A Review on Oral Fast Dissolving Tablet an Efficient Drug Delivery Approach

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Abstract: Presto-dissolving drug delivery systems are becoming more and more popular as innovative medicine delivery systems since they are simple to use and improve patient compliance. Typically, elderly individuals have trouble swallowing traditional lozenge forms (tablet, capsule, result, and suspensions) due to dysphasia and extremity tremors. Delivery systems for fast-dissolving medications might provide a solution to these issues. The first pass effect and gastrointestinal tract declination can be avoided because the medication is directly absorbed into the systemic circulation. These reasons make this term the most well-liked and respected among pediatrics, senior, and choking-related cases. In the US, over-the-counter medications for pain management and motion sickness are prioritized. Many businesses are experimenting with thin film forms by using transdermal drug delivery technology. Recent developments in rapidly dissolving buccal film expression and their evaluation metrics are gathered in the current study.(1,2) Keywords: Oral route, mouth-dissolving tablet, fast-dissolving tablet, super disintegrant.

Keywords : Fast-dissolving Tablet , Super disintegrant , oral route, Mouth Dissolving tablet .

Introduction:

Up to 50–60% of all lozenge forms, including tablet and pill, are commonly accepted. Because tablets are portable, simple to manufacture, and can be delivered in precise cure, they are still the most used conventional lozenge forms at the moment. The difficulty swallowing (dysphagia) or biting in some circumstances, particularly those involving children and the elderly, is a significant drawback of solid lozenge forms. The difficulty swallowing is a common miracle in elderly cases because of a fear of choking, hand tremors, dysphasia, in young people because of underdeveloped nerve and muscular systems, and in schizophrenia cases because of poor case compliance. When water isn't accessible, when someone has diarrhea, when they cough during a common cold wave, when they have an antipathetic condition, or when they have a bronchial infection, tablets and capsules can be difficult to swallow. A third of the population, mostly children and seniors, have trouble swallowing, which makes them less compliant with oral tablet medication treatment and lowers the effectiveness of the treatment as a whole. Because of this, pills that quickly dissolve or disintegrate in the oral depression have garnered a lot of interest. the Food and Drug Administration of the United States.(3) These new kinds of pills dissolve, disintegrate, or disperse in a short period of time without water. According to the European Pharmacopoeia, these MDTs should dissolve or disintegrate in fewer than three twinkles. The expression is particularly helpful for those who are bedridden and have swallowing issues. Because of their improved patient compliance, quick start of action, higher absorption, and good stability, MDTs are preferred as a lozenge form of medication in the current market. 1, 2, 3. Orodispersible pills, presto disintegrating tablets, orally dissolving tablets, quick disintegrating tablets, fast dissolving tablets, rapid-fire dissolving tablets, pervious tablets, quick melt tablets, and rapid-fire melt tablets are additional names for mouth-dissolving tablets. Still, the USP has authorized these lozenge forms as ODTs out of all the terms listed below. ODTs were described by the US Food and Drug Administration (FDA) as "solid lozenge forms containing medications. (4) Colorful methods including as direct contraction, wet granulation, contraction moulding, vitalization, and snap drying can be used to administer fast-dissolving medications. They use various strategies, such as the use of large amounts of hydrophilic disintegration agents, which enable the lozenge forms to dissolve quickly in the slaver's mouth upon contact with the case.

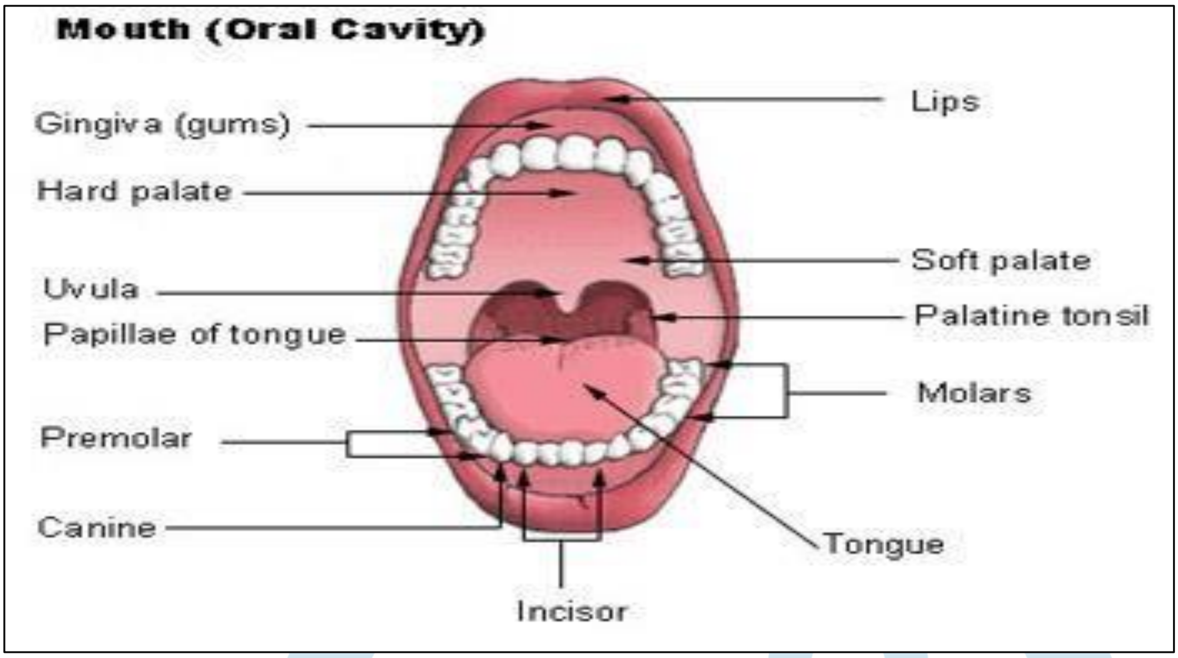


Fig.1 : Mouth (Oral cavity)

Definition:
Oral Disintegrating Tablets (ODT) are "a solid lozenge form containing medicinal substances, which disintegrates swiftly, generally within a matter of seconds, when placed upon the tongue," according to the Centre for Medicine Evaluation and Research (CDER), US FDA.
A solid lozenge that can break down into smaller grains that slowly dissolve in the mouth is what is meant by a fast-dissolving tablet. Depending on the tablet's expression and size, the decomposition period for fast-dissolving tablets ranges from several seconds to more than a millisecond. (1)

Criteria for fast-dissolving drug delivery:

1. It shouldn't be swallowed because it will melt or disintegrate quickly in the mouth.
2. Work well with flavor muffling.
3. Be mobile without any fragility issues.
4. Display a friendly mouth feel.
5. After oral delivery, leave little to no residue in the mouth.
6. Displays that are less sensitive to external factors including moisture and temperature (4)

Salient Feature of Fast Dissolving Drug Delivery System:
• Ease of administration for patients who are unable to swallow, such as elderly patients, stroke patients, patients who are bedridden, patients who have renal failure, and patients who refuse to swallow, such as pediatric, senior, and mental patients.
• The lozenge form does not require water to be swallowed, making it generally feasible for people who are travelling and do not have immediate access to water.
• The medication will dissolve and submerge quickly, causing a rapid onset of
•Pre-gastric immersion can influence Advanced bioavailability and as a result of Reduced lozenge, and it can also improve clinical performance by lowering the number of unwanted items.
• A higher bioavailability, especially in the case of unusable and hydrophobic medications, as a result of the tablets' quick breakdown and dissolution.
• Longer-lasting stability since the medicine stays in the shape of a firm lozenge until it is swallowed. As a result, it combines the benefits of liquid lozenge form in terms of bioavailability with those of solid lozenge form in terms of stability.
• FDT won't cause choking or airway obstruction, making it safer than traditional lozenge formulations.
• Additional commercial opportunities in areas such as life cycle management, product countersign, product isolation, and patent extensions.
• Favorable in situations when there is an abrupt and rapid-fire initiation of action, such as stir sickness, unanticipated instances of an antisocial assault, or coughing. Both solid (higher stability) and liquid (greater bioavailability) lozenge versions have advantages. (4,5)
•Pre-gastric immersion can improve bioavailability and result in a smaller lozenge, which can improve clinical performance by reducing waste.
• Good mouth feels property helps to change the perception of drug as a bitter lozenge particularly in the pediatric case.

