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Oral Fast Dissolving Tablet: Best Approach for Faster Therapeutic Effect

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ABSTRACT: - The preferred medicine delivery technique is still oral administration. Fast-acting pills have becoming more popular. Because they dissolve in the mouth without additional water, enabling convenient administration of active medicinal substances, they have gained considerable recognition as a novel drug delivery mechanism for the treatment of a variety of disorders. FDTs eliminate the disadvantages of conventional dosage forms, including dysphagia (difficulty swallowing) in paediatric and geriatric patients. The advantages of both conventional tablet and liquid dosage forms are offered by FDT formulations. For the production of FDTs, a variety of technologies have been developed, including spray drying, the cotton candy process, sublimation, melt granulation, direct compression freezes drying/lyophilization, phase transition process, mass extrusion, and others. The main advantages, desirable traits, disintegration procedure, and development methods for fast-dissolving tablets are briefly discussed in this article.

Keywords: oral fast-dissolving tablet, melt granulation, disintegration, sublimation, lyophilization.

INTRODUCTION: -

Up to 50–60% of all dosage forms are administered by oral methods, which are well accepted. Solid dose forms are preferred because they are inexpensive, simple to administer, accurate, allow for self-medication, reduce pain, and, most significantly, increase patient compliance. The most common solid dosage forms are tablets and capsules; nevertheless, for certain individuals, these dosage forms are difficult to swallow. The size, appearance, and flavour of tablets are frequently mentioned as reasons why taking pills is difficult. Water consumption is crucial to successfully ingesting oral dose forms. People frequently find it difficult to take conventional dosage forms like tablets when water is not available, when they have motion sickness (kinetosis), or when they suddenly start coughing due to the common cold, an allergic reaction, or bronchitis.

[1] The largest need for simple-to-swallow dosage forms is among the elderly, young patients, patients who are travelling, and patients who might not have easy access to water [2].

Difficulty in swallowing is a common occurrence in elderly patients because of anxiety about choking, hand tremors, and dysphasia, in young people because of underdeveloped neurological and muscular systems, and in schizophrenia patients because of poor patient compliance. A third of the population, mostly children and the elderly, has swallowing problems, which causes them to not take their oral tablet medication as prescribed, decreasing the effectiveness of their treatment as a whole. These factors have led to a lot of interest in tablets that can quickly dissolve or disintegrate in the oral cavity [3].

Pharmaceutical technologists have created an innovative oral dosage form known as orally disintegrating (dispersible) tablets (ODTs), fast disintegrating (dissolving) tablets (FDTs), mouth melting tablets (MMTs), or mouth dissolving tablets (MDTs), which dissolve quickly in saliva without the need for water, typically within a few seconds [4].

When compared to conventional dose forms, medication solubility and absorption, as well as the time it takes for a therapeutic effect to start and its bioavailability, may be much higher. The medication is released by oral fast-dissolving tablets or orodispersible tablets in the mouth for local oromucosal tissue as well as pre-gastric (oral cavity, pharynx, and oesophagus), gastric (stomach), and post-gastric (small and large intestine) segments of the gastrointestinal tract to absorb (GIT) [2]. Additionally, less medication than in conventional tablets is vulnerable to first-pass metabolism [5].

These dosage forms have been approved as Orally Disintegrating Tablets by the United States Pharmacopoeia (USP) (ODTs). Orodispersible tablets are those that quickly dissolve in the mouth before being swallowed, as defined by the European Pharmacopoeia [2].

A fast-dissolving tablet (FDT) is a solid dosage form containing a medication or active ingredient that dissolves quickly, typically in a matter of seconds, when placed on the tongue, according to the United States Food and Drug Administration (USFDA) [3].

In order to provide paediatric and geriatric patients with an alternative to traditional dose forms, fast-dissolving medication delivery devices were initially created in the late 1970s. These pills are made to break down or dissolve quickly in the saliva, usually in less than 60 seconds [3].

More than half of the patient population prefers FDTs over other dose forms, according to recent market research. Mouth-dissolving tablets are made primarily using two techniques: first, super disintegrants such as crospovidone, sodium starch glycolate, and croscarmellose sodium are used. Another technique involves freeze-drying and vacuum-drying the tablets to maximise their pore structure [5].

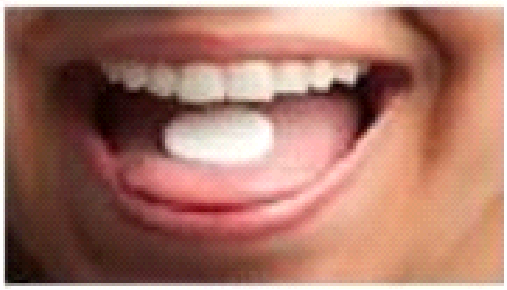

Fig. 1: Administration of Oral FDT [6]

Criteria for a Quickly Dissolving Drug Delivery System [6]:

- The pills should dissolve or disintegrate in the mouth in a matter of seconds without the need for water.
- be tolerant of flavour masking.
- be lightweight and unafraid of breaking.
- Feel good in the mouth.
- After oral administration, leave little to no aftertaste.
- Low sensitivity to environmental factors like humidity and temperature.

Advantages of FDTs [2,7,8]: -

- Can be easily administered to patients who are unable to swallow, such as the elderly, those who have had strokes, and those who are bedridden, as well as those who shouldn't swallow, such as those with renal failure, and those who refuse to swallow, such as children, geriatric and psychiatric patients, or patients who are mentally disabled.
- Patient compliance for patients who are unable to leave their beds, as well as for busy persons on the go.
- As saliva descends into the stomach, some medications are absorbed from the mouth, pharynx, and oesophagus, decreasing first-pass metabolism.
- Faster medication absorption through the mouth, pharynx, and oesophagus, which may result in a quick beginning of the effect.
- Pregastric absorption can enhance the bioavailability, lower dose requirements, and enhance clinical performance by minimising side effects.
- Due to the improved taste of bitter medications, good mouth feel property helps to transform the basic perception of medication as a "bitter pill,", particularly for young patients.
- There is no need for water when taking the tablet.
- They can disguise tastes and offer a pleasant mouthfeel.
- After administration, there is no leftover material in the mouth.
- The production of tablets can be done for a reasonable price with traditional processing and packaging machinery.
- Permit heavy drug loading.
- The medicine has a quick rate of dissolution and absorption, providing an immediate commencement of effect.
- When compared to liquid medications, it is easier to administer and transport.
- FDTs are appropriate for controlled and sustained release actives.

