AN UPDATED PRECISE REVIEW ON SUPERDISINTEGRANTS

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ABSTRACT

Superdisintegrants are an emerging trend in the Pharmaceutical field. In the application oral disintegration tablets (ODTs), fast-dispersible tablets, capsules, mouth-dissolving films superdisintegrants have found to be an important existence especially for ODTs and fast dispersible tablets based on their decentralization time. Thus these formulations always achieved a better patience compliance in case of Pediatric, Geriatric or Psychiatric Patients suffering from Dysphasia as Dysphasia has grown to be an alarming concern all over the Globe. The superdisintegrants works on mechanisms like wicking, swelling, deformation etc. The superdisintegrants are used at a very low concentration in solid dosage forms. With the rapid demand of novel drug delivery, the drug delivery system has become one of the mile stone of present research. The use of super disintergants is not new. Only with the recent development of superdisintegrants agents it has become possible to manufacture ODTs.

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INTRODUCTION
Disintegrants or disintegrating agents are the excipients added to the various pharmaceutical formulations mainly in tablets and some encapsulated formulations to enhance the breakdown of these into smaller particles in the aqueous media by increasing the surface area and enhancing the quick release of the drug substances. These are having very important role in fast releasing tablet formulations. Superdisintegrants are the agents added to tablet mostly and some encapsulated formulations to initiate the breakup of the tablet and capsule “slugs” into smaller fragments in an aqueous environment there by increasing the available surface area and promoting a more rapid release of the drug substance. They promote moisture penetration and dispersion of the tablet matrix. There are some methods of putting disintegrating agents into the tablets:-
A. Internal Addition (Intragranular)
B. External Addition (Extragranular)
C. Partly Internal and External. [1]
The disintegration of dosage forms depends upon some physical factors of disintegrants/superdisintegrants. These are as follow:

i. Percentage of disintegrants present in the formulation.
ii. Proportion of disintegrants used.
iii. Compatibility with other excipients.
iv. Presence of surfactants.
v. Hardness of the tablets.

vii. Mixing and types of addition. [16]
Superdisintegrants are usually used at a low amount in the solid dosage forms, typically 1-10% by weight relative to the total weight of the dosage form. Disintegrants are added to tablet to promote the breakdown of the tablet and capsule “slugs” into smaller portions in an aqueous environment thus increasing the surface area and initiate a more rapid release of the drug substance. Tablet disintegration gives first drug release. The function of disintegrant is the capacity to interact very much with water. The various mechanisms of disintegrants are the combinations of swelling or wicking or deformation. Disintegrants used intragranularly and extragranularly provide more effectiveness thus enabling to breakdown the tablet into granules and the required granules further disintegrate to release the drug into solutions. When compare, intragranularly used disintegrant are more compelling than extra granularly as extragranularly used disintegrant exposes to wetting and drying thus reducing the activity and shelf life of the disintegrant. The conventional tablets are intended to be swallowed whole and desired to disintegrate releasing the desired medicaments for resolution providing a suitable curative efficacy in the Gastro Intestinal Tract. Superdisintegrants offer much improvements over starch. But a problem is always associated with it which is hygroscopic nature. So, it quite mandatory for a pharmacist to manufacture superdisintegrants which are effective at low concentration and efficiency of disintegrating & intra granularly effective. The choice of a super disintegrants and its performance are of much crucial. [28, 56, 57, 58]

INFLUENCE OF SUPERDISINTIGRANTS ON THE RATE OF DISSOLUTION FROM ORAL SOLID DOSAGE FORMS
Solid Dosage Form must undergo drug solubility as drugs must be absorbed but poorly soluble cannot be absorbed so common superdisintegrants are preferred. It is mandatory for a drug required to be absorbed into systemic circulation for its proper therapeutic efficacy via the different membranes which are biological. For its significant drug dissolution tablets formulations which are conventional requires proper rapid disintegration.
Some commonly used superdisintegrants are Crospovidone, Croscarmellose Sodium & Starch Glycolate which are highly efficient at very low concentration levels (2-5% W/W) [10-14]. Drugs like Ciprofloxacin disintegrate in the oral cavity on its contact with saliva thus improving curative efficacy. Ciprofloxacin is a chemotherapeutic antibiotic which is a synthetic one of the fluoroquinolonone drug class. As most oral dosage forms are manufactured for direct ingestion or for chewing purpose or dissolution in water where some of them are absorbed in mouth.

