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REVIEW ARTICLE

New Approach on Rapid Mouth Dissolving Tablets: A Review

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ABSTRACT

Mouth Dissolving Tablet (MDT) technology has been gaining significance now-a-days with wide variety of drugs serving many purposes. Mouth Dissolving Tablets (MDT) has ever increased their demand in the last decade since they disintegrate in saliva in less than 60 seconds. Mouth Dissolving Drug Delivery Systems serves as a major benefit over the conventional dosage forms since the drug gets rapidly disintegrated & dissolves in the saliva without the use of water. In spite of the downside i.e., lack of immediate onset of action; these oral dosage forms have beneficial such as self-medication, increased the patient compliance, ease of manufacturing and lack of pain as comparison to conventional technologies. The objective of this article is to review the development of MDTs, challenges in formulation, he objective of this article is to review the development of MDTs, challenges in formulation, benefit, limitation ,new MDT technologies and evaluation methodologies.benefit, limitation ,new MDT technologies and evaluation methodologies.

KEYWORDS: Mouth Dissolving Drug delivery systems, MDT, conventional technologies, Patient compliance.

INTRODUCTION:

1. MOUTH DISSOLVING TABLET:

Mouth dissolving tablets (MDT) are useful in patients, such as pediatric, geriatric, bedridden, or developmentally disabled, who may face difficulty in swallowing conventional tablets or capsules and liquid orals or syrup, leading to ineffective therapy, with persistent nausea, sudden episodes of allergic attack, or coughing for those who have an active life style. Over the past three decades, mouth dissolving tablets have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance.

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. The reason that the oral route achieved such popularity may be in part attributed to its ease of administration.

All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage forms (solid, dispersion or liquid) must be developed within the intrinsic characteristics of GI physiology. Therefore, a fundamental understanding of various disciplines, including GI physiology, pharmacokinetics, pharmacodynamics and formulation design are essential to achieve a systemic approach to the successful development of pharmaceutical dosages forms. The more sophisticated a delivery system, the greater is the complexity of these various disciplines involved in the design and optimization of the delivery system. In any case, the scientific framework required for the successful development of an oral drug delivery system consists of a basic understanding of the following three aspects.

- Physicochemical, pharmacokinetic and pharmacodynamics characteristics of the drug.
- The anatomic and physiologic characteristics of the GIT.
- Physicochemical characteristics and the drug delivery mode of the dosage form to be designed[1].

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow.

Solid dosage forms are popular because of

- accurate dosage
- self-medication
- ease of administration
- pain avoidance
- Patient compliance.

Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden

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episodes of coughing during the common cold, allergic condition and bronchitis. For these reasons, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Rapidly dissolving or disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people[2].

Mouth dissolving tablets are also called as fast dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. Mouth dissolving tablets are those when put on tongue, disintegrate instantaneously releasing the drug which dissolves or disperses in the saliva .Faster the drug into solution, quicker the absorption and onset of clinical effect.

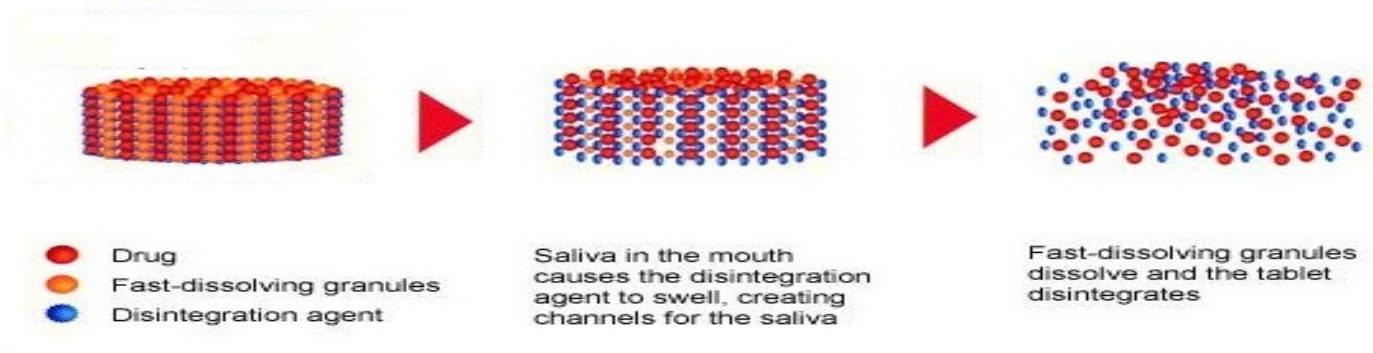

Figure No. 1: Conceptual Diagram of MDT's

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 tablets dosage form. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics[3].

