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A Review: The Fast Dissolving Tablets

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ABSTRACT

Fast dissolving tablets are disintegrating and/or dissolve quickly in the saliva without the need of water. Fast dissolving tablets are emerged as alternative dosage form for patients who faced difficulty in swallowing i.e. dysphagia such as pediatric and geriatric patients. Fast dissolving tablets are more reliable than conventional dosage form such as tablets, capsules due to better patient compliance. Fast dissolving tablets is a novel drug delivery system with least disintegration time and convenience of self administration. Fast dissolving tablets are also called as orodispersible tablet, rapimelt tablets, mouth dissolving tablets, quick dissolving tablets, rapid dissolving tablets, porous tablets etc. Fast dissolving tablets are formulated by various technologies with aid of superdisintegrant. This review article contains different techniques used for preparing fast dissolving tablets like lyophilization technologies, tablet moulding method, spray drying techniques, sublimation techniques, mass extrusion method, direct compression method. This review article also contains various patented technologies for formulating fast dissolving dosage form, mechanism of superdisintegrant, challenges faced, advantages and limitation of fast dissolving dosage forms.

INTRODUCTION:

Oral route of administration is most preferred route for administration of various drugs due to it is regarded as safest, most convenient and economical route [1]. Tablets and capsule are widely consuming dosage forms for oral route of administration of various drugs because of its benefit of self-administration, compactness and ease of production. However, many patient group such as elderly, children and patients who are unamenable, feel like vomiting have difficulty in swallowing these dosage form [2]. To overcome this problem fast dissolving tablet emerged as alternative dosage form. Fast dissolving tablets are also called as orodispersible tablet, rapimelt tablets, mouth dissolving tablets, quick dissolving tablets, rapid dissolving tablets, porous tablets etc. [3]. These tablets disaggregate in the mouth within a very short time interval i.e. 20-30 sec and comes in contact with saliva resulting in the pharmacological action of drug.

Fast dissolving tablets show better patient compliance and acceptance with improved bioavailability, efficacy and biopharmaceutical properties, in contrast to conventional tablets. Fast dissolving concept is a very supportive route for life-threating diseases patients like AIDS, Parkinson disease etc. [4]. United States Food and Drug Administration (USFDA) defined fast dissolving tablet (FDT) as "a solid dosage form containing a medicinal substance or active ingredient which disintegrates rapidly usually within matter of seconds when placed upon tongue" [5]. According to European Pharmacopoeia, "the FDT should disperse/disintegrates in less than three minutes" [8]. Fast dissolving tablets are available in two types that should be distinguished: While one tablet formulation rapidly dissolves in the mouth and can be ingested without the need for water, the other tablet formulation dissolves readily in water to form a dispersion that is simple for the patient to consume. In most cases, a tablet that dissolves or disintegrates in the oral cavity without the requirement for water or chewing is a fast-dissolving drug delivery system [13]. Currently these fast dissolving tablets are available in market for treating disease condition such as Parkinson's disease, schizophrenia, hypertension nausea, vomiting and migraine.

Advantages of fast dissolving tablets: [1-2]

1. Ease of administration to patients who cannot swallow, such as pediatric, geriatric and psychiatric patients.

2. Good mouth feel property of fast dissolving tablets helps to modify the basic view of medication as "bitter pill", particularly for pediatric patients due to improved taste of bitter drugs.

3. Advantage of liquid medication in the form of solid preparation.

4. Ease of administration and accurate dosing as compared to liquid Formulations.

5. Faster drug absorption through the mouth, throat, and esophagus, which may result in a quick onset of action.

6. By decreasing side effects, pregastric absorption can improve bioavailability, reduce dose, and improve clinical performance.

7. Quick drug therapy intervention.

8. Advantageous in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action required.

9. Adaptable and compatible with current packaging and processing machinery.

10. Permit high drug loading, cost effective.

11. Protection from the danger of suffocation due to physical obstruction, thus increasing protection.

12. Novel business opportunity will be getting produced due to the product differentiation.

Disadvantage of fast dissolving tablets: [8-9]

1. Fast dissolving tablet is hygroscopic in nature i.e. having moisture absorbing property from atmosphere so must be keep in dry place.

