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A COMPREHENSIVE REVIEW ON USE OF NATURAL POLYMERS IN MOUTH DISSOLVING TABLETS AS SUPERDISINTEGRANTS

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ABSTRACT

Mouth dissolving tablets are a solid dosage form containing medicinal substance which disintegrates fast, typically within a matter of seconds, when placed against the tongue. Its popularity is increasing day by day due to its ease of administration, for patient having problem in swallowing, particularly pediatrics, geriatrics and, patients with dysphagia. The aim of this article is to study the use of natural polymer as superdisintegrants in mouth dissolving tablets. Natural polymer such as Soy Polysaccharide, Lepidium sativun mucilage, Fenugreek gum, Dehydrated banana powder, orange peel pectin, Mangifera indica gum, Hibiscus rosa sinenses mucilage, Locust bean gum, etc. improve the physicochemical properties of tablets, viz., increased the solubility of poorly water soluble drug, decreased disintegration time and add nutritional value as well. Natural polymers are economic, non-toxic, biodegradable, environmentally friendly, more reliable and safe than synthetic polymers.

Keywords: Mouth dissolving tablets, natural polymer, superdisintegrants

INTRODUCTION

Tablet is the most commonly prescribed dosage form because of its wide advantages in terms of self-administration, handling, low cost and simplicity in development. It is however associated with some drawbacks such as difficulty in swallowing, particularly pediatrics, geriatrics and, patients having difficulty in swallowing conventional tablets and capsules. This problem may prove worst during the traveling conditions due to the non-availability of water.[1,10]

Mouth dissolving tablets are a new dosage type that has been created to overcome these issues. As name suggests, these tablets break down in the mouth in a matter of 20 to 30 seconds, and when they come into touch with saliva, the active ingredient begins to work therapeutically.[10]

Fast disintegrating tablets, fast dispersing tablets, rapid dissolve tablets, rapid melt tablets, quick disintegrating tablets, and orally disintegrating tablets are other names for the technology. The Food and Drug Administration (FDA) describes the FDT formulation as "a solid dosage form containing medicinal substance which disintegrates fast, typically within a matter of seconds, when placed against the tongue".[28]

The purpose of this review is to evaluate the impact of different natural polymers used in mouth dissolving tablets as superdisintegrants and comparing with synthetic polymers. Natural polymers used as superdisitegrant speed up the disintegration of tablets, causing the tablet to disintegrate quickly within a few seconds.[3,31]

Natural polymers are more efficacious and reliable. They are favored over synthetic polymers because they are easily accessible in natural areas all over the world. They are very economical having low cost and easily available in abundant quantity. They are non-toxic in nature and have no side effects, safer for human use. Also natural polymers are biodegradable, so they do not have adverse impact in environment. Patients generally prefer natural polymers over synthetic ones since they are more effective and safe and have higher patient compliance. [25]

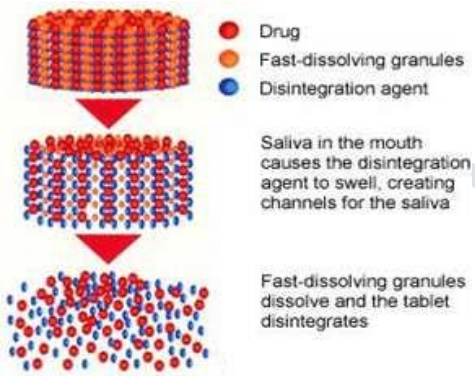

Fig.1: Conceptual Diagram Mouth Dissolving Tablets.[17]

MERITS OF MOUTH DISSOLVING TABLETS [8,18, 35]

1. Ease of administration for patient having problem in swallowing, particularly pediatrics, geriatrics and, patients with dysphagia.
2. Rapid onset of action as tablet break down, dissolve, and are absorbed quickly.
3. Provides accurate dosage compared to liquids.
4. There is no requirement of water to swallow medicine, which is a very helpful feature for people traveling without immediate access to water.
5. Greater stability.
6. First pass metabolism is decreased, improving bioavailability and lowering adverse effects.
7. Offers increased safety because there is no chance of choking from physical impediment when swallowing.

