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MOUTH DISSOLVING TABLETS: A REVIEW

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ABSTRACT

Mouth dissolving Drug Delivery Systems (MSDDS) have the unique property of rapidly disintegrating and/or dissolving and releasing the drug as soon as they come in contact with saliva, thus obviating the requirement of water during administration. Mouth dissolving tablets constitute an innovative dosage form that overcomes the problems of swallowing and provides a quick onset of action. Orally disintegrating tablets provide an advantage particularly for paediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. This review describes the various disintegrants employed and different patented technologies and their products, and their mechanism of action and evaluation tests, marketed formulations of MDDS. This article also reviews the earlier applications and methodologies of taste masking and also emphasize on the recent developments and approaches of bitterness reduction for orally used pharmaceuticals

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Key Words

Mouth dissolving tablets, patented technologies, superdisintegrants, Taste masking.

INTRODUCTION

The tablet is the most widely used dosage form existing today because of its convenience in terms of self administration, compactness and ease in manufacturing. However, geriatric, paediatric and mentally ill patients experiences difficulty in swallowing conventional tablets, which is common among all age groups, especially in elderly and dysphasic patients ^[1] which leads to poor patient compliance. To overcome these problems, scientists have developed innovative drug delivery system know as mouth dissolving/disintegrating tablets (MDTs) ^[2].

This dosage form dissolves and disintegrates in the oral cavity within minutes without need of water or chewing. This formulation is useful in administration of drug in paediatrics, geriatric patients ^[3]. Mouth dissolving tablets are also known as Fast-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving tablet. Suitable drug candidates for such systems include neuroleptics, cardiovascular agents, analgesics, antiallergics and drugs for erectile dysfunction ^[4]. It has been shown in Table 1.

Most Mouth dissolving tablets contain substances to mask the bitter taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients ^[4,5]. MDTs are formulated

mainly by two techniques first the use of superdisintegrants like Cross linked carboxymethyl cellulose (Croscar- meliose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. Another method is maximizing pore structure of the tablets by freeze drying and vacuum-drying. Mouth dissolving drug delivery system emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and gelatin capsules. Hence they do not comply with prescription, which results in non-compliance and ineffective therapy. In some cases such as motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult. Paediatric and geriatric patients experience particularly this difficulty. Such problems can be resolved by means of mouth dissolving tablet. When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.

Table 1: Some of Promising Drug Candidates for Mouth Dissolving Tablets ^[6]

Sr no	Category	Examples
1	Antibacterial agents	Ciprofloxacin, tetracycline, erythromycin rifampicin, penicillin, doxycyclin, nalidixic acid, trimethoprim, sulphacetamide,
2	Anthelmintics	Albendazole, mebendazole, thiabendazole, ivermectin, praziquantel, pyrantel embonate, dichlorophen etc.
3	Antidepressants	Trimipramine maleate, nortriptyline HCl, trazodone HCl, amoxapine.
4	Antidiabetics	Glibenclamide, glipizide, tolbutamide, tolazamide.
5	Analgesics/anti-inflammatory	Diclofenac sodium, ibuprofen, ketoprofen, mefenamic acid, naproxen, oxyphenbutazone, indomethacin, piroxicam, phenylbutazone, etc.
6	Antihypertensives:	Amlodipine, carvedilol, diltiazem, felodipine, minoxidil, nifedipine, prazosin HCl, terazosin HCl etc.

7	Antiarrhythmics	Disopyramide, quinidine sulphate, amiodarone HCl, etc
8	Antihistamines	Acrivastine, cetirizine, cinnarizine, loratadine, fexofenadine, trinrolidine etc
9	Anxiolytics, sedatives hypnotics and neuroleptics	Alprazolam, diazepam, clozapine, amylobarbitone, lorazepam, haloperidol, nitrazepam midazolam phenobarbitone, thioridazine,
10	Diuretics	Acetazolamide, clorthiazide, amiloride, furosemide, spironolactone, bumetanide ethacrynic
11	Gastro-intestinal agents	Cimetidine, ranitidine HCl, famotidine, domperidone, omeprazole, ondansetron HCl, granisetron HCl, etc.
12	Corticosteroids	Betamethasone, beclomethasone, hydrocortisone, prednisone, prednisolone, methyl prednisolone, etc.
13	Antiprotozoal agents	Metronidazole, tinidazole, omidazole, benznidazole, clioquinol.