2. The tablets usually have inadequate mechanical strength. As a result, careful handling is necessary.

3. The tablets may leave unpleasant taste and/or grittiness in mouth if not developed properly.

4. Drugs with relatively higher doses are difficult to formulate into fast dissolving tablets e.g. Ciprofloxacin (500mg), Clozapine (900mg), Thioridazine (800 mg) etc.

5. Dryness of the mouth due to reduced saliva production may not be good candidates for these tablet formulations.

6. Patients who simultaneously take anticholinergic medications may not be the best candidates for fast dissolving tablets.

7. Fast dissolving tablets are very absorbent and soft moulded metrics or compacted in a tablet with low compression, which makes tablet friable and breakable which complicated to handle.

8. It needs special packaging for protection during storage and transportation.

9. Drugs that require controlled or sustained release, frequent dosing, and short half-life are not good candidates for fast dissolving tablets.

Salient feature of fast dissolving tablets: [7-10]

1. Patient compliance is easy and the administration of tablet especially for patients suffering from dysphagia, cardiac and renal complications, bedridden patients, and patient who refuse to swallow the dosage form such as pediatric, geriatric & psychiatric patients.

2. Oral disintegration of tablet eliminates the use of water which is suitable for patients who are traveling and cannot access water easily.

3. Rapid onset of action due to rapid disintegration followed by dissolution.

4. Increased bioavailability, due to absorption via mouth buccal mucosa which has better permeability properties.

5. The fast dissolving tablets will give a good mouth feel, especially in pediatric patients due more emphasis on organoleptic properties.

6. Favourable in cases which require an immediate and rapid onset of action e.g. motion sickness, sudden occurrence of allergic attack or coughing.

7. Increased bioavailability, due to absorption via mouth buccal mucosa which has better permeability properties.

8. Can be administered orally without water.

9. Insensitive to environmental conditions such as humidity and temperature.

Ideal properties of fast dissolving tablets: [9-13]

1. Require no water for oral administration.
2. It should have a pleasing mouth feel.
3. It should have an acceptable taste masking property.
4. It should be harder and less friable.
5. It should leave minimal or no residue in mouth after administration.
6. It should exhibit low sensitivity to environmental conditions.
7. It should allow tablet manufacturing by conventional processing and packaging.

Equipment's.

8. It should be cost effective.
9. Dissolve or disintegrate easily within a few seconds in salivary fluid.
10. During manufacturing processes and after manufacturing handling, it should have an adequate hardness to resist rigors.
11. It should allow high drug loading.
12. It should be adaptable and amenable to existing processing and packaging machinery.

Drug selection criteria for fast dissolving tablet: [18-21]

1. Drug should have to permeate via oral mucosal tissue.
2. Drug should be partially non ionized at pH in oral cavity.
3. Drug having the ability to diffuse and partition into the epithelium of the upper GIT.
4. Fast-dissolving tablets are not suitable for drugs with a short half-life or frequent dosages.
5. Drug should have good stability in saliva and water.
6. Very bitter or unacceptable taste and odour drugs are unsuitable for fast dissolving tablets.

CHALLENGES FOR FORMULATING FAST DISSOLVING TABLETS:

A) Palatability:

As most drugs are unpalatable, fast dissolving tablets usually contain the medicament in a taste masked form. Upon administration, it disintegrates or dissolve in patient's mouth cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes crucial factor to patient compliance. This is challenge as most drugs are bitter in nature [2-5].

B) Hygroscopicity:

Several drugs are hygroscopic in nature i.e. they having ability to absorb moisture under normal condition of temperature and humidity. Hence they require protection from humidity which calls for specialised product packaging [7-10].

C) Aqueous solubility:

Aqueous solubility becomes a major issue if the drug is hydrophobic in nature or highly lipophilic, thus it doesn't dissolve/disintegrate in mouth leading to grittiness and residue in mouth.

D) Size of tablet:

The convenience of administration of tablet is depends upon its size. It has been reported that the easiest size of tablet to ingest is 7-8 mm while the easiest size to handle was one larger than 8 mm. Hence, it is challenging to create tablets that are both easy to handle and easy to swallow.

E) Mechanical strength:

The tablet should have appropriate mechanical strength accompanying its additives added, should not break easily, nor be friable. This is a challenge as the drug should rapidly disintegrate in oral cavity and yet have good mechanical strength [7].

