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FAST DISSOLVING TABLET – AN INNOVATIVE APPROACH

Kaur Kiranpreet* and Garg Rajeev

Department of Pharmaceutics, Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial College of Pharmacy, Bela (Ropar), Punjab, India

Abstract:

Fast dissolving tablets are the most supportive and widely accepted dosage forms, commonly for pediatric patients. Some solid dosage forms like capsules and tablets have issue like worry of swallowing called dysphagia, resulting in matter of patient non-compliance and making the therapy inefficient. FDT disintegrate or dissolve quickly in the saliva in lack of water in within a few seconds (less than 60 seconds) and are real fast dissolving tablets. FDTs are designed to disintegrate speedily, absorb faster so,in vitro drug release time improve and this property of drugs enhanced bioavailability. The fast dissolving solid dosage form turns into a soft paste or liquid form for easy swallowing, and thus it is free of risk of choking without obstruction.

Keywords: *Fast dissolving tablet, Oral dissolving tablet, Superdisintegrants etc.*

Corresponding author:

Kaur Kiranpreet,

Department of Pharmaceutics,
Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial College of Pharmacy,
Bela (Ropar), Punjab, India
kiranassarpur96@gmail.com

QR code

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INTRODUCTION:

The concepts of Fast Dissolving Drug Delivery System become apparent to provide patient with conventional means of taking their medication. Because of physiological changes especially, elderly and pediatrics are quite unable to swallow called Dysphagia; comparatively, this is a common problem of all age groups patients [1]. Solid dosage forms that can be disintegrated, dissolved, or suspended by saliva in smaller particles resulting in easy swallowing which is very beneficial to the pediatric and geriatric population who are disable to take medicine , as well as other patients who favour the convenience of easily swallowable dosage forms. This tablet breaks immediately without delay when it set down on tongue in the mouth, releasing the drug that dissolves or disperses in the saliva and shows its action [2].

United States Food and Drug Administration (USFDA) defined fast dissolving tablet (FDT) as "a solid dosage form containing a medicinal substance or active ingredient which disintegrate quickly usually within seconds when placed upon the tongue" [3]. These tablets are develop to dissolve or disintegrate speedily in the saliva usually less than 60 seconds in the mouth to show its fast action[4].

A tablet which can rapidly disintegrate in saliva is an attractive and most promising dosage form and a patient-oriented pharmaceutical preparation[5]. The disintegrated mass can slide down smoothly along the esophagus with the help of saliva, so even people who have swallowing or chewing difficulties we can take it easily [6].

MERITS OF FAST DISSOLVING TABLETS

1. Administered without water, any time and any place you are.
2. Suitability for geriatric and pediatric patients, who have more difficulties in swallowing and for the other groups that may experience problems , due to being mentally ill, the developmentally disable to take and the patients who are uncooperative[7].
3. Beneficial in cases such as motion sickness, allergic attack or coughing, where an ultra rapid onset of action required of through dosage form.
4. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets and make the dose effective to use.
5. Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed so no matter of stability. It has advantages of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability [8].

DEMERITS OF FAST DISSOLVING TABLETS

1. Mechanical strength of final product.
2. Drug and dosage form stability.
3. Mouth feel is not so better because large particles cause grittiness [9].
4. The tablets may leave unpleasant taste if not masked the taste and not formulated properly.
5. Dryness of the mouth due to decreased saliva production may not be good suitability for these tablet formulations [10].

METHOD OF PREPARATION OF FAST DISSOLVING TABLET

1. Freeze-Drying or Lyophilization

Freeze drying is the process in which water is sublimed from the product after it is frozen under low temperature by the application of vaccum to remove water [11]. This technique creates an amorphous porous structure that can dissolve rapidly and to prevent melt-back or collapse during primary and secondary drying [12].

