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A RECENT REVIEW ON TECHNOLOGICAL ADVANCEMENT AND THE USE OF NATURAL SUPERDISINTEGRANT IN THE FORMULATION OF FAST DISINTEGRATING TABLET

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ABSTRACT

Fast dissolving tablet are the novel dosage form which is well accepted now a days by geriatric and pediatric patients as it does not need water to swallow. The aim of the present article is to study the natural polymers and the technology used in fast dissolving tablets. Natural polymers like plantagovata seed mucilage, *Mangiferaindica*gum, gum karaya, *Hibiscus rosasinenses* mucilage, dehydrated banana powder, orange peel pectin, Locust bean gum, improve the properties of tablet and used as binder, diluent, superdisintegrant, increase the solubility of poorly water soluble drug, decrease the disintegration time and provide nutritional supplement. Natural polymers are obtained easily from the natural origin and they are cost effective, non-toxic, biodegradable, eco-friendly, devoid of any side effect, renewable and also provide nutritional supplement. It is proved from the studies that natural polymers are more safe and effective than synthetic polymers.

KEY WORDS

Mouth dissolving tablets, Superdisintegrants, Bioavailability and ODT Technology.

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INTRODUCTION[1-3]

Fast disintegrating tablets are very popular now-days as they get dissolved or easily disintegrated in mouth within few seconds of administration without the need of water. Active drug is released immediately from the tablet when is placed on the tongue. Orodispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active peoples. Orodispersible tablets are also known as mouth dissolving tablets, melt-in-

mouth tablets, fast dissolving tablets, rapimelts, porous tablets and quick dissolving tablets.

Disintegrants are important excipient of the tablet formulation, they are always added to tablet to induce breakup of tablet when they are comes in contact with aqueous fluid and this process of desegregation of constituent particles before the drug dissolution occurs, is known as disintegration process and excipients which induce this process are known as disintigrents.

Advantages of Fast Dissolving Tablets[4]

- Ease of administration to patients who cannot swallow, such as the elderly, strokes victims and bedridden patients; patients who should not swallow, such as renal failure patients; and who refuse to swallow, such as pediatrics, geriatric and psychiatric patients.
- Patient's compliance for disabled bedridden patients and for travelling and busy people, who do not have ready access to water.
- Good mouth feel property of MDDDS helps to change the basic view of medication as "bitter pill", particularly for pediatric patients due to improved taste of bitter drugs.
- Convenience of administration and accurate dosing as compared to liquid Formulations.
- Benefit of liquid medication in the form of solid preparation.
- More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and esophagus which may produce rapid onset of action.

Drug Selection Criteria[5]

The ideal characteristics of a drug for oral dispersible tablet include

- Ability to permeate the oral mucosa.
- At least partially non-ionized at the oral cavity pH.
- Have the ability to diffuse and partition into the epithelium of the upper .GIT
- Small to moderate molecular weight.
- Low dose drugs preferably less than 50mg.
- Short half life and frequent dosing drugs are unsuitable for ODT.
- Drug should have good stability in saliva and water.
- Very bitter or unacceptable taste and odour drugs are unsuitable for ODT.

Influencing Factors for Sublingual Absorption[6]

- Lipophilicity of Drug: For effective sublingual drug absorption the drug must have slightly higher lipid solubility for passive absorption.
- pH and pKa of Saliva: The pH of saliva is 6.0.This pH is favorable for the drugs which remain unionized. For acidic drug pKa of saliva should be greater than 2.0 and for basic drug pKa of saliva should be less than 10.
- Solubility in salivary secretion: The drug should be soluble in aqueous buccal fluids.
- Binding to oral mucosa: Binding between drug and oral mucosa should be poor.
- Thickness of oral mucosa: The thickness of oral mucosa is 100-200 micrometer which is less as compared to buccal thickness (500-800 micrometer).
- Partition co efficient: The drugs which have oil to water partition co efficient within the value of 40-2000 are suitable for absorption through sublingually.

Selection Criteria for Superdisintegrants[7]

Superdisintegrants primarily affect the rate of disintegration, but when used at high levels it can also affect mouth feel, tablet hardness and friability. Hence, various ideal factors to be considered while selecting an appropriate superdisintegrants for a particular formulation should:

- Proceed for rapid disintegration, when tablet comes in contact with saliva in the mouth/oral cavity.
- Be compactable enough to produce less friable tablets.
- Produce good mouth feel to the patients. Thus, small particle size is preferred to achieve patient compliance.
- Have good flow, since it improves the flow characteristics of total blend.

