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AN OVERVIEW ON FAST DISSOLVING DRUG DELIVERY SYSTEM - A PIONEERING DRUG DELIVERY TECHNOLOGY

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ABSTRACT

Among the various novel drug delivery systems the fast dissolving drug delivery system is rapidly gaining interest in pharmaceutical Industry. Fast-dissolving drug-delivery systems were first developed in the late 1970 as an alternative to tablets, capsules, and for pediatric and geriatric patients who experience difficulties swallowing traditional oral solid dosage forms. These are used in the form of fast dissolving tablet and fast dissolving oral films. Today, fast dissolving drug delivery system is a proven and accepted technology for the systemic delivery of active pharmaceutical ingredient for over-the-counter medications. Fast dissolving drug delivery has become a significant priority worldwide. It can be easily swallowed without requirement of water is a major advantage over conventional dosage form. It may be possible to achieve rapid absorption of drugs and increased bioavailability, reduced toxicity, rapid onset of therapeutic action, improved delivery of poorly water-soluble drugs and also it is regarded as the most economical and safest method of drug delivery.

KEYWORDS

Fast dissolving drug delivery system, Fast dissolving tablet, Fast dissolving oral film, Bioavailability and Absorption.

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INTRODUCTION

The concept of Fast dissolving drug delivery system emerged as a preferred alternative to conventional oral dosage form with an objective to increase patient compliance. As the development of a new generic molecule is costly, the research has been focused on the development of new dosage forms with better compliance as compared to different dosage forms. Recent advances in novel drug

delivery system aims to enhance the safety of drug while maintain its therapeutic efficacy. Fast dissolving drug delivery system rapidly disintegrate and dissolves to release active pharmaceutical ingredient when it comes in contact with saliva, eliminating the need of water during administration and makes it highly attractive for pediatric and geriatric patients¹.

Fast dissolving dosage form includes tablets and films. Fast dissolving tablets are solid dosage forms which disintegrate rapidly when placed in tongue, instantaneously releasing the drug. Fast dissolving film is a dosage form which when placed on patients tongue or any oral mucosa, gets instantly wet by saliva, adheres onto the site of application and releases the drug^{2,3}.

Ideal characteristics for fast dissolving drug delivery system⁴

- It doesn't require water for administration and dissolves in a fraction of seconds.
- It leaves no or minimal residue in mouth after oral administration.
- Have a pleasing mouth feel.
- Rapid dissolution of drug produces a quick onset of action.
- Drugs may be absorbed from mouth, pharynx and esophagus as the saliva moves down into the stomach, results in improved bioavailability.
- Pregastric absorption results in increased bioavailability and reduction in dose.

Requirements of ideal drug candidate⁵

- No bitter taste
- Dose should be less than 20mg
- It should be stable in water and saliva
- Small to moderate molecular weight
- It should have ability to permeate oral mucosal tissue
- It must be able to diffuse and partition into epithelium of upper GIT.

FAST DISSOLVING TABLETS

Fast dissolving tablets are also called as mouth disintegrating tablet, quick dissolving tablet, and melt in mouth tablet, porous tablet, rapid melt tablet or orally disintegrating tablet. Orally disintegrating tablet has been defined in the 'Orange Book' as "a

solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds when placed upon the tongue". It combines the benefits of both liquid and conventional tablet formulations. They are distinguished from lozenges, buccal tablets and conventional sublingual tablets, which need more than a minute to dissolve in the mouth⁶. (Figure No.1).

Advantages of fast dissolving tablet⁷

- Ease of administration to persons with swallowing difficulties
- They are cost effective
- It doesn't require chewing
- Convenience of administration and accurate dosing
- Increase in bioavailability in the case of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of tablet.

Limitations of fast dissolving tablet⁸

- Tablet require careful handling because of insufficient mechanical strength
- It requires special packaging for proper stabilization.
- Drugs with large dose can't be formulated
- If the tablets are not formulated properly, it may leave an unpleasant taste in the oral cavity.

Techniques for preparing fast dissolving tablet^{4,9,10}

The various techniques for the preparation of quick dissolving tablet includes

- Freeze drying/ lyophilization
- Tablet moulding
- Sublimation
- Spray drying
- Direct compression
- Mass extrusion.