F) Amount of drug:

The application of technologies used for fast dissolving tablets is limited by the amount of drug that can be incorporated into each unit dose. The drug dose must be less than 400 mg for

insoluble drugs and 60 mg for soluble drugs for lyophilized dosage forms. This parameter is particularly challenging when developing a fast dissolving oral films or wafers.

G) Mouth feel:

Fast dissolving tablets should not break into larger particles in the oral cavity. The particles produced after disintegration of the fast dissolving tablets should be as small as possible. Additionally, incorporating flavours and cooling substances like menthol enhances the mouth feel [5-16].

NEED OF FAST DISSOLVING TABLETS:

1. Patient factor [16-19]

Fast dissolving dosage forms are suitable for those patients such as pediatric and geriatric patients who are not able to ingest conventional tablets and capsules with an 8-oz glass of water. These include the following.

1. Patients who have difficulty in ingesting or masticating solid dosage forms.
2. Patients implacability due to fear of unpleasant.
3. Very older patients who may not be able to swallow solid dosage forms of antidepressant drug.
4. An eight-year-old allergy patient prefers a dosage form other than antihistamine syrup.
5. A patient with persistent nausea, who may be a journey, or has little or no access to water.

2. Effectiveness factor [19-21]

1. Improved bioavailability and rapid onset of action are a major assert of these formulations.
2. Dispersion in saliva in oral cavity causes pregastric absorption from some formulate ions in those cases where drug dissolves rapidly.
3. Buccal, pharyngeal and gastric region are all areas of permeation of many drugs.
4. Any pregastric absorption bypasses presystemic metabolism and can be great benefit in drugs that undergo hepatic metabolism.

5. Furthermore, safety profiles may be enhanced for drugs that produce significant amounts of toxic metabolites produced by presystemic metabolism and for drugs that have a considerable fraction of absorption in the oral cavity and pre-gastric segments of gastrointestinal tract.

3. Manufacturing and marketing factor [5,20]

1. Formulating novel drug delivery technologies and utilizing them in product development is crucial for pharmaceutical industries to survive, regardless of their size.

2. As a drug close to end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form.

3. A new dosage form permits a manufacturer to extend market exclusivity, unique product differentiation and extend patent protection. For examples, Eisai Inc. launched Aricept fast dissolving tablets, a line extension of donepezil for Alzheimer's disease, in Japan in 2004 and in the U. S. June 2005 in response to a generic case Ranbaxy filed in the US.

EXCIPIENT USED IN FAST DISSOLVING TABLETS:

Excipients used in fast dissolving tablets contain one superdisintegrant, a diluent/bulking agent, a lubricant and alternately swelling agent, permeabilizing agent sweeteners and flavourings agents.

SUPERDISINTEGRANTS:

Superdisintegrant are novel polymers having more disintegrating capacity than disintegrants. A superdisintegrant is an excipient, which is added to a tablet blend to aid in the breakup of the compacted mass when it is put into a fluid environment [13]. Utilisation of superdisintegrant is the basic approach of formulation of fast dissolving tablet. It is essential to select a suitable superdisintegrant in appropriate concentration so as to ensure rapid disintegration and high dissolution rates [14]. They are used in less concentration of 1-10% by weight relative to the total weight of dosage units.

Selection criteria for superdisintegrants:

1. Superdisintegrant particle should be small.

2. Superdisintegrant should be compatible with other excipients and drugs.

3. Superdisintegrant should be non-toxic.

4. Superdisintegrant should show good hydration capacity.

5. Superdisintegrant having good flow property.

6. Superdisintegrant should effective in low concentration.

7. Superdisintegrant should produce quick disintegration, when tablets are coming in contact with saliva in oral cavity.

MECHANISM OF SUPERDISINTEGRANTS:

A) Swelling: [3-8]

Swelling may be the most widely accepted general mechanism for tablet disintegration. Tablets with high porosity show poor disintegration due to lack of appropriate swelling force. Moreover, sufficient swelling force is exerted in the tablet with low porosity. It is valuable to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

B) Porosity and capillary action (wicking): [21]

The capillary action must be considered as first step in mechanism of disintegration. When we put the tablet into suitable water medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which fragile the intermolecular bond and breaks the tablet into fine particles.

Water uptake by tablet depends upon hydrophilicity of the drug /additives and on tableting conditions. For these types of disintegrants continuation of porous structure and low interfacial tension towards aqueous fluid is essential which helps in disintegration by producing a hydrophilic network around the drug particles.

