ejpmr, 2020,7(10), 215-229

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

MOUTH DISSOLVING TABLETS – AN UPDATE PROSPECTS FOR ORAL DRUG DELIVERY SYSTEM

Poonam Verma, Rudra Pratap Singh*, Chandrika Chouhan, Suman Sahu and Rishabh Sahu

Department of Pharmaceutics, Columbia Institute of Pharmacy, Raipur – 493111, Chhattisgarh.

***Corresponding Author: Rudra Pratap Singh**

Department of Pharmaceutics, Columbia Institute of Pharmacy, Raipur – 493111, Chhattisgarh.

Article Received on 16/08/2020 **Article Revised on 05/09/2020** **Article Accepted on 26/09/2020**

ABSTRACT

Fast dissolving drug delivery system is the process to deliver a drug in a case of severe pain, attack gives the rapid action and this type of tablets rapidly dissolve in saliva within a 15 sec to 3 min without need of water. It's regarded as the safest economical and most convenient method of drug delivery system in its having the higher patient compliance. In this article, Different methods are described for the preparation of fast dissolving tablets such as a methods are- freeze drying, direct compression, Durasolv technology etc. and analytical parameters are a size, shape, thickness, weight uniformity, friability, dissolution test, disintegration etc. This review article are a focused on mainly advantages, disadvantages, synonym, methodology, ideal characteristics and analytical parameters of fast dissolving tablets at laboratory level.

KEYWORDS: Mouth dissolving tablet, fast dissolving drug delivery system, methodology and analytical parameters.

Graphical Abstract

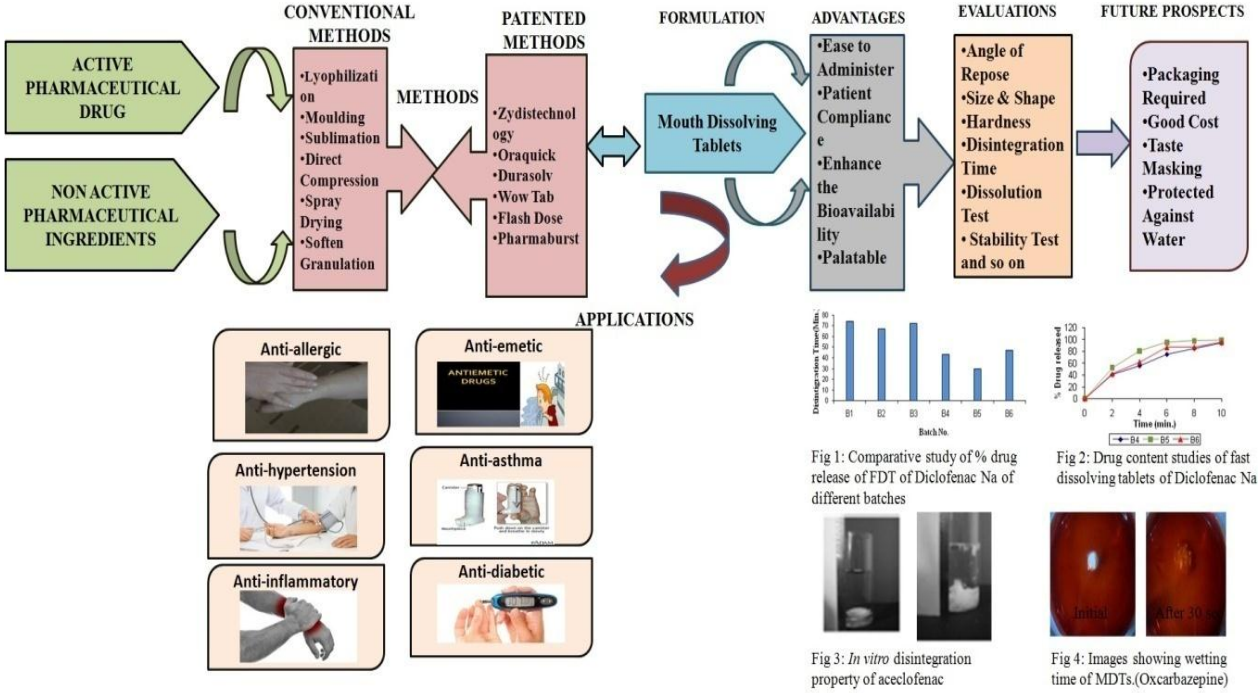

Fig 1: Comparative study of % drug release of FDT of Diclofenac Na of different batches

Fig 2: Drug content studies of fast dissolving tablets of Diclofenac Na

Fig 3: *In vitro* disintegration property of aceclofenac

Fig 4: Images showing wetting time of MDTs.(Oxcarbazepine)

INTRODUCTION

Drug delivery system is economical tool for enhancing market, extending product life cycles and making opportunities. Drug delivery system (DDS) makes a big contribution to world pharmaceutical sales through market segmentation and is moving quickly. Despite of tremendous innovations in drug delivery, the oral route remains the well-liked route for administration of therapeutic agents as a result of correct dose, low price medical aid, self medication, non invasive methodology and easy administration resulting in high level of patient compliance. Unit

dosage forms are popular as a result of low price, easy administration, correct unit dosage forms self medication, pain ignore and also the most significantly the patient compliance. The primary popular solid dosage forms are being tablets and capsules.[1-5]

Tablets

According to Pharmacopoeia of India, Pharmaceutical tablets are solid, flat or biconvex discs, prepared by compressing a drug or a mixture of drugs, with or without diluents. They vary in shape and differ greatly in size and weight, depending on the amount of medicinal substance and the intended mode of administration." Tablet fabrication by compression was initiated in 1843 by Brockedon .Since then the popularity of this dosage form has been increasing and today tablets remain the most popular of all the dosage forms, intended for oral use. This may be attributed in part to the availability of variety of compression machines and advances in tablet technology. [6]

According to accumulation of India " Pharmaceutical tablets are a solid unit, flat or bulging discs, ready by press a drug or a mix of medication, with or while not diluents. They terribly in form and take issue greatly in size and weight, looking on the number of healthful substance and also the meant mode of administration." Tablet fabrication by compression was initiated in 1843 by Brockedon .Since then community |the recognition} of this dose kind has been increasing and nowadays tablets stay the foremost popular of all the dose forms, meant for oral use. this could be attributed partly to the provision of kind of compression machines and advances in pill technology.[6]

Classifications of Tablets[6]

- Sugar coated tablets (SCT)
- Film coated tablets (FCT)
- Enteric coated tablets (ECT)
- Chocolate coated tablets (CCT)
- Multiple compressed tablets (MCT)
- Buccal or sublingual tablets
- Dispensing tablets (DT)
- Hypodermic tablets (HT)
- Time release tablets
- Sustained release tablets

History

Fast-dissolving drug-delivery systems were 1st developed within the late 1970s as an alternate to tablets, capsules, and syrups for pediatric and geriatric patients World Health Organization expertise difficulties in swallowing ancient oral solid-dosage type. The novel technology of oral quick-dispersing dose forms is also known as fast dissolve, fast dissolve, fast soften and fast disintegrating tablets. However, the perform and beginning of of these dose forms square measure similar.[7]

Introduction of a therapeutic substance into the body to enhance its effectuality and safety is called a drug-delivery system that interfaces between the patient and also the drug. Drug could also be introduced into the flesh by several routes, however oral route has been one preferred and used route for each standard furthermore as novel drug delivery due to low value of medical care, pain evading, self-medication, simple uptake, resulting in high levels of patient compliance, and it didn't need sterile conditions.[8]

To beat these issues, mouth dissolving tablets (MDT) are developed, that having smart hardness, dose uniformity, simple administration and is the primary alternative of dose type for pediatric medicine, medical specialty and move patients. MDTs also are called "fast-melting, fast-dissolving, oral disintegrating or disperse". Mouth dissolving tablets will outline as "A solid dose type containing meditative substances that disintegrates quickly, typically at intervals a matter of seconds, once placed below the tongue.[9] Mouth Dissolving pill incorporates a pleasing mouth feel, and it not needed water to swallow. MDT simply dissolved or disintegrates in discharge at intervals a couple of seconds (15s to 3min) while not the requirement of drinkable or change of condition, leaves no residue within the mouth once administered and fewer sensitive to environmental conditions like temperature, humidity.[10-12] All MDTs approved by FDA are classified as orally disintegrating tablets. Recently, the European Pharmacopeia adopted the term mouth dissolving pill for a pill that disperses or disintegrates in 3 min within the mouth before swallowing. Such a pill disintegrates into smaller granules or melts within the mouth from a tough solid to a gel-like structure, permitting simple swallowing by patients.[11-15]

Mouth dissolving tablets also are referred to as as quick dissolving tablets, melt-in-mouth tablets, orodispersible tablets, rapimelts, porous tablets, fast dissolving tablets etc. The quick dissolving tablets square measure quickly dissolved or disintegrated by the utilization of superdisintegrants (FDAs).[16] The FDT technology, that makes tablets dissolve or disintegrate within the mouth while not further water intake. The FDT preparation is outlined by the Food and Drug Administration (FDA) as "a solid dose form containing medical substances which disintegrates quickly, typically at intervals a seconds, once placed upon the tongue." consistent with European Pharmacopoeia "the FDT have to to disperse/disintegrate in 3 min.[17]

Synonyms[7]

- Orodispersible Tablets
- Orally Disintegrating Tablets
- Quick Dissolving Tablets
- Fast Melt Tablets
- Rapid Disintegrating Tablets

Advantages of Fast Dissolving Tablets

- Ease of administration and Patients compliance:- These tablets are simple to administer just in case of patients United Nations agency cannot swallow (Bedridden patients, stroke victims, and elder patients), United Nations agency shouldn't swallow (like nephritic failure) and United Nations agency refuse to swallow (Paediatrics, geriatric and medical specialty patients). These tablets provide patients compliance just in case of sick-abed disabled patients and for peoples United Nations agency are busy or traveling as water isn't needed for administration.
- Rapid onset of action:- These tablets are having quick onset of action as these tablets are becoming absorbed through pre-gastric space.
- Enhanced bioavailability:- Bioavailability of poorly soluble medicine will increase by adding hydrophilic disintegrating agents which ends in quick disintegration and dissolution. Due to the pre stomach absorption, these tablets bypass the primary pass metabolism which ends in reduced dose, less aspect impact and increased bioavailability.
- Fast dissolving tablets are palatable:- Property of getting elegant feel, it's a lot of accepted among pediatrics patients, because it improves the technique of bitter medicine.
- batter alternative to conventional tablets and liquid dosage forms:- Mouth dissolving tablets are solid unit dose forms having correct dosing, having no risk of choking and suffocation with benefit of each solid and liquid dose forms.[20-24]

Disadvantages of Fast Dissolving Tablets

Mechanical strength:-These tablets square measure terribly brittle, fragile and porous in nature as they're ready by low compression force. Thus, needs correct packing and handling where as transportation.

Unpleasant taste:-If not properly ready, these tablets will leave unpleasant taste or feeling of grittiness within the mouth.

Required dry condition for storage:- tablets are absorptive in nature and to be keep in dry condition.

Expensive and time intense method.

Required special packaging as obtained tablets are poorly stable. [20-24]

SALIENT FEATURES OF FAST DISSOLVING DRUG DELIVERY SYSTEM

- Ease of administration- For patients who are a unit unsafe, disabled and uncooperative.
- No would like of water to swallow the solid dose kind.
- Bioavailability – improve bioavailability, especially in cases of insoluble and hydrophobic medicine, because of quick disintegration and dissolution of those tablets.
- Disintegration and dissolution- fast disintegration and dissolution of the dose kind.
- Absorption -Drugs absorbed from the mouth, esophagus and muscular structure because the spittle passes down into the abdomen. In such cases bioavailability of the drug is exaggerated.
- Improve safety -The risk of chocking or suffocation throughout oral administration of standard formulation because of physical obstruction is avoided, so providing improved safety.[25-29]

IDEAL CHARACTERISTICS OF A DRUG TO BE SELECTED FOR FDDS

Drug needs no water for oral administration for dissolve/disintegrate in mouth in an exceedingly matter of seconds.

• Drug must have pleasant taste.
• Have an appropriate taste masking property.
• Be more durable and fewer fragile.
• The Incorporated drug must have low dose but 30mg.
• The medication with smaller and moderate relative molecular mass are desirable.
• Drug must have elegant stability and solubility in water also as in spit.
• Exhibit low sensitivity to environmental conditions (temperature and humidity).
• The drug must to be partly unionized at the pH of oral cavity.
• The drug must have the flexibility to permeate oral tissue layer tissue.
• Leave negligible or no residue in mouth once administration.
• permits the manufacture of pill mistreatment standard process and packaging instrumentality.[25-29]

METHODS

Various technologies used to manufacturing of mouth dissolving tablets shown in **Figure 1**.[52]

Lyophilization or Freeze-Drying

Freeze-drying, conjointly referred to as freezing, or cryodesiccation, during this methodology water is change from the merchandise when temperature reduction. This method creates associate degree amorphous porous structure which will dissolve quickly. The active drug is dissolved in associate degree solution of a carrier. Then the mixture is treated by weight and poured into the wells of the preformed blister packs. The trays holding the blister packs are responded to a cryogen temperature reduction tunnel to freeze the drug resolution or dispersion. Then the frozen blister packs are placed in cold cupboards to continue the lyophilization. When lyophilization, the foil backing is applied on a blister-

sealing machine. Finally, the blisters area unit prepackaged. Ex (Bauhinia variegata linn /Tectone grandis linn).

The major disadvantage of freezing technique is high price of kit and process. Alternative disadvantages embrace lack of resistance necessary for normal blister packs of the ultimate dose forms.[30]

Moulding

Moulded tablets are designed to facilitate the absorption of active ingredients through tissue layer linings of mouth. during this technique, pill disintegrates and dissolves quickly appreciation to the presence of soluble ingredients. Moistened powder mix is wrought in to pill victimization compression pressure below utilized in typical tablet's compression. Then the solvent is removed by air-drying. wrought tablets have a porous structure that enhances dissolution. the two major issues with molding are less mechanical strength and poor taste masking.

Sublimation

In this method, extremely volatile ingredients like ammonia carbonate, carbonate, carboxylic acid, camphor, hydrocarbon, urea, etc., are added that change pronto, to different pill excipients and also the mixture is then compressed in to tablets. Volatile material is then removed via sublimation, leaving a extremely porous matrix. These compressed tablets that have high porousness (approximately 30%) speedily dissolved at intervals 15 seconds in secretion. The process of sublimation method is shown in Figure 2. Ex (Promethazine theoclate, Candesartan cilexetil).[31-32]

Direct Compression

It is that the best and most well liked technique to manufacture tablets by mistreatment standard equipments. During this technique, tablets are compressed directly from the mixture of It the drug and excipients. This system will currently be applied to quick dissolving pills as a result of the provision of improved tablet excipients (superdisintegrants) and sugar primarily based excipients. This technology is cost-efficient and easy to implement at the commercial level. The process of direct compression method is shown in Figure 3. Ex (Oxcarbazepine, Chlorpromazine HCL, Cimetidine).[33-35]

Spray Drying

In this system, process solvent is evaporated quickly and might manufacture extremely porous and fine powder, that was compressed into tablets. Hydrolyzed and non hydrolyzed gelatin used as a supporting agent for the matrix, Osmitrol as a bulking agent and sodium starch glycolate or croscarmellose as a disintegrant. Tablets prepared by this technique shows disintegration time < 20 sec in an liquid medium. The process of spray drying method is shown in **Figure 4**. Ex (Nizatidine/Eudragit E100).[36]

Mass Extrusion

This methodology involves softening the active mix victimization the solvent mixture of soluble polythene glycol and methyl alcohol and subsequent expulsion of softened mass through the extruder or syringe to induce a cylinder of the merchandise into even segments victimization the heated blade to make tablets. The dried cylinder can even be accustomed coat granules for bitter medicine and there by reach taste masking. The process of mass extrusion method is shown in Figure 5.

Nanonization

Nanomelt technology has been recently developed methodology, that involves the reduction within the particle size of drug to nano size by wet-milling technique. Surface sorption of the nano crystals of the drug is completed on hand-picked stabilizers for helpful them against agglomeration, that are then incorporated into MDTs. this system is especially advantageous for poor water soluble medicine and alternative blessings of this technology represent quick disintegration/dissolution of nanoparticles resulting in multiplied absorption and therefore higher bioavailability and reduction in dose, value effective producing method, standard packaging appreciation exceptional strength and big selection of doses.

Soften granulation

In this method, MDTs may be ready by incorporating a deliquescent waxy binder (super polystate) PEG-6-stearate. Super polystate may be a waxy material with a freezing point of 33-37 °C and a hydrophilic- oleophilic balance of 9. It not solely acts as a binder and will increase the physical resistance of tablets, however additionally helps within the disintegration of tablets because it melts within the mouth and solubilizes speedily deed no residue. Super polystate was incorporated into the formulation of MDTs by soften granulation methodology wherever granules are produced by the liquified category of this material.[10-15]

PATENTED TECHNOLOGIES FOR PREPARATION OF MDTs

Zydistechnology

Zydis formulation was initial marketed and quick disintegrating pill preparation's technique during which the pill dissolves within the mouth within seconds when placement of the tongue. it's a novel freeze dried pill during which drug is physically entrapped or dissolved within the matrix of quick dissolving carrier material. Once Zydis units are place to the mouth, the freeze-dried structure disintegrates absolute. To produce strength and resilience to tablet'spolymers like gelatin, dextran or alginates square measure incorporated with it that additionally from glossyamorphous structure. Saccharides like diuretic or sorbitol are incorporated to

get crystallinity, class and hardness. Water is employed for the producing method to make sure production of porous units to achieve fast disintegration various gums are used to prevent sedimentation of spread drug particles throughout the producing method. The process of Zydis technology is shown in Figure 6.

Oraquick technology

The OraQuick fast-dissolving/disintegrating pill formulation is proprietary by K.V Pharmaceuticals. It utilizes taste masking microsphere technology referred to as micromaskin that doesn't utilize solvents of any kind, that provides superior mouth feel, vital mechanical strength, and fast disintegration/dissolution of product, therefore, results in quicker and a lot of economical production. Lower heat of production than different fast-dissolving/disintegrating technologies create OraQuick applicable for heat-sensitive medicine.

Ziplets/Advatab Technology

This technology is proprietary by passano con Barnago, Italy. It utilizes water-insoluble ingredient combined with one or more practical disintegrants. AdvaTab tablets disintegrate speedily in but 30 seconds. These tablets are ready victimization polymer-coated drug particles that are uniformly spread in associate ultra-fine, low-water content, speedily disintegrating matrix with superior organoleptic properties. AdvaTab tablets are compressed employing a proprietary, patented, external lubrication system during which the lubricator is applied solely to the pill surface, leading to strong tablets that are arduous and fewer friable and might be prepacked in bottles or blister.

Lyoctechnology

Lyoc technology is proprietary by pharmalyoc. Oil in water emulsion is ready and placed directly into blister cavities followed by freezing. Non-homogeneity throughout freeze drying is avoided by incorporating inert filler to extend the viscousness finally the deposit. High proportion of filler reduces consistency of tablets due to that disintegration is down.

Durasolv Technology

Durasolv is that the patented technology of CIMA labs. The tablets created by this technology incorporate a drug, fillers and a lubricator. During this system, active medicinal drug is taste masked. It additionally contains effervescent disintegrating agent. DuraSolv has abundant higher mechanical strength than its forerunner appreciation to the utilization of upper compaction pressures throughout tableting. DuraSolv tablets are ready by victimization standard tableting instrumentation and have smart rigidity (friability but that 2%). The DuraSolv product is therefore created during a quicker and more cost effective manner. One disadvantage of DuraSolv is that the technology isn't compatible with larger doses of active ingredients, as a result of the formulation is subjected to such high pressures on compaction.

Wowtab Technology

Wowtab Technology is patented by Yamanouchi Pharmaceutical Co. WOW means that "Without Water ".during this method, combination of low mouldable and high mouldable saccharides is employed to get a speedily melting, strong pill. The active ingredient is mixed with a low mouldability sugar (e.g. lactose, glucose, and mannitol) and coarse with a high mouldability sugar (e.g. Maltose, oligosaccharides) and compressed into the table. Tablets developed by Wowtab technology offers the superior mouth feel due to the graceful soften action and appropriate for each standard bottle and blister packaging.

Flash dose technology

Flash will technology has been patented by Fuisz. This technology based mostly is predicated relies upon the preparation of sugar based matrix called floss, that is formed from a mixture of excipients either alone or together of medicine by flash heat process. Tablets are created by direct compression technique. the ultimate product incorporates a terribly high extent for dissolution. It disperses and dissolves quickly once placed on the tongue. curiously, by dynamic the temperature and alternative conditions throughout production, the characteristics to the products may be altered greatly. The process of Flash dose technology is shown in Figure 7.

Pharmaburst Technology

Pharmaburst technology is patents by SPI company, New Castle. It utilizes the coprocessed excipients to develop MDTs, that dissolves inside 30-40 s. This technology involves dry mixing of drug, flavour, and lubricator followed by compression into tablets. Tablets obtained have the decent strength, in order that they may be packed in blister packs and bottles.

Nanocrystal technology

Nanocrystaltechnology is patented by Elan, King of Prussia. Nanocrystal Technology which has evaporation of mixture dispersions of drug substance and water soluble ingredients stuffed into blister pockets. This methodology avoids the producing method like granulation, mixing and tableting that is a lot of blessings for extremely potent and unsafe medicine. [10-15]

The examples of mouth dissolving tablets by the various methods are given in **Table 1.**

EVALUATION OF MOUTH DISSOLVING TABLETS

Pre Evaluation Parameters

Angle of Repose

Determined by funnel technique and standard of flow property is given in Table 2. Weigh the mix accurately and absorb a funnel. Modify the peak of the funnel in such the simplest way that funnel tip touches the peak of the heap of the mix. The mix of drug and excipients was allowed to flow through the funnel freely on to the surface and live the diameter of the powder cone created.

Angle of repose calculated exploitation the equation:

$\tan \theta = h/r$ **…….. Eq. (1)**

Where,

h =height of the powder cone

r = radius of the powder cone.

Bulk Density

A weighed amount of mix was poured into a graduated measurement cylinder and volume and weight area unit measured.

BD =Weight of the powder/Volume of the packing. **…….. Eq. (2)**

Tapped Density

Take a graduated measurement cylinder and place a familiar mass of drug-excipients mix. At a height of 10 cm and interval of 2 seconds, the cylinder was allowed to comprise its own weight on to a tough surface and sound was continues until any no amendment in volume noticed.

Tapped density (TD) = weight of the powder/Volume of the tapped packing **….. Eq. (3)**

Carr's Index

Carr's sponginess index (**Table 3**), is employed to see the sponginess Index of the blends.

Carr's compressibility (CI%) = [(TD-BD)X100]/TD **…….. Eq. (4)**

#Similar index used to calculate the flow property of the blend

Hausner's Ratio

Hausner's ratio = (Tapped densityx100)/Poured density **…….. Eq. (5)**

Hausner's ratio < 1.25 - Good flow = 20% Compressibility Index

Hausner's ratio >1.25-Poor flow = 33% Compressibility Index. [20-24]

Post Analysis Parameters [10-15]

Size And shape

Size and form the scale and form of the pill may be dimensionally represented, monitored and controlled.

Thickness and Diameter

Thickness and diameter pill thickness is investigating by exploitation filling instrumentation. Some filling instrumentation utilizes the uniform thickness of the tablets as a investigating mechanism. 10 tablets were taken, and their thickness was recorded exploitation micrometer (digital vernier calipers).

Uniformity of weight

Weight of the tablets determined one by one and conjointly on a digital balance. The common weight of 1 pill was resolute from the collective weight. For Example Meloxicam (Weight variation check is finished with 20 tablets. It's the individual variation of pill weight from the common weight of 20 tablets).[50]

Tablet hardness

Hardness of pill is outlined as for applied across the diameter of the pill within the order to break off the pill. Hardness of the pill of every formulation was resolute use the standard hardness tester (Monsanto Hardness tester, Pfizer hardness tester, etc.). It's expressed in weight unit or pound. The pressure needed to break off the tablets is measured as a operate of hardness (kg/ cm^2). The worth's obtained should meet the quality value. For Example Meloxicam = The crushing strength or hardness of the tablets was measured with facilitate of a Monsanto hardness tester and expressed in kg/cm^2.[50]

Content Uniformity

5 tablets were small-grained and also the mix like as an example 4 mg of Tizanidine HCl drug was weight and dissolved in appropriate amount of pH1.2 solutions. resolution was filtered and diluted and drug content analyzed spectrophotometrically at 228 nm.[53]

Friability

Friability of the pill was resolute exploitation friability check equipment (Campbell physics,India). Friability is to live the extent of pill breakage throughout physical stress conditions like Packing, transportation, etc. A sample of every which way chosen six tablets was evaluated for friability exploitation Roche friabilator at 25 RPM for 4 minutes. The half of weight loss is calculated by measurement the whole weight of 6 tablets before and once operation. The friability check was performed for all the developed Oro-dispersible tablets. Twenty tablets were taken and their weight was resolute. Then they were placed within the Roche friabilator and allowed to form100revolutions. The tablets were then de-dusted and reweighed. The share weight loss was calculated.

Percentage Friability

$$= \frac{(W1 - W2)}{W1} \times 100$$ **…….. Eq. (6)**

Where, W1 = Initial weight of the 20 tablets.
W2 = Final weight of the 20 tablets after testing.

Friability values below 1% are generally acceptable" [54]
For Example Sulbutamol Sulphate: The friability of sample of tablets ware measured employing a Roach Friabilitor. This device consists of a plastic chamber that's set to revolve around twenty five revalut for four minutes dropping the tablets at a distance of six inches with every revolution. Pre weighed sample of twenty tablets was placed within the friabilator and were subjected to one hundred revolutions. Tablets were dusted employing a soft cloth fabric and reweighed.[57]

Wetting time
The significant parameters for mouth dissolving tablets area unit the quantitative relation of Wetting time and water absorption reportable by Yunixia et al. a bit of double folded tissue paper (circularly cut) was placed during a small petri plate containing water soluble dye resolution (Sorenson"s buffer pH6.8). Pill was placed within the paper, and also the time needed for complete wetting of the pill was resolute. 3 trials for every batch additionally the variance were also determined. For Example Lornoxicam (A small piece of circular paper (8cm) Folded twice was placed during a Petri dish (Internal Diameter = 9cm) containing 10 metric capacity unit of solution simulating spit pH 6.8). A pill was placed on the paper and also the time taken for complete wetting was noted. 3 tablets from every formulation were every which way chosen and also the average wetting time was noted. [58] Wetting time and water absorption quantitative relation reportable the utilization of a bit of double folded paper placed during a petridish containing 6 metric capacity unit (pH 6.8) of water. One pill was placed on this paper and also the time for complete wetting of pill was noted as wetting time. The wetted pill was then weighed and also the water absorption quantitative relation, R, was resolute in step with equation (7)
Eq. R = 100 (Wa.Wb)/Wb **…….. Eq. (7)**

Where Wb and Wa are the weights of tablet before and after water absorption, respectively .[53]

Disintegration Time
Disintegration time for every which way chosen six tablets was measured exploitation the disintegration check equipment (specified in I.P.-1996). the common time needed for disintegration was calculated and compared with standards. For Example a Valsartan = Disintegration time was measured in 900 metric capacity unit artificial spit (pH 5.8) in step with the USP 24 technique while not disc at 37 ± $0.5C^0$ temperature. The disintegration time of six individual tablets were recorded and also the average was reportable .[59]

Dissolution Test
The conventional technique of dissolution might be extended to in-vitro analysis of MDT The dissolution conditions for the reference listed medicine out there in USP may be used for preliminary in-vitro studies to mimic higher in-vivo conditions. A side from the on top of, multimedia system dissolution studies in numerous buffer solutions of various pH viz. 0.1 N HCl; PH4.5 and 6.8 buffers must to be allotted for interpretation of their in-vivo performance and pharmaceutical equivalence. USP equipment II (paddle) with a speed of 50 revaluation looks to be best suited and customary selection with acceptable dissolution media volume to keep up sink condition. For Example Lornoxicam = in vitro unleash of Lornoxicam from tablets was monitored by exploitation 900 metric capacity unit of simulated internal organ fluid, SIF (USP phosphate solution, pH 7.4) at 37 ± 0.5^0C and 50 RPM dissolution tester [Paddle sort, model TDT-08L Electrolab, (USP), India]. 5 metric capacity unit Aliquots were withdrawn at one minute time intervals and were replenished forthwith with an equivalent volume of recent buffer medium. Aliquots, following appropriate dilutions, were assayed spectrophotometrically (UV-1700, Shimadzu, Japan) at 378nm.[58]

Weight variations
20 tablets were chosen at a random and so the common weight was resolute. All the twenty pills were weight done by one and compared with the common weight the tablets meet USP specifications if no over a pair of tablets area unit outside the share limit and if no tablet differs by over a pair of times the share limit.[54] Propranonol HCL = the technique was applied to live pill wetting time. a bit of double folded paper was placed during a small petridish (i.d. = 6.5 cm) containing 10 metric capacity unit of water, a pill was placed on the paper, and also the time for complete wetting was measured. 3 trials for every batch were performed and variance was additionally determined.[60]

Stability as per ICH
The stability studies were allotted for a amount of three months within the Stability chamber (Rimek). The tablets were packed in appropriate packaging and hold on beneath the subsequent conditions as prescribed by the ICH tips [40°C ± 2°C and seventy five ± five-hitter RH (Q1C)]. The tablets were withdrawn sporadically with associate interval of thirty days and analyzed for Hardness, Disintegration, Dissolution, wetting time, drug content etc.[35]

MARKETED FORMULATION FOR MOUTH DISSOLVING TABLETS[6,61]
The examples of marketed formulations for mouth dissolving tablets are given in **Table 4.**

FUTURE CHALLENGES

Fast dissolving intraoral merchandise face several challenges as given below, these challenges area unit associated with new technologies and goods as they mature. Most of the medication would like taste masking. Tablets area unit fragile and should be protected against water. thus special packaging is required. A novel producing method may be a challenge, due to new instrumentation,technology and method. Limited drug loading due to technology limitation, taste masking and pill size.Need a lot of clinical trials to check a lot of clinical/medical advantages. Older patient advantages by amendment in taste, flavor and dissolve too quick. Cost of the goods may be a major challenge.[25]

Figure Captions

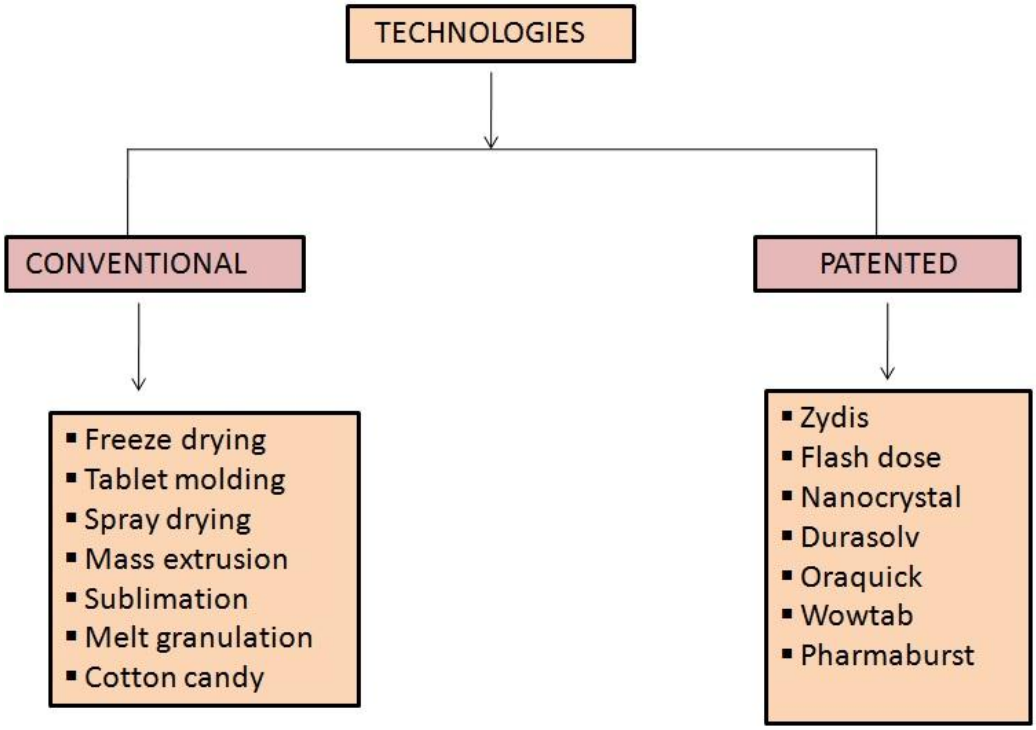

Figure 1: Various Technologies of Mouth Dissolving Tablet.

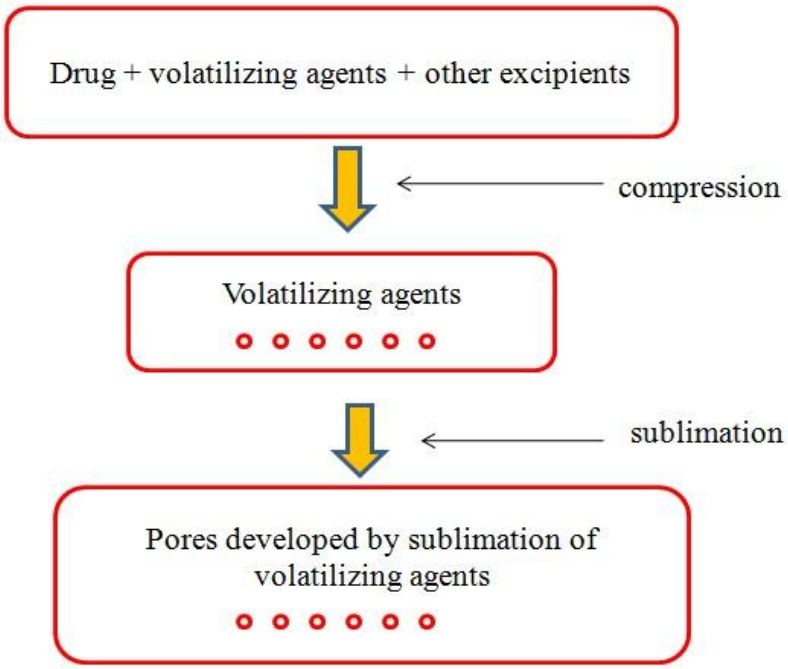

Figure 2: Process of Sublimation Method.

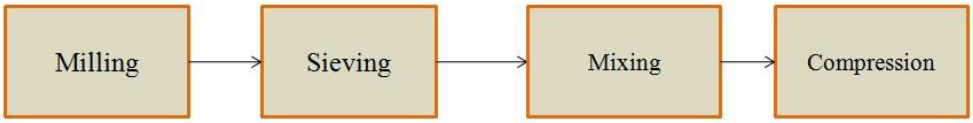

Figure 3: Process of Direct Compression Method.

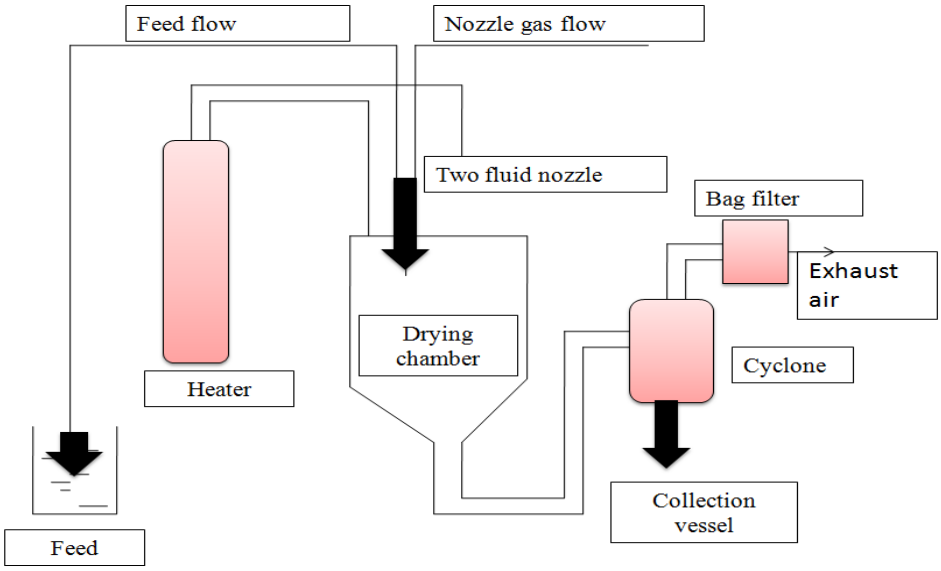

Figure 4: Process of Spray Drying Method.

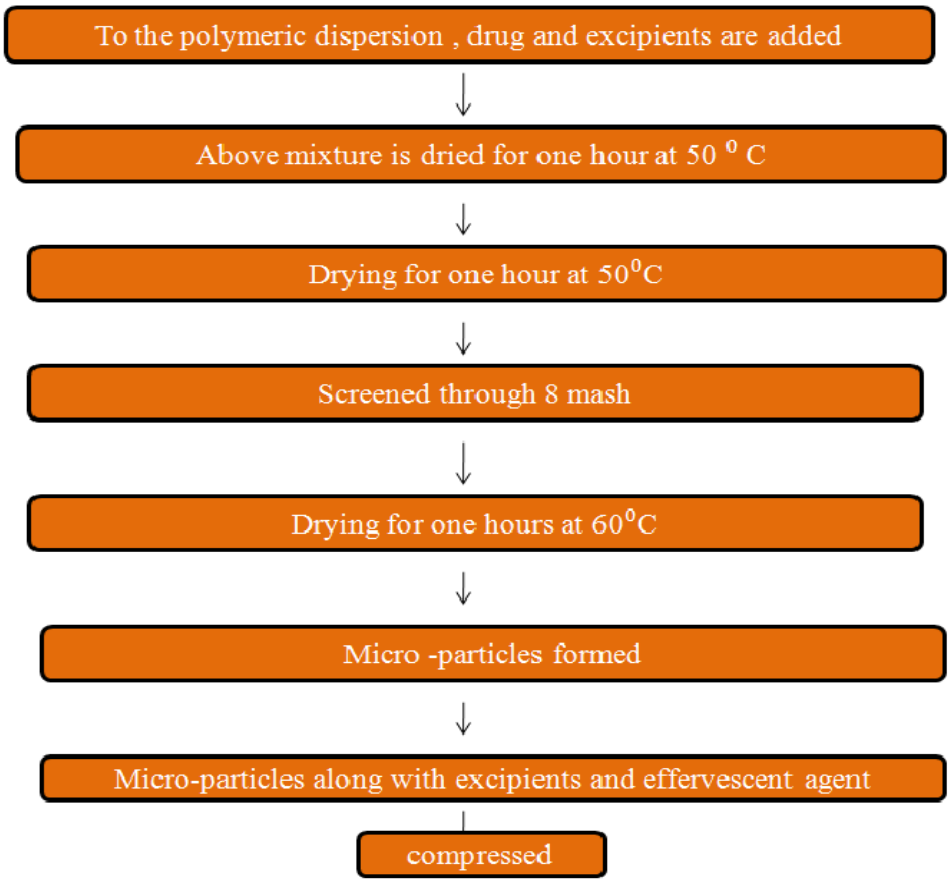

Figure 5: Process of Mass Extrusion.

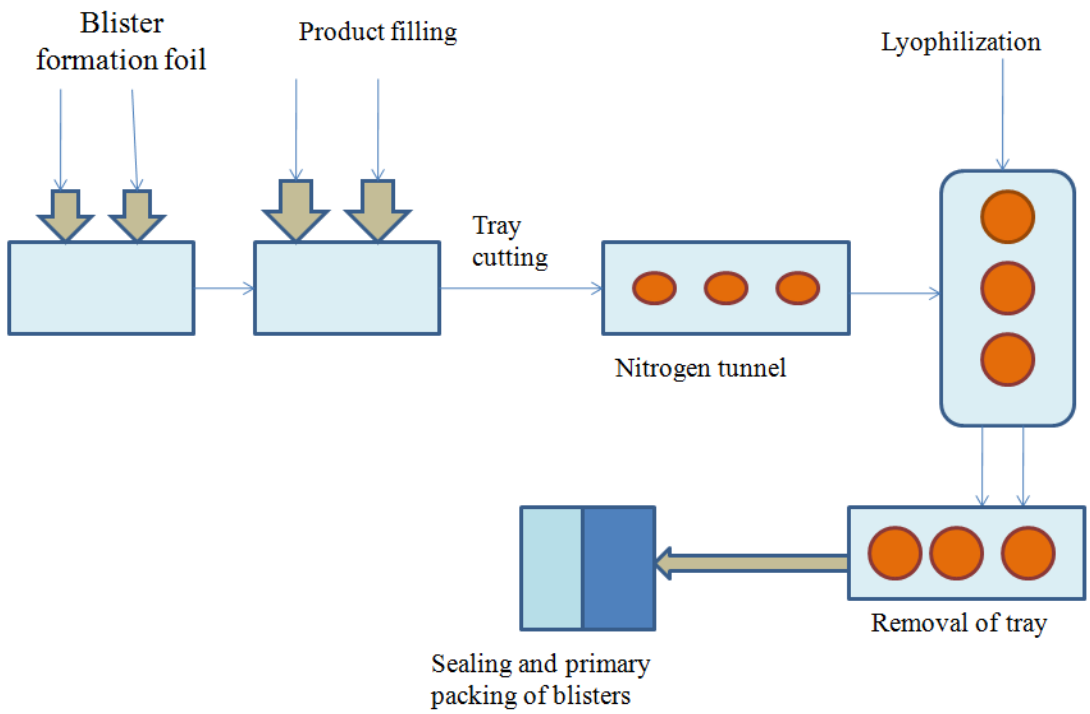

Figure 6: Process of Zydis Technology.

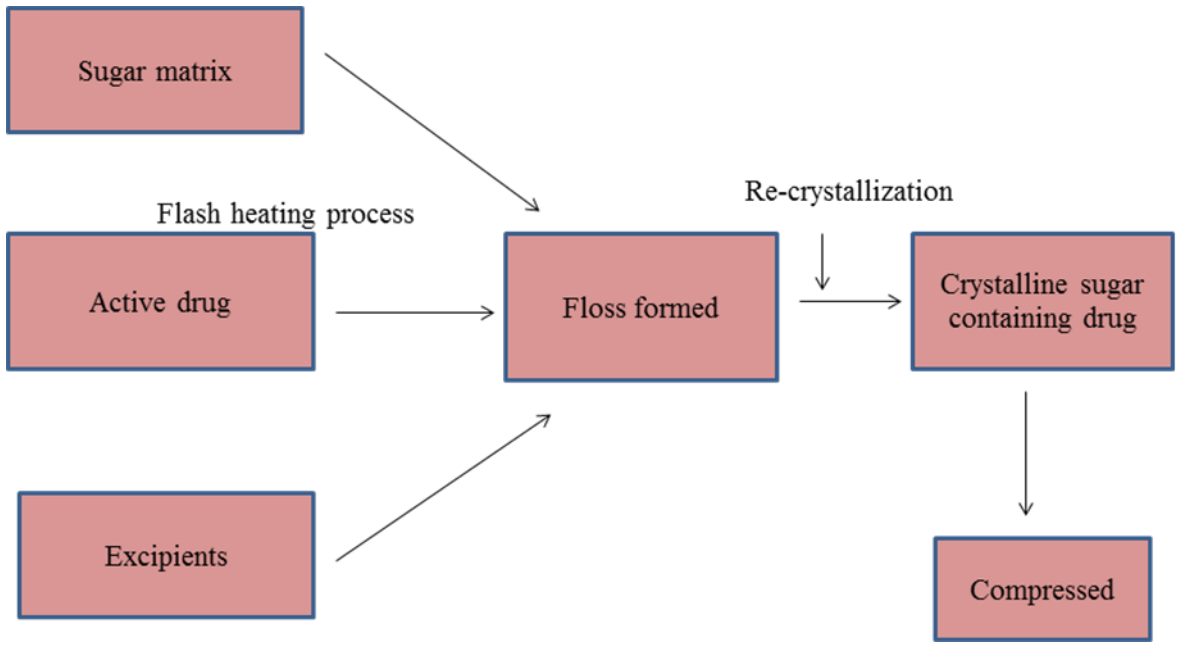

Figure 7: Process of Flash Dose Technology.

Table Captions

Table 1: Examples of Mouth Dissolving Tablets

S. No.	Drugs	Additives	Methods (C/P)	Treatments	Reference
1.	Ibuprofen	Cross carmellose sodium, microcrystalline cellulose, sodium starch glycolate, polyethylene glycol 4000, tween80,tartrazine,pineapple	Solid dispersion	Oral drug delivery	[1]
2.	Oxcarbazepine	Dicalcium phosphate, mannitol, microcrystalline cellulose, crospovidone, croscarmellose sodium, Mg stearate, aspartame, PEG6000	Direct compression, solid dispersion	Antiepileptics	[36]
3.	Promethazine theoclate	PMT, camphor, menthol, talc, dextrose, avicel pH102, urea, crospovidone, lactose, monohydrate, Mg stearate	Sublimation	Anti-emetic	[30]
4.	Levocetrazine	Kyron T-134, sodium starch glycolate, mannitol, croscarmellose sodium, magnesium, colloidal silicon dioxide, talcum, menthol, aspartame, MCC pH(102)up to	Direct compression	Anti-allergic	[38]
5.	Gliclazide	Cross carmellose sodium, mannitol, Mg stearate, talc, sodium saccharin, PVP K-30, PEG 6000	Solvent evaporation	Treat non-insulin dependent diabetes mellitus	[39]
6.	Curcumin	Lycoat RS720, Glycerin, Tartaric acid, Polaxamer 907, sorbital, water, PEG 6000, PVP K30.	Solid dispersion method	Antibacterial, Antioxidant, Ant diabetic.	[40]
7.	Nizatidine /Eudragit E100 complex	Crospovidone,soy- polysaccharide, microcrystalline cellulose, mannitol, lactose, ethanol, methanol, Mg stearate	Spray drying	Treat gastroesophogel reflex disease	[36]
8.	Chlorpromazine HCL	Microcrystalline cellulose, mannitol, sodium starch, glycolate, L-HPC, aerosil, aspartame, magnisum stearate, strawberry flavor, crospovidone, sodium starch glycolate, croscarmellose sodium	Direct compression	Anti-emetic	[34]
9.	Cimetidine	Crosscarmellose sodium, crosspovidone, Mg stearate, mannitol, talc, isopropyl alcohol	Direct compression	Treat peptic ulcers, treat gastric ulcer, treat abdominal cramps	[35]
10.	Coca butter	Corn starch, sodium starch glycolate type A(SSG), microcrystalline cellulose	Fusion molding	Skin care	[41]
11.	Tolvapton	Lactose monohydrate, microcrystalline cellulose, sodium starch glycolate, crospovidone, HPMC, sodium larryal sulphate	Wet granulation	Acute disease and cronic illness	[42]
12.	Candesartan Cilexetil	Cross carmellose sodium, crospovidone, sodium starch glycolate, microcrystalline cellulose, camphor, Mg stearate	Sublimation	Acute disease and cronic illness	[33]
13.	Ondansetron Hydrochloride	Sodium starch glycolate, microcrystalline cellulose, croscarmellose sodium, mannitol, magnisum stearate, sodium saccharin, mint flavour, aerosil	Direct compression	Quite effective in emesis	[43]
14.	Zolpidem tartrate	Inclusion complex of drug, microcrystalline cellulose, croscarmellose sodium, crospovidone, sodium starch glycolate, aspartame, magnesium stearate, aerosil	Direct compression	Treatment of insomnia as well as in brain disorder	[44]
15.	Norfloxcin	Avicel PH 101,starch 1500X, Croscarmellose sodium, husk, Stearic acid, fumed silica, Mg stearate,	Direct compression	Treatment of urinary tract infection	[45]

		menthol			
16.	Granisetron hydrochloride	Seeds of plantago ovata, croscarmellose sodium, crospovidone, sodium starch glycolate, camphor, aspartame, mannitol, talc, Mg stearate	Vaccum drying	Treatment of vomiting and nausea	[46]
17.	Sertraline hydrochloride	Dibasic calcium, phosphate, dextrose, talc, Mg stearate, sodium starch glycolate, crospovidone	Direct compression	Treatment of depression	[47]
18.	Chlorthalidone	Crospovidone, microcrystalline cellulose, Mg stearate, talc	Direct compression	Treatment of hypertension	[48]
19.	Aceclofenac	Mannitol, sucrose, Mg stearate, Ac-di-sol,	Direct compression	Anti-inflammatory	[49]
20.	Meloxicam	Crospovidone, PVP solution in ethyl alcohol, colloidal silica dioxide, camphor, lactose, talc, Mg stearate	Wet granulation	Anti-inflammatory	[50]
21.	Diclofenac sodium	Crospovidone, sodium starch glycolate, croscarmellose sodium, mannitol, talc	Direct compression	Analgesic Antipyretic	[51]

Table 2: Relation Between Angle of Repose and Flow Property.

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

Table 3: Relation between % Compressibility and Flow ability.

% compressibility	Flow property
5-12	Excellent
12-16	Good
18-21	Fairly passable
23-35	Poor
33-38	Very poor
>40	Very very poor

Table 4: Marketed Formulation For Mouth Dissolving Tablets.

Name of the Product	Active Ingredients	Pharmacological activity
Imodium Lingual	Imodium	--
Remeron Soltab	Quick releasing antiulcer preparation of pepcid Mirtazepine (15, 30,or 45 mg), orange flavor	--
Mosid-MT	Mouth melt tablet mosapride citrate	--
Calritin Reditabs	Immediate dissolving formulation of calritin	--
Nimulid-MD	Nimesulide	--
Zyrof Meltab	Rofecoxib	--
Claritin Reditab	Micronized loratadine	--
Feldene Melt	piroxicam (10 or 20 mg)	--
Maxalt-MLT	Rizatriptan (5 or 10 mg)	--
Pepcid RPD	Faotidine (20 or 40 mg)	--
Zyprexa Zydis	Olanzapine (5, 10,15,20 mg)	--
Zofran ODT	Ondansetron (4 or 8 mg), strawberry flavor	--
Pepcidin Rapitab	Quick releasing antiulcer preparation of pepcid	--
--	Amodiaquine, Chloroquine	Anti-malarials
--	Felodipine, Nicardipine, Nifedipine	Anti-Hypertensive
--	Butoconazole nitrate, Clotrimazole	Anti-fungal
--	Probenecid, Sulphinpyrazone	Anti-gout

--	Clonazepam, Ethotoin	Anti-Epileptics
--	Ciclazindol, Maprotiline HCl	Anti-depressants
--	Glibenclamide, Gliclazide	Anti-diabetics
--	Bromocriptine Mesylate, Lysuride Maleate	Anti-parkinsonian
--	Disopyramide, Flecainide Acetate	Anti-Arrhythmic
--	Chlorambucil, Cyclosporin, Dacarbazine	Anti-neoplastic Agents and Immunosuppressants
--	Barbitone, Bentazeparn, Bromazepam	Anxiolytic, Sedatives
--	Dipyridamole, Nicoumalone, Phenindione	Anti-coagulants

CONCLUSION

This review article is focused on mainly advantages, disadvantages, synonym, methodology, ideal characteristics and analytical parameters of fast dissolving tablets at laboratory level. The challenges for the researcher is to unable to find out the overcoming solutions for the physiological and biologically facing drugs or active constituents. An incompatible polymer and solvents are creating a lot of issues during the phase of formulations and also at the time of storage. Through this paper, we are overcoming the issue related to the drugs and polymers and also providing the applications and future prospects of nano sized granules in the form of Mouth dissolving tablets.

REFERENCES

1. Beri Chiman, Sacher Isha. Development of fast disintegration tablets: As oral drug delivery system. Indian Journal of Pharmaceutical & Biological Research, 2013; 1(3): 80-99.
2. Kashyap S., Sharma V., Singh L., Fast disintegrating tablet: A boon to pediatric and geriatric, Imperial Journal of Pharmaceutics & Cosmetology, 2011; 1(1): 1-11.
3. Pahwa R., Piplani M., Sharma PC., Kaushik D., Nanda S., Orally Disintegrating Tablets - Friendly to Pediatrics and Geriatrics, Archives of Applied Science Research, 2010; 2(2): 35-48.
4. Debjit B., Chiranjib B., Krishna K., Chandira R.M., Fast Dissolvingtablet: An Overview, Journal Of Chemical And Pharmaceutical Research, 2009; 1(1): 163-177.
5. Sastry V.S., Ram N.J., Joseph A.F., Recent technological advances in oral drug delivery – a review, PSTT, 2000; 3: 139-144.
6. Jain NK, Sharma SN. A text Book of Professional Pharmacy. 5th edition, Vallabh Prakashan, 2007, 295-314.
7. Sehgal Prateek, Gupta Ramdayal, Singh Umesh Kumar. Fast dissolving tablets: A New Venture in drug delivery. American journal of Pharma tech Research, 2012; 2(4): 253-278.
8. Dey Paramita, Maiti Sabyasachi. Orodispersible Tablets: A New Trend In Drug Delivery. J Natural Sci. Biology And Medicine, 2010; 1(1): 2-5.
9. Patel AR, Prajapati DS, Raval JA. Fast Dissolving Films (FDFs) as a Newer Venture In Fast Dissolving Dosage Forms. Int J Drug Devt Res, 2010; 2(2): 232-246.
10. Masih Daljit, Gupta Rajesh. Mouth Dissolving Tablets. UK Journal of Pharmaceutical and Biosciences, 2013; 1(1).
11. Chein YW. Oral Drug Delivery and Delivery Systems, 2nded. New York: Marcel Dekker; 1992.
12. Konare AS, Chaudhari PS, Oswal RJ, Kshirsagar SS, Antre RV, Chorage TV. Mouth Dissolving Tablets-An Innovative Technology. Int J Applbiol Pharm Tech, 2011; 2(1): 496-503.
13. Kumar VD, Sharma I, Sharma V. A Comprehensive Review On Fast Dissolving Tablet Technology. J Applied Pharma Sci, 2011; 1(5): 50-58.
14. Parkash V, Maan S, Yadav DSK, Jogpal HV. Fast Disintegrating Tablets: Opportunity In Drug Delivery System. J Advanced Pharma Tech Res, 2011; 2(4): 223-35.
15. Gohel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation Design And Optimization Of Mouth Dissolve Tablets Of Nimesulide Using Vacuum Drying Technique. AAPS Pharm Sci Tech, 2004; 5: 36.
16. Yadav Ajit Kumar, Sharma Anamika, Saxena Shivangi. Mouth Dissolving Tablets: General Overview and Formulation Aspects.Bulletin of Pharmaceutical Research, 2014; 4(1): 43-57.
17. Yadav Garima, Kapoor Anupriya, Bhargava Shilpi. Fast Dissolving Tablets Recent Advantages: A Review. International Journal of Pharmaceutical Sciences and Research, 2012; 3(3): 728-736.
18. Bhowmik Debjit, B. Chiranjib, Kant Krishna, Pankaj, R. Margret Chandira. Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research, 2009; 1(1): 163-177.
19. Shukla Dali, Chakraborty Subhashis, Singh Sanjay, Mishra Brahmeshwar. Mouth Dissolving Tablets: An Overview of Formulation Technology. Scientia Pharmceutica, 2009; 77: 309–326.
20. R. Santosh Kumar, Kumari Annu. Fast Dissolving Tablets: Waterless patient compliance dosage forms. Journal of Drug Delivery and Therapeutics, 2019; 9(1): 303-317.
21. Panigrahi R, Behera S, Panda C, A Review on Fast Dissolving Tablets. Webmed Central: Review articles, 2011; 1(11): 1-15.
22. Singh S, Nautiyal U, Singh R, Kaur S, Fast Dissolving Tablets – Future Aspects. International

Journal of Pharmaceutical and Medicinal Research, 2015; 3(2): 216-231.
23. Abay FB and Ugurlu T, Orally Disintegrating Tablets: A Short Review.Journal of Pharmaceutics & Drug Development, 2015; 3(3).
24. Hannan PA, Khan JA, Khan A, Safiullah S, Oral Dispersible System: A New Approach in Drug Delivery System. Indian Journal of Pharmaceutical sciences, 2016; 78(1): 2-7.
25. Heer Deepak, Aggrawal Geeta. Recent Trends of Fast Dissolving System: An Overview of formulation technology. Pharmacophore, 2013; 4(1): 1-9.
26. Prajapati BP And Ratnakar N. A Review On Recent Patents On Fast Dissolving Drug delivery System. International Journal Of Pharmtech Research, 2009; 1(3): 790-798.
27. Nandy BC., Mazumder B., Pathak K And Saxena N.An Overview On Fast Dissolving Drug Delivery System.AJPSR, 1(2): 2249-4898.
28. S. Neelam,S.Vipin,G. Summet.Recent Advances In Novel Mouth Dissolving Tablets.Novel Science International Journal Of Pharmaceutical Science, 2012; (3): 1204-211.
29. D. Bhowmik, Chiranjib, B; Krishnakanth, Pankaj and Chandra, RM.Fast Dissolving Tablet: An Overview. Journal Of Chemical And Pharmaceutical Research, 2009; 1 (1): 163-177.
30. Kagalkar Amrita A., Nitava Sachin A. Developments & Evaluation of Herbal Fast Dissolving Tablets of Tectone grandis linn & Bacchenia veriagate linn. Mixture. International Journal of Pharm Tech Research, 2014; 6(5): 1600-1607.
31. Hardenia Shive, Darwhekar Gajanan. Formulation and Optimization of fast dissolving tablets of Promethazine Theoclate using 3^2 factorial designs. Journal of Drug Delivery and Therapeutic 2017; 7(7): 12-14.
32. Prasad SGB., Gupta VRM.,N. Devanna. Formulation and Evaluation of Candesartan Cilexetil Porous Tablets by Sublimation Technique. Journal of Global Trends in Pharmaceutical sciences, 2014; 5(4): 2125-2131.
33. Kalia Anupama, Khurana Shelly, Bedi Neera. Formulation and Evaluation of Mouth Dissolving Tablets of Oxcarbazepine. International Journal of Pharmacy and Pharmaceutical Science, 2009; 1(1): 12-13.
34. Gudas G K., B. Manasa, VV. Rajesham. Formulation and Evaluation of Fast Dissolving Tablets of Chlorpromazine HCL. Journal of Pharmaceutical Science and Technology, 2010; 2(1): 99-102.
35. Prajapati B., Kaur S. Formulation and Evaluation of Mouth Dissolving Sublimation Tablets of Cimetidine to Treat Abdominal Cramps. International Journal of Pharmaceutical Science Invention, 2014; 3(9): 41-46.
36. Balagani P.K., G.Arcgana. Formulation and Evaluation of Nizatidine Fast Dissolving Tablets. World Journal of Pharmaceutics Research, 2014; 4(2): 1358-1372.
37. Jain SK, Shukla M. Development and in Vitro Evaluation of Ibuprofen Mouth Dissolving Tablet Using Solid Dispersion Technique, 2010; 58(8): 1037-1042.
38. Garg Ashish, Gupta M M. Taste Masking And Formulation Developement and Evaluation Of Mouth Dissolving Tablets Of Levocetrizine Dihydrochloride. Journal of Drug Delivery & Therapeutics, 2013; 3(3): 123-130.
39. Kamble Sharad K and Shinde Sunita S. Design and Development of Fast Dissolving Tablet of Gliclazide. Journal of Developing Drugs, 2017; 6(3): 2-13.
40. Sultana Shaik Shaheda, Rao Sk, S Swati. Formulation And Evaluation Of Herbal Fast Dissolving Buccal Film Containing Curcumin. World Journal Of Pharmacy And Pharmaceutical Sciences, 2018; 7(4): 1617-1635.
41. Zulkifli NA, Razak FSA, Long CM. The Effect Of Disintegrants On The Physical Properties Of A Cocoa Butter Based Fast Melt Tablet Developed By A Fusion Moulding Method. International Pharmaceutical Excipients Council, 2019; 10(2): 55-61.
42. Prasad SG, Gupta VRM. Formulation And Evaluation Of Fast Dissolving Tablet Of Tolvaptan. Journal Of Global Trends In Pharmaceutical Sciences, 2015; 6(1): 2403-2410.
43. Gosai AR, Patil SB, Sawant K. Formulation And Evaluation Of Oro Dispersible Tablets Of Ondansetron Hydrochloride By Direct Compression Using Superdisintegrants. International Journal Of Pharmaceutical Sciences And Nanotechnology, 2008; 1(1): 107-111.
44. Prasad SG, Gupta VRM, N. Devanna. Formulation And Evaluation Of Taste Masked Fast Dissolving Tablet Of Zolpidem Tartrate By Direct Compression Method. Journal Of Global Trends In Pharmaceutical Sciences, 2014; 5(4): 2167-2176.
45. Chaturvedi S, Agrawal VK, Verma A. Comparative Evaluation of Natural and Semi-Synthetic Superdisintegrants In The Formulation Of Oro-Dispersible Tablets Of Norfloxacin. International Journal of Pharmacy and Pharmaceutical Sciences, 2012; 4(2): 576-583.
46. Patil BS, Rao NGR. Formulation And Evaluation Of Fast Dissolving Tablets Of Granisetron Hydrochloride By Vacuum Drying Technique. Journal Of Applied Pharmaceutical Science, 2011; 1(4): 83-88.
47. Mehta M, Bhagwat DP, Gupta Gd. Fast Dissolving Tablets Of Sertraline Hydrochloride. International Journal Of Chemtech Research, 2009; 1(4): 925-930
48. Rao NGR, Kota RK, Setty CM. Formulation And Evaluation Of Fast Dissolving Chlothalidone

Tablets. International Journal Of Pharmacy And Pharmaceutical Sciences, 2009; 1(1): 79-87.
49. Bhardwaj S , Jain V, JAT RC. Formulation And Evaluation Of Fast Dissolving Tablet Of Aceclofenace. International Journal Of Drug Delivery, 2010; 2 : 93-97.
50. Khemariya P, Gajnhiye KR, Vikas VD. Preparation And Evaluation Of Mouth Dissolving Tablets Of Meloxicam. International Journal Of Drug Delivery, 2010; 2: 76-80.
51. Modi A, Singh V. Formulation And Evaluation Of Fast Dissolving Tablets Of Diclofenac Sodium Using Different Superdisintigrants By Direct Compression Method. International Journal Of Pharmaceutical & Biological Archives, 2012; 3(4): 1003-1007.
52. Kapse NK, Vilas PB, Birajdar AS. Co-Processe Superdisintegrants: Novel Technique For Design Orodispersible Tablets. Journal Of Innovations In Pharmaceuticals And Biological Sciences, 2015; 2(4): 541-555.
53. Konapure SA, Chaudhari PS, Oswal RJ. Mouth Dissolving Tablets" An Innovative Technology. International Journal Of Applied Biology And Pharmaceutical Technology, 2011; 2(1): 496-503.
54. Prasad BSG, Subhramaniam SN,M Swetha. Formulation And Evaluation Of Oro-Dispersible Tablets Of Levocetrizine By Melt Granulation Technology. Der Pharmacia Lettre, 2013; 5 (1): 107-115. [21] Sree Giri Prasad. B, V. R.
55. Gupta M., Devanna. N. Der Pharmacia Lettre, 2012; 4(5): 1505-1514.
56. T. Satyanarayana, J. Murali Krishna, P. Suresh Kumar, S. Navaneetha Krishnan, G. Shaji. Der Pharmacia Lettre, 2011; 3(6): 125-130.
57. S. Dineshmohan, K Vanitha, A Ramesh. Formulation And Evaluation Of Salbutamol Sulphate Fast Dissolving Tablet. International Journal of Research In Pharmaceutical And Biomedical Sciences, 2010; 1(2): 105-108.
58. Metker Vishal, Kumar Annj, Pathak Naveen. Formulation And Evaluation Of Orodispersible Tablets Of Lornoxicam. International Journal of Drug Development & Research, 2011; 3(1): 281-285.
59. Jain CP, Naruka PS. Formulation And Evaluation Of Fast Dissolving Tablets Of Valsartan. International Journal Of Pharmacy And Pharmaceutical Sciences, 2009; 1(1): 219-226.
60. Singh VK, Singh Utkarsh,Maurya JK.Formulation And Evaluation Of Mouth Dissolving Tablet Of Propranolol HCL Using Different Superdisintegrant. Journal of PHAR Tech Research, 2013; 3(6): 583-590.
61. Khan Tarique, Nazim Sayyed, Shaikh Siraj. An Approach For Rapid Disintegrating Tablet: A Review. International Journal Of Pharmaceutical Research And Development, 2011; 3(3): 170-183.