Mouth dissolving drug delivery systems (MDDDS) are a new generation of formulations which combine the advantages of both liquid and conventional tablet formulations and at the same time, offer added advantages over both traditional dosage forms. They provide the convenience of a tablet formulation and also allow the ease of swallowing provided by a liquid formulation. MDDDS offer the luxury of much more accurate dosing than the primary alternative, oral liquids. This segment of formulation is especially designed for dysphagic, geriatric, pediatric, bed-ridden, travelling and psychotic patients who are unable to swallow or refuse to swallow conventional oral formulations. They do not require water for administration, thus are good alternative for travelers and for bed ridden patients. They simply vanish when placed in the mouth, so cannot be hidden in mouth by psychotic patients. These products not only increase the patient's compliance but also fetch large revenues to manufacturers due to line extension of the existing formulation. In the recent past, several new advanced technologies have been introduced for the formulation of mouth dissolving tablets (MDTs) with very interesting features, like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients. The technologies utilized for fabrication of MDDDS include lyophilization, moulding, direct compression, cotton candy process, spray drying, sublimation, mass extrusion, nanonization and quick dissolve film formation. These techniques are based on the principles of increasing porosity and/or addition of superdisintegrants and water soluble excipients in the tablets. The formulations prepared from these techniques differ from each other on the basis of the factors like mechanical strength of final product, drug and dosage form stability, mouth feel, taste, rate of dissolution of the formulation in saliva, rate of absorption from saliva and overall drug bioavailability[5].

Although, numerous technologies had been developed for the fabrication of these unique dosage forms in last two decades, but so far, no standardized technique has been designed or mentioned in pharmacopoeias for their evaluation except in European Pharmacopoeia (EP), which defines Orodispersible tablets as "uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed". EP also specifies that the Orodispersible tablets should disintegrate within 3 minutes when subjected to conventional disintegration test used for tablets and capsules. Orally Disintegrating (OD) tablet technology has been approved by United state Pharmacopoeia (USP), Center for Drug Evaluation and Research (CDER). USFDA defined OD tablet as " A solid dosage form containing medicinal substance , which disintegrate rapidly ,usually within a matter of seconds , when placed upon the tongue"[6].

Despite various terminologies used, Mouth dissolving tablets are here to offer unique form of dug delivery with advantages over the conventional oral solid dosage forms.

1.1. CRITERIA FOR MOUTH DISSOLVING DRUG DELIVERY SYSTEM:[7]

The tablets should:

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasant mouth feel.
- Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition like temperature and humidity
- Allow the manufacture of the tablet using conventional processing and packaging equipment's, at low cost.

1.2. SALIENT FEATURE OF MOUTH DISSOLVING DRUG DELIVERY SYSTEM: [7]

- Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients and patient who refuse to swallow such as pediatric, geriatric & psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- 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 increased.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.
- The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation, product promotion, patent extensions and life cycle management.

Table 1-
Benefits of rapid mouth dissolving tablets
Clinical
Improved oral absorption
Faster onset of action
Minimized first-pass effect
Improved bioavailability
Medical
No tablet or capsule to swallow or chew
Better taste, no water needed
Improved safety and efficacy
Improved compliance
Technical
Accurate dosing compared to liquid products
Contain sugars and other GRAS excipients
Improved stability due to better packaging
Use common process and conventional equipment
Business
Unique product differentiation
Value-added product line extension
Provide exclusive marketing
Extend patent protection

1.3 ADVANTAGES OF MOUTH DISSOLVING TABLETS [7]:

- Administered without water, anywhere, any time.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

- Pregastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.