Disadvantage of FDT [2]

- Because of its hygroscopic nature, FDT must be stored in a dry environment and occasionally has a mouthfeel.
- For the correct stabilisation and safety of a stable product, particular packaging is needed.
- Dose homogeneity is a difficult technical problem.

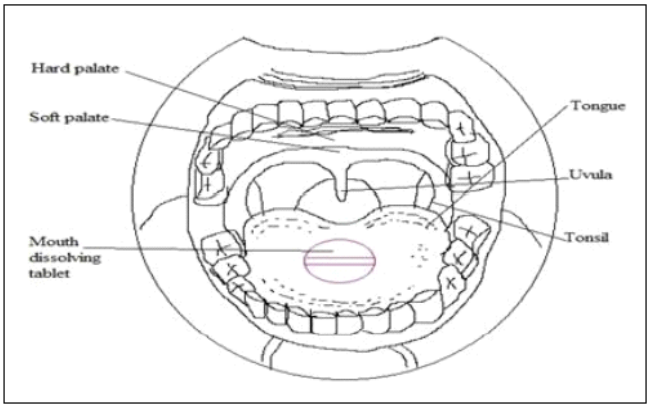

Fig. 2: Administration of Oral Fast Dissolving Tablets [9]

- **Potential Drug Candidates for Oral Fast Dissolving Tablets [9]:**

- **Non-steroidal Anti-Inflammatory Drugs**: Ketoprofen, Piroxicam, Paracetamol, Rofecoxib, Nimesulide, Ibuprofen.
- **Anti-ulcer Drugs**: Famotidine, Lansoprazole.
- **Antidepressants Drugs**: Mitraxepine, Fluoxetine.
- **Antiparkinsonian Drugs:** Selegiline.
- **Antimigrane Drugs**: Sumatriptan, Rizatriptan benzoate, Zolmitriptan.
- **Anti-histaminic Drugs**: Loratadine, Diphenhydramine, Meclizine.
- **Antiemetic Drugs**: Ramosetoron HCl, Ondansetron, Baclofen.

- **Mouth Dissolving Phenomenon**: Superdisintegrants pay considerably more attention while creating mouth-dispersing tablets. By causing swelling and water absorption in the pill, they offer quick disintegration. The swelling process of the superdisintegrants wets the carrier's surface, which enhances tablet disintegration and causes increased dissolution to occur [9]. The swelling capacity in the dissolution media and the density of the generated matrix both affect how well super disintegrants operate. A greater degree of disintegration results from the matrix's higher swelling capacity and density [9].

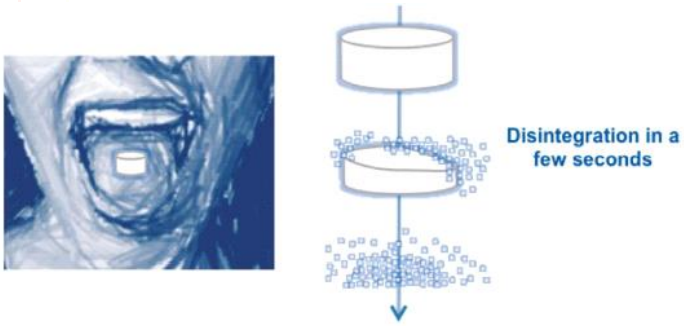

Fig. 3: Representing the administration of Oral Fast Dissolving tablets and the simulation of rapid disintegration in the oral cavity[10]

Ideal Properties of Fast Dissolving tablets [10]: -

Fast Dissolving tablets,

1. Does not require water or substitute liquid to swallow.
2. Rapidly dissolves and disintegrates in saliva within a matter of seconds.
3. Have a pleasant taste and mouth feel.
4. Easily transportable and mobile.
5. Leave no/negligible residue in the mouth after administration.
6. Be able to manufacture in a simple conventional way with low cost.
7. Withstand environmental conditions like humidity, temperature etc.

Difficulties with existing oral dosage form: - [11]

- The patient can have tremors, which makes it challenging for them to swallow powdered or liquid medications. Gastrointestinal ulcers may result from physical obstructions and adhesion to the oesophagus in dysphasia.
- Solid dose forms, such as tablets and capsules, can hinder the development of the neurological and muscular systems in young people, which can lead to problems.
- Because liquid medications like suspensions and emulsions are placed in multi-dose containers, content homogeneity in each dose might not be maintained.
- Sublingual and buccal formulations may irritate the oral mucosa.

Challenges in the formulation of FDTs: - [2,12,13]

- **Mechanical strength and disintegration time:** Fast-dissolving tablets are designed to have a disintegration time that is typically under a minute. Maintaining adequate mechanical strength while doing so is a major difficulty. There is a high likelihood that a fragile FDT will shatter when being packed, transported, or handled by a patient. A solid working relationship between these two factors is always required because it is only normal for the disintegration time to increase with increasing mechanical strength.
- **Taste masking**: - The taste of many medications is harsh. Patient compliance and acceptance of the dosage form will be significantly impacted if a bitter medicine tablet dissolves or disintegrates in the mouth. Therefore, it is essential to effectively disguise the flavour of bitter medications so that the mouth is not affected by their taste.
- **Mouth feels**: - Tablets that dissolve quickly shouldn't break up into bigger pieces inside the mouth. After the FDT disintegrates, very minute particles should be created. After being administered orally, FDT shouldn't leave any aftertaste in the mouth. Additionally, the tongue feel is improved by the inclusion of flavours like orange, raspberry, and strawberry as well as cooling agents like menthol.
- **Aqueous solubility:** Because they produce eutectic mixtures, which lower the freezing point and lead to the production of a glassy solid that may collapse upon drying due to the loss of supporting structure during the sublimation process, water-soluble pharmaceuticals present a variety of formulations issues. Using different matrix-forming excipients like mannitol, which can induce crystallinity and hence contribute rigidity to the amorphous composite, it is occasionally possible to prevent such collapse.

- **Size of tablets:** The size of the tablet affects how easy it is to take. 7-8 mm tablets are reportedly the simplest to swallow, while tablets larger than 8 mm were said to be the easiest to handle. Consequently, it is challenging to create tablets that are both easy to grasp and easy to swallow.
- **Amount of drug: -** The amount of medication that can be included in each unit dose restricts the use of technologies used for fast-dissolving tablets. Generally speaking, the fast-dissolving tablet weight should not be greater than 500 mg, according to USP.
- **Sensitivity to environmental conditions**: Many FDT dosage forms are hygroscopic and unable to keep their physical integrity at standard temperatures and humidity levels. As a result, they require humidity protection, which necessitates particular product packaging. The sensitivity of FDTs to environmental factors like humidity and temperature needs to be minimal.
- **Cost**: - An FDT should use technology that is reasonable in terms of the cost of the finished good.
- **Good packaging design**: - The package design should be taken into account early on in the development stages to safeguard tablets from moisture and other environmental risks.

