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Oral disintegrating tablets: A review

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ABSTRACT

Oral route is the most prescribed route of administration and tablet and capsules are regarded as the dosage form which is most prescribed by medical practitioners as they can be taken easily, but several limitations of that kind of dosage forms like chocking and swelling discomfort in geriatric and pediatric population is observed. Due to high development costing constrains of a new drug molecule, Pharmaceutical companies are framing their ways which allows patient's convenience of intake. Companies in this era while developing a medicine are focused on trending drug dosage form in comparison with other dosage forms with improved safety and more effects with lesser frequencies ,which are effective to the people. In present study author has compared traditional techniques with patented techniques for preparation of oral disintegrating tablets.

Introduction

Oral disintegrating tablets or orally dissolving tablets (ODTs) is a dosage form containing medicinal substance which disintegrates rapidly (usually within few seconds) in the oral cavity (mouth, under the tongue) rather than swallowing. It is difficult to convince infants and juveniles to swallow medicines, as they may cause choking hazards [1]. ODT serve as a substitute dosage form used by patients who are suffering from or experiencing difficulty in swallowing(dysphagia) or in instances where compliance is a well known issue and therefore a simpler dosage form will ensures that the medication is taken by patient. It was reported that 35% of the entire population suffer from dysphagia and population is highly prone to this condition [1]. Adults have difficulty in swallowing too especially in bariatric patients, and patients of Parkinson's disease. Oral disintegrating tablets provide a solution or an alternative to overcome these challenges [2]. They resemble but differ from traditional tablets in the sense that; they disintegrate rapidly in the buccal cavity and there is no need of swallowing. As pharmacist and other scientist attain better understanding of biochemical and

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physiochemical parameter of drug delivery system is becoming more sophisticated. For some time now oral disintegrating tablets are gaining more prominence in the field of pharmaceuticals as a preferred option to traditional or conventional tablets [3]. No liquid or water is required when taking Oral disintegrating tablets, which is a significant advantage. It's very important for acute conditions such as; migraine, insomnia, psychiatric incidence etc due to its rapid onset of activity. If drug is absorbed in the oral cavity it avoids first pass metabolism by liver hence can reduce side effects caused by pre-gastric absorption [4].

Advantages of ODTs

The chief advantage of Oral Disintegrating Tablet formulation is the fact that, they merge both the advantages and features of liquid and conventional or traditional tablet dosage form. They provides ease of a tablet dosage form, and also allows the convenience of patient swallowing as liquid formulation [5].

Others advantages are:

1. Water and other liquids is not required for swallowing.
2. Ease of dissolution and rapid disintegration in saliva just within a short period or span of time.
3. Taste is pleasing.
4. Leaves no residue in the mouth.
5. Portable and ease of transportation.
5. Cost effective as manufacturing is done by direct compression method.
6. Ease of administering to juveniles, mentally unstable and old patients.
7. Dose is accurate as compared to liquids.
8. Absorption and dissolution is faster and hence offers fast action [6].

Limitations of ODTs

1. ODTs show high affinity to water naturally (hygroscopic) and hence should not be kept in a wet or humid environment.
2. They shows effervescence, fragile granules property

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3. ODT require particular packaging for stabilization & maintenance of safety [2]

Mechanisms of ODTs

In order to achieve a desirable rapid or fast dissolving action of a tablet these important steps were taken into consideration and followed;

- Water will promptly enter into the tablet matrix when placed in the mouth to enable rapid disintegration and immediate dissolution of the tablet [7].
- A suitable disintegrating agent is used in this case for preparation and the disintegrating agent used should be soluble in water in the formulation of the tablet.
- Solution or suspension of the drug is formed due to disintegration of the tablet into smaller particles [8]

When drug is placed in the mouth there is capillary action due to surface wetting hence water penetrates into the tablet leading to swelling. Swelling and capillary air expansion causes a localized stress which is known as “heat of wetting”. Particle then disintegrates to release drug. A theory was proposed by Guyot- Hermann known as Particle repulsion theory. According to this theory elective repulsive forces which exist between the particles leads to their disintegration and for this to occur water is required.

TECHNIQUES FOR PREPARATION OF ODTs

Some techniques used in the manufacturing of ODTs may be divided into two main groups:-

1) Conventional method

2) Patented method

Conventional technologies

Some conventional method which have been brought up for the effective preparation of these type of dosage form includes;

a) Melt granulation and Sublimation

b) Mass Extrusion

c) Spray drying

d) Process Molding

e) Freeze drying

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f) Phase transition Process

g) Direct compression

h) Phase transition Process

i) Cotton Candy Process [2, 9]

j)

Patented Method

Fast-dissolving feature of ODTs is accredited to rapid influx of water in the matrix of tablet leading to its rapid disintegration. Quite a few techniques technologies are been developed and improved based on formulation aspects and their consequential dosage forms may differ on various parameters like its taste, hardness, dose, porosity, residues, stability and disintegrating time, and all together its bioavailability [1].

