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AN EYE REPORT ON RECENT ADVANCEMENTS IN FAST-DISSOLVING DRUG DELIVERY SYSTEM

Amit Kumar, Vishal kumar, Ashish Jaiswal, Anjana Devi[1]*
School of Pharmacy, Career Point University Bhoranj (Tikker - kharwarian),
Hamirpur, Himachal Pradesh 176041, India

ABSTRACT

Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. Mouth dissolving tablet are solid dosage forms containing drugs that disintegrate in the oral cavity with in less than one minute that development of mouth dissolving tablets formulation is emerging and gaining popularity because it is easy to administer and leads to better patient compliance. Als for the drugs that have poor bioavailability, these dosage forms are widely used as they provide large acceptance of such drugs by avoiding first pass metabolism tablets that disintegrate with in few seconds. According to European pharmacopoeia, the ODT should disperse in less than three minutes. MDTs can be administered anywhere and anytime, without the need of water and are thus quite suitable for children, elderly and mentally disabled patients. This is seen to afflict nearly 35% of the general population and associated with a number of conditions like parkinsonism, mental disability, motion sickness, unconsciousness, unavailability of water etc.to overcome such problems, certain innovative drug delivery systems, like 'mouth dissolving tablets'(MDT) have been developed.

KEYWORDS: MDT, Oral Delivery, Patients, Disperse, Mouth dissolving tablets

INTRODUCTION

FAST-DISSOLVING DRUG DELIVERY SYSTEM

FDDDS were first came into existence in 1970 as an alternative to tablets, syrups and capsules, for pediatric and geriatric patients which rapidly disintegrate and dissolve in saliva and then easily swallowed without need of water which is a major benefit over conventional dosage form.

Fast dissolving drug delivery system have acquired great importance in the pharmaceutical industry due to their unique properties and advantages like availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity, no need of water, accurate dosing, rapid onset of action, ease of transportability, ease of handling, pleasant taste and improved patient compliance especially for pediatric and geriatric. There are multiple fast-dissolving over the counter (OTC) and Prescribed (Rx) products on the market worldwide, most of which have been launched in the past 3 to 4 years.

There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology.

A fast-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrants in the oral cavity without the need of water or chewing. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. These are also called melt-in-mouth tablets, repimelts, porous tablets, oral-dispersible, quick dissolving or rapid disintegrating tablets.

AN IDEAL PROPERTIES OF FDT6

Require no water for oral administration, yet dissolve / disperse/ disintegrate in mouth in a matter of seconds. Have a pleasing mouth feel. Have an acceptable taste masking property. Be harder and less friable Leave minimal or no residue in mouth after administration Exhibit low sensitivity to environmental conditions (temperature and humidity). Allow the manufacture of tablet using conventional processing and packaging equipment.

ADVANTAGES OF MDT

1. No need of water to swallow the tablet.
2. Can be easily administered to pediatric, elderly and mentally disabled patients.
3. Accurate dosing as compared to liquids.
4. Dissolution and absorption of drug is fast, offering rapid onset of action.
5. Bioavailability of drugs is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into the stomach.
6. Advantageous over liquid medication in terms of administration as well as transportation
7. First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side

effects.

8. Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
9. Suitable for sustained/controlled release actives.
10. Allows high drug loading.

DISADVANTAGES

1. Fast dissolving tablet is hygroscopic in nature so must be kept in a dry place.
2. Sometimes it possesses a mouth feeling.
3. MDT requires special packaging for proper stabilization & safety of stable products.
4. The tablets usually have insufficient mechanical strength. Hence, careful handling is required
5. The tablets may leave an unpleasant taste and/or grittiness in the mouth if not formulated properly.

CHALLENGES IN FORMULATING FAST-DISSOLVING TABLETS

FAST-DISSOLVING ORAL FILMS

Fast-dissolving oral films (FDOFs) are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improves the efficacy of drugs by dissolving within minute in oral cavity after contact with saliva without chewing and no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability. FDOFs are useful in patients such as pediatric, geriatrics, bedridden, emetic patients, diarrhea, sudden episode of allergic attacks, or coughing for those who have an active life style. It is also useful whether local action desired such as local anesthetic for toothaches, oral ulcers, cold sores or teething.8, 9 Fast dissolving oral films are based on the technology of the transdermal patch. Films are very similar to postage stamp in their shape, size and thickness. Sometimes taste masking agents are also added to mask the taste of the active ingredient.

FAST-DISSOLVING ORAL FILMS HAVE ADVANTAGES LIKE

More stable, durable and quicker than other conventional dosage forms, avoid first pass metabolism,11 pleasant mouths feel, accurate dosing, rapid onset of action and no need of water with patient compliance. More over ease of handling and transportability.

