



A SHORT REVIEW ON FAST DISSOLVING ORAL FILMS

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ABSTRACT

Fast dissolving drug delivery system was initially developed in late 1970s as an alternative conventional oral dosage forms like tablets, capsules and syrups for paediatric and geriatric patients who experience difficulties in swallowing of traditional oral dosage forms. For this purpose, a variety of orally disintegrating tablet formats were commercialized. In recent times fast dissolving oral thin films gain importance because of its wide benefits. Most of these products were designed to dissolve in less than one minute when exposed to saliva to form solution that could then be more easily swallowed. In the present review the classification of fast dissolving films and the role of formulation factors along with the evaluation parameters have been discussed. Now a days these are proven and accepted technology for the systemic delivery of active pharmaceutical ingredients for over the counter medications and are in the early to mid-development stages for prescription drugs.

KEY WORDS

Oral dosage forms, Fast dissolving films, Classification, Formulation and Evaluation.

INTRODUCTION

The oral is the most preferable route for drug administration as it is more convenient, economical, and ease of administration lead to higher levels of patient compliance. The oral route is some time a problem because of swallowing difficulties for paediatric and geriatric patients who have fear of choking. Patient convenience and compliance-oriented research has resulted in bringing out safer and better drug delivery systems. Recently, fast dissolving drug delivery systems have started gaining popularity and acceptance for reason of rapid disintegration or dissolution, self-administration even without water or chewing. Buccal drug administration has lately become an important route of drug administration. Various bioadhesive mucosal dosage forms have been developed, which includes adhesive tablets, gels, ointments, patches, and more recently the use of polymeric films for buccal delivery, also known as mouth dissolving films¹. Permeability of buccal is approximately 4-4000 times greater than that of skin,

but less than that of intestine. Hence, the buccal delivery serves as an excellent platform for absorption of molecules that have poor dermal penetration. The primary barrier to permeability in oral mucosa is membrane coating granules as of intercellular derived materials. These dosage forms have average shelf life of 2-3 years, depending on active chemical ingredient but are extremely sensitive to environmental moisture.

Ideal characteristics for fast dissolving oral films¹:

- High stability
- High transportability
- Ease of administration
- Ease of handling
- No special packaging material or processing requirements No water requirement for application
- Pleasant taste

Therefore, they're very suitable for paediatric and geriatric patients, bedridden patients and patients suffering from dysphasia, Parkinson's disease, mucositis, or vomiting. These were initially introduced

in the market as breath fresheners and personal care products such as dental care strips and soap strips. Formulation of fast dissolving oral films involve materials like strip forming polymers, flavoring agents, coloring agents, stabilizing agents, plasticizers, active pharmaceutical ingredients, sweetening agents, saliva stimulating agents, thickening agents, permeation enhancers and super disintegrants.

Special features of fast dissolving oral films:

- Thin elegant film
- Available in various sizes and shapes
- Unobstructive
- Excellent mucoadhesion
- Fast disintegration Rapid release

Advantages of fast dissolving oral films:

- Improved patient compliance
- Convenient dosing
- No water requirement No risk of choking Taste masking Enhanced stability
- Drug enters the systemic circulation with reduced hepatic first pass effect. Large surface area for absorption
- Dose accuracy is possible

Advantages over oral dissolving tablets:

- ODTs are difficult to carry,store,and handle due to fragility and friability. ODTs are expensive to prepare

Disadvantages of fast dissolving oral films:

- High dose cannot be incorporated beyond 1 to 30 mg Technical limitations during manufacturing. Drugs which can be formulated as fast dissolving oral films:
- Antitussives
- Expectorants Anti asthmatics Anti epileptics Expectorants
- Drugs used in treatment of GIT diseases
- Drugs used in treatment of nausea due to cytostatic therapy, pains i.e migraine Anti Parkinson's therapy

CLASSIFICATION OF FAST DISSOLVING ORAL FILMS¹:

For ease of description fast dissolving oral films are divided into 3 broad groups

Lyophilized systems:

It has been by far the most successful among them.The technology involved in these is taking a suspension or solution of drug with other structural excipients and

through the use of mould or blister pack forming tablet shaped units,which are then frozen and lyophilized in the pack or mould.Resulting units have high porosity,which allow rapid water or saliva and resulting in rapid disintegration.Dose handling capability differs depending on whether the active ingredient are soluble or insoluble drugs,dose capability may differ.

Compressed tablet-based systems:

They are produced using standard tablet technology by direct compression of excipients.The speed of disintegration for fast dissolving tablets compared with a standard tablet is achieved by formulating using water soluble excipients or super disintegrate or effervescent components to allow rapid penetration of water in of the tablet.These systems can theoretically accommodate relatively high doses of drug material, including taste masked coated particles.The potential disadvantage is that they take longer time to disintegrate than thin films or lyophilized dosage forms.

Oral Thin Films (OTF) :

Oral films, also called oral wafers are group of flat films which are administered into the oral cavity.

