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RESEARCH ARTICLE

ORODISPERSIBLE TABLET

Mr. Dharashive V.M. and *Mrs. Kapse V.N. YELAM

Pharmaceutical Department, Shivlingeshwar College of Pharmacy, Almala Dist. Latur, Maharashtra, 413520

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ABSTRACT

The most common, convenient and preferred route of drug administration is oral route. Oral disintegrating tablets are the solid dosage forms that disintegrates in the saliva in less than 60 seconds, and are thus taken without the need of extra water. The oral disintegrating tablets are launched in 1980 and hence now-a-days it is one of the fastest growing segment of oral dosage form due to its improved solubility, stability and patient compliance. The versatile manufacturing technologies of orally disintegrating tablet is now no longer limited by dosage strength, bitter active pharmaceutical ingredients (API) and narrow therapeutic applications. scientists have prepared ODTs by following various methods like compression, molding, melt granulation, phase transition process, sublimation, freeze-drying, spray drying, effervescent methods etc.

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INTRODUCTION

This type of drug delivery helps to peoples who have difficulty in taking conventional solid dosage forms e.g childrens, elders, patients, mentally ill persons, disabled etc. Thus this has encouraged both academia and industry to generate new orally disintegrating formulations and technological approaches in this field. Drug delivery sytems are the strategic tool for expanding market, extending product life cycles and generating opportunities. The oral drug delivery system is the most preferred way of administration, due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliances, many patient groups such as childrens, elder patients, mentally ill persons disabled, nauseated, patients having dysphagia (difficulty in swallowing) motion sickness complications etc patients are non compliance with the traditional oral form, so over a decade the demand for development of orally disintegrating tablets (ODTs) has enormously increased. A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds when placed upon the tongue are called orally disintegrating tablets. The term orodispersible Tablet as appears in European Pharmacopoeia (suppl.4.1, Iv ED) is defined as "uncovered tablet for Buccal cavity, where it disperse before ingestion ". Thus it has significant impact on the patient compliance. ODTs with good taste and flavor increase the acceptability of bitter drugs by various group of population. Orodispersible tablets are also known as Mouth dissolving tablets, Orally disintegrating tablets, Melt-in-mouth, Fast dissolving drug delivery, Rapimelt tablets, Porous tablets, Quick dissolving tablets etc. Developing new drug delivery technologies and utilizing them in product development is critical for all the pharmaceutical industries. A new dosage form allows a manufacturer to extend market exclusivity, unique product differentiation, product life extension and offers a more convenient dosage form to the the patient. marketers build a better brand and company image when they offer a unique easier-to-take form that satisfies the need of an underserved patient population.

Corresponding author: **Mrs. Kapse V.N. YELAM**
Pharmaceutical Department, Shivlingeshwar College of Pharmacy, Almala Dist. Latur, Maharashtra, 413520.

SELECTION OF ODT DRUG CANDIDATES

Several factors must be considered when selecting drug candidates for delivery of ODTs as dosage form. In general an ODT is formulated as a bioequivalent line extension of an oral dosage form. But in some cases an ODT may have varying degrees of pregastric absorption and thus the pharmacokinetic profile will vary. Therefore the ODTs will not be equivalent to the conventional oral dosage form. It is possible that these differences may be fully or partly attributed to the drug molecule, formulation or combination.

Drugs having ability to diffuse and able to permeate oral mucosal tissue are considered ideal for ODT formulations.Patients who concurrently take anti-cholinergic medications may not be the best candidates of these drugs. Similarly patients with siogren's syndrome or dryness of the mouth due decreased saliva production may not be good candidates for these tablet formulation. Patients who require drugs with a short half-life and frequent dosing, drugs which are very bitter or otherwise unacceptable taste because taste masking cannot be achieved or those which require controlled or sustained release are unsuitable candidates of rapidly dissolving oral dosage form.

IDEAL PROPERTIES

- ODTs can be manufactured by using conventional processes and packaging equipments.
- It required no external water for administration.
- It leave minimal or no residue in mouth after administration.
- It have improved compliance with added convenience.

ADVANTAGES

- ODTs are cost effective, lower production, packaging and distribution cost as compared to current commercially available products.
- No chewing needed.
- Ease in administration for patients who are mentally ill, disabled and uncooperative.
- Ability to provide advantages of liquid medications in the form of solid preparation.
- Allows high drug loading.

DISADVANTAGES

- It is a cost-intensive production process.
- Lack of physical resistance in standard blister packs.
- Limited ability to incorporate higher concentrations of active drug.
- Patients who concurrently take anti-cholinergic medications may not be the best candidates for ODTs.
- Hygroscopic in nature.
- Sometime it posseses mouth feeling.
- Highly fragile.
- ODTs requires special packaging for properly stabilization and safety of stable product.