1.4. LIMITATIONS OF MDT: [8]

- The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

1.5. CHALLENGES IN MOUTH DISSOLVING DRUG DELIVERY SYSTEMS: [9]

1.5.1. PALATABILITY:

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

1.5.2. MECHANICAL STRENGTH:

In order to allow ODTs to disintegrate in the oral cavity, they are made of either very porous and soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, difficult to handle and often requiring specialized peel-off blister packing that may add to the cost.

1.5.3. HYGROSCOPICITY:

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

1.5.4. AMOUNT OF DRUG:

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

1.5.5. AQUEOUS SOLUBILITY:

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

1.5.6. SIZE OF TABLET:

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

2. TECHNIQUES OF MDT FORMULATION:

The fast-dissolving property of the MDTs is attributed to quick ingress of water into tablet matrix resulting in rapid disintegration. Hence, the basic approaches to develop MDTs include:

- Maximizing the porous structure of the tablet matrix.
- Incorporating the appropriate disintegrating agent/agents.
- Using highly water-soluble excipients in the formulation

2.1 TECHNIQUES FOR PREPARING MDT: [10]

Many techniques have been reported for the formulation of Mouth dissolving tablets or Orodispersible tablets.

1. COMPACTION
a. Direct Compression by using Sugar Based Excipients
b. Wet/Dry Granulation using Superdisintegrants
2. Lyophilization
3. Phase transition process
4. Sublimation
5. Tablet Moulding
6. Mass extrusion
7. Spray drying
8. Cotton Candy Process

METHODS FOR DESIGNING MDT:[4, 7, 10]

2.1.1. COMPACTION:

a. DIRECT COMPRESSION BY USING SUGAR BASED EXCIPIENTS:

This method consists of directly compressible blend, which consists of an excipient and an active ingredient. The excipient consists of a disintegrating agent and one hydrophilic diluent selected from the polyols having less than 13 carbon atoms. Polyols most commonly

used are xylitol, sorbitol, mannitol and maltitol. Directly compressible form or various ratios of compressible and powder form of polyols are used in these methods. Disintegrating agents most commonly used are Crospovidone, Croscaramellose sodium and Sodium starch glycollate. In addition to these ingredients, sweeteners and lubricants are incorporated in the formulation. Good aqueous solubility and sweeteners impart a pleasing mouth feel and good taste masking. But not all the sugar based excipients have fast dissolving action and good compressibility and/or compatibility. However, technologies were developed to make use of the sugar-based excipients in the design of fast dissolving tablets.

b. WET/DRY GRANULATION USING SUPERDISINTEGRANTS:

Wet/Dry granulation techniques with superdisintegrants can be used to prepare fast dissolving tablets. Crospovidone, Croscaramellose sodium and Sodium starch glycollate are used as superdisintegrants. Active drug, diluents, binder, lubricants, glidants are used along with disintegrates. In wet granulation technique, disintegrates are added in both wet granulation step and dry blending step. Disintegrating agents have the ability to swell when exposed to GIT fluids resulting in rapid disintegration. Sweeteners and flavors are also added to dry blending step to improve palatability.

2.1.2. LYOPHILIZATION:

Lyophilization can be used to create an amorphous, porous structure that commonly dissolves rapidly. The lyophilization process imparts glossy amorphous structure to the bulking agent and sometimes to the drugs, thus enhancing the dissolution characteristics of the formulation. But this method is not commonly used because of its high cost of equipment and processing. It also produces dosage forms with lack of physical resistance. The most commonly used matrix forming agents are gelatins and sugar based excipients.

2.1.3. PHASE TRANSITION PROCESS:

Tablets were produced by compressing a powder containing two sugar alcohols, with high and low melting points and they are subsequently heated to a temperature between their melting points. Before heating process, the tablets do not have sufficient hardness because of low compatibility. The tablet hardness was increased after heating process, due to the increase of inter particle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol.

