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A Review on Development and Evaluation of Mouth Dissolving Anti-inflammatory Tablet Containing Fenopufen

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ABSTRACT

The objective of this paper was to attempt to investigate a review the Development and evaluation of mouth dissolving antinflammatory tablet containing fenopufen. MDT is used methods to improve patient's compliance have always attracted scientists towards the development of fancy oral drug delivery systems. Among them, mouth dissolving drug delivery systems (MDDDS) have acquired an important position in the market by overcoming previously encountered administration problems and contributing to extension of patent life. In the present scientific scenario the drug delivery technology has become highly competitive and rapidly evolving with ever increasing demand. Fast dissolving tablet (FDT) is one such type of an innovative and unique drug delivery system which is swiftly gaining much attention in the research field of rapid dissolving technology. Oral route is the most expedient and safest route of drug delivery because of wide range of drugs are administered through this route. Recently researchers have developed fast dissolving tablet (FDT) which dissolve or disintegrate rapidly in mouth saliva without intake of water. This novel drug delivery such as FDT or MDT (mouth dissolving tablet) has overcome many disadvantages like dysphagia or non accessibility of water while travelling. When compared with conventional dosage form FDT can be a useful alternative as well. This review article contains different techniques used for preparing FDT, silent features, various patented technologies, and mechanism of super disintegration, challenges faced and the limitations.

Keywords: Oral route, Mouth dissolving tablet, Super disintegrants, Dysphagia, fenopufen.

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INTRODUCTION

Conventional dosage forms are pioneer of drug administration systems. The most widely used and accepted is the oral route of drug administrations. The oral dosage forms are widely used for ease of self-administration and low cost as compared to other dosage forms.¹ It is however associated with some drawbacks such as dysphasia (difficulty in swallowing), low bioavailability and delayed onset of action. In order to overcome these issues researchers have long explored the “oral cavity” to harness its drawback to enhance the drug’s permeability as well as bioavailability. The “oral cavity” has a good permeability because of mucosal lining being relatively less keratinized in the buccal mucosa.² Drug absorbed via “oral cavity” directly enters into systemic circulation by a jugular vein ensuring, a rapid onset of action, avoidance of first pass metabolism, and drug degradation in gastric region and enzymatic hydrolysis in intestine.³ Keeping in mind the advantages of the “oral cavity”, an Oral Dispersible Tablet, commonly known as the Fast Dissolving Tablets are a widely accepted formulations. According to European pharmacopoeia “ODT (Oral Dispersible Tablet) should disperse or disintegrate in less than 3 minute when placed on tongue”. Fast dissolving drug delivery system (FDDDS) is a newer concept which combines the advantages of both liquid and solid formulations and at the same time, offer advantages over the traditional dosage forms. Many patients, especially elderly find it difficult in swallowing tablets, capsules, fluids and thus do not comply with prescription, which results in high incidence of non-compliance oriented research has resulted in bringing out many safer and new drug delivery system. Rapidly disintegrating/dissolving tablet is one of such example, for the reason of rapid disintegration or even with saliva. Considering quality of life, most of these efforts have been focused on ease of medication. Among the various dosage forms developed to improve the ease of administration, the mouth dissolving tablet (MDT) is the most widely preferred commercial products.⁴ The oral cavity is an attractive site for the administration of drugs because of ease of administration. Various dosage forms like Tablets, Capsules, and Liquid preparations are administered by oral route. During the last decade, mouth dissolving tablet (MDT) technologies that make tablets disintegrate in the mouth without chewing and additional water intake have drawn a great deal of attention. The MDT is also known as fast melting, fast dispersing, rapid dissolve, rapid melt, and or quick disintegrating tablet. All MDTs approved by the Food and Drug Administration (FDA) are classified as orally disintegrating tablets. Recently, the European Pharmacopoeia adopted the term orodispersible tablet for a tablet that disperses or disintegrates in less than 3minutes in the mouth before swallowing. Such a tablet disintegrates into smaller