a)Primary drying

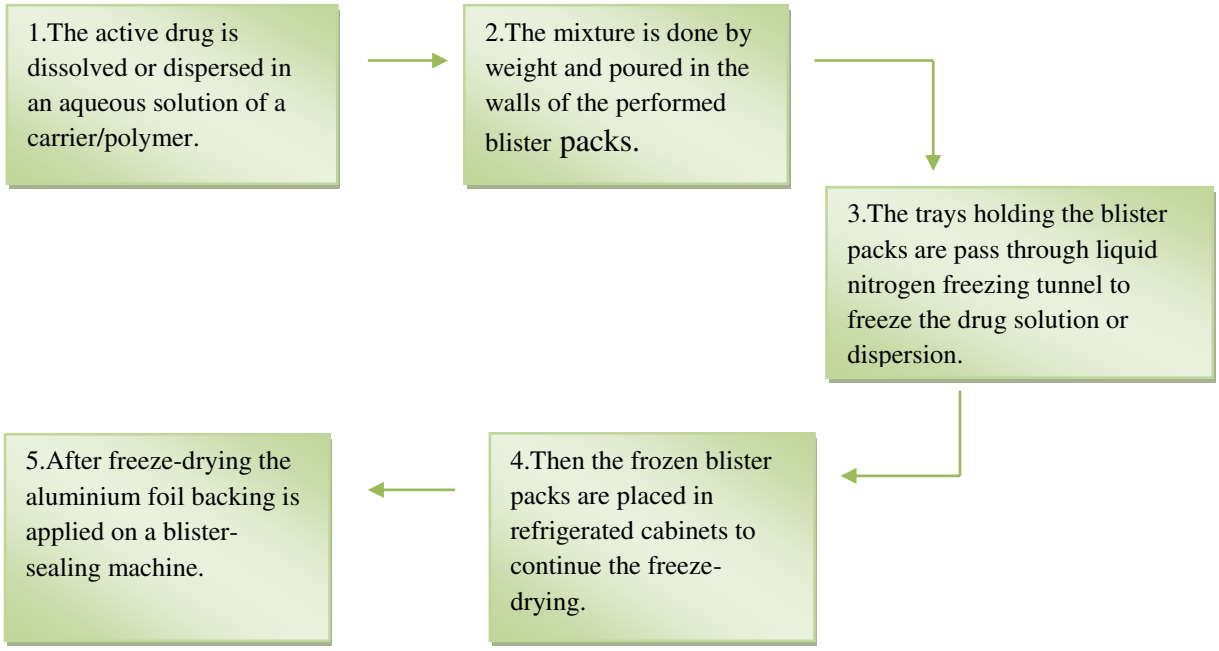
During the primary drying phase, the pressure is decline, and sufficient heat is supplied to the material for the ice to sublime. In this initial drying phase of the process, about 95% of the water in the material is sublimated through this technique. This phase may be slow, because, if too much heat is added, the material's structure could be altered [13].

In this phase, pressure is controlled through the application of partial vaccum. The vacuums quicken the sublimation, making it useful as a purposive drying process.

b)Secondary drying

The secondary drying phase aims to remove unfrozen water molecules which are not frozen by this process, since the ice was removed in the primary drying phase. This section of the freeze-drying process is conducted by the material's adsorption isotherms. In this phase, the temperature is raised above than in the primary drying phase, and can even be above 0 °C, to split any physico-chemical interactions which are formed between the water molecules and the frozen material [14].

A typical procedure involved in the manufacturing of FDT using this technique is given below:

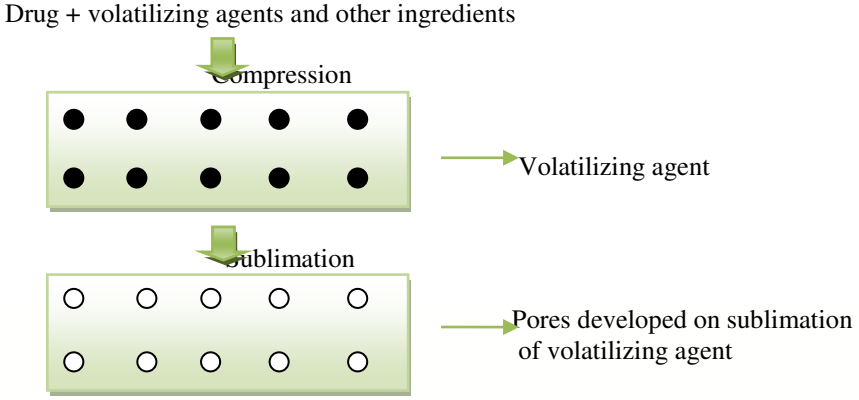


The freeze-drying technique has indicated improved absorption and increase in bioavailability. The major disadvantages of lyophilization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions[15].

2.Sublimation

This process include incorporation of some inert volatile substances like urea, urethane, naphthalene, camphor, etc to other excipients and the compression of blend into tablet. Removal of volatile material by sublimation creates pores in tablet structure, so after comes in contact with saliva tablet dissolves. In addition several solvents like cyclohexane, benzene etc can also be used as pore forming agents. Fast dissolving tablets with highly porous structure and good mechanical strength have been developed by this method[16].

Solvents like cyclohexane and benzene were also recommend for the generation of porosity in the matrix. Mannitol is used as a matrix former, and camphor was used as a sublimating agent in this process for sublimation. The tablets dissolved in 10-20 s and displayed satisfactory handling properties[17].



3.Direct compression

The disintegrant addition technology is the most preferred and better technique to manufacture the tablets due to following advantages:

1.High doses can be accommodated and final weight of the tablet can more than of other methods of formulation.

2.The easiest way to manufacture the tablets[18].

3.Conventional equipment and commonly available excipients are used.

4.A limited no. of processing steps are involved.

5.Cost effectiveness.

Because of the accessibility of improved excipients especially superdisintegrants and sugar based excipients, this technique can now be utilized for preparation of Fast Dissolving Tablets[19].

a.Superdisintegrants: Superdisintegrants are the principally affecting disintegration and ultimately dissolution of the fast dissolving tablets, mainly for direct compression techniques. The presence of other ingredients like water-soluble excipients and effervescent agents further quicken the disintegration process.

b.Sugar Based Excipients: This is another route to approach the direct compression technique. The use of sugar based excipients especially bulking agents like lactilol, dextrose, fructose, maltose, mannitol, sorbitol, polydextrose, xylitol, and starch hydrolysate which show high aqueous solubility and sweetness, and hence give taste masking property and a pleasant mouth feel[20]. Sugar-based excipients are categorized into two types on the basis of molding and dissolution rate.

Type 1 saccharides (mannitol and lactose) exhibit low mould-ability but high dissolution rate.

Type 2 saccharides (maltilol and maltose) exhibit high mould-ability and low dissolution rate[21]

4.Moulding method

Tablets are designed using hydrophilic ingredients, with the aim to get high rate of drug dissolution. For compression of dosage form powder mass is wetted with hydroalcoholic solvent. The solvent system is then allowed to evaporate. When spray congealing the molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethene glycol with an active ingredient into lactose based tablet triturate the taste of drug particles is developed . Characteristics of moulding method are, in this rapid dissolution when solvents are removed by drying leaving porous mass which increase the dissolution. In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly and give the effect. The powder blend is moistened with a hydroalcoholic solvent and is molded into tablets under lower pressure than which used in conventional tablet compression. The solvent is then removed through air-drying .Molded tablets are very less compact than compressed tablets because these posses porous structure that increase dissolution[22,23].

5.Melt granulation

Melt granulation technique is a process by which the pharmaceutical powders are aggregated by a meltable binder. The benefit of this technique compared to a conventional granulation is that no water or organic solvents is required so there is no drying step and the process is less time consuming. It requires less energy than wet granulation. It is a technique useful to enhance the dissolution rate of poorly water-soluble drugs, such as griseofulvin[24].

To succeed this process, high shear mixers are utilized, where the product temperature is raised above the melting point of binder by a heating jacket or by the heat of friction generated by impeller blades. Perissutti et al prepared carbamazepine fast-release tablets by melt granulation technique using polyethylene glycol 4000 as a melting binder and lactose monohydrate as hydrophilic filler[25].

CHALLENGES IN FORMULATING FDTs

1.Palatability

Most orally disintegrating drug delivery systems disintegrate or dissolve in patient's oral cavity, thus releasing the active ingredients which come in contact with the taste buds give the bitter taste; hence, taste-masking of the drugs becomes critical to patient compliance and it is more challenging[26].

2.Mechanical strength

In order to allow FDTs to disintegrate in the mouth, they are made with very low compression force, which makes the tablets friable or brittle thus it exhibit low mechanical strength, difficult to handle, and often requiring specialized peel-off blister packing that may increase the cost of product.

3.Hygroscopicity

Several FDTs are hygroscopic tending to absorb moisture from the air and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need special protection from humidity so need specialized packaging of product and a limiting step[27].

4.Amount of drug

For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs[28]. It have narrow therapeutic index and in the formulation minimum excipients and low concentration of drug is use.

5.Aqueous solubility

Aqueous solubility becomes a major issue if the drug is hydrophobic in nature or highly Lipophilic, thus it won't dissolve/disintegrate in mouth leading to

grittiness and residue in mouth.

6.Size of tablet

It has been reported that the easiest size of tablet to swallow is 7-8 mm and should not exceed it. Therefore, the tablet size that is both easy to take and easy to handle[29].

EVALUATION

Evaluation parameters of tablets mentioned in the Pharmacopoeias and some special tests are discussed here.

1. Weight variation

20 tablets were selected randomly for evaluation and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in table 1[30].

Average weight of tablet	% Deviation
80 mg or less	10.0
More than 80 mg but less than 250 mg	7.5
250 mg or more	5.0

2. Hardness

The limit of hardness for the FDT is in lower range to enable early disintegration in the mouth. The hardness of the tablet may be measured using conventional hardness testers are Monsanto tablet hardness tester and Pfizer tester. It is expressed in kg or pound[31].

3. Friability

FDT is a challenge for a formulator to achieve % friability within limits (0.1-0.9%) since all methods of manufacturing of FDT are responsible for increasing the % friability values. Friability of each batch is determine in "Roche friabilator"[32]. Ten pre-weighed tablets were rotated at 25 rpm for 4 min or total 100 revolutions, the tablets were then reweighed and the percentage of weight loss during friability is calculated by the following equation.

$$F = (W \text{ initial} - W \text{ final}) / W \text{ initial} \times 100$$

4. Moisture uptake studies

Moisture uptake studies for FDT should be conducted to check the stability of the dosage form. Ten tablets from each formulation were kept in a desiccator over calcium chloride at 37ºC for 24h for study. The tablets are weighed and then exposed to 75% relative humidity, at room temperature for period of 2 weeks. Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the dessicator for 3 days[34]. One tablet as control which is without super disintegrants is kept to check the moisture uptake by the other excipients in process. Tablets are then weighed and the percentage increase in the weight was recorded for study.

5.In-vitro dispersion time

Tablet was added to 10 ml of phosphate buffer solution, pH 6.8 at 37+0.5°C for dispersion. Time required for complete dispersion of a tablet was measured for determination.

6. Dissolution test

The dissolution method for FDT is practically same as conventional tablet when FDT does not employ taste masking. Commonly the drugs may have dissolution conditions as in USP monograph. 0.1N HCl, pH 4.5 and pH 6.8 buffers should be used for evaluation of FDT to determine the dissolution. USP 2 paddle apparatus is most suitable and common choice for dissolution test of FDT tablets as compared to USP1 (basket) apparatus due to specific physical properties of tablets[35]. In paddle apparatus the paddle speed of 25-75 rpm is commonly used for dissolution testing. Then the analysis for API content by UV-Vis. Since the dissolution of FDTs is very fast when using USP monograph conditions hence slower paddle speeds may be employed to obtain a comparative profile.

PATENTED TECHNOLOGIES FOR FAST DISSOLVING TABLETS

Several technologies have been developed on the basis of formulation aspects and different processes and patented by several pharmaceutical companies. Patented technology is described below:

1.Zydis technology

Zydis formulation is a unique or different freeze-dried tablet in which drug is physically entrapped or dissolved within the matrix of fast dissolving carrier material. When zydis units are put into the mouth, the freeze-dried structure disintegrates immediately and does not require water for swallowing. The zydis matrix is composed of many materials designed to achieve a number of objectives like to impart strength and elasticity during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength to tablet.[37].

Advantages

• Buccal pharyngeal and gastric regions are all areas of absorption from this formulation. Any pre-gastric absorption avoids first-pass metabolism so advantage of 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 in the formulation.

• Patients who have difficulty swallowing oral medication due to dysphagia and unable to take medicine, stroke or medical conditions such as

gastroesophageal reflux disease, multiple sclerosis or Parkinson's disease.

Disadvantages

• The process of freeze-drying is a relatively expensive manufacturing process [38].

• The formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses so difficult to store.

2. Orasolv technology

In this system, the active medicament is taste masked. It also contains the effervescent disintegrating agent. in order to minimize oral dissolution time tablets are made by direct compression technique at low compression force. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable and packaged in specially designed pick and place system.

Advantages

Taste-masking is two-fold, quick dissolution. This technology has been used for drug strengths in the range of 1 mg to 750 mg. Depending on formulation and tablet size, the disintegration time of the tablet can be designed in the range of 10 to 40 seconds.

Disadvantages

They are sensitive to moisture due to the presence of the effervescent system and must be packaged appropriately. Low mechanical strength [39].

3. Durasolv technology

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

Advantages

DuraSolv technology is good for tablets having a low amount (125 mcg to 500 mg) of active ingredients and tablets are compressed to a greater hardness of 15-100 N, resulting in a more durable ODT. As a result, this technology enables packaging flexibility; tablets can be bottled and blistered [40].

Disadvantages

The technology is not compatible with larger doses of active ingredients because the formulation is subjected to high pressure during compaction. The drug powder coating in Durasolv may become fractured during compaction, exposing the bitter tasting drugs to the patient taste buds.

4. Wow tab technology

Wow, tab technology is patented by Yamanouchi Pharmaceutical Co. WOW means "Without Water". In this process, a combination of low moldability saccharides and high moldability saccharides is used to obtain a rapidly melting strong tablet. The combination of high and low moldability is used to produce tablets of adequate hardness.

Advantages

Adequate dissolution rate and hardness. Wow, tab product can be packed in both into the conventional bottle and blister packs.

Disadvantages

No significant change in bioavailability [41].

5. Flash dose technology

Flash dose technology has been patented by Fuisz. Nurofen melt let, a new form of Ibuprofen as melt-in-mouth tablets, prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of self-binding shear form matrix termed as floss. Shearform matrices are prepared by flash heat processing.

Advantages

High surface area for dissolution

Disadvantage

• High temperature required to melt the matrix can limit the use of heat-sensitive drugs, sensitive to moisture and humidity.

• The dosage form can accommodate only up to 600 mg of drug.

• Tablets produced are highly friable, soft and moisture sensitive. Therefore specialised packing is required.

6. Flashtab technology

The flashtab technology is yet another fast-dissolving/disintegrating tablet formulation.

Prographarm laboratories have patented the flashtab technology. It utilizes most of the same excipients as in conventional compressed tablets. A disintegrating agent and a swelling agent are used in combination with coated drug particles in this formulation to produce a tablet that disintegrates in the mouth in less than one minute [42].

MARKET FORMULATIONS OF FAST DISSOLVING TABLETS

Table 2:

Product	Generic	Company
Nimulid-MD	Nimesulide	Panacea Biotech, New Delhi, India
Feldene fast melt	Piroxicam	Pfizer Inc. NY, USA
Zyrob meltab	Rofecoxib	Zydus Cadila, India
Pepcid RPD	Famotidine	Merck and Co. , NJ, USA
Romilast	Montelukast	Ranbaxy Labs Ltd. , New Delhi, India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, India
Olanex instab	Olanzapine	Ranbaxy Labs Ltd., New Delhi, India
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Mosid-MT	Mosapride citrate	Torrent Pharmaceuticals, India
Febrectol	Paracetamol	Prographarm, Chateauneuf, France
Maxalt MLT	Rizatriptan	Merck and Co. , NJ, USA
Zelapar TM	Selegiline	Amarin Corp. , London, UK
Benadryl fast melt	Diphenhydramine	Pfizer
Imodium (instant melts)	Loperamide HCL	Janssen
Klonopin wafers	Clonaxepam	Roche
Zyprexa	Olanzapine	Eli lilly

EXCIPIENTS USED IN FAST DISSOLVING TABLETS

Excipients balance the properties of the actives in fast-melting tablets. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives.

1. Bulking Materials

Bulking materials are significant in the formulation of fast-dissolving tablets. The material contributes functions of a diluents, filler and cost reducer. Bulking agents improve the textural characteristics that in turn enhance the disintegration in the mouth, besides adding bulk also reduces the concentration of the active in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. Mannitol in particular has high aqueous solubility and good sensory perception. Bulking agents are added in the range of 10 percent to about 90 percent by weight of the final composition[43].

2. Emulsifying agents

Emulsifying agents are important excipients for formulating fast-melting tablets they aid in rapid disintegration and drug release without chewing, swallowing or drinking water. In addition, incorporating emulsifying agents is useful in stabilizing the immiscible blends and enhancing bioavailability. A wide range of emulsifiers is recommended for fast-dissolving tablet formulation, including alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition[44].

3.Lubricants

Lubricants, though not essential excipients, can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach. Examples are magnesium stearate and stearic acid[45].

4. Flavours and Sweeteners

Flavours and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients. Both natural and synthetic flavours can be used to improve the organoleptic characteristic of fast-melting tablets. Formulators can choose from a wide range of sweeteners including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose. The addition of sweeteners contributes a pleasant taste as well as bulk to the composition[46].

5. Superdisintegrants

Disintegrants are substances routinely included in tablet formulations and in some hard shell capsule formulations to promote moisture penetration and dispersion of the matrix of dosage form in dissolution fluids. An oral solid dosage form should ideally disperse into the primary particles from which it was prepared. Superdisintegrants are generally used at a low concentration, typically 1-10% by weight relative to total weight of dosage unit. Generally employed superdisintegrants are crosscarmellose sodium (Ac-Di-Sol), Crospovidone (CP), sodium starch glycolate (SSG) etc. which represent example of crosslinked

cellulose, crosslinked polymer and crosslinked starch respectively[47].

6. Taste masking technologies

Taste masking is an essential requirement for fast dissolving tablets for commercial success. Taste masking of the active ingredients can be achieved by various techniques. Drugs with unacceptable bitter taste can be microencapsulated into pH sensitive acrylic polymers. Cefuroxime axetil is microencapsulated in various types of acrylic polymers (e.g., Eudragit E, Eudragit L-55 and Eudragit RL) by solvent evaporation and solvent extraction techniques. These polymer microspheres showed efficient taste masking and complete dissolution in a short period. Fine granules of drug and disintegrant (e.g. low substituted Hydroxypropyl cellulose) when coated with a water insoluble polymer (e.g. ethylcellulose) masked the bitter taste of sparfloxacin. The addition of low substituted Hydroxypropyl cellulose as disintegrant to the drug in cores resulted in increased dissolution rate and bioavailability of sparfloxacin compared to its conventional tablets[48].

CONCLUSION:

Fast dissolving tablets are innovative dosage forms developed and specially designed to minimize problems that seen in conventional solid dosage form i.e. difficulty in swallowing of the tablet in geriatric and pediatric patients. Fast dissolving tablets are disintegrating quickly in the saliva generally within less than 60 seconds. Fast dissolving tablets have better patient compliance, bioavailability improved efficacy, convenience, and better safety compared with conventional oral dosage forms. FDTs need to be formulated for psychotic patients, bedridden, geriatric, pediatric patients, for those patients who may not able to take water, patients who are busy in traveling. FDTs formulations formulated by some of these conventional and patent technologies and FDTs have sufficient mechanical strength, quick disintegration/dissolution in the buccal cavity without water. The newer technologies utilized for the formulation of the FDTs that provide more effective dosage forms with more advantages and minimal disadvantages.

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