2.1.4. SUBLIMATION:

Tablets prepared by a water soluble material like Mannitol, give slow dissolution rates due to low porosity. Porosity can be increased by incorporating subliming agents like Urea, Ammonium bicarbonate, Ammonium carbonate, Camphor to the other tabletting ingredients and the mixture is compressed into tablets. The volatile materials are then removed by sublimation, which generates porous structures. Additionally, several solvents such as water, Cyclohexane, and Benzene can be used as pore forming agent.

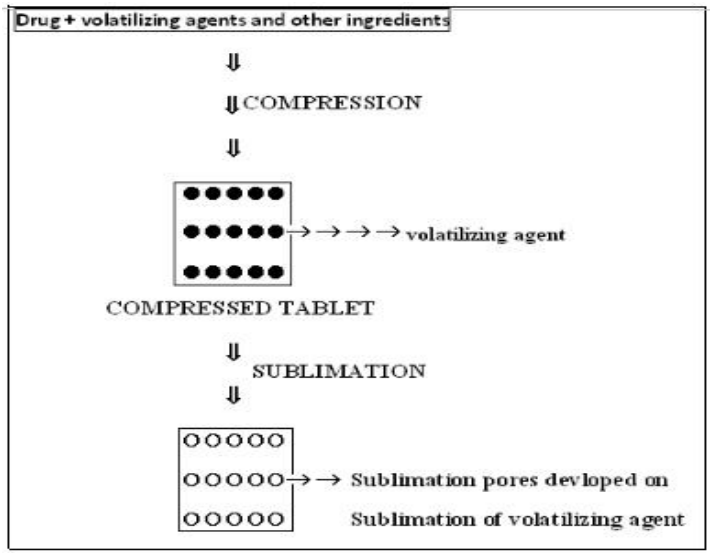

Figure No. 2: - Sublimation method

2.1.5. TABLET MOLDING:

This method consists of suspending an active ingredient and a sugar into agar aqueous solution. Suspension is filled in molds to solidify into a jelly and subsequently dried. Drying can be affected by reduced pressure drying or aeration drying. Additional components like flavor, sweeteners, colors and preservatives may be added to improve taste, stability, appearance, etc.

Another method where sugar, active component, and other excipients are mixed with a small volume of volatile liquid binder to form slightly wet lump. This lump is then forced into molds and evaporated the liquid binder. Sugars, which can be used, are Mannitol or Lactose. These types of products disintegrate or dissolve within 5 to 20 seconds.

2.1.6. MASS EXTRUSION:

This technology involves softening the active blend using the solvent mixture of water-soluble Polyethylene glycol, using Methanol and expulsion of softened mass through the extruder or syringe, to get a cylindrical product and cut into even segments using heated blade to form tablets.

2.1.7. SPRAY DRYING:

Compressing highly porous support matrix, produced by spray drying, with active ingredient gives fast dissolving tablets. The support matrix composed of non-hydrolyzed gelatin or hydrolyzed gelatin, bulking agent, volatizing agent like Ethanol, acidifying or alkalizing agent to maintain the net charge. Most commonly used bulking agents are Mannitol, Sorbitol, Sucrose, Lactose, etc. Croscaramellose sodium, Crospovidone, Sodium starch glycollate and a small amount of effervescent material may be added to assist in the disintegration of the tablet. Additionally sweeteners, flavors and lubricants may be added.

2.1.8. COTTON CANDY PROCESS:

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides 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 ODT. This process can accommodate high doses of drug and offers improved mechanical strength. However, high-processing temperature, limits the use of this process.