granules or melts in the mouth from a hard solid to a gel-like structure, allowing easy swallowing by patients. The disintegration time for good MDTs varies from several seconds to about a minute.⁵ Orally disintegrating tablets provide an advantage particularly for pediatric and geriatric. Fast dissolving tablets are novel drug delivery system that dissolves, disintegrate or disperse the API in saliva within few seconds with or without intake of water. The faster the dissolution of drug into the solution, quicker is the absorption and onset of clinical effect. The bioavailability of some drugs may increase due to absorption of drugs in oral cavity or also due to pregastric absorption of drug from saliva that pass down into the stomach. Natural and synthetic Superdisintegrants like mucilage, cross linked carboxymethyl cellulose (croscarmellose) and sodium starch glycolate (primogel), poly vinyl pyrrolidone etc provide immediate disintegration of tablets and facilitate the design of delivery system with desirable characteristics. These types of formulations are widely recommended for the drugs used in emergency. e.g., Cardiac agents, Asthma, Brain stroke, Anti-hyper-lipidemic etc.

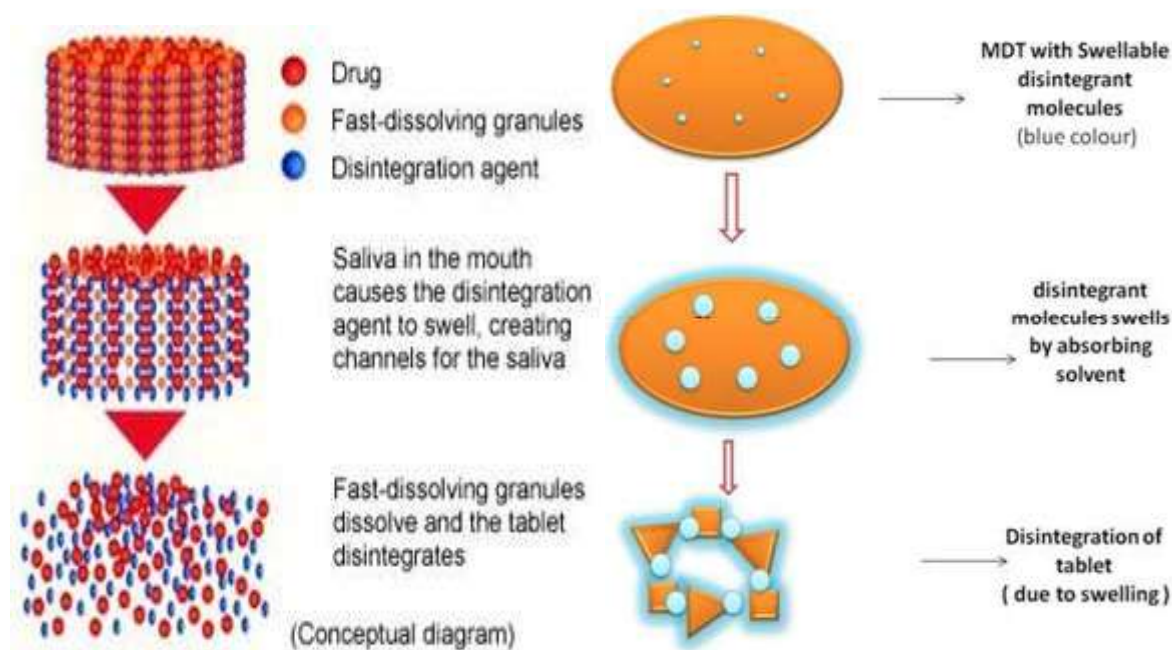


Figure 1: Mechanism involved in FDT

Need of oral route of administration

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, relatively low cost of manufacture, packaging, shipment increased stability, avoidance of pain, flexibility and most importantly patient compliance. Oral drug delivery systems are divided into immediate release and

modified release systems. Immediate release drug delivery systems are intended to disintegrate rapidly, and exhibit instant drug release. They are associated with a fast increase and decrease, and hence fluctuations in drug plasma levels, which leads to reduction or loss in drug effectiveness or increased incidence of side effects. Administration of the drug delivery systems several times per day is therefore necessary to compensate the decrease in drug plasma concentration due to metabolism and excretion.⁶