Approaches For Preparation of FDTs: -

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Good packaging design: - The package design should be taken into account early on in the development stages to safeguard tablets from moisture and other environmental risks.

❖ **Patented Technologies for Fast Dissolving Tablets [14]:**

- Zydis Technology
- Durasolv Technology
- Orasolv Technology
- Flash Dose Technology
- Wow tab Technology
- Flash tab Technology
- Melt Ease technology
- Quick Dis technology
- OraQuick
- NanoCrystal
- AdvaTab technology
- Frosta technology
- AdvaTab technology
- Ceform technology
- Pharmaburst technology
- Lyo(Pharmalyoc)
- Dispersible tablet technology
- Orodis technology

- **Zydis Technology**: The Zydis formulation is a special freeze-dried tablet in which the medicine is physically confined or dissolved within the matrix of a quickly evaporating carrier substance. The freeze-dried structure instantly disintegrates when zydis units are placed in the mouth; water is not necessary to facilitate swallowing. The zydis matrix is made up of a variety of materials with various goals in mind. Polymers such as gelatin, dextran, or alginates are included to add strength and resilience during handling. These take the shape of a shiny, amorphous structure that provides strength. Saccharides like sorbitol or mannitol are added to provide crystallinity, beauty, and hardness. While different gums are employed to prevent the sedimentation of dispersed medication particles in the manufacturing process, water is used to ensure the formation of porous units to accomplish quick disintegration. Glycine and other collapse protectors stop zydis units from contracting during the freeze-drying process or during long-term storage. Products from Zydis are packaged in blister packets to shield the formulation from environmental moisture [14].
- **Durasolv Technology**: The unique technique of CIMA labs is called Durasolv. This method creates tablets with a medicine, a filler, and a lubricant. The technology used to make tablets is typical, and they are well-rigid. These can be put into a standard packaging method, such as blisters. The Durasolv technology is suitable for products that only need small amounts of active chemicals [14].
- **Orasolv Technology:** Orasolv Technology was created in CIMA labs. This technique masks the taste of the active medication. An effervescent disintegrating agent is also present. To reduce the amount of time needed for oral dissolving, tablets are manufactured using the direct compression technique at low compression force. The tablets are produced using standard blenders and tablet presses. The manufactured tablets are pliable and squishy [14].
- **Flash Dose Technology**: Fuisz has patented flash dosage technology. The first commercial product released by Biovail Corporation is the Nurofen meltlet, a novel formulation of ibuprofen in the form of melt-in-mouth tablets created using flash dosage technology. Flash dosage tablets are made of "floss," a self-binding shear form matrix. Flash heat processing is used to create shear form matrices [14].
- **Wow tab Technology**: Yamanouchi Pharmaceutical Co. has a patent on the Wow tab technology. WOW is short for "Without Water." To create a rapidly melting, robust tablet, a combination of low mouldability and high mouldability saccharides is used in this procedure. The active component is blended with a low mouldability saccharide (such as lactose, glucose, and mannitol) and granulated with a high mouldability saccharide (such as maltose, and oligosaccharides), then compacted into table form. [14]
- **Flash tab Technology**: - The Flash tab technology has a patent from Prographarm laboratories. The active ingredient in the tablet created using this technology is in the form of tiny crystals. The traditional methods of coacervation, microencapsulation, and extrusion spheronization can be used to create drug micro granules. All processing was done using standard tabletting technology [14].
- **Melt Ease technology: -** Nutrition formulators are the ones who created this technology. Tablet dissolution is possible in 5 seconds (average 400 mg tablet). The best approach currently available to

assure compliance is provided by this technology. For many nutritional supplements, sales can be raised in two significant markets—children and the elderly—at a relatively low development cost [15].

- **Quick Dis technology**: - QuickDis, a trademarked intraoral fast-dissolving medication delivery technology, was developed by Lavipharm laboratories. It is a quick-dissolving, thin, and flexible film. The tongue's top or bottom is where the film is placed. Unit-dose pouches and multiple-dose blister packages are just two of the packaging options for the Quick-Dis medication delivery system. 2 mm Quick-Dis film often disintegrates in only 5–10 seconds. For Quick Dis film with a thickness of 2 mm, the dissolving time—which is defined as the period of time at which at least 80% of the tested film dissolves in aqueous media—is around 30 s. A Quick-Dis medication delivery system's unique active ingredient release profile includes 50% release within 30 s and 95% release within 1 min [15].
- **OraQuick (KV Pharmaceuticals)**: - The MicroMask microsphere technology, according to KV Pharmaceutical, has a better mouth feel than other taste-masking solutions. Since there is no need for a solvent in the flavour masking process, production is quicker and more productive. Heat-sensitive medications can be processed with OraQuick. Additionally, according to KV Pharmaceuticals, the matrix that encases the medication powder in microencapsulated particles is more malleable, allowing for amazing mechanical strength without compromising taste masking [15].
- **NanoCrystal (Elan)**: - Elan's unique NanoCrystal technology for FDT can facilitate formulation, enhance compound activity, and improve final product attributes. The surface area will rise as the particle size is reduced, which accelerates the rate of disintegration. The advantages of this technology include remarkable strength, enabling the use of conventional packaging tools and forms (such as bottles or blisters), and pharmacokinetic advantages of orally delivered nanoparticles in the form of fast disintegrating tablet matrix (up to 200 mg of active pharmaceutical ingredient per unit) [15].
- **AdvaTab technology**: - Eurand Pharmaceuticals is the company behind the AdvaTab technology. It manufactures ODT tablets using a unique tablet formulation created and patented by Kyowa Hakko Kogyo (Tokyo, Japan), in which the lubricant is sprayed onto each tablet as it is being made. The internal lubrication technique used to create conventional tablets disperses lubricant both inside and on the tablet's outside surface. The manufacturing process for AdvaTab uses 10–30 times less hydrophobic lubricant, and the strength of these tablets may be 30–40% higher than that of regular tablets. This technique creates tablets that are incredibly robust and hard. When the tablet comes into touch with saliva, its hardness does not prevent liquid from entering [15].
- **Frosta technology: -** Strong tablets with high porosity are created by compressing highly plastic granules at low pressure. The porous and plastic substance, the water penetration enhancer, and the binder are the three different sorts of components that make up the highly plastic granules. A water penetration enhancer and a porous plastic material can be combined in specific ratios to create tablets. The possibility of bonding by compression is increased by the close contact between porous and plastic materials. The binder holds the porous substance and water penetration enhancer during granulation. The porous structure of the porous materials shouldn't be destroyed if the binder is in a liquid or semi-solid form. This can be accomplished using aqueous binder solutions with very low water activity [15].

