



A REVIEW ON THE BENEFIT OF ORODISPERSIBLE TABLET

¹Piyush Jain, ²Gita Sahu, ³Neha Mandle, ⁴Surekha Beghel

Assistant Professor, Sanskar city College of Pharmacy, Rajnandgao, Chhattisgarh, India

Associate Professor, Gracious College of Pharmacy, Raipur, Chhattisgarh, 492015

Abstract: The concept of fast dissolving drug delivery system emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatine capsules. Hence, they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. In some cases such as motion sickness, sudden allergic attacks or coughing, swallowing conventional tablets may be difficult. Such problems can be resolved by means of orodispersible tablets. These tablets disintegrate and dissolve rapidly in mouth. Hence no need to swallow the dosage form, which is highly convenient feature for patients. Hence preparing orodispersible tablet would provide a rapid action during these physiological conditions which may occur any time and a quick therapy being required for them.

I. INTRODUCTION

Hence the review is based on the orodispersible tablet. Tablet are popular for several reasons. The oral route represents a convenient and safe way of drug administration. The preparation procedure enables accurate dosing of the drug. Tablets are convenient to handle and can be prepared in a versatile way with respect to their use and to the delivery of the drug. Tablets can be mass produced with robust and quality-controlled production procedures giving an elegant preparation of consistent quality. Tablets are the manufacturer's dosage form of choice because of their relatively low cost of manufacturing, package and shipment, increased stability and virtual tamper resistance.⁴

Among the different routes of administration, the oral route of administration continues to be the most preferred route due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance.⁵ To overcome these problems, formulators have considerably dedicated their effort to develop a novel type of tablet dosage form for oral administration, i.e., one, which disintegrates and disperse rapidly in drinking water. These tablets usually disperse within 15 sec. to 2 min. The faster the drug goes into solution, the quicker the absorption and onset of clinical effect. The bioavailability of a drug from rapidly disintegrating tablets may be even greater than that observed for other standard dosage forms. The rapidly disintegrating tablets also offer advantages over other oral dosage forms such as effervescent tablets, suspensions, chewing gum or chewing tablets, which are commonly used to enhance patient compliance.⁶ Effervescent tablets and suspensions require preparatory steps before administration of the drug. The elderly, who often are unable to chew large pieces of gum or tablets, sometimes experience unpleasant taste when bitter drugs are consumed. The advantages of rapidly disintegrating tablets are being recognized in both industry and academia.⁷

Ideal characteristics of orodispersible tablets (ODTs):^{8,9,10}

- Does not require water for oral administration. Should easily disintegrate and dissolve. Mask or overcome unacceptable taste of drug. They should have high drug loading. They should have pleasant feel in the mouth. They should have negligible or no residue in oral cavity after administration. They should have low sensitivity against environmental conditions like moisture, temperature etc. Ease of administration for patients who are mentally ill, disabled and uncooperative. Should be portable without fragility concern. They should be manufactured using conventional tablet processing and packing equipment at low cost.

Advantages of ODTs:¹¹

- Ease of administration to patients who refuses to swallow a tablet such as paediatrics, geriatric patients and psychiatric patients. Achieve increased bioavailability / rapid absorption through pregastric absorption of drugs from mouth, pharynx and esophagus as saliva passes down. Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric Patients. Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety. Rapid disintegration and absorption of drug, which will produce quick onset of action. New business opportunities like product differentiation, line extension and life cycle management. Exclusivity of product promotion. Patients for whom chewing is difficult or is painful can use these new tablets easily.

Developmental Challenges in formulation of ODTs:

Fast Disintegration:⁹

ODTs should disintegrate in the mouth without additional water or with a very small amount (e.g., 1-2ml) of water. The disintegration fluid is provided by the saliva of the patient. The disintegrated tablet should become a soft paste or liquid suspension, which can provide good mouth feel and smooth swallowing. The ODTs usually means disintegration of tablets in less than 1 minute, but it is preferred to have disintegration as soon as possible.

Drug properties:⁹

For the ideal ODT technology, the drug properties should not significantly affect the tablet property. Many drug properties could potentially affect the performance.

Taste of the active ingredient:¹³

Some drugs have relatively no taste, and simply adding a suitable flavour can hide any slight unpleasant sensation. However, most drugs do require taste masking if they are to be incorporated into fast dissolving formulations. Numerous methods exist to achieve this, including simple wet granulation or roller compression with other excipients to minimize the presented surface area of the drug. Spray drying can also be employed to the drug. If further taste masking is needed, the resultant particle can be sealed with a suitable coating material (like hydroxy propyl methyl cellulose, ethyl cellulose, methacrylate and polyvinylpyrrolidone). The choice of coating material will determine the mechanism of taste masking. In addition, the quantity of coat applied, how it is applied will all affect the quality of taste masking. Cyclodextrins (cyclic linked oligosaccharides) have been shown to prove some measure of taste masking by trapping the drug within the cyclic structure long enough to render initial dissolution. Other taste masking methods are namely coating methods including electrochemical, hot melt and super critical fluids. Encapsulation using coacervation has also been employed to encapsulate certain drugs.

