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A NOVEL APPROACH TO ORAL DRUG DELIVERY FAST DISSOLVING FILM

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ABSTRACT

In the recent years, many of the pharmaceutical groups are focusing their research on rapid dissolving technology. This technology evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers, so OFDFs are gaining the interest of large number of pharmaceutical industries Numerous FDT products entered the market in the nineteen eighties. This novel drug delivery like FDT or mouth dissolving tablet (MDT) has overcome several disadvantages like dysphagia or non-accessibility of water whereas travel. Compared with typical dosage form FDT is an alternative as well as helpful for the patient. The basic approach employed in the development of FDT is that the use of superdisintegrants likecrosspovidone, croscarmellose sodium or maximizing pore structure within the formulation. This review article contains different techniques used for preparing FDT, silent features, numerous proprietary technologies, mechanism of super disintegration, and also the limitations.

KEYWORDS: Fast dissolving tablet, Mouth dissolving tablet, Dysphasia, Super disintegrants.

INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, selfmedication, pain avoidance and most importantly the patient compliance. 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. 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 episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Or dispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people4. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva5. The faster the drug into solution, quicker the absorption and onset of clinical effect. 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 advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics.[1] Their growing importance was underlined recently when European pharmacopoeia adopted the term " Orodispersible tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach in development of FDT is the use of superdisintegrants like cross linked carboxymethyl cellulose (croscarmellose), sodium starch glycolate (primogel, explotab), polyvinylpyrollidone (polyplasdone) etc, which provide instantaneous disintegration of tablet after putting on tongue, their by release the drug in saliva. 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. More ever, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet. The technologies used for manufacturing fast-dissolving tablets are freeze-drying, spray-drying, tablet molding, sublimation, sugar-based excipients, tablet compression, and disintegration addition. As a result of increased life expectancy, the elderly constitute a large portion of the worldwide population today. These

people eventually will experience deterioration of their physiological and physical abilities.[2]

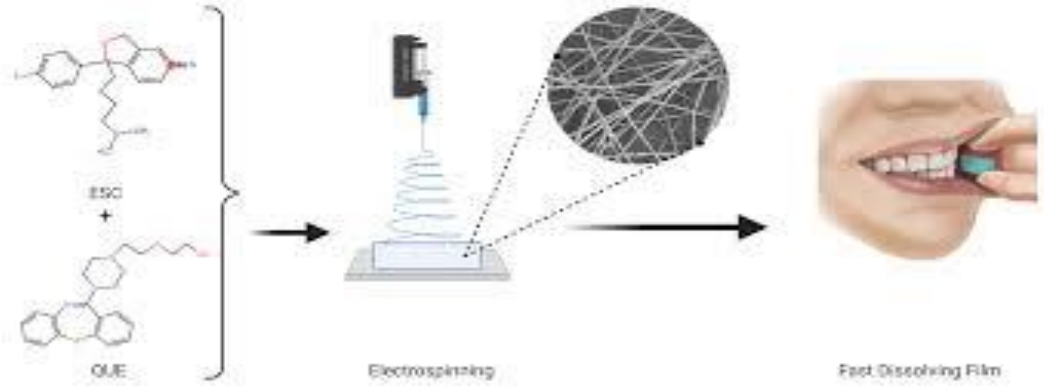

Fig. No. 1: Fast dissolving tablet.[1]

Criteria for Fast dissolving Drug Delivery System

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 as temperature and humidity.
- Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost.[3]

Salient Feature of Fast Dissolving Drug Delivery System

- Ease of administration for patients who are unstable, disabledand uncooperative.
- No demand of water to the patient.
- It ought to be the quick disintegration of fast dissolving in nature.
- Overwhelm unsatisfactory taste of the drug.
- Can be designed to leave lowest or no residue within the mouth
- once administration and additionally to produce a nice mouth feel.
- It permits high medication stacking.
- Ability to create advantages of the fluid solution inside the sortof strong preparation.[4]

BENEFITS OF FAST DISSOLVING TABLETS

- Patient having problem in swallowing like medicine, geriatric and psychiatrically patients will simply administer this kind of dosage form.
- Improved quiet consistence.
- Rapid begins of activity and ought to give an enhanced bioavailability.
- Comfort of taking and precise dosing when contrasted with fluids.
- Gives correct dosing as compared to liquids.
- Free need to measure, an important disadvantage in liquids.
- Better stability.
- No need of water to swallow the measurement from, that is to a great degree helpful component for patients who are voyaging and don't have prompt access to water.
- Good mouth feel property fluctuates the basic perspective of the drug as "bitter drug".
- Some medicines are absorbed from the mouth, throat and oesophagus because the secretion passes down into the abdomen, and in such cases bioavailability of the medication in exaggerated.
- Pregastric assimilation may bring about enhanced bioavailability enhanced clinical execution through a markdown of undesirable impacts.
- The oral or buccal membrane being extremely vascularized, medicines are often absorbed directly and may enter the circulation while not undergoing first -pass internal organ metabolism.[5]

DEMERITS OF FAST DISSOLVING TABLETS

- The disadvantage is that they are fragile and brittle.
- It wants a special package for defense throughout storage and transportation.[6]

LIMITATION OF FAST DISSOLVING TABLETS

- The tablets once in a while have lower mechanical quality. Hence, careful handling is needed throughout producing method.
- The tablets may leave a disagreeable taste as well as abrasiveness in mouth if not grew appropriately.
- Drugs with bigger measurements are hard to formulate into FDT e. g. Rifampin (600 mg), ethambutol (1000 mg) etc.[7]

IDEAL PROPERTIES OF FDTs

They should

- Not need water to swallow and may dissolve or disintegrate within the mouth inside many seconds.
- Permit high medication stacking.
- Be good with taste covering and diverse excipients.
- Have a delightful mouth feel.
- Leave little or no deposit inside the mouth.

- ❖ Have adequate strength to resist the trials of the producing method and Post producing, handling.
- ❖ Exhibit low affectability to natural conditions like stickiness and temperature.
- ❖ Be adaptable and agreeable to existing procedure.
- ❖ Permit the fabricate of tablets utilizing standard process and equipment at low Cost.[8]

TECHNIQUES FOR PREPARING FAST DISSOLVING TABLETS

- ❖ Many techniques have been reported for the formulation of Fast dissolving tablets or Orodispersible tablets.[9]

1. Freeze drying / lyophilization
2. Tablet Moulding
3. Spray drying
4. Sublimation
5. Direct compression
6. Mass extrusion.

Freeze-Drying or Lyophilization

Freeze drying is the process in which water is sublimed from the product after it is frozen. This Technique creates an amorphous porous structure that can dissolve rapidly. A typical procedure In evolved in the manufacturing of ODT using this technique is mentioned here. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer.[10] The mixture is done by weight and poured in the walls of the preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying.[11] Afte rfreeze-drying the aluminum foil backing is applied on a blister-sealing machine. Finally theblisters are packaged and shipped. The freeze-drying technique has demonstrated improved absorption and increase in bioavailability.[12] The major disadvantages of lyophillization techniqueare that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions.[13]

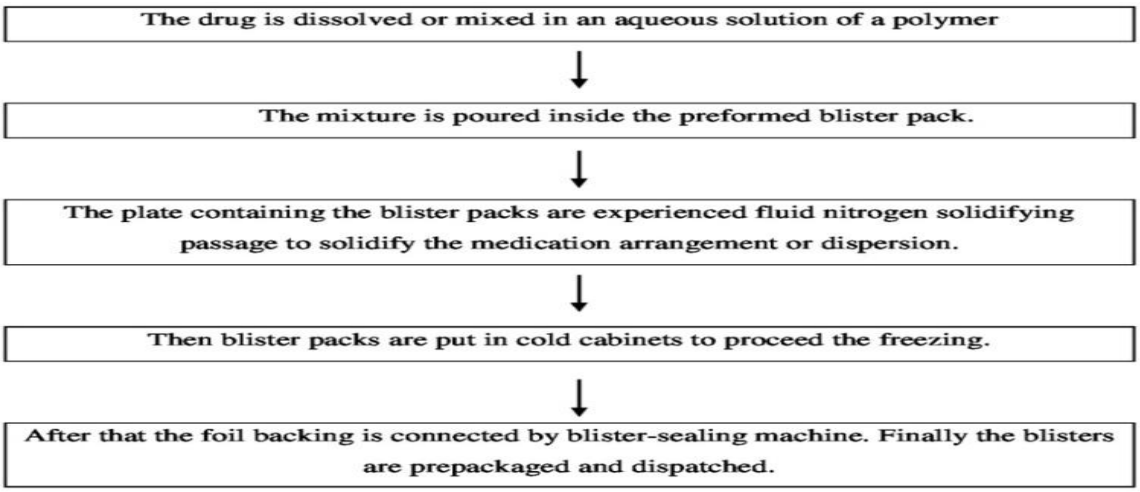

Fig.2: Systemic representation of Freeze drying process

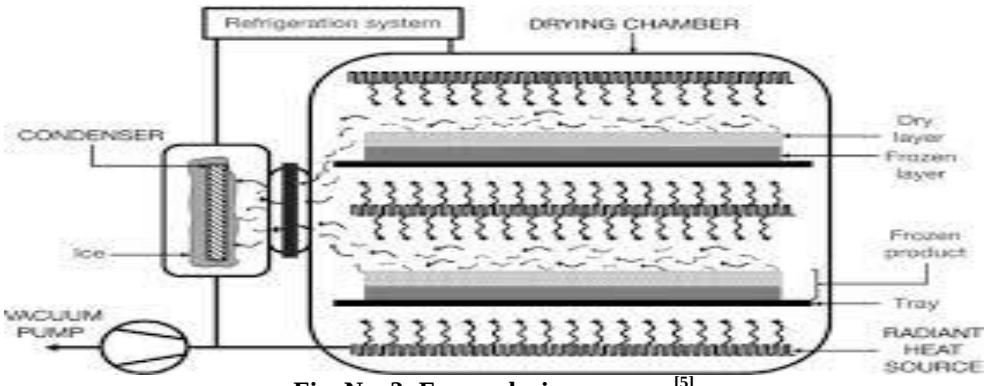

Fig. No. 2: Freeze drying process.[5]

Tablet Molding

Molding process is of two types i.e. solvent method and heat method. Solvent method involve moistening the powder blend with a hydro alcoholic solvent followed by compression at lopressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying.[14] The tablets manufactured in this manner are less compact than compressed tablets and posses a porous structure that hastens dissolution. The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. mannitolor lactose) and pouring the suspension in the

blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30○C under vacuum.[15] The mechanical strength of molded tablets is a matter of great concern. Binding agents, which increase the mechanical strength of the tablets, need to be incorporated. Taste masking is an added problem to this technology.[16] The taste masked drug particles were prepared by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and an active ingredient into a lactose based tablet triturate form. Compared to the lyophillization technique, tablets produced by the molding technique are easier to scale up for industrial manufacture.[17]

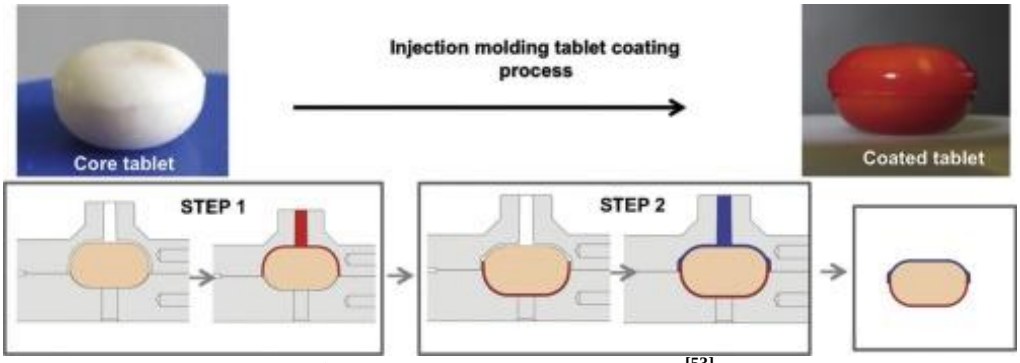

Fig. No. 3: TABLET MOLDING.[53]

Spray Drying

In this technique, gelatin can be used as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or cross carmellose or crospovidone are used as Super disintegrates.[18] Tablets manufactured from the spray-dried powder have been reported to Disintegrate in less than 20 seconds in aqueous medium. The formulation contained bulking agent like mannitol and lactose, a super disintegrant like sodium starch glycolate & croscarmellose sodium and acidic ingredient (citric acid) and/or alkaline ingredients (e.g. sodium bicarbonate).[19] This spray-dried powder, which compressed into tablets showed rapiddisintegration and enhanced dissolution.[20]

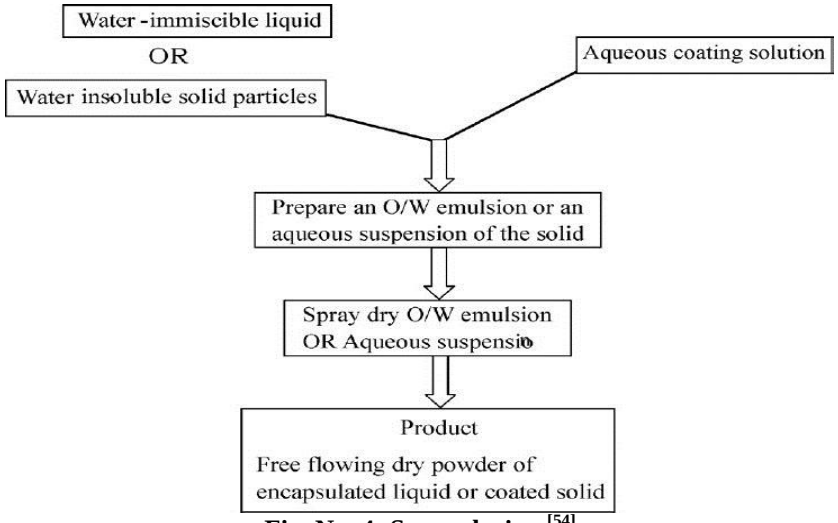

Fig. No. 4: Spray drying.[54]

Sublimation

To generate a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalicanhydride may be compressed along with other excipients into a tablet.[21] This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured bythis technique has reported to usually disintegrate in 10-20 sec. Even solvents like cyclohexane; benzene can be used as pore forming agents.[22]

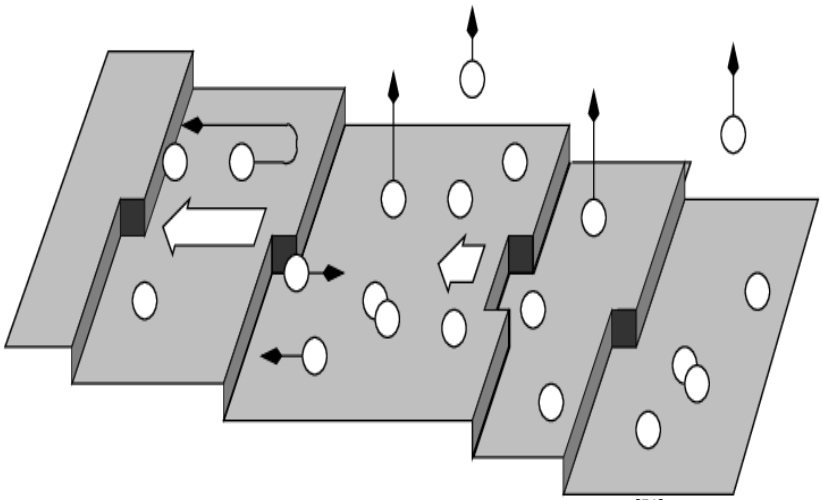

Fig. No. 5: Representation of sublimation.[51]

Direct Compression

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of ODT because of the availability of improved excipients especially superdisintegrants and sugar based excipients.[23]

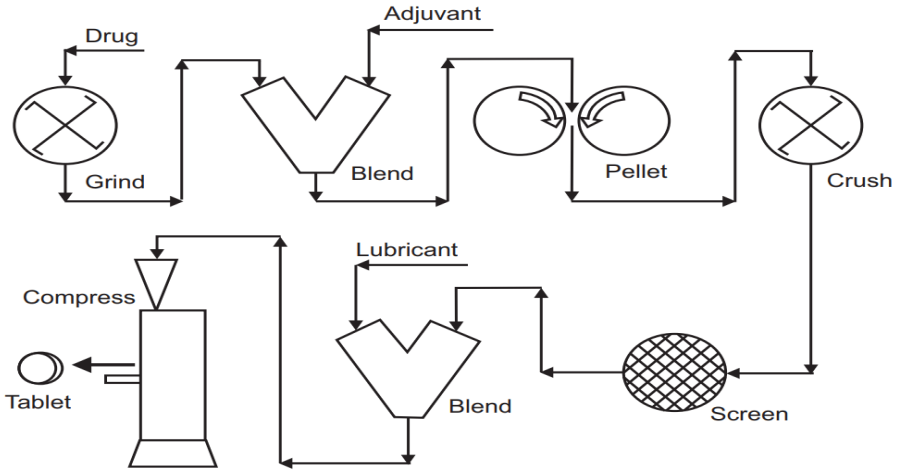

Fig. No. 6: Direct Compression Method.[56]

(a) Super disintegrates

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration.[24]

(b) Sugar Based Excipients

This is another approach to manufacture ODT by direct compression. The use of sugar based Excipients especially bulking agents like dextrose, fructose, isomalt, lactilol, maltilol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous Solubility and sweetness, and hence impart taste masking property and a pleasing mouthfeel. Mizumito et al have classified sugar-based excipients into two types on the basis of molding and dissolution rate.[25]

Type 1 saccharides (lactose and mannitol) exhibit low mouldability but high dissolution rate.

Type 2 saccharides (maltose and maltilol) exhibit high mouldability and low dissolution rate.[26]

Mass-Extrusion

This technology involves softening the active blend using the solvent mixture of water-solublepolyethylene glycol and methanol and subsequent expulsion of softened mass through theextruder or syringe to get a cylinder of the product into even segments using heated blade toform tablet. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.[27,28,29,30]

LIMITATIONS

- The quantity of drug may be incorporated ought to usually be but 400 mg for insoluble drug and less than 60 mg for soluble drugs.[31]
- The particle size of the insoluble drugs should not be less than 50µm and not more than 200µm to stop deposit throughout the process.[33]

ADVANTAGES

- The buccal tubular cavity and internal organ regions are all areas of absorption from this formulation. Any pre-gastric absorption avoids first-pass metabolism and may be a plus in medication that ensures an excellent deal of hepatic metabolism.[34]
- The zydis formulation self-preserving as a result of the ultimate water concentration within the freeze-dried product is simply too low to permit for microbic growth.[35]

DISADVANTAGES

- The method of lyophilization may be a comparatively costly manufacturing method.
- The formulation is extremely light-weight and fragile, and so should not be kept in backpacks or the lowest of handbags.[36]
- It has poor stability at more temperatures and humidities.
- The lyophilization is a time severe system. It has poor physical resistance. Loading of a high dose of soluble medication is not potential.[37]

❖ **DURASOLV TECHNOLOGY**

DuraSolv is Cima's second-generation fast-dissolving/disintegrating pill formulation like OraSolv, DuraSolv has a lot of higher mechanical strength than its precursor because of the utilization of upper compaction pressures throughout tableting.[38]

ADVANTAGES

- ❖ Durasolv tablets are formulated by utilizing conventional tableting and show great 2% friability.
- ❖ The durasolv product is cost-effective as good as a faster manufacturing product.[39]
- ❖ Durasolv is long lasting seeing that it is prepackaged in blister packaging, pouches or vials.
- ❖ The durasolv innovation is most appropriate to plans and similarly little dosages of the drug.[40]

DISADVANTAGES

- ❖ One disadvantage of this science will not be compatible with higher doses of a drug, for that reason of the formula is subjected to such excessive pressures on compaction.[41] Unlike orasolv, the structural integrity of any style masking can also be compromised with excessive drug doses.[42]
- ❖ The drug powder coating in durasolv would grow to be damaged due to compaction, unlock the bitter-tasting drug to a sufferer's style buds.[43]

Orasolv technology

CIMA labs have created Orasolv Technology. In the course of this method, drug taste masked. It furthermore carries the effervescent disintegrating agent. Tablets are created by means of direct compression process at low compression drive so that you could decrease oral dissolution time. Standard blenders and tablet machine are employed to produce the tablets. The tablets made are delicate and friable.[44] Effervescent agent is that the main ingredient utilized in this technology. The drug microparticles are gently compressed together with the effervescent agent. The developed pills have the look of a standard compressed tablet.[45] However, they are weaker and additional fragile than the standard tablets. Thus, there is a demand for a special packaging. The particle coating that is employed for taste masking purpose is not cracking at the time of compression due to a low compression force.[46]

Wow technology

It is proprietary by Yamanouchi Pharmaceutical Corporation wherever wow tends for "without water". During this method high mould ability carbohydrate like saccharide, a diuretic is mixed with low mouldability carbohydrate like glucose, disaccharide, and mannitol to get quickly melting tablet.[47]

Flashdose technology

This technology is much like candy floss, employing a distinctive spinning mechanism to provide crystalline floss structure. The medication will then be fused into this crystalline sugar and packed into a pill. Such product contains a high area for dissolution, dissolving quickly on tongue and simple dispersion. The Flash dose pills involves self–binding shear kind matrix termed as "floss".[48]

Flashtab technology

This technology aims to form the drug have fast release in git, small encapsulated drug with effervescence, and simply flash diffusion pill. Typically the chemical compound used is Eudragit for fast release. This technology uses standard approach of wet/dry granulation follow by classical methodology of compression.[49] Micro granules of medication, taste masking agents, disintegrating agent, and swelling agents are utilized to formulate medicine. These tablets have smart physical resistance, and extremely recommended for hygroscopic materials for blister packing as materials like PVC/aluminum foils cater higher moisture protection compared to traditional polyvinyl chloride or polypropylene foils.[50]

CONCLUSION

Due to the increasing demand for novel drug delivery, the quickdisintegrating drug delivery a system has become one in the entiremilestone within the novel drug delivery system. The introduction of quick-dissolving drug delivery system has encountered the delivery of standard dosage form.

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