Table 2: Common reasons and conditions for using ODT ^[7]

Medication type	Indication
Fast – acting	Pain , fever, heartburn, diarrhoea, migraine, anxiety,
Complian- cecritical	Parkinson’s disease, Alzheimer’s disease, psychosis, Hypertension,
Paediatric	Cough/cold/allergy, Pain, fever, ADHD

Ideal properties of MDT:

1) Not require water or other liquid to swallow but it should dissolve or disintegrate in the mouth within matter of seconds^[6,7].

2) Be compatible with taste masking.

3) Be portable without fragility concern.

4) Have a pleasing mouth feel.

Leave minimal or no residue in the mouth after oral administration.

Exhibit low sensitivity to environmental conditions as humidity and temperature

More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and oesophagus which may produce rapid onset of action^[8,9]

Be adaptable and amenable to existing processing and packaging machinery.

Allow the manufacture of tablets using conventional processing and packaging Equipments at low cost. ^[10]

Allow high drug loading

Have sufficient strength to withstand the rigors of the manufacturing process and post manufacturing handling Easily dissolve or disintegrate in saliva within a few seconds

Advantages of MDTs

^[4-12]

Rapid drug therapy intervention

Bitter taste can be masked by use of flavour and sweetener to produce good mouth feel particularly for paediatric patients

The risk of choking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety. This is beneficial for travelling patients and busy people, who do not have easy access to water.

Accurate dosing as compared to liquids.

First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.

MAIN INGREDIENTS USED IN PREPARATION OF MDT:

Important ingredients that are use should allow quick release of drug resulting in faster dissolution. This includes both the actives and the excipients.

Super disintegrants:

Use of disintegrants is the basic approach in development of MDTs. Disintegrants play a major role in the disintegration and dissolution of MDT.

Super disintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases, which promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution^[13-15].

Table 3: Superdisintegrants employed in MDT^[16]

Super Disintegrants	Nature	Mechanism of Action	Brand Names
Crosscarmellose	Modified cellulose or Cross linked Cellulose	Wicking due to fibrous Structure swelling with Minimal gelling	Ac-Di-Sol Nymce 25 X
Crosspovidone	Cross linked PVP	Water wicking, swelling and possibly some deformation recovery	Kollidon Polyplasdne
Aliginic acid NF	Cross linked Aliginic acid	Wicking action	Satialgine
Soy Polysaccharides	Natural disintegrants	--	EMCOSOY
Calcium silicate	--	Wicking action	--
Sodium starch Glycolate	Modified starch	Rapid and extensive swelling with minimal gelling	Explotab Primogel
Ion exchange resin	Resins		Amberlite (IPR 88)
L-HPC	Low hydroxyl propyl cellulose	Both swelling and wicking	--
Acrylic acid derivatives	Poly (Acrylic acid) Superporous	Wicking action	--

MECHANISM OF ACTION OF DISINTEGRANTS:

1. By capillary action.
2. By swelling.
3. Because of heat of wetting.
4. Due to release of gases.
5. By enzymatic action.

6. Due to disintegrating particle/particle repulsive forces.

7. Due to deformation.

1. By capillary action:^[17]

When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. For these types of disintegrants,

maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

2. By swelling:

Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

3. Because of heat of wetting (air expansion):

When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet .

4. Due to release of gases:

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet.

5. By enzymatic reaction:

Here, enzymes present in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration. Actually due to swelling, pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

Table.4: List of drugs using flavours and sweeteners: ^[19-26]

Sr no	Drug(s)	Taste masking agent(s)
1	Aspirin	Sodium phenolate
2	Chlorpheniramine, Phenyl propanolamine	Sod. bicarbonate, citric acid, orange/cream flavour
3	Famotidine	Sod. bicarbonate, citric acid, lemon flavour

6. Due to disintegrating particle/particle repulsive forces:

Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

7. Due to deformation:

Hess had proved that during tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. The swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch.

Sugar based excipient:

Sugar based excipients are used for taste masking and as bulking agents. Most of the drugs are having unpleasant or bitter taste. So taste masking is necessary in most of the cases. Sorbitol, mannitol, xylitol, dextrose, fructose, etc. are mainly used. Aqueous solubility and sweetness impart a pleasing mouth feel and good taste masking ^[18].