- **Ceform technology: -** Dry powder comprising either pure drug material or a mixture of drug material and excipients is inserted into a precisely built, quickly spinning machine during the manufacture of ceform microspheres. The rotating machine head's centrifugal force propels the dry drug mixture through tiny, heated holes at a high rate of speed. After that, the microspheres are mixed and made into tablets via compression. When both the drug and the excipient are processed simultaneously, a certain microenvironment is created. This milieu can be used to incorporate components into the microsphere, which can change the properties of the drug substance [15].
- **Pharmaburst technology: -** Utilizing off-the-shelf coprocessed excipients, Pharmaburst technology (SPI Pharma, New Castle, Delaware) produces an ODT that dissolves in 30–40 seconds, depending on the active component type and loading (up to 700 mg). The active pharmacological ingredient in a tablet determines how much pharmaburst is needed in a formulation. Initial experiments must be conducted on a formulation using pharmaburst concentrations ranging from 50 to 80%, depending on the desired mouth feel and disintegration time. Dry mixtures containing a medicine, flavour, and lubricants are compacted into tablets on a tablet press using standard tooling throughout the manufacturing process [15].
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- **Lyo (Pharmalyoc)**: - In this method, oil in water emulsion is prepared and can be immediately applied to blister cavities before being freeze-dried. By adding inert filler to boost viscosity, non-homogeneity during freeze-drying is prevented. A large filler content decreases the porosity of tablets, which lowers the rate of disintegration [15].
- **Dispersible tablet technology: -** In this method, oil in water emulsion is prepared and can be immediately applied to blister cavities before being freeze-dried. By adding inert filler to boost viscosity, non-homogeneity during freeze-drying is prevented. A large filler content decreases the porosity of tablets, which lowers the rate of disintegration [15].
- **Orodis technology: -** Orodis technology is compacted and disintegrates quickly (15 to 30 s). This technology creates incredibly robust, manageable tablets. Push-through blisters can be used to package tablets. This technology's materials are compliant with USP and EP requirements [15].
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Conventional technology for Preparing FDTs [2]:

- Spray drying.
- Sublimation.
- Freeze-drying or lyophilization.
- Tablet Molding.
- Mass extrusion.
- Direct compression.
- Phase transition.
- Nanonization.
- Cotton candy process.

Basic pharmaceutical processes to manufacture FDTs are explained as follows:

- **Spray drying: -**

The use of spray drying techniques is widespread in biochemical and pharmaceutical processes. Spray drying creates highly porous and fine powders and offers a quick and cost-effective method of eliminating solvents. In the pharmaceutical sector, spray dryers are always employed to create very porous powders. Drying is mostly used to produce dry particles with desired characteristics. In a spray dryer, the formulation is dried by spraying. ODTs made with this technique dissolve after around 20 seconds.

The formulations consist of mannitol as a bulking agent, croscarmellose sodium or sodium starch glycolate as a dissolving agent, and hydrolyzed and non-hydrolyzed gelatins as supporting agents. To enhance disintegration and dissolving behaviour, a material that is either alkaline (such as sodium bicarbonate) or acidic (such as citric acid) is utilised. When submerged in an aqueous media, tablets made by compressing spray-dried powder displayed a 20-second disintegration time [16].

- **Sublimation: -**

Due to the reduced porosity of the tablets, which prevents water from penetrating into the matrix and causing rapid breakdown, compressed tablets containing highly water-soluble components may exhibit sluggish dissolution behaviour. Conventional methods compress volatile substances into tablets, which can then be sublimated to remove them, creating structures that are incredibly porous. Ammonium carbonate, urea, ammonium bicarbonate, camphor, and hexa methylene tetramine are among the volatile substances that can be employed. In a few instances, the volatile components included thymol, menthol, camphor, an organic acid like adipic acid, and fatty acids including arachidic acid, myristic acid, capric acid, and palmitic acid. The sublimation temperature varied from 400C to 600C. It was discovered that the disintegration period in the oral cavity was roughly 25 s [17].

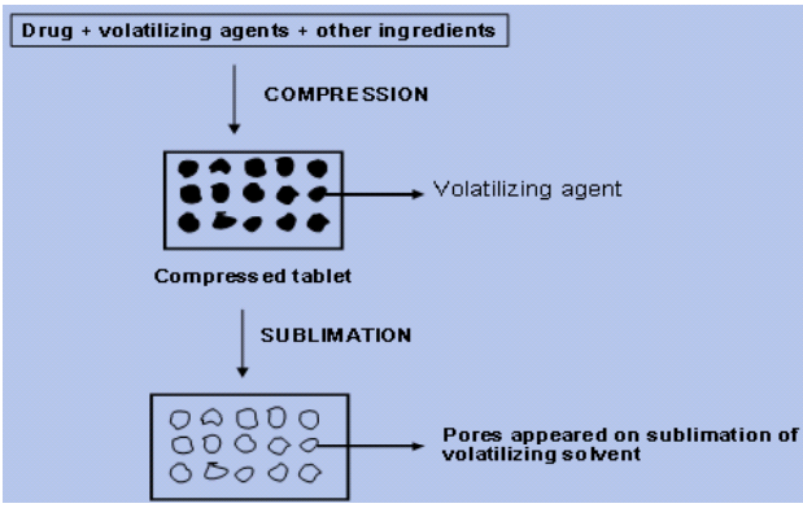

Fig 4: Diagrammatic representation of sublimation technique [18]

- **Freeze drying or lyophilization: -**

Compressed tablets that contain highly water-soluble components may display sluggish dissolving behaviour because of the reduced porosity of the tablets, which restricts water absorption into the matrix. Volatile chemicals are compacted into tablets using conventional methods. By sublimating these volatile chemicals, extremely porous structures can be created. Urea, ammonium bicarbonate, camphor, and hexa methylene tetramine are among the volatile compounds that can be used. The volatile compounds used infrequently included thymol, menthol, camphor, adipic acid, myristic acid, capric acid, and palmitic acid. The sublimation temperature ranged from 400°C to 600°C. The oral cavity's disintegration time was found to be approximately 25 s.