Still it is a major problem for pediatric & geriatric, psychiatric & travelling patients to swallow the tablets. But the disintegrating tablet in oral drug delivery system overcome all the mentioned problems and readily forms a substitutional form of oral medication. They are characterized by high porosity, low density & quite true hardness. [31, 44]

MECHANISMS OF DISINTEGRATION OF SUPERDISINTEGRANTS
A. Swelling of the Disintegrate:- It is a phenomenon in which certain disintegrating agents. E.g. Starch impart the disintegrating effect. Swelling action provides coming in contact with water. This is the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force.[49]

B. Porosity and Capillary Action (Wicking):- Disintegrants that do not readily swell exert their action through porosity by providing the track for the penetration of fluids into tablets and the liquids are sucked into their pathways through the various capillary action and breaks the inter particulate bonds and finally the tablet. Particles not swelling facilitate disintegration via their physical nature of cohesiveness and compressibility.[48]

C. Deformation: - During tablet formation the disintegrate particles get deformed and this deformed particles finally get turn to their normal & stable structure when they come in contact with water. Starch grains under deformation will return to their original shape when the initial pressure is removed. But after applying the compression forces, the starch grains are considered to be deformed more permanently and are referred to be
energy rich as their energy being released upon exposure to water. High compression leads the elasticity to be deformed to plasticity with energy much higher.

D. By Enzymatic Action:- The enzymes present in the body act as disintegrants. They help in disintegration by destroying the binding action and thus helps in disintegration and dissolution.

E. Due to disintegrating particle/particle repulsive forces:- Another mechanism of disintegration attempts explaining the swelling of tablet made with non swallow able disintegrants. Guyot- Hermann has proposed a particle repulsion theory based on the observation that non-swelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is mandatory for it. Researchers found that repulsion is secondary to wicking. It is believed that no single mechanism is responsible for the action of most disintegrants. [32, 33, 50]

F. By the release of gases:-Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet gets disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very quickly dissolving tablets or fast disintegrating tablet. [18, 36]
DIFFERENT COMMONLY USED SUPER DISINTEGRANTS ARE:-

1. Modified Starches: Sodium Carboxy Methyl Starch (Sodium Starch Glycolate): Potato Starch (Solanum tuberosum) gives the product with the best disintegrating properties though it is possible to synthesis starch glycolate from a wide range of native starches. After selecting the potato starch, the second step involves the cross linking of the starch which is carried out by using an FDA approved. Starch esterifying agent such as tri metaphosphate or phosphorous oxychloride in alkanine suspension. [38]

![Diagram of a cross-linked polymer](image)

2. Cross linked Polyvinyl Pyrrolidone: Also known as crospovidone immediately wicks saliva into the tablet thus generating the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth. It involves the principal of swelling and wicking unlike other disintegrants which constitutes only swelling. Crospovidone particles appears highly porous and granules when examined under electron microscope. They are highly compressible materials as a result of their unique particle morphology. [4-9]

![Diagram of crospovidone](image)

3. Croscarmellose Sodium: Croscarmellose is a modified cellulose whose DS is higher than that of Sodium Starch Glycolate. Croscarmellose sodium is described as a cross-linked polymer of carboxy methylcellulose. Apart from the differences between the starch and cellulose polymer backbones, there are Differences between the synthetic processes used to modify the polymer.

![Diagram of croscarmellose sodium](image)

4. Soy polysaccharide: Natural superdisintegrant do not contain any starch or sugar thus readily used in nutritional products. It has significant effect on gastrointestinal functions, nutrient balance, steroid excretions, glucose tolerance, serum lipids, and other parameters in humans.

5. Crosslinked Alginic acid: Gets easily disintegrate by swelling or wicking action, a hydrophilic colloidal substance having high sorption capacity.
6. Gellan gum:- Polysaccharide which is anionic of linear tetrasaccharides obtained from *Pseudomonas elodea* which is a bacterium. The repeating unit of the polymer is a tetrasaccharide, which consists of two residues of D-glucose and one of each residues of L-rhamnose and D-glucuronic acid.

