the two gums, leading to the formation of a denser gel compared to using either gum individually. This gel serves as a binder and disintegrant at varying concentrations. Locust bean gum finds application in numerous pharmaceutical scenarios, including the development of novel drug delivery systems. Additionally, it is commonly employed in the food industry as a thickening and gelling agent. It has been reported that locust bean gum shares bioadhesive properties with guar gum and can enhance solubility. Several studies have also highlighted the potential utility of locust bean gum in pharmaceuticals and biotechnology (Gandhi & Akhtar, 2019).

E. Superdisintegrant mechanism

The drug release mechanism associated with fast-disintegrating formulations containing super disintegrants involves various processes. These processes include wicking (absorption), swelling, deformation, and electrostatic repulsion, all of which exert significant effects, particularly on tablet disintegration (Kumar & Saharan, 2017).

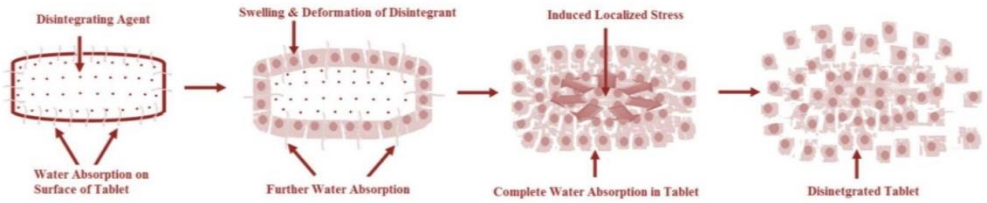

Figure 1. Superdisintegrant mechanism (Gupta *et al*., 2011).

The swelling and deformation are mechanisms by which disintegrants, including super disintegrants, contribute to the destruction of tablets in formulations. This mechanism is based on the swelling of the disintegrant when absorbing water, which causes the rupture of the tablet matrix due to the local pressure generated inside the tablet. This effectively increases the space available for rapid release of the drug (Gupta *et al*., 2011).

The mechanism of action of super disintegrants involves several processes:

The "**swelling**" In this mechanism, disintegration occurs when certain materials, such as starch, swell when exposed to water. This overcomes the adhesion of the other ingredients in the tablet, thereby causing the tablet to disintegrate. For example, sodium starch glycolate uses this mechanism (Safitri *et al.*, 2019).

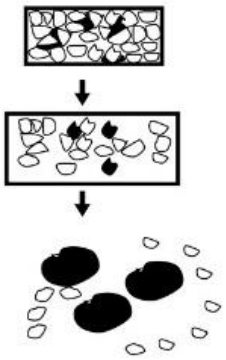

Figure 2. Swelling mechanism

The particles swell and rupture the matrix after swelling upwards propagating local stress throughout the matrix (Rakesh Pahwa1 *et al*., 2010).

"wicking" In this mechanism, disintegration occurs through the physical properties of particles that are compact but have low compressibility. Particles with these properties undergo disintegration which increases porosity and provides a pathway for fluid penetration into the tablet via capillary action. This breaks the bonds between the particles and results in the tablet breaking (Safitri *et al.*, 2019).

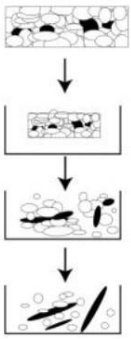

Figure 3. The mechanism in the picture is that water is drawn into the pores by disintegration and reduces the tightness of the physical bonds between particles (Gandhi & Akhtar, 2019)

Because of the heat of wetting

As disintegrants come into contact with moisture, their exothermic properties lead to capillary air expansion, generating local pressure that aids in tablet disintegration. While this mechanism elucidates the action of certain disintegrants, it fails to account for the mechanism of action of modern disintegrants. (Zhao N, 2005).

Enzymatic reactions

Several enzymes found in our body also act as disintegration agents. The ability of enzymes to bind to binders helps in the tablet disintegration process. The swelling produced by this enzyme exerts outward pressure, causing the tablet to break and increasing water absorption, which in turn produces large amounts of granules to support a more effective disintegration process (Vandana & Priyanka, 2012).

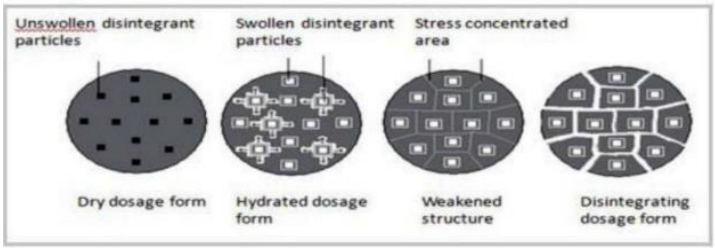

Figure 4. Enzymatic reaction

Due to Gas Release

When carbonates and bicarbonates react with citric acid or tartaric acid within the tablet upon wetting, carbon dioxide is liberated, leading to pressure buildup within the tablet. This pressure contributes to tablet disintegration. Effervescent mixtures are utilized by pharmacists aiming to formulate ultra-fast dissolving tablets or tablets that disintegrate rapidly. However, these effervescent agents are highly sensitive to minor fluctuations in humidity and temperature levels. Therefore, stringent environmental control is imperative during tablet manufacturing (Vandana & Priyanka, 2012).