Factors for ODT

Taste masking

Many drugs are bitter in taste. A tablet of bitter drug dissolving / disintegrating in mouth will seriously affect patient compliance and acceptance for the dosage form. So effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.

Number of techniques are developed for masking the bitter taste of most of the drugs that includes

- formation of pellets by extrusion.
- speronization or mass extrusion.
- coating of drug using a taste masking polymer.
- Spray drying the drug dispersed in a polymeric solution.
- Complexation of drugs by inclusion in cyclodextrin.
- Drug-resinate complex formation.
- Microencapsulation of drug by polymer.

Mechanical strength & disintegration time

Mechanical strength and disintegration time are directly proportional to each other i.e increasing the mechanical strength of tablet will increase the disintegration time of tablet. So a good compromise between these two parameters is always essentials. As the ODTs must be formulated to obtain disintegration time usually less than a minute. Many ODTs are fragile and there are many chances that such fragile tablet will break during packing, transport or handling by the patients.

Mouth feel

To get better mouth feel ODTs should leave minimal or no residue in mouth after oral administration. ODTs should not disintegrate into larger particles in the oral cavity, it must be as small as possible. Moreover addition of flavours and cooling agents like menthol improve the mouth feel.

Sensitivity to environmental conditions

ODTs should generally show low sensitivity to environmental conditions such as humidity and temperature as most of the materials used to manufacture ODTs are meant to dissolve in minimum quantity of water.

Cost

The technology used to manufacture ODTs must be acceptable in terms of costs. some methods like Zydis & Orasolv require special technologies & specific packaging which increase the cost to a remarkable range.

Technologies used to manufacture orodispersible tablets

- Freeze Drying.
- Tablet Moulding.
- Spray Drying.
- Sublimation.
- Direct compression.
- Mass Extrusion: -
- Nanonization : -

FREEZE DRYING OR LYOPHILISATION

A process in which water is sublimated from the product after freezing is called lyophilisation. It is a pharmaceutical technology which allows drying of heat sensitive drugs and biologicals at low temperature under conditions that allows removal of water by sublimation. Lyophilisation results in preparations which are highly porous, with a very high specific surface area and which dissolve rapidly and show improved absorption and bioavailability. Tablets prepared by lyophilisation are fragile and possesses low mechanical strength which make them difficult to handle and they also exhibit poor stability on storage under stressed conditions. Jaccard and Leyder used lyophilisation to create an oral pharmaceutical preparations that not only dissolves rapidly but also improved the bioavailability of several drugs such as Spironolactone and Trolendomycin.

MOULDING

Moulded tablets disintegrates more rapidly and offer improved taste because the dispersion matrix is generally made from water soluble sugars. The active ingredients in most cases is absorbed through the mucosal lining of the mouth. In the manufacturing process of moulding tablets 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 and possesses porous structure.

SPRAY DRYING

Spray drying is a process by which highly porous, fine powders can be produced. The formulations that were produced contained hydrolyzed & unhydrolyzed gelatin as a support agent for the matrix, mannitol as a bulking agent and sodium starch glycolate or crosscarmellose as a disintegrant. Disintegration & Dissolution was further enchanced by adding an acid or an alkali. The formulation was spray dried to yield a porous powder and the tablet manufactured from this powder disintegrates in less than 20 seconds in an aqueous medium.

SUBLIMATION

The presence of porous structure in the tablet matrix is the key for rapid disintegration of tablet. A porous matrix is formed by compressing the volatile ingredients along with other excipients into tablets, which are finally subjected to a process of sublimation. Ammonium bicarbonate, Ammonium carbonate, benzoic acid, camphor, Hexamethonium teramine, Napthalene, Pthalic anhydride, Urea, & Urethane were compressed along with other excipients into a tablet. The volatile material was then removed by sublimation leaving behind a porous matrix

DIRECT COMPRESSION

It is the easiest way to manufacture tablets. conventional equipments, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablets can easily exceed than that of other production methods.

MASS EXTRUSION

This technology involves softening of the active blend using solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby making their bitter taste.

NANOZINATION

It is the process of size-reducing of the drug particles with or without stabilizer to less than 1000nm and preferably less than 100 nm. Nanomelt technology involves reduction in the particle size of drug to nanosize by milling the drug using a proprietary wet-milling technique.

The nano crystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into the ODTs. This technique is especially advantageous for poor water soluble drugs that leads to fast disintegration, increased absorption and hence higher bioavailability. Nanonization is a cost effective manufacturing process needs conventional packaging due to exceptional durability and wide range of doses.