Dose:¹³

Molecules requiring high doses present three challenges to development of fast dissolving dosage forms: 1) Taste masking of active substance, 2) mouth-feel or grittiness and 3) tablet size. These challenges are not unrelated because most drugs will require taste masking depending on the degree of bitterness relative to the dose of the drug, which will affect the final tablet size. As mentioned previously, drug may require coating, which will result in an increase in the particle size. The extent to which this increase will affect the mouth feel and tablet size will depend on the dose of the drug and the amount of coating material required masking its taste.

Hygroscopy:¹⁴

Several fast dissolving dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence they need protection from humidity that calls for specialized product package.

Friability:¹⁵

In order to allow fast dissolving tablets to disintegrating rapidly in the water, they are made of either very porous or soft moulded matrices or compressed into tablets with low compression force, which makes the tablet friable and/or brittle, which are difficult to handle, often require specialized peel-off blister packing.

The techniques used in the preparation of rapidly disintegrating tablets are:

CONVENTIONAL TECHNIQUES:^{9,16}

Tablet moulding:

In this method, the delivery system is prepared in the form of tablets using water-soluble additives to allow the tablets to dissolve rapidly and completely in water. All the ingredients of the formulation are passed through fine mesh, dry blended, wetted with a hydro-alcoholic solvent and then compressed into tablets using low compression forces.

Freeze drying (Lyophilization):¹⁶

Lyophilization is a pharmaceutical manufacturing technology, which allows drying of heat sensitive drugs and biological products at low temperatures 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.

Spray drying:¹⁷

Spray drying is a process by which highly porous, fine powders can be produced. The composition contains a bulking agent (e.g. mannitol and lactose), a disintegrate (e.g. sodium starch glycolate, croscopolidon and croscarmellose sodium), an acidic ingredient (citric acid) and/or alkaline ingredients (e.g. sodium bicarbonate) which when compressed into tablets shows fast disintegration and enhanced dissolution.

Sublimation:¹⁸

This method includes the addition of a sublime salt to the tableting components, compressing the blend and removing the salt by the process of sublimation. The active ingredient, a diluent, a sublime salt (ammonium carbonate, ammonium bicarbonate), a binder and other excipients are blended and tablets are prepared.

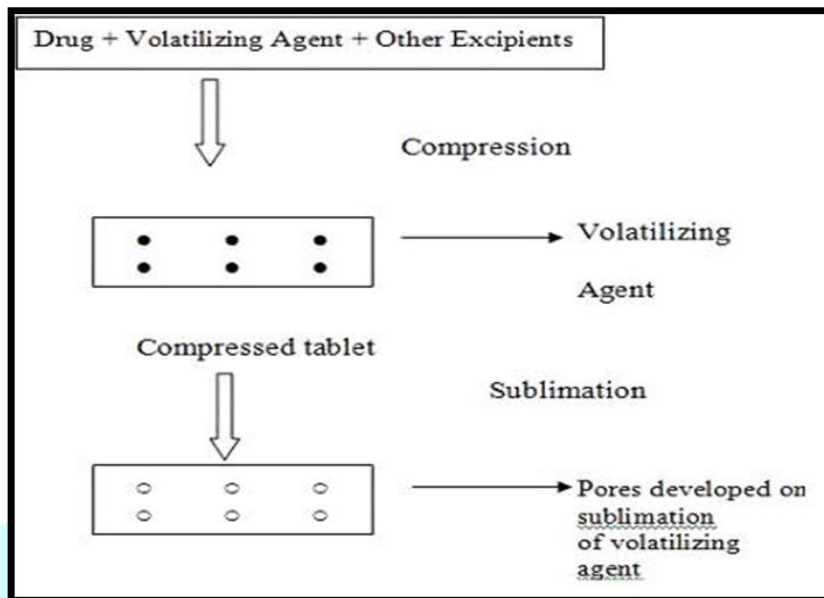


Fig. 1: Schematic Representation of Sublimation tablet.

