Asian Journal of Pharmaceutical Education and Research
Vol -7, Issue-1, January-March 2018
ISSN : 2278 7496

REVIEW ARTICLE Impact Factor: 4.101

FAST DISSOLVING TABLET AND TASTE MASKING APPROACHES – AN OVERVIEW

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Received 28 Dec. 2017; Revised 31 Dec. 2017; Accepted 2 Jan. 2018, Available online 20 Jan 2018.

ABSTRACT

Fast disintegrating tablets (FDTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. Oral drug delivery remains the preferred route for administration of various drugs. Recent developments in the technology have prompted scientists to develop FDTs with improved patient compliance and convenience. Upon introduction into the mouth, these tablets dissolve in the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. The popularity and usefulness of the formulation resulted in development of several FDT technologies. Particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. This review describes various formulations and technologies developed to achieve fast dissolution/dispersion of tablets in the oral cavity. In particular, recent development in fast disintegrating technology mainly works to improve the disintegration quality of these delicate dosage forms without affecting their integrity. This article focuses on the patented technologies available and the advances made so far in the field of fabrication of fast disintegrating tablets. Apart from the conventional methods of fabrication, this review also provides the detailed concept of some unique technologies like freeze drying, direct compression, spray drying, tablet molding, sublimation fast dissolving films cotton candy process, along with their advantages and limitations.

Keywords: Fast Dissolving Tablet, Patented Technology, Taste Masking Approaches, Superdisintigrant.

INTRODUCTION

In recent decades, a wide variety of pharmaceutical research is directed at developing new dosage forms. Most of these efforts have focused on either formulating novel drug delivery systems or increasing the patient compliance.[1] Among the dosage forms developed for facilitating ease of medication, and enhance the patient compliance; mouth dissolving tablet (MDT) is the most widely preferred commercial products.[2] Drug delivery through oral route is the most preferred and accepted way of application by the patients. Solid dosage forms in the shape of tablets used orally have the most substantial and significant place among the entire pharmaceutical formulations. Over the last 30 years, orally disintegrating tablets

(ODTs) are gaining considerable importance. These tablets disperse in the saliva in the mouth within a short period of time. Saliva containing the dispersed drug is then swallowed through the oesophagus. In the European Pharmacopeia, orally disintegrating tablets are specified as "orodispersible tablets" and defined as "orodispersible tablets are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed" while in the United States.[2]

Food and Drug Administration (FDA) Regulation (U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research), they are classified as "orally disintegrating tablets" and defined as "A solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue". [1]

Advantages of Fast Dissolving Tablet [3,4]

- No need of water to swallow the tablet.
- It can provide accurate dosing as compare to liquid.
- Fast dissolution and absorption of drug, hence offering rapid onset of action.
- Useful in cases like motion sickness, suede episodes of attack of allergy, or coughing, where ultra-rapid onset of action is necessary.
- It has ability to provide similar advantage of liquid medication in the form of solid dosage form.
- Bioavailability of drug is increase because some drugs are absorbed from mouth, pharynx, and oesophagus through saliva passing down into stomach.
- Reduce hepatic first pass metabolism, hence offering rapid onset of action.
- Reduce the risk of suffocation.
- Allow high drug loading.
- Cost effective.

Ideal properties of FDT's [4,5]

- Require no water for oral administration, yet dissolve/disperse/ disintegrate in mouth in a mattr of seco nds
- Have a pleasing mouth feel.
- Have an acceptable taste masking property.
- Leave minimal or no residue in mouth after administration.
- Exhibit low sensitivity to environmental conditions (temperature and humidity)
- Be compatible with taste masking.
- Be portable without fragility concern.
- Leave minimum or no residue in the mouth after oral administration.
- Allow the manufacture of the tablet using conventional processing and packaging equipments.

Limitation of FDT's [5,6]

- Mechanical strength of final products.
- Drug with larger dose are difficult to formulate FDT.
- Patient who take anticholinergic medication are not good candidate for FDT.5
- Patient who have problem of dryness of mouth due to decrease production of saliva, are not good candidate for FDT.
- Tablet may leave unpleasant taste in the mouth, if not formulated properly.
- Careful handling is require because tablet have insufficient mechanical strength.[6]

Drug selection criteria for FDT [7]

- Ability to permit oral mucosa.
- Partially non-ionized at the oral cavity PH.
- Drug should have small to moderate molecular weight.
- Drug have dose less than 50mg.
- Drug with bitter taste are unsuitable for FDT.