FORMULATION METHODOLOGY EMPLOYED FOR FAST-DISSOLVING TABLETS

Lyophilization or freeze-drying Formation of porous product in freeze-drying process is exploited in formulating FDT. Lyophilization is a process, which includes the removal of solvent from a frozen suspension or solution of drug with structure-forming additives. Freeze-drying of drug along with additives imparts glossy amorphous structure resulting in highly porous and lightweight product.

The resulting tablet has rapid disintegration and dissolution when placed on the tongue and the freeze-dried unit

dissolves instantly to release the drug. The FDTs formed by lyophilization has low mechanical strength, poor stability at higher temperature, and humidity. Along with above complications and its expensive equipment freeze-drying use is observed to be limited.

TABLET MOLDING

Tablets formed by molding process are highly porous in structure, resulting in high rate of disintegration and dissolution. This process includes moistening, dissolving, or dispersing the drugs with a solvent then molding the moist mixture into tablets by applying lower pressure in compression molding, but always lower than the conventional tablet compression. The powder mixture may be sieved prior to the preparation in order to increase the dissolution. Molded tablets have low mechanical strength, which results in erosion and breakage during handling

FREEZE DRYING

A process in which water is sublimated from the product after freezing. Lyophilization is a pharmaceutical technology that allows drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by sublimation. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability.

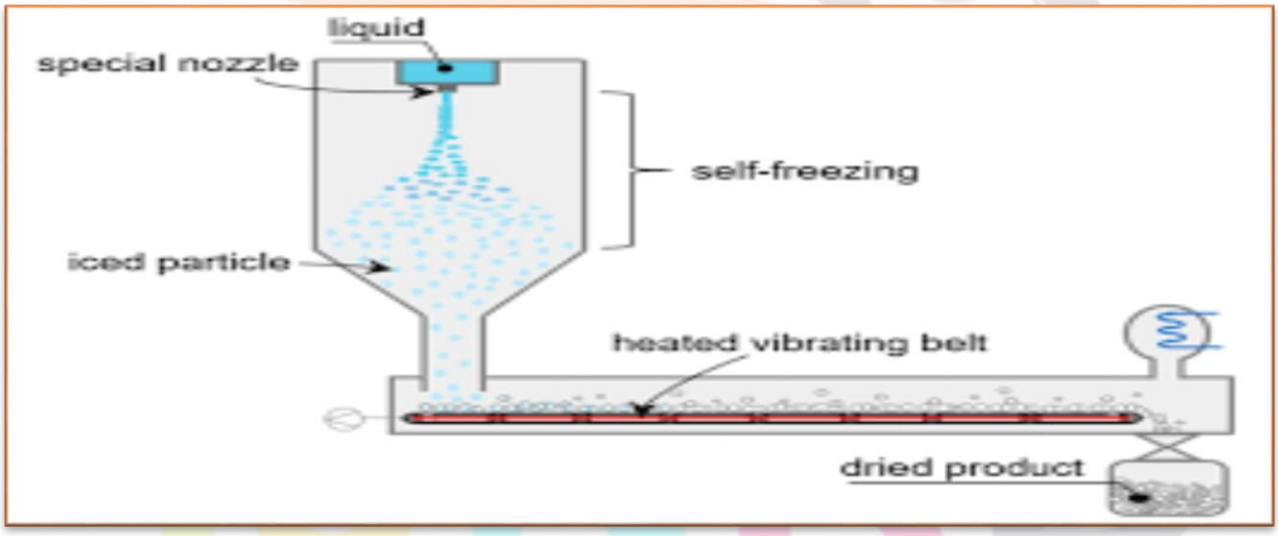

Fig: Freeze Drying

SUBLIMATION

The key to rapid disintegration for fast dissolving tablets is the presence of a porous structure in the tablet matrix. Conventional compressed tablets that contain highly water-soluble ingredients often fall to dissolve rapidly because of low porosity of the matrix. Hence, to generate porous matrix, volatile ingredients are used that are later subjected to a process of sublimation. The volatile material was then removed by sublimation, leaving behind a porous matrix. In which Mannitol is used as a matrix former, and camphor was used as a sublimating agent. That yields highly

porous tablets with satisfactory mechanical strength and a high dissolution rate.

SPRAY-DRYING

Spray drying can produce highly porous and fine powders that dissolve rapidly. The formulations are incorporated by hydrolyzed and nonhydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or cross came lose sodium as disintegrating and an acidic material (e.g. citric acid) and or alkali material (e.g. I sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium.

