FDA-Approved Natural Superdisintegrants and their comparision in formulation of mouth Dissolving Tablet

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Abstract: For administration of any drug oral route is generally preferred than any other route because it is easy and best route for drug administration. Many patient feel uneasiness to swallow the tablet i.e paediatric and geriatric patient. So to avoid their inconvenience mouth dissolving tablet has been preferred now a days. These tablet have various advantages as it improve bioavailability and drug action and response to the body. Mouth dissolving tablet dissolve rapidly in mouth without any requirement of water which makes patient more convenient. In this study we will see how natural superdisintegrate are more effective like Fenugreek seed mucilage, Plantago ovate husk and dehydrated banana powder is used and compared in the formulation of mouth dissolving formulation. Natural superdisintegrant has numerous benefits as chemically inert, nontoxic, less expensive, widely available. So in this article we will study about natural superdisintegrant which are FDA approved used in formation of mouth dissolving formulation

Keywords: Mouth dissolving formulation; Superdisintegrant; fenugreek seed mucilage; Plantago ovate husk.

1) INTRODUCTION

Comparing various route for drug administration still oral route is preferred as it is easy and convenient to take without any irritation and pain. But many people face difficulty in swallowing the tablet especially paediatric, geriatric and mentally retarded people(1). To avoid this inconvenience mouth dissolving tablets are prepared as they rapidly melt and without the need of water they dissolve in saliva and give its action. Mouth dissolving tablets are also called as Fastly dissolving tablet, orodispensible tablet, quick dissolving tablet etc(2) so this type of mouth dissolving tablet are Novel type of tablet(3,4). Recently orodispersible term used by the European pharmacopeia. Orodispersible or mouth dissolving tablet are solid dosage form having superdisintegrant due to which these formulation get dissolve within a minute in a mouth so there is no difficulty in patient for swallowing these tablets.

Mouth dissolving tablets when placed in the saliva automatically melts and dissolve in the saliva without any requirement of water for disintegration and gets quickly absorbed. ODT target is for patient such as pediatric and geriatric, mentally retarded, bedridden patient and the patient who are travelling can take these medication without the requirement of water(4,8).

Mouth dissolving tablets which are approved by the FDA are also termed as orally disintegrating tablet. These tablet firstly disintegrate in smaller granules and then melt in the mouth which make patient to swallow easily without requirement of water. Mouth dissolving tablet works on the principle of disintegration, dissolution and absorption of drug. Disintegration of generally affected by disintegrant added in the tablet and aqueous fluid present in the surrounding to penetrate the tablet. Disintegrants are added in the tablet as it insert the aqueous fluid in the tablet which swells the tablet and finally break the particles to disintegrate. Disintegrating agent which are added in the tablet to promote breakdown of tablet or capsule for faster disintegration and quick absorption. In many orally disintegrating tablet superdisintegrant play a major role in its formulation. Superdisintegrant in comparison to disintegrating agent increases the rate of disintegration and dissolution more better in comparison to disintegrating agent. Superdisintegrant used may be synthetic or natural in origin(5). In the present article we will study and compare natural superdisintegrant over synthetic superdisintegrant because they are safe, non-toxic, environment-friendly, biodegradable in nature, have more patient compliance and they are renewable in nature. This review basically used to study different natural polymer which are beneficial to us, their pharmaceutical action in mouth dissolving tablet formulation and comparision between different natural polymers which are used in the formulation of mouth dissolving tablet and how it helps in the betterment of tablet and capsule then synthetic one. (6) Natural polymers improve some tablet properties in the fast dissolving tablets like it improves disintegration time of tablet so that tablet disintegrate fast and for this some superdisintegrant work as a natural polymer like plantago ovate husk, fenugreek seed mucilage and dehydrated banana powder.

FDA approved natural superdisintegrant-

All the polymers should be recognized by united state Food and drug administration. These Approved polymers are listed in the category of generally safe according to code of federal regulation 21. Some are considered as safe food additive because these polymers meet fully standard of safe criteria.

2) SUPERDISINTEGRANT –

Superdisintegrants are those substance which when added in the tablet formulation it enhances the breakdown of tablet and capsule into smaller granules in the presence of aqueous fluid which penetrate and swell the tablet to disintegrate. One gram of superdisintegrates break on absorbing 10-40 gram of water.