7. Xanthan gum:- Obtained from *Xanthomonas campestris*. Hydrophilicity is quite high, gelling tendency & water solubility very low. Xanthan gum is a polysaccharide secreted by the bacterium *Xanthomonas campestris*, used as a food additive and rheology modifier, commonly used as a food thickening agent (in salad dressings, for example) and a stabilizer (in cosmetic products, for example, to prevent ingredients from separating).[15-18]

8. Calcium Silicate:- Highly porous, light weight basically acting by wicking action.

9. Pharmaceutical Superdisintegrants, quick disintegrating enzyme having solid oral dosage compositions, rapid disintegrating tablets etc. also constitute the super disintegrants in various formulations.

10. L-HPC: (Low substituted hydroxyl propyl cellulose)- It is insoluble in water, very quickly swells in water. Grades LH-11 and LH-21 exhibit the greatest degree of swelling. Certain grades can also provide some binding properties while retaining disintegration capacity.
TABLE 1: LIST OF SOME SUPERDISINTEGRANTS IN TABULAR FORM: [45]

<table>
<thead>
<tr>
<th>SUPERDISINTEGRANTS</th>
<th>EXAMPLE</th>
<th>MECHANISM OF ACTION</th>
<th>SPECIAL COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crosscarmellose®</td>
<td>Crosslinked Cellulose</td>
<td>-Swells 4-8 folds in&lt;10 seconds.</td>
<td>-Swells in two dimensions</td>
</tr>
<tr>
<td>Ac-Di-Sol®</td>
<td></td>
<td>-Swelling and wicking both</td>
<td>-Direct compression or granulation</td>
</tr>
<tr>
<td>Nymce ZSX ®</td>
<td></td>
<td></td>
<td>-Starch Free</td>
</tr>
<tr>
<td>Primellese®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solutab®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vivasol®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L-HPC®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crosspovidone</td>
<td>Crosslinked PVP</td>
<td>-Swells very little and returns to original size after compression but act by capillary action</td>
<td>Water Insoluble and spongy in nature so get porous tablet.</td>
</tr>
<tr>
<td>Crosspovidon M®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kollidon ®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyplasdone®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium starch glycolate</td>
<td>Crosslinked linked starch</td>
<td>-Swells 7-12 folds in &lt;30 seconds</td>
<td>-Swells in three dimensions and high level serve as sustain release matrix</td>
</tr>
<tr>
<td>Explotab ®</td>
<td></td>
<td></td>
<td>-Promote disintegration in both dry or wet granulation</td>
</tr>
<tr>
<td>Primogel®</td>
<td></td>
<td></td>
<td>-Does not contain any starch or sugar. Used in nutritional products.</td>
</tr>
<tr>
<td>Alginic Acid NF</td>
<td>Crosslinked alginic acid</td>
<td>-Rapid swelling in aqueous medium or wicking action</td>
<td></td>
</tr>
<tr>
<td>Satialgine ®</td>
<td></td>
<td></td>
<td>-Highly porous</td>
</tr>
<tr>
<td>Soy Polysaccharides</td>
<td>Natural super disintegrant</td>
<td></td>
<td>-Optimum concentrations is between 20-40%</td>
</tr>
<tr>
<td>Emcosoy ®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium Silicate</td>
<td>Wicking action</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ADVANTAGES OF SUPERDISINTEGRANTS: [25,55]

i. Wetting causing fast disintegration.

ii. Lump formation is hardly on disintegration.

iii. No stickness to the punches and dyes.

iv. Having good mechanical strength to the tablet formulation.

v. Easy packing and transportation.

vi. Disintegration is maximum followed by dissolution.
vii. Superdisintegrants improve disintegrant efficiency resulting in decreased use levels when compared to traditional disintegrants.

viii. Superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs.

ix. Superdisintegrants achieves increased bioavailability & immediate adsorption from mouth, pharynx and oesophagus as saliva emerges down.

x. Contains an acceptable masking property of taste & is stronger as well as friable.

DISADVANTAGES:- [55]

i. Hygroscopic nature

ii. Anionic may cause a little *in-vitro* attachment with other cationic drugs.

