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Various Aspects of Oral Fast Disintegrating Dosage Form



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ABSTRACT

Oral fast disintegrating drug delivery systems were first developed in the late 1970s as an alternative to tablets, capsules, & syrups for paediatric & geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms. These dosage forms either dissolve or disintegrate generally within a 3 minute, without needing water. Oral fast Disintegrating dosage form have started gaining popularity & acceptance as new drug delivery system because they are easy to administer & lead to better patient compliance .Oral fast Disintegrating dosage form consist of mouth dissolving tablets & fast dissolving films. Mouth dissolving tablets contains drug, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue. Fast dissolving films, a new drug delivery system for the oral delivery of the drugs, was developed based on the technology of the transdermal patch. Present review focused on various aspects of Oral fast disintegrating dosage forms.

INTRODUCTION

Reason behind preference of oral route for drug administration is due to its ease of swallowing, distress avoidance, versatility & most significantly, patient compliance. The large number of patients find it difficult to swallow tablets & capsules, & do not take their medicines as prescribed. It is estimated that 50 % of the population was affected by this problem, which finally results in a higher chance of non-compliance & ineffective therapy. For these reasons, tablets that can disintegrate in the oral cavity, have attracted enormous attention.¹ Solid dosage forms as oral tablets have the most considerable place among the entire pharmaceutical Preparations.²

Drinking water is required for the swallowing of oral dosage forms. Most of the times patient are in compliant with conventional tablets & capsules. Without water there is motion sickness & sudden episodes of coughing during the common cold, allergic conditions & bronchitis.

The elderly constitute a major portion of today's population mainly because of increased life expectancy of individuals. Dysphagia or difficulty in swallowing is common problem.² This problem is now overcome by Oral fast disintegrating tablets. Synonyms of fast Dissolving dosage forms are 'Quick Dissolve', 'Rapid Melt', 'Quick Disintegrating', 'Mouth Dissolving', 'Orally Disintegrating', 'Oro Dispersible', 'Melt-in-Mouth'.

Advantages of Oral fast disintegrating tablet

The several advantages of mouth dissolving dosage forms are

- 1) Orally disintegrating tablets have dosage advantages of solid as well as liquid dosage forms.
- 2) The primary benefit of this technology is to improve patient compliance.
- 3) Easy to administer for paediatric, geriatric, & hospitalized patients.
- 4) Ease of administration for patients, those who are not cooperative.
- 5) Pleasant mouth feel can be designed to leave minimal or no residue in the mouth after administration.
- 6) Quick dissolution & rapid absorption which provide rapid onset of action
- 7) No need of water to take this dosage form.

Limitations of Oral fast disintegrating tablets

- I. The tablets usually have insufficient mechanical strength. Hence, required careful handling.
- II. The tablets may leave unpleasant taste & grittiness in mouth
- III. Drugs with relatively large doses are difficult to formulate into FDTs.
- IV. Patients who concurrently take anti-cholinergic medications may not be the best candidates for FDTs. ¹¹

Ideal Properties of ODT

- It should be compatible with taste masking & other Excipients.
- It should have a pleasing mouth feel.
- It should leave minimal or no residue in mouth after administration
- It should be harder & less friable.
- It should exhibit low sensitivity to environmental conditions.
- It should have an acceptable taste masking property.
- It should allow the manufacture of tablets using conventional processing & packaging equipment's at economy cost.

Model drug selection criteria for ODT

- No bitter taste.
- Small to moderate molecular weight.
- In water & saliva good stability.
- Partially non-ionized at the oral Cavities pH.
- Ability to diffuse & partition into the epithelium of the upper GIT.
- Ability to permeate oral mucosal tissue. ¹²

Unsuitable drug characteristic for ODT

- Short half-life & frequent dosing.
- Very bitter
- Unacceptable taste.

Ingredients mostly used in Oral Mouth dissolving Tablets Drug should have

1. Low dose E.g. Terazosin HCl.
2. Have better availability to permeate oral mucosal tissue.
3. Less or not bitter in taste.
4. Good stability in water as well as in saliva.
5. Better solubility. E.g. Promethazine^{23,24,25}

Table 1: Various excipients & their percentage in ODT

Name of the excipients	Percentage Used
Disintegrant	1 to 15%
Binder Antistatic Agent 0 to 10%	5 to 10%
Diluents	0 to 85%

Various Evaluation tests on OFDT

1. General Appearance

The general appearance of a tablet, its visual identity & overall “elegance” is essential for consumer acceptance. It includes size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws & consistency.

