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ORAL DISPERSIBLE TABLETS IN ADVANCED DRUG DELIVERY SYSTEM

PREPARATION AND EVALUTION

Srilatha Gangula ,Dr k.v ratnamala Department of pharmaceutics, RBVRR women's college of pharmacy , affiliated to osmania university ,hyderabad .

ABSTRACT

Oral dispersible drug delivery systems are extremely used to improve bioavailability and improve patient compliance .oral dispersible tablets(OTDs) have used alternative to conventional tablets and capsules due to better patient compliance. The purpose of the article is to review potential advancements of ODT technology in drug delivery applications .various techniques are used to prepare OTDs compression of tablets , freeze drying , tablet moulding ,sublimation and mass extrusion . OTDs are mostly used for drugs sensitive to GI fluids and it is more conventional for pediatrics , geriatric and bed ridden patients. OTDs when placed on the tongue they disintegrate within seconds releases the drug . this article reviews the preparation methods and advantages and disadvantages , selection of proper drug for formulating OTDs.

Key words : oral dispersible tablets , improve bioavailability , improved solubility

INTRODUCTION

Oral disintegrating tablets are unit solid dosage forms they are formulated with the aim of improving the disintegration and dissolution rates . the tablet must be prepared with high porosity , low density and low hardness to achieve rapid disintegration rates .oral dispersible tablets also called as oral disintegrating tablets , quick disintegrating tablets , mouth dissolving tablets , fast dissolving tablets , porous tablets, rapimelts .united states food and drug administration (FDA) defined ODT as " a solid dosage form contain medicament which disintegrates within few seconds when placed upon the tounge .

The special advantages of OTDs over the solid and liquid dosage forms includes

• OTD are unit solid dosage forms they provide good stability , accurate dosing , easy manufacturing , small packing size, and they are easily handled by patients.

• OTD present no risk of obstruction of gastrointestinal tract .

• Easy administration for pediatric, geriatric and inpatients (especially for mentally retarded and psychiatric patients)

• The rapid disintegration of the resulting tablets results in a quick dissolution of the drug and fast absorption that provide rapid onset of action.

•The bioavailability of drugs that are absorbed in mouth , pharynx and esophagus is increased .

• Pre gastric absorption of drugs avoid hepatic metabolism .which reduces the dose and increase the bioavailability of the drug .

Various processes are employed to obtain ODT tablets such as molding , lyophilization ,spray drying , sublimation ,mass extrusion, compaction and other patented technologies . these technologies require specific equipments and expensive process compared with the standard manufacturing process also special packing required.

ODTs are being preferred as advanced dosage form in most instances over conventional immediate release dosage form for various drugs . For instance ODT disintegrate or dissolves in mouth within a very short time .Further, they do not require water on administration, present acceptable taste masking properties, should have high drug loading capacity, better feel after administration , stable in environmental condition and should not leave any residue in mouth after oral administration . Due to their rapid action of drug at the buccal cavity ODTs would be always first choice in case of drugs that are unsuitable to be delivered through GI for many reasons. The advantages offered by ODTs over immediate release formulations may include ease of formulation designing and manufacturing, unit packaging, easy to handle by patients, no need of water to administer, the tablet disintegrates rapidly in the mouth releases the drug and shows rapid absorption may leads to high therapeutic efficacy due to increased bioavailability .

LIMITATIONS

• Most of the cases soluble diluents used for formulating ODTs they may be hygroscopic dosage which may lead to stability issues.

• The tablets may leave unpleasant in taste if not formulated properly.

• hygroscopic and light sensitive drugs may requires special packing .

• Precautions can be taken while administration of the tablet ,should be taken instantaneously after removing from pack.

ideal properties

- After oral administration they should leave no residue in mouth.
- It should be disintegrate in mouth within few seconds.
- drug loading capacity is high
- They should be compatible with the other excipients used in the formulation.
- They should be withstand environmental conditions such as humidity and temperature.
- They gives the pleasant taste after administration.
- They must have sufficient strength to withstand the manufacturing process and handling.