USES OF SUPERDISINTEGRANTS:-

i. Application of Oral Disintegration Tablets

ii. Fast Dispersible tablets, capsules, mouth dissolving films etc.

iii. Gets optimized on their disintegration time.

iv. *Superdisintegrants are used* to improve the efficacy of solid dosage forms.

v. They promote moisture penetration and dispersion of the tablet matrix.

vi. Their major use is to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablet

SUPERDISINTEGRANT’S EFFECT ON DRUG RELEASE OF ORALLY DISINTEGRATING TABLET (ODT’S) -

ODT’S are defined as those which disintegrate or dissolve in saliva without the need of water. Tablet disintegrating in mouth, enhancing the clinical effect of the drug via pregastric adsorption through the mouth, pharynxyal, esophagus. They overcome the difficulty of swallowing associated with gagtric, pediatric or psychiatric patients. Some conventional tablets take several minutes to dissolve in mouth while ODT’s disintegrates & dissolve in mouth in less than 10 seconds producing a rapid action. The effect of superdisintegrant, on ODT’s was evaluated by measuring the in-vitro disintegration time, wetting time, water absorption ratios, drug release by dissolution and in-vivo oral disintegration time. The disintegration of orally disintegrating tablets is dependent on the nature of superdisintegrant, concentration in the formulation and its source. [14]

METHOD OF INCORPORATION OF DIFFERENT SUPERDISINTEGRANTS:-

Incorporation of Superdisintegrants are of three types in the dosage forms:-

1) Internal Addition (Intragranular):-During this process the superdisintegrants are incorporated within the granules by blending with other powders carrying out the granulation. In Internal Addition (Intragranularly), the disintegant is mixed with other powders before wetting the powder mixtures with the granulating fluid. Thus the disintegant is incorporated within the granules. [60]

2) External Addition (Extragranular):- In external addition method, the disintegant is added to the sized granulation with mixing before compression.
3) Partly Internal and External:– In this method, part of disintegrant can be added internally and part externally. This results in immediate disruption of the tablet into previously compressed granules while the disintegrating agent within the granules produces additional erosion of the granules to the original power particles. [17, 18]

SELECTING SUPERDISINTEGRANTS FOR ORALLY DISINTEGRATING TABLET FORMULATION:–

There has been rapid growth in the number of orally disintegrating tablets (ODT) available on the market during the past years. An ODT is generally recognized as a solid dosage form containing a medicinal substance that disintegrates and dissolves quickly and dissolves in the mouth without water within 60 seconds or less. ODTs are also known as quick dissolves, fast melts, or fast-dissolving, rapid-dissolve, or orally dissolving tablets. Products of ODT’s have entered in the 1980’s. These products have increased in popularity because consumers, old and young, find them convenient and easy to use. In general, ODTs can accommodate as much as 500 mg of active ingredient, although 100–200 mg is a reasonable limit for more rapid disintegration. The ODT’s should disintegrate immediately within a second when placed on the tongue. They should meet the patience compliance for pediatric, geriatric, psychiatric patients with dysphagia.

CRITERIA FOR CHOOSING A SUPER DESINTIGRANT

Although the superdisintegrant primarily affects the rate of disintegration, then the rate of dissolution when used at high levels it can also affect mouth feel, tablet hardness, and friability. Thus, several factors must be considered when selecting a superdisintegrant.

Disintegration:– The disintegrant must immediately wick saliva into the tablet to generate the volume expansion and hydrostatic pressures essential to provide immediate disintegration into the oral cavity.

Compactability:– It is quite essential for a super disintegrant to have a good hardness at a given compression force to produce stronger tablets. Thus, a more compactable disintegrant will produce stronger, less-friable tablets.

Feel of the mouth:– For getting the desired patient compliance, disintegrants must provide a palatable experience to the patient. Big particles can result in a awkward feeling in the mouth. Thus, tiny particles are chosen.

Flow:– As with all direct-compression tablet formulations, achieving suitable flow and content uniformity is utmost essential to attain the required dosage per unit. It improves the flow properties of the total blends. In a standard tablet formulations, superdisintegrants are used at 2–5 wt % of the tablet formulation. With ODT formulations, disintegrant levels can be significantly higher. An ideal disintegrant should have poor solubility, poor gel formation, good hydration capacity, good compressibility, flow properties and no tendency to form complexes with the drugs.

The selection of the optimal disintegrant for a formulation depends on a consideration of the combined effects of all of these factors.