• The threat of choking or suffocation during oral administration of conventional expression due to physical inhibition is avoided therefore furnishing advanced safety. (7)

Advantages of solid dispersion :

- ✓ It reduces the flyspeck size of the product.
- ✓ It makes the medication more wettable.
- ✓ Increases porosity.
- ✓ It transforms liquid into an unformed state. (8, 9)
- ✓ The tablet can be swallowed dry.
- ✓ Children, the elderly, and patients with mental impairments can all receive FDTs without difficulty.
- ✓ More precise dosage than with liquids.
- ✓ More cost-effective in terms of administration and transportation than liquid drugs.
- ✓ First pass metabolism is decreased, resulting in improved bioavailability and decreased cure and adverse effects. (7)

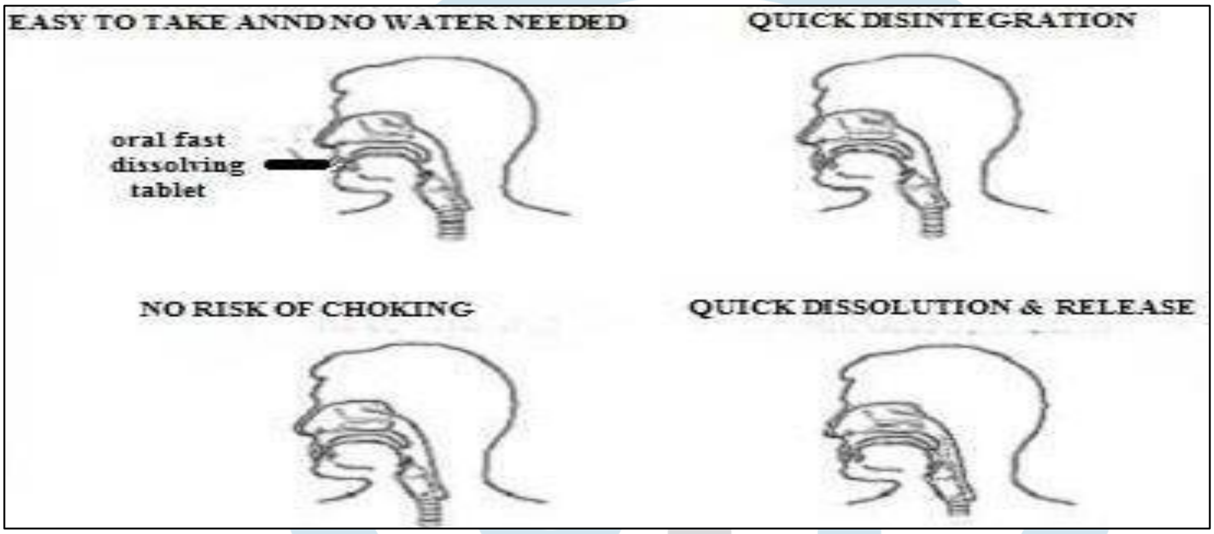


Fig.2: Advantages of FDT

Limitations of FDT :

- ✓ The mechanical strength of tablets is one of the main drawbacks of FDTs.
- ✓ FDT are genuinely transparent and softly moulded criterion or squeezed into a tablet with low contraction, making tablet brickle and brittle Which delicate to handle.
- ✓ Bad-tasting medications are difficult to manufacture as FDT; particular palladium must be taken prior to creating medications of this type.
- ✓ Some FDT cannot sustain physical integrity because they are hygroscopic. Under typical circumstances, moisture causes specialized packaging to be needed.
- ✓ Slaves who are unable to speak owing to dropped slaver products might not make good advocates for these tablet phrasings.
- ✓ The slaver result's rate of immersion and overall bioavailability.
- ✓ Lozenges and medications maintain stability. (10, 11)

Pharmacokinetics

It covers ingestion, dissemination, metabolism, and excretion. Following immersion, medicine takes on a curative role and produces a pharmacological effect. Therefore, the rate and extent of immersion are both crucial. There is detention in the breakdown and dissolution of traditional lozenge form. However, the oral depression and rapid dissolution in the case of quickly dissolving pills. The tablet dissolves quickly when it is immersed in the mouth, throat, and esophagus. Age, coitus, pH, and blood inflow through the gastrointestinal tract are a few elements that are taken into account because elderly may be deemed to require separate, special medical care. Numerous variables, such as towel permeability, perfusion rate, list of medicines to towel, and complaint state pharmaceutical trade, affect how medicines are distributed. Reduced body mass and total body water in elderly patients lead to decreased distribution of lipid-responsive medications. The length of the effect and its strength depend on how quickly the body transforms the medication. Reduced renal volume and native blood input to the liver slow down the oxidation, reduction, and hydrolysis of drugs in the memory. Excretion through renal concurrence is slowed, resulting in an extension of the half-life of drugs excreted through the kidneys. Fast-acting pill metabolism is genuinely simple and achievable very quickly. Water consumption is crucial to successfully digesting oral lozenge forms. (12)

Pharmacodynamics:

pharmaceutical event commerce bloody in older adults as well as young adults due to delayed organ development. decreased capacity of the body to react in a reflexive manner Orthostatic hypotension, heart issues, and stimuli may be seen after taking an anti-hypertensive drug such prazosin. decreased CVS sensitivity to beta adrenergic agonist While administering antibiotics, antagonist impunity is minimized and taken into account. Senior show: Modified response to medication remedy Theophylline's reduced bronchodilator action causes an increase in barbiturate receptivity. Seniors typically have accompanying illnesses, which are taken into account when various pharmaceutical remedies are recommended. Clinically evaluated medication combinations for the various classes of cardiovascular drugs, diuretics, and antihypertensives in elderly patients have been developed by researchers. The combination is determined by the case's complaint state. (12)

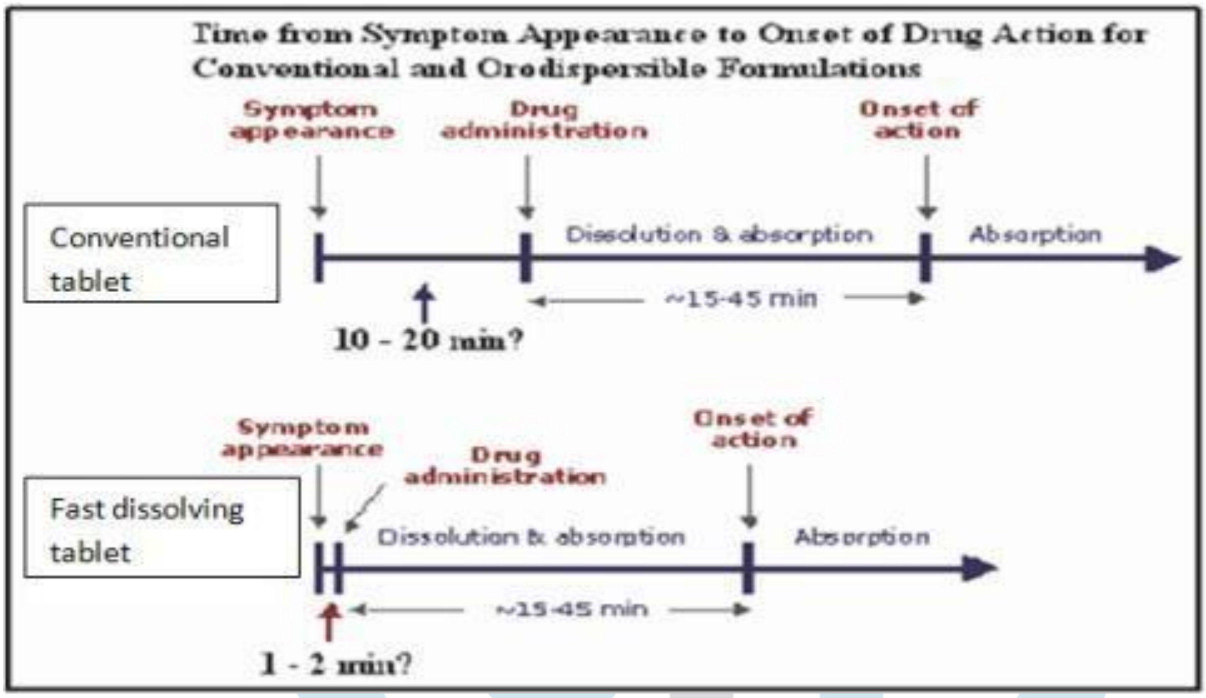


Fig.3 : timely comparison between conventional and fast dissolving tablet

Drugs used in fast dissolving delivery system :