Formulation of fast dissolving oral films²:

Fast dissolving oral films are thin films with an area of 5 to 20 sq.cm containing an active ingredient. Drugs can be incorporated up to a single dose of 15 mg. Excipients plays important role in mechanical properties of the films.

Composition of fast dissolving oral films:

Drug:1-25%

Water soluble polymer:40-50%

Plasticizers Up to 20%

Filters, colours, flavour etc.: Up to 40%

1) Drug:

Several classes of drugs can be formulated as fast dissolving oral films including anti-ulcer drugs like omeprazole; anti asthmatic like salbutamol sulphate; anti tussive, expectorants, antihistamines, NSAID'S like paracetamol, meloxicam, valdecocib.

2) Water soluble polymers:

Water soluble polymers are used as film formers. The use of film forming polymers is they have rapid dissolution, disintegration, good mouth feels and mechanical properties to films. The disintegration rate of polymers is decreased by increased the molecular weight of polymers.

Eg: Water soluble polymers used in film preparation- HPMC E-3 and K-3; methylcellulose, pullulan, carboxymethylcellulose, PVP, pectin, gelatin, sodium alginate, hydroxyethylcellulose, polyvinyl alcohol, maltodextrins, and Eudragit. Polymerized rosin is ideal film forming polymer.

3) Plasticizer:

Formulation considerations (plasticizers) play an important factor affecting the mechanical properties of films. The mechanical properties such as tensile strength and elongation to the films are improved by addition of plasticizers. E.g.: glycerol, di butyl phthalate, polyethylene glycols etc.

4) Surfactants:

5) Surfactants are used as solubilising or wetting or dispersing agents so that the film getting dissolved within seconds and release active agent immediately.

E.g.: sodium lauryl sulphate, benzalkonium chloride, benzethonium chloride, tweens, etc. Poloxamer 407 is used as solubilising, wetting, and dispersing agent.

6) Flavour:

Any flavour can be used such as intense mints, sour fruit flavours or sweet confectionery flavours.

7) Colouring agents:

A full range of colours are available, including FD&C colours and custom Pantone matched colours

8) Saliva stimulating agents:

9) These may also be added to enhance the disintegration and to get rapid release. E.g.: citric acid, tartaric acid, malic acid, ascorbic acid and succinic acid.

MANUFACTURING METHODS³:

One or combination of the following process can be used to manufacture the mouth dissolving films 17.

- i) Solvent casting
- ii) Semi Solid casting
- iii) Hot melt extrusion
- iv) Solid dispersion extrusion
- v) Rolling

1) Solvent casting method:

In solvent casting method water soluble polymers are dissolved in water and the drug along with other Excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted into the Petri plate and dried.

2) Semisolid casting:

In semisolid casting method firstly, a solution of water- soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which was prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally, the gel mass is casted in to the films or ribbons using heat-controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4

3) Hot melt extrusion:

In hot melt extrusion method firstly, the drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. Finally, the melt is shaped in to films by the dies. There are certain benefits of hot melt extrusion 18.

-Fewer operation units -Better content uniformity - An anhydrous process

4) Solid dispersion extrusion:

In this method immiscible components are extruding with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.

5) Rolling Method:

In rolling method, a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cut into desired shapes and sizes 3.

EVALUATION PARAMETERS⁴

Thickness

The thickness of film is measured by micrometer screw gauge or calibrated digital Vernier Calipers. The thickness of film should be in range 5-200 μm . The thickness should be evaluated at five different locations (four corners and one at center) and it is essential to ascertain uniformity in the thickness of film as this is directly related to accuracy of dose distribution in the film.

Dryness/tack test

In all there have been eight stages identified for film drying and these are set-to-touch, dust-free, tack-free (surface dry), dry-to touch, dry-hard, dry-through (dry-to-handle), dry-to-recoat, and dry print-free. Tack is the

tenacity with which the strip adheres to an accessory (a piece of paper) that has been pressed into contact with strip. Instruments are also available for this study. [22]

Tensile strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of strip as given in the equation below:

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

Elastic modulus

Elastic modulus is calculated by formula

$$\text{Elastic modulus} = \frac{\text{force at corresponding strain}}{\text{Cross sectional area (mm}^2\text{)} \times \text{Corresponding strain}}$$

Percent elongation

When stress is applied on a film (2 × 2 cm²) sample it gets stretched, this is referred to strain. Strain is basically the deformation of strip before it gets broken due to stress. It is measured by using hounsfield universal testing machine. Generally, elongation of strip increases as the plasticizer content increases. It is calculated by the formula:

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

Tear resistance

Tear resistance is the resistance which a film offers when some load or force is applied on the film specimen. The load mainly applied is of very low rate 51 mm/min. The unit of tear resistance is Newton or pounds-force. In other words, it is the maximum force required to tear the specimen.

Young's modulus

Young's modulus or elastic modulus is the measure of stiffness of strip. It is represented as the ratio of applied stress over strain in the region of elastic deformation as follows:

$$\text{Young's modulus} = \frac{\text{Slope} \times 100}{\text{Strip thickness} \times \text{Cross head speed}}$$

Hard and brittle strips demonstrate a high tensile strength and Young's modulus with small elongation.