Description of Natural Superdisintegrants

Plantagoovata seed mucilage

Psyllium or Ispaghula is the common name used for several members of the plant genus Plantago whose seeds are used commercially for the production of

mucilage. Mucilage of Plantagoovata has various characteristics like binding, disintegrating and sustaining properties. In an investigation fast disintegrating tablets of Amlodipine Besylate was prepared by direct compression method using different concentrations of plantagoovata mucilage as a natural superdisintegrant. All formulations were evaluated for weight variation, hardness, friability, disintegration time, drug content and dissolution. The optimized formulation shows less in vitro disintegration time 11.69 seconds with rapid *in vitro* dissolution within 16 minutes. *In-vitro* disintegration time decreases with increase in concentration of natural superdisintegrant.

Hibiscus rosasinensis mucilage and treated agar

It is also called shoe flower plant, China rose, Chinese hibiscus belonging to family Malvaceae. Mucilages are used as thickeners, suspending agent, water retention agent, disintegrants. The plant is easily available and its leaves contain mucilage and in mucilage L-rhamnose, D-galactose, D-galactouronic acid and D-glucuronic acid is present. Treated agar is prepared by treating it with water for one day.

***Lepidiumsativum* mucilage**

Lepidiumsativum (family: Cruciferae) is known as Asaliyo and is widely used as herbal medicine in India. It is widely available in market and has very low cost. Parts used are leaves, root, oil, seeds etc. Seeds contain higher amount of mucilage, dimeric imidazole alkaloids lepidine B, C, D, E and F and two new monomeric imidazole alkaloids semilepidinoside A and B. Mucilage of Lepidiumsativum has various characteristic like binding, disintegrating, gelling etc.

Gum karaya

Gum Karaya is a vegetable gum produced as an exudate by trees of the genus *Sterculia*. Chemically, Gum Karaya is an acid polysaccharide composed of the sugars galactose, rhamnose and galacturonic acid. The high viscosity nature of gum limits its uses as binder and disintegrant in the development of conventional dosage form. Karaya gum has been investigated for its potential as a tablet disintegrant. Various results showed that modified Gum Karaya produce rapid disintegration of tablets. Gum Karaya can be used as an alternative superdisintegrants to commonly available synthetic and semi synthetic superdisintegrants due to their low cost, biocompatibility as well as easily availability.

Fenugreek seed mucilage

Trigonella Foenum-graceum commonly known as Fenugreek is an herbaceous plant of the Leguminous family. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). Although it does not dissolve in water, mucilage forms a viscous tacky mass when exposed to fluids. Like other mucilage-containing substances, fenugreek seeds swell up and become slick when they are exposed to fluids. Hence, the study revealed that this natural disintegrant (fenugreek mucilage) showed better disintegrating property than the most widely used synthetic superdisintegrants like Ac-di-sol in the formulations of FDT's. Studies indicated that the extracted mucilage is a good pharmaceutical adjuvant, specifically a disintegrating agent.

Mango peel pectin

Mango peel which constitutes 20-25% of the mango processing waste was found to be a good source for the extraction of pectin of good quality, suitable for the preparation of fiim and acceptable jelly. Pectin is a complex hetro-polysacharides which is a hydrophilic colloid. Mango peel pectin stand as a good candidate as superdisintegrant though, not as stronger a**s** synthetic superdisintegrant but due to its good solubility and higher swelling index, it may be used in the formulation of fast dispersible tablets.

Agar and treated agar

Agar is the dried gelatinous substance obtained from *Gelidiumamansii*(Gelidanceae) and several other species of red algae like *Gracilaria*(Gracilariaceae) and *Pterocadia*(Gelidaceae). Agar is yellowish gray or white to nearly colorless, odorless with mucilaginous taste and is available in the form of strips, sheet flakes or coarse powder. Agar consists of two polysaccharides as agarose and agar pectin. Agarose is responsible for gel strength and Agar pectin is responsible for the viscosity of agar

solutions. High gel strength of agar makes it a potential candidate as a disintegrant.