- **Tablet Molding: -**

To make moulded tablets, ingredients that dissolve in water are employed. The powder mixture is sprinkled with a solvent (usually water or ethanol). The mixture is formed into tablets under pressure. Less pressure than what is generally used to compress tablets should be applied. Another name for this method is compression moulding. Air drying can get rid of the solvent. Low pressure causes a highly porous structure to form, which enhances the dissolution. The powder mixture needs to be put through a very fine screen in order to speed up the rate of dissolving. Recently, the moulded forms have also been created by either evaporating the solvent from a drug solution or suspension at room pressure or by melting a matrix in which the drug is dissolved or distributed (novacuum lyophilization). Due to the extremely water-soluble sugar components of moulded tablets, they dissolve more quickly and have a better flavour. However, the mechanical strength of moulded tablets is typically low. The chance of the moulded tablets breaking when handling pills and opening blister pockets is very high. When compounds that increase, hardness are introduced to the formulation, disintegration rates are observed to be reduced. The mechanical strength and effective disintegration of the tablets can be increased by using non-standard equipment and multistep processes [20].

- **Mass extrusion: -**

The water-soluble polyethylene glycol and methanol solvent mixture is used in the mass extrusion method to soften the active blend. To create a cylinder of the product, softened mass is ejected by an extruder or syringe. The product is then sliced into even segments with a hot blade to create tablets [20].

- **Direct compression: -**

Given that conventional tablet manufacturing and packaging equipment can be used to create them, as well as the availability of tabletting excipients with improved flow, compressibility, and disintegration properties, particularly tablet disintegrants, effervescent agents, and sugar-based excipients, direct compression represents the simplest and most cost-effective tablet manufacturing technique. Superdisintegrants, when added to many FDTs based on direct compression, primarily affect the rate of disintegration and subsequently the dissolution. Other formulation elements like effervescent agents and water-soluble excipients speed up the disintegration process even further. The patented Orasolv technology (OT), which is frequently utilised in the development of over-the-counter medicines, is based on effervescent agents, the evolution of CO2 as a disintegration mechanism. The substance is slightly effervescent and has microparticles in it. The effervescent component is activated by saliva, leading to the tablet's disintegration. excipients made with sugar This is an additional method for producing FDTs using direct compression. In particular, bulking agents with high water solubility and sweetness, such as dextrose, fructose, isomalt, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose, and xylitol, are used as excipients in sugar-based products to mask the taste and create a pleasant mouthfeel [21].

- **Phase transition: -**

A unique technique that uses the sugar alcohol phase transition to create FDTs that are sufficiently hard. By compressing a powder containing two sugar alcohols with contrasting melting points and then heating it to a temperature in the middle of their melting points, tablets were created using this method. Due to poor compatibility, the tablets don't have enough hardness before heating. Due to the phase change of lower melting point sugar alcohol, which increased interparticle linkages or the bonding surface area in tablets, the hardness of the tablet rose after heating [14].

- **Nanonization: -**

Through the use of a patented wet-milling procedure, a drug's particle size is reduced to nanosize using the recently created Nanomelt technology. The drug's nanocrystals are protected from agglomeration by surface adsorption on certain stabilisers, which are then added to FDTs. This method is especially useful for medications that are poorly soluble in water.

- **Cotton candy process**: -

This method gets its name from the floss-like crystal structures it creates using a special spinning mechanism, which resembles cotton candy. By simultaneously spinning and flash-melting polysaccharides or saccharides, cotton candy technique 10 creates a matrix of these substances. For better flow and compressibility, the matrix created is partially recrystallized. This candy floss matrix is then compacted into FDTs after being processed and combined with the active components and excipients [14].

- **Medications that meet the following criteria are likely to be appropriate for use in FDTs [22]:**
  - If administered orally, medications may penetrate the upper GIT epithelium (log P > 2).
  - Medicines with brief half-lives that must be taken often.

- The FDTs' first-pass metabolism resulted in the production of hazardous by-products. Pharmaceuticals with controlled and sustained release cannot be used in multi-drug safe medications.
- Speedy drug breakdown and absorption will allow for a rapid start to action.
- Strong enough to withstand the strain of assembly and subsequent maintenance. It is therefore both adaptable and susceptible to current packaging and handling techniques and allows for a high drug loading while being exposed to low-sensitivity environmental conditions, such as temperature and humidity.

Excipients Commonly Used for FDTs Preparation: - [23]

The following excipients are typically found in FDT: at least one lubricant, diluent, swelling agent, permeabilizing agent, sweetener, and flavour.

Table 1: - Name and weight percentage of different excipients

Types of Excipients	Examples	Percentage Used
Superdisintegrants	Croscarmellose sodium, crospovidone, sodium starch glycolate, microcrystalline cellulose, carboxy methyl cellulose, modified corn starch, polacrilin potassium etc.	1 to 15%
Diluents /Bulking agents / Filler	Dextrose, Fructose, Maltose, Mannitol, Sorbitol, Starch hydrolysate, Polydextrose, Xylitol, Lactitol & Directly compressible lactose, Magnesium carbonate, calcium sulphate, magnesium trisilicate etc.	10 to 85%
Binder	Polyvinylpyrrolidone, polyvinyl alcohol, hydroxy propyl methylcellulose etc.	5 to 10%
Antistatic Agent	Sodium laury lsulfate, sodium dodecyl sulfate, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene stearates etc.	0 to 10%
Lubricant	Stearic acid & Magnesium stearate.	1 to 5%
Flavouring agent	Peppermint flavor, Cooling flavor, aromatic flavor oil, vanilla, citrus oils & fruit essences.	-
Sweeteners and sugar-based excipients	Dextrose, Sugar, Fructose, Aspartame, Sodium saccharine, Sucralose and sugar alcohols.	-

Excipients play a significant part in the formulation and design of oral fast-dissolving tablets. Excipients in oral disintegrating pills balance the characteristics of the activities. To avoid interactions and activity inhibition, a complete understanding of the chemistry and mechanism of these excipients is required. The formulator must take into account the cost factor. When excipients are included in a formulation, they give the product the required organoleptic qualities and increased efficacy. Excipients can be utilised for a variety of purposes [10].

- **Superdisintegrants**: - Superdisintegrants are chemicals that, in comparison to disintegrants, aid in quicker disintegration at low concentrations. In relation to the total weight of the solid dosage unit, they are utilised in a weight range of 1 to 10%. Superdisintegrant is used as an excipient in the formulation of fast-dissolving tablets, and as such, it must meet certain requirements in addition to its swelling property, which are listed in the section below [6].

❖ **Properties of a superdisintegrant: -**

Poor gel formation, good hydration, good moulding and flow properties, no drug complexation, compatibility with other excipients, no toxicity, and inertness are all desirable characteristics.

The swelling mechanism is how these substances work. Due to swelling, either an increase in swelling pressure in the tablet's outer direction that causes the tablet to burst or an increase in water absorption that increases the volume of the granules that facilitates disintegration. Super disintegrant is in higher demand due to recent advancements in drug delivery systems. As a result, we must create a superdisintegrant that is more effective at disintegrating materials at low concentrations. Superdisintegrants affect the rate at which a tablet disintegrates, as is well known, but at high concentrations, they also affect the tablet's hardness, friability, and mouth feel. Consequently, we must take into account a number of factors before choosing a superdisintegrant for the formulation. [15].

❖ **Selection criteria for superdisintegrants [6]: -**

• Able to disintegrate quickly.

• Excellent Flow Property.

• Compatible

• The particles should be small because larger ones can leave a gritty taste in the mouth.

Any solid tablet or capsule formulation must take into account the proper superdisintegrant choice and its consistent functioning. The various ways they work to break down tablets into small particles in an aqueous environment include swelling, wicking, deformation, heat of wetting, gas release, enzymatic action, and combination action [6].

❖ **Mechanisms of Superdisintegrants [15]:**

1. **Swelling**: Through this mechanism, some disintegrating ingredients, such as starch, cause the tablet to break down when it comes into contact with water. For instance, sodium starch glycolate and plantain ovate.

2. Porosity and Capillary Action (Wicking): Some super disintegrants work by capillary action and porosity to disintegrate. The disintegrating particles work to increase porosity, which creates pathways for liquid to permeate into tablets. The liquid is then exhausted by capillary or wicking activity, which

causes the breakdown of inter-particle bonding and finally the disintegration of the tablet, such as Croscarmellose and Crosspovidone

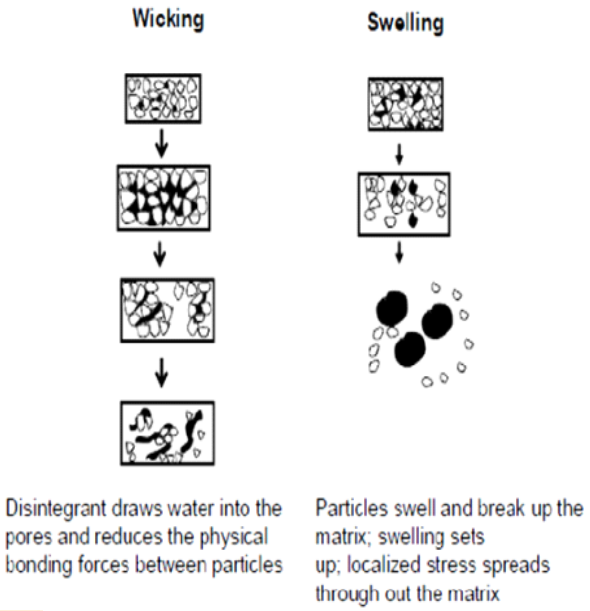

Fig. 5: Wicking and swelling mechanism of tablets [21]

3. Deformation: The starch grains distorted when pressure was applied, but they will return to their original shape when pressure is released. However, they irreversibly distorted when crushed into tablets, releasing their energy when in touch with water.

4. Due to Disintegrating Particle/Particle Repulsive Forces: Non-swellable disintegrants are connected to this mechanism. Guyot-Hermann responded with the particle repulsion theory. According to this theory, water is caused by electric repulsive forces between particles that cause particle disintegration. The majority of disintegrants are thought to operate through many mechanisms. However, it is the outcome of the interactions between these important systems.

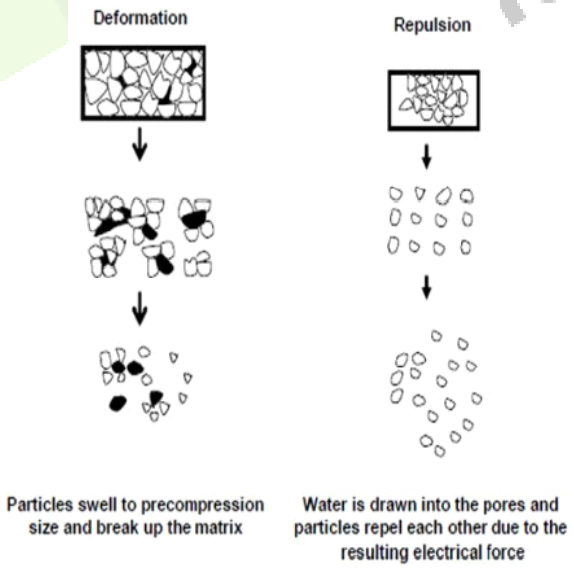

Fig. 6: Deformation and repulsion of tablet disintegration [21]

5. Chemical Reaction (Acid-Base reaction): Due to the interaction of tartaric acid and citric acid (acids) with alkali metal carbonates or bicarbonates (bases) in the presence of water, the tablet is swiftly broken apart by internal CO2 liberation in water. The tablet breaks down as a result of internal pressure buildup. The solubility of active medicinal components in water as well as the taste-masking effect are improved as a result of CO2 gas liberation. The environment must be strictly controlled when the tablets are being prepared because these disintegrants are extremely sensitive to even the smallest variations in temperature and humidity. Either the effervescent blend is added right before compression, or it can be added in two different formulation fractions.

6. Enzymatic Reaction: Biological Reaction The body's natural enzymes also function as disintegrants. These enzymes aid in disintegration and eliminate the binding action of the binder. The swelling causes pressure to be applied in the tablet's outer direction, which causes it to rupture, or the water's faster absorption generates a huge rise in the amount of granules, which encourages disintegration. Table 1 lists several illustrations of dissolving enzymes along with the binders that they are active against.

7. Heat of Wetting: Exothermic disintegrants that are wet cause localised tension as a result of capillary air expansion, which helps the tablet dissolve. The majority of modern disintegrating agents, however, cannot be well described by this theory since it only applies to a small subset of disintegrants.

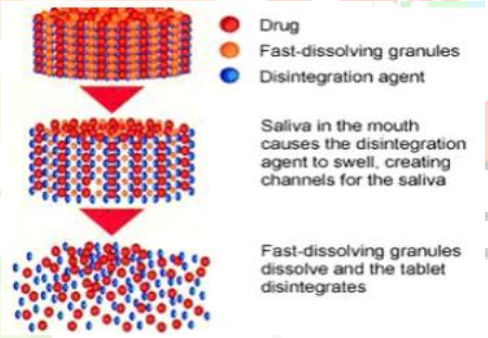

Fig. 4: Conceptual Diagram of Fast dissolving Tablet [10]

Depending on their source, there are two different kinds of superdisintegrants: one is natural and the other is synthetic.

❖ **Superdisintegrants are classified into two categories** [10],

- **Natural Superdisintegrants**: Examples: Plantago ovata seed mucilage, Lepidium sativum mucilage, Gum Karaya, Guar gum, Gellan gum, Xanthan gum, Cassia fistula gum, Fenugreek seed mucilage, Mango peel pectin, Agar and treated agar etc.
- **Synthetic Superdisintegrants**: Examples: croscarmellose sodium (Ac-Di-Sol) sodium starch glycolate (Primogel and Explotab) and crospovidone (Polyplasdone XL) etc.

- **Bulking agents:** The use of bulking agents is essential in the creation of FDTs since they serve as a diluent, filler, and cost-saving tool. Bulking agents improve the textural features and mouth disintegration. More sugar-based bulking agents, such as mannitol, polydextrose, lacitol, DCL (directly compressible lactose), and starch hydrolysate for water solubility, are recommended for the distribution. Particularly high aqueous solubility and good sensory perception are characteristics of mannitol. In the final composition range of 10% to 90% by weight, bulking agents are applied. [10].
- **Lubricants:** Lubricants aid in the manufacturing process even if they are not a necessary part. When punching, lubricants stop the powder mixture from sticking to the die cavity. Lubricants help the medicine travel from the mouth along the oesophagus and into the stomach by reducing the grittiness. Depending on the characteristics of the medicine employed in the formulation, several hydrophilic and hydrophobic lubricants are used [10].
- **Sweeteners and flavours:** Lubricants aid in the manufacturing process even if they are not a necessary part. When punching, lubricants stop the powder mixture from sticking to the die cavity. Lubricants help the medicine travel from the mouth along the oesophagus and into the stomach by reducing the grittiness. Depending on the characteristics of the medicine employed in the formulation, several hydrophilic and hydrophobic lubricants are used [10].
- **Surface acting agents**: Surfactants are employed in FDTs, such as sodium lauryl sulphate, polyoxyethylene sorbitan fatty acids esters (tweens), sodium doecyl sulphate, sorbitan fatty acid esters (span), and polyoxyethylene sterates. [10].
- **Colours:** FDA approved colours are permitted in the formulation. Examples are sunset yellow, amaranth etc. [10].
- **Drug:** The characteristics of the medicine should not significantly alter the characteristics of the tablet for the best ODT technology. For instance, the drug's solubility, crystal morphology, particle size, hygroscopicity, compressibility, and bulk density can have a big impact on how strong and how easily tablets break down in the final formulation. ODT technology needs to be adaptable enough to manage each drug's distinct characteristics [10].
  - **Evaluation Of FDTs: -**
    - **Pre-compression Characterization of Tablet [21]:** - Prior to compression, the bulk and tapped densities of the powder blends should be examined. Based on these values, the compressibility index and Hausner's ratio should be computed, and the flow characteristics of the powder blends should be evaluated based on the angle of repose.
  - **Angle of repose: -**The angle of repose can be used to calculate the frictional forces in loose powder or granules. This is the angle formed by a mass of grains or powder and the horizontal plane. The funnel method determines it. Fill a funnel that can be lifted vertically to a maximum cone height with the mixture and pour it through (h). Consider measuring the heap's radius (r). The following formula is used to determine the angle of repose:

    $\tan \Theta = h/r$

Table 2: - Relation between Angle of repose and Flow property [6]

Angle of repose	Flow property
< 0	Excellent
20-30	Good
31-34	Passable
>34	Very poor

- **Bulk density and tapped density: -**

The 100 ml measuring cylinder should contain a precise weighted quantity of powder. Note the initial volume, then tap the cylinder 100 times on a hard, level surface while recording the tapped volume of packing [85]. Utilizing the following formula, bulk density (BD) and tapped density (TD) should be determined:

$$\textbf{BD} = \frac{\textbf{weight of power}}{\textbf{Volume of packing}}$$

$$\textbf{TD} = \frac{\textbf{Weight of Powder}}{\textbf{Tapped volume of Packing}}$$

BD = weight of powder/ volume of packing

TD = weight of powder/tapped volume of packing

- **Carr's index** (Compressibility): - Compressibility index of powder can be determined by the following formula:

$$\textbf{Carr's Index (\%)} = \frac{\textbf{(Tapped density - Bulk density) *100}}{\textbf{Tapped density}}$$

Table 3: - Relation between % Compressibility and Flow ability [14]

% Compressibility property	Flow
5-12	Excellent
12-16	Good
18-21	Fairly Passable
23-35	Poor
33-38	Very Poor

- **Hausner's ratio: -** Hausner's ratio is an index of ease of powder flow. It is calculated by the following formula:

$$\text{Hausner's ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Hausner's ratio1.25-Poor flow=33%Compressibility Index

❖ **Post-compression Characterization of Tablets**: -

- **Organoleptic properties:** Dimensionally describing, tracking, and controlling the tablet's size and shape is possible. Tablet thickness is a crucial element in both duplicating appearance and counting with filling machinery. The uniform thickness of the tablets is used as a counting mechanism by some filling equipment [14].
- **Uniformity of weight:** Twenty tablets were ingested, and their weights were calculated individually and collectively on a digital weighing balance in accordance with the I.P. procedure for uniformity of weight. The total weight was used to calculate the average weight of one pill. The weight variation test would provide a reliable way to assess the uniformity of the medication content [14].

Table no. 4: - Maximum percentage difference allowed

Average weight of Tablets (mg)	Maximum percentage difference allowed
130 or less	10
130-324	7.5
More than 324	5

- **Tablet hardness: -**: The force needed to break a tablet across its diameter is referred to as the tablet's hardness. The hardness of the tablet determines how resistant it is to breaking, chipping, or abrasion when handled before use and during storage transformation. Using a Monsanto Hardness tester, the hardness of each formulation's tablet was evaluated [14].
- **Tablet Friability [14]**: - The mechanical strength of tablets is measured. The following approach was done to determine the friability using the Roche friabilator. The friabilator was loaded with a pre-weighed tablet. With each revolution, the plastic chamber of a friabilator, which rotates at 25 revolutions per minute, drops the tablets six inches away. For at least 4 minutes, the tablets were spun in the friabilator. After being dusted and reweighed, the test tablets' weight loss is a measure of friability and is stated as a percentage as follows:

$$\% \text{ Friability} = \frac{(w1-w2) * 100}{W1}$$

Where W1 = Weight of tablets before test (initial weight)

W2 = Weight of tablets after test (final weight)

- **Thickness**: - The die and punches chosen for creating the tablets will determine the tablet's diameter and punch size. A screw gauge is used to measure tablet thickness. Tablet thickness should not deviate

from the target value by more than 5%. To make packaging easier, the thickness must also be kept under control. Ten preweighed tablets should each have their specific thickness measured in millimetres (mm) using a screw gauge. Report the standard deviation and average thickness [14].

- **In vitro disintegration time: -** Using a tablet disintegration tester, six tablets are used in water at 37 °C for this test. The amount of time needed for the pills to dissolve and totally flow through the sieve is noted [14].
- **In vitro dissolution study**: - USP dissolving testing apparatus 2 is used to determine the drug's release rate from FDTs (paddle method). 900 ml of 0.1 N HCl are used in the dissolution test, which is carried out at 370.5 0C and 100 rpm [14].
- **Wetting time**: - Use a piece of tissue paper that is 10.75 mm x 12 mm, fold it twice, and put it in a culture dish with a diameter of 6.5 cm and a water content of 6 ml. Record the amount of time needed for the paper to be completely soaked using a tablet [14].
- **In vitro dispersion time: -** The tablets should be dissolved in 10 ml of pH 7.4 phosphate buffer solution at 37 0.5 °C. Calculate how long it takes for the tablets to dissolve completely [14].
- **Water absorption ratio (R): -** - Using a digital weighing balance, record the tablet's weight (Wb) before putting it in the petri dish. Take note of the tablets' weight after being wettened (Wa). The following equation can be used to calculate the water absorption ratio, R.

  $$R = \frac{Wa - Wb}{Wb} * 100$$

  where Wb and Wa are tablet weights before and after water absorption, respectively.
- **Stability studies [6]**: Fast-dissolving tablets with an improved formulation are packaged and stored for stability experiments in accordance with ICH requirements, and their physical stability and release characteristics were examined.

Table 5: Marketed formulations of FDTs [15]: -

Trade Name	Active Drug	Manufacturer
Felden fast melt	Piroxicam	Pfizer Inc., NY, USA
Ugesic	Piroxicam	Mayer organic Ltd.
Esulide MD	Nimesulide	Doff Biotech
Kazoldil MD	Nimesulide	Kaizen Drugs
Mosid MD	Mosapride	Torrent Pharma
Valus	Valdecoxib	Glenmark
Vomidon MD	Domperidone	Olcare
Claritin redi Tab	Loratidine	Schering Plough Corp., USA
Maxalt MLT	Rizatriptan	Merck and Co., NJ, USA
Zyprexia	Olanzapine	Eli Lilly., Indianapolis, USA
Pepcid RPD	Famotidine	Merck and Co., NJ, USA
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Zofer MD	Ondansetron	Sun Pharma
Ondem MD	Ondansetron	Alkem Pharma
Zoming-ZMT	Zolmitriptan	AstraZenecea, USA
Zeplar TM	Selegilline	Amarin Corp. London
Tempra Quiclets	Acetaminophen	Bristol Myers Squibb. USA
Febrectol	Paracetamol	Prographarm. France
Nimulid MDT	Nimesulide	Panacea Biotech. India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, India
Rofixx md	Rofecoxib	Cipla ltd. Mumbai, India
Olanex Instab	Olanzapine	Ranbaxy Lab. Ltd, India
Romilast	Monteleukast	Ranbaxy Lab. Ltd, India
Zontec MD	Cetrizine Zosta	Pharma India
Lonazep MD	Olnazepine	Sun Pharma
Nime MD	Nimesulide	Maiden Pharma
Imodium lingual	Imodium	R.P. Scherer Corp., U.S.A
Pepcidin Rapitab	Pepcid	Merck & Co., U.S.A
Cibalginadue Fast	Ibuprofen	Novartis Consumer Health
Nurofen Flashtab	Ibuprofen	Boot healthcare
Hyoscyamine sulphate ODT	Hyoscyamine sulfate	Ethex Corporation
Risperdal M Tab	Risperidone	Janssen
Imocdium Instant Melts	Lopermide HCl	Janssen
Propulsid Quick Sol	Cisapride monohydrate	Janssen
Alavert	Loratadine	Wyeth Consumer Healthcare
NuLev	Hyoscyamine sulfate	Schwarz Pharma

Kemstro	**Baclofen**	**Schwarz Pharma**
Nasea OD	**Ramosetoron HCl**	**Yamanouchi**
Gaster D	**Famotidine**	**Yamanouchi**
Fluoxetine ODT	**Fluoxetine**	**Biovail**
Zolpidem ODT	**Zolpidem tartrate**	**Biovail**
Excedrin Quick Tabs	**Acetaminophen**	**Bristol-Myers Squibb**
Abilify Discmelt	**Aripiprazole**	**Otsuka America**
Aricept ODT	**Donepezil**	**Eisai Co.**
FazaClo	**Clozapine**	**Azur Pharma**
Relivia Flash dose	**Tramadol HCl**	**Fuisz Technology, Ltd**
Domray MD	**Domperidone**	**Ray Remedies**
Nurtec ODT	**Rimegepant**	**Biohaven**

CONCLUSIONS: -

This study shows that an Oral fast-dissolving tablets are one of the novel approaches in the world of pharmaceutical sciences. With no risk of choking and higher safety and efficacy than conventional forms, these fast-acting tablets provide the patient with instant relief from migraine discomfort. Many diseases required fast action for that diseases oral FDTs are very important and helpful.

This has improved both patient compliance and acceptance of the medication. To assist dysphasic patients who had trouble swallowing typical oral dosage forms, oral rapid dissolving tablets were created. Today, a wide range of OFDTs are accessible for illnesses like acidity, Parkinson's, Parkinson's disease, anxiety, diarrhoea, hypertension, allergies, and anxiety. In addition to satisfying the population's need for convenience in drug administration, their administration without the use of water avoids hepatic metabolism, improving therapeutic response. The patient will benefit from it.

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