An ideal Properties of FDT

Require no water for oral administration, yet dissolve / disperse/ disintegrate in mouth in a matter of seconds. Have a pleasing mouth feel. Have an acceptable taste masking property. Be harder and less friable Leave minimal or no residue in mouth after administration Exhibit low sensitivity to environmental conditions (temperature and humidity). Allow the manufacture of tablet using conventional processing and packaging equipments.⁷

Advantages of FDT

Administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure & patients who refuse to swallow such as pediatric, geriatric & psychiatric patients rapid drug therapy intervention. Achieve increased bioavailability/rapid absorption through pregastric absorption of drugs from mouth, pharynx & oesophagus as saliva passes down. Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, who do not always have access to water.⁸ Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients. The risk of choking or suffocation during oral administration

Criteria for Drug Selection: FENOPROFEN

The ideal characteristics of a Fenprofen for *in- vivo* dissolution from an MDT include:- Dose lower than 20mg. Small to moderate molecular weight. Good stability in water and saliva. Partially non-ionized at the oral cavities pH, ability to diffuse and partition into the epithelium of the upper GIT, ability to permeate oral mucosal tissue. Unsuitable drug characteristic for MDT: Short half-life and frequent dosing very bitter or otherwise unacceptable taste because taste masking cannot be achieved. Required controlled or sustained release.⁹

DRUG (FENPROFEN)

Fenopufen is a Nonsteroidal anti-inflammatory drug (NSAID). Fenopufen calcium is used for symptomatic relief for rheumatoid arthritis, osteoarthritis, and mild to moderate pain. Fenopufen is marketed in the USA as Nalfon.

Decreases inflammation, pain, and fever, probably through inhibition of cyclooxygenase (COX-2 inhibitor) activity and prostaglandin synthesis.¹⁰

Super Disintegrants Used in MDTs¹¹

As day's passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrants i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. This superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration. Various types of Super disintegrants used are as follows –

- Crosspovidone
- Microcrystalline cellulose
- Sodium starch glycollate
- Sodium carboxy methyl cellulose or ross
- carmelose sodium
- Crosscarmellose sodium
- Calcium carboxy methyl cellulose
- Modified corn starch.
- Sodium starch

Superdisintegrants

Table: 1. Classification of superdisintegrants

Name	Description	Trade name
1. Modified starches (Sodium starch glycolate. NF)	Sodium carboxy methyl starch, the carboxymethyl groups induced hydrophilicity and cross-linking reduces solubility	Explotab, Primojel, T a b l o
2. Modified cellulose (Croscarmallose. NF)	Sodium carboxy methyl cellulose which has been cross-linked to render the material insoluble	Ac-Di-Sol, Nymcel, S o l u t a b
3. Cross-linked Polyvinylpyrrolidone (Crospovidone. NF)	Crosslinked Polyvinylpyrrolidone, high molecular rending the material	Crospovidone, K o l l i d o n , Polyplasdone

Methods of Incorporating Disintegrants into Tablets: -¹²

There are three techniques of incorporating disintegrating agents into the tablet as described below:

- **Internal Addition (Intra-granular):** In this method, the disintegrant is properly mixed with few other powders before wetting powder mixtures with granulating fluid. Thus the disintegrant is included within the granules.
- **External Addition (Extra-granular):** In this method, the disintegrants are added to the sized granulation with mixing before compression.
- **Partly Internal and External:** In this method, part of disintegrant could be added internally and part externally which results in immediate interruption of the tablet into previous compressed granules while disintegrating agent within granules produce extra attrition to the granules in comparison to the powder particles.

The most popular disintegrants are soluble starch, corn starch etc. which are well dried and powdered. Starches have good affinity for water and swell when moistened thus facilitate the breaking of the tablet matrix, its disintegration action in tablets is because of capillary action. Spherical shape of starch enhances the porosity of tablet and thus promotes capillary action. Cellulose and gums are considered to be valuable when used as disintegrants. Cellulose and gums are higher swell ability with water and break the tablets into smaller particles. Alternative method for the disintegration of tablet is including of tartaric acid and citric acid with sodium carbonate, sodium bicarbonate, potassium bicarbonate or calcium carbonate. They react in contact with water releasing carbon dioxide that disrupts the tablet.