TRADITIONAL TASTE MASKING TECHNIQUES IN ORAL PHARMACEUTICALS:

Taste masking using flavours and sweeteners:

4	Ibuprofen	Sod. Citrate, dehydrate, sod. saccharin, refined sugar
5	Theophylline	D-sorbitol, sodium saccharin, sodium glutamate, and vanilla essence
6	Acetaminophen	Sod. bicarbonate, citric acid, cherry flavour
7	Caffeine	Starch, lactose, and mannitol

Taste masking using Lipophilic Vehicles: -

It is the property of oils, surfactants, poly alcohols and lipids to increase the viscosity in the mouth

and to coat the taste buds and therefore they are potential taste masking agents

Table.5: List of drugs and Lipophilic Vehicles¹

Sr no	Drug(s)	Taste masking agent(s)
1	Isoprothiolane	Hydrogenated oil and HPMC
2	Acetaminophen	Molten stearyl stearate
3	Talampicillin HCl	Magnesium aluminum silicate & soyabean lecithin
4	Clarithromycin	Glyceryl monostearate and AMCE
5	Indeloxazine HC	Hydrogenated oil and surfactants

Taste masking by Coating with Hydrophilic Vehicles: -

Carbohydrates can be used as a coating material to mask the taste of orally administered drugs. Various

forms of proteins have been used extensively for taste masking.

Table.6: List of drugs and Hydrophilic Vehicles^[3, 32-40]

Sr no	Drugs	Polymer(s) used
1	Pinaverium bromide	Cellulose or shellac
2	Ibuprofen	Methacrylic acid copolymer (Eudragit)
3	Sparfloxacin	L-HPC, EC, HMC/EC, HPMC, Tio ₂ , sucrose, fatty acid ester mixture
4	Amoxicillin trihydrate	MCC, L-HPC
5	Clarithromycin	Carbopol, PVP
6	Roxithromycin	PEG, Eudragit L 100–55
7	Cefuroxime axetil	Eudragit L-55 and RL
8	Pirenzepine & Oxybutynin	Eudragit E-100, MCC, HPC
9	Levofloxacin	Eudragit E100, cellulose acetate

Taste masking by Ion-Exchange Resins (IERS):

To stabilize the sensitive components, to sustain the drug release, to disintegrate tablets and to mask taste, ion-exchange resins are used in formulations.

Table 7: List of drugs and taste masking ion exchange resins ^[41-45]

Sr no	Drug(s)	Resin/complexing agent
1	Carbetapentane citrate	Cyclodextrin

2	Ibuprofen	Hydroxypropyl b-cyclodextrin
3	Diphenhydramine HCl	Indion CRP 244, indion CRP 254
4	Buflomedil	Amberlite IRP 69
5	Orbifloxacin	Amberlite IRP 69

MDTs with Patented Taste Masking Technology**Table .8: Patented Technology**

Sr no	Technology	Mechanism of Action
1	CIMA Labs'	coating of drug with dissolution retarding excipient
2	Microcaps	microencapsulation by coacervation-phase separation technique
3	Solutab	coating of drug with sustained release agent followed by coating with enteric polymer and finally with mannitol
4	OraQuick	produces microspheres, known as MicroMask
5	AdvaTab	combination of Microcaps technology for taste masking and Diffuscap controlled release technology

APPROACHES FOR PREPARATION OF MDT:

1. Freeze-drying or lyophilisation
2. Sublimation
3. Spray drying
4. Moulding
5. Mass extrusion
6. Direct compression
7. Cotton-candy process
8. Nanonization.
9. Fast dissolving films.
10. Melt granulation.

1. Freeze drying or lyophilisation:

A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze-dried forms offer more rapid dissolution than other

available solid products. The lyophilisation process imparts glossy amorphous structure to the bulking agent and sometimes to the drug ^[46]. The ideal drug characteristics for this process are relative water insolubility with fine particle size and good aqueous stability in suspensions. The advantage of using freeze-drying process is that pharmaceutical substances can be processed at non elevated temperature, thereby eliminating adverse thermal effects. However high cost of equipment and processing limits the use of this process. Other disadvantages include lack of resistance necessary for standard blister packs of the final dosage forms ^[47-48, 4].