DEMERITS OF MOUTH DISSOLVING TABLETS [24,17]

1. Formulating drugs into mouth dissolving tablet is difficult for medications with relatively high dosages.
2. If tablets are not properly formed, they may leave an unpleasant taste and/or grittiness in the mouth.
3. They are more prone to deterioration from temperature and humidity
4. Some people may not respond well to these tablet formulations if they have dry mouth as a result of reduced saliva production.
5. Tablets typically lack adequate mechanical strength. As a result, it needs to be handled and packaged carefully.

CRITERIA FOR MOUTH DISSOLVING TABLETS [20,22,41]

1. They should dissolve or disintegrate in the mouth in a matter of seconds without the need for water during administration.

2. When using sweeteners to conceal tastes, they should be compatible.
3. Ideally, it should have pleasant taste.
4. Should not leave much residue in the mouth after use.
5. Must be suitable for heavy drug loading
6. Should have enough strength to endure the rigors of the manufacturing process and post-manufacturing handling.
7. Should not get affected by external factors like humidity and temperature.
8. Manufacturing and packaging should be economically feasible.

NATURAL POLYMERS USED IN MOUTH DISSOLVING TABLETS

1. Lepidium sativum mucilage:
   Lepidium sativum Linn. belonging to family Brassicaceae is one of the edible, quickly growing annual herbs that contains mucilage. Its numerous components, including the roots, leaves, and seeds, have been utilized to cure a variety of human illnesses. As its principal phytochemical components, it mostly consists of alkaloids, saponins, anthracene glycosides, carbohydrates, proteins, amino acids, flavanoids, and sterols.[26]
   A. Bharathi et al, 2020, formulated and evaluated Roflumilast fast dissolving tablets using Lepidium sativum mucilage employing 23 factorial design. Tablets were evaluated for various parameters, viz., hardness, friability, disintegration time, wetting time, in vitro drug release. The optimized formulation showed disintegration time of less than 52 seconds, in vitro wetting time less than 90 seconds and in vitro dissolution of 99 % with 5 minutes.[9]

2. Soy Polysaccharide:
   Soy polysaccharide is a high molecular weight polysaccharides extracted from soy beans and has been used as a disintegrant in direct compression tablets containing lactose and dicalcium phosphate dihydrate as diluents.[4]
   Singh et al, 2019, mouth dissolving tablet of atorvastatin using Soy Polysaccharide as natural superdisintegrant. Tablets were prepared by direct compression method. A formulation containing 10% soy polysaccharide showed good results terms of tablet disintegration, wetting time, and dissolution rate. Prepared tablets disintegrate in a matter of seconds without water.[16]

3. Chitin and Chitosan:
   Chitin is a naturally occurring polymer of N-acetylglucosamine and glucosamine residues that is non-toxic, biodegradable, and found throughout nature. It's monosaccharide building blocks are connected by (1-4) glycosidic linkages. Chitosan, deacetylated form of chitin is prepared by deacetylation of acetamide group into amino group.[42]
   Gailute Draksiene et al, 2021, prepared fast disintegrating tablets of Meloxicam by using chitosan. Tablet compressed with compression force 10.8 kN and 11.0 kN had satisfactory mechanical and disintegration qualities as well as good dissolution rate.[5]

4. Gum karaya:
   Gum karya (Family: Sterculiaceae), a dried gummy exudate is obtained from Sterculia urens which is large bushy tree bearing height of 30 ft., and is native to India. The gum is an acid polysaccharide whose primary components are d-galactose, d-glucouronic acid, l-rhamnose, xylose residues, and acetyl groups. Previous studies have also revealed that it can be employed as a disintegrant as an alternative for synthetic superdisintegrants. It has wide availability, biocompatibility, and low cost. Due it's great capacity for retaining water, viscosity, swelling behavior, antibacterial activity, and widespread availability, it has a variety of purposes.[14]

Baviskar et al, 2020, formulated and evaluated mouth dissolving tablets of Lornoxicam. Tablets were prepared by using natural superdisintegrants Gum Karaya and Plantago ovata husk and other synthetic superdisintegrants. Tablets containing 6% of gum karaya showed better performance over formulations containing other disintegrants.[11]