C) Due to disintegrating particle/particle repulsive forces: [8-14]

Another mode of disintegrating attempts to explain the swelling of tablet made with ‘non-swellable’ disintegrants. Guyot Hermann has put forward a particle repulsion theory based on the observation that non-swelling particle also cause disintegration/disaggregation of tablets. The electric repulsive forces between particles are the mode of disintegration and water is required for it. Researchers found that repulsion is next mechanism after wicking.

D) Due to deformation: [17]

During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with water. Occasionally, the swelling capacity of starch was enhanced when granules were highly deformed during compression. This enhancement in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

E) Because of heat of wetting: [14]

When disintegrants with exothermic properties i.e. heat evolving properties gets wetted, localized stress is produced due to capillary air expansion, which aids in disintegration of tablet. This mechanism, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents.

TYPES OF SUPERDISINTEGRANTS:

1. Natural Superdisintegrants:

Natural superdisintegrant are commonly used in fast dissolving tablet formulation which aids in disintegration/disaggregation of tablets. Examples of natural superdisintegrant are Banana powder, apple pectin, plantago ovata mucilage, hibiscus rosa sinesis mucilage, gum karaya, fenugreek powder etc.

2. Synthetic Superdisintegrants:

Synthetic superdisintegrant are most widely used in fast dissolving tablets formulation which aids in disintegration/disaggregation of tablets. Examples of synthetic superdisintegrant are sodium starch glycolate, crosspovidone, croscarmellose sodium, ion exchange resin etc.

CONVENTIONAL TECHNOLOGIES FOR FORMULATING FAST DISSOLVING TABLETS:

Many conventional techniques have been reported for development of fast dissolving tablets.

1. Lyophilization/ freeze drying
2. Tablet moulding
3. Sublimation

4. Spray drying
5. Mass extrusion
6. Direct compression

1. Lyophilization/ freeze drying: [3-7]

Freeze drying is procedure in which water is sublimed from the product after it is frozen. This technology produced an amorphous porous structure that can dissolve quickly. A typical procedure involves in formulation of fast dissolving tablets utilizing this technique is mentioned here.

1. The active drug is dissolved or dispersed in aqueous solution of carrier/polymer.
2. The mixture is done by weight and poured in the walls of preformed blister packs.
3. To freeze the drug solution or dispersion, the trays containing the blister packs are moved through a liquid nitrogen freezing tunnel.
4. Then the frozen blisters are placed in refrigerated cabinet to continue the freeze drying.
5. After freeze drying the aluminium foil backings is applied on a blister sealing machine.
6. The blisters are then sealed and shipped.

The freeze drying technique has demonstrated enhanced absorption and improvement in bioavailability. The major limitation of lyophilization technique are that it is expensive and time consuming; Conventional packaging is inappropriate for these products due to their fragility and poor stability under pressure.

2. Tablet moulding: [7-8]

In moulding process there are two types i.e., solvent method and heat method solvent method involves moistening the powder mixture with hydro alcoholic solvent followed by compression at low pressure in moulded plates to form wetted mass. Air drying is then utilized to remove the solvent. The tablets formed in this manner are less compact than compressed tablets and possess a porous structure that accelerate dissolution. The heat moulding process involves the preparation of suspension that contains drug, agar sugar e.g. mannitol or lactose and pouring the suspension in blister packaging wells, solidifying the agar

at room temperature to form jelly and drying at 30^0 c under vacuum. The mechanical strength of moulded form of tablets is matter of great concern.

Binding agents which enhances the mechanical strength of tablets, need to be incorporated. Taste masking is added concern to this technology. The taste masked drug particles are formulated by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and active ingredient into a lactose based tablet triturate form. Compared to lyophilization technique, tablets formulated by moulding technique are easier to scale up for industrial manufacture.

3. Sublimation: [7-8]

To produce a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like camphor, benzoic acid, naphthalene, urea, urethane, ammonium bicarbonate, ammonium carbonate may be compressed with other additives into tablet. Sublimation is then used to remove this volatile substance, leaving behind a very porous matrix. The reported average disintegration time for tablets made using this method is 10 to 20 seconds. As pore-forming agents, even solvents like cyclohexane and benzene can be utilised.