ADVANTAGES :

• Ease of administration to patients , such as pediatric, geriatric, mentally ill, disabled and uncooperative patients.

- Rapid release of drug and rapid absorption may produce rapid onset of action.
- Pregastric absorption can result in improved bioavailability.
    - water is not required for the dosage form,which is highly convenient for patients who are travelling and do not have immediate access to water.

• bioavailability of drug increases in Some cases of drugs which are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach.

• it gives good feel after administration of drug which changes the psycology of the patient

DISADVANTAGES

• due to hygroscopic in nature of oral disintegrating tablets they must be kept at controlled environment conditions like humidity and temperature.

• ODT requires special packaging for proper sterilization and mainatin stability .

• ODTs have less mechanical strength. Hence, careful handling is required.

• they Leave unpleasant taste when they formulated with less care .

ODT DRUG RELEASE MECHANISM:

The main action of oral dispersible tablets depends on the release mechanism of superdisintegrants used in it. The superdisintegrants may release drug through following mechanisms .

1. Deformation : the disintegrant particles are deformed during compression stage while formulating the tablet but while administration when they came in contact with water, the disintegrants come back to their precompression size through swelling and the tablet breaks.

2. Porosity and capillary action [wicking]:

during administration the tablets are may first dissolved in small amount of liquid, so that the water can easily penetrate inside the tablet and break it into minute particles.

3. Swelling :

some disintegrants shows their action through swelling when they came contact with water they ultimately swell causes tablet breaking.

PREPARATION METHODS :

The formulation of tablet is most important step. The formulator has to be very careful during the manufacturing because if a product is not formulated properly then it will for sure it doesn't show its therapeutic action . Different techniques are there for the manufacturing of ODT's. Each technique have its own merits and demerits; depending on the type of drug-excipient used any of the following method can be employed

Freeze drying:

it isalso called as lyophilization technique ,it ismostly used for thermolabile drugs. Because it performed at low temperature for drying of drug. The moisture fom the drugs escape through sublimation. here the drug is kept in a water soluble matrix, which is then passesd through a freezing tunnel to dry it. The product formed is porous nature disintegrates in a few of seconds thus increasing its bioavailability .

Moulding:

This is most commonly used method for preparing oral dispersible tablets. Only the water soluble ingredients dissolved in water so that the product dissolves quickly and all the solid ingredients are dissolved in solvents, the dispersible tablets are compressed at low pressure . After compression the solvent is removed .

by air-drying method. The formed product is very porous in nature which is having great dissolution .

Spray drying:

This method is generally employed when there is a need to formulate extremely porous and fine powders. In this method the gelatin is used as a supportive agent and Mannitol is used as bulking agent. For better dissolution and disintegration characteristics effervescent agents also used . and the porous powder is formed when prepared mass is spray dried .

Sublimation

the dissolution rate is delayed due to the low porosity incase of compressed tablets. In sublimation technique, the active ingredient, the volatilizing agent and the other adjuvant are combined to form a tablet. the volatile material is evaporated after compression by sublimation. Tablets prepared by this method , usually disintegrates quickly

Mass extrusion:

In this method softened mass is placed into an extruder or syringe, to obtain a cylinder shaped product which is further cutted into small segments to from tablets. In case of bitter drugs, tablet is coated for taste

CHALLENGES IN FORMULATING ,MANUFACTURING OF ODTS :

Mechanical strength and disintegrating time :

by enhancing the mechanical strength of the tablet, the Disintegrating time will also rise. So a perfection is needed in between these two parameters. Usually the disintegrating time ofless than one minute is required in orally dispersible tablets. so maintaing good mechanical strength is a major task for the formulator along with good disintegration time .