3. IMPORTANT PATENTED TECHNOLOGIES FOR FAST DISSOLVING TABLETS:[4, 7, 10]

3.1. Zydis Technology

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

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

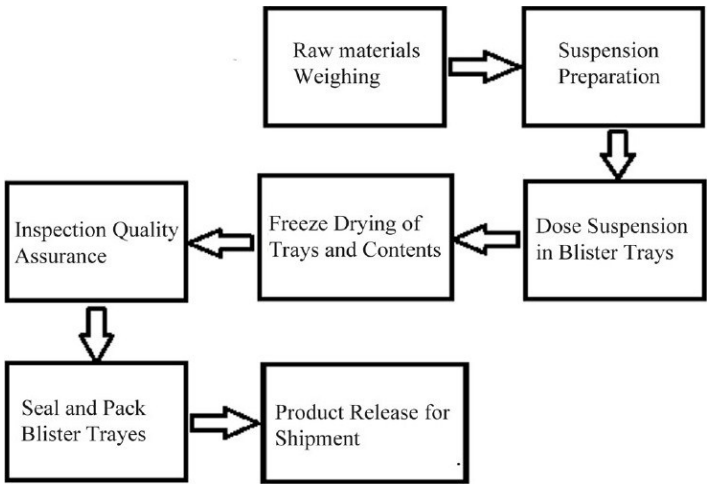

Figure No. 3:- Zydis tablet manufacturing process. : step by step preparation.

3.2. DURASOLV TECHNOLOGY:

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

3.3. ORASOLV TECHNOLOGY:

CIMA labs have developed Orasolv Technology. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique, low compression force in order to minimize oral dissolution time.

Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable.

3.4. FLASH DOSE TECHNOLOGY:

Flash dose technology has been patented by fuisz. Nurofen meltlet, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology & is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of self-binding shear form matrix termed as “floss”. Shear form matrices are prepared by flash heat processing.

3.5. WOW TAB TECHNOLOGY:

Wow tab technology is patented by Yamanouchi Pharmaceutical Co. WOW means “Without Water”. In this process, combination of low mouldable and high

mouldable saccharides is used to obtain a rapidly melting, strong tablet. The active ingredient is mixed with a low mouldable saccharides (e.g. lactose, glucose, and mannitol) and granulated with a highly mouldable saccharides (e.g. Maltose, oligosaccharides) and compressed into tablet.

3.6. FLASH TAB TECHNOLOGY:

Prographarm laboratories have patented the Flash tab technology. Tablet prepared by this system consists of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like coacervation, micro encapsulation and extrusion spheronisation.

3.8. LYOC TECHNOLOGY:

This was the first freeze drying- based technology introduced for ODTs. The process involves preparation of a liquid solution or suspension of the drug containing fillers, thickening agents, surfactants, non-volatile flavoring agents, and sweeteners. This homogenous liquid is deposited in blister cavities and subjected to freeze drying. Advantages of Lyoc compared to other freeze-dried dosage forms include absence of preservatives.

3.9. ORAQUICK TECHNOLOGY:

KV Pharmaceutical's two proprietary taste-masking technologies, FlavorTech and MicroMask , are utilized for developing OraQuick tablets. MicroMask provides taste masking by incorporating a drug into matrix microspheres. The first step involved in formulating the tablet include dissolving the sugar (sucrose, mannitol, sorbitol, xylose, dextrose, fructose, or mannose), and protein (albumin or gelatin) in a suitable solvent such as water, Ethanol, Isopropyl alcohol, and Ethanol– water mixture. The porosity of the product is determined by the quantity of solvent used in the formulation. The solution of the matrix is then spray dried, yielding highly porous granules. The matrix granules are mixed with other excipients such as binder, lubricant, sweeteners, flavors, coloring agent, fillers, disintegrants, surfactants, etc. The drug can be added at this stage in the form of taste-masked granules, otherwise added first in the matrix granule. The granules or powder obtained is then compressed at low compression force to form tablets that are soft and friable but highly porous. After the tablets are compressed, they are subjected to a sintering step. Tablets are sintered in an oven, typically at temperature of about 50°C to 100°C for few minutes to an hour's or at 90°C for about 10 min. During this step, the compressed tablets containing binder (Polyethylene glycol) in the earlier step melts and binds particles to form stronger tablet.

3.10. ADVATAB TECHNOLOGY:

The primary ingredients in the dosage form include sugar alcohols and saccharides with particle size less than 30 µm along with disintegrant and lubricant. The lubricant used in the formulation is added as an external lubricant compared to conventional formulations, which contain an internal lubricant. This make tablets stronger in comparison to conventional tablets, as internal lubricants are hypothesized to decrease binding of the drug particles. The dosage forms are manufactured using conventional tableting and packaging equipments. The tablets, which can handle high drug loading and coated particles, can be packed in both bottles and pushed through blisters.