4. Spray drying: [3,8]

In this technique, gelatin can be utilized as a supporting agent and as a matrix, mannitol as a bulking agent and croscarmellose sodium or crospovidone or sodium starch glycolate are utilised as superdisintegrants. Tablets manufactured from the spray-dried powder have been observed to disintegrate in less than 20 seconds in aqueous medium. The formulation contained bulking agent like lactose and mannitol, a superdisintegrant like croscarmellose sodium and sodium starch glycolate and acidic ingredient such as citric acid and/or alkaline ingredients such as sodium bicarbonate. This spray-dried powder, which compressed into tablets showed quick disintegration and improved dissolution.

5. Mass extrusion: [1]

In this method active blend is softened using the solvent mixture of water soluble polyethylene glycol and methanol and then subsequent expulsion of softened mass through the extruder or syringe is made to get a cylinder of product into even segments using heated

blade to form tablet. The dried cylinder can also be utilised to coat granules for bitter drugs and thereby achieving taste masking.

6. Direct compression: [8]

Direct compression represents the simplest and cost effective tablet manufacturing technique. In this method, tablets are prepared directly by compression of the mixture of drug and additives without any initial treatment. The mixture which is to be compressed must have good flow properties. This method completes within 3 steps i.e.

a) Milling of drug and additives

b) Mixing of drug and additives

c) Tablet compression

PATENTED TECHNOLOGIES FOR FORMULATING FAST DISSOLVING TABLETS:

1. Zydis technology: [7]

Zydis formulation is unique technology for formulating fast dissolving tablets. Zydis is the first fast dissolving dosage form in market. Zydis formulation is unique freeze dried tablet in which drug is entrapped or dissolved within matrix of fast dissolving carrier material. When zydis units are put into the mouth, the freeze-dried structure disintegrates immediately and does not require water to aid swallowing. The zydis matrix is composed of many materials designed to achieve a number of objectives. To impart strength and flexibility during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which provides strength.

To obtain crystallinity, elegance and hardness, saccharides such as sorbitol or mannitol are incorporated. Water is utilised in the manufacturing process to ensure production of porous units to achieve quick disintegration while various gums are utilised to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the contraction of zydis units during freeze-drying process or long-term storage. Zydis products are packed in blister packs to save the formulation from moisture in the environment.

2. Durasolv technology: [3-13]

Durasolv technology is patented by CIMA labs. Durasolv technology is based upon direct compression technology which utilizes suitable additives with enhanced properties, especially superdisintegrants that improved the rate of disintegration and hence dissolution. The tablets made by this technology consist of drug, filler and lubricant. Tablets are prepared by using conventional tabletting equipment have good rigidity. These can be contained in standard packaging systems, such as blisters. Durasolv is an appropriate technology for product requiring low amounts of drug.

3. Orasolv technology: [1-19]

Orasolv is unique technology is patented by CIMA labs. This involves use of effervescent disintegrating agents compressed with low pressure to produce the fast dissolving tablets. This evolution of carbon dioxide from the tablet produces effervescence sensations, which is a positive organoleptic property. Concentration of effervescent mixture usually used is 20-25% of tablet weight. As tablets are formulated at low compression force, they are soft and fragile in nature. This initiated to develop pakslov, a special packing to protect tablets from breaking during storage of transport. Paksolv is a dome-shaped blister package, which stops the vertical movement of tablet within the depression. Paksolv offers moisture, child and light resistance packing.

4. Flash Dose Technology: [3-21]

Flash dose technology is patented by fuisz. The flashdose technology uses a unique spinning mechanism to generate floss like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the drug and be compressed into a tablet. flashdose tablet consists of self binding sheaform matrix termed as “floss’’ structure. The process has been patented by fuisz and known as “Shearform”.

Interestingly, by altering the temperature and other conditions during production, the characteristics of the product can be changed greatly. Instead of floss- like material, small spheres of saccharide can be generated to carry the drug. The procedure of producing microspheres has been patented by fuisz and known as “Ceform”.

5. Wow tab Technology:

Wow tab technology is patented by Yamanouchi Pharmaceutical Company. WOW Stands for "without water''. In this process high mouldability saccharide like oligosaccharide, mannitol is mixed with low mouldability saccharide like glucose, lactose and mannitol to obtain rapidly melting strong tablet. The active substance is combined with a saccharide that is low in mouldability, granulated with a saccharide that is high in mouldability, and compressed into a tablet.