S. No	Therapeutic activity	Drugs used
1.	Analgesic and anti-flammatory agents	Aloxiprin, fenbufen, meclofenamic acid, oxaprozin, oxyphenbutazone, ibuprofen, nabumetone, piroxicam
2.	antihelmentics	Albendazole, cambendazole, ivermectin, pyrantel, praziquantel, mebendazole, thiabendazole, hydroxyl naphthoate
3.	Anti –arrhythmic agents	Amiodarone hcl, disopyramide, flecainite acetate, vanidine sulphate,
4.	Anti-bacterial agents	Cinoxicam, clofazimine, cloxacillin, doxycycline, nitrofurantoin, ehionamide, banethamine, pencillin, sulphadoxine, sulphabenzamide, sulphapyridine, trimethoprim.
5.	Anti-**c**oagulants	Dicoumarol, dipyrimidine, phenindione, nicoumalone.
6.	anti-depressant	Amoxapine, ciclazindol, mianserinHCL, trazodoneHCL, trimipramine maleate, maprotilineHCL.
7.	ANTI-DIABETICS	acetohexamide, chlorpropamide, glibenclamide, gliclzide, glipizide, tolbutamide.
8.	Anti-epileptics	Clonazepam, methion, phenacemide, phenobarbetone, sulthiame, phenatoin**,** oxecarbazepine, methylphenobarbitone.
9.	Anti-fungal	Clotrimazole, flucytocin, grisiofulvin, natomycin, amphitercin, terconazole, tioconazole, itraconazole,
10.	Anti-malarial	Amodiaquine, chloroproguanil HCL, pyramethamine, chloroquine, mefloquine**,**
11.	Anti-muscarnic agents	Atropine, biperdine, hyoscyamine, oxyphencyclamine HCL, tropicamide
12.	Anti-protozoa agents	Clioquinol, benznidazole, diloxamidesfuroate, metronedazole, benznidazole, tinidazole.
13.	Anxiolytics, seditives, hypnotics and neuroleptics	Alprazolam, barbitone, bentazepam, bromazepam, clozapin, bromperidol, diazepam, ethinamate, flurazepam, droperidol.
14.	Cardiac inotropic agents	Amrinone, digitoxin, digoxin, medigoxin, enoximone.
15.	Anti-parkinsonian agents	Bromocriptine, mesylate, ysuride maleate.

Table1: Drug used in fast dissolving delivery system

Techniques for Preparing Fast dissolving Tablets:

Numerous ways have been reported for the expression of Fast dissolving tablets or Orodispersible tablets. Then we have bandied the six major ways which are extensively used for the expression of these tablets.

1. Drying/ Lyophilization
2. Tablet moulding
3. Spray drying
4. Sublimation
5. Direct Compression
6. Mass Extrusion
7. Cotton Candy
8. Nonionisation
9. Oral disintegrating or presto dissolving thin flicks

1. Freeze Drying or Lyophilization

Snap drying is the procedure used to remove water from a product after it has been firmed. In this way, a pervious structure that can quickly dissolve is created. An ordinary process used in the production of FDT Then it is mentioned to use this fashion. The use of snap-drying has shown to improve immersion and boost bioavailability. Lyophilization is expensive and time-consuming; these products are fragile, making standard packaging ineffective for them; and they have poor stability under stressful circumstances. (5).

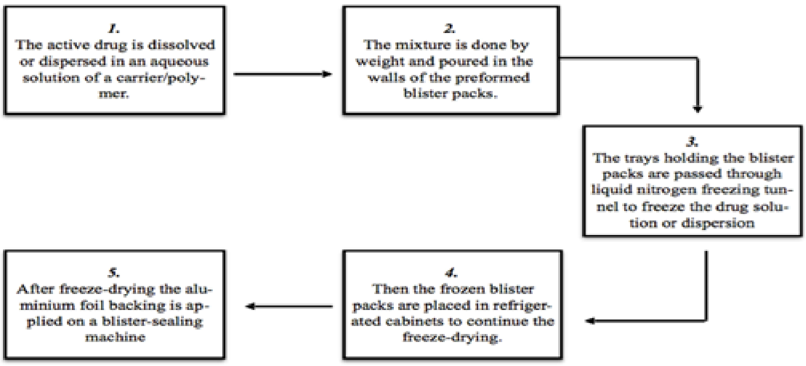
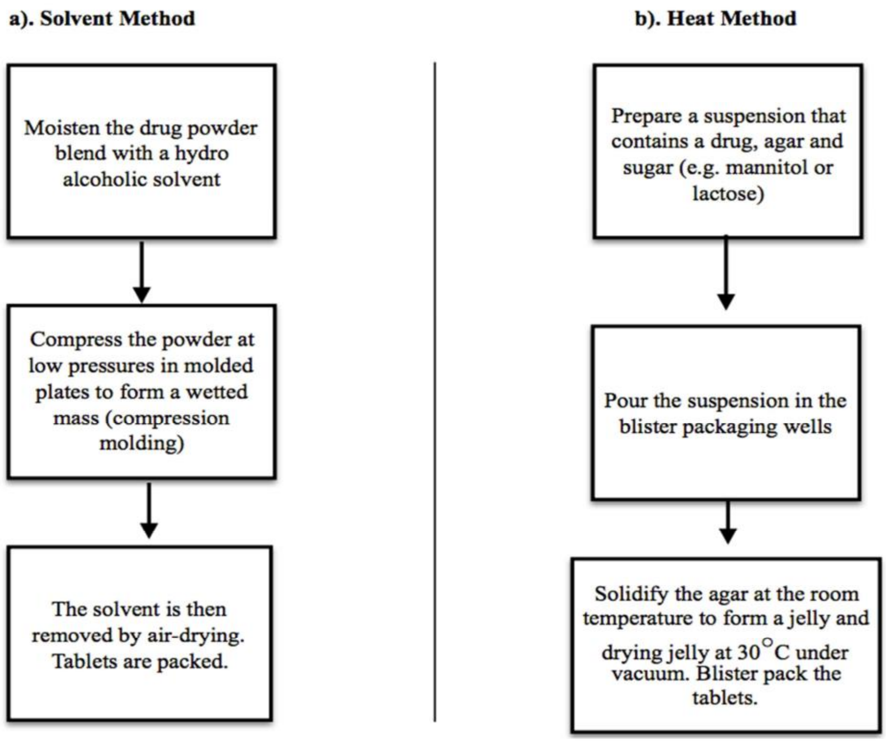


Fig.4 : Steps by step procedure of Lyophilisation of FDT

2. Tablet Molding

There are two different types of moulding processes: solvent systems and heat systems. Less compact than compressed tablets, tablets made using a solvent system have a porous structure that speeds up dissolution. A major worry is the mechanical strength of tablets that have been formed. It is necessary to contain list agents that improve the mechanical strength of the tablets. The masking of taste is a further issue with this technology. To solve this, the masked medicine patches are made by spray-congealing a molten mixture of hydrogenated polyethylene glycol, cottonseed oil painting, lecithin, and sodium carbonate, an active ingredient, into a lactose-ground tablet triturate form. Comparatively to the lyophilization fashion, tablets made in the moulding fashion are simpler to gauge up for artificial manufacturers. (5)