Freeze drying

It is the process in which water is sublimed from the product after it's frozen. This technique produces an amorphous porous structure which dissolves rapidly. A typical procedure for the manufacture of quick dissolving tablet using above technique is mentioned here. The drug is dissolved /dispersed in an aqueous solution of a carrier/polymer. The

mixture is poured into the wells of preformed blister packs. Trays that are holding blister packs are passed through liquid nitrogen freezing tunnel in order to freeze the drug solution or dispersion. The frozen blister packs are then placed in refrigerated cabinets to continue freeze drying, after which the aluminum foil backing is applied on a blister-sealing machine. Finally, they are packed and shipped. This technique has demonstrated improved absorption and bioavailability. The major limitation of this technique is that its time consuming and expensive, poor stability in stressed conditions.

Tablet moulding

There are 2 types of molding process (a) solvent method, (b) heat method. In solvent method, the powder blend is moistened with a hydro alcoholic solvent and compressed at low pressure in molded plates to form wetted mass which are then air dried to remove the solvent. Heat method involves preparation of a suspension drug, agar and sugar, which is poured into the blister packaging wells. The agar is solidified at room temperature to form jelly and dried under vacuum at 30°C. The molded tablets are less compact than compressed tablets, which enhances disintegration/dissolution and finally absorption is increased.

Sublimation

In this technique, highly volatile ingredients like urea, naphthalene, benzoic acid, ammonium bicarbonate, phthalic anhydride are added to the tablet excipients and compressed. The volatile material is removed by sublimation to generate a highly porous matrix. This technique produces tablet with enhanced dissolution.

Spray drying

In this method, gelatin can be used as matrix and supporting agent, mannitol as bulking agent and sodium starch glycolate/ crosscarmellose/ crosspovidone as super disintegrants. This spray dried powder which is then compressed into tablet showed quick disintegration and enhanced dissolution.

Direct compression

This technique is the simplest and cost effective method to manufacture tablet. It can be applied to the preparation of fast dissolving tablet due to the

availability of improved excipients like super disintegrants and sugar based excipients. The addition of super disintegrant enhance rate of disintegration and dissolution, the choice of suitable type and amount is a critical factor. The presence of other water soluble excipients and effervescent agents hastens the disintegration process.

Mass extrusion

It involves softening the active blend using water soluble polyethylene glycol and methanol. The softened mass is then expelled through extruder or syringe to get a cylinder of product into even segments using heated blade to form tablet. The dried product can be used for coating bitter drug granules and hence mask their taste.

Important patented technologies for fast dissolving tablets¹¹

Zydis Technology

Zydis formulation is the first marketed new tablet technology. It's a unique 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 instantaneously and does not require water to aid swallowing. To impart strength and resilience during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength. This technology claims for increased bioavailability as compared to other conventional tablets. The main advantage of this technology is convenience and limitation is that the freeze drying process is quite expensive manufacturing process.

Durasolv Technology

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of drug, filler and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. The tablets have low friability, about 2%. The disintegration time is less than 60 seconds. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for product requiring low amount of active ingredients.

Flash Dose Technology

Flash dose technology has been patented by fuisz. It utilizes most of the same excipients as in conventional compressed tablets. A disintegrating agent and 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 a minute.

Oraquick Technology

This technology is being patented by CIMA labs. The Oraquick fast dissolving/ disintegrating tablet formulation utilize a patented taste masking technology. The taste masking process does not utilize solvents, and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast dissolving/ disintegrating technologies which makes Oraquick appropriate for heat-sensitive drugs. Oraquick claims quick dissolution in a matter of seconds, with good taste masking.

Wow tab

Wow tab technology was developed by Yamanouchi Pharma Technologies. "Wow" means without water. The active ingredients may constitute up to 50% w/w of the tablet. Here, saccharides of both low and high mold ability are used to prepare the granules. Highly Moldable substance has high compressibility and thus slow dissolution. The combination of high and low moldability is used to produce tablets of adequate hardness and a rapidly melting strong tablet. The low moldability saccharides include lactose, mannitol, glucose, sucrose, and xylitol and high-moldability saccharides are maltose, sorbitol, and oligosaccharides Active ingredients are mixed with low moldability saccharides and then with high moldability saccharides and then compressed into tablet. Wow tab product dissolves quickly in 15 s or less. Wow tab product can be packed in both into conventional bottle and blister packs. This technology utilizes conventional granulation and tableting methods and used for both water-soluble and insoluble drugs.