Guar gum

Guar gum is mainly consisting of the high molecular weight (approximately 50,000-8,000,000) polysaccharides composed of galactomannans and is obtained from the endosperm of the seed of the guar plant, *Cyamopsistetragonaloba*(L) *Taub*. (syn. *Cyamopsispsoraloides*). It is used as thickener, stabilizer and emulsifier, and approved in most areas of the world (e.g. EU, USA, Japan, and Australia. It is naturally occurring gum (marketed under the trade name jaguar). It is free flowing; completely soluble, neutral polymer composed of sugar units and is approved for use in food. It is not sensitive to pH, moisture contents or solubility of the tablet matrix. It is not always pure white and sometimes varies in color from off-white to tan tends to discolor with time in alkaline tablets.

Gellan gum

Gellan gum Gellan gum is a water-soluble polysaccharide produced by *Pseudomonas elodea*, a bacterium. Gellan gum is an anionic, high molecular weight, deacetylatedexocellular polysaccharide gum produced as a fermentation product by a pure culture of Pseudomonas elodea, with a tetrasaccharide repeating unit of one α-L-rhamnose, one β-D-glucuronic acid and two β-D-glucose residues. Antony et al 1997 studied the Gellan gum as a disintegrant and the efficiency of gum was compared with other conventional disintegrants such as dried corn starch, explotab, avicel (pH 10.2), Ac-di-sol. and Kollidon CL. The disintegration of tablet might be due to the instantaneous swelling characteristics of gellan gum when it comes into contact with water and owing to its high hydrophilic nature. The complete disintegration of tablet was has proved itself as superior disintegrant.

Chitin and Chitosan

Chitin (β-(1→4)-N-acetyl-D-glucosamine) is a natural polysaccharide obtained from crab and shrimp shells. It possesses amino group covalently linked to acetyl group as compared to free amino group in chitosan. Chitosan is produced commercially by deacetylation of chitin, which is the structural element in the exoskeleton of crustaceans (such as crabs and shrimp) and cell walls of fungi. Bruscato et al 1978 reported that when chitin was included in the conventional tablets, the tablets disintegrated with in 5 and 10 minutes irrespective of solubility of the drug. The disintegration time in the oral cavity as well as wetting time could be analyzed by surface free energy. Chitosan is the best known natural polysaccharide used for its versatile applications in pharmaceutical industry.

Table No.1: ODT products in Indian market[2]

S.No	Brand Name	Active Ingredients	Company
1	Nimulid-MD	Nimesulide	Panacea
2	Biotech Zyrofmeltab	Rofecoxib	Zydus Cadila
3	MOSID-MD	Mosapride Citrate	Torrent Pharmaceuticals
4	Feledine Melt	Piroxicam	Pfizer
5	Maxalt ODT	Famotidine	Merck
6	Remeron Sol Tab	Mirtazapine	Organon
7	Romilast	Montelukast	Ranbaxy
8	Manza BDT	Olanzepine	Orchid
9	Olanexinstab	Olanzepine	Ranbaxy
10	Valus	Valdecoxib	Glenmark
11	Rofaday MT	Rofecoxib	Lupin
12	Torrox MT	Rofecoxib	Torrent

Table No.2: ODT products available in international market[2]

S.No	ODT products	Drug Name	Company Name
1	Nimpain MD	Nimesulide	Prompt cure Pharma
2	Imodium lingual	Imodium	R.P. Scherer Corp., U.S.A
3	Pepcidin Rapitab	Pepcid	Merck & Co., U.S.A
4	Calritin Reditabs	Calritin	Schering Plough, U.S.A
5	Nurofen Flashtab	Ibuprofen	Boot healthcare
6	Hyoscyaminesulfate ODT	Hyoscyaminesulfate	Ethex Corporation
7	Cibalginadue Fast	Ibuprofen	Novartis Consume Health
8	Zyprexa	Olanzepine	Eli Lilly
9	Zofran ODT	Ondansetron	Glaxo Smithkline
10	Risperdal M Tab	Risperidone	Janssen
11	Imocdium Instant Melts	Lopermide HCl	Janssen
12	Propulsid Quick Sol	Cisapride Monohydrate	Janssen
13	Zomig-ZMT and Rapimelt	Zolmitriptan	Astra Zeneca
14	Alavert	Loratadin	Wyeth Consumer Healthcare
15	NuLev	Hyoscyamine Sulfate	Schwarz Pharma
16	Kemstro	Baclofen	Schwarz Pharma
17	Benadryl Fast Melt	Diphenhydramine Citrate	Pfizer
18	Nasea OD	Ramosetoron HCl	Yamanouchi
19	Gaster D	Famotidine	Yamanouchi
20	Excedrin Quick Tabs	Acetaminophen	Bristol-Myers Squibb
21	Zolpidem ODT	Zolpidem tartrate	Biovail
22	Fluoxetine ODT	Fluoxetine	Biovail