2. Sublimation:

The sublimation process involves addition of some inert volatile substances like urea, urethane, naphthalene, camphor, etc to other excipients and the

compression of blend into tablet. Removal of volatile material ^[49] by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. To improve the porosity, volatile substances such as camphor can be used in tableting process, which sublimated from the formed tablet 33 Developed MDTs utilizing camphor, a subliming material that is removed from compressed tablets prepared using a mixture of mannitol and camphor. Camphor was sublimated in vacuum at 80°C for 30 min after preparation of tablets ^[50]

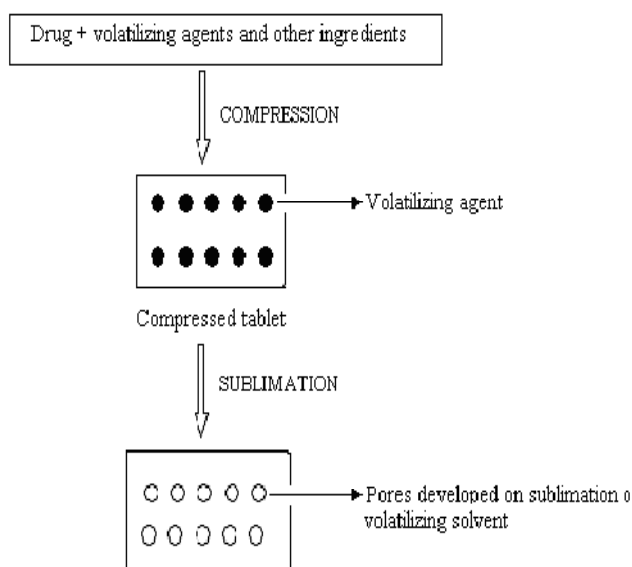


Fig. 1.5: Schematic Diagram of Sublimation Technique for Preparation of MDT

3. Spray drying:

The spray drying produces highly porous and fine powders as the processing solvent is evaporated during the process. In this method to prepare MDTs hydrolyzed and non- hydrolyzed gelatin were used as supporting matrix, mannitol as bulking agent and sodium starch glycolate or crosscarmellose sodium as superdisintegrant. Disintegration and dissolution were further increased by adding acidic substances like citric acid or alkali substance like sodium bicarbonate. This

formulation technique gives porous powder and disintegration time < 20 sec ^[5].

4. Moulding:

Molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution. They disintegrate very quickly because these are made from water soluble excipients ^[51]. Different moulding techniques can be used to prepare mouth-dissolving tablets:

a. Compression moulding: The powder mixture previously wetted with a solvent like ethanol/water is compressed into mould plates to form a wetted mass.

b. Heat moulding: A molten matrix in which drug is dissolved or dispersed can be directly moulded into Mouth dissolving tablets ^[52].

c. No vacuum lyophilisation: This process involves evaporation of solvent from a drug solution or suspension at a standard pressure ^[53].

5. Mass extrusion: ^[54, 55]

In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then the softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and there by masking their bitter taste.

6. Direct compression methods:

This technique is easy way to formulate MDTs since limited number of processing steps, low manufacturing cost. The disintegration and dissolution of directly compressed tablets depends on single or combined effect of disintegrant, water soluble excipients and effervescent agents. Tablet size and

hardness strongly affect the disintegrant efficacy. Hard and large tablets have more disintegration time than normally required. Very soft and small tablets have low mechanical strength. So, an optimum kind and concentration of disintegrant should be chosen to achieve quick disintegration and high dissolution rates [56].

Advantages

- 1) High doses can be accommodated and final weight of the tablet can exceed that of other methods
- 2) Conventional equipment and commonly available excipients are used [57]

7. Cotton candy process:

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimics cotton candy. Cotton candy process [58] involves formation of matrix of polysaccharides or saccharides (floss)- sucrose, dextrose, lactose and fructose at temperatures ranging between 180–266°F by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to MDTs [59].

8. Nanonization:

In this process, the particles of the drug are reduced in size to nanoparticles by milling the drug in the proprietary wet milling process. The agglomeration can be prevented by surface adsorption of the nanocrystals. These are then compressed and changed into a tablet. This technique is advantageous for less water soluble drugs. The bioavailability of the drug is increased as the disintegration time is reduced to a significant extent [64].

9. Fast dissolving films:

This is a new technique through which medications can be taken more conveniently. In this technique, a non-aqueous solution is prepared containing water soluble film forming polymers (carboxy methylcellulose, hydroxypropyl methylcellulose,

hydroxyl ethylcellulose, hydroxyl propylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking ingredients, which is allowed to form a film after evaporation of solvent [56]. In case of a bitter drug, resin adsorbate or coated microparticles of the drug can be incorporated into the film [60]. This film, when placed in mouth, melts or dissolves rapidly, releasing the drug in solution or suspension form. The features of this system include paper thin films of size less than 2X2 inches, dissolution in 5 sec, instant drug delivery and flavoured after taste [61].

