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Review Article

A review on orally disintegrating tablet: As a new potential approaches for drug delivery system

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ABSTRACT

In the current scenario, orally disintegrating tablet are gaining more prominence as a novel potential drug delivery system & emerges as one of the popular & widely accepted dosage forms, especially for pediatric due to its troubleshoots the problem of dysphagia and geriatric patients suffering from Parkinson's disorder or hand tremors. An orally disintegrating tablet is a drug dosage form available for imitated amount of the over the counter (OTC) and prescription medication. Over the past three decades, orally disintegrating tablets (ODTs) have gained substantial popularity as a preferable alternative to traditional tablets and capsules due to improved patient compliance. ODTs are solid dosage forms containing medicinal substances which disintegrate rapidly, typically in a matter of seconds, when placed on the tongue. It has been developed for oral administration, also called as fast-melt, rapid-melt, porous tablet or fast disintegrating tablet (FDTs). This article focuses on the patented technologist available and the advance made so far in the field of fabrication of orally disintegrating table. Apart from that this article also provide the detail information of need for development of ODT's, formulation challenges and desired characteristics of orally disintegrating tablet, ingredient to be used in formulation of ODT's, mechanism of tablet disintegration and evaluation.

Keywords: Over the counter, direct compression, super-disintegrates, Mechanism of disintegration, Formulation Challenges, patented technologies

INTRODUCTION

Now a day, pharmaceutical companies are focus on the new drug delivery systems to ensure the delivery of the drugs to the patients efficiently and with fewer side effects [1]. The oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, non-invasive method and ease of administration leading to high level of

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patient compliance[2,3,4]. Tablets and capsules are the most popular dosage forms, but drawback of such dosage forms is Dysphagia or difficulty in swallowing [4]. To take care of these issue, pharmaceutical technologists have invested in their best amounts of energy to build up a quick dissolving drug delivery, i.e. Mouth Dissolving Tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing [4,5].

Mostly the mouth dissolving delivery system must include excipient to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients[5,6]. Oral disintegrating tablet are also called as melt-in-mouth tablets, repimelts[5], porous tablets, snappy deteriorating tablets[7], oro-dispersible, quick dissolving or rapid disintegrating tablets, Mouth dissolving tablets, fast dissolving, rapid –dissolve, fast melts[7], Effervescent Drug Absorption system[5,7].

Mouth Dissolving Tablets as characterized as "A strong dose structure containing restorative substances, which disintegrates rapidly, more often than not inside a matter of seconds, when put upon the tongue"[7]. Orodispersible tablets are uncoated tablets proposed to be set in the mouth where they disperse quickly before being swallowed [8]. Orodispersible tablet can be prepared by various methods like freeze drying, sublimation of volatile salt, incorporation of super disintegrating agent, wet compression method and sugar based excipient. The problem that tablet is low physical resistance and high friability. Sugar have a good compatibility as well as good solubility property which help to improve the disintegration[9]. The center for drug Evaluation and Research states an ODT to be: "A solid dosage form containing therapeutic substances, which break down quickly, usually within a matter of seconds, when put upon the tongue"[10,11]. According to European Pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach behind the development of MDT is the use of superdisintegrants like Cross linked carboxymethyl cellulose (Croscarmellose), Sodium starch glycolate (Primogel, Explotab) , Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva[12]. U.S. Food and Drug Administration approved Zydis, ODT formulation of Claritin (loratadine) in December 1996. It was followed by a Zydis ODT formulation of Klonopin (clonazepam) in December 1997, and a Zydis ODT formulation of Maxalt (rizatriptan) in June 1998. Further a number of drugs have been approved by regulatory authorities for ODT formulations[14]. Recent market studies show that more than half of the patient population prefers ODTs to other dosage forms and most consumers would ask their doctors for ODTs (70%), purchase ODTs (70%), or prefer ODTs to regular tablets or liquids (>80%)[15]. As disintegration of tablet in the mouth this could enhance the clinical effect of the medicine through pre-gastric absorption from the mouth, pharynx and esophagus. This leads to an increase in bioavailability by avoiding first pass metabolism[16,17]. Fast dissolving drug delivery can be accomplished different strategies like direct compression, wet granulation, compression molding, volatization and freeze – drying. They include various mechanisms like use of high amounts of hydrophilic disintegrating agents which allow the dosage forms to disintegrate quickly in the patient's mouth on contact with saliva[17]. United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs ranges from several seconds to about a minute [18,19]. A disintegrant utilized in granulated formulation processes can be increasingly successful whenever utilized both "Intragranularly" and "Extragranularly" thereby acting to break the tablet up into granules and having the granules further disintegrate to release the drug substance into solution[20, 21].

Properties of superdisintegrants with special emphasis on correlating these functional properties to disintegrate efficiency and drug release rate. Water penetration rate and rate of disintegration force development are generally positively related to disintegrate efficiency in non-soluble matrix in a direct compression process, drug is blended with a variety of excipients, subsequently lubricated and directly compressed into a tablet[21,22].

From the point of view of the pharmaceutical business, ODTs may provide new business opportunities in the form of product differentiation, life extension and life cycle management, exclusivity, uniqueness and patent life extension[25]. Recently there is an enormous development of various technologies for the preparation of orally fast disintegrating tablets.

SALIENT FEATURE OF ORALLY DISINTEGRATING TABLET [16,26-29]

i. Ease of administration to patients who are mentally ill, disabled and uncooperative such as pediatric and geriatric patients and, psychiatric patients.
ii. Convenience of administration and accurate dosing as compared to oral liquids.

iii. Quick disintegration and dissolution of dosage form and absorption which may produce rapid, onset of action.
iv. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.
v. Ability to provide advantages of liquid medication in the form of solid preparation.
vi. Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.
vii. 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.
viii. Good mouth feels property of MDTs helps to change the basic view of medication as bitter pill, particularly for pediatric patients.
ix. Can be designed to allow high drug loading.
x. Cost effective therapy.

LIMITATIONS[27,30]

i. It is difficult to formulate FDTs of drug which are having high dose, example like antibiotics ciprofloxacin with adult dose tablet containing about 500mg of the tablet.
ii. Patients who concurrently take anticholinergic medication may not be the best candidates for MDTs and patients like Sjogren's syndrome or dryness of the mouth due to decrease saliva production may not be good candidates for these tablet formulation.
iii. Drugs with short half-life, frequently dosing and those who requires sustained or controlled action are difficult to formulate as a FDTs.
iv. FDTs usually have insufficient mechanical strength which calls for careful handling by patient.
v. If such tablets are not formulated properly then they may leave unpleasant taste or grittiness in the mouth

NEED FOR DEVELOPMENT OF ODT'S[4,15,31]

The demand of non-invasive drug delivery systems persists due to patient's poor acceptance and compliance with existing delivery system. The pediatrics and geriatric patient populations are the main targets, as both the groups are difficult to swallow conventional tablets and capsule.

Patient Related Factors: Mouth dissolving dosage forms are suitable for patients, who for one reason or the other, find it inconvenient to swallow traditional tablets and capsules with glass of water such as pediatrics and geriatric patient. These include the following

i. Pediatric and geriatric patients who have difficulty in swallowing or chewing traditional tablets dosage forms.
ii. The risk of chocking or suffocation during oral administration of conventional solid dosage form due to physical obstruction is avoided, thus providing safety.
iii. Elderly patients who are not able to swallow a daily dose of antidepressant.
iv. An eight-year old with allergies who desires a more convenient formulation than antihistamine syrup formulation.
v. Middle-aged women who take radiation therapy for breast cancer may be too nauseous to swallow her H2- blocker.
vi. A schizophrenic patient who may try to hide a conventional tablet under tongue to avoid their daily dose of an atypical antipsychotic.
vii. A patient with nausea problem, who may be travelling, or no access to water.

Effectiveness factors:

i. Improved the bioavailability and rapid onset of action are a major claim of these dosage form. Because the tablets disintegrate inside the mouth, drugs may be absorbed in the buccal, pharyngeal, and gastric regions. Thus, quick drug therapy intervention and improved the bioavailability of drugs are possible.
ii. The pre-gastric drug absorption avoids the first-pass metabolism and drug dose can be reduced if a significant amount of the drug is lost through the hepatic metabolism.

Safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism, and for drugs that have a substantial fraction of absorption in the oral cavity and pre-gastric segments of GIT.

FORMULATION CHALLENGES AND DESIRED CHARACTERISTICS OF ORALLY DISINTEGRATING TABLET[15,30,32]

Mechanical strength :ODTs are allow to disintegrate in oral cavity , they are made of porous or soft molded matrices , this makes tablet friable and handling becomes difficult and often requiring specialized peel-off blister packing that may add to the cost. Orodispersible tablets with highly porous structure and good mechanical strength have been developed by sublimation method. Therefore it is important to find the porosity of tablet which should offer faster disintegration and at the same time should maintain high mechanical strength. Also Durasolv® has much higher mechanical strength than Orasolv due to the use of higher compaction pressures during compression.

Palatability: ODTs are intended to be dissolved in mouth. Most of the drugs are unpalatable. Orally disintegrating drug delivery systems contain the medicament in a taste-masked form. Bitter taste can be masked with enough sweetener and flavors. Methods of taste masking include lipophilic vehicles, coating with polymers, carbohydrates, lipids or proteins complexion with cyclodextrins or ion-exchange resins, formation of salts, use of salting out layers and solid dispersions.

Hygroscopicity: Most of drugs in form of ODTs are hygroscopic in nature and hence need to be protected from humidity which calls for specialized product packaging. To overcome humidity problem special working facilities can be designed by simple methods and special air-conditioning systems can be set up.

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.

Aqueous solubility :Drug should be stable both in water and in saliva, should not ionize at oral cavity pH and should be able to permeate oral mucosal tissue to diffuse and partition in upper GI epithelium (log P > 1, or preferably > 2, not have short half-life). To optimize solubility problem of the active pharmaceutical ingredient some solid buffers and surfactants can also be chosen. 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.

***Size of tablet*:** The degree of easy administration of tablet depends on its size. Size of tablet 7 and 8 mm are easy to swallow while tablets of size 8mm are easy to handle. Hence, tablet sizes which are both easy to handle and swallow are difficult to achieve. For the patient compliance, to make the swallowing easier, round shape punches having optimum dimensions can be used.

Rapid disintegration of tablet: FDTs should disintegrate in the mouth without or with the presence of very small amount of water, for disintegration to occur, disintegration fluid is provided by the saliva of the patient. After disintegration, disintegrated tablet should become a soft paste or liquid suspension. The " Fast disintegration " means disintegration of tablet in less than 1 minute, but it is preferred to have disintegration as soon as possible.

INGREDIENT TO BE USED IN FORMULATION OF ODT'S[8-10,21-23]

Wide variety of the ingredients is used for the preparation of FDTs which may be from natural or synthetic origin. The ingredient which is to be incorporated in the FDTs should allow the faster disintegration of the tablet to achieve quick onset of action. Pharmaceutical codes require that all ingredients in drugs, as well as their chemical decomposition product are identified and guaranteed to be safe. Various active and inactive excipient, plant material are used for the preparation of FDTs that are as follow.

Fillers or diluents: These are the agent who improves the textural characteristics that in turn enhance the disintegration in the mouth and also help to reduce the concentration of the active in the composition. These agents increase the bulk of the product and make it possible for the final product to have the proper volume for patient handling. More commonly used Diluents are cellulose derivatives and preferably microcrystalline cellulose, maltodextrins, beta-cyclodextrins, starches, lactose, polyols and preferably mannitol.

Lubricant: They are used to reduce the friction during compaction and ejection of tablets. They remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach. E.g. Stearic acid, magnesium stearate, calcium stearate, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, colloidal silicon dioxide.

Emulsifying agents*:* Incorporation of emulsifying agent is useful in stabilizing the immiscible blends and enhancing bioavailability. They promote rapid disintegration and drug release without chewing, swallowing or drinking water. E.g. Alkyl sulfate

Binders: Binder help to keep the composition of these fast melting tablets together during compression stage. The choice of a binder is critical for achieving the desired sensory and melting characteristics, and for the faster release of drug. The right selection of a binder or combination of binders is essential to maintain the integrity and stability of the tablet. Binders can either be liquid, semi-solid, solid or mixtures of varying molecular weights such as polyethylene glycol.

Antistatic agent: used to promote powder flow by reducing interparticle friction and cohesion. E.g. silica, talc, magnesium carbonate.

Flavors and Sweeteners: Flavors and sweeteners make the products more palatable and pleasing for patients. They are used to overcoming bitterness and undesirable tastes of some active ingredients. Both natural and synthetic flavors can be used to improve the organoleptic characteristic of fast-melting tablets. Example of sweeteners includes sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose.

Gas producing disintegrants: Gas producing disintegrants are used especially where extra rapid disintegration or readily soluble formulation is required. Composition is based upon the same principles as those used for effervescent tablets, the most common being mixtures of citric & tartaric acids plus carbonates or bicarbonates.

Superdisintegrants: Superdisintegrants added to tablet or capsule blend to aid in the breakup of the compacted mass, when put into a fluid environment. It is especially design for immediate release product where rapid release of the product is required. These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. They provide rapid disintegration due to the combination effect of swelling and water absorption by the formulation. Due to swelling criteria of superdisintegrants the wetted surface of carrier increase, these increase the wet ability and dispersibility of system thus improve the disintegration and dissolution. Superdisintegrants improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs, Example of superdisintegrants are cross linked carboxymethyl cellulose (crosscarmellose), SSG, PVP, Sago starch, Isphagula husk, calcium silicate, soy polysaccharides etc.

Mode of addition **[21,22,34]**

There are three methods of incorporating disintegrating agents into the tablet:

Internal addition (Intragranular): In both wet and dry granulation process the superdisintegrants are mixed with other excipient and granulation is carried out. Thus the superdisintegrants are incorporated within the granules.

External addition (Extragranular): In both wet and dry granulation process, the superdisintegrant is added to the granules during dry mixing prior to compression.

Partly internal and external: In this method part of superdisintegrants are added to intragranular and a part to extragranules. This method usually produces better results and more complete disintegration than Intragranular and Extragranular process.

The proper choice of disintegrant and its consistency of performance are of critical importance to the formulation development of FDTs. In more recent years, increasing attention has been paid to formulating not only fast dissolving and /or disintegrating tablet that are swallowed, but also orally disintegrating tablet that are intended to dissolve and / or disintegrate rapidly in the mouth.

MECHANISM OF TABLET DISINTEGRATION **[33-36]**

Following are the four major mechanism of disintegration of tablet

Swelling: The most common mechanism of action for tablet disintegration is swelling. Tablets with low porosity show high disintegration due to lack of adequate swelling force. By swelling in contact with fluid, the adhesiveness of other ingredients in a tablet is causing the tablet fall apart. On the other side, sufficient swelling force is exerted in the tablet with low porosity. It is note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

Capillary action & Wicking: Capillary action is the first step action. When tablet come in contact with 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.

Deformation: When tablet compressed, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch such as potato or corn starch was improved when granules were extensively deformed during compression. When these tablets are comes to contact with aqueous environment, the energy potential of deformed starch grain will be triggered to cause disintegration.

Particle repulsive force**:** Another one mechanism of disintegration is swelling of tablet made with 'nonswellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non-swelling particle also cause disintegration of tablets. The electric repulsive

forces between particles are the mechanism of disintegration and water is required for it.

TECHNIQUE USED FOR THE PREPARATION OF ORALLY DISINTEGRATING TABLET:

Various technologies used for the preparation of FDTs are broadly classified into two categories.

1. Patented
2. Nonpatented (Conventional)

Patented Technique[26,32,37-39]

FlashtabTechnology: Ethypharm France has patented the Flashtab Technology. This technology involves the preparation of granules of drug by using conventional technique like by simple wet or dry granulation or by coacervation, micro encapsulation, and extrusion spheronisation. Tablet prepared by this system consist of an active ingredient in the form of micro crystal. This micro crystal of the drug are then added to the granulated mixture of excipient and compressed into tablet. Excipient used in this system is of two types such as disintegrating agent and swelling agent. Disintegrating agent include reticulated PVP and carboxy methylcellulose. Swelling agent include starch and microcrystalline cellulose. Disintegrating time is within 1 min.

Wowtab Technology: Yamanouchi Pharmaceutical Co. has patented the Wowtab Technology.WOW means "Without Water ". This system used sugar and sugar-like excipients. The two different types of saccharides are combined to obtain a rapidly melting strong tablet formulation with adequate hardness and fast dissolution rate. The active ingredient is mixed with a low mouldability saccharide (lactose, glucose) and granulated with a high mouldability saccharide (mannitol, sorbitol) and compressed into tablet. Formulated tablet produced from this technology will have sufficient hardness to maintain the physical characteristics of the dosage form during in process production process until it comes in contact with moisture such as saliva in mouth.

Flash Dose Technology: Fuisz have patented the Flash Dose Technology. Nurofenmeltlet, a new form of ibuprofen as melt-in-mouth tablets, prepared using flash dose technology is the first commercial product launched by" Biovail Corporation". This system based on the preparation of the sugar based matrix known as the floss, which is made from the combination of excipient either alone or with drug. Two platforms are available called Sheaform or ceform which are currently utilized in preparation of wide range of ODTs. The advantage of this system is to provide tablet with high surface area for dissolution. High temperature is required to melt the matrix which limits the use of heat sensitive drugs.

Orasolv Technology: "CIMA" labs developed the Orasolv Technology. Here the taste masking of active ingredient is achieved and it also contain effervescent disintegrating agent which is activated by saliva. The amount of effervescent agent (citric, tartaric, malic, fumeric, adipic and succinics and a carbonate source like sodium bicarbonate, sodium carbonate, potassium bicarbonate and potassium carbonate, magnesium carbonate) is in general about 20-25% of the total weight of the tablet. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to produce the tablets. The tablet produced by this technique is soft and friable which calls for packaging in specially designed pick and place system. The major disadvantage of this technique is its low mechanical strength.

Durasolv Technology: CIMA labs have patented the Durasolv Technology. The tablets made by this technology consist of a drug, fillers and a lubricant. These systems involves the preparation tablets by using conventional tableting equipment and have good rigidity and tablet can be packed into the conventional packaging system like blister. Durasolv is an appropriate technology for products requiring low amounts of active medicament. Disadvantage of the Durasolv is that the technology is not compatible with high dose of active medicament, because the formulation is subjected to high pressure during compaction.

Zydis Technology: Zydis was the first marketed technology developed by R.P.Scherer, Inc. The dosage form dissolves in the mouth within seconds after placement on the tongue. The primary principle involved in this technique is freeze drying of tablet in which active ingredient is physically intrapped within the matrix of fast dissolving carrier material. This technology consist of softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of this softened mass through the syringe or extruder to get a cylinder of the product into even segment using heated blade to form tablets. Drying is carried out. Dried cylinder can also use to coat granules having bitter taste.

Nonpatented(Conventional)[36,40-43]

Freeze drying/Lyophilization: A process in which water is sublimated from the product after freezing. The formulations show improved dissolution rate due to the appearance of glossy amorphous structure to bulking agents and sometimes to drug resulting in highly porous and lightweight product.

The ideal drug characteristics for this process are relative water insolubility with fine particle size and good aqueous stability in suspensions. Primary problem associated with water soluble drugs are formation of eutectic mixture, because of freezing point depression and formation of glassy solid on freezing, which might collapse on sublimation. Freeze drying process normally consists of three steps:

I. Material is frozen to bring it below the eutectic point.
II. Primary drying to reduce the moisture around 4% w/w of dry product.
III. Secondary drying to reduce the bound moisture up to required final volume.

Molding: There are two types i.e. solvent method and heat method. This process is achieved by using water soluble excipient like sugars. Drug and excipients powder blend is pushed through a very fine screen to improve the dissolution rate then moistened with a hydroalcoholic solvent and molded into tablets under pressure, the process ended by air drying to evaporate the solvent . The tablets manufactured so formed are less compact than compressed tablets and possess a porous structure that improved the dissolution. In the heat molding process, a suspension consists of a drug, agar and sugar (e.g. mannitol or lactose). This suspension is poured into the blister packaging wells, and then agar is solidified at the room temperature to form a jelly and dried at 30°C under vacuum. The main concern about these molded tablets is their mechanical strength, which can be achieved by using binding agents.

Sublimation: The presence of a highly porous structure in the tablet matrix is the main factor for quick disintegration of ODT; this process is achieved by addition of some inert volatile substances like urea, naphthalene, camphor, etc. to other ingredient and the compression of blend into tablet. Camphor was sublimated in vacuum at 80°C for 30 min after preparation of tablets. Removal of volatile material by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc. can also be used as pore forming agents.

Spray Drying: Spray dryer are used in the pharmaceutical industry to produce highly porous powder. This technique is mainly based on a particular support matrix mannitol as a bulking agent and sodium starch glycolate or crosscarmellose or crosspovidone are used as superdisintegrants. Tablet formulated by this spray dryer powder get disintegrated in less than 20s in an aqueous medium. The principle behind this technique is the active drug is dissolved or dispersed in an aqueous solution of polymer. Disintegration and dissolution rate were further improved by addition of effervescent agents, i.e. citric acid and sodium bicarbonate.

Direct Compression: Direct compression is most popular and well known technique for the preparation of FDTs. The advantage of this method includes the simplest and most cost effective tablet manufacturing technique. The principle behind this technique is use of the availability of improved excipients especially super-disintegrants and sugar based excipients in optimum concentration so as to improved disintegration along with pleasant mouth feel.

Mass Extrusion: This technique involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol and expulsion of softened mass through the extruder or syringe to obtain cylinder of the product into even segment employing heated blade to form tablet. The dried cylinder can be used to coat the granules of bitter tasting drugs and thereby masked their bitter taste.

Nanonization: It involves the reduction of the particle size of drug to nano size by wet-milling technique. Surface adsorption of the nano crystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into tablet. This technique is beneficial for poor water soluble drugs and also for a wide range of doses (up to 200 mg of drug per unit).

Cotton Candy Process: They utilize the spinning mechanism to produce floss like crystalline structure, which mimic cotton candy. This technique involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to improve the flow properties and compressibility. This candy floss matrix is then milled and blended with active medicament and excipients and subsequently compressed to ODT. These processes are suitable for high doses of drug and produce a tablet with improved mechanical strength.

Fast Dissolving Films: This technique offers very convenient means of taking medication and supplements. In this technique, water soluble film forming polymer (pollutant, carboxy methylcellulose, hydroxypropyl methylcellulose, hydroxyl ethylcellulose, hydroxyl prpylcellulose, sodium alginate etc.) drug and other taste masking ingredient are dissolved in nonaqueous solvent to prepare non-aqueous solution, which forms a film after evaporation of solvent.

EVALUATION[44,45]

Tablet Thickness (mm): Tablet thickness is an important characteristic for size and appearance. The thickness of tablet was measured by using Vernier Caliper, placing tablet between two arms of the Vernier Caliper. 5 tablets were taken and their thickness was measured.

Hardness (kg / cm2): The tablet hardness, which is the force required to break a tablet. The tablet hardness was measured using Monsanto hardness tester. The hardness was measured in terms of kg /cm2. The resistance of tablets to shipping or breakage, under condition of storage, transportation and handling before usage, depends on its hardness.

Friability (%): Friability measures the tablet strength. Roche Friabilator was used to test the friability of tablets using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 20min, the tablets were weighed and the percentage loss in tablet weigh was determined.

Wetting time (s): A piece of tissue paper folded twice was placed in a small petri dish containing 6ml of water. A tablet was placed on the paper and the time taken for complete wetting of tablet was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted.

Water absorption ratio (%): A piece of tissue paper folded twice was placed in a small petridish having Internal Diameter = 6.5cm containing 6ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The wetted tablet was taken and reweighted[24].

Water absorption ratio(R) was determined using following equation.

$$R = 100 (Wa – Wb) / Wb$$

Where, Wa = weight of tablet after water absorption

Wb = weight of tablet before water absorption

Weight Variation: Twenty tablets were selected randomly and weighed individually. Average weight of the tablets was determined. Deviation of each tablet weight from average weight was determined. The specification used for weight variation test was as per IP (not more than 2 of the individual masses deviate from the average mass by more than the 5% and none deviate by more than 10 %).

Drug Content Uniformity(%): Five tablets were crushed and from this, quantity equivalent to 10mg of sample was taken into a 100ml volumetric flask and dissolved in fluid , and assayed for drug content using a UV spectrophotometer .

In-Vitro disintegration time (s): The in-vitro disintegration time was determined using USP disintegration test apparatus at $37^0C \pm 2^0C$. The tablets were placed in each of six tubes of the apparatus and the time taken for complete disintegration of the tablet was noted.

In-vitro Dissolution study: The dissolution studies of formulated tablet of sample were performed by using USP type II dissolution test apparatus (United States Pharmacopoeia, 2006) in 900 ml of fluid respectively. Temperature was maintained at 37 ±0.5°C and 60 rpm stirring was provided for each dissolution study. Samples were collected periodically and replaced with a fresh dissolution medium. After filtration through Whatman filter paper 41(pore size 0.45µm), concentration of drug was determined spectrophotometrically on UV Visible spectrophotometer.

CONCLUSION

Orally disintegrating tablets have potential leads over conventional dosage forms, with improved patient compliance, convenience, bioavailability and rapid onset of action. They're a great way to get medications to geriatric and pediatric patients. They have major advantages over both solid and liquid dosage forms in that they remain solid during storage, assisting in dosage form stabilization, and then turn into liquid form within seconds of administration. Several consumer products are available on the market as a result of the range of innovations used in its formulation. As a result, ODT has a lot of potential to become the delivery mechanism for most drugs in the near future.

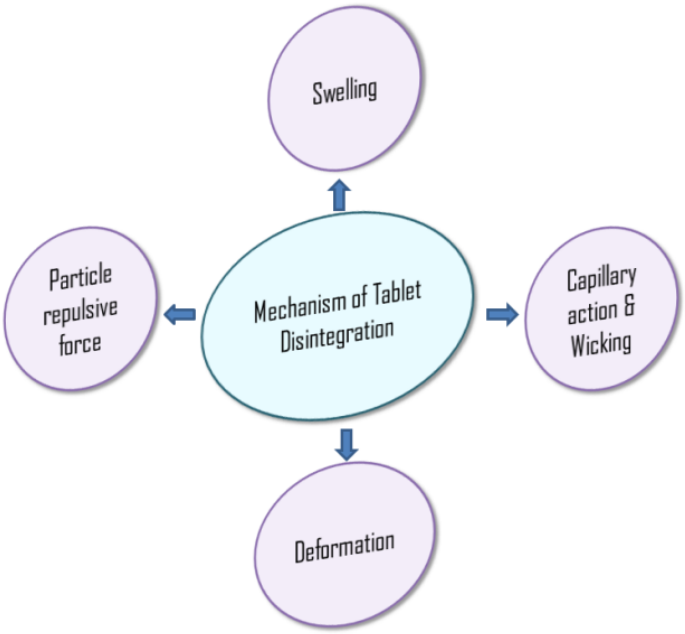

Fig.No. 1: Mechanism of tablet disintegration

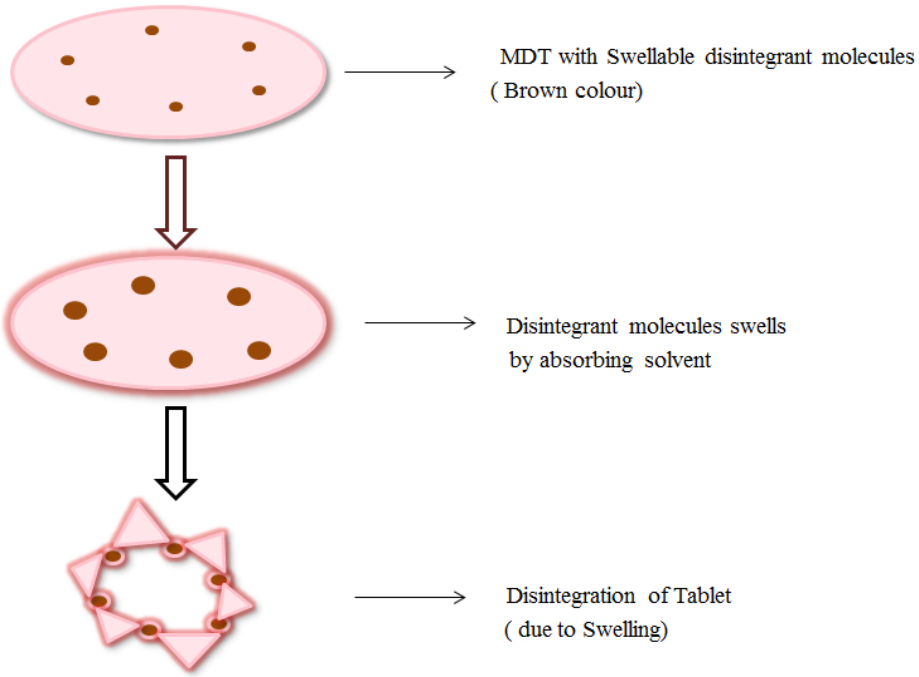

Fig.No.2:Swelling Mechanism of a Disintegrant in which the disintegrant swell, absorbs the surrounding medium aiding in fast disintegration[20]

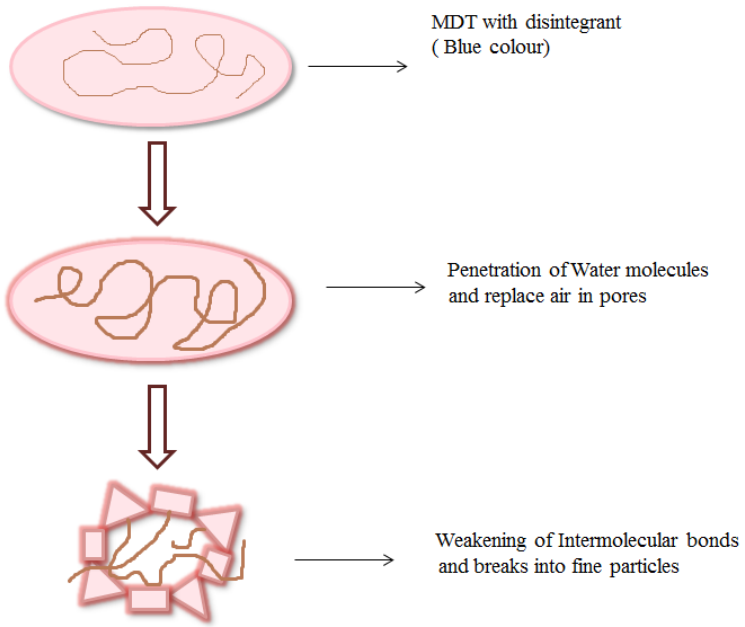

Fig.No.3: Wicking Mechanism. This mechanism involves Capillary action aiding faster disintegration[20]

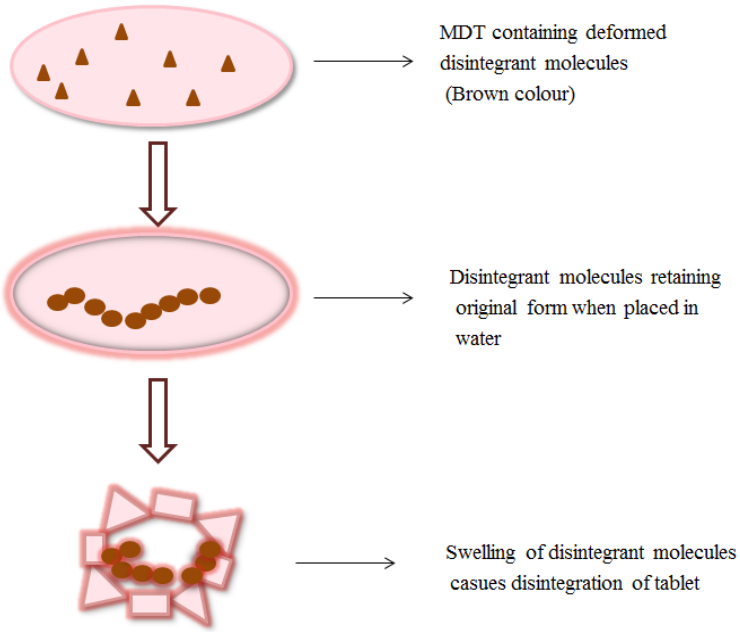

Fig.No.4: Deformation mechanism of Disintegrant. In this mechanism, irregular arrangement of molecules (in contact with medium) causes fast disintegration[20]

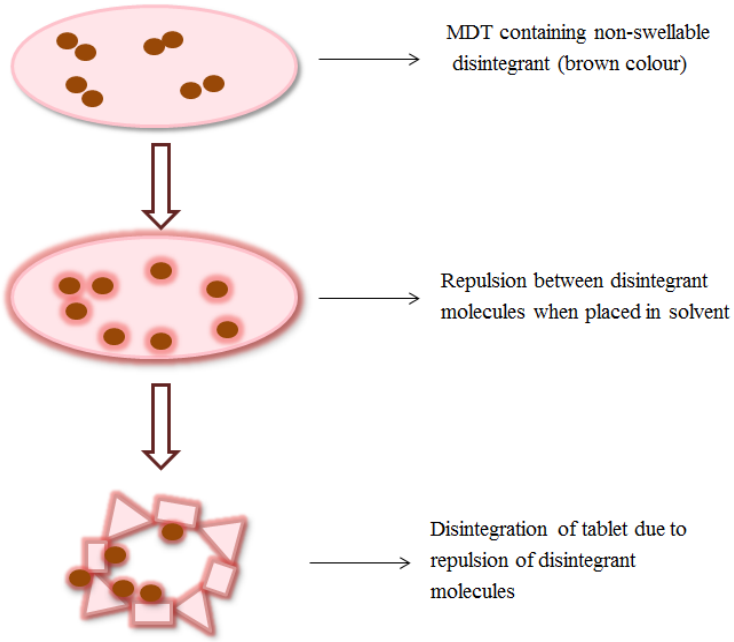

Fig.No.5: Repulsion mechanism of Disintegrant[20]

Table 1: Percentage deviation in weight variation

Average weight of a tablet	Percentage deviation
80 mg or less	10
More than 80 mg and less than 250 mg	7.5
250 mg or more	5

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