The acid-base reactions (Chemical reactions)

Through the internal release of CO2 in water resulting from the interaction of citric acid and tartaric acid (acids) with alkali metal bicarbonates or carbonates (base) within the tablet when exposed to water, rapid fragmentation occurs. The tablet undergoes

disintegration due to the pressure exerted on it. As carbon dioxide gas is released, the dissolution of the active pharmaceutical ingredient (API) in water is enhanced, along with a taste-masking effect. However, this disintegration agent is highly sensitive to even slight variations in temperature and humidity levels, necessitating stringent environmental controls during tablet manufacturing. The effervescent mixture is preferably added rapidly before compression and can be incorporated into the formulation in two separate fractions (Ishikawa T, 2001).

Deformation

It is a mechanism by which starches such as potato or corn starch, which are initially elastic, become plastic under high compaction pressure during tableting. When these tablets are exposed to water, the potential energy of the starch granules is triggered, causing disintegration (Safitri *et al*., 2019).

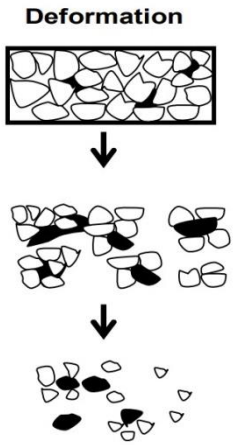

Figure 5. Disintegrants draw water into the pores and reduce the physical bond strength between particles. (Rakesh Pahwa1 *et al*., 2010).

Combination Reactions

In this mechanism of action, the disintegrating agent uses a combination of both wicks and swelling action, for example, Crospovidone (Vandana & Priyanka, 2012).

Electrostatic repulsion mechanism

Particle repulsion theory is one of the disintegration mechanisms that tries to explain the swelling phenomenon of tablets made from disintegrating materials that do not expand. According to the concept proposed by Guyot-Hermann, particles that do not undergo extensive swelling, such as starch, are still capable of causing tablet disintegration. This theory explains that water will penetrate into the tablet through hydrophilic pores, forming a continuous starch network that allows the flow of water from one particle to another, generating significant hydrostatic pressure. Then, water will penetrate between the starch granules due to its affinity for the starch surface, thereby breaking the hydrogen bonds and other forces that hold the tablet together. Electrical repulsion between particles is also an important disintegration mechanism, and the presence of water is necessary to facilitate this process. (Rakesh Pahwa1 *et al*., 2010). Involves electrostatic repulsion, Electrical repulsion between particles acts as a disintegration mechanism, and the presence of water is necessary for the particles not to swell, ultimately leading to disintegration of the tablet (Safitri *et al*., 2019).

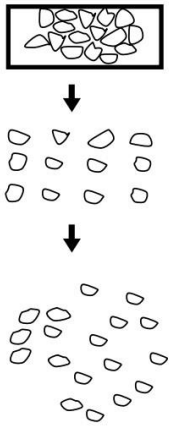

Figure 6. Water is drawn into the pores and the particles repel each other due to the resulting electrical force.

In making FDT tablets, of course, there are different drug release mechanisms in the mouth. The following are several drug release mechanisms based on the type of superdisintegrant group used.

Table II. Mechanism of drug release based on the type of superdisintegrant group

Group	Superdisintegrant	Mechanism of Action	Information
Crosslinked Cellulose	1. Croscarmellose 2. Ac-Di-Sol 3. Nymce ZSX 4. Primellose Solutab 5. Vivasol L-HPC	Inflates 4-8 times in less than 10 seconds expands and absorbs water.	Expanding in 2 dimensions can be printed directly or with free granulation.
Crosslinked PVP	1. Crospovidone 2. Crospovidone M 3. Kolidon 4. Polyplasdone	Slightly expands and returns to its initial size after printing, but acts by a capillary system	Insoluble in water and can be absorbed to obtain porous tablets
Crosslinked Strach	1. Sodium starch Glycolate 2. Explotab 3. Primogel	Inflates 7-12 times and takes less than 30 seconds	Expands in 3 dimensions.
Natural Super disintegran	1. Soy Polysaccharides 2. Emcosoy	Contains no sugar or starch for a nutritional product	
Calcium Silicate		Absorption action	Maximum concentration 20-40%

(Gupta, 2010)

Various kinds of super disintegrant results when combined with other super disintegrants :