Table No.3: Drugs used in the formulation of sublingual dosage

S.No	Drugs	Category	Dosage form
	Physostigmine Salicylate	Anti-alzheimers	Tablet
2	Scopolamine	Opoid analgesic	Spray
3	Captopril	Anti hypertensive	Tablet
4	Furosemide	Diuretic	Tablet
5	Nifedipine	Anti-anginal	Tablet
6	Nitroglycerine	Anti-anginal	Tablet
7	Vinpocetine	Neurotropic	Tablet
8	Terbutaline Sulphate	Bronchodialator	Tablet
9	Amlodipine Besylate	Antihypertensive	Tablet
10	Ondanstron Hcl	Antiemetic	Film
11	Buprenonpine	Opoid analgesic	Tablet
12	Asenapine	Antiphychotic	Tablet

Technology for mouth dissolving tablets[10-12]

Conventional techniques for FDTs

Tablet moulding

In this method water soluble additives are used to form tablets. The ingredients used in the formulation are passed through the fine mesh, dry blended and wetted with hydro alcoholic solvent and then by using low compression forces compressed into tablets.

Freeze drying (Lyophilization)

In this method water is removed by sublimation of the heat sensitive materials and biologicals. The porous tablets formed having improved absorption and bioavailability.

Spray drying

In this method highly porous fine powders are produced which when compressed into tablets show fast disintegration and enhanced dissolution.

Sublimation

In this method sublime salt is added to the components of tablets and by the process of sublimation the salt is removed and blend is compressed.

Addition of disintegrants

To improve the dissolution and disintegration, disintegrants are added in the FDTs.

Direct compression method

In this method the drug and the excipients are uniformly blended in a prescribed manner and directly compressed into tablet, without any pretreatment. The uniform blend of powders should have good flow properties, the disintegrants are added as excipients in direct compression method.

Patented technologies for FDTs

Zydias technology

Zydis is patented by R.P. Scherer. In this, drug is physically trapped in the matrix of saccharide and polymer. The Polymers used in this technology are hydrolyzed gelatin, hydrolyzed dextran, dextrin, alginates, polyvinyl alcohol, polyvinyl pyrrolidine, acacia and mixtures of these. Solution or dispersion of the ingredients is prepared and filled in the blister cavities; liquid nitrogen is used to freeze it. Then remove the fozen solvent or porous wafers are produced by sublimation. To pack zydis units' peelable backing foil is used.

Durasolv technology

CIMA labs patented this technology. In this technique active drug is required in low amount. Drug, lubricant and fillers are used and the same equipments used in the conventional tablets are used in durasolv technique. The tablets formed are rigid due to higher compaction force and the tablets formed are packed in the blister packing.

Orasolv technology

First orodispersable tablet are prepared by CIMA labs. In this technique effervescent disintegrating agent is used. The equipments used in conventional tablets are used in orasolv technology. The taste of active drug is masked and tablet is formed by applying less compaction force. These soft tablets are packed in special packaging system.

Wowtab technology

This is the patented technology of Yamanauchi Pharmaceutical Company. The meaning of wow is "without water". In this technique the combination of high and low mouldable substances are used. The active ingredients are mixed with low mouldable saccharide and then granulated with high mouldable saccharide and compressed into tablets. These tablets are dissolved with in less than 15 sec. These tablets are packed into conventional bottles and blister packs.

Flash dose technology

This technology is patented by fuisz. The taste of bitter drugs is masked by sugar based matrix called floss. Nurofen meltlet, it is the mouth dissolving tablet of ibuprofen.

Flash tab technology

This technology is patented by prographarm lab. In this technique taste masked microgranules of active ingradients is prepared. These granules along with swelling agent, disintegrating agent and other excipient are compressed to form a maltiparticulate tablet. These tablets are rapidly disintegrated.

CONCLUSION

The development of a fast-dissolving tablet also provides an opportunity for linextension in the market place, a wide range of drugs (e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs for erectile dysfunction) can be considered candidates for this dosage form. Pharmaceutical marketing is another reason for the increase in available fast dissolving/ disintegrating products. As a drug entity nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a

manufacturer to extend market exclusivity, while offering its patient population a more convenient dosage form. In this regard, fast dissolving/ disintegrating tablet formulations are similar to many sustained release formulations that are now commonly available.

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