Addition of Disintegrants:¹⁸

Addition of disintegrants in fast dissolving tablets, leads to quick disintegration of tablets and hence improves dissolution. Microcrystalline cellulose, cross-linked Carboxy methyl cellulose Sodium, cross-linked polyvinyl pyrrolidone and partially substituted Hydroxypropyl cellulose, absorb water and swell due to capillary action and are considered as effective disintegrants in the preparation of fast dissolving tablet.

Direct Compression Method:^{5,17}

Direct compression is the easiest method to manufacture Oro Dispersible tablets (ODTs) and fast-melting tablets (FMTs). The great advantage of direct compression is its low manufacturing cost. It uses conventional equipment, commonly available excipients and a limited number of processing steps.

Step	Direct compression	Dry granulation	Wet granulation
I	Mixing / blending of active drug and adjuvant	Mixing/blending of Active drug and adjuvant	Mixing/blending Active drug and adjuvant
II	Compression	Compression to slugs	Preparation of binder solution
III		Size reduction of slugs and sieving	Massing of binder solution of step 2 with powder mixture of step 1
IV		Mixing of granules with pharmaceutical additives.	Wet screening of damp mass
V		Compression	Drying of wet granules

VI

Resifting of dried granules and blending with pharmaceutical additives.

VII

Compression

There was no much attention to the direct compression of pharmaceuticals in the previous days (late 1950). Now a days great deal of attention has been given to both product and process development. The availability of new materials, new forms of old materials and the invention of new machinery has allowed the production of tablets by simplified and reliable methods. In early 1960, the introduction of spray dried lactose (1960) and Avicel (1964) had changed the tablet manufacturing process and opened avenues of direct compression tableting. Previously, the word direct compression was used to identify the compression of a single crystalline compound (i.e. sodium chloride, potassium chloride, potassium bromide, etc.) into a compact form without the addition of other substances. Current usage of the term direct compression is used to define the process by which tablets are compressed directly from the powder blends of active ingredient/s and suitable excipients. No pre-treatment of the powder blends by wet or dry granulation is involved.

PATENTED TECHNOLOGIES:³¹

Each technology has a different mechanism, and each fast disintegrating dosage form varies regarding the following

- Mechanical strength of final product
- Drug and dosage form stability
- Mouth feel
- Taste
- Rate of dissolution of drug formulation in saliva
- Swallow ability
- Rate of absorption from the saliva solution and
- Overall bioavailability

Table 1: A list of Patented Technologies using manufacturing techniques:^{8,10,31}

Technology	Basis for technology	Company
Zydis	Lyophilization	R. P. Scherer Inc.
Quicksolv	Lyophilization	Janseen Pharmaceutical
Lyoc	Lyophilization	Farmlyoc
Flashtab	Multiparticulate Compressed tablets	Ethypharm
Orasolv, Durasolv	Compressed Tablets	CIMA Labs Inc.
Rapitab	Compressed Tablets	Schwarz Pharma
Wowtab	Compressed Molded Tablets	Yamanouchi PharmaTechnologies, Inc.
Fastmelt	Molding	Élan Corp.
Ziplets	Molding	Eurand
Flashdose	Cotton-candy process	Fuisz Technology Ltd.

SUMMARY

For the treatment of various disease conventional oral dosage form like tablets and capsules etc. are available in the market but the major drawback with these are many patients find it difficult to swallow tablets and hard gelatine capsules. The difficulty experienced in particular by paediatric, geriatrics, mentally ill and uncooperative patients and hence do not take their medicines as prescribed, leading to patients noncompliance. The concept of formulating ODTs offer a suitable and practical approach in serving desired objective of rapid disintegration and dissolution characteristics with increased bioavailability after the administration without water is being undertaken. The formulation of ODTs

was done by three methods direct compression, sublimation and mould method. The following excipients were selected in the direct compression method Sodium starch glycolate, Croscopolvidone, Micro crystalline cellulose, Lactose spray dried, Saccharin sodium, Magnesium stearate and Talc. Addition of superdisintegrant such as croscopolvidone at the level of 2% concentration in the formulation, leads to quick disintegration of the tablet after penetration of physiological fluid and hence improves dissolution characteristics. For the sublimation method the following excipients were selected Camphor, Menthol, Micro crystalline cellulose, Lactose spray dried, Saccharin sodium, Magnesium stearate and Talc. After preparation of the tablets it was subjected to sublimation of Camphor and Menthol in hot air oven at 50°C. The prepared tablets are evaluated for different parameter like hardness, friability, in-vitro dissolution and disintegration time.

Addition of superdisintegrant such as croscopolvidone at the level of 2.5% concentration in the formulation, gives the maximum hardness and rapid disintegration.

In the present study ODTs were developed with sufficient strength, desirable taste and pleasant mouth feel by simple and low cost manufacturing processes using material with proven safety as excipients.

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