1. Sodium starch glycolate with crospovidone uses the active substance Diphenhydramine Hcl, FDT Diphenhydramine HCl Tablet Formulation produces the fastest disintegration time, namely 41.4 seconds, which does not exceed the disintegration time limit for FDT tablets. (Rahmawati *et al*., 2022).
2. Sodiumstrach glycolate with croscarmellose sodium using the active substance Metoclopramide produces the fastest disintegration time, namely 52.25 seconds. This shows that the combined concentration of croscarmellose and sodium starch glycolate (SSG) in this formula can produce fast disintegration of the metoclopramide HCl tablet formula over time. short one (Ikasari *et al*., 2022).
3. Jackfruit seed starch is a natural super disintegrant, a combination of croscarmellose, and the active substance irbesartan. From the results of this research, we can conclude that the use of 5% alkaline extracted jackfruit seed starch (JFS2) and 5% croscarmellose sodium as super disintegrants can produce faster disintegration conditions and a better dissolution rate in the Irbesartan fast disintegrating tablet formulation (Suryadevara *et al*., 2017)
4. Chitosan and glycine with the active substance Domperidone produced disintegration times ranging from 21 ± 3 seconds to 85 ± 5 seconds. This can show that tablets with the addition of chitosan-glycine conjugate can disintegrate quickly (Kumari, 2021)
5. *Plantago ovata* with *Lepidium sativum* uses the active substance Flurbiprofen. Data in the article show that the isolated natural super disintegrant, especially PO, is effective in increasing tablet disintegration to produce flurbiprofen FDT which disintegrates quickly, in accordance with the criteria for this dosage form. (Mohammed *et al*., 2016).
6. Cassia tora polysaccharide (small *ketepeng*) and Natrium Starch glycolate produce Valsartan. Optimum conditions are found at a Cassia tora polysaccharide content of 7.5% (Pawar, H., 2014).
7. Crospovidone and Croscarmellose Sodium with the active ingredient Hydrochlorothiazide. The results show that all formulas meet the disintegration time requirements set by the British Pharmacopoeia. The tablet disintegration time is influenced by the combination of crospovidone and the combination of croscarmellose sodium with a higher super disintegrant resulting in a faster disintegration time (Farahiyah&Syaifullah Sulaiman, 2021).

The advantages of adding super disintegrants in making tablet formulations are as follows:

Accurate dosing: As a solid unit dosage form, tablets offer the convenience of accurate dosing, allowing precise dosing, especially suitable for pediatric and geriatric patients.

1. Increased bioavailability: These tablets can increase drug absorption in the pre-gastric period, thereby increasing bioavailability and clinical effectiveness with lower doses.
2. Patient compliance: Requiring no water to swallow, these tablets are a convenient option for patients who travel frequently or have limited access to water
3. Ease of administration: Convenient for dosing, particularly beneficial for individuals with swallowing difficulties, including the elderly, children, or individuals with cognitive impairments.
4. Barrier-free: The risk of choking due to physical obstruction during swallowing is reduced, increasing safety and compliance of use.
5. Enhanced palatability: Ensures a residue-free mouthfeel, enhancing the overall user experience. Additionally, taste-masking methods can be applied to diminish the bitter taste associated with medications.
6. Excellent stability: The tablet exhibits robust stability and is less susceptible to environmental fluctuations.

7. Straightforward packaging: This can be efficiently packaged using blister packs without the need for specialized packaging materials.
8. Business opportunities: Provide new business opportunities through product differentiation, promotions, and product line expansion.
9. Cost-efficient: Demonstrated to be economically advantageous in terms of production, packaging, and distribution when compared to alternative commercial products.
10. Versatile technology: Suitable for advanced product development, including veterinary, over-the-counter, and prescription drugs (Pahwa & Gupta, 2011).

CONCLUSION

Fast Disintegrating Tablets (FDT) are an important innovation in drug delivery, especially for special patients such as children, geriatrics, and patients with mental disorders. These tablets disintegrate rapidly in the mouth, increasing drug bioavailability and patient compliance with treatment. The use of super disintegrants in FDT formulations plays a crucial role in facilitating the rapid disintegration of tablets when in contact with water. Synthetic super disintegrants are used to increase the disintegration speed and dissolution rate of drugs, thereby accelerating the pharmacological effects of drugs. The mechanism of action of superdisintegrants involves swelling, deformation, electrostatic repulsion, and wicking. These processes contribute to rapid tablet disintegration and drug release, increasing the effectiveness of rapid-disintegrating tablet formulations. Various types of super disintegrants such as croscarmellose, crospovidone, sodium starch glycolate, alginic acid, and soy polysaccharides have different mechanisms of action but aim to facilitate rapid tablet disintegration. Thus, the use of rapid disintegrating tablet formulations with super disintegrants can provide significant benefits in improving patient quality of life and adherence to treatment.

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