5. Gellan Gum:

Gellan gum is anionic polysaccharide obtained from Pseudomonas elodea. It is mostly made up of a repeating unit of tetrasaccharide, which consists of two residues of D-glucose and one residue of each of D-glucuronic acid and L-rhamnose. By using fermentation, it is produced. It comes in two forms: High acyl (HA) and Low acyl (LA).[3]

Medha et al, 2018, prepared sublingual tablets of Rizatriptan using Gellan gum as superdisintegrant. Gellan gum as superdisintegrant showed maximaum drug release at the concentration of 6.66%.[19]

6. Mango peel pectin:

Mango peel pectin is extracted from mango (Magnifera Indica L,) peels. Mango peel can be used as a significant source of pectin for use in the pharmaceutical and food sectors.[2]

Pectin is heteropolysaccharide made of D galacturonic acid. These polysaccharides are made free or methyl esterified carboxyl groups connected by 1,4-glucosidic bonds.[6]

Malviya et al, 2010, studied the effect of mango peel pectin as a superdisintegrant in fast dispersible tablets of Diclofenac Sodium. Study revealed that mango peel pectin did not act as promising superdisintegrant. Though, because of its better swelling index and good solubility properties it can be used in fast dispersible tablets.[40]

7. Fenugreek gum:

Fenugreek is a leguminous plant from the Fabaceae family that is widely grown as a semiarid crop. A significant portion of the mucilage found in seeds can be employed as a disintegrant in the formulation of tablets that dissolve in the mouth. Mucilage is an amorphous powder of an off-white to cream-yellow color that dissolves quickly in warm water to create a viscous colloidal solution.[36]

M. Uday Kumar et al, 2014, formulated and evaluated Diclofenac Sodium fast dissolving tablets using different concentration of Fenugreek gum as natural superdisintegrant. Tablets were evaluated for various physicochemical characteristics such as hardness, friability, disintegration time, wetting time, in vitro drug release and it was depicted that formulation containing 6 % of Fuenugreek gum produced least disintegration time of 21 seconds and drug released of 93.74 % within 25 minutes.[27]

8. Agar and Treated Agar:

Agar is dried gelatinous substance derived from Gelidium amansii (Family, Gelidanceae) and many other species of red algae such as Gracilaria (Family, Gracilariaceae) and Pterocadia (Family, Gelidaceae). Agar is a mucilaginous substance that comes in the shape of strips, sheet flakes, or coarse powder. It is a yellowish gray, white, or virtually colorless substance with no odor.[30]

Prakash Pawan et al, 2011, formulated and evaluated, mouth dissolving tablets of Piroxicam using treated agar as natural super disintegrant. Study revealed that formulation containing 6% of treated agar exhibits most satisfactory result with disintegration time 21 seconds.[37]

9. Guar Gum:

Guar gum (Family, leguminosae) is powdered endosperm of seeds of Cyamopsis tetragonolobus. Galactomannan, a complex polysaccharide made of d-galactose and d-mannose, is found in the endosperm. It finds use in a wide range of industries due to its thickening, emulsifying, binding, and gelling capabilities, fast solubility in cold water, wide pH stability, film-forming capacity, and biodegradability.[21]

Dr. Rambabu Sharma et al, 2013, compared superdisintegrating nature of guar gum in mouth dissolving tablets with Sodium Starch Glycolate and found that guar gum showed good swelling property than Sodium Starch Glycolate causing faster disintergration and drug released. But at concentration more than 8% guar gum formed gel layer around the tablet and showed poor disintegrating activity.[29]

10. Locust bean gum:
    Locust bean gum is also known as carob bean gum. It is galactomannan vegetable gum extract derived from the seeds of the Mediterranean tree Ceretonia silique. According to reports, it also possesses a solubility-enhancing quality and an adhesive property.[7]
    Karan Malik et al, 2011, prepared and evaluated Nimesulide orodispersible tablets using locust bean gum as natural super disintegrant. Disintegration time of formulation containing 10% locust bean gum was found to be 13 seconds.[38]