3. Spray Drying:

In this way, super disintegrants like croscarmellose, sodium bounce glycolate, or crospovidone are combined with gelatin to act as a matrix and supporting agent, as well as bulking agent and superdisintegrant, respectively. The tablets made from spray-dried greasepaint that contain a superdisintegrant, a bulking agent, a citric acid component, and/or an alkaline component, such as sodium bicarbonate, have been found to dissolve in less than 20 seconds in a waterless media. This greasepaint that had been compacted into tablets and sprayed dried did so quickly and with improved dissolving. (5)

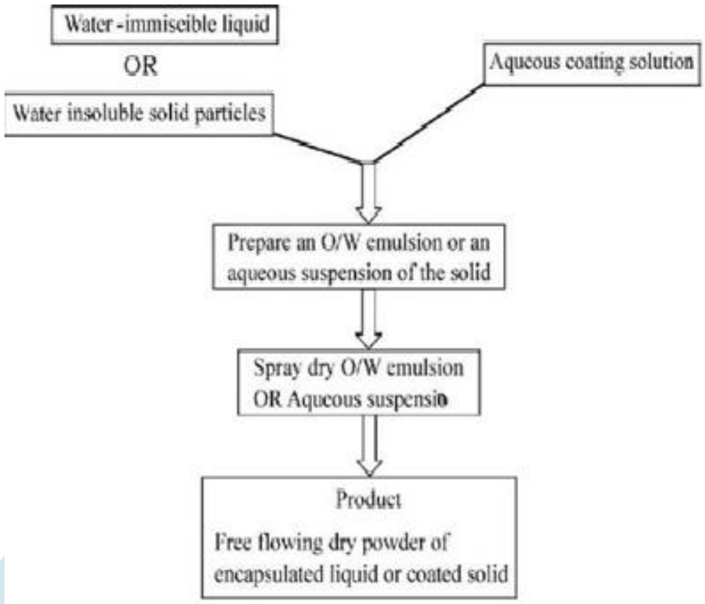


Fig.6: Flow chart for coating liquid and solid particles using spray-drying process

4. Sublimation:

By integrating quickly volatilizing inert solid ingredients such urea, camphor ammonium carbonate, ammonium bicarbonate, and hexamethylenetetramine into pervious matter, rapid decomposition and dissolution can be achieved. They were compressed after being combined with other ingredients. Reduced pressure and a modest increase in temperature cause the unexpected material to evolve, leaving the mass in a transparent state. The permeable nature of sublimation systems allows for the use of cleaners like cyclohexane and benzene. (13)

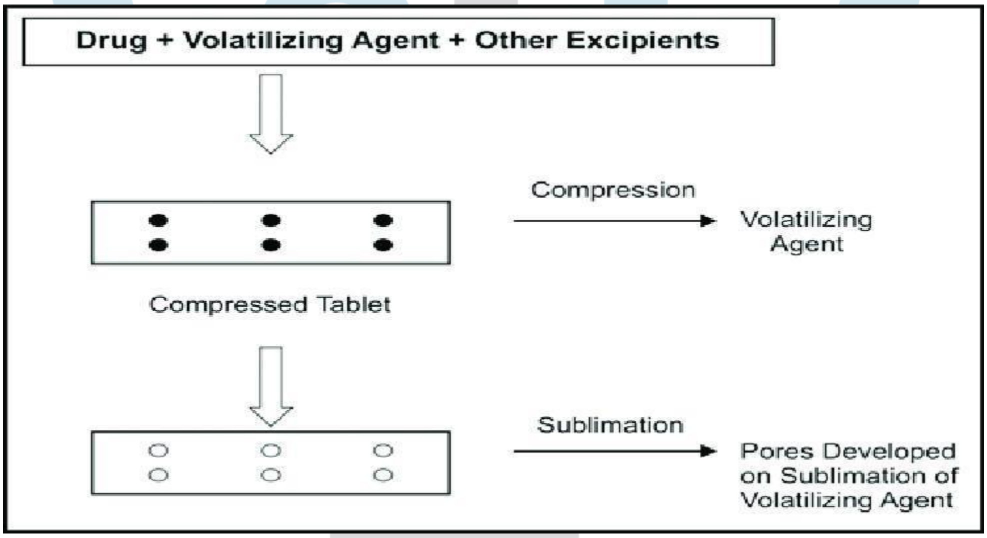


Fig.7: Schematic diagram of sublimation techniques for FDP [14]

5.Direct Compression:

The disintegrant addition technology (direct contraction) is the utmost preferred fashion to manufacture the tablets due to certain advantages:

- High boluses can be tolerated, and the tablet's final weight can be greater than that of other designs.
- The simplest method of producing the tablets.
- Usage of conventional equipment and widely accessible excipients.
- There are only a few processing methods involved.
- Economical.

The disintegrant effectiveness is drastically impacted by tablet size and hardness. Large, brittle pills require more decomposition time than is usually necessary. Tablets that are genuinely soft and tiny have weak mechanical properties. Therefore, it is important to choose the best type and concentration of disintegrant in order to accomplish rapid disintegration and high dissolution rates. Still, decomposition time increases or stays essentially constant above the critical attention position (10)

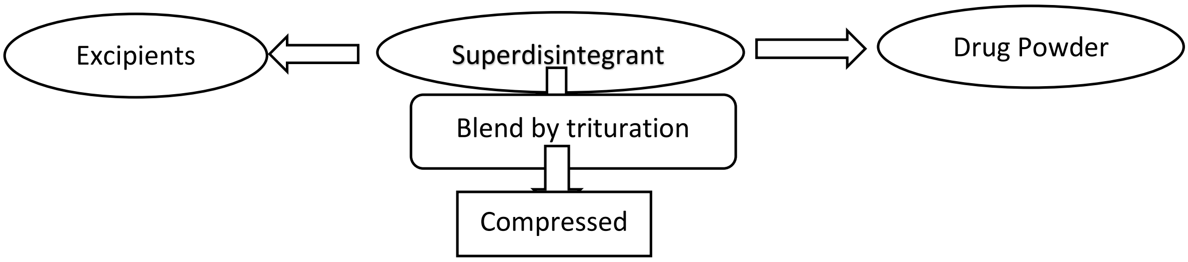


Fig. 8: Direct compression

6.Mass Extrusion:

Using methanol as a detergent and polyethene glycol as the water-soluble component, the combined ingredients in this process are softened before being extruded into thin cylinders. They are then cut into smaller tablets using a hot blade. The goods in this system have the ability to cover up the bitter taste of medications. Creating tiny grains and increasing their oral bioavailability.(14, 15)

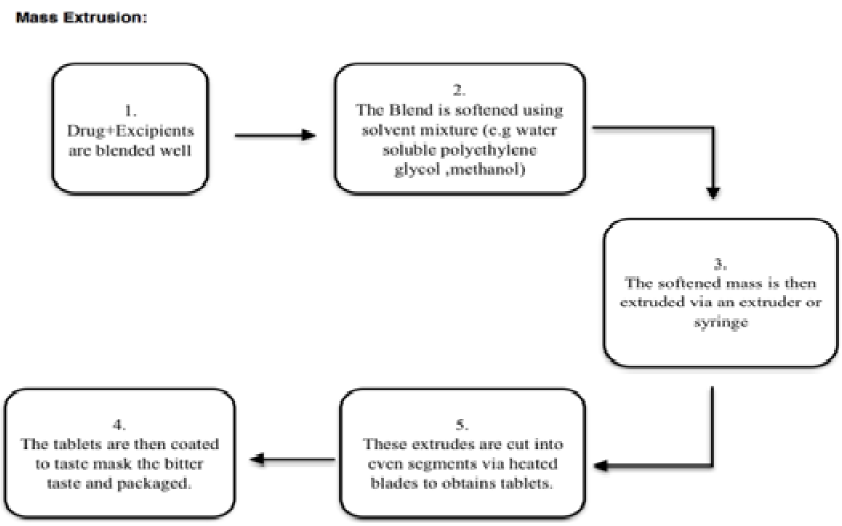


Fig.9: Formulations by Mass Extrusion

7.Cotton candy process:

This method gets its name from the use of a special spinning media to create a crystalline structure that resembles fluff and is delicate like cotton. The cotton delicacy method entails the simultaneous action of flash melting and spinning to conform a matrix of polysaccharides or saccharides. In order to improve the inflow parcels and compressibility, the matrix produced is only partially recrystallized. This delicatessen Additionally, the floss matrix is mulled and combined with the active ingredients and excipients before being compacted into FDTs. However, filaments can be produced from other polysaccharides, such as poly maltodextrins and polydextrose, at temperatures up to 40 degrees lower than those required for sucrose. With this change, thermolabile medications may now be safely objectified within the statement. The tablets manufactured by this process are largely pervious in nature and offer veritably affable mouth feel due to fast solubilization of Sugars in the presence of slaver. (7)

8. Nanoionization:

A recently developed nano-melt technology comprises personal wet-milling of the medication to reduce the flyspeck size of the medication to nano size. By face adsorption on designated stabilizers, which are also included in MDTs, the drug's nanocrystals are protected against agglomeration. This approach is particularly advantageous for drugs that are not suitably water-responsible. Other benefits of this technology include its cost-effective manufacturing process, conventional packaging due to exceptional continuity, and a wide range of boluses (up to 200 mg of medication per unit). Nanoparticles also quickly decompose or dissolve, increasing immersion and, consequently, improving bioavailability and reducing cure time. (15, 16,17)

9. Oral disintegrating or fast dissolving thin films:

It's a cutting-edge innovation in rapid release tablets that offers a genuinely Accessible way to take medications and nutrients. In this way, a non-aqueous result with water accountability is set. After the detergent has evaporated, a film-forming polymer (such as pullulan, carboxymethylcellulose, hydroxypropyl methylcellulose, hydroxyl ethyl cellulose, hydroxyl propyl cellulose, polyvinyl pyrrolidone, polyvinyl alcohol, or sodium alginate, etc.), medication, and other taste-muffling ingredients are allowed to form. If the medication is bitter, the film may also contain resin adsorbate or carpeted microparticles of the medication. When this film is put in the mouth, it quickly melts or dissolves, releasing the medication in either result or suspense form. The features of this system include Paper-thin flicks of size lesser than 2 × 2 elevation, dissolution in 5 sec, instant medicine delivery and flavored shadow. (15, 17)

Important patented technologies for preparation of FDTs :

Tabal 2: Important patented technologies for preparation of FDTs [3]

S. No.	Technique	Advantages	Disadvantages
1.	Zydis	Quick dissolution, Self-preserving and increased bioavailability.	Expensive process, poor stability at higher temperature and humidity.
2.	Orasolv	Taste-masking is twofold, quick dissolution.	Low mechanical strength.
3.	Durasolv	Higher mechanical strength than Orasolv, Good rigidity.	Inappropriate with larger dose.
4.	Flashdose	High surface area for dissolution.	High temperature required to melt the matrix can limit the use of heat-sensitive drugs, sensitive to moisture and humidity.
5.	Flashtab	Only conventional tabletting technology	--
6.	Wow tab	Adequate dissolution rate and hardness.	No significant change in bioavailability.
7.	Oraquick	Faster and efficient production, appropriate for heat-sensitive drugs.	--

For patented technology and their brand product:

S. No.	Technology	Process involved	Patent owner	Drugs Used (Brand name)
1.	Zydis	Lyophilization	R.P.Scherer Inc.	Loratidine (Claritin Reditab and Dimetapp Quick Dissolve)
2.	Quicksolv	Lyophilization	Jansen Pharmaceutical	Cisapride monohydrate (Propulsid Quicksolv), Risperidone (Risperdal M-tab)
3.	Flashtab	Lyophilization	Ethypharm	Ibuprofen (Nurofen Flashtab)
4.	Lyoc	Multiparticulate Compressed tablets	Farmlyoc	Phloroglucinol Hydrate (Spasfon Lyoc)
5.	Orasolv	Compressed Tablets	Cima Labs Inc.	Paracetamol (Tempra Quicklets), Zolmitriptan (Zolmig Repimelt)
6.	Durasolv	Molding	Cima Labs Inc.	Hyoscyamine Sulfate (NuLev) Zolmitriptan (Zolmig ZMT)
7.	RapiTab	Compressed Tablets	Schwarz Pharma	--
8.	Wow tab	Compressed Molded Tablets	Yamanouchi Pharma Technologies, Inc.	Famotidine (Gaster D)
9.	Fast melt	Molding	Elan Corp.	--
10.	Ziplets	Molding	Eurand	Ibuprofen (Cibalgina Due Fast)
11.	Flashdose	Cotton-candy process	Fuisz Technology Ltd.	Tramadol HCl (Relivia Flash dose)
12.	Oraquick	Micromask taste Masking	KV Pharm. Co., Inc.	Hyoscyamine Sulfate ODT
13.	Advatab	Microcaps and diffuscap CR Technology	Eurand International	AdvaTab cetrizine, AdvaTab Paracetamol

Table 3: For patented technology and their brand product

Excipients used in FDT preparation:

1. Superdisintegrant
2. Sugar based excipients
3. Emulsifying agent

4. Lubricants
5. Flavor and sweeteners
6. Anti-adherent
7. Binders
8. Diluents
9. Colorant
10. Disintegrant
11. Glidants
12. Sublimating agents.

1. Superdisintegrant:

Superdisintegrant primarily affect the breakdown and ultimate dissolution of fast-dissolving tablets, particularly for direct contraction methods. The decomposition process is accelerated further by the presence of additional components, such as bouncy agents and water-responsive excipients.

Rational of using of Superdisintegrant:
Many therapeutic situations require an instantaneous start to the activity, hence an immediate release of the medication is required. This problem results in an advanced prevalence of ineffective remedies and is predicted to affect 50% of the population. In order to achieve the desired bioavailability, druggists strive to create super-disintegrants that give the quickest rate of dissolving and disintegration. pills that dissolve slowly almost always ensure slow bioavailability, whereas pills that dissolve quickly don't necessarily ensure fast bioavailability. In response to the significant need for speedier dissolution requirements, "Super Disintegrants," a brand-new creation, are now readily available. The majority of the time, expression scientists utilize superdisintegrant to create FDTs or improve the solubility of pharmaceuticals. Synthetic polymers including crospovidone (XPVP), croscarmellose sodium (CCS), and sodium bounce glycolate (SSG) are frequently used as disintegrants.
Mechanism of Super disintegrants:

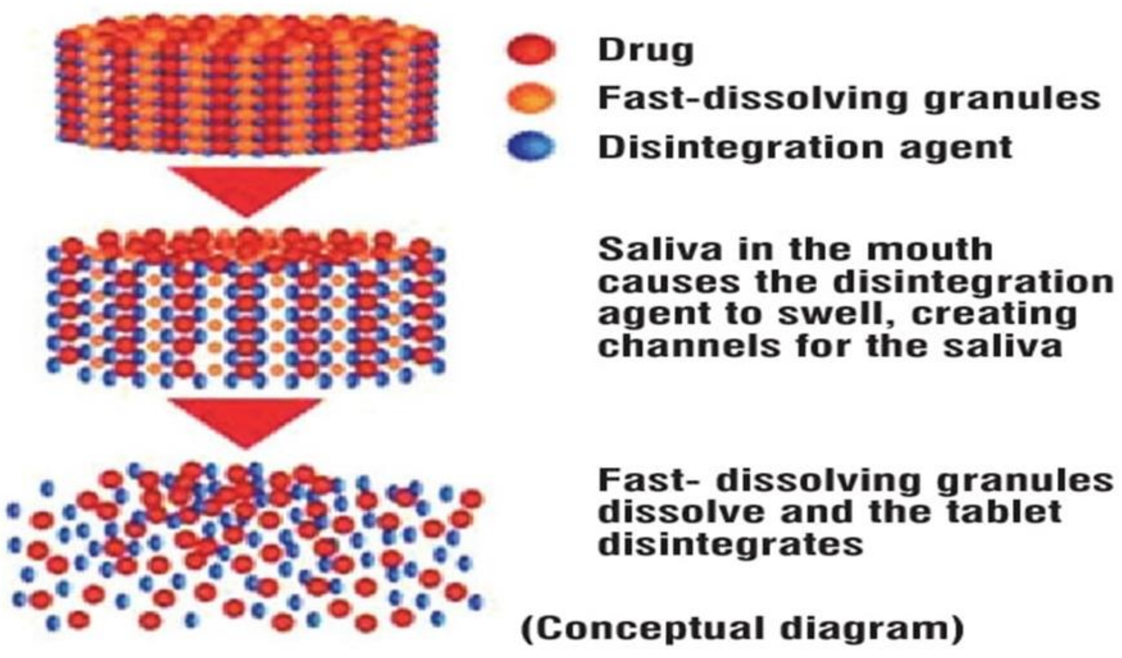


Fig.10 : Mechanism of Super disintegration

The following list identifies the four main processes of tablet disintegration:

a) Swelling:

Superdisintegrant that function in this manner exhibit the basic properties of "swell" and "burst". In comparison to other excipients or the drug, the aqueous component contributes more adhesive power to the super-disintegrant when it comes into contact with water or saliva, causing the tablet to expand and crumble or break apart.

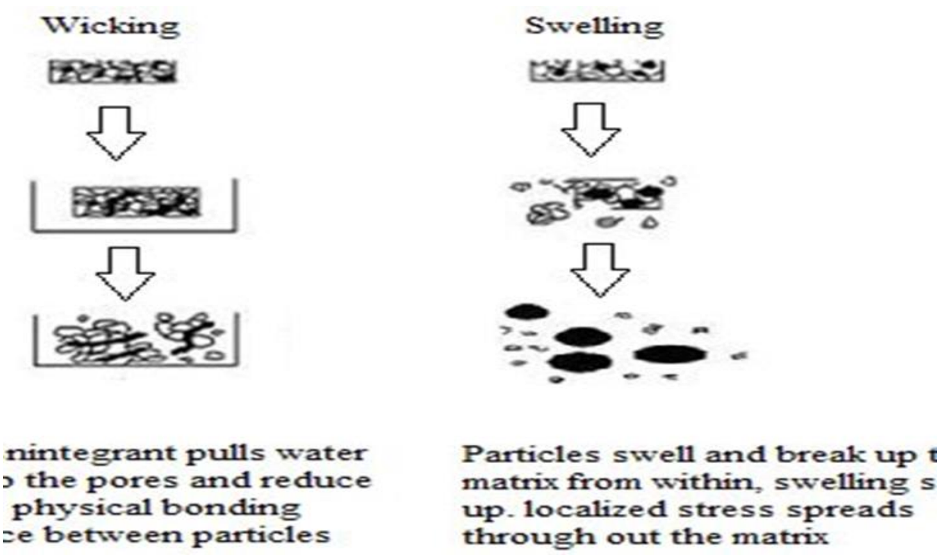


Fig.11: Diagrammatic Depiction of Mechanism of Swelling

This process is used by the majority of superdisintegrant. The most popular of them are carbohydrate and its derivatives. The inventory of natural and synthetic superdisintegrant with swelling mechanisms is provided below. [5]

Superdisintegrants	Brand names	Mechanism of action	Special comments
Crosslinked cellulose	Crosscarmellose®, Ac-Di-Sol®, Nymce ZSX®, Primellose®, Solutab®, Vivasol®, L-HPC, Nymcel	Swelling and Wicking both	Swelling two dimensions, Direct compression or Granulation starch free.
Crosslinked PVP	Crosspovidone M®, Kollidone®, Polyplasdone®, polyplasdone XL®, Kollidone CL®	Capillary action	Water insoluble and spongy in nature so get porous tablet
Crosslinked Starch	Explotab®, Primogel®, Tablo®, Vivastar®	Swelling	Swells in three dimensions and high level serve as sustain release matrix
Crosslinked alginic acid	Alginic acid NF®, Staialgine®	Swelling or Wicking	Promote disintegration in both dry and wet granulation
Soy polysaccharides	Emcosoy®	-	Does not contain any starch or sugar. Used in nutritional products.
Gallen Gum	Kilcogel®	-	Natural superdisintegrant
Xanthum Gum	Grindsted®, Xanthum SM®	-	Natural superdisintegrant
Ion Exchange Resin	Indion 414®, Tusion 339®, Amberlite IRP 88®	-	-

Tabal 4: The list of the natural as well as the synthetic Superdisintegrants

b) Porosity and capillary action:

Capillary action is the initial phase of breakdown in every case. When we immerse the tablet in a suitable waterless media, which permeates the tablet and replaces the air adsorbed on the patches, the intermolecular connection is compromised and the tablet is split up into small patches. The degree to which water is absorbed by the tablet depends on the hydrophilicity of the excipient or medication and the tableting conditions. These types of disintegrants are required for the preservation of a pervious structure and low interfacial pressure towards waterless fluid, which facilitate disintegration by establishing a hydrophilic network surrounding the medication patches. (18)

c) Particle/Particle Repulsive Forces and deformation:

Guyot-Hermann has proposed the idea of particle repulsion. This hypothesis states that swelling is produced by a tablet containing "non-swellable" disintegrants. The concept of the electric repulsive force of electrons governs how this works. Water must come into contact with the tablet for it to break apart since water's power of attraction makes particles repel one another.

Starch grains are thought to generally have an "elastic" nature, returning to their original shape once the applied pressure is relaxed. However, these grains are believed to be permanently damaged and "energy rich," with this energy being released when the grains come into contact with water, due to the compression pressures utilized in tableting. In other words, "energy rich" starch grains have a greater capacity for swelling than starch grains that have not undergone pressure-induced deformation. [5]

2. Sugar Based Excipients:

This is a brand-new method for making FDT through direct compression. The use of bulking agents, such as Dextrose, fructose, isomalt, lactilol, maltilol, maltose, mannitol, sorbitol, bounce-hydrolysate, Polydextrose, and xylitol, which exhibit high Waterless solubility and agreeableness, and therefore conduct taste masking property and a pleasing Mouth sense.

