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MOUTH DISSOLVING TABLETS- A NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

The past decade has thrown open the doors for continuous technological advancements in the pharmaceutical sector. Mouth Dissolving Tablets are one of the fruitful results of these technological advancements. MD tablets play a major role in improving the patient's compliance. They rapidly disintegrate in the saliva hence obviating the need of the water. With the increasing incidences of non-compliance among the patients, Mouth dissolving tablets are the perfect answer to all these problems. A variety of drugs can be administered in the form of MD tablets as they give the advantage of the liquid medication in the solid preparation. These novel types of dosage forms have found acceptance among the geriatric, pediatric and dysphasic patients.

Keywords: Mouth dissolving tablets, Patient's compliance, Novel Drug Delivery

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1.0 INTRODUCTION

Patient compliance is one of the most important aspects in the pharmacy practice. Now days, pharmacy companies are coming up with development of new drug delivery systems to ensure the delivery of the drugs to the patients efficiently and with fewer side effects. This objective led to the emergence of the concept of Mouth Dissolving Tablets. These dosage forms rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration. This attribute makes these dosage forms highly attractive product for the pediatric, geriatric and dysphagic patients.

The disorder of dysphagia is associated with many diseases like stroke, Parkinson's disease, AIDS, thyroidectomy, head and neck radiation therapy and other neurological disorders including cerebral palsy. Earlier reports revealed that 26% out of 1576 patients experienced difficulty in swallowing tablets due to their large size, followed by their surface, shape and taste. The problem of swallowing tablets is also evident in travelling patients who may not have ready access to water.¹ below² below

There are number of dosage forms available like effervescent tablets, dry syrups and chewing gum tablets, which are commonly used to enhance the

patient's compliance but MD tablets that can dissolve or disintegrate in oral cavity have attracted a great deal of attention. They dissolve fast in the mouth and water quickly egress into the tablet matrix to cause rapid disintegration and instantaneous dissolution of the tablet. The basic approach to design MDT is by maximizing the porous structure of the tablet matrix, incorporating the suitable disintegrating agents and highly water soluble excipients in the tablet formulation.

Following are the characteristics of an ideal mouth dissolving tablet -

- A. It should not require the water to swallow and should dissolve or disintegrate in the mouth within a few seconds.
- B. It should allow high drug loading.
- C. It should provide pleasant mouth feeling with minimal or no residue in the mouth after oral administration.
- D. It should have sufficient strength not to disintegrate during the manufacturing and post manufacturing handling period with a low sensitivity to the environmental conditions such as humidity and temperature.

- E. It should be adaptable to the existing packaging and processing Techniques.^{1,2}

MD tablets are also known as fast dissolving, rapid-dissolve, rapimelt, fast melts, porous tablets, EFVDAS or Effervescent Drug Absorption system (Elan Corporation), Orosolv (Cima Labs Inc. USA), Zydis (R.P.Scherer, UK) etc.

There are some of the advantages that make MDT beneficial over other dosage forms.

- I. MD tablets are easy to administer to the patients who have difficulty in swallowing like children, old people, bed-ridden and psychiatric patients.
- II. Patients which do not always have access to the water like travelling patients use MD tablets.
- III. It gives the benefit of the liquid dosage form as it dissolves in the mouth and acts like syrup or a solution because of the homogeneity offered by MD tablets with good chemical stability.
- IV. It provides better bioavailability by rapid drug absorption in the pre-gastric area like esophagus and buccal cavity and can be handled easily.

Common techniques for manufacturing of MD tablets are:

1. Lyophilization
2. Moulding

3. Direct Compression
4. Cotton Candy Process
5. Spray Drying
6. Sublimation
7. Mass Extrusion
8. Nanonization
9. Fast Dissolving Films

1. LYOPHILIZATION

In this technique tablets form have a porous matrix structure. Due to the presence of open matrix structure, the saliva goes into the matrix resulting in the dissolution of the matrix. Hence the tablets are dissolved very rapidly. The drug is entrapped in a water soluble matrix which is freeze dried to produce a unit which rapidly disperses when placed in mouth. The final formulation may contain other excipients, such as suspending agents, wetting agents, preservatives, antioxidants, colors and flavors which improve the process characteristics or enhance the quality of final product. Essential characteristics for Freeze drying formulations include small particle size with low dose and water-insoluble, chemically stable drug molecule. Technologies like Zydis, Quicksolv and Lyoc are commonly used to manufacture MDTs worldwide.