Taste masking:

The taste of an orally administered drug has always been important . almost all drugs are bitter in taste. while formulating the orally dispersible tablets the taste masking is one of the most important factors. So, a suitable taste masking agent should be used in their formulation Delivery systems disintegrate or dissolve in patient oral cavity, thus releasing the active ingredients which come in contact with toungue ; hence taste masking of drugs become critical parameter to patient compliance .

Aqueous solubility:

eutectic mixtures is formed by water soluble drugs , freezing point depression occurs while forming eutectic mixture and the formation of a glassy solid that can crumble after drying sublimation . so problem can be avoided by using matrix-forming excipients, such as mannitol, which can cause crystallinity and impart rigidity .

Hygroscopicity:

orally disintegrating tablets are hygroscopic in nature and are unable bear even ordinary conditions of temperature and humidity. So the only way to preserve the product from unfavourable environmental conditions is to provide them a specialized packaging .

Amount of drug:

For lyophilized dosage forms, the drug dose must be less than 400 mg for insoluble drugs and less than 60mg for soluble drug. the amount of drug is particurarly challenging when formulating a fast-dissolving oral films or wafers. Size of tablet: It has been suggested that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was larger than 8 mm. the tablet size that is both easy to take and difficult to achieve .

Mouth feel:

The orally dispersible tablets after administration do not cause any discomfort in the oral cavity to the patient as it will result in poor patient compliance. The formulator must ensure that the tablet should breakdown into small particles Also, some flavouring and cooling agents can be incorporated to give a pleasant mouth feel to the patient .

Advancements in ODT technologies

Zydis technology:

The Zydis technology was one of the most important milestones in the history of dispersible tablets. It was discovered by R.P. Scherer. With the aid of lyophilization technique, the tablet is surrounded within a fast-dissolving carrier material . So that when it reaches the oral cavity it should disintegrate quickly. different types adjuvants are used in these tablets to make the final product more stable. Due to freeze drying process the tablet is not prone to microbial contamination .These tablets generally are packed in blister

packs to preserve from moisture in the environment. The examples of some marketed formulation are Grazax®ODT, Maxalt® MLT, Xilopar® 1.25, Zofran® Zydis, CůĂrŝtin®Reditabs®

Pepcid®RPD etc

Orasolv technology:

This technique was invented by CIMA labs. effervescent disintegrating agent is added along with a taste masking agent, in order to

mask the bitter taste of A.P.I. conventional type of tablets are prepared various kind ofequipment. The compression force applied for compressing the tablets should be very low, so that the final product obtained is soft and should be disintegrate very rapidly. Also, the storage of these dosage forms requires special attention to make them stable during their shelf-life. This technology has already been used for six marketed formulation and More than two ingredients can be incorporated using this technology .

Durasolv technology:

This technique was also developed by CIMA labs. The main constituent of this formulation include drug, lubricant and fillers The traditional instruments used for conventional tablets can be used for making tablets by Durasolv technology. Also, special packaging is not required for storage of these products. This technology is generally suitable for tablets which contain relatively low amount of active ingredient .

Wowtab technology:

This technology is patented by Yamanouchi pharmaceutical Company. The term WOW in Wowtab means without water. The ratio between active ingredients and excipients is kept 50:50. The saccharides of both

low and high mouldability are employed to formulate the granules. Mouldability can be expressed as the ability of a substance to be compressed. The blend of low and high mouldability in the tablet results in the formation of tablets with appropriate hardness. The tablets prepared with the aid of Wowtab technology dissolves rapidly within lessthan 15 seconds or less. Any kind of packaging can be used to pack the tablet .

Flashtab technology:

This method is another novel method of preparing oro-dispersible tablets. The novel technology was invented by Prographarm laboratories. The active ingredient used in the formulation is in the form of micron crystals.different types of traditional tablet making techniques can be used for the manufacturing. The final product prepared dissolves in the mouth in less than one minute .