2. Size & Shape

The size & shape of the tablet can be dimensionally described, monitored & controlled.

3. Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance & also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism

4. Weight variation

5. Friability

Friability 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.

6. Hardness

Tablet hardness is measured with hardness testers like Monsanto or Pfizer tester. A tablet is placed in the hardness tester & load required to crush the tablet is measured.

7. Wetting time

The initial process in the disintegration of ODT involves water uptake & wetting of the tablet. So determination of wetting time is also important. It also helps in studying the effect of various excipients in the disintegration of the tablet.

8. Disintegration time

As described in pharmacopoeia, tablets are placed in the disintegration tubes & time is noted. According to the European pharmacopoeia, the fast disintegrating or ODTs should disintegrate within 3 minutes without leaving any residue on the screen.

9. *In vitro* Dispersion Time

In vitro dispersion time was measured by dropping a tablet in glass cylinder containing 6 ml of Sorenson's buffer (pH 6.8)..

10. Dissolution test

The dissolution method for oral disintegrating tablets is the same as that of conventional tablets. USP 2 paddle apparatus is most suitable & common choice for dissolution test of oral disintegrating tablets, where the paddle speed is 50 rpm is used. The USP 1 or 2 basket or paddle apparatus may have certain application for such tablets but is used less frequently due to specific physical properties of tablets.

11. Stability study

The ODT are packed in suitable packaging & stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

- (i) 40 ± 1 °C
- (ii) 50 ± 1 °C
- (iii) 37 ± 1 °C & RH 75% \pm 5%^{41, 42}

12. *In vivo* evaluation of ODT

Pharmacokinetic & Pharmacodynamics of ODT formulation is carried out in suitable animal or human model [5].

Ideal characteristic of fast dissolving films

- Thin elegant film
- Available in various size & shapes
- Unobstructive
- Excellent mucoadhesion
- Fast disintegration
- Rapid release

Advantages of fast disintegrating film

- Convenient dosing
- No water needed
- Taste masking
- Enhanced stability
- Improved patient compliance [6]

Disadvantages

- It is hygroscopic in nature, so it must be kept in dry places.
- It also shows the fragile, effervescent granule property.
- They require special packaging for the products stability & safety [7].

Composition of the OFD Film

OFD film is a thin film with an area of 5-20 cm² containing an active ingredient. The immediate dissolution, in water or saliva respectively, is reached through a special matrix from water-soluble polymers. Drugs can be incorporated up to a single dose of 15mg.

Formulation considerations have been reported as important factors affecting mechanical properties of the films, such as shifting the glass transition temperature to lower temperature [8].

A typical composition contains the following

Table 2: Various excipients & their percentage in ODF

Name of the excipients	Percentage Used
Polymers	40 to 50 %
Plasticizers	5 to 10%
Additives	0 to 40%

1) Drugs

Following category of drugs can be formulated as mouth dissolving films including antiulcer, antiasthmatics, salbutamol sulphate, antitussives, expectorants, antihistaminics, NSAID'S [9,10,11,12,13].

2) Water soluble polymers

Water-soluble polymers are used as film formers. The use of film forming polymers in dissolvable films has attracted considerable attention in medical & nutraceutical application. The water-soluble polymers achieve rapid disintegration, good mouth feel & mechanical properties to the films. Example are A-15, Pullulan, HPMCE-3 & K-3, Methylcellulose A-3, A-6 & carboxymethylcellulose cekl 30, Polyvinylpyrrolidone PVP K-90, Pectin, Polyvinylalcohol, Gelatin, Sodium Alginate, Hydroxypropyl cellulose, [8,9,10,11,12].

3) Plasticizers

Formulation considerations (plasticizer, etc.) have been reported as important factors affecting mechanical properties of films. Such as tensile strength & elongation to the films have also been improved by the addition of plasticizers. Variation in their concentration may affect these properties. The commonly used plasticizers are glycerol, di-butylphthalate, & PEG.etc.[13].

4) Surfactants

Role of Surfactants is for solubilising or wetting or dispersing agent, so that the film is getting dissolved within seconds & release active agent immediately. Example of the

commonly used is sodium lauryl sulphate, benzalkonium chloride, bezthonium chloride, tweens, etc. One of the most important surfactant is poloxamer 407 that is used as solubilizing, wetting & dispersing agent. [14].

5) Flavour

Any flavor can be added, such as intense mints, sour fruit flavours or sweet confectionery flavours. [15].