3.11. FROSTA TECHNOLOGY:

This technology incorporates manufacture of highly plastic granules using a plastic material, a material enhancing water penetration, and a wet binder. These granules can then be compressed into tablets at low pressure, thus enabling fast disintegration upon administration.

Table No. 2: List of commercially available orally disintegrating tablets[4]

Trade Name	Active Ingredient	Category	Technology	Manufacturer
Feldene Fast Melt	Piroxicam	Anti-rheumatic	Zydis	Pfizer Inc. NY. USA
Claritin Redi Tab	Loratidine	Anti-histaminic	Zydis	Schering Plough Corp. USA
Maxallt MLT	Rizatriptan	Anti-migrain	Zydis	Merck & Co., Nj, USA.
Ppcid RPD	Famotidine	Anti-histaminic	Zydis	Merck & Co., Nj, USA.
Rispetdal M-tab	Risperidone	Schizophernia	Zydis	Jannsen
Zubrin (pet drug)	Tepoxalin	Canine NSAID	Zydis	Schering Plough Corp. USA
Zofran ODT	Ondansetron	Anti-emetics	Zydis	Glaxo Wellcome, Middlesex, UK.
Klonopin Wafer	Clonazepam	Sedation	Zydis	Roche

Imodium Instant Melts	Loperamide HCl	Anti-Diarrheal	Zydis	Jannsen
Tempra Quicklets	Acetaminophen	Antipyretic	OraSolv	Bristol Myers Squibb, NY, USA.
Remeron SolTab	Mirtazapine	Anti-depression	OraSolv	Organon Inc.
Triaminc Softchews	Various combinations	Pediatriccold, cough and allergy	OraSolv	Novartis Consumer Health
Zoming- ZMT	Zolmitriptan	Anti-migignaine	Durasolv	Astra Zeneca, Wilmington, USA.
Alavert	Loratadine	Anti-histaminic	Durasolv	Wyeth Consumer Healthcare
NuLev	Hyoscyamine sulfate	Anti-ulcer	Durasolv	Schwarz Pharma
Kemsstrro	Baclofen	Anti-spastic analgesic	Durasolv	Schwarz Pharma
Benadryi Fast Melt	Diphenhydramine & Pseudophidrine.	Anti –allergic	WOWTAB	Warner Lambert NJ, USA.
Nasea OD	Ramosetoron HCl	Anti-emetics	WOWTAB	Yamanouchi
Gaster D	Famotidine	Anti-ulcer	WOWTAB	Yamanouchi
Ralivia FlashDose	Tramadol Hcl	Analgesics	FlashDose	Biovail
Zolpidem ODT	Zopidem Tartrate	Sleep Disorders	FlashDose	Biovail
Fluoxetine ODT	Fluoxetine	Anti-depression	FlashDose	Biovail
Hyoscyamine sulfate ODT	Hyoscyamine sulfate	Anti-ulcer	OraQuick	ETHEX Corporation

3.4. SUPERDISINTEGRANTS:

Superdisintegrants are used to improve the efficacy of Mouth Dissolving dosage forms, by decreasing their disintegration time, which in turn enhances drug dissolution rate. Disintegrates are substances or mixture of substances added that are to drug formulations to facilitates their breakup or disintegration into smaller particles that dissolve more rapidly than in the absence of disintegrants.[11]

Superdisintegrants are generally used at a low level in the solid dosage form, typically 1% to 10 % w/w.

MECHANISM OF SUPERDISINTEGRANTS:[7]

There are four major mechanisms for tablets disintegration as follows

1. SWELLING:

Perhaps the most widely accepted general mechanism of action for tablet disintegration is 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.

2. POROSITY AND CAPILLARY ACTION (WICKING):

Disintegration by capillary action is always the first step. 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. Water uptake by tablet depends upon hydrophilicity of the drug/excipient and on tableting conditions. 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.