PATENTED TECHNOLOGIES

ZYDIS TECHNOLOGY

ZYDIS are the inventors of this technology. It is the best known of the fast dissolving / disintegrating tablet preparations, and was the marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. Zydis tablet is produced by lypophilizing or freeze-drying the drug in a matrix usually consisting of gelatine. The product is very light weight and fragile and must be dispensed in a special blister pack.

ORASOLV TECHNOLOGY

Cima labs are the inventors of this technology. The orasolv tablets are lightly compressed, yielding a weaker and more brittle tablet in comparison with conventional tablets but it has the appearance of a traditional compressed tablet. In orasolv tablet the particle coating used for taste masking is not compromised by fracture during processing.

DURASOLV TECHNOLOGY

Cima labs are the inventors of this technology. It is the second-generation fast-dissolving / disintegrating tablet formulation. Durasolv has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting thus it is produced in faster and more cost effective manner.

FLASH DOSE TECHNOLOGY

Fuisz is the inventor of this technology. The flash dose technology utilizes a unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. The final product has a very high surface area for dissolution. It disperse and dissolves quickly once placed onto the tongue.

WOWTAB TECHNOLOGY

Yamanouchi pharmaceuticals are the inventors of this technology. The WOW in WOWTAB signifies the tablet is to be given " wit out water". The wowtab technology utilizes sugar and sugar-like excipients. This process uses a combination of low mouldability saccharides and high mouldability saccharides. The two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate.

EVALUATION OF FAST DISSOLVING TABLETS

TABLET THICKNESS

Tablet thickness is an important characteristics in reproducing appearance and also in counting by using filling equipment.

WEIGHT VARIATION

Standard procedures are followed as described in the official books.

FRIABILITY: - Increase in the friability of ODTs than conventional tablets decreases the disintegration time. It is a measure of mechanical strength of the tablet. If a tablet has more friability it may not remain intact during packaging, transport, or handling. Roche friabilator is used to determine the friability by following the procedure.

HARDNESS (CRUSHING STRENGTH)

Tablet hardness is measured with hardness tester like Monsanto. The hardness of ODTs is generally kept lower than conventional tablets as increased hardness delays the disintegration of the tablet.

WETTING TIME

The method by Yunixia et.al. was followed to measure tablet wetting time. A piece of tissue paper (12cm*10.75cm) folded twice was placed in a small petridish (ID=6.5) containing 6ml of sorensons buffer ph 6.8. A tablet as put on the paper, and the time for complete wetting was measured.

DISINTEGRATION TIME

Several new methods have been used to find disintegration time. One of these methods uses a charge couple device (CCD) camera or texture analyzer to evaluate the disintegration time of tablets. Another simplest method is to take 6ml of simulated saliva in a measuring cylinder and place the tablet in it. The liquid is neither shaken nor stirred & DT is noted.

IN VIVO DISINTEGRATION TIME

It is determined using healthy human volunteers. The DT noted by the volunteers by placing the tablet in mouth.

DISSOLUTION TEST

The dissolution method for oral disintegrating tablets is the same as that of conventional tablets. USP 2 paddle apparatus is most suitable and common choice for dissolution test of oral disintegrating tablets.

STABILITY STUDY (TEMPERATURE DEPENDENT)

The fast dissolving tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

- 40±1°c
- 50±1°c
- 37±1°c
- RH 75%±5%

The tablets were withdrawn after 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegrations and Dissolution etc.) and drug content. Accelerated stability data are plotting according Arrhenius equation to determine the shelf life at 25°c.

INDUSTRIAL APPLICATION

- To develop new orally disintegrating dosage forms.
- To improve the existing technology of ODTs.
- To optimize the blend of disintegrants or excipients to achieve ODTs.
- To select and develop proper packaging material and system for enhanced stability & distribution of the product and also develop a cost-effective product.
- To use various taste-masking agents and prepare palatable dosage forms to increase patient compliance.
- To develop disintegrants from different polymers which are used as coating materials by certain modifications & use them for formulating ODTs.

Conclusion

Oral drug delivery is the most demanded route of administration due to its safest, most convenient & most economical method of drug delivery. A novel tablet concept which offers ease of oral administration & benefits of increased patient compliance is the ODTs. They have better patient acceptance and compliance and may offer improved biopharmaceutical properties, improved efficacy, and better safety compared with conventional oral dosage forms. Prescription ODT product initially were developed to overcome the difficulty in swallowing conventional tablets among pediatric, geriatric & psychiatric patients with dysphagia. Today, ODTs are more widely available as OTC product for treatment of allergies, cold, flu symptoms. The target population has expanded to those who want convenient dosing anywhere, anytime, without water. Such product provide opportunity for the product line extension in the market place. Due to this wide significance of ODTs, this drug delivery system may lead to better patient compliance and ultimate clinical output. Future might provide many more classes of drugs developed in the form of ODT.

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