Pharmaburst technology:

As the name suggests, this technique's goal is to release the medicament instantaneously in the mouth. SPI Pharma from New Castle patented this technology . In this technique, combinations of specialized excipients are employed, which ultimately gave rise to such a final product which immediately releases the drug from dosage form. One ofthe special ingredients used is mouldability saccharine which forms a rapid melting strong tablet .

Ora-Quick:

The taste-masking has always been a major issue of concern n oral dosage forms. The KV pharmaceutical has come with a unique microsphere technology, called as micromask, which can definitely overcome this obstacle. The technique is also suitable for thermo-labile drugs. After tablet Formulation the tablet is coated with micro-encapsulated so that the mechanical strength of the tablet remains The particles Ora-quick technology .

Characterisation of ODTS:

Weight variation test:

This test is carried out to ensure that the each tablet of a batch has equal amount of drug in it according to its claim. For this we had to select 20 tablets randomly and weigh them. all the tablets are weighed ,the average weight is calculated. If the results are within the prescribed range then the batch is passed the weight variation test and if the tablets weights do not comply within the prescribed range then the batch is rejected for marketing .

Tablet thickness:

The thickness of a tablet is also an important parameter of evaluation It can be evaluated easily with the help of equipment called as Vernier Caliper. Randomly five tablets are choosen from the batch under test and one by one are placed in the equipment and results are interpreted .

Tablet hardness:

The hardness of a tablet is very crucial in order to protect it from handling and ŧransportation errors. But in case of oral dispersible tablets the excess hardness may lead to poor patient compliance. So the hardness of a oral dispersible tablet should be less than that of an ordinary tablet. The hardness of a tablet is related to the force required to break a tablet in the radial direction while compression it is testedby using monsanto hardeness tester and pfizer tester .

Tablet friability test:

The friability test apparatus is generally employed to test the friability of the tablets. This test mainly performed to evaluate the ability of the tablets to bear handling and transportation errors. According to the Pharmacopoeia the prescribed no of tablets are taken and are placed in the friability test apparatus. No. of revolutions and time is set as prescribed manner and results are recorded.

Wetting time:

wetting property of tablet must be evaluated , because disintegration time of tablet must depends on wetting property Also, the impact of excipients excipients on disintegrating time of a tablet can also be concluded. For this purpose, a tablet is placed on a piece of ŧissue paper folded twice and kept in a small Petri dish (ID=6.5 cm) containing 6 ml of water, and the ŧime for complete wetting is measured.

In-Vitro disintegration test:

The disintegration test apparatus is generally used for determination of disintegration time of tablets under test. Sis tablets are taken from the batch under evaluation and are place into the six tubes of the apparatus. These tubes contain a suitable dissolution medium a specified in the pharmacopoeia and the temperature of the medium must be maintained within 37°+_2°C. the apparatus was started after setting the all the parameters , the results are concluded after the completion of test .

In-Vitro dissolution study:

The dissolution time of oral dispersible tablets can be performed by using dissolution apparatus. The procedure given in the monograph for a particular drug and tablet form can also be considered for the dissolution time of that drug in oro-dispersible form. Other media such as 6.8 pH phosphate buffer can be evaluated for ODTs. commonly the USP 2 paddle type of apparatus can be utilized for orally disintegrating tablets, with a paddle speed of 50 rpm .

Marketed formulation :

Oral dispersible tablet name	Manufactured company
Domperidone	Olcare labs
piroxicam	Pfizer USA
Cetrizine	Zosta Pharma ltd.
Ibuprofen	Novartis
Famotidine	Merk and co,USA

Conclusion

The Oro-dispersible tablet is the newly emerged dosage-form in the era of solid dosage forms. It better patient compatability ,rapid disintegration and enhanced bio-availability make it a perfect carrier for the active pharmaceutical ingredient. we have to summaries that the basic concepts and basic techniques involved in the formulation of oral-dispersible tablets. As it is a new addition in solid dosage form, so more and more research is desired, more and more technologies are to be invented so that the remaining demerits of this formulation can be converted into merits .

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