

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

Anshika shukla^{*1}, Archana gautam²

Faculty of Pharmacy, Aryakul college of pharmacy and Research, Lucknow, Uttar Pradesh, India

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 tablets have various advantages as they improve bioavailability and drug action and response to the body. Mouth dissolving tablets dissolve rapidly in mouth without any requirement of water which makes patient more convenient.

In this study we will see how natural superdisintegrants 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 superdisintegrants 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 routes 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, orodispersible tablet, quick dissolving tablet etc⁽²⁾ so this type of mouth dissolving tablets are Novel type of tablet⁽³⁻⁴⁾. Recently orodispersible term used by the European pharmacopoeia. Orodispersible or mouth dissolving tablet are solid dosage form having superdisintegrant due to which these formulations get dissolved 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 melt and dissolve in the saliva without any requirement of water for disintegration and get quickly absorbed. ODT target is for patient such as paediatric and geriatric, mentally retarded, bedridden patient and the patient who are travelling can take these medications without the requirement of water⁽⁴⁸⁾.

Mouth dissolving tablets which are approved by the FDA are also termed as orally disintegrating tablets. These tablets firstly disintegrate into smaller granules and then melt in the mouth which makes patient to swallow easily without requirement of water. Mouth dissolving tablets work on the principle of disintegration, dissolution and absorption of drug. Disintegration is 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 they insert the aqueous fluid in the tablet which swells the tablet and finally break the particles to disintegrate.

Disintegrating agents which are added in the tablet to promote breakdown of tablet or capsule for faster disintegration and quick absorption. In many orally disintegrating tablets superdisintegrants play a major role in their 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 superdisintegrants over synthetic superdisintegrants 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 polymers which are beneficial to us, their pharmaceutical action in mouth dissolving tablet formulation and comparison between different natural polymers which are used in the formulation of mouth dissolving tablets and how it helps in the betterment of tablets and capsules then synthetic one.⁽⁶⁾ Natural polymers improve some tablet properties in the fast dissolving tablets like it improves disintegration time of tablets so that tablets disintegrate fast and for this some superdisintegrants 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 States 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 additives because these polymers meet fully standard of safe criteria.

2) SUPERDISINTEGRANT –

Superdisintegrants are those substances which when added in the tablet formulation it enhances the breakdown of tablets and capsules into smaller granules in the presence of aqueous fluid which penetrate and swell the tablet to disintegrate. One gram of superdisintegrant breaks on absorbing 10-40 gram of water.

2.2) Best properties of Superdisintegrants^(8,9)

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 nontoxic 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 solves the problem and tablet gets easily disintegrated and dissolves.⁽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 slows down the dissolution of drug as drug firstly goes 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. Superdisintegrant may be natural or synthetic in nature.

Synthetic superdisintegrant e.g. -SSG, Crospovidone, Croscarmellose sodium etc.⁽⁷⁾

2.1.1) **Natural superdisintegrant-**

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

e.g. -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, croscarmellose sodium etc.

2.3) **Criteria for selection of superdisintegrant**

Superdisintegrants primarily increase 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-1 Natural superdisintegrants used in formulation of Tablet –

Drug	Superdisintegrant	Compression method	References
Lisinopril	Plantago ovate mucilage, aloe vera mucilage, hibiscus rosasinensis	Direct compression	
Nimesulide	Lipidium sativum	Direct compression	⁽¹⁴⁾
Ondansetron HCl	Plantago ovate husk	Direct compression	⁽⁴⁷⁾
Granisetron HCl	Plantago ovate husk	Direct compression	⁽⁴⁷⁾
Piroxicam	Treated agar	Direct compression	⁽¹⁵⁾
Oflaxacin	Locust bean gum	Solvent evaporation method	⁽⁴⁷⁾
Diclofenac sodium	Fenugreek gum		M.Udaykumar 2014
Cinnarizine	Chitosan	Wet granulation	
Famotidine	Plantago ovate mucilage, seed powder	Non aqueous wet granulation method	⁽¹⁶⁾

Table-2 Action of various superdisintegrants

Disintegrants	Action
starch	It works on the principle of capillary action, water penetrates inside the tablet, which leads to disruption of tablet
Chitin and Chitosan	Water uptake occurs causes moisture sorption
Isapgghula 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

Sr. No	Natural Superdisintegrants	Source	References
1	Plantago Ovata Seed Mucilage	Seeds of Plantago ovate	(17)
2	Lapidium sativum mucilage	Seeds of Lapidiumsativum	(18)
3	Gum karaya	Dried exudation of sterculiaurens tree	(19)
4	Fenugreek seed mucilage	Seed of fenugreek, Trigonella foenum-graceum	(20)
5	Guar gum	Seed of guar plant, Cyamopsis tetragonoloba	(21)
6	Cassia Fistula gum	Seed of Cassia fistula tree	(22)
7	Locust Bean Gum	Seed of Carob tree Ceretonia Siliqua	(23)
	Hibiscus rosa-sinensis Linn Mucilage	Fresh Leaves of Hibiscus rosa-sinensis Linn	(24)

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 t

5.1) Plantago ovata

Husk of Plantago ovate 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 Isapgghula husk of a plant called as plantago ovata. The swelling index of the tablets is around 89+ 2.2%v/v. Mucilage 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 - Granisetron HCl

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 | P a g e agent were dispersed rapidly within 15 sec and showed 92.09% drug release in 15 min⁽³⁵⁾

Natural polymer- Dehydrated Banana powder

Marketed drug- Ondansetron HCl

Disintegration time -15.3%

Concentration used -6% w/w

Arun N et al. formulated orodispersible tablets of Ondansetron HCl, Propranolol, and Gabapentin using DBP as superdisintegrant.

The tablets were evaluated for hardness, friability and wetting time. Result is founded that Dehydrated banana powder increases the release of the 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

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 by 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 Plantago Ovata Husk⁽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 mucilage 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 powdered 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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