10. Melt granulation:

Abdelbary *et al.* prepared ODT by incorporating a hydrophilic waxy binder (super polystate) PEG- 6-Sterate. Superpolystate is a waxy material with a melting point of 33–37°C and a hydrophilic/lipophilic balance of 9. It is not only acts as a binder and increases the physical resistance of tablets, but also helps the disintegration of tablets as it melts in the mouth and solubilizes rapidly leaving no residue. Super polystate was incorporated in the formulation of ODT by melt granulation technique where granules formed by the molten form of this material. Crystallized paracetamol was used as model drug and in addition the formulation included mannitol as a water-soluble excipient and croscarmellose sodium as disintegrating agent [62].

PATENTED TECHNOLOGIES FOR PREPARATION OF MDT: Zydis Technology:

It was the first marketed technology developed by R.P.Scherer, Inc. patented as the Zydis technology. Zydis, the best known of the fast dissolving/disintegrating tablet preparations, and the tablet dissolves in the mouth within seconds after placement on the tongue. Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatine.

Advantages:

- 1) The product is very lightweight and fragile, and must be dispensed in a special blister pack

Disadvantages:

- 1) The Zydys formulation has poor stability at higher temperatures and humidity. It readily absorbs water, and is very sensitive to degradation at humidity greater than 65%.^[48,63]

Durasolv technology:

The tablets made by this technology which was developed by CIMA labs, consist of a drug, fillers and the lubricants. The tablets are prepared by conventional tableting equipment and have good rigidity. They can be packed in the conventional tableting equipment and have good rigidity^[51]

Advantages:

- 1) This technology is good for tablets having low amount of active ingredients.

Disadvantages:

- 1) The technology is not compatible with larger doses of active ingredients, because the formulation is subjected to high pressure during compaction. The drug powder coating in Durasolv may become fractured during compaction, exposing the bitter tasting drugs to the patient taste buds^[7]

Orasolv technology:

This technology is patented by CIMA Labs. This includes use of effervescent disintegrating agents compressed with low pressure to produce the MDTs. The evolution of carbon dioxide from the tablet produces fizzing sensation, which is a positive organoleptic property. Concentration of effervescent mixture usually employed is 20-25% of tablet weight^[64].

Because of the soft and fragile nature of OraSolvR tablets, a special packaging system, known as PakSolvR, was developed to protect the tablets from breaking during transport and storage. PakSolvR is a “dome-shaped” blister package that prevents the vertical movement of the tablet within the depressions, because the diameter of the lower portion of the dome is too narrow to accommodate the tablet. PakSolvR also offers light, moisture, and child resistance^[65].

Wow tab technology:

The WOW in the WOWTAB signifies the tablet is to be given without water. This technology utilizes sugar

and sugar-like excipients. The two different types of saccharides having high moldability like maltose, mannitol, sorbitol, and oligosaccharides.(good binding property) and low moldability like lactose, glucose, mannitol, xylitol (rapid dissolution) are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate^[66].

Pharmaburst technology:

SPI Pharma, New Castle, patents this technology. It utilizes the coprocessed excipients to develop MDTs, which dissolves within 30-40 s. This technology involves dry blending of drug, flavour, and lubricant followed by compression into tablets. Tablets obtained have sufficient strength so they can be packed in blister packs and bottles^[67].

Dispersible Tablet Technology

Lek in Yugoslavia was issued patents for dispersible tablets of dihydroergotoxine^[68] and cimetidine, which were claimed to disintegrate in less than 1 minute when in contact with water at room temperature. Dihydroergotoxine is poorly soluble in water in the free base form. An improved dissolution rate of dihydroergotoxine methanesulphonate was observed with dispersible tablets containing 0.8–10%, preferably about 4% by weight, of an organic acids. One of the essential excipients in the cimetidine formulation was a disintegrating agent. The disintegrating agents include starch or modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose, and cyclodextrin polymers.