The Need for Development of ODTs¹³

The need for non-invasive delivery systems persists due to patients' poor acceptance of, and compliance with, existing delivery regimes, limited market size for drug companies and drug uses, coupled with high cost of disease management. Patient factors¹⁷⁻²⁰ orally disintegrating dosage forms are particularly suitable for patients, who for one reason or the other, find it inconvenient to swallow traditional tablets and capsules with an 8-oz glass of water.

These include the following:

- Pediatric and geriatric patients who have difficulty in swallowing or chewing solid dosage forms
- Patients who are unwilling to take solid preparation due to fear of choking
- Very elderly patients who may not be able to swallow a daily dose of antidepressant.
- An eight-year old with allergies who desires a more convenient dosage form than antihistamine syrup
- A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H₂- blocker

- A schizophrenic patient in an institutional setting who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic
- A patient with persistent nausea, who may be journey, or has little or no access to water

Effectiveness factor¹⁴

Increased bioavailability and faster onset of action are a major claim of these formulations. Dispersion in saliva in oral cavity causes pregastric absorption from some formulations in those cases where drug dissolves quickly. Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs. Any pregastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo a great deal of hepatic metabolism. Furthermore, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism, and for drugs that have a substantial fraction of absorption in the oral cavity and pregastric segments of GIT

Manufacturing and marketing factors¹⁵

Developing new drug delivery technologies and utilizing them in product development is critical for pharmaceutical industries to survive, regardless of their size. As a drug nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, unique product differentiation, value-added product line extension, and extend patent protection, while offering its patient population a more convenient dosage form. This leads to increased revenue, while also targeting underserved and under-treated patient populations. As examples, Eisai Inc. launched Aricept ODT, a line extension of donepezil for Alzheimer's disease, in Japan in 2004 and in the U.S. in 2005 in response to a generic challenge filed in the U.S. by Ranbaxy. Merck's Japanese subsidiary launched Lipola M (simvastatin ODT), a line extension of its block-buster, Zocor, a cholesterol-lowering drug, in response to seventeen generic registrations of simvastatin applied for in Japan in 2004²⁴. Marketers build a better brand and company image when they offer a unique easier-to-take form that satisfies the need of an underserved patient population.¹⁶

Challenges in Formulating ODTs Palatability¹⁷

As most drugs are unpalatable, orally disintegrating drug delivery systems usually contain the medicament in a taste-masked form. Delivery systems disintegrate or dissolve in patient's oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes critical to patient compliance.

Mechanical strength¹⁸

In order to allow ODTs to disintegrate in the oral cavity, they are made of either very porous and soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, difficult to handle, and often requiring specialized peel-off blister packing that may add to the cost. Only few technologies can produce tablets that are sufficiently hard and durable to allow them to be packaged in multidose bottles.

Hygroscopicity¹⁹

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging.

Amount of drug²⁰

The application of technologies used for ODTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving oral films or wafers.

Aqueous solubility²¹

Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process. Such collapse sometimes can be prevented by using various matrix-forming excipients such as mannitol than can induce crystallinity and hence, impart rigidity to the amorphous composite. **Size of tablet²²**

The degree of ease when taking a tablet depends on its size. It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.

Selection of ODT Drug Candidates²³

Several factors must be considered when selecting drug candidates for delivery as ODT dosage forms. In general, an ODT is formulated as a bioequivalent line extension of an existing oral dosage form. Under this circumstance, it is assumed that the absorption of a drug molecule from the ODT occurs in the postgastric GIT segments, similar to the conventional oral dosage form. But this scenario may not always be the case. An ODT may have varying degrees of pregastric absorption and thus, the pharmacokinetic profiles will vary.