Effect of Combination of Natural Super disintegrants on Fast Dissolving Tablets of Linisopril:–

Main objective of this study was to formulate & evaluate the rapidly dissolving tablets of Linosopril using natural super disintegrants in combination. Isolated mucilage of Montago ovato, Aloe vera & extracted mucilage of Hibiscus rosainensis to release significant exemption profile for proper disintegration in desired time.[40,43]. Lisinopril is the main drug of the angiotensin conventional enzyme (ACE inhibitor) used in the
treatment for many respiratory disease including congestive heart failure. The IUPAC name of Lisinopril is \( N^2-(1S)-1\text{-carboxy-3-phenylpropyl}\)-L-lysyl-L-proline. Lisinopril were obtained as a gift sample from Modern Lab., Indore (M.P). Plantago ovata seeds, Aloe vera and Hibiscus rosasinesis leaves were purchased from local market, Berhampur, India. Microcrystalline cellulose, mannitol, magnesium stearate, talc were purchased from Noble Enterprises, Berhampur, India. [40-42]

**TYPES OF SUPER DESINTIGRANTS:**

Natural Superdisintegrants: -These super disintegrating agents are natural in origin and are preferred over synthetic substances because they are quite cheaper, abundantly available, non-irritating and nontoxic in nature. The natural materials like gums and mucilages have been extensively used in the field of drug delivery for their easyavailability, cost effectiveness, Eco friendliness, emollient and non-irritant nature, non-toxicity, capable of multitude of chemical modifications, potentially degradable and compatible due to natural origin. There are several gums and mucilages are available which have super disintegrating activity. [37]

Synthetic Superdisintegrants:- A group of superdisintegrants including croscarmellose sodium (Ac-Di-Sol) sodium starch glycolate (Primojel and Explotab) and crospovidone (Polyplasdone XL) lighten most of these problems. Use of the superdisintegrants in fast dispersible tablet is possible as tablet shows optimum physical properties. They are expensive, not easily available and toxic in nature. Super disintegrants are Effective in lower concentrations than starch. Less effect on compressibility and flow ability. More effective intragranularly. Effective in lower concentrations than starch. [37]

Examples of Natural Superdisintegrants:-
- Nemusulide, Famotidine, Ofloxacin, Piroxicam, Amlodiphine Beysilate etc.

Examples of Synthetic Superdisintegrants:-
- Terbutaline Sulphate, Carvidilol, Balsatan, Ziduvudine, Felodiphine, Lisinopril etc.

**Formulation and evaluation of Norfloxacin Dispersible tablets using natural substances as Disintegrants:**

Norfloxacin is a man-made a synthetic chemotherapeutical antibacterial used in curative treatment of Urinary Tract Infections. Norfloxacin’s dispersible tablets were prepared using natural substances as disintegrant. e.g., Ispaghula husk powder, Cassia tora powder, Cassia tora powder (defatted), and Cassia nodosa powder in varying concentration by direct compression method. Norfloxacin was provided as a gift sample by Ankur drugs & pharma. Limited, Daman, Gujarat, Ispaghula husk powder, Cassia tora powder, Cassia nodosa powder were provided by Prasad Traders Pusad and Gautam Global, Dehra Dun, India, authenticated by Agarker research Institute, Pune. The present investigation was carried out to prepare dispersible tablets of Norfloxacin using Plantago ovata a natural disintegrant, seed husk (Isapghula), Cassia tora and Cassia nodosa as a disintegrants to establish standards required for the dispersible tablet, to attain the perfection level of the impelling concentration of the disintegrant and to compare the formulations with marketed & the trade product. [44]

1-ethyl-6-fluoro-4-oxo-7-piperazin-1-yl-1H-quinoline-3-carboxylic acid
CONCLUSION:
Overall summary of superdisintegrants which are available and essential are being discussed as far as possible. The ease of availability of these particular agents have always been a realistic approach in the preparation of ODT’s. The availability of the various technologies and manifold advantages of Fast dissolving tablets may be ODT’s will surely increase its demand in the near future. Disintegrants which are prepared by intra and extra granulation method was found to be the most effective & curative as they disintegrate rapidly when compared to other disintegrants, and the percentage drug clemency also shows a higher disintegration profile.

REFERENCES:
1. Rudnic EM, Lausier JM, Chilamkarti RN, Rhodes CT. Studies on the utility of cross-linked polyvinyl pyrrolidone as a tablet disintegrant. Ind. Pharm. 1980, 6, 291-309.
32. http://formulationvinesia.com