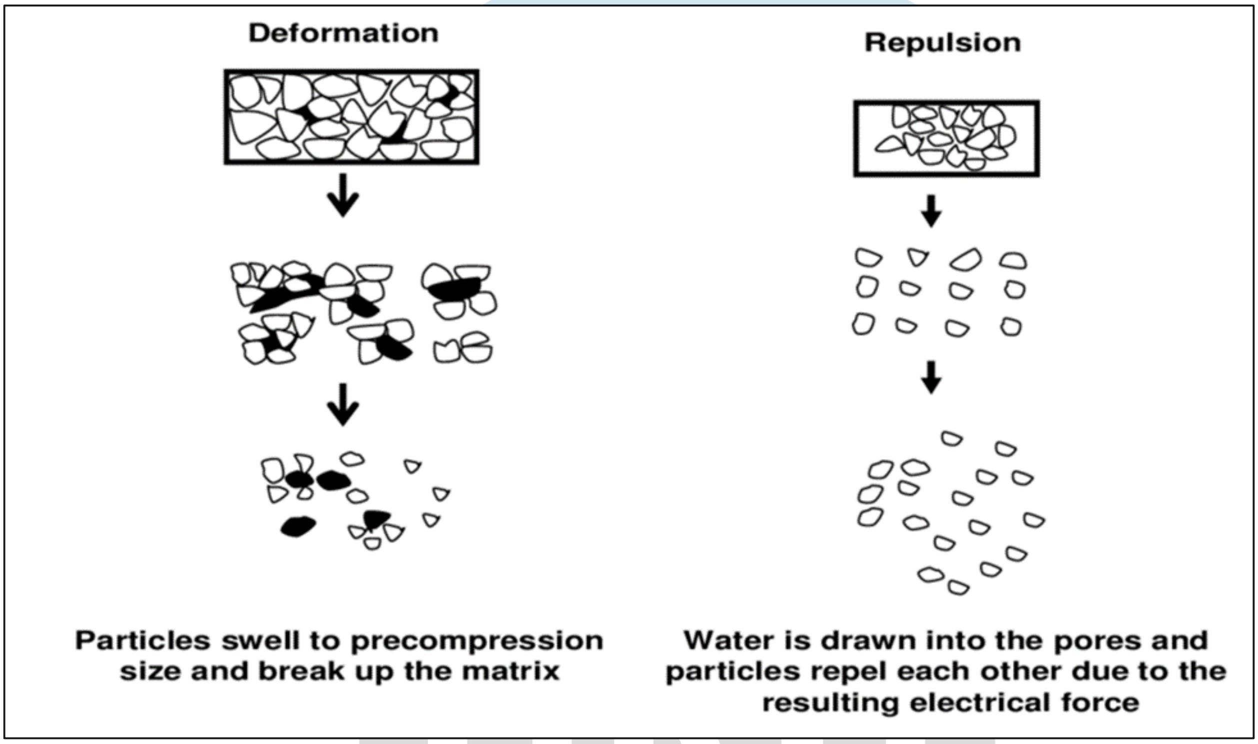


Fig.12: Diagrammatic description of Mechanism of Particle/Particle Repulsion and deformation

Advantages of Sugar Based Excipients:

- High doses can be used, and the final pill weight can be greater than with other methods.
- Easiest way to manufacture the tablets.
- Excipients that are readily available and conventional tools are used.
- A limited no. Of processing steps are involved

3.Emulsifying agents

Because they enable quick medication release without the need for chewing, swallowing, or water consumption, emulsifying agents are essential in the development of fast-dissolving tablets. Aside from increasing bioavailability, emulsifying agents help stabilize immiscible mixtures. Fast-dissolving tablets can be made with a variety of emulsifying agents, including alkyl sulphates, propylene glycol esters, lecithin, sucrose esters, and others. These can range in weight percentage from 0.05% to 15% of the final composition. [11,19]

4.Lubricants

Lubricants Reduce grittiness and aid in the transit of drugs from the oral cavity to the stomach, while they are not necessary excipients, and can help make tablets more palatable when they break down in the mouth. [7]

5. Flavors (taste masking agents) and Sweeteners

By adding tastes and taste-masking ingredients, the products are made more edible and enticing for patients. Some active compounds lose their bitter and disagreeable tastes when these Ingredients are added. Natural and synthetic tastes can both enhance the organoleptic qualities of fast-dissolving tablets. In addition to natural sweeteners like aspartame, sodium saccharin, sugar alcohols, and sucralose, there are numerous other sweeteners available, such as sugar, dextrose, and fructose. The addition of sweeteners gives the composition bulk and a tasty flavor. (11,19)

6. Antiadherents

Antiadherents are used to reduce the adhesion between the powder (granules) and the punch faces in order to prevent sticking to tablet punches. They also aid in preventing pills from sticking. Magnesium stearate is the most commonly used ingredient.

7. Binders

Binder holds the parts of a tablet collectively. Binders provide low active dosage tablets volume and ensure that tablets and granules can be made with the required mechanical strength. Typically, binders include cellulose ethers like hydroxypropyl cellulose (HPC), xylitol, sorbitol, or maltitol, as well as saccharides and their derivatives including sucrose, lactose, starches, microcrystalline cellulose, and gelatin. Polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) are examples of synthetic polymers.

8. Disintegrants

When wet, disintegrants grow and disappear. In the digestive tract, this causes the pill to disintegrate, releasing the active components for absorption.

Types of disintegrants include:

- Water uptake facilitators
- Tablet rupture promoters

Example: cross linked polyvinyl pyrrolidone (crospovidone), cross linked sodium Carboxymethyl cellulose (croscarmellose Sodium), sodium starch glycolate.

9. Fillers or diluents

A tablet or capsule's size is increased by fillers, which reduces production costs and improves usability. A good filler should be neutral to the other ingredients in the formulation, non-hygroscopic, affordable, and preferably tasteless or pleasant. Tablets and hard gelatin capsules frequently contain pure plant filler, also known as plant cellulose. The popular tablet filler calcium phosphate dibasic is another one. More examples of fillers include lactose, sucrose, glucose, mannitol, sorbitol, calcium carbonate, magnesium stearate, and vegetable fats and oils.

10.Colours

Colours are added to formulations to improve their visual appeal. Because it makes it straightforward to identify a drug, colours homogeneity is essential**.**

11.Glidants

Utilizing sublimating agents including camphor, menthol, and thymol was studied. The disintegration time (30 s) was further slashed with the addition of camphor, although the percentage of friability increased.[20]

12. Agents that Sublimate

Utilizing sublimating agents including camphor, menthol, and thymol was studied. When camphor was added, the disintegration time (30 s) was reduced even more, but the percentage of friability increased.[20]

Natural Polymers used in FDT:

S. no.	Natural polymer	Marketed drug	Disintegration time	Concentration used
1	Chitin and chitosan	Cinnarizine	60 sec	3% w/w
2	Guar gum	Glipizide	30 sec	1% w/w
3	Gum karaya	Amlodipine, granisetron hydrochloride	17.10 sec	4% w/w
4	Agar and treated agar	Theophylline	20 sec	1-2% w/w
5	Fenugreek seed mucilage	Metformin hydrochloride	15.6 sec	4% w/w
6	Soy polysaccharide	Lornoxicam	12 sec	8% w/w
7	Gellan gum	Metronidazole	155 sec	4% w/w
8	Mango peel pectin	Aceclofenac	11.59 sec	0.1–4% w/w
9	*Lepidium sativum* mucilage	Nimesulide	17 sec	5–15% w/w
10	*Plantago ovata* seed mucilage	Granisetron HCl	17.10 sec	5% w/w
11	Aegle marmelos gum	Aceclofenac	8–18 min	6% w/w
12	Locust bean gum	Nimesulide	13 sec	10% w/w
13	*Lepidium sativum*	Nimesulide	17 sec	10% w/w
14	*Mangifera indica* gum	Metformin HCL, paracetamol	3–8 min	6% w/w
15	*Hibiscus rosa-sinensis* mucilage	Aceclofenac	20 sec	6% w/w
16	Dehydrated banana powder	Ondansetron HCl/propranolol, gabapentin	15–36 sec	6% w/w

Table 5: Natural Polymers used in FDT [21]

Evaluation parameter of FDT:

1. Hardness
2. Weight variation
3. Friability
4. Dissolution
5. Wetting Time
6. Disintegration
7. Water Absorption ratio
8. In-vitro dispersion time

1) Hardness

The force needed to shatter the tablet across the test is a good indicator of the strength of the tablet. For uncoated tablets, a hardness of roughly 3-5 kg/cm2 is sufficient for measuring force in kilograms. The Monsanto hardness tester was used to measure the tablets' hardness. [12]

Mechanical Strength:

Tablets should have enough durability to withstand mechanical shocks during production, packaging, and shipping. When evaluating a tablet's mechanical strength, two crucial aspects to take into account are frangibility and crushing strength.

Crushing Strength:

The amount of force required to break a tablet by contraction in the radial direction is known as the crushing force, and it is a crucial component in the formulation of mouth dissolve tablets since excessive crushing force significantly reduces the time it takes for the tablet to dissolve. The current investigation evaluated the tablet's resistance to crushing using Pfizer hardness testers. Three normal compliances are provided.