Patented technologies for fast dissolving tablet [8,9]

- Zydis Technology
- Durasolve Technology
- Orasolve Technology
- Wowtab Technology
- Flashtab Technology
- Flashdose Technology
- Oraquick Technology
- Nanocrystal Technology
- Sherform Technology

Zydis Technology-

Zydis is well known fast dissolving/disintegrating tablet preparation was the first marketed new technology tablet.[8] After placing on tounge it dissolves in few second. Lyophilizing or freeze drying technology are used for preparation of zydis tablet, the drug in a matrix usually consist of gelatin. To improve strength during handling polymer like, gelatin, dextran, or alginate are added in formulation. It forms glossy, amorphous structure which can impart strength. Water are used for preparation of zydis

tablet to ensure production of porous unit it can provide rapid disintegration. To prevent sedimentation of dispersed drug particle in manufacturing process, various types of gum can be used. Glycerin prevent the shrinkage of zydis unit. It can act as a collapse protectant.[9]Zydis formulation is self-preserving because final water concentration in freeze dried product is too low to allow for microbial growth.[8]

Drawback-

In zydis product water insoluble drug can be incorporated only up to 400 mg / tablet or less. On other hand water soluble drug can be incorporated up to 60 mg.[9]

Zydis formulation is very light weight and fragile and hence should not be store at bottom of per or in backsce. Very sensitive to degradation at humidity greater than 65%.

Durasolve Technolog

Durasolve is a patented technology of CIMA lab's second generation fast dissolving tablet formulation.[8] Product require low amount of active ingredient that can be prepare by durasolve technology. Tablet can be prepare by this technology contain drug, fillers, and lubricant. Tablet have good rigidity that can be prepare by conventional tableting equipment. Generally, mannitol, lactose, sucrose, sorbitol, dextrose are used as fillers.[9]More amount of hydrophobic lubricant cab be used in this formulation. For compression of tablet low compressive force is require. The production cost is low because direct compression is required.

Orasolve Technology-

Orasolve technology is the patented technology of CIMA lab's. In this system active medicament is taste masked. In this technique effervescent disintegrants are used. For preparation of tablet conventional equipment and blender are used. Less compaction force is required for formulation of tablet to minimize oral dissolution.[8]It is best technology for fast dissolving tablet. The tablet matrix dissolve in less than one min, leaving coated drug powder. It contains single or multiple active ingredients and tablet contain greater than 1.0 g of drug have been develop. Disintegration time less than 30 sec.

Drawback-

One of the major disadvantage of the orosolve formulation is it's mechanical strength. Tablet are fragile hence need special packing.[9]

Wowtab Technology

Wow means "without water". This technology is patented by Yamanouchi Pharmaceutical Co. In this process combination of low moldability saccharides and high moldability saccharide (eg. Maltose) are used to obtain proper hardness and instant melting strong tablet.[9] It is an intrabuccaly soluble, compressed tablet contain granule made by saccharide of low and high mouldability. To obtain tablet of adequate strength the combination of high and low mould abilities are used. Because of hardness of tablet it can be stable in environment. The wowtab formulation in japanees market from no of years. This technology can used sugar and sugar-like excipient. Wowtab formulation is more stable in environment than tablet prepare by zydis or Orasolve.[8]

Flash Dose Technology

This technology has been patented by FUISZ. With the help of this technology Nurofen meltlet, new form of ibuprofen melt in mouth tablet can be prepare. This is a first commercial product had been launched by Biovail corporation.[9] Flash dose technique apply a unique spinning mechanism to produce a floss-like structure as like cotton candy. It consists of self-binding matrix called as floss. In this technology swelling and disintegrating agent are usually mainly two components.[8]

Drawback

The prepared tablets are highly friable, soft and moisture sensitive, hence special packing is needed.[9]

The dosage form can accommodate only up to 600 mg of drug.

Flash Tab Technology

Rapidly disintegrating tablet which consist of active ingredient in the form of microcrystal can be prepare by flash tab technology.[8] With the help of conventional technique like coacervation, microencapsulation drug microgranule can be prepare. All the processing used conventional tableting technology. In this technology swelling and disintegrate are mainly two components. Tablet can be prepare by wet granulation and compressed tablet. The tablet produce has good mechanical strength, and disintegration time less than one min.[9]

Nanocrystal Technology

The colloidal dispersion of drug along with water-soluble ingredient mixes thoroughly. The size of nanocrystal particles are less than 1000 nm in diameter which can be produced by milling for the fast dissolving tablet. Nanocrystal technology can enable formulation and improve compound activity and

final product characteristics. Surface area cab be increase by decreasing particle size, which can increase dissolution rate.[8]

Oraquick Technology-

The oraquick fast dissolving tablet formulation utilizes a patented taste making technology. This taste masking technique does not utilize solvent of any kind hence lead to rapid and more efficient production. During production less heat is produced therefore this technology is used for heat sensitive drug.