2.2) Best properties of Superdisintegrants

1. It must be poorly soluble.
2. Formation of poor gel.
3. Having hydration capacity
4. Must be having good flow properties,
5. No complexation property with the drug
6. Good feeling in mouth
7. It must be non-toxic and inert in nature

1) **Good Compressibility and Flow Properties** - For an ideal superdisintegrant it should be highly compressible and flow property must be good \( ^{(49-51)} \)

2) **Good capacity of hydration** - Drug and additives which are hydrophobic in nature may create problem in disintegration, so in that case if disintegrant of highly hydrated capacity is being added to the drug it solve the problem and tablet gets easily disintegrates and dissolve. \( ^{(52)} \)

3) **Poor solubility** - Solubility of drug is main in the tablet preparation as disintegration and dissolution highly depends on the solubility of the tablet \( ^{(53)} \)

4) **Poor gel forming capability** - Gel generally slow down the dissolution of drug as drug firstly go through the layer of gel and then after release in the body. In the formation of tablet gel concentration must be 4-6% only \( ^{(54)} \)

2.1) **Types of superdisintegrant used in formulation of mouth dissolving tablet**

Superdisintegrant can be defined as the substance which takes less onset of time for disintegration. Supedisintegrant may be natural or synthetic in nature.

Synthetic superdisintegrant e.g.- SSG, Crospovidone, Croscarmellose sodium etc. \( ^{(7)} \)

2.1.1) **Natural superdisintegrant**

These polymer are found in nature i.e plant and animal origin  

- Plantago ovate, fenugreek seed mucilage, Dehydrated banana powder

2.1.2) **Synthetic superdisintegrant**

The polymers which are manufactured in laboratory by polymerization process are called synthetic polymers. e.g.- crospovidone, croscarmelose sodium etc.

2.3) **Criteria for selection of superdisintegrant**

Superdisintegrants primarily increases the rate of disintegration \( ^{(10)} \)

2.3.1) **Essential factors considered for selection of suitable superdisintegrants:**

1. Disintegration process increases when tablet comes directly in contact with saliva.

2. Water is not required for swallowing

3. Produce good mouth feel.

4. Have good flow \( ^{(11-12)} \)

5. Good for patient who avoid taking tablet.

6. Good taste

<table>
<thead>
<tr>
<th>Drug</th>
<th>Superdisintegrant</th>
<th>Compression method</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lisinopril</td>
<td>Plantago ovate mucilage, aloevera mucilage,</td>
<td>Direct compression</td>
<td></td>
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<tr>
<td></td>
<td>hibiscus rosinensis</td>
<td></td>
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<tr>
<td>Nimesulide</td>
<td>Lipidium sativum</td>
<td>Direct compression</td>
<td>( ^{(14)} )</td>
</tr>
<tr>
<td>Ondensetron HCl</td>
<td>Plantago ovate husk</td>
<td>Direct compression</td>
<td>( ^{(47)} )</td>
</tr>
<tr>
<td>Granisetron HCl</td>
<td>Plantago ovate husk</td>
<td>Direct compression</td>
<td>( ^{(47)} )</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>Treated agar</td>
<td>Direct compression</td>
<td>( ^{(15)} )</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>Locust bean gum</td>
<td>Solvent evaporation</td>
<td>( ^{(47)} )</td>
</tr>
<tr>
<td>Diclofenac sodium</td>
<td>Fenugreek gum</td>
<td></td>
<td>M.Udaykumar 2014</td>
</tr>
<tr>
<td>Cinnarizine</td>
<td>Chitosan</td>
<td></td>
<td>Wet granulation</td>
</tr>
<tr>
<td>Famotidine</td>
<td>Plantago ovate mucilage, seed powder</td>
<td>Non aqueous wet granulation method</td>
<td>( ^{(16)} )</td>
</tr>
</tbody>
</table>

**Table-2** Action of various superdisintegrants

- **starch** - It works on the principle of capillary action, water penetrate inside the tablet, which lead to disruption of tablet

- **Chitin and Chitosan** - Water uptake occur causes moisture sorption

- **Isapghula Husk** - It is having high swelling property which causes rapid disintegration

- **Gums** (Guar Gums, Gum Karaya, Agar, Gellan Gum) - Swells in water and rapidly disintegrate

**Table-3** Sources of some common natural Superdisintegrants
4) **Natural superdisintegrant**

Natural superdisintegrant are derived from natural sources and are preferred over synthetic superdisintegrant which are derived in lab by polymerization. There are several gums and mucilage’s are available which have super disintegrating activity (25).