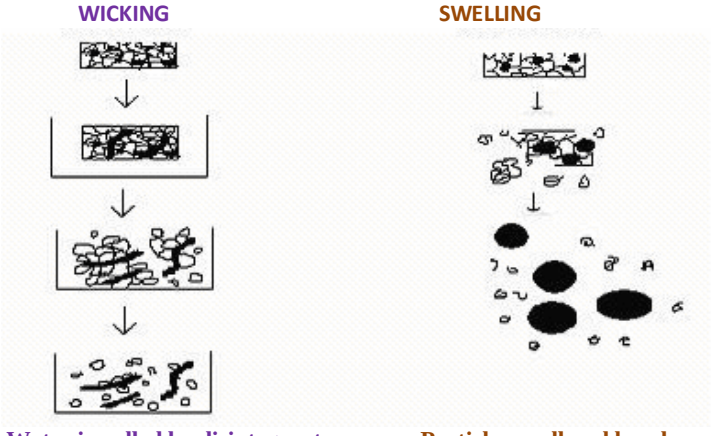

Figure No. 4: Wicking and Swelling mechanism of Superdisintegrant's action

3. DUE TO DISINTEGRATING PARTICLE-PARTICLE REPULSIVE FORCES:

Another mechanism of disintegrant attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non-swelling particle also cause disintegration of tablets[7]. The electric repulsive forces between particles are the mechanism of disintegration that requires water. Researchers found that repulsion is secondary to wicking.

4. DUE TO DEFORMATION:

During tablet compression, particles get deformed and these deformed particles return back to their normal structure, when they come in contact with aqueous media or water. Occasionally, 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.

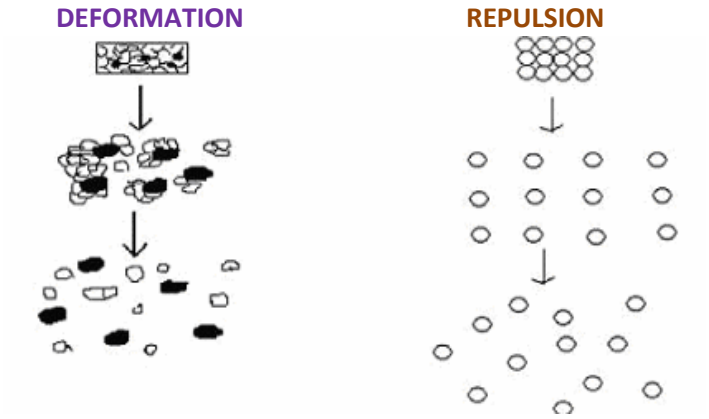

Figure No. 5: Deformation and Repulsion mechanism of Superdisintegr-ant's action

Table No. 3: Classification of Superdisintegrants and their mechanism of action[11].

Superdisintegrants	Example	Mechanism Of action	Special comment
Crosslinked cellulose	Crosscarmellose , Ac-Di-Sol, Nymce ZSX, Primellose, Solutab, Vivasol, L-HPC	Swells 4-8 folds in less than 10 seconds, Swelling and wicking both.	Swells in two dimensions. Used in Direct compression or Starch free granulation.
Crosslinked PVP	Crosspovidone, Crosspovidon M, Kollidon, Polyplasdone	Swells very little and returns to original size after compression but act by capillary action.	Water insoluble and spongy in nature, makes porous tablet.
Crosslinked starch	Sodium starch glycolate, Explotab, Primogel	Swells 7-12 folds in less than 30 seconds.	Swells in three dimensions and high level serve as sustain release matrix.
Crosslinked alginic acid	Alginic acid NF, Satialgine	Rapid swelling in aqueous medium or wicking action.	Promote disintegration in both dry and wet granulation.
Natural super disintegrant	Soy polysaccharides Emcosoy		Does not contain any starch or sugar. Used in nutritional products.
Calcium silicate		Wicking action	Highly porous, Optimum concentration is between 20-40%

EVALUATION OF MOUTH DISSOLVING TABLETS:

4.1. DESCRIPTION:

Took 10 tablets in a Petri-dish and observed for uniformity of colour distribution, edge damages, cracks and shape of the tablet.