11. Plantago Ovata seed mucilage:
    Psyllium, also referred to as ispaghula, is the common name for several Plantago species whose seeds are used commercially to make mucilage. The mucilage from the plantago ovata has a number of functions, including as binding, dissolving, and maintaining qualities.[7]
    Khinchi et al, 2011, studied the disintegrating properties of Seed powder, Husk powder and mucilage of Plantago Ovata by formulation orodispersible tablets. The study revealed that Plantago Ovata seed mucilage showed the highest swelling index and exhibited comparable disintegration properties to the most used synthetic superdisintegrants.[39]

12. Hibiscus rosa-senansis leaf mucilage:
    It is a member of the Malvaceae family and is also known as the Chinese hibiscus, the China rose, and the shoe flower plant. Mucilage contains L-rhamnose, D-galactose, D-galacturonic acid, etc.[8]
    Surya kumari et al, 2019, formulated and evaluated fast dissolving tablets if Imipramine using Hibiscus rosa-senansis leaf mucilage as superdisintegrant. Formulation containing 6% of mucilage showed disintegration time of 24 seconds.[15]

13. Ocimum sanctum seed:
    Ocimum sanctum, often known as Holy Basil in English or "Tulsi" or "Tulasi" in Hindi, is recognized as a holy plant in Hindus. Linalool and a variety of other natural products, such as polyphenols like flavonoids and anthocyanins, are among the phenolic components found in a variety of essential oils found in basils.[32]
    K. Malik et al, 2012, formulated and evaluated Nemesulide fast melt tablets containing ocimum sanctum as superdisintegrant. Formulation containing 10% ocimum sanctum powder showed disintegration time 10±1 seconds. Hence, concluded that it can be used as natural super disintegrant agent in fast dissolving tablets.[34]

14. Aegle marmelos gum:
    It is produced from the fruits of the Aegle marmelos tree, a tree native to India and a member of the Rutaceae family. The ripe fruit pulp has a mucilaginous, astringent flavor and is reddish-brown in color. The pulp is rich in protein, carbohydrates, vitamins C and A, dictamine, marmeline, o-methyl fordinol.[7]
    Aceclofenac fast-dissolving tablets were created by Kulkarni et al, 20 using a modified Aegle marmelos gum. Solubility of Aceclofenac was found to be increased with increase in concentration of Aegle marmelos gum and modified Aegle marmelos gum.[23]

15. Ficus Indica Fruit Mucilage:
    The pulp of the ficus indica fruit contains mucilage, which is used as a superdisintegrant. Fruits of Fructus indica are the size of cherry. It has both therapeutic and nutritional value. Ficus indica is an astronomically immense tree up to 3 m and very fast-growing with spread branches and aerial roots.[12]
    Pandit et al, 2020, formulated fast dissolving tablets of Pioglitazolne and Cilnidipine using Opuntia Ficus Indica as an innate superdisintegrant. Formulation with 2.94% Opuntia Ficus Indica showed disintegration time of 18.53 seconds and drug release of more than 90 % for Pioglitazolne and near to 70% for Cilnidipine within 30 minutes.[13]

ADVANTAGES OF NATURAL POLYMERS [25, 33]

Natural polymers have a number of benefits, including the following.

1. Biocompatible and non-toxic: Nearly all plant components are made up of repeating monosaccharide units, which are carbohydrates in nature. They are therefore not harmful.
2. Biodegradable: Most of the natural polymer are biodegradable and they do not have adverse effect on human and environment.
3. Economic: They are more affordable to use as natural resources. In comparison to synthetic material, the production cost is lower.
4. Environmentally friendly processing: They involve simple production process.
5. Local availability: They are easily available in most of the developing countries.
6. Patient tolerance and public acceptance: Due to less side and adverse effects, their patient tolerance and public acceptance is high.

CONCLUSION

The article discussed overview of various type of natural super disintegrants available at present. They provide predominant effect on in vitro disintegration time of tablets. Hence, by evaluating the outcome of different formulations with natural polymer, we can draw a conclusion that mouth dissolving tablets can be prepared by using different natural super disintegrants which will improve the patient compliance in population who finds difficulty in swallowing. These substances improve drug release and shorten wetting time. Additionally, it has benefits over synthetic disintegrants, such as being nontoxic, conveniently accessible, affordable, and biocompatible.

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