Quicksolv Technology

This technology is patented by Janssen Pharmaceuticals. It utilizes two solvents in

formulating a matrix, which disintegrates instantly. Methodology involves dissolving matrix components in water and the solution or dispersion is frozen. Then dry the matrix by removing water using an excess of alcohol (solvent extraction). Thus the product formed has uniform porosity and adequate strength for handling.

Pharmabrust Technology

Pharmaburst technology is being patented by SPI pharma. The tablet manufactured by this process involves a dry blend of a drug, flavors, and lubricant then followed by compression into tablets which then dissolve within 30-40 seconds. Tablets manufactured by this methodology have sufficient strength can be packed in blister packs and bottles

Advatab

Advatab tablets disintegrate rapidly in the mouth, typically in less than 30 seconds and allow convenient oral drug administration without water. These tablets are especially suited to those patients that experience difficulty in swallowing capsules and tablets. The pairing of AdvaTab with Microcaps creates products that offer the dual advantage of a patient friendly dosage form, together with a superior taste and smooth mouth feel. This is a critical advantage as the unpleasant taste of drugs is a significant restriction in the application of other technologies.

Evaluation of Fast dissolving tablet^{7,13,14}

Hardness

The hardness of orally disintegrating tablets are determined using Monsanto or Pfizer tester.

Friability

The friability of 20 tablets can be determined using Roche friabilator. The pre weighed tablets are placed in friabilator and then rotated at 25 rpm for 4 min. the operated tablets were dusted and reweighed. The compressed tablets shouldn't lose more than 1% of their weight. The % friability is given by

$$\% F = \frac{(\text{Initial weight} - \text{final weight})}{\text{initial weight}} \times 100$$

Wetting time

A piece of twice folded tissue paper was placed in a petridish having 5ml of water. A pre weighed tablet was placed on that paper and time required for

complete wetting was characterized by coloring of tablet.

Weight variation

20 tablets are randomly selected and weighed individually for determining weight variation. According to IP weight variation specification is given in Table No.2.

Disintegration test

The standard procedure of disintegration test has to be modified as disintegration is required without water. The test must mimic disintegration in mouth within saliva. It should be less than 1 min.

Modified disintegration test

A tablet was carefully placed in the centre of petridish containing 10 ml of water. The time for the tablet to completely disintegrate into fine particles was noted.

Dissolution study

The dissolution study for fast dissolving tablet is identical to that of conventional tablets using USP dissolution apparatus 2 (paddle type) at 25-75 rpm. Buffers of pH 4.5 and 6.8, 0.1 N HCl should be used for the evaluation of these tablets.

Accelerated stability studies

The suitably packed fast dissolving tablets are stored under the following conditions as per ICH guidelines for accelerated studies (a) $40 \pm 1^\circ\text{C}$ (b) $50 \pm 1^\circ\text{C}$ (c) $37 \pm 1^\circ\text{C}$ and relative humidity = $75 \pm 5\%$. The tablets which are withdrawn after 15 days are analyzed for physical characterization and drug content. The data obtained are fitted into first order equation to determine the degradation kinetics and are plotted according to Arrhenius equation to determine the shelf life at 25°C .

Packaging of fast dissolving tablet¹⁵

Expensive packaging, specific processing, and special care are required during manufacturing and storage of fast-dissolving dosage forms to protect it. The dosage form can be packaged using various options, such as single pouch, blister card with multiple units, multiple-unit dispenser, and continuous roll dispenser, depending on the application and marketing objectives.

FAST DISSOLVING FILM

Fast dissolving film, a new drug delivery system that has been developed for the oral delivery of drug based upon the technology of transdermal patch. It consists of a thin oral strip which is placed on patient's tongue or oral mucosal tissue, gets instantly wet by saliva, dissolves rapidly to release the medicament for oral mucosal absorption. Fast dissolving film is a new dosage form made using hydrophilic polymers which dissolve rapidly on tongue or buccal cavity releasing the drug to systemic circulation through buccal mucosa. Fast dissolving films are the most advanced solid dosage form in terms of flexibility. They are also called as mouth dissolving strip, orodispersible films, and oral strips. The formulation of fast dissolving buccal film involves material such as strip-forming polymers, plasticizers, active pharmaceutical ingredient, sweetening agents, saliva stimulating agent, flavoring agents, coloring agents, surfactant, permeation enhancers, and super disintegrants. All the excipients used in the formulation of fast dissolving film should be approved for use in oral pharmaceutical dosage forms as per regulatory perspectives^{16,17}. (Figure No.2).

List of marketed fast dissolving oral films is given in Table No.3¹⁶.