Flashtab technology:

Prographarm laboratory has patented the Flashtab technology. This technology involves the preparation of rapidly disintegrating tablet which consists of an active ingredient in the form of microcrystals. Drug microgranules may be prepared by using the conventional techniques like coacervation, extrusion-spheronization, simple pan coating methods and microencapsulation^[69]. Excipients used in this technology comprise two groups of components: disintegrating agents, such as carboxymethylcellulose or

insoluble reticulated polyvinylpyrrolidone; and swelling agents, such as carboxymethylcellulose, starch, modified starch, carboxymethylated starch, microcrystalline cellulose, and possibly directly compressible sugars. The mixture of excipients is prepared by either dry or wet granulation methods^[70].

Nanocrystal technology:^[71]

This is patented by Elan, King of Prussia. Nanocrystal technology includes lyophilization of colloidal dispersions of drug substance and water-soluble ingredients filled in to blister pockets. This method avoids manufacturing process such as granulation, blending, and tableting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drug.

Frosta technology:^[75]

Akina patents this technology. It utilizes the concept of formulating plastic granules and compressing at low pressure to produce strong tablets with high porosity. Plastic granules composed of:

- i. Porous and plastic material,
- ii. Water penetration enhancer, and
- iii. Binder.

The process involves usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 s depending on size of tablet.

Oraquick:

This technology is patented by K.V.S. Pharmaceuticals^[72]. It utilizes taste masking microsphere technology called as micromask, which provides superior mouth feel, significant mechanical strength, and quick disintegration/dissolution of product.

CHARACTERIZATION OF DISINTEGRATE POWDER:

Angle of Repose:

The angle of repose was determined by the funnel method. The accurately weighed powder was taken in a funnel. The height of a funnel was adjusted in such a way that its tip just touches the apex of the heap of the powder. The powder was allowed to flow through funnel freely onto the surface. The diameter of the powder heap was measured and angle of repose was calculated using following equation

$$\tan(\theta) = h/r$$

Where, h and r indicate the height and radius of the powder heap.

Swelling capacity:

Disintegrant (1g) was taken in the measuring cylinder. Then distilled water (10 ml) was poured in it. The measuring cylinder was shaken vigorously for 10 minutes and allowed to stand for 24 hrs at 37 ± 1 OC. Swelling capacity⁵ was expressed as percentage and calculated using following equation,

$$\text{Swelling capacity} = (X_v/X_i) 100$$

Where, X_v : Final volume occupied by swollen material after 24 hrs.

X_i : Initial volume occupied by powder in measuring cylinder^[73].

Compressibility:

The compressibility index (Carr's Index) was determined by using following equation,

$$\text{Carr's Index (\%)} = [(TBD - LBD) \times 100] / TBD$$

Table 9: Patented technologies for fast dissolving tablets

Patented Technology	Basis of Technology	Developing Company	Brand Names	Drug Release
Zydis	Lyophilization	R.P.Scherer, Inc.	Claritin Reditab	Dissolves in 2 -10 s
Orasolv	Direct compression	Cima Labs, Inc.	Tempra Quicklets, Zolmig Repimelt	Disintegrates in 5 – 45
Durasolv	Direct compression	Cima Labs, Inc.	NuLev , Zolmig ZMT	Disintegrates in 5 – 45 s
Wowtab	Direct compression	Yamanouchi Pharma Tech. Inc.	Gaster D	Disintegrates in 5 – 45 s
Flashdose	Cotton Candy Process	Fuisz Technology Ltd.	Relivia Flash dose	Dissolves within 1 min.
Flashtab	Direct compression	Ethypharm	Nurofen FlashTab	Dissolves within 1 min
Oraquick	Taste masking	KV Pharm.Co., Inc.	Hyoscyamine Sulfate ODT	--
Advatab	CR Technology	Eurand International	AdvaTab	Disintigreat less than 30 sec.
Ziplets	Direct compression	Eurand International	Cibalgina DueFast	--
Lyoc	Lyophilization	Farmalyoc	Spasfon Lyoc	--
Quicksolv	Lyophilization	Janssen pharmaceuticals	Propulsid Quicksolv, Risperdal M Tab	--

Hydration Capacity (H. C.):

Disintegrant (1g) was taken in the 15 ml tarred centrifuge tube. Then 10 ml of distilled water was added to it and allowed to centrifuge for 10 minutes. After the centrifugation process the tarred centrifuge tube was taken out and inverted to remove the supernat. The decanted tube then weighed on digital balance (Shimadzu) and the hydration capacity 5 was calculated using following equation,

H. C. = weight of hydrate sample/ weight of dry sample.

Density:

The loose bulk density (LBD) and tapped bulk density (TBD) of disintegrant were determined. LBD and TBD were calculated using following equation,

LBD = weight of the powder / volume of the packing

TBD = weight of the powder / tapped volume of the packing^[74].