Techniques for formulation of FDT 10

- Freeze drying or lyophilization
- Direct compression method
- Sublimation method
- Moulding method
- Spray drying method
- Taste masking method

Direct compression method-

For preparation of fast dissolving tablet direct compression method is a commonly used. It is a simple method for preparation of FDT. Diluents, directly compressible disintigrants, effervescent agent are used as excipient for FDT production. The blend prepare from excipient and drug are directly compressed. Superdisintigrant are used in optimum quantity. This help in faster disintegration of tablet. Different types of superdisintigrants are used like crosspovidone, sodium starch glycolate, microcrystalline cellulose etc.

Table no-1 list of superdisintigrants.[11]

Superdisintigrants	Nature	Mechanism of action	Brand name
Crosscarmellose	Modified cellulose or cross linked cellulose.	Wicking due to fibrous structure.	AC-Di-ol Nymcel
Crosspovidone	Cross linked PVP	Water wicking , sweelind and possibly some deformation recovery.	Kollidon, Polyplasdone
Sodium starch glycolate	Modified starch	Rapid and extensive sweeling with minimal gelling.	Explotab Primogel

Mechanism of superdisintigrants[12]

- By porosity capillary action (wicking)
- By swelling
- By enzymatic reaction
- Due to disintegrating particle
- Due to deformation

Freeze drying or lyophilization method

For drying of heat sensitive drug this method can be used. At low temperature drying is done, and water can be removed by sublimation process. Through lyophilization highly porous tablet may be form. More fragile tablet can be form by lyophilization technique therefore specialized packing is required.

Drawback-

The main disadvantages of lyophilized drug are that they have very poor stability when store under stressed conditions.

Sublimation method-

This process involve addition of napthalene, camphor, urea. Tablet with highly porous structure are form with this technology. By this technique, the active drug, volatilized substance and other ingredient are compressed to form a tablet, and sublimation of volatilizing substance is done. This can result in the formation of pores tablet. Volatile substance like Camphor, ammonium bicarbonate, hexamethylene tetramine etc. are used in sublimation method

Moulding method-

Tablet prepare by this method is solid dispersion. Drug can exist in a matrix as a discrete particle or micro particle. In this method the ingredient blends are moistened with hydro-alcoholic or aqueous solvent. Then blend is moulded into tablet, for that low compression force is require. The pressure require for moulded tablet is low as compare to conventional tablet. For conventional tablet high pressure is required. Air drying is used to remove solvent.

Drawback

Tablet possess poor mechanical strength.

Spray drying method

A highly porous powder is preparing by this method. This method involves spray drying of blend containing drug, bulking agent, effervescent and disintegrating agent. It results in the formation of porous powder which can instantly dissolve in water. Finally, the porus powder is then compressed to formulate tablet.

Taste Masking Technologies [13,14]

To achieve the goal of taste abatement of bitter or unpleasant taste of drug. Various techniques reported in the literature are as follows

- Taste masking with flavors, sweeteners & amino
- Acids
- Polymer coating of drug
- Formation of inclusion complexes
- Ion exchange resin complexes
- Solid dispersion
- salt preparation

Taste masking with flavors, sweeteners & amino acid

This technique is simplest approach for taste masking. But for very bitter drug this apparoach is not successful. Artificial sweeteners and flavors can be generally used alone with other taste-masking method to improve the efficiency of these techniques.

Flavors

Basis of Choosing a Flavor

- Complementary to existing flavor of the drug
- Known popularity of particular flavors
- Age of patients
- Allergy

Natural Vs Synthetic

- Cheaper
- More readily available
- Less variable in chemical composition
- More stable Flavoring agents for taste masking [4]

Natural Flavors- Raspberry Juices, Liquorices Extract, Lemon & Orange Spirits, Blackcurrant Syrups, Ginger Tinctures, Anise & Cinnamon Aromatic Waters, Peppermint & Lemon Aromatic Oils.

Synthetic Flavors- Alcoholic solutions, Aqueous solutions, powders.

Sweeteners

- Complement flavors associated with sweetness
- Soothing effect on the membranes of the throat

Natural Sweetener- Sucrose, Glucose, Fructose, Sorbitol, Mannitol, Honey, Glycerol, Liquorice.

Artificial Sweetener- Saccharin, Saccharin Sodium, Aspartame.

Nutritive Sweeteners- Sucrose, Fructose, Glucose.

Non-Nutritive Sweeteners- Aspartame, Sucralose, Neotame, Saccharine.

Polyols- Mannitol, Sorbitol, Xylitol, Erythritol, Maltitol.

Novel Sweeteners- Trehalose, Tagatose.

Amino acids

Amino acids and their salts (alanine, taurine, glutamic acid, glycine) in combination with bitter drugs it can reduces the bitterness of the drugs for example, taste of ampicillin improved markedly by preparing its granules with glycine and mixing them with additional quantity of glycine, sweeteners, flavors and finally compressing them into tablets.

Table no-2 [13]

Sr no	Drug	Flavor	Result
1	Nimesulide	Camphor	Camphor significantly masked the taste of tablet with sufficient strength, friability, disintegration and dissolution
2	Oflaxacin	Aspartame	Aspartame significantly masked the taste of tablet

Polymer coating of drug

Some bad taste drugs are not be masked by incorporation of sweetners and flavours. Therefore, coating of drug is an alternative option for taste masking. This process retard dissolution and solubalization of drug. This is a simplest method for taste masking. Coating act as a physical barrier to drug particle hence drug and taste bud interaction can be minimizing. Taste masking of ibuprofen has been successfully achieved by using the air suspension coating technique to form microcapsules, which comprises a pharmaceutical core of a crystalline ibuprofen and methacrylic acid copolymer coating that provides chewable taste masked characteristics.

Agents used for coating

- Carbohydrates (Cellulose)
- Synthetic polymers (Eudragits etc)
- Proteins, Gelatine, and Prolamines (Zein)
- Zeolites

Table no-3 [13]

Sr no	Drug	Polymer	Result
1	Indeloxazine hydrochloride	mixture comprising hyd rogenated oil and surfa ctants	Powders of Indeloxazine hydrochloride without this bitter taste, microparticles (medi an diameter, 130 m) of IDX were coated to m ask the tast
2	Sparfloxacin	Low substituted hydrox ypropyl cellulose, ethyl cellulose	Degree of Taste masking increases by ethyl cellulose and HPMC ratio. Complete tast e masking was done EC: HPMC

Formation of inclusion complexes

In inclusion complex formation drug molecule fits into cavity of complexing agent. Host of molecule is a stable complex. Bitterness reduction is depend upon the extent of complexation of guest molecule. In inclusion complex vander walls force are mainly involve. The bitter taste of drug can be reduced by complexing agent either by decreasing it's oral solubility. Third method is suitable for low dose drug. Hydrophobic drugs form complex by replacing, inclusion water. while easily migrating (hydrophilic, well soluble) drugs form complex, assuming replacement of crystal water.

Table no-4 [13]

Sr no	Drug	Polymer	Result
1	Terfenadine	B-cyclodextrin	A palatable syrup of terfenadine-cyclodextrin complex was formulated

Ion exchange resin complexes

In this method drug are attached to oppositely charged resin sunstrate, forming insoluble substance or resonate through weak ionic bonding. Ion-exchange resin are high molecular weight polymer with anionic and cationic functional group which are join to water insoluble polymer backbone.

Classification

- Strong cation exchanger- sulphuric acid sites
- Weak cation exchanger- carboxylic acid moieties

- Strong anion exchanger- quaternary amine ionic sites
- Weak anion exchanger- predominantly tertiary amine substituents

Solid dispersion

Dispersion of one or more active ingredient is an inert carrier or matrix at solid state prepare by melting solvent or melting solvent method. Solid dispersion of drug like polymers, sugar, or other suitable agents, is very useful for taste masking. povidone, polyethylene glycols, hydroxypropyl methylcellulose, urea, mannitol and ethylcellulose are used as carrier in solid dispersion. Various approaches for preparation of solid dispersion are enlist below: -

- Melting method
- Solvent method
- Melting solvent method

Table no-5

Sr no	Drug	Polymer	Result
1	Artemether	Mono Amino Glycyrrhyzinate Pentahydrate (GLY)	Successful masking of taste and rapid disintegration of formulated tablets in the oral cavity with improved Dissolution
2	Rofecoxib	Poloxamer 188	The melting method was used to prepare solid dispersions and MDT was formulated.

CONCLUSION

Introduction of fast disintegrating dosage forms has solved some of the problems encountered in administration of drugs to the pediatric and elderly patient, which constitutes a large proportion of the world's population. Hence, patient demand and the availability of various technologies have increased the acceptance of Fast disintegrating tablets, which in turn prolongs the patent life of a drug. Keeping in view of the advantages of the delivery system, fast disintegrating dosage forms have been successfully commercialized, and these dosage forms very well accepted at doctors as well as patient level.

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