Advantages of fast dissolving film¹⁸

- Fast and accurate dosing in a safe and efficacious manner
- No risk of choking
- Ease of handling and transportation
- Faster dissolution rate and quick onset of action
- Large surface area is available for drug absorption
- No special training required for its administration
- No special set is required for the industry
- Non-invasive.

Limitations of fast dissolving film¹⁹

- Higher doses can't be incorporated into film
- They are moisture sensitive.
- They require special packaging for the product stability and safety.

Methods of Preparation of Fast dissolving films^{20,21}

- Solvent casting
- Hot melt extrusion
- Semi solid casting
- Rolling method
- Solid dispersion

Solvent casting

In this technique, water soluble polymers are dissolved in suitable solvent. Drug and other excipients are dissolved in suitable solvent. Both the solutions are mixed, which is stirred and finally poured on to the petridish and dried.

Hot melt extrusion

The initial mass is formed by mixing the drug with carrier which is then dried and the dried granular material is introduced into extruder. The extrudate is then pressed into a cylindrical calendar to get film. In this method, fewer operation units are required, better content uniformity and have minimum product wastage.

Semisolid casting

This technique is used when film ingredient has acid insoluble polymer. Here, the water soluble polymers are dissolved in water and it's added to acid insoluble polymer in ammonia solution which is separately made. After proper mixing of the solution, plasticizers are added to obtain final solution. The gel mass obtained is casted as films or ribbons using heat controlled drums. The ratio of acid insoluble polymer to that of film forming polymer must be 1:4.

Rolling method

A solution or suspension of drug is prepared with film forming polymer and subjected to roller. The solvent is usually water and mixture of water and alcohol. The film is dried on roller and then cut into desired size and shape. The solution or suspension must have specific rheological consideration.

Solid dispersion

In this technique, immiscible components are extruded with drug and then the solid dispersions are made. The drug is dissolved in suitable liquid solvent and obtained solution is added to the melt of suitable polymer, obtainable below 70°C without removing the liquid solvent to obtain the solid

dispersion finally, solid dispersions are shaped into films by means of dies.

Technologies in the development of oral film²²

SOLULEAVES technology is used to produce a range of oral delivery films that can incorporate active ingredients, colors and flavors. SOLULEAVES films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients and flavors. This quality makes edible films an excellent delivery method for a large range of products requiring fast release in the mouth. This method of administration is especially useful for pediatric or geriatric patients who may have difficulty swallowing traditional tablets or capsules. The delivery system can be used for the cough/cold, gastrointestinal and pain therapeutic areas and delivering nutritional products. SOLULEAVES films can also be designed to adhere to mucous membranes and slowly release the active ingredient.

WAFERTAB system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The WAFERTAB filmstrip can be flavored for additionally improved taste masking. The active ingredient is precisely dosed and integrated into film after casting, thus preventing exposure to unnecessary heat and moisture and potentially enhancing product stability. The WAFERTAB system lends itself to many possibilities for innovative product design, enabling multiple films with different actives to be bonded together. WAFERTAB can be prepared in a variety of shapes and sizes and is an ideal method for delivery of medicines, which require fast release or for use by patients who have difficulty in swallowing.

RAPID FILM offers unique potential to deliver a variety of drugs, particularly when a fast onset of action is required. This technology can be used with poorly soluble drugs. Classes of drugs that can benefit from delivery via the Rapid Film system include hypnotics, anxiolytics, antiemetics, NSAIDs and pain killers, 5HT1 agonists for migraine treatment, antiallergics, antacids, vitamins, minerals, asthma and treatments for the oral cavity.

FOAMBURST is a special variant of the SOLULEAVES technology, which got a new patent granted in 2004. In this, an inert gas is passed into the film during production. This results in a film with a honeycombed structure, which dissolves rapidly giving a novel mouth sensation. FOAMBURST has attracted interest from food and confectionary manufacturers as a means of carrying and releasing flavors.

XGEL film is at the heart of Meldex International's intellectual property, used in all its film systems and its ingestible dosage delivery technologies. XGEL film provides unique product benefits for healthcare and pharmaceutical products. It's is non animal derived, approved on religious grounds and is suitable for vegetarians; the film provides an economic and competitive manufacturing platform. XGEL film can be taste masked colored, layered, and capable of being enteric properties whilst also having the ability to incorporate active pharmaceutical ingredients. The XGEL film systems can be made to encapsulate any oral dosage form, and can be soluble in either cold or hot water. XGEL film is comprised of a range of different water-soluble polymers, specifically optimized for the intended use. All of the XGEL ingredients are well known and generally regarded as safe.