4.2. DIAMETER & THICKNESS:

The diameter & thickness of the tablets were determined by using digital Vernier caliper by picking tablets randomly. The tablet was hold between the jaws of caliper and slides the adjustable jaws toward the tablet till it was hold firmly between jaws. Recorded the reading of

diameter & thickness of tablet in mm. Took the reading of 6 tablets and calculated the SEM value.

4.3. AVERAGE WEIGHT:

Took 20 tablets from composite sample and weighed accurately on electronic weighing balance. The average weight was calculated by formula:

Average weight (mg) = Total weight of 20 tablets (gm) *1000 / 20

4.4. UNIFORMITY OF WEIGHT (%):

Weighed each 20 tablets individually and noted the highest and the lowest weight then with the help of average weight test, Uniformity of weight (%) was calculated by using formula;

For (-) variation = Minimum weight – Average weight*100 / Average weight

For (+) variation = Maximum weight – Average weight*100 / Average weight

Table No. 4: Weight Variation Specification as per IP.

Sr. No.	**Average Weight of Tablet**	**% Deviation**
1	80 mg or less	± 10
2	More than 80 mg but less than 250 mg	± 7.5
3	250 mg or more	± 5%

4.5. HARDNESS:

The strength of tablet is expressed as tensile strength (Kg/cm^2). The tablet crushing load, which is the force required to break a tablet into pieces by compression. It was measured using a tablet hardness tester (Monsanto hardness tester). Took the hardness of 6 tablets and calculated the SEM value.

4.6. FRIABILITY:

The friability of the tablets was determined using Roche friabilater. This device subjects the tablets to the combined effect of absorption and shocks in a plastic chamber revolving at a height at 6 inches in each revolution. Pre-weighted sample of taste was placed in the friabilater and were subjected to 100 revolutions.

Tablets were deducted using a soft muslin cloth and reweighted. The friability (F) is gives by the formula.

Friability F (%) = (W_0-W/ W_0)*100

Where, w_0 is the weight of the tablets before the test and w is the weight of the tablets after the test.

4.7. *IN-VITRO* DISINTEGRATION TIME:

Disintegration of fast disintegrating tablets is achieved by saliva in the mouth, however, amount of saliva in the mouth is limited and no tablet disintegration test was found in USP and IP to simulate *In-vivo* condition. So it was done with water.

Placed 1 tablet each in six cylindrical tubes with basket, using distilled water maintained at 37±2 ^{0}C as the as the immersion fluid & apparatus operated to observed and note the time in which all the tablets have disintegrated completely. The test was repeated three times and recorded the reading and calculated SEM value.

4.8. DETERMINATION OF UNIFORMITY OF DRUG CONTENT:

Ten randomly selected tablets were taken into separate volumetric flasks and completely dissolved in Sorenson's buffer (pH 6.8) by sonication. The volume makeup was done with the buffer solution and filtered. An aliquot of 1.0 ml from these solutions were diluted to 10 ml with Sorenson's buffer (pH 6.8) in separate volumetric flask and determined the concentration by UV spectrophotometrically by using calibration curves. Thus drug content of each of 10 tablet was determined and the same procedure was followed for every formulation.

4.9. IN- VITRO DISSOLUTION STUDY:

Tablet test condition for the dissolution rate studies were used according USP specification using USP 24, type I apparatus. The dissolution medium was 900 ml of Phosphate buffer (pH 6.8). The temperature of the dissolution medium and the rate of agitation were maintained at 37± 0.50 ^{0}C and 50 rpm respectively. Aliquots of 10 ml of dissolution medium were withdrawn at specific time interval and same volume is replaced by fresh dissolution medium, pre-warmed to 37 ± 0.50^{0}C. The drug concentration was determined spectrophotometrically by using UV spectrophotometer.

4.10. EVALUATION OF THE TASTE OF THE TABLET:

The taste of tablet was checked by panel method. Firstly a panel of 10 human volunteers was selected and the study protocol was explained to volunteers. Then tablet randomly selected from each batch for the study is given one by one to volunteers and written consent was obtained from them. Mouth should be properly washed with purified water before tablet was placed on tongue. Observations from volunteers were recorded for all formulations after placing 15 seconds of the tablet on tongue.

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