Zydis Technique

Zydis technique, an important technique for the production of ODT tablets using freeze drying. Tablets made by this method is taken with no water because they dissolves rapidly on tongue within few seconds. Drug will be trap physically into the matrix (normally soluble in water).We proceed with freeze drying to generate a tablet which which dissolve or disintegrate faster. Water soluble matrix which has been used in this method are composed of; soluble saccharides and compound polymers to permit rapid or fast dissolution and also allows sufficient physical and mecahnical strength to withstand handling. During this process water is added to enhance porosity for the fast dissolution or disintegration of the tablet [10].

Limitations of Zydis Technique

- Drug amount added should not be more than 400 mg (in case of insoluble drugs) and not more than 60 mg (in case of drugs which are soluble). Not adhering to this leads difficulty in release of drug.
- Size of particle should be more than 50μm and less than 200 μm to help prevent the sedimentation drug. Not adhering to this leads difficulty in release of drug.

Advantages

- Absorption of these formulation takes place inside the mouth or pre gastric region. This helps to avoid first-pass metabolism, which is important or useful for drugs which undergo hepatic metabolism.

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- Advantageous for patients having difficulty to swallow oral medications or dosage forms due to Parkinson's disease, stroke, or dysphagia.

Disadvantages

- Freeze-drying employed in this process a relatively cost intensive manufacturing process.
- Formulations of this technique are lightweight and fragile.
- Stability of this formulation is poor at higher temperatures and humidities.
- Drugs which are not soluble in water can be integrated only up to 400 mg per tablet and should not be more than that. alternatively water, the drugs which are soluble should only be integrated up to 60 mg [2, 4, 5].

Orasolv technology

CIMA labs developed the Orasolv technique. Here, we taste mask the active medicament. They contains the disintegrating agent which are effervescent in nature. Oral Disintegrating Tablets are made using a method of direct compression method or technique at very low compression, to minimise time taken for the drug to disintegrate or dissolve. We use tablet machine as well as conventional blenders for production of tablets. Tablets produced by this technique will be friable or soft and are to be packaged in a particularly packaging system.

Advantages

Taste-masking is two-fold, quick dissolution. This technique has been employed for drugs with strengths ranging from 1 mg to 750 mg. Considering the size of tablet, its disintegration time can be designed considering a range of 10 to 40 seconds.

Disadvantages

- Tablets produced by Orasolv technique are very sensitive to moisture, which is due to the presence of an effervescent system and hence they should be packaged in the most suitable and appropriate manner.
- Low mechanical strength [7, 8, 11].

Durasolv technology

CIMA labs patented the Durasolv technology. Tablets which are made using this method are composed of the active ingredient, suitable bulk enhancer and a preferred glidant. When ODTs are made using this technology they turn to have very good rigidity. This technology is employed when product requires less amount of active pharmaceutical ingredient.

Advantages

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- Dura solv method is good and highly employed in preparing tablets which have very low amount of active pharmaceutical ingredients (125mcg to 500 mg)
- Tablets are compressed to greater hardness when this technology is used (15 to100N) which results in more durable ODT.
- This technology offers flexibility of Packing as tablets can be easily bottled.

Disadvantages

Fracturing of drug powder coating during compaction may occur, and patient will feel bitterness [3].

Wow tab technology

Yamanouchi Pharmaceutical Co patended the Wow tab technology. WOW means "Without Water". In this technology, there is a combination of low moldability saccharides and moldability saccharidesis are used to develop a fast dissolving oral disintegrating hard tablet. The method involves the addition of both low and high mold ability are employed to yield an Oral disintegrating tablet which has enough mechanical strength.

Advantages

- Has adequate dissolution rate and hardness.
- Wow tabs product can be packed either the conventional bottles or in blister packs.

Disadvantages

There is no significant change in bioavailability [9, 12].

Flash dose technology

Fuisz Nurofen developed the technique of Flash dose method, its a latest form of Ibuprofen in the market which melts in the mouth, made or prepared by flash dose method. This technology was the foremost commercial product of its kind introduced by Biovail Corporation. Tablets made by flash dose method are made of a binding shear form a matrix which is called floss. Example; Shear form matrice is normally developed by a technique known as flash heat processing technique.

Advantages

Tablets produced by this technique has high surface area assisting in dissolution of the tablet..