EVALUATION OF MOUTH DISSOLVING TABLET:^[4, 75]**General Appearance:**

It includes general appearance of a tablet, its visual identity, tablets size, shape, colour, presence or absence of an odour, taste, surface texture, physical

flaws and consistency and legibility of any identifying marking.

Uniformity of weight:

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight.

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

Hardness:

A significant strength of ODT is difficult to achieve due to the specialized processes and ingredients used in the manufacturing. The limit of hardness for the ODT is usually kept in a lower range to facilitate early disintegration in the mouth. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester [76].

Friability test:

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator was employed for finding the friability of the tablets. 20 tablets from each formulation were weighed and placed in Roche friabilator that rotated at 25 rpm for 4 minutes. The tablets were dedusted and weighed again. The percentage of weight loss was calculated again. The percentage of weight loss was calculated using the formula

$$\% \text{ Friability} = [(W1-W2)100]/W1$$

Where,

W1= Weight of tablet before test

W2 = Weight of tablet after test

Dissolution test:

The development of dissolution methods for ODT is comparable to approach taken for conventional tablets and is practically identical when ODT does not utilize taste masking. Commonly the drugs may have dissolution conditions as in USP monograph. Other media such as 0.1 N HCl, pH 4.5 and pH 6.8 buffers should be used for evaluation of ODT in the same way as their ordinary tablet counterparts. Experience has indicated that USP 2 paddle apparatus is most suitable and common choice for dissolution test of ODT tablets, where a paddle speed of 50 rpm is commonly used^[71,54].

In Vivo Disintegration test:

The time for disintegration of ODTs is generally <1min and actual disintegration time that patient can experience ranges from 5 to 30s. The standard procedure are that the test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37°C ± 2°C was used as a disintegration media and the time in second is taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

Uniformity of dispersion:

Two tablets were kept in 100ml water and gently stirred for 2 minutes. The dispersion was passed through 22 meshes. The tablets were considered to pass the test if no residue remained on the screen^[77].

Stability studies^[78, 79]

The best formulation of Gliclazide MFDTs containing (CPV + CCM in 75:25 ratio) were subjected to stability study by keeping them at 40°C/75% RH for 1 month to assess their stability with respect to their physical appearance and release characteristics. The physical characteristics like weight variation, hardness, friability, wetting time, water absorption ratio, disintegration time, mouth feel & in vitro release profile were determined at interval of 15 & 30 days.

FUTURE PROSPECTS OF MDT:

Mouth dissolving tablets can offer several biopharmaceutical advantages such as improved efficiency over conventional dosage forms. For example, they require smaller amounts of active ingredient to be effective, improve absorption profiles, and offer better drug bioavailability than regular tablets and capsules. The safety and efficacy profile of drugs in orodispersible

tablet is same like their conventional tablet dosage form. Based on conventional techniques, new techniques are developed like Zydis, Wow Tab, Orasolv and many more, which leads to getting a patent and new market strategy for orodispersible tablets. This dosage form are gaining market share day by day and becoming a better choice of acceptance. Following are the some marketed product of ODT .

Table .10: Marketed Products of MDT

Trade Name	Active Drug	Manufacturer
Nimulid-MD	Nimesulide	Panacea Biotech, New Delhi, +India
Feldene Fast Melt	Piroxicam	Pfizer Inc., NY, U.S.A
Zyrof Meltab	Rofecoxib	Zydus, Cadila, India
Pepcid RPD	Famotidine	Merck and Co., NJ, U.S.A
Romilast	Montelukast	Ranbaxy Labs Ltd., New Delhi, India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, Ahmedabad, India
Olanex Instab	Olanzapine	Ranbaxy Labs Ltd., New Delhi, India
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Mosid-MT	Mosapride Citrate	Torrent Pharmaceuticals Ahmedabad, India
Febrectol	Paracetamol	Prographarm, Chateaufneuf, France
Maxalt MLT	Rizatriptan	Merck and Co., NJ, U.S.A
Zelapar TM	Selegiline	Amarin Corp., London, UK

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