Therefore, the ODT will not be bioequivalent to the conventional oral dosage form. For example, ODT formulations of selegiline, apomorphine, and buspirone have significantly different pharmacokinetic profiles compared with the same dose administered in a conventional dosage

form. It is possible that these differences may, in part, be attributed to the drug molecule, formulation, or a combination of both. If significantly higher plasma levels have been observed, pregastric absorption leading to the avoidance of first-pass metabolism may play an important role. This situation may have implications for drug safety and efficacy, which may need to be addressed and assessed in a marketing application for an ODT. For example, safety profiles may be improved for drugs that produce a significant amount of toxic metabolites mediated by firstpass liver metabolism and gastric metabolism and for drugs that have a substantial fraction of absorption in the oral cavity and segments of the pregastric GIT. Drugs having ability to diffuse and partition into the epithelium of the upper GIT ($\log P > 1$, or preferable > 2); and those able to permeate oral mucosal tissue are considered ideal for ODT formulations. Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs. Similarly, patients with Sjögren's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations²⁰. Drugs with a short half-life and frequent dosing, drugs which are very bitter or otherwise unacceptable taste because taste masking cannot be achieved or those which require controlled or sustained release are unsuitable candidates of rapidly dissolving oral dosage forms. Researchers have formulated ODT for various categories of drugs used for therapy in which rapid peak plasma concentration is required to achieve the desired pharmacological response. These include neuroleptics, cardiovascular agents, analgesics, anti-allergic, anti-epileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and drugs used for erectile dysfunction

Salient Features of Fast Dissolving Drug Delivery System²⁴

Ease of administration to patients who refuse to swallow a tablet, such as paediatric and geriatric patients and, psychiatric patients. Convenience of administration and accurate dosing as compared to liquids. No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water. Good mouth feels properly of MDSS helps to change the basic view of medication as "bitter pill", particularly for paediatric patients, rapid dissolution of drug and absorption which may produce rapid, onset of action. Some drugs are absorbed from the mouth pharynx and oesophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased. Ability to provide advantages of liquid medication in the form of solid preparation. Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

Conventional Techniques used for preparation of FDDDS²⁵

Disintegrant Addition Disintegrant addition technique is one popular techniques for formulating Fast-dissolving tablets because of its easy implementation and cost-effectiveness. The basic principle involved in formulating Fast-dissolving tablets by disintegrant addition technique is addition of superdisintegrants in optimum concentration so as to achieve rapid disintegration along with the good mouth feel. Microcrystalline cellulose and low substituted hydroxypropylcellulose were used as disintegrating agents in the range of 8:2 – 9.1 to prepare fast dissolving tablet. Agar powder is used as disintegrant for the development of rapidly disintegration tablets by enhancing the porosity of agar by water treatment. Rapidly disintegrating tablets of bitter drugs oxybutynin & pirenzepine were prepared by using the taste masked granules and h mixture of excipients consisting of crystalline cellulose (Avicel PH 02) and low-substituted hydroxypropy cellulose HPC, LH-11), prepared rapidly disintegrating tablets using microcrystalline cellulose (Avicel PH-M series) that was spherical and had a very small particle size 7-32 μm). Instead of conventional microcrystalline cellulose (PH 102). Tablets prepared using microcrystalline cellulose; PH-M06 and L-HPC in the ratio of 9:1 were very rapidly disintegrating) in saliva. They concluded that Avicel PH-M06 was superior to Avicel PH 102 in terms of the feeling of roughness in the mouth. Fast dissolving table of efavirenz (anti HIV agent) were formulated by using combination of microcrystalline cellulose and sodium starch glycolate as super disintegrant. Gillis et al, prepared a fast-dissolving tablet of galanthaminehydrobromide which comprises of spray dried mixture of lactose monohydrate and microcrystalline cellulose (75:25) as a diluent, a cross linked polymeric disintegrant such as cross povidone and with a direct compression process of preparing such fast-dissolving tablets. Fast-dissolving tablets having analgesic activity was formulated using a combination of superdisintegrants. Rapid oral disintegration tablets were developed by direct compression using co-ground mixture of D-mannitol and crospovidone. CIMA labs patented Orasolv technology by employing the evolution of carbon dioxide or the effervescence as disintegration mechanism in the formulation of fast-dissolving tablets.