Disadvantage

- One drawback of this method is that, melting of matrix requires a high temperature hence this method cannot be used for drugs which are thermolabile, and hygroscopic drugs.

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- Tablets produced are normally highly friable, moisture sensitive and soft hence special packing is required
- Each dosage for can only lodge up to just 600 mg of active pharmaceutical ingredient [5, 13]

Flash tab technology

This method of formulating ODTs was patented by Prographarm laboratories. In this technology active ingredient is in the form of microcrystals. It normally utilizes the same excepients used in conventional compressed tablets. There is a combination of disintegrating and swelling agent with coated drug particle to form a tablet which will disintegrate rapidly in the mouth in less than a minute [14].

Oraquick technology

This technique was developed by K. V. S. Pharmaceuticals and they have patent for same. It uses a technique to mask the taste of bitter drug and this is known as "taste masking microsphere technique" or micro mask. Micro mask provides advanced mouth feel above taste masking alternatives.

Advantages

- Significant mechanical strength
- Quick disintegration/dissolution of the product [10]

Advatab technology

Advatab is different and is very different from the other techniques because this method can be combined used together with Eurand's complimentary particle techniques such as its renowned Microcaps R, which masks the taste of bitter drug and its DiffucapsR, which controls the release of active drug. Tablets produce by this technique disintegrates in the mouth within few seconds. Very useful to treat patients experiencing difficulty in swallowing capsules and tablets [12].

Nanocrystal technology

Nano crystal technique improves activity of compound and final product. This technique decreases the particle size thereby reducing surface area and subsequently dissolution rate increases. Nano particles are atypically not more than 1000 nanometer in its diameter. Oral

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disintegrating tablets are produced using this method by milling the active ingredients by a process known as wet milling method.

Pharmaburst technology

This technology is being patented by SPI Pharma. Technique involves the dry blend of drug together with flavours and lubricants followed by compression into tablets. Tablets produced by this technique dissolve rapidly within 30 – 40 sec and have sufficient strength to be packed in blisters and bottles.

Frosta technology (Akina)

Frosta method of formulating ODTs is a unique technique which was developed and patented by Akina. This technique uses core motive of forming plastic granules and compressing at a relatively less pressure yielding tablets of high strength and are porous in nature. This technique involves mixing of porous plastic together with a diluent which enhances water penetration. The mixture is the granulated using a blender for uniformity and consistency in the blend produced [8, 11, 15].

Table 1: Patented techniques and drugs they are used for [7, 16]

S. No.	Technology	Process involved	Drugs Used
1	RapiTab	Compressed Tablets	_
2	Zydis	Lyophilization	Loratidine (Claritine Reditab and Demitapp Quick Dissolve)
3	Quicksolv	Lyophilization	Cisapride monohydrate (Propulsid Quicksolv), Risperidone (Rispedal M-tab)
4	Oraquick	Micromask taste masking	Hyoscyamine Sulfate ODT
5	Wow tab	Compressed Tablets Moulded Tablets	Famotidine (Gaster D)
6	Flashtab	Lyophilization	Ibuprofen (Nurofen flashtab)
7	Lyoc	Multiparticulates Compressed tablets	Phloroglucinol Hydrate(Spasfon Lyoc)
8	Flashdose	Cotton candy process	Tramadol HLC
9	Orasolv	Compressed tablets	Paracetamol (Tempra Quicklets), Zolmitriptan (Zolmig ZMT)
10	Flash dose	Cotton candy process	Tramadol HLC
11	Ziplet	Molding	Ibuprofen
12	Advatab	Microcap and Diffucap CR Technology	AdvaTab Citrizine AdvaTab Paracetamol

Evaluation of Oral Disintegrating Tablets

All parameters to be evaluated has been given in various Pharmacopoeias should be adhered to strictly and thoroughly analyzed and addressed to ensure they match up to standards, along with some unique tests. Tablet's quality, when established, is normally determined by the quality of the physiochemical characteristics of excipients used to manufacture it. Various

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processes employed in formulation, example mixing, drying, packing etc can affect the characteristics of blends produced. Prepared blends are evaluated by the following test methods:

- The angle of repose
- Bulk density
- Hardness
- Hauser's ratio
- Tapped density
- Carr's index
- Friability
- Wetting time

Angle of repose

Critical angle, another name for angle of repose is defined as the angle at which the particle or material on slope is on the verge of sliding. To determine this angle funnel method was used. Blend was weighed accurately and taken into clean dry funnel set on a stand. Distance between tip of funnel and the base was adjusted for the tip of the funnel to touch the apex of the heap. Solid dispersion (drug excipients blend) was made to pass through funnel smoothly onto the surface. Diameter and height of the heap was measured. The angle of repose was calculated as:

$$\tan\theta = \frac{2h}{D}$$

Where h= height and r= radius [2].

Bulk density

To determine the bulk density of the blend weighed quantity of the prepared blend was poured into a clean and dry measuring cylinder, volume and weight were then taken and recorded.

$$\rho b = \frac{M}{Vb}$$

Here, ρb = Bulk density; Vb = Bulk volume; M = Weight of powder [3, 9].

Tapped density

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To determine tapered density by taking the mass of drug excipient blend in a graduated cylinder. Tapped to make the blend settled and compact. Continued tapping until there was no change noticed in the volume of the blend.

$$\rho t = \frac{M}{Vt}$$

Where, Vt = Minimum volume occupied by the blend in the cylinder; M = Weight of the blend [3, 9]

Compressibility index

$$CI = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \text{ X 100}$$

Oral disintegrating tablets evaluation

Weight variation

Uniformity and consistency is a very important factor when formulating tablets, this is why weight variation is performed to ensure that the active pharmaceutical ingredient is evenly distributed throughout the blend and subsequently the tablet produced. To perform this method, 20 tablets were taken and their individual weights were taken and recorded. Average of the weights was calculated. Weight variation is determined using the formula:

% Weight variation = Iw-Aw/Aw ×100

where Iw= Individual weight and Aw= Average weight [1]

Hardness

Tablet hardness which is also known as crushing strength (fc) of the tablet. Various instruments are used to test for hardness of a tablet, examples include; Monsanto tablet hardness tester, Strong cob, Pfizer hardness tester. Hardness is expressed by in kg/cm^2 [2, 14].

Friability (F)

Tablet friability is determined using Roche friabilator. When weight of the tablet is lost in container due to factors which remove fine particles from its surface we term it as friability. This method of evaluation helps to determine the mechanical strength of the oral disintegrating tablet produced. Ability of the produced ODT to withstand during packing and transportation and well as vibration can be determined by this method. As per IP 20 tablets are to be taken from each batch and weighed We then place then in a roche friabilator which

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rotates at 25 rpm for 4 min. All tablets and weigh after dedusting. The friability (F) is calculated by the formula:

F= I – W/W where I=Initial weight of drug and W= Final weight of drug

Wetting time

The wetting time is associated with the hydrophilicity of the excipient and inner structure of the tablets. In accordance with the Washburn E. W equation, the rate at which water penetrates into the bed of powder is directly proportional to the radius of pore and its highly affected by hydrophilicity of the given powders [1, 17].

$dl/dt = r\Upsilon\cos\theta/(4\eta l)$

Where l= penetration length , r= radius of capuillary, ¡= surface tension, h= viscosity of liquid, t= time, and q= contact angle

***In vitro* release of drug**

To determine the in vitro release of the Oral disintegrating tablet which has been prepared its dissolution profile has to be estimated first, USP 2 Paddle instrument has been employed in this process under the condition of; rotation at 50rpm, and phosphate buffer having PH 6.8 (900 ml) has been used in this method to achieve a desired results [16]

Table 2: ODT products available in Indian market [5, 10, 15]

Brand name	**API**	**Manufacturer**
Valus	Valdecoxib	Glenmark, India
Torrox	Rofecoxib	Torrent Pharmaceuticals, Ahmedabad, India
Rofaday MT	Rofecoxib	Lupin,, India
Kemstro	Baclofen	Schwarz Pharma, India
Romilast	Montelukast	Ranbaxy Lab. Ltd. Delhi, India
ZyrofMeltab	Rofecoxib Zydus	Cadila, India
Torrox	Rofecoxib	Torrent Pharmaceuticals, Ahmedabad, India
Minoclav DT-TAB	Amoxycillintrihydrate and Potassium clavulanate	Minova life Sciences, India
Numoxylin CV DT	Amoxycillintrihydrate and Potassium clavulanate	Gepach international, India
Nimulid MDT	Nimulid MDT	Panacea Biotech, New delhi, India
Nulev	Hyoscyamine sulfate	Schwarz Pharma, India
ZyrofMeltab	Rofecoxib Zydus	Cadila, India
Romilast	Montelukast	Ranbaxy Labs Ltd., New Delhi, India
OlanexInstab	Olanzapine	Ranbaxy Labs Ltd., New Delhi, India
Clonazepam ODT	Clonazepam Par Pharmaceutical	Par Pharmaceutical
Bigcef DT-TAB	Cefuroxime	Bestochem, India
Alepam	Amoxycillin trihydrate and Potassium clavulanate	Scoshia Remedy, India
Acufix DT-TAB	Cefixime	Macleods, India
Acepod	Cefpodoxime	ABL Lifecare, India

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