6. Flash tab Technology: [18]

Flashtab technology is patented by prographarm laboratories. Active ingredient is used in the form of micro crystals. The traditional methods of coacervation, micro encapsulation, and extrusion spheronization can be used to create drug micro granules. All processing was done using standard tabletting technology.

7. Sheaform technology: [21]

The technology is based on the preparation of floss that is also known as 'Shearform Matrix', which is produced by subjecting a feed stock containing a sugar carrier by flash heat processing. In this process, the sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which raises the temperature of the mass to create an internal, flow condition, which permits part of it to move with respect of the mass. The floss so produced is amorphous in nature so it is further chopped and recrystallized by various techniques to provide aciform flow properties and this facilitate blending the recrystallized matrix is then blended with other tablet excipients and an active ingredient. The resulting mixture is compressed into tablet.

8. Ceform technology: [14]

This technology includes preparation of microspheres of the active drug. Drug material alone or in combination with other pharmaceutical substances, and additives is placed into a precision engineered rapidly spinning machine. The centrifugal force comes into action, which throws the dry drug blend at high speed through small heated openings. Due to the heat provided by carefully controlled temperature, drug blend liquefies to form a sphere, without affecting the drug stability. The microspheres thus formed are compressed into tablets. As the drug and excipients both can be processed simultaneously, it creates unique

microenvironment in which the materials can be incorporated into the microspheres that can change the characteristics of the drug, such as increasing solubility and stability.

9. Nanocrystal technology: [7]

The technology increases dissolution rate by decreasing particles size and increasing surface area. Nanocrystal particles are drug particles (less than 1000 nm in diameter), produced by milling the drug substance, and obtained through wet milling technique. Nanocrystal fast dissolving technology provides, Wide range of doses per unit (up to 200 mg of API per unit), based on proprietary and patent protected technology elements products can be well classified. Improved Pharmacokinetics of oral drug. Use of non-moisture sensitive in actives, and is economic and Cost-effective.

Combining drug Nano crystal colloidal dispersions and water-soluble GRAS (Generally Regarded as Safe) ingredients, then filled into blisters, and lyophilized product wafers are formed. They are highly robust, yet dissolve in very small quantities of water in seconds, which is agreeable when working with highly potent or hazardous materials reducing operations, like granulation, blending, and tableting. This approach is also allowing small quantity of drugs to be converted into fast dissolving tablets because manufacturing loss is negligible.

10. Frosta technology: [19]

It uses the concept of formulating plastic granules and compressing at low pressure to formulate strong tablets with high porosity. Plastic granules made up of porous and plastic material, Water penetration enhancer and binder. The procedure involves usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The tablets obtained have excellent hardness and quick disintegration time ranging from 15 to 30s depending on size of tablet 30. filler decreases porosity of tablets due to which disintegration is lowered.

PREFORMULATION STUDIES OF BLENDS:

1. Bulk density: [3-18]

Bulk density can be determined by pouring blend into a graduated measuring cylinder using a funnel and weigh. It is the ratio of weight of powder to the bulk volume of powder. The bulk density can be calculated using the formula

$$\text{Bulk density} = \frac{\text{Weight of powder}}{\text{Bulk volume}}$$

2. Tapped density: [18]

Same measuring cylinder should be set for the determination of tapped density that was used for the determination of bulk volume. Set measuring cylinder to 300 taps per minute and operate for 500 taps. The tapped density is calculated by the following formula-

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume}}$$

3. Angle of repose:

The angle of repose was determines using funnel method. The angle of repose was then calculated by measuring the height and radius of heap of granules formed.

$$\theta = \tan^{-1}(h/r)$$

Table no. 1 Angle of repose as an indication of powder flow properties

Sr.no.	Angle of repose	Type of flow
1	< 20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very Poor

4. Carr's index (or) % compressibility:

A simplex way of measurement of the free flow of powder. Carr's index measures the propensity of powder to be compressed and the flow ability of powder. Carr's index can be calculated from the bulk and tapped density by using following formula-

$$\text{Carr's index} = \frac{(\text{Tapped density} - \text{Bulk density}) \times 100}{\text{Tapped density}}$$

Table no.2 Relationship between % compressibility and flow ability

% Compressibility	Flow ability
5-12	Excellent
12-16	Good
18-21	Fair passable
23-35	Poor
33-38	Very poor
<40	Very very poor

5. Hausner ratio:

Hausner ratio is ratio of tapped density to bulk density. Hausner ratio can be calculated from following formula-

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

6. Identification of drug sample: [3]

It was confirmed by melting point determination and also by FTIR spectral analysis.