The Zydis technology (ZT) is a patented technique which had been used for drugs like famotidine, enalapril, loperamide, piroxicam, oxazepam, lorazepam, domperidone, brompheniramine, olanzepine, ondansetron and rizatriptan. Numbers of products are available in the market, which had been manufactured using this technology. In U.S., the MDT products

available are: Claritin Reditab, Dimetapp Quick Dissolve, Feldene Melt, Maxalt- MLT, Pepcid RPD, Zofran ODT and Zyprexa Zydis.

The major advantage of this technology is that it offers less disintegration time but the technique is quite expensive and special packaging procedures are required. The storage conditions should be properly maintained as these tablets are less stable to changing environment; hence special packaging procedures are required.

During lyophilization, formulation excipients and process variables play an important role. Hydrochlorothiazide was used as a model drug¹⁰,¹¹ for detecting the influence of various formulations and process parameters on the characteristics of MD tablets. According to them, maltodextrins are useful for the formulation of tablets formed by lyophilization technique. Similarly results revealed the role of formulation excipients⁴ in the development of lyophilised fast disintegrating tablets. It was concluded that the use of 5% gelatin in combination of mannitol is the ideal formulation. Carbopol 974P-NF and Pluronic F127 (6%) were concluded to have the best viscosity modifying properties.

2. TABLET MOULDING

Molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The

solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution. They disintegrate very quickly because these are made from water soluble excipients. These properties are enhanced with porous structures or are physically modified by the molding process. In comparison to lyophilization process, tablets produced by moulding technique are easier to adapt to the industrial scale. Moulded tablets are cheaper and have poor mechanical strength. They can break or get eroded during the process of handling and storing. To overcome the poor taste, drug⁵ containing discrete particles was incorporated, which was formed by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium bicarbonate, lecithin, polyethylene glycol and active ingredient into a lactose based tablet triturate form.

3. DIRECT COMPRESSION

It is the simplest and most cost effective tablet manufacturing technique for MDTs as they can be fabricated using conventional tablet manufacturing and packaging machinery and also due to availability of tableting excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrants, effervescent agents and sugar based excipients. A type of disintegrant and its proportion are of prime importance. There are number of factors which affect disintegration like particle size distribution, contact angle, pore size distribution,

tablet hardness, water absorption capacity and type and proportion of disintegrants.

FLASHTAB, a DC based technology contains coated crystals of drug and micro granules along with disintegrants. In this technology, two types of disintegrants are used: a disintegrating agent (e.g., modified cellulose), which has a high swelling force and a swelling agent (e.g., starch) which has a low swelling force. Cousin et al⁶ formulated a rapidly disintegrable multi particular tablet using carboxymethyl cellulose as disintegrating agent and swelling agent consisting of modified starch or microcrystalline cellulose. The disintegration time of this tablet was 60 sec.

The evolution of carbon dioxide as a disintegrating mechanism forms the basis of another DC based technology called as ORASOLV. J. Michaelson⁷ describes the use of a combination of alginic acid and a water-soluble metal carbonic acid to prepare tablets. An acid-base reaction occurs when they are dissolved in water. The salt causes the tablet to swell and the carbonic acid produced carbon dioxide within the swelling tablet so that rapid disintegration can be possible. Similarly, the use of sugar-based recipients like dextrose, fructose, isomalt, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol is appreciated in masking the bad taste of the tablets and impart sweetness while formulating MD tablets

4. COTTON-CANDY PROCESS

In this process Shearform technology is used in the preparation of a matrix known as FLOSS, made from the combination of the recipients either alone or with the drugs. The fibrous nature of the floss is similar to the cotton-candy fibers. The floss is commonly made of saccharides such as sucrose, dextrose, lactose and fructose at temperatures ranging between 180–266 °F. Other polysaccharides such as polymaltodextrins and polydextrose can be transformed into fibers at 30-40% lower temperature range.

5. SPRAY DRYING

Allen et al⁸ used spray drying process to provide products with high porosity in fine powder because the processing solvent can be easily dried. Hence rapidly disintegrating tablets can be prepared where tablets disintegrates in less than 20 seconds. This technique is based on particulate support-matrix, which is prepared by spray drying the solvent. This matrix then becomes the carrier for the active ingredients. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and / or alkali material (e.g. sodium bicarbonate) to enhance disintegration and dissolution.