Folding endurance

Folding endurance gives the brittleness of a film. The method followed to determine endurance value is that the film specimen (2 × 2 cm²) are repeatedly folded at the same place until it breaks or a visible crack is observed. The number of times the film is folded without breaking or without any visible crack is the calculated folding endurance value.

In vitro disintegration test

Disintegration time is the time when an oral film starts breaking when brought in contact with water or saliva. For a fast dissolving film, the time of disintegration should be in range of 5-30 s. United State Pharmacopoeia (USP) disintegration apparatus can be 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 should be shaken gently and the time was noted when the film starts to break or disintegrates.

In vitro dissolution studies

Dissolution is defined as the amount of drug substance that goes into the solution per unit time under standardized conditions of liquid/solid interface, temperature, and solvent concentration. The standard basket or paddle apparatus described in any of the pharmacopoeia can be used for dissolution testing. The selection of dissolution medium will essentially depend as per the sink conditions and highest dose of API. The temperature of dissolution medium should be maintained at 37 ± 0.5°C and rpm at 50. When the paddle apparatus is employed, it has a disadvantage that oral films tend to float over the dissolution medium.

Drug content uniformity

This is determined by any standard assay method described for the particular Active pharmaceutical ingredient (API) in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. Limit of content uniformity is 85-115%.

Organoleptic test

The desired organoleptic properties of a fast dissolving formulation should have are color, flavor, and taste. As the formulation will disintegrate in the oral cavity so it should provide acceptable organoleptic palatable characteristics. Color makes a formulation acceptable among the patients and moreover oral films should have attractive color as they are administered to children. Hence, color of formulation should be uniform and attractive. Color can be evaluated by visual inspection. The other organoleptic property is the odor. The flavor used in the formulation should provide good odor to the formulation. The odor of the polymer, drug, and any other excipient should be masked with use of flavoring agent. Taste is also an important factor which

has to be evaluated. To evaluate the taste, special human taste panels are used. Experiments using electronic tongue measurements have also been reported to distinguish between sweetness levels in taste masking formulation. Electronic tongue technique works on the principle of potentiometric titration method. In this liquid samples can be analyzed directly, whereas solid samples need to be dissolved in a suitable solvent before analyzing. In this method, reference electrode and sensors are dipped in a beaker containing a test solution for 120 s and a potentiometric difference between each sensor and a reference electrode is measured and recorded by the E-tongue software.

Surface pH test

The surface pH of fast dissolving strip can cause side effects to the oral mucosa, so it is necessary 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, OS was made slightly wet and the pH was measured by bringing electrode in contact with surface of oral film. This study should be done on at least six films of each formulation and their mean $\pm$ SD can be calculated. In another method to determine the surface pH, the films are placed 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.

Contact angle

Contact angle measurement predicts the wetting behavior, disintegration time, and dissolution of oral film. These measurements are performed with help of goniometer and the measurements should be done at room temperature. The water used to determine contact angle should be double distilled water. A drop of double distilled water is placed on the surface of dry film. Images of water droplet are recorded within 10 s of deposition by means of digital camera. Digital pictures can be analyzed.

Transparency

To determine transparency of oral film, a simple ultraviolet (UV) spectrophotometer can be used. The film specimen is placed on the internal side of spectrophotometer cell. The transparency of films is calculated as follows:

$$\text{Transparency} = (\log T600)/b = -\epsilon c$$

Where T600 is the transmittance at 600 nm and b is the film thickness (mm) and c is concentration.

Scanning electron microscopy

To study the surface morphology of film between different excipients and drug scanning, electron microscopy can be used. The film sample should be placed in sample holder and at $\times 1000$ magnification, various photomicrographs can be taken using tungsten filament as an electron source.

Permeation studies⁵

Even though permeability of oral mucosa is 4-1000 times greater than that of skin, permeation studies should be carried out. To study the permeability, modified Franz diffusion cell can be used along with porcine buccal mucosa. The Franz diffusion cell consists of a donor and a receptor compartment. In between the two compartments, mucosa is mounted and 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 to maintain thermodynamics 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 1 ml 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 can be determined.

Percentage moisture loss

To determine percentage moisture loss films of area 2×2 cm² are cut and weighed accurately on an electronic balance. After weighing, the films were kept in desiccators containing fused anhydrous calcium chloride. The films should be kept for 72 h in the desiccator. After 72 h, they are taken out and again weighed and the percentage moisture loss of films was measured by using the formula:

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

The percentage moisture loss studies are done to determine physical stability and integrity of the film.

Determination of % yield of buccal patches

Percentage yield of buccal patches can be calculated by the following formula:

$$\% \text{ yield} = \text{Mass of the buccal patches obtained}/\text{Total weight of drug and polymer} \times 100$$

Stability study

Stability study should be carried out according to the International Conference on Harmonization (ICH) guidelines. The prepared formulation was wrapped in a

special way. Firstly, it was wrapped in a butter paