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Review article

Review on Fast Dissolving Tablets Technology and Superdisintegrants

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Abstract

The convenience of administration and improved patient compliance are important in the design of oral drug delivery system which remains the preferred route of drug delivery inspite of various disadvantages. Fast dissolving tablets (FDTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. It has more significance to geriatric, Paediatric, bedridden patients because they have a problem in swallowing and the patient with dysphasia. It is more useful for the traveller and busy patients who don't have easy access to water. Fast dissolving tablets are prepared by various technologies with the aid of superdisintegrants. Fast dissolving tablets are more reliable than conventional dosage forms like tablets, capsules because of better patient compliance. The advancement in this field allows the development of an economic and better way of disease management with avoidance of several problems related to the other delivery systems.

Introduction

Oral route of drug administration have wide acceptance. 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, in the case of motion sickness and sudden episodes of coughing during the common cold, allergic conditions and bronchitis. For this reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. These problems lead to the development of novel type of solid oral dosage form called "Fast dissolving tablets" [1,2].

A solid dosage form containing medicinal agent or active ingredient which disintegrates rapidly usually within a matter of seconds when placed up on the tongue [3]. The performance of FDTs depends on the technology used in their manufacturing process. The fast dissolving property of these tablets is attributable to the quick ingress of water into the tablet matrix, which creates porous structure and results in rapid disintegration. Hence, the basic approaches to develop FDTs include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water-soluble excipients in the formulation.

FDTs disintegrate instantaneously when placed on tongue, releases the drug that dissolves or disperses in the saliva. Most drugs are absorbed through the oral mucosa, which is highly vascularised, can directly enter into the systemic circulation, by passing first pass metabolism in the liver. This result in rapid onset of action and greater bioavailability of the drug than those observed from conventional tablet dosage form. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down in to the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form [4].

During the last decade, several new advanced technologies have been introduced for the formulation of FDTs with very interesting features, like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients. Various technologies utilized for fabrication of FDTs and these techniques are based on the principles of increasing porosity by addition of superdisintegrants or water-soluble excipients in the tablets.5

Advantages of FDT

- FDT can be administer to the patients who cannot swallow tablets/capsules such as the elderly, stroke victims, bedridden patients, patients with esophageal problems & patients who refuse to swallow such as pediatric, geriatric & psychiatric patients and thus improves patient compliance.
- Increased bioavailability and rapid absorption of drugs through pre-gastric absorption of drugs from mouth, pharynx & esophagus as saliva passes down.

- FDT is most convenient for disabled, bedridden patients, travelers and busy people, who do not always have access to water.
- Good mouth feel property of FDT helps to change the perception of medication.
- The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
- FDT opened new business opportunity like product differentiation, product promotion, patent extension and life cycle management.
- Conventional manufacturing equipment and cost effective.
- Good chemical stability as conventional oral solid dosage forms and allow high drug loading.
- Provides rapid drug delivery from dosage forms and rapid onset of action
- Provide advantage of liquid medication in form of solid preparation.
- Rapid drug therapy intervention.
- Adaptable and amenable to existing processing and packaging machinery [6, 7].

Disadvantages of FDT

- Drugs with relatively larger doses are difficult to formulate into FDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500mg of the drug.
- Patients with dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.
- FDT is hygroscopic in nature so must be keep in dry place.
- Some time it possesses mouth feeling.
- It shows fragile nature, effervescence granules property.
- FDT requires special packaging for properly stabilization & safety of stable product [6, 7].

Challenges in formulation of Fast dissolving tablets

Mechanical strength and disintegration time

FDTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge. Many FDTs are fragile and there are many chances that such fragile tablet will break during packing, transport or handling by the patients. Tablets based on technologies like zydis need special type of packaging. It is very natural that increasing the mechanical strength will delay the disintegration time. So a good compromise between these two parameters is always essential [7, 8].

Taste masking

Many drugs are bitter in taste. A tablet of bitter drug dissolving/disintegrating in mouth will seriously affect patient compliance and acceptance for the dosage form. So effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity [8].

Mouth feel

FDTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the FDTs should be as small as possible. FDTs should leave minimal or no residue in mouth after oral administration. Moreover addition of flavors and cooling agents like menthol improve the mouth feel [7].

Sensitivity to environmental conditions

FDTs generally should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in FDTs are meant to dissolve in minimum quantity of water.

Technologies for preparing FDTs

FDTs are formulated by utilizing several processes which differ in their methodologies and the FDTs formed vary in various properties such as mechanical strength of tablets, taste and mouth feel, drug dissolute, in saliva, bioavailability, stability, swallowability [7].

Zydis technology

Zydis the best known of the fast-dissolving/disintegrating tablet preparations was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. A zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The zydis product is made to dissolve on the tongue in 2 to 3 seconds.

To obtain crystalline, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration. Various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of zydis units during freeze drying process or long term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment [9].

Advantages

- Buccal pharyngeal and gastric regions are all areas of absorption from this formulation. Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism.
- The zydis formulation self preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth [10].

Disadvantages

- The process of freeze-drying is a relatively expensive manufacturing process.
- The formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses.
- It has poor stability at higher temperatures and humidity.
- The freeze-drying is time consuming process.
- It has poor physical resistance.
- Loading of high dose of water-soluble drugs is not possible [10].

Wowtab technology

The wowtab fast dissolving/disintegrating tablet formulation has been on the Japanese market for a number of years. Wowtab technology is patented by Yamanouchi Pharmaceutical Company. The wow in wowtab signifies that tablet is to be given "without water". It has just recently been introduced into the U.S. The wowtab technology utilizes sugar and sugar like (e.g. mannitol) excipients. This process uses a combination of low mould ability saccharides (rapid dissolution) and high mouldability saccharide (good binding property). The two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate. Due to its significant hardness, the wowtab formulation is a bit more stable to the environment than the zydis or orasolv. It is suitable for both conventional bottle and blister packaging. The taste masking technology utilized in the wowtab is proprietary, but claims to offer superior mouth feel due to the patented smooth melt action. The wowtab product dissolves quickly in 15 seconds or less [10].

Orasolv technology

Orasolv was Cima's first fast dissolving/disintegrating dosage form. The orasolv technology, unlike zydis, disperses in the saliva with the aid of almost imperceptible effervescence. The orasolv technology is best described as a fast disintegrating tablet; the tablet matrix dissolves in less than one minute, leaving coated drug powder. The taste masking associated with the orasolv formulation is twofold. The unpleasant flavor of a drug is not merely counteracted by sweeteners or flavors both coating the drug powder and effervescence are means of taste masking in orasolv. This technology is frequently used to develop over-the-counter formulations. The major disadvantage of the orasolv formulations is its mechanical strength. The orasolv tablet has the appearance of a traditional compressed tablet. However, the orasolv tablets are only lightly compressed, yielding a weaker and more brittle tablet in comparison with conventional tablets. For that reason, Cima developed a special handling and packaging system for orasolv. An advantage that goes along with the low degree of compaction of orasolv is that the particle coating used for taste masking is not compromised by fracture during processing. Lyophilization and high degrees of compression, as utilized in orasolv's primary competitors, may disrupt such a taste masking approach. The orasolv technology is utilized in six marketed products. These formulations can accommodate single or multiple active ingredients and tablets containing more that 1gm of drug have been developed. Their disintegration time is less than 30sec. The orasolv formulations are not very hygroscopic.

Advantages

The orasolv formulations are not very hygroscopic, the formulation can accommodate high doses, and it also provides a distinct, pleasant sensation of effervescence in the mouth [10].

Disadvantages

A weaker and more brittle tablet in comparison with conventional tablets, poor mechanical strength, and the cost of fast dissolving tablets is higher than the cost of standard tablets made by direct compression; manufacturing requires a controlled environment at low relative humidity [11].

Durasolv technology

Durasolv is Cima's second-generation fast-dissolving/disintegrating tablet formulation. Produced in a fashion similar to orasolv, durasolv has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tabletting. Durasolv tablets are prepared by using conventional tabletting equipment and have good rigidity (friability < than 2%). The durasolv product is thus produced in a faster and more cost-effective manner. Durasolv is so durable that it can be packaged in traditional blister packaging, pouches or vials.

One disadvantage of durasolv is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction. Unlike orasolv, the structural integrity of any taste masking may be compromised with high drug doses. The drug powder coating in durasolv may become fractured during compaction, exposing the bitter tasting drug to a patient's taste buds. Therefore, the durasolv technology is best suited for formulations including relatively small doses of active compound [10].

Flashdose technology

Flashdose technology has been patented by Fuisz. Nurofen meltlet, a new form of ibuprofen as melt-in-mouth tablets, prepared using flash dose technology is the first commercial product launched by Biovail Corporation. A flashdose tablet consists of self binding shear form matrix termed as "floss". Shear form matrices are prepared by flash heat processing [10].

Flashtab technology

Prographarm laboratories have patented the flashtab technology. This technology involves the preparation of rapidly disintegrating tablet which consists of an active ingredient in the form of micro-crystals. Drug micro-granules may be prepared by using the conventional techniques like coacervation, extrusion-spheronization, simple pan coating methods and micro-encapsulation. The micro- crystals of micro-granules of the active ingredient are added to the granulated mixture of excipients prepared by wet or dry granulation, and compressed into tablets. All the processing utilized the conventional tabletting technology, and the tablets produced are reported to have good mechanical strength and disintegration time less than one min [10].

Oraquick

The oraquick fast dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its microsphere technology, known as micro mask, has superior mouth feel over taste masking alternatives. The taste masking process does not utilize solvents of any kind, and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast dissolving/disintegrating technologies makes oraquick appropriate for heat sensitive drugs. KV Pharmaceutical also claims that the matrix that surrounds and protects the drug powder in micro-encapsulated particles is more pliable, meaning tablets can be compressed to achieve significant mechanical strength without disrupting taste masking. Oraquick claims quick dissolution in a matter of seconds, with good taste masking. There are no products using the oraquick technology currently on the market, but KV Pharmaceutical has products in development such as analgesics, scheduled drugs, cough and cold, psycho tropics, and anti-infective.

Nanocrystal technology

For fast dissolving tablets, Elan's proprietary nanocrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using nanocrystal technology. Nanocrystal particles are small particles of drug substance, typically less than 1000 nanometers (nm) in diameter, which are produced by milling the drug substance using a proprietary wet milling technique. Nanocrystal colloidal dispersions of drug substance are combined with water-soluble GRAS (Generally Recognized as Safe) ingredients, filled into blisters, and lyophilized. The freeze-drying approach also enables small quantities of drug to be converted into fast dissolving dosage forms because manufacturing losses are negligible [10].

Freeze drying

A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze dried forms offer more rapid dissolution than other available solid products. The lyophilization process imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristics of the formulation. However, the use of freeze drying is limited due to high cost of the equipment and processing. Other major disadvantages of the final dosage forms include lack of physical resistance in standard blister pack. A tablet that rapidly disintegrates in aqueous solution includes a partially collapsed matrix network that has been vacuum dried above the collapse temperature of the matrix. The matrix is partially dried below the equilibrium freezing point of the matrix. Vacuum drying the tablet above its collapse temperature instead of freeze drying below its collapse temperature provides a process for producing tablets with enhanced structural integrity, while rapidly disintegrating in normal amounts of saliva [11].

Moulding

Tablet produced by moulding are solid dispersion. Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is in general made from water soluble sugars. The active ingredients in most cases are absorbed through the mucosal lining of the mouth. The manufacturing process of molding tablets involves moistening the powder blend with a hydro-alcoholic solvent followed by pressing into mold plates to form a wetted mass (compressing molding). The solvent is then removed by air drying. Thus the process is similar to what is used in the manufacture of tablet triturates. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution.

Molded forms are also prepared using a heat molding process that involves setting the molten mass that contains a dispersed drug. The heat molding process uses an agar solution as a binder and a blister packaging well as a mold to manufacture a tablet. The process involves preparing a suspension that contains a drug, agar, and sugar (e.g., mannitol or lactose), pouring the suspension into the blister packaging well, solidifying the agar solution at room temperature to form a jelly, and drying at -30°C under vacuum.

Another process used is called no vacuum lyophilization, which involves the evaporation of a solvent from a drug solution or suspension at standard pressure. Erosion and breakage of the moulded tablet often occur during handling and opening of blister packs. Recently, moulded forms also have been prepared directly from a molten matrix in which the drug is dissolved or dispersed (heat moulding) or by evaporating the solvent from a drug solution or suspension at standard pressure (no vacuum lyophilization). Tablets produced by moulding are solid dispersions. The physical form of the drug in the tablets

depends on whether, and to what extent, it dissolves in the molten carrier [11].

Direct compression

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression, also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. Directly compressed tablets disintegration and solubilization depends on single or combined action of disintegrate, water soluble excipients and effervescent agent. Disintegrate efficacy is strongly affected by tablet size and hardness. Large and hard tablets have disintegration time more than that usually required. As consequences, products with optimal disintegration properties often have medium to small size, high friability and low hardness. Breakage of tablet edges during handling, tablet rupture during the opening of blister packing, all results from insufficient physical resistance. Disintegrants have major role in the disintegration and dissolution process of mouth dissolving tablets made by direct compression. To ensure a high disintegration rate, choice of suitable type and an optimal amount of disintegrant is important. Other formulation components such as water soluble excipients or effervescent agents can further enhance dissolution or disintegration properties. But main drawback of using effervescent excipients is their highly hygroscopic nature.9

Spray drying

Highly porous and fine powders can be produced by spray drying, as the processing solvent is evaporated rapidly during spray drying. Spray drying technique has been employed to prepare fast dissolving tablets. They developed formulation by using mannitol as bulking agent, hydrolysed and non-hydrolysed gelatin as support matrix, sodium starch glycolate as disintegrant and acidic material (e.g. citric acid) and/or alkali material (e.g. NaHCO3) to enhance disintegration and dissolution. When immersed in an aqueous medium, the tablets compressed from spray-dried powder, disintegrated within 20 seconds [11].

Mass extrusion

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.10

Sublimation

Because of low porosity, compressed tablets composed of highly water-soluble excipients as tablet matrix material often do not dissolve rapidly in the water. Porous tablets that exhibit good mechanical strength and dissolve quickly have been developed. Inert solid ingredients (e.g. urea, urethane, ammonium carbonate, camphor, naphthalene) were added to other tablet excipients and the blend was compressed into tablet. Removal of volatile material by sublimation generated a porous structure. A method of producing fast dissolving tablet using water as the pore forming material has been described by Makino. Compressed tablets containing mannitol and camphor have been prepared by sublimation technique. The tablet dissolves within 10-20 seconds and exhibit sufficient mechanical strength for practical use. Koizumi have developed a new method of preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material [11].

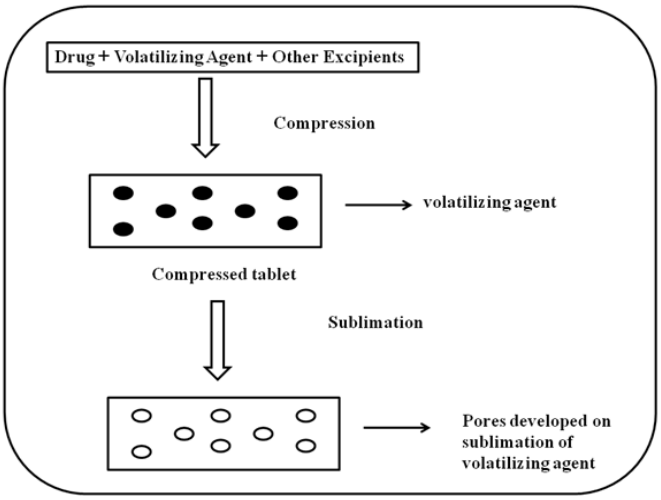

Fig 1 Steps involved in sublimation

Cotton candy process

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially re-crystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to FDT. This process can accommodate high doses of drug and offers improved mechanical strength. However, high process temperature limits the use of this process [12].

Melt granulation

This method describes a new approach of preparing dispersible tablet with sufficient mechanical strength, involving the use of a hydrophilic waxy binder (super-poly-state-R, PEG-6-stearate) by melt granulation. Because super-poly-state-R is a waxy material with a melting point of 33–37°C and a hydrophilic to lipid balance (HLB) value of 9, it will not only act as a binder and increase the physical strength of tablets but also help the disintegration of the tablets. In case of melt granulation, granules were prepared in a high speed blade

mixer at 40–44°C, according to the conventional hot melt procedure. The melt granulation disintegrating tablets had better hardness results than the wet granulation disintegrating tablets. The disintegration times of melt granulation tablets, was more than one min [12].

Wet granulation

Bonadeo et al., described a process of producing FDTs by wet granulation. It was found that even with effervescent agents presented in the tablet with lower than 5%, quick disintegration times could be achieved. Furthermore, it was also found that fast disintegration time could be achieved using only the acid component of the effervescent couple. In the patent, the formulation includes poly-alcohols (e.g. mannitol, xylitol, sorbitol, maltitol, erythritol and lactitol), 1–30% of an edible acid, and an active ingredient as the dry mixture. This mixture was wet granulated with an aqueous solution of a water-soluble or water-dispersible polymer (e.g. polyethylene glycols, carrageenan and ethylcellulose), which consisted of 1–10% of the final weight of the granule in a fluid bed. Granules with high porosity and low apparent density were obtained, and the tablets made by such granules had rapid disintegration times ranging from 3 to 30 seconds in the saliva. Jian et al., developed FDT for a poorly water-soluble active ingredient. First nanoparticles were formed by mechanical grinding, precipitation, or any other suitable size reduction process. Those nanoparticles, less than 2μm, were stabilized by surfactants. The particles were granulated with at least one pharmaceutically acceptable water-soluble or water dispersible excipient using a fluid bed, and the granules were made into tablets. The tablets had complete disintegration or dissolution in < 3 minutes.13

Formulation Aspects

Important ingredients that are used in the formulation of FDTs should allow quick release of the drug, resulting in faster dissolution. This includes both the pharmacologically active ingredients (drug) and the excipients (additives) [14].

Selection of the drug

Several factors may be considered while selecting an appropriate drug candidate for development of fast dissolving tablets.

The ultimate characteristics of a drug for dissolution in mouth and pre-gastric absorption from fast dissolving tablets include

- Ability to permeate the oral mucosa.
- At least partially non-ionized at the oral cavity pH.
- Have the ability to diffuse and partition into the epithelium of the upper GIT.
- Small to moderate molecular weight.
- Low dose drugs preferably less than 50mg.
- Short half life and frequent dosing drugs are unsuitable for FDT.
- Drug should have good stability in saliva and water.
- Very bitter or unacceptable taste and odor drugs are unsuitable for FDT.

There are no particular limitations as long as it is a substance which is used as a pharmaceutical active ingredient. Researchers have formulated FDT for various categories of drugs used for therapy in which rapid peak plasma concentration is required to achieve the desired pharmacological response. These include neuroleptics, cardiovascular agents, analgesics, anti-allergic, anti-epileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and drugs used for erectile dysfunction.

In contrast, the following characteristics may render unsuitable for delivery as an orally disintegrating tablet

- Short half life and frequent dosing.
- Very bitter or otherwise unacceptable taste because taste masking cannot be successfully achieved.
- Require controlled or sustained release.
- Combination with anticholinergics.

Selection of excipients

Mainly seen excipients in FDT are as follows at least one disintegrant, a diluent, a lubricant, and optionally, a swelling agent, sweeteners, and flavoring agents etc. Ideal bulk excipients for orally disintegrating dosage forms should have the following properties [6].

- Disperses and dissolves in the mouth within a few seconds without leaving any residue.
- Masks the drug's offensive taste and offer's a pleasant mouth feel.
- Enables sufficient drug loading and remains relatively unaffected by changes in humidity or temperature. The role of excipients is important in the formulation of fast-melting tablets. The temperature of the excipients should be preferably around 30–350C for fast melting properties [6].

Role of superdisintegrants in FDT

The basic approach in development of FDTs is use of disintegrant. Disintegrant play an important role in the disintegration and dissolution of FDT. It is essential to choose a suitable disintegrant, in an optimum concentration so as to ensure quick disintegration and high dissolution rates [7].

Superdisintegrant provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrant, the wetted surface of the carrier increases; this promotes the wet ability and dispersibility of the system, thus enhancing the disintegration and dissolution. Care should be taken to taken while selecting concentration of the super disintegrant. Superdisintegrates are selected according to critical concentration of disintegrant. Below

this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if concentration of superdisintegrant is above critical concentration, the disintegration time remains almost constant or even increases [7].

Common disintegrants used in this formulation are croscarmellose sodium (vivasol, ac-di-sol), crospovidone (polyplasdone), carmellose (NS-300), carmellose calcium (ECG-505), sodium starch glycolate (SSG) etc. Recently few ion-exchange resins (e.g. indion 414) are found to have superdisintegrant property and are widely used in pharmaceutical industry. Swelling index of the superdisintegrants is commonly studied in simulated saliva. Volume occupied by the material at the end of 4h should be noted and swelling index is calculated by the formula: (final volume-initial volume/initial volume) X 100.

Taste masking technologies of dissolving tablets

Taste is one of the most important parameters governing patient compliance. Undesirable taste is one of several important formulation problems that are encountered with certain drugs. Oral administration of bitter drugs with an acceptable degree of palatability is a key issue for health care providers, especially for pediatric patients. Taste masking is defined as a perceived reduction of an undesirable taste that would otherwise exist.

General taste masking practices in oral pharmaceuticals

Various techniques available for masking bitter taste of drugs include taste masking with ingredients such as flavors, sweeteners, and amino acids; taste masking by polymer coating; taste masking by conventional granulation; taste masking with ion-exchange resins; taste masking by spray congealing with lipids; taste masking by formation of inclusion complexes with cyclodextrins, taste masking by the freeze-drying process; taste masking by making multiple emulsions; and taste masking with gelatin, gelatinized starch, liposomes, lecithins or lecithin like substances, surfactants, salts, or polymeric membranes15.

Taste masking with flavors, sweeteners, and amino acids

This technique is the foremost and the simplest approach for taste masking, especially in the case of pediatric formulations, chewable tablets, and liquid formulations. But this approach is not very successful for highly bitter and highly water-soluble drugs. Artificial sweeteners and flavors are generally being used along with other taste-masking techniques to improve the efficiency of these techniques. The cooling effect of the taste masking agents also aids in reducing the bitterness. Menthol reduces the bitter taste, and low calorie formulations show beneficial anti-caries effects.

Aspartame is used as a prominent sweetener in providing bitterness reduction. A very small concentration (0.8%) is effective in reducing the bitterness of 25% acetaminophen. Starch, lactose, and mannitol have also exhibited taste-masking properties of caffeine. Artificial sweeteners such as neohesperidine dihydrochalcone and hesperidine dihydrochalcone 4'-β-D glucoside have the ability to mask bitterness and saltiness by virtue of their lingering sweetness [16].

Taste masking with lipophilic vehicles

Oils, surfactants, poly-alcohols, and lipids effectively increase the viscosity in the mouth and coat the taste buds, and therefore they are potential taste masking agents.

- Guaifenesin melt-granulation carnauba wax and magnesium aluminium silicate.
- Cimetidine granulation glyceryl monostearate.

Lecithin and lecithin like substances formulations with a large excess of lecithin or lecithin like substances are claimed to control bitter taste in pharmaceuticals. Magnesium aluminum silicate with soybean lecithin is used to mask the unpleasant taste of talampicillin HCl. The drug is dissolved in or dispersed into an organic solvent such as chloroform.

Taste masking by coating with hydrophilic vehicles

This is the simplest and most feasible option to achieve taste masking. The coating acts as a physical barrier to the drug particles, thereby minimizing interaction between the drug and taste buds. Coating of chewable tablets provides excellent taste masking while still providing acceptable bioavailability. A specialized technique, i.e., micro-emulsion technology, has been used for taste masking of powders, chewable tablets, and liquid suspensions.

Carbohydrates (cellulose)

The taste of orally administered drugs can be masked by coating the drug with carbohydrates. Bitter solid drugs such as pinaverium bromide, as spasmolytic, has no bitter taste when formulated in an organoleptically acceptable manner by polymer coating with a mixture of cellulose or shellac and a second film forming polymer soluble at pH less than 5.

Taste masking of ibuprofen has been successfully achieved by using the air-suspension coating technique to form micro-capsules, which comprise a pharmaceutical core of crystalline ibuprofen and a methacrylic acid copolymer (eudragit) coating that provides chewable taste masked characteristics [17].

Taste masking by inclusion complexation

In inclusion complex formation, the drug molecule fits into the cavity of a complexing agent, i.e., the host molecule, forming a stable complex. The complexing agent is capable of masking the bitter taste of drug by either decreasing its oral solubility on ingestion or decreasing the amount of drug particles exposed to taste

buds, thereby reducing the perception of bitter taste. This method is most suitable only for low dose drugs. Vander walls forces are mainly involved in inclusion complexes. β - cyclodextrin is the most widely used complexing agent for inclusion type complexes. It is a sweet, nontoxic, cyclic oligosaccharide obtained from starch.

The strong bitter taste of carbetapentane citrate syrup was reduced to approximately 50% by preparing a 1:1 complex with cyclodextrin. Palatable ibuprofen solutions are prepared by forming a 1:11 to 1:15 inclusion complex with ibuprofen and hydroxypropyl β-cyclodextrin, respectively. The complex masked the bitter component but created a sore taste that was masked by sweeteners [17].

Taste masking by ion-exchange resins (IERs)

IERs are high molecular weight polymers with cationic and anionic functional groups. The most frequently employed polymeric network is a copolymer of styrene and divinylbezene. Ion-exchange resins are used in drug formulations to stabilize the sensitive components, sustain release of the drug, disintegrate tablets, and mask taste. Drug can be bound to the resin by either repeated exposure of the resin to the drug in a chromate graphic column or by prolonged contact of resin with the drug solution.

Drugs are attached to the oppositely charged resin substrate, forming insoluble adsorbates or resonate through weak ionic bonding so that dissociation of the drug-resin complex does not occur under the salivary pH conditions. Drug molecules attached to the resin are released by exchanging with appropriately charged ions in the GIT, followed by diffusion of free drug molecule out of the resins [17].

FDTs with patented taste masking technology

Cima lab's taste masking technique involves coating of drug with dissolution retarding excipient. Micro-caps process involving micro-encapsulation by co-acervation phase separation technique solutab technology involving coating of drug with sustained release agent followed by coating with enteric polymer and finally with mannitol and mixing of drug with cyclodextrins are some of the tastes masking approaches [17].

Mechanism of disintegration

When fast dissolving tablets placed in the mouth, upon contact with saliva the tablets disintegrates or dissolve instantaneously. There are four major mechanisms for tablets disintegration as follows19

Swelling

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

Porosity and capillary action (wicking)

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipients and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

Due to disintegrating particle/particle repulsive forces

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

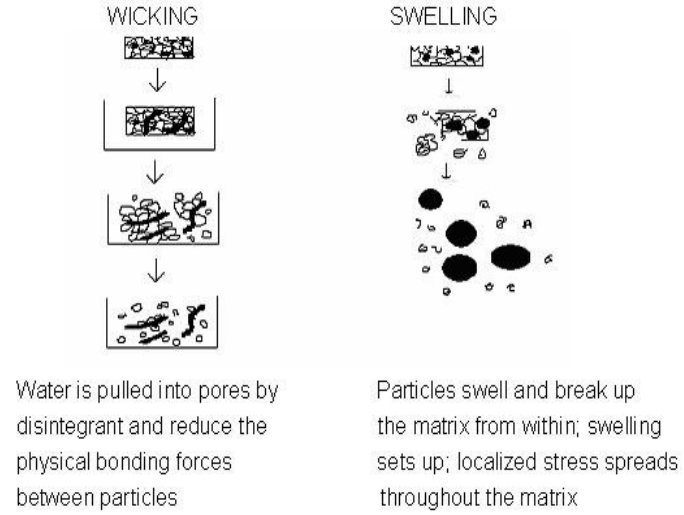

Figure 2 Disintegration of tablet by swelling and wicking

Due to deformation

During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

Patient counseling in effective use of FDT

Storage of this dosage form as some of FDT developed may not have sufficient mechanical strength, which needs to be handled carefully. Patients with dryness of mouth or who take anticholinergic drugs may not be suitable

candidates for administering FDT. Although no water is required to allow drug to disperse quickly and efficiently but decreased volume of saliva may slow the rate of disintegration/dissolution and may reduce the bioavailability of the product. Patients need to be clearly told about the difference between effervescent and FDT. Some of technologies use effervescence, which experience a pleasing tingling effect on the tongue.[20]

Conclusion

FDTs technology is growing day by day with offering considerable benefits for lifecycle management, development timelines and patient convenience. The advanced technologies provides pharmaceutical companies can take advantage of FDTs for product line extensions or for first- to-market products with continued development of new pharmaceutical excipients, one can expect the emergence of more novel technologies for FDTs in the days to come. These FDTs mechanism is to achieve fast dissolving effect and to enhance the bioavailability. The effect of super different superdisintegrants and different sublimating agents can be known for manufacuturing of FDTs, The new technologies of manufacturing provide tablets with rapid onset of action, increased bioavailability, low side effects and better safety.

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