Evaluation of fast dissolving film^{21,23}

Thickness

The thickness of film is measured by micrometer screw gauge or calibrated digital vernier caliper at 5 different locations. It is essential to determine uniformity in the thickness of the film as this is directly related to the accuracy of dose in the film.

Folding Endurance

Folding endurance is determined by repeated folding of the film at the same place till the film breaks. The number of times the film is folded without breaking is measured as the folding endurance value.

Surface pH test

The surface pH of fast dissolving film can cause side effects to the oral mucosa, so it is essential to evaluate the surface pH of film. The surface pH of film should be 7 or close to neutral. For this purpose, a combined pH electrode can be used.

With the help of water, film was made slightly wet and the pH was measured by bringing electrode in contact with surface of oral film. In another method, surface pH of films are determined by placing it on the 1.5% w/v agar gel and then the pH paper are placed on the film, change in color of pH paper gives surface pH of the film.

Tensile strength

Tensile strength is the maximum stress applied to a point at which the film breaks. It is calculated by the equation

$$\text{Tensile strength} = \frac{\text{Load at failure} \times 100}{\text{Film thickness} \times \text{film width}}$$

Percent elongation

When stress is applied, film stretches and this is referred to as strain. Strain is the deformation of film divided by original dimension of the sample. Generally elongation of film increases as the plasticizer content increases.

$$\% \text{ Elongation} = \frac{\text{Increase in length of strip} \times 100}{\text{Initial length of strip}}$$

In vitro disintegration test

Disintegration time is the time when film starts breaking when it is brought in contact with water or saliva. For fast dissolving film, the time of disintegration should be in range of 5-30 s. United State Pharmacopoeia (USP) disintegration apparatus is used to study disintegration time. In another method, the disintegration time can be visually determined by dipping the film in 25 ml water in a beaker. The beaker must be shaken gently and the time when the film starts to breaks or disintegrates was noted.

Dissolution Test

Dissolution testing can be performed using the standard basket or paddle apparatus described in any of pharmacopoeia. The selection of dissolution medium will essentially depend as per the sink conditions and highest dose of drug. The temperature of dissolution medium must be maintained at $37 \pm 0.5^\circ\text{C}$ and rpm at 50. When the paddle apparatus is employed, it has limitation that oral films have a tendency to float over the dissolution medium.

Permeation studies

To study the permeability, modified Franz diffusion cell mould be used with porcine buccal mucosa. The Franz diffusion cell consists of a donor and a receptor compartment where in between the mucosa is mounted. The size of the mucosa should be of the same size as that of the head of receptor compartment. The receptor compartment is filled with buffer and maintained at $37\pm 0.2^{\circ}\text{C}$ and a magnetic bead stirring at a speed of 50 rpm is used. A film specimen moistened with a few drops of simulated saliva should be kept in contact with mucosal surface. The donor compartment should consist of 1ml simulated saliva fluid of pH 6.8. At particular interval, samples are withdrawn and replaced by same amount of fresh medium. By suitable analytical method, percentage of drug permeated is determined.

Percentage moisture loss

To determine percentage moisture loss films of area $2\times 2\text{ cm}^2$ are cut and weighed accurately. After weighing, the films were kept in desiccators containing fused anhydrous calcium chloride. The films should be kept for 72 h in the desiccators. After 72 h, they are taken out and again weighed and the percentage moisture loss of films was measured by equation.

$$\text{Percent moisture loss} = (\text{Initial weight} - \text{Final weight}) / \text{Initial weight} \times 100$$

Drug content uniformity

It is determined by any standard assay method described for the particular drug in any of the standard pharmacopoeia. Content uniformity is determined by estimating the drug content in individual film. Limit of content uniformity is 85-115%.

Stability study

Stability study must be carried out as per International Conference on Harmonization (ICH) guidelines. The prepared formulations are wrapped in a special manner. Firstly, it was wrapped in a butter paper then in an aluminum foil and the packing should be placed in an aluminum pouch and make it heat sealed. The storage conditions at which formulations are kept should be $30^{\circ}\text{C}/60\%$ relative humidity (RH) and $40^{\circ}\text{C}/75\%$ RH. After 3 months, the films were evaluated for drug content, disintegration time, and physical appearance observation.