7. Drug excipient compatibility study: [3]

Compatibility of the drug with excipients was determined by FTIR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients. The samples were taken for FTIR study.

EVALUATION OF FAST DISSOLVING TABLETS:

1. General appearance:

Tablets of different formulations were randomly selected and organoleptic properties such as colour, odour, taste, shape, were evaluated.

2. Tablet thickness: [18]

Tablet thickness is an important characteristic and is expressed in mm. The thickness and diameter of the tablets was determined using a micrometer screw gauge.

3. Tablet hardness: [13]

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet, them resistance of the tablet to abrasion, chipping or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet was determined using Pfizer Hardness Tester.

4. Friability of tablets: [9]

Friabilator consist of plastic chamber revolves at 25 rpm, dropping those tablets at distance of 6 inches with each revolution. The tablets were rotated in the friabilator for at least 4 min. At the end of these test tablets are required to be dedusted and reweighed, the loss in the weight of tablet is the measured of friability and is expressed in percentage as-

$$\% \text{ Friability} = \frac{\text{initial weight} - \text{final weight}}{\text{Initial weight}} \times 100$$

5. Weight variation:

20 tablets are selected randomly from the lot and weighted individually to check for weight variation. Weight variation of tablet specification as per I.P.

Table no.3 Weight variation specification as per I.P.

Average weight of tablets	% Deviation
80 mg or less	±10
80-250 mg	±7.5
250 mg or more	±5

6. Wetting time: [3]

Five circular tissue papers of 10 cm diameter are placed in petri dish with a 10 cm diameter. Ten millimetres of water containing eosin, water soluble dye, is placed in petri dish. A tablet

is carefully placed on surface on surface of tissue paper. The time required for water to reach upper surface of tablet is noted as wetting time.

7. In-vitro disintegration time: [18]

This test is performed on 6 tablets, by placing tablet into each tube (3 inches long and have 10 mesh screen) of apparatus using the distilled water (used as disintegration medium) at a frequency of 28-32 cycle/minute and 37 ± 2^0c and the time in second was noted when no lumps remaining in the apparatus.

8. Modified disintegration test:

The traditional method of conducting a disintegration test for these dosage forms has a number of drawbacks and is insufficient for measuring very quick disintegration times. Fast dissolving tablets need to have their disintegration times adjusted since they need to dissolve without water for the test, which should imitate salivary disintegration. A petri dish (10 cm in diameter) with 10 ml of water inside of it was used for this. The time it took for the tablet to totally break down into tiny particles was recorded after it was carefully placed in the centre of the petri dish.

9. In-vitro dispersion time: [19]

To determine dispersion time 10 ml measuring cylinder was taken in which 6 ml distilled water was added and tablet was dropped in it. Time required for complete dispersion was determined.

10. In-vitro dissolution study: [9]

In vitro dissolution study has to be performed by using USP type II apparatus (paddle type) [Electro lab (ETC -11L) Tablet dissolution tester] at 50 rpm. Phosphate buffer pH 6.8, 900 ml is mainly used as dissolution medium which is required to maintain at 37±0.5°C. Aliquot of (10ml) dissolution medium is required to withdraw out at specific time interval (2min) and then it is required to subject for process of filtration. The amount of drug dissolved was determined by UV Spectrophotometer (Shimadzu, japan) by measuring the absorbance of the sample. Three trials of each batch were performed and average % drug release with standard deviation was calculated and recorded.

11. Stability studies: [18

Stability testing of tablets is done to check whether it is a stable product or not and to check integrity of formulations during its shelf life. The formulation prepared should be packed in a special way, firstly the formulation is wrapped in a butter paper then aluminium foil is wrapped over it, then this is packed in an aluminium pouch and heat sealed. Storage conditions of formulation should be 45^0c/ 75% RH. Formulations should be stored for 3 months. During the course of stability study triplicate samples should be taken at three sampling intervals i.e. 0, 1 and 3 months, and tablets should be evaluated for physical changes and drug content.

DRUGS TO BE INCORPORATED IN FAST DISSOLVING TABLETS:

a. Antihypertensive: Felodipine, Amlodipine, Nifedipine, Nimodipine, Diltiazem, Carvedilol, Prazosin hydrochloride, Terazosin hydrochloride, Benidipine, Darodipine, Minoxidil, Nicardipine

b. Antiarrhythmics: Quinidine sulphate, Amiodarone hydrochloride, Disopyramide, Flecainide acetate

c. Analgesics/Anti-inflammatory agents: Ibuprofen, Ketoprofen, Naproxen, Oxyphenbutazone, Phenylbutazone, Indomethacin, Piroxicam**,** Mefenamic acid, Diclofenac sodium, Flurbiprofen, Sulindac

d. Antidepressants: Nortryptaline hydrochloride, Trazodone hydrochloride, Amoxapine, Mianserin hydrochloride, Paroxetine hydrochloride, Imipramine, Amitryptaline hydrochloride, Sertraline hydrochloride

e. Antidiabetics: Tolbutamide, Tolazamide, Chlorpropamide, Glibenclamide, Glipizide

f. Antibacterial agents: Ciprofloxacin, antibiotic medication, erythromycin, rifampicin, penicillin, doxycyclin, nalidixic acid, trimethoprim, sulphacetamide, sulphadiazine

g. Anthelmintics: Albendazole, mebendazole, thiabendazole, livermectin, praziquantel, pyrantel etc.

h. Diuretics: Amiloride, Furosemide, Acetazolamide, Clorthiazide, Spironolactone, Bumetanide, Ethacrynic acid etc.

i. Gastrointestinal agents: Famotidine, Ranitidine hydrochloride, Cimetidine, Ondansetron, Omeprazole hydrochloride, Granisetron hydrochloride etc.

j. Anxiolytics, sedatives hypnotics & Neuroleptics: Alprazolam, Diazepam, Clozapine, Lorazepam, Nitrazepam, Midazolam, Phenobarbitone, Thioridazine, Oxazepam etc.

k. Corticosteroids: Betamethasone, Beclometasone, Hydrocortisone, Prednisone, Prednisolone etc.

l. **Antiprotozoal agents:** Metronidazole, Tinidazol, Omidazole, Benznidazole, Clioquinol, Decoquinate etc.

INDUSTRIAL APPLICATION OF FAST DISSOLVING TABLETS: [20]

1. To formulate an orally disintegrating dosage forms and to work with existing disintegrants.

2. To further improvise upon existing technology of fast dissolving tablets.

3. To optimize the blend of disintegrants or additives to achieve fast dissolving tablets.

4. To select and develop proper packing material and system improved stability of the product and also develop cost effective product.

5. To arrive at various taste masking agents and formulate palatable dosage form thereby enhanced patience compliance.

6. To develop disintegrants from different polymer which are used as coating material by certain modification and use them for formulating fast dissolving tablets.

FUTURE PROSPECTS OF FAST DISSOLVING TABLETS:

These dosage forms might be acceptable for the oral administration of medications like protein- and peptide-based therapies, which have a poor bioavailability when consumed as regular tablets. In the stomach, these compounds usually break down quickly. If the majority of the pharmaceuticals of the next generation are protein or peptide based, tablets may no longer be the most common way to dose such compounds. Patients typically do not choose to utilise injections until advanced auto-injectors make it easier for them to do so. Although one effective alternate delivery method for these medications is inhalation, recent advances in biopharmaceutical research have primarily resulted in chemical substances with low molecular weights. The advancement of faster dissolving tablets that could release these

medications in the oral cavity and increase the administration of oral proteins is very promising.

CONCLUSION:

The fast dissolving tablets have enormous advantages over conventional dosage forms with enhanced patience compliance, convenience, bioavailability and faster onset of action had drawn attention of many manufactures over decade. Fast dissolving tablet is acceptable for pediatric, geriatric and bedridden patients. Faster dissolution as well as disintegration is the main goal of fast dissolving tablets. Incorporating superdisintegrants or developing a porous structured tablet matrix can accomplish this. Fast dissolving tablets formulated by some of these technologies have sufficient mechanical strength, rapid disintegration/dissolution in mouth without water. The future scope for these products is promising due to availability of new technologies combined with strong market acceptance and patient demand. Future possibilities for enhancement in fast dissolving drug delivery system are bright, but technology is still new.

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