Many investigations on natural polymers having disintegrant activity are being focussed on polysaccharides and proteins, as they are having ability to produce a wide range of materials and properties on the basis of their molecular structures (26).

Natural disintegrant are preferred over synthetic superdisintegrant due to following reasons:

1) cheaper
2) Easily and abundantly available
3) Non-toxicity.
4) Eco-friendly in nature (27)

**Method of Extraction or Isolation of natural superdisintegrant**

Rebamipide is a white crystalline powder and has no odor but has a bitter taste.

5.1) **Plantago ovata**

Husk of Plantago ovata is used for polysaccharide formation (family plantaginaceae). Polysaccharide derived from plantago ovate considered as superdisintegrant. Plantago ovate mucilage is used as natural superdisintegrant having characteristics like Binding properties, disintegrating, sustaining properties and high Swelling index. (28).

The dried seeds of Isapghula husk of a plant called as plantagoovata. The swelling index of the tablets is around 89+ 2.2%/v/v. Muclilage of plantago ovate is responsible for swelling property and disintegration of tablet (29).

The mucilage is clear, colourless gel; obtained from the seed coat of psyllium. Milled seed mucilage is white fibrous material which is hydrophilic in nature (30).

Natural Polymer- Plantago ovate seed mucilage

Marketed drug - GranisetronHCl

Disintegration time- 17.10 sec

Concentration used – 5% w/w (31)

5.2) **Fenugreek seed mucilage**

It is an herbaceous plant of leguminous family obtained from the seeds of Trigonella-foenum-graecum. Fenugreek seed contain natural gummy substance called Mucilage. It has numerous medicinal use as gastroprotective, Diuretic, anti-inflammatory. Mucilage show better disintegrating property. It also used for lactating mothers to increase the lactation (32).

Natural polymer- Mucilage of fenugreek seed

Marketed drug- Metformin hydrochloride

Disintegration time- 15.6sec

Concentration used-4% w/w

5.3) **Dehydrated banana powder**

Dehydrated banana powder (family Musaceae). containing vitamin A and vitamin B6. It is used for the treatment of diarrhoea, gastric ulcer related problem, Stress and anxiety (33).

Banana powder has excellent natural superdisintegrant property as it contains potassium, which is well being used for brain functioning (34).

Tablets containing banana powder as disintegrating Bharathi M et al. / International Journal of Pharmacy & Therapeutics, 8(3): 2017, 96-103. 101 | Page agent were dispersed rapidly within 15 sec and showed 92.09% drug release in 15 min (35).

Natural polymer- Dehydrated Banana powder

Marketed drug- OndansetronHCl

Disintegration time - 15.3%

Concentration used -6%/w/w

Arun N et al. formulated orodispersable tablets of Ondansetron HCl, Propanalol, and Gabapectin using DBP as superdisintegrant. The tablets were evaluated for hardness, friability and wetting time. Result is founded that Dehydrated banana powder increases the release ofthe drug from the tablet.

6) **Future Application of superdisintegrant in Future trends**

6.1. **Oral Disintegrating Tablet formulation**

Major application of superdisintegrant is the formation of mouth dissolving formulation. MDT is the type of dosage form which is taken inside buccal cavity or sublingually without the use of water, within 60 sec or less.

6.2. **Pharmaceutical Superdisintegrants**

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Natural Superdisintegrants</th>
<th>Source</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Plantago Ovata Seed Mucilage</td>
<td>Seeds of Plantago ovate</td>
<td>(17)</td>
</tr>
<tr>
<td>2</td>
<td>Lapidium sativum mucilage</td>
<td>Seeds of Lapidium sativum</td>
<td>(18)</td>
</tr>
<tr>
<td>3</td>
<td>Gum karaya</td>
<td>Dried exudation of sterculiaurens tree</td>
<td>(19)</td>
</tr>
<tr>
<td>4</td>
<td>Fenugreek seed mucilage</td>
<td>Seed of fenugreek, Trigonellafoenumgraecum</td>
<td>(20)</td>
</tr>
<tr>
<td>5</td>
<td>Guar gum</td>
<td>Seed of guar plant, Cyamopsis tetragonoloba</td>
<td>(21)</td>
</tr>
<tr>
<td>6</td>
<td>Cassia Fistula gum</td>
<td>Seed of Cassia fistula tree</td>
<td>(22)</td>
</tr>
<tr>
<td>7</td>
<td>Locust Bean Gum</td>
<td>Seed of Carob tree Ceretonia Siliqua</td>
<td>(23)</td>
</tr>
<tr>
<td></td>
<td>Hibiscus rosa-sinensis</td>
<td>Fresh Leaves of Hibiscus rosa-sinensis</td>
<td>(24)</td>
</tr>
<tr>
<td></td>
<td>Mucilage</td>
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</tr>
</tbody>
</table>
The super disintegrants containing agglomerate of co processed starch or cellulose and enough quantity of an augmenting agent to increase the compatibility of tablets.

6.3. Mouth Dissolving Tablets
MDT are the formulation which dissolve and disintegrate in the mouth without need of water . The benefits of superdisintegrating agents is that they swell when comes in contact with saliva but do not dissolve or have an adhesive affinity. Thus the tablet disintegrates equally. Ion exchange resins are effective at considerable lesser levels.(36,37)

7) METHOD OF ISOLATION OF SUPERDISINTEGRANT FROM NATURAL SOURCE
7.1) Isolation of Mucilage from Fenugreek Seeds
Fenugreek seed are firstly powdered and this powder is further extracted with hexane so that all lipophilic compound get removed. Now boiled in ethanol for 20 min and soaked in 10 litres of water with pH using 0.5M HCl. The mixture is stirred for 12hr occasionally using mechanical stirrer then filter it using the filter paper. Now the filtrate which is obtained is gone through centrifugation process and then the supernatant formed is concentrated to make its final volume. Now supernatant is mixed with 96% of ethanol of same volume and stored in refrigerator for 4 hr. Using centrifugation technique mucilage gets precipitated which is then precipitated out and finally gets separated. Now the mucilage is again suspended in water and agitated for 20 min then again gone with reprecipitation to remove chloride ion as an impurity. The residue obtained is now washed with diethyl ether and acetone then dried overnight at 45°C forming white coloured powder. (38)

7.2) Isolation of Mucilage from PlantagoOvataHusk
(39-40)
Plantago ovate is soaked in water for 48hrs for extracting the mucilage. Now it is boiled for 2hrs so that all mucilage comes completely in the water. Now take the muslin cloth and squeezed out the mucilages with it so that seeds gets separated. Then this mucilage is precipitated using 3 times of 95% ethanol which is then dried in the oven at 50-55°C. Now take the dried mucilage and powder it using mortar and pestle and finally sieved it using mesh no 60. (41)

7.3) Preparation of Dehydrated Banana powder
Take Banana pulp which is chopped in small pieces and shear it using colloidal mill to form its smooth paste. Now sodium metabisulfite is added which works as to brighten the colour of pulp formed of banana. Now this paste is dried using drum dryer results in the formation of dehydrated banana powder which can be used for years. (42)

12) Regulatory Status of Polymers
The natural polymer used in the current study are approved by USFDA. These polymers considered and approved by USFDA are recognized as generally safe by GRAS and these polymers are also listed in the Code of Federal Regulations (CFR 21), for example fenugreek seed, Plantago ovate, Dehydrated banana powder fills all specifications as described in the Food Chemicals Codex. (46)

13) Conclusion and future prospective
In the current study we have concluded the properties of natural superdisintegrant i.e. Mucilage of Fenugreek seed, Plantago ovate husk and Dehydrated Banana powder which are used in the formulation of mouth dissolving formulation and their comparative study. The natural superdisintegrant have better disintegrating, dissolving property and bioavailability which help in effective therapy and Patient compliance. So we can conclude that natural superdisintegrant can be used in formulation of mouth dissolving. Due to highly acceptance of mouth dissolving tablet by using natural superdisintegrant by patients is growing day by day in the market

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