6) Colour

A full range of colors is available, including FD & C colors, EU Colours, Natural Colours [15].

Some saliva stimulating agents may also be added to enhance the disintegration & to get rapid release. Some of these agents are citric acid, tartaric acid, malic acid, ascorbic acid & succinic acid [16].

Methods of manufacture of Oral fast dissolving films:

One (or a combination) of the following processes may be used to manufacture the oral films:

- a) Solvent casting
- b) Solid dispersion extrusion
- c) Semisolid casting
- d) Hot-melt extrusion
- e) Rolling

The wet film is then dried using controlled bottom drying [19].

Characterization of fast dissolving films:

Drug-excipients interaction studies:

Fourier Transformer Infra Red Spectrum Differential scanning calorimeter thin layer chromatography & X Ray Diffraction can be used to assess possible drug excipient interaction.

Thickness: Thickness test can be carried out using an electronic micrometer. The thickness of the film sample should be measured at five locations (center & four corners), & the mean thickness is calculated. Samples with air bubbles, nicks or tears & having mean thickness variation of greater than 5% are excluded from analysis [21].

Swelling index: The studies for swelling index of the film are conducted in stimulated salivary fluid. The film sample is weighed & placed in a pre-weighed stainless steel wire sieve. The mesh containing the film is submerged into 50 ml of stimulated salivary medium contained in a mortar. Increase in weight of the film is determined at each interval until a constant weight is observed. The degree of swelling is calculated using the formula:

$$SI = wt - wo / wo$$

Where SI is the swelling index,

wt is the weight of the film at time "t", &

wo is the weight of film at t = 0

Uniformity of drug content: This parameter can be determined by dissolving known weight of film by homogenization in 100 ml of stimulated saliva of pH 6.8 for 30 min with continuous shaking.

Tensile strength: The tensile strength (Psi) is the property of the film that requires a load to cause load deformation failure of film using is measured by Instron tester. [22].

$$\text{Tensile strength (N/mm}^2\text{)} = \text{breaking force (N)} / \text{cross-sectional area of sample (mm}^2\text{)}$$

Percent elongation: The percent elongation is measured when the film snaps as sufficient force applied so as to exceed the elastic limit. Percentage elongation can be obtained by following equation:

$$\text{Elongation at break (\%)} = \text{increase in length at breaking point (mm)} / \text{original length (mm)} \times 100\%$$

Palatability test: On the basis of taste, Palatability study is conducted, after bitterness & physical appearance. All the batches are rated A, B & C grades as per the criteria. When the formulation scores at least one grade, formulation is considered as average. When the

formulation scores two a grade then it would be considered as good & the one with all three a grade it would be the very good formulation.

Grades: A= very good, B= good, C=poor

Folding endurance: To determine folding endurance, a strip of film is cut & repeatedly folded at the same place. The number of times the film could be folded at the same place without breaking gives the value of folding endurance.

Disintegration test: Disintegration test is done by using Disintegration apparatus.

Dissolution test: This drug release studies are carried out in modified USP XXIII apparatus (paddle over disk) [24,28,30].

Permeation studies:

Permeation studies are carried using the modified Franz diffusion cell by using porcine buccal mucosa. The mucosa is mounted between the donor & receptor compartment of Franz diffusion cell. The receptor compartment is filled with buffer & maintained at $37\text{ }^{\circ}\text{C} \pm 0.2\text{ }^{\circ}\text{C}$ & the hydrodynamics were maintained by stirring with a magnetic bead at 50 rpm. One previously weighed film is placed in intimate contact with the mucosal surface of the membrane that should be previously moistened with a few drops of simulated saliva. The donor compartment is filled with 1 ml of simulated saliva of pH 6.8. Samples are withdrawn at suitable interval, replacing the same amount with the fresh medium. The percentage of drug permeated is determined by measuring the absorbance by selected analytical method [31].

Stability study:

Stability study of fast dissolving films is carried out for all the batches according to ICH guidelines [31].

CONCLUSION

Oral FDD like tablets & films have several advantages over the conventional dosage form have gained popularity because of better patient compliance, rapid drug delivery system, drug is directly absorbed into systemic circulation, first pass metabolism & degradation in gastrointestinal tract can be avoided.

Oral disintegrating dosage forms are generally benefited to patients who are busy & traveling & may not have access to water. FDTs have gained considerable attention for those patients who have difficulties in swallowing because of dysphagia & tremors. By looking above mentioned various aspects of Oral disintegrating dosage forms we conclude that this dosage form very useful in various conditions like dysphagia, during travelling.

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