Storage and packaging of fast dissolving strip²³

Fast dissolving strips can be packed using single pouches, blister card with multiple units, multiple-unit dispenser, and continuous roll dispenser. There are certain patented packaging systems for fast dissolving films. The criteria's that are taken into consideration for packaging include need for unit dose packaging, bar- code labeling, child resistant seal and senior friendly packaging.

Table No.1: Commercially available Fast Dissolving Tablets

S.No	Trade name	Active pharmaceutical ingredient	Manufacturer
1	Pepcid RPD	Famotidine	Merck and co., NJ, USA
2	Claritin redi Tab	Loratadine	Schering plough Corp., USA
3	Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
4	Febrectol	Paracetamol	Prographarm, Chateaufneuf, France
5	Romilast	Montelukast	Ranbaxy lab. Ltd, New Delhi, India
6	Benadryl Fastmelt	Diphenhydramine and pseudoephedrine	Warner Lambert, NY, USA
7	Tempra Quiclets	Acetaminophen	Bristol myers Squibb, NY, USA
8	Felden fast melt	Piroxicam	Pfizer Inc., NY, USA
9	Olanex instab	Olanzapine	Ranbaxy lab. Ltd, New Delhi, India

Table No.2: IP Weight Variation Specification of Fast Dissolving Tablet

S.No	Average tablet weight	% deviation
1	80 mg or less	±10
2	80-250 mg	±7.5
3	250 mg or more	±5

Table No.3: Commercially Available Fast Dissolving Film

S.No	Brand name	Drug	Manufacturer
1	Listrine cool mint	Cool mint	Pfizer ,Inc.
2	Klonopin wafers	Clonazepam	Solvay pharmaceuticals
3	Triaminic	Diphenhydramine HCl	Novartis
4	Chloraseptic	Menthol	Prestige
5	Benadryl	Diphenhydramine HCl	Pfizer
6	Gas- X	Simethicone	Novartis

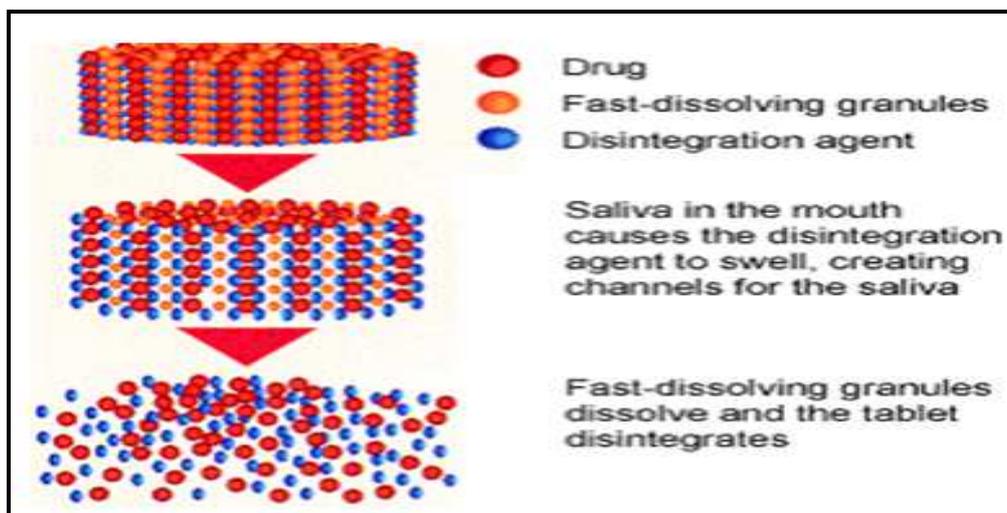


Figure No.1: Fast Dissolving Tablet



Figure No.2: Fast Dissolving Film

CONCLUSION

Drug delivery system has become an important subject in the past few decade. Development of fast dissolving drug delivery system has significantly boosts the pharmaceutical market by extending product life cycles. With the advancement in fast disintegrating dosage form, it has solved problems encountered in the administration of drugs to pediatric and elderly population, that constitute a major proportion of world's population. To overcome the difficulty in swallowing conventional tablets, scientist has developed innovative drug delivery system such as fast dissolving drug delivery system. These can be administered any time without water leading to their suitability to mentally ill, bedridden patients as well as geriatric and pediatric population. The benefits in terms of patient compliance, rapid onset of action and bioavailability make this delivery system as dosage form of choice in the current market.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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