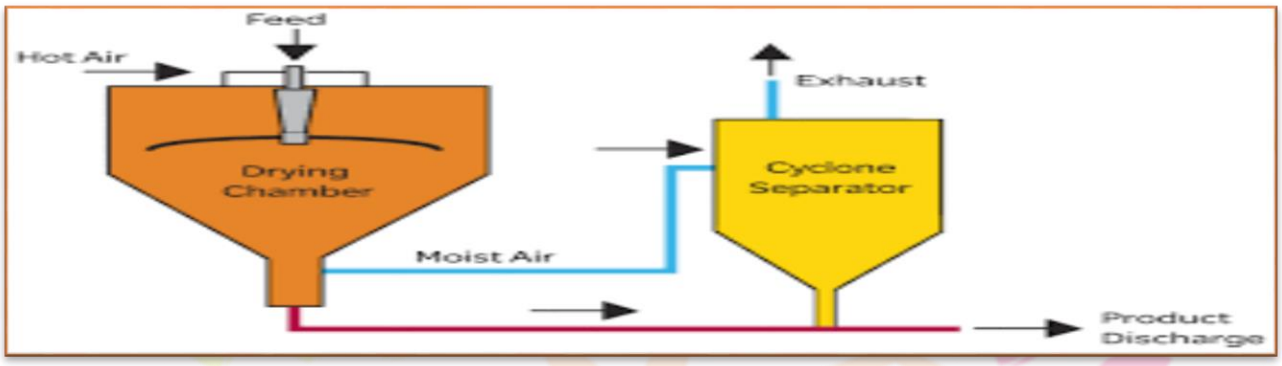

Fig**:** Spray-Drying

MASS EXTRUSION

This technology involves softening the active blend using the 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.

DIRECT COMPACTION

Direct compaction method is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Als high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. Directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agent.

COTTON CANDY PROCESS

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved

flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to FDT. This process can accommodate larger drug doses and offers improved mechanical strength. However, high-process temperature limits the use of this process.

SUPER DISINTEGRANTS USED IN MDTS

As day's passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrants, Super disintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intra granularly. This super disintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

VARIOUS TYPES OF SUPER DISINTEGRANTS USED ARE AS FOLLOWS:

1. Cross povidone
2. Microcrystalline cellulose
3. Sodium starch glycollate
4. Sodium carboxy methyl cellulose or cross came to lose sodium
5. Pre-gelatin starch
6. Calcium carboxy methyl cellulose
7. Modified corn starch. Sodium starch glycollate has good flowability than cross came lose sodium.

EVALUATION OF MOUTH-DISSOLVING TABLETS BY:

THICKNESS

Tablet thickness can be measured using a simple procedure. 5 tablets were taken and their thickness was measured using Varier calipers.

HARDNESS

It is the force required to break a tablet by compression in the radial direction, it is an important parameter in the formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. In the present study, the crushing strength of the tablet was measured using Pfizer hardness testers. An average of three observations is reported.

UNIFORMITY OF WEIGHT

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content

uniformity.

DISINTEGRATION TIME

The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

Fig: DISINTEGRATION TIME

FRIABILITY TEST

Friability of the tablets was determined using Roche friability (Electro lab Mumbai). This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the fryabilator and were subjected to 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (f) is given by the formula. $f = (1- W0 / W) \times 100$ Where, W0 is weight of the tablets before the test and W is the weight of the tablet after the test.

Fig: friability test

PACKAGING

Packaging special care is required during manufacturing and storage to protect the dosage of other fast-dissolving dosage forms. Quick-dispersing and/or dissolving oral delivery systems, the system can be packaged using various options, such as single pouch, blister card with multiple units, multiple unit dispenser, and continuous roll dispenser, depending on the application and marketing objectives.

SUMMARY AND CONCLUSION

The basic principle involved in formulating fast dissolving tablets is by maximizing the pore structure. a vacuum-drying technique was adopted in the present investigation after addition of a subliming agent to increase porosity of the tablets. The main focus of this category of drug is basically on nongeriatric and geriatric populations and patients suffering from heart disease as these provide instant relieve from the attack as taken by the patient itself without water as it disintegrates rapidly within the saliva which help in quick recovery and helpful to those patients founding difficulty in swallowing of tablets, as FDT has a potential advantage on conventional dosage form as the increases the bioavailability and onset of action of the drugs.

FUTURE ASPECTS

The key ingredient of the formulation is the addition of a super disintegrates agent in optimum concentration which provide rapid disintegration along with excellent mechanical strength. the product offers a promising future potential because of the availability of new technologies along with strong market acceptance and patient demand Several drug delivery technologies that can be leveraged on improving drug therapy from these dosage forms.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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