The OraSolv technology is an oral dosage form, which combines taste-masked drug ingredients with a quick dissolving effervescent excipient system. Taste masking is achieved through a process of microencapsulation, which coats or entraps the active compound in an immediate release matrix. The effervescent excipient system aids in rapid disintegration of the tablet, permitting swallowing of pharmaceutical ingredients before they come in contact with the taste bud. The OraSolv tablet dissolves quickly without chewing or without water and allows for effective taste masking of a wide variety of active drug ingredients, both prescription and nonprescription.²⁶

Flashtab technology is a patented technology of Prographarm, which employ combination of taste-masked multiparticulate active drug substances, a disintegrating agent, a swelling agent and other excipients to form a multiparticulate tablet that disintegrates rapidly. Rapidly disintegrating multiparticulate tablet was prepared by using taste-masked microcrystals of drugs, crosslinked disintegrating agent and soluble diluent with binding properties.

Freeze Drying²⁷

A process in which water is sublimated from the product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature 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

Moulding²⁸

In this method, molded tablets are prepared by using water soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution. The slow dissolution of the compressed tablet containing even highly water-soluble ingredients is due to the low porosity of the tablets. Inert solid ingredients that volatilize readily (e.g. urea, ammonium carbonate, ammonium bicarbonate, hexamethylenetetramine, camphor etc.) were added to the other tablet ingredients and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates porous structures. Additionally, several solvents (e.g. cyclohexane, benzene) can be also used as pore forming agents,

Spray-Drying²⁹

Spray drying can produce highly porous and fine powders that dissolve rapidly. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and / or alkali material (e.g. I sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium.

Mass-Extrusion³⁰

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or

syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

Direct Compression³¹

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods, directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agent.

Patented Technologies for Fast Dissolving Tablets 10- 14 Zydis Technology Zydis, the best known of the fast-dissolving/disintegrating tablet preparations was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. A Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The Zydis product is made to dissolve on the tongue in 2 to 3 seconds. The Zydis formulation is also self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth.

Durasolv Technology

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of a drug, fillers and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. These can be packed into conventional packaging system like blisters. Durasolv is an appropriate technology for products requiring low amounts of active ingredients.

Orasolv Technology

Orasolv Technology has been developed by CIMA labs. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable and packaged in specially designed pick and place system. Flash Dose Technology Flash dose technology has been patented by Fuisz. Nurofenmeltlet, a new form of ibuprofen as melt-in-mouth tablets, prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consists of self binding shear form matrix termed as "floss". Shear form matrices are prepared by flash heat processing.

Wowtab Technology

Wowtab Technology is patented by Yamanouchi Pharmaceutical Co. WOW means “Without Water “In this process, combination of low mould ability saccharides and high mould ability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldabilitysaccharide and granulated with a high mould ability saccharide and compressed into tablet.

Flashtab Technology

Prographarm laboratories have patented the Flash tabtechnology. Tablets prepared by this system consist of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like coacervation, micro encapsulation, and extrusion spheronisation. All the processing utilized conventional tableting technology. Promising Drugs to be in corporated In Fast Dissolving Tablets¹⁵⁻¹⁷ There are no particular limitations as long as it is a substance which is used as a pharmaceutical active ingredient.

Evaluation of Powder Properties of Tablet³¹

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulation and process variables involved in mixing and all these can affect the characteristics-of blends produced. The various characteristics of blends tested are as given below:

Angle of Repose

The frictional force in a loose powder can be measured by the angle of repose? It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle θ , is in equilibrium with the gravitational force. The angle of repose was determined by the funnel method suggested by Newman.

Angle of repose is determined by the following formula $\tan \theta = h/r$ Therefore $\theta = \tan^{-1} h/r$ Where θ = Angle of repose h = height of the cone r= Radius of the cone base Angle of Repose less than 30° shows the free flowing of the material.

Compressibility index (Carr's index)- Percent compressibility of granules as determined by Carr's compressibility index was calculated by the following formula:

$$Carr's\ index = \frac{TD - BD}{TD} \times 10$$

Table 2: Flow properties as indicated by Carr's index

Percent compressibility	Type of flow
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-25	poor
33-38	Very poor
>40	Extremely poor

Bulk Density

Density is defined as weight per unit volume. Bulk density, p_b , is defined as the mass of the powder divided by the bulk volume and is expressed as gm/ cm

The bulk density of a powder primarily depends on particle size distribution, 'particle shape and the tendency of particles to adhere together. There are two types of bulk density. The particles are pack in such a way so as to leave large gaps between their surfaces 'resulting up in light powder of low bulk density. Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. A standard procedure used for obtaining bulk density or its reciprocal bulkiness is given, below A sample of about 50 cm³ (blend) is carefully introduced in a 100ml graduated cylinder.

(i) The cylinder is dropped onto a hard wood surface three times from a height of 1 inch at two second interval.

The bulk density is then obtained by dividing the weight of sample in gms by final volume in cm

(ii) $P_b = M / V_p$ Where p_b = Bulk Density " M = Weight of sample in gm V = Final volume of blend in cm³

(iii) Bulkiness Specific bulk volume or reciprocal of bulk density is called bulkiness or bulk. Bulkiness increases with a decrease in particle size. In mixture of material of different sizes, however the smaller particle shifts between the larger particles and tends to reduce the bulkiness.

The bulkiness can be calculated by the following formula Bulkiness= $1 / p_b$ where, p_b = Bulk Density. Loose bulk density It is defined as the ratio of weight of blend in gms to the loose bulk volume (untapped volume) in cm³ Loose bulk density is given by Loose bulk density $p_u = \text{Weight in gms} / V_b$ Where V_b = Bulk volume (untapped volume)

(iv) Void Volume

The volume of the spaces is known as the void volume "v" and is given by the formula $V = V_b - V_p$ Where V_b = Bulk volume (volume _ before tapping) V = True volume (volume after tapping)

(v) Porosity The porosity ϵ of powder is defined as the ratio of void volume to the bulk volume of the packaging. The porosity of the powder is given by $\epsilon = \frac{V_b - V_p}{V_p} = 1 - \frac{V_p}{V_b}$ Porosity is frequently expressed in percentage and is given as $\% \epsilon = (1 - \frac{V_p}{V_b}) \times 100$ The porosity of powder indicates the types of packaging a powder undergoes when subject to vibrations, when stored, or in tablet machine when passed through hopper or feed frame.

(vi) Percent Compressibility It is an important measure obtained from bulk density and is defined as, $C = \frac{P_b - P_u}{P_b} \times 100$ If the bed of particles is more compressible the blend will be less flowable and flowing material.

Hausner's Ratio (HR) - It is the ratio of tapped density to the bulk density. It is given by-

$$HR = TD / BD$$

TD- Tapped density

BD- Bulk density

Table 3. Flow properties as indicated by Hausner's ratio

Hausner's Ratio	Flow of powder
1-1.2	Free Flow
1.2-1.6	Cohesive Flow

(i) The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

(ii) Size and Shape The size and shape of the tablet can be dimensionally described, monitored and controlled.

(iii) Tablet thickness Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

(iv) Uniformity of weight I.P .procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity

5. Porosity The porosity ϵ of powder is defined as the ratio of void volume to the bulk volume of the packaging. The porosity of the powder is given by $\epsilon = \frac{V_b - V_p}{V_p} = 1 - \frac{V_p}{V_b}$ Porosity is frequently expressed in percentage and is given as $\% \epsilon = (1 - \frac{V_p}{V_b}) \times 100$ The porosity of powder indicates the types of packaging a powder undergoes when subject to vibrations, when

stored, or in tablet machine when passed through hopper or feed frame. 6. Percent Compressibility It is an important measure obtained from bulk density and is defined as, $C = \frac{Pb - Pu}{Pb} \times 100$ If the bed of particles is more compressible the blend will be less flowable and flowing materials.

Evaluation Test for Fast Dissolving³⁰

Tablets from all the formulation were subjected to following quality control test The general appearance of a tablet, its visual identity and over all “elegance” are essential for consumer acceptance. Include in are tablet’s size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

Size and Shape

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

Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

Uniformity of weight I.P.

Procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

Disintegration test-

By doing Disintegration test we came to know whether dosage form disintegrate within a particular time when it is placed in a suitable liquid medium under the prescribed experimental conditions. The end point of Disintegration test comes at that state at which no residue of the tablet remains on the screen of the testing apparatus or, if a residue remains, it consists of fragments of insoluble coating of the tablets. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets; not less than 16 of the total of 18 tablets tested should disintegrate.

Method: First of all we have to place one tablet in each of the 6 tubes of the basket. Then we add a disc to each tube and operated the apparatus, using water maintained at $37 \pm 2^\circ\text{C}$ at the concentration liquid.

***In- vitro* dissolution studies-**

This test is performed to measure the duration of time required by a dosage form to reach to the systemic circulation in the body. This test is carried out under precise condition

Method: First of all we have to take 1000 ml of dissolution media which in the dissolution apparatus. After that we have to warm the dissolution medium between 36.5°C and 37.5°C temperature. Then allow put tablet in the dissolution apparatus before rotation of paddle. In this process we have to use a suitable device which help to keep tablet in the base of the pot otherwise the dosage form will float to the surface. We should keep in mind that air bubbles are barred from the surface of the dosage form. The in-vitro dissolution study should be carried out immediately at the 75 rpm. Within the specified time interval, or as the time assured, withdrawn a sample from the dissolution basket, the withdrawal sample should not be less than 10ml except in the case of single sampling, after withdrawal of sample we have to add equal volume of dissolution media which is equal to volume of sample taken out From the basket of dissolution apparatus. The in-vitro dissolution test should be carried out as specified in Table 5.14. Repeat the whole procedure five times. For each of the dosage form dissolution test is carried out, calculated the percentage of the active pharmaceutical ingredient dissolved in the solution by using a suitable spectroscopy method.

Table: 4 Acceptance Table for Dissolution

Period	No tested	Approval criteria
A1	6	Every element should not be less than $E^* + 5\%$
A2	6	Average of 12 elements (A1 +A2) must be equivalent to Or greater than E, and no elements should be less than $E - 15\%$.
A3	12	Average of 24 element (A1+A2+A3) should be equal to or greater than E, not more than 2 units should be less

*E = Total of dissolved active ingredient precise in individual monograph, articulated as percentage of assured quantity.

Recognized criteria for Dissolution: In case results do not match with the criteria area given in acceptance Table for Dissolution (table 5.14) continue the test with extra dosage forms (tablets or capsules) through stages S2 and S3 unless the result conformed.

CONCLUSION

Fast Dissolving tablets are considered to be contemporary dosage forms. These dosage forms and their route of administration results in better efficacy, rapid onset of action, enhanced bioavailability, and improved patient compliance. There are many marketed product of this category which have been introduced in the recent past. Some of the recent product in the Indian and global market are listed in table for ready reference. The primary attractive factor of MDT is quick disintegration in oral cavity without the aid of water, along with sufficient mechanical strength. This feature makes this formulation a highly recommendable choice for geriatric and

pediatric patients. FDT in the near future is expected to grow at a great and rapid pace, owing to the advancement in the scientific research and discovery of new excipients, resulting in a future-ready, combative arena of pharmaceutical drug delivery systems. Orally disintegrating tablets have better patient acceptance and compliance and may offer improved biopharmaceutical properties, improved efficacy, and better safety compared with conventional oral dosage forms. Prescription ODT products initially were developed to overcome the difficulty in swallowing conventional tablets among pediatric, geriatric, and psychiatric patients with dysphagia. Today, ODTs are more widely available as OTC products for the treatment of allergies, cold, and flu symptoms.

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