2) Weight variation

To verify for weight variation, 20 pills were randomly chosen from the lot and individually weighed. Table No.6 displays the weight variation specification according to the I.P. [18]

Average weight of tablet (According to IP /BP)	Limit	Average weight of tablet (According to USP)
80 mg or less	10%	130 mg or less
More than 80 mg or less than 250 mg	7.5%	130 mg or 324 mg
250 mg or more	5%	More than 324 mg

Table 6: Weight variation specification as per I.P

3) Friability:

Tablets' mechanical toughness is assessed. The Roche friabilator was used to determine the frangibility using the following method. A pre-weighed pill was placed inside the friabilator. The tablets are dropped at a distance of 6 elevation with each rotation of the plastic chamber that makes up the friabilator. The tablets were spun in the friabilator for at least four twinkles. The loss in weight of the pill is the indicator of frangibility and is expressed as a chance as follows after being dusted and checked again at the end of the test. Frangibility is equal to 100 times the original weight divided by the weight lost. (4)

4) Dissolution:

USP 2 Paddle apparatus was used and paddle was allowed to rotate at 50 rpm. phosphate buffer (PH 6.8) (900 ml) was used as a dissolution medium.

5) Wetting time:

In a little Petri dish with 6 ml of water, a piece of tissue paper that had been folded twice was placed. The amount of time needed for the paper to completely wet was measured after placing a tablet on it. Next, the wet Tablet was weighed. The following equation was used to obtain the water absorption ratio, R.

R=10(wa/wb) where,

Wb is weight of tablet before water absorption & wa is weight of tablet after water Absorption.

6) Disintegration: Disintegration in oral cavity

Six healthy volunteers who received tablets made with the ideal formulation were asked to record the amount of time it took for the tablets to completely dissolve in their mouths.

7) Water absorption Ratio:
A towel paper that had been folded twice was put in a little Petri dish with 6 cc of water. After setting a tablet on the paper, the amount of time needed for it to completely wet was calculated. The wet Tablet was subsequently counted. R = 10(wa/wb), where Wb is the weight of the tablet before water immersion and wa is the weight of the tablet after water immersion, was used to calculate the water immersion rate.

8) In-vitro dispersion time:
The amount of time it took for a tablet to completely dissolve in 10 ml of phosphate buffer solution, which had a pH of 6.8 at 37+0.5°C, was measured. [18]

<u>Challenges of Fast Dissolving Tablet's:</u>
Despite the advantages of this formulation, it faces number parameters that come across as a challenge. These are Listed below

Sr. no	Challenges	Description
1	Mechanical strength and disintegration time	MDTs are frequently made to disintegrate in less a minute. Maintaining strong mechanical strength at this time is a major difficulty. Many MDTs are sensitive, and when they are packed, shipped, or handled, they all break down. The process of decommissioning would be delayed if the mechanical capacity were increased.
2	Mouth feel	The tablet does not break up into larger pieces in the mouth. After the tablet dissolves, the fragments it produces should be as small as possible. The tablet should leave very little or no aftertaste in the mouth after oral intake.
3	Palatability	Since most medications are undesirable, the flavour of the tablet should be concealed.
4	Mechanical strength	In order to allow ODTs to disperse in the oral cavity, they are manufactured from incredibly porous and soft modelled matrices or packed in very weak compressing strength tablets, which makes them fragile and/or brittle and frequently necessitates a professional pullout blister packaging that can fit the bill.
5	Hygroscopic property	Many other doses disintegrating oral tablets are hygroscopic and under natural circumstance of humidity and temperature, cannot retain physical integrity. They also need moisture protection which needs special product packaging.
6	Cost	In terms of the final product cost, the technologies adopted for an ODT should be appropriate.
7	Taste masking	The bitter taste of drugs is masked effectively; therefore, the taste in the oral cavity is not felt.

Table 7: Challenges faced while preparing FDT

<u>Patent on Fast Disintegrating Drug delivery system:</u>

Sr. No.	Author	Drug	Method/polymer	Inference
1	Lee *et al.* (2013)	Megestrol	Spray drying	Quicker dissolve and mask the bitter taste of drugs.
2	Szamosi *et al.* (2013)	Phenyl Propano-Lamine HCl	Direct compression	Melt at 37. c and low compression force.
3	Constantine (2011)	Ondasetron	Polyethylene glycol	Used of the bioactive agent and in the treatment of dysphagia.
4	Singh *et al.* (2006)	Nimesulide	Sodium starch glycolate	Dissolve or disintegrate in digestive organs.
5	Aggarwal et al. (2005)	Galanthamine	Direct compression	Used in Alzheimer's disease.
6	Callihan et al. (2005)	Aspirin	Direct compression	Mannose provide rapid dis-integration anddissolution.
7	Szamosi et al. (2005)	Ibuprofen	Direct compression	Provide excellent mouth feel.
8	Khawla et al. (2004)	Ibuprofen	Melt extrusion	Very low compression force.

9	Callihan et al. (2004)	Caffeine	Direct compression	Rapid dissolution.
10	John et al. (2003)	Active Substance	Freeze drying	Rapid disintegration.
11	Abu-lzzakawla et al. (2005)	Ibuprofen	Direct compression	Low melting point of compound use.
12	William et al. (2001)	Efavirenz	Wet granulation	Used in HIV.
13	Gilis et al.(2000)	Galanthamine HBr	Direct compression	Used in treatment of Alzheimer’s dementia.
14	Warner Lambert Co. et al. (1998)	Active substance	Direct compression	Use low density granules.
15	Makino et al. (1996)	Active substance	Compression molding	High adequate strength disintegration and dissolving rate

Table 8: Patent on FDD delivery system:

List of commercially available FDTs:

Brand Name	**Drug**	**Company Name**
Maxalt-MLT	Rizatriptan Benzoate	Merck
Mosid MT	Mosapride	Torrent
Nulev	Hyoscyamine sulfate	Schwarz Pharma
Nimulid MD	Nimusulide	Panacea
Orthoref MD	Rofecoxib	Biochem
Olanex Instab	Olanzepine	Ranbaxy
Pepcid ODT	Famotidine	Merck
Rofaday MT	Rofecoxib	Lupin
Torrox MT	Rofecoxib	Torrent
Valus	Valdecoxib	Glenmark
Zotacet MD	Cetrizine Hcl	Zota Pharma
Zyprexa	Olanzapine	Eli lilly
Zofran ODT	Ondansetron	GSK
Zomig ZMT and Rapimelt	Zolmitriptan	Astra Zeneca
Claritin redi Tab	Loratidine	Schering plough Corp., USA
Olanex instab	Olanzapine	Ranbaxy lab. Ltd. New-Delhi, India
Romilast	Montelukast 0	Ranbaxy lab. Ltd. New-Delhi, India
Romilast	Montelukast	Ranbaxy lab. Ltd
Felden fast melt	Piroxicam	Pfiser Inc., NY ,USA

Table 9: Marketed product [3]

Conclusion:

In terms of market share, lifecycle management, and development lead times, FDTs are a rapidly evolving technology. A third of the population, primarily the elderly and young, have swallowing issues, which makes it challenging for them to take their oral tablet prescriptions as directed and lowers the overall efficacy of therapy. Fast dissolving tablets are a brand-new kind of tablet that combine the advantages of simple administration and the convenience of dosing without water or other liquids. Fast-dissolving tablets are designed to dissolve or break down in saliva in less than 60 seconds, frequently between 5 and 60 seconds. Fast-dissolving tablets provide greater patient compliance and acceptance when compared to conventional oral dosing forms. Additionally, they might possess superior biopharmaceutical properties, bioavailability, increased efficacy, practicality, and safety. It is projected that FDT will grow significantly and quickly in the near future as a result of advances in scientific research and the development of new excipients, which have created a competitive, future-ready market for pharmaceutical drug delivery systems.

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