6. SUBLIMATION

In the sublimation process, the tablet is formed with active ingredients and the recipients which are volatile in nature. After the compression of the tablets, the volatile ingredients are evaporated and the remnant is highly porous tablet which can be easily disintegrated. Inert solid ingredients such as urea, ammonium carbonate, ammonium bicarbonate, hexa methylene tetramine, camphor etc are added which can volatilize very easily. Highly porous⁹ and compressed tablets were prepared by sublimation that were rapidly soluble in saliva. Mannitol and camphor were used as a tablet matrix material and subliming the material respectively. Sublimation of camphor was done in vacuum at 80 C for 30 minutes to develop pores in the tablets.

7. MASS EXTRUDER

This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol and expulsion of softened mass through the extruder or syringe to get a cylindrical shaped extrude which are finally cut into even segments using heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste.

8. NANONIZATION

In this process, the particles of the drug are reduced in size to nanoparticles by milling the drug in the proprietary wet milling process. The agglomeration can be prevented by surface

adsorption of the nanocrystals. These are then compressed and changed into a tablet. This technique is advantageous for less water soluble drugs. The bioavailability of the drug is increased as the disintegration time is reduced to a significant extent.

9. FAST DISSOLVING FILMS

This is a new technique through which medications can be taken more conveniently. In this technique, a non-aqueous solution is prepared containing water soluble film forming polymers (carboxy methylcellulose, hydroxypropyl methylcellulose, hydroxyl ethylcellulose, hydroxyl propylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking ingredients, which is allowed to form a film after evaporation of solvent.

Nowadays MD tablets are successfully evolved as the alternative way of administering tablets. There are number of patented technologies which were developed for the formation of MD tablets and are described as under:

PATENTED TECHNOLOGIES FOR MD TABLET FORMATION:

Zydis Technology

Zydis was the first marketed technology developed by R.P.Scherer, Inc. for formation of new generation tablets. Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product

is very light weight and fragile, which is dispensed in a special blister-packing. The preparation is also self-preserving because due to freeze drying, there is very little amount of water left in the drug for the attack of the microorganisms. The disintegration time of the tablets made by Zydis technology is few seconds.

Durasolv technology

The tablets made by this technology which was developed by CIMA labs, consist of a drug, fillers and the lubricants. The tablets are prepared by conventional tableting equipment and have good rigidity. They can be packed in the conventional tableting equipment and have good rigidity. This technology is good for tablets having low amount of active ingredients.

Orasolv Technology

CIMA labs developed this technology where the tablets are made by direct compression but with less of the pressure than the conventional DC. The active ingredient is taste masked and it also contains the effervescent disintegrators. The tablets produced are soft and friable and packaged in specially designed pick and place system.

Wowtab technology

Wowtab Technology is patented by Yamanouchi Pharmaceutical Co. where the word "WOW" means "without water". It is the combination of low mouldability saccharides and high mouldability saccharides used to obtain a rapidly melting strong tablet. The active ingredient is

mixed with a low mouldability saccharide and granulated with a high mouldability saccharide and compressed into tablet.

Flashtab technology

The tablet prepared by this technology was patented by Prographarm laboratories. It consists of active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like coacervation, microencapsulation, and extrusion spheronisation.

Beside these, there are some other patented technologies like Lyoc patented by Farmalyoc, Quicksolv patented by Janssen pharmaceuticals, Zipllets and Advatab patented by Eurand International, Oraquick patented by KV Pharm.Co.,Inc. etc

CONCLUSION:

Today there is significant amount of non-compliance among the patients and hence there is a need to design the patient-oriented drug delivery systems. Mouth dissolving tablets are ideal for many groups of patients including geriatrics, pediatrics, psychiatrics and for those people who have difficulty in swallowing. By using such manufacturing technologies, many drugs can be formulated in the form of mouth dissolving tablets to provide the advantages of liquid medication in the form of solid preparation. With the continuous innovations in the pharmaceutical technologies, one can expect the emergence

of more novel technologies for MDTs in the days to come. It is reasonable to expect that future trends in innovations of drug delivery systems will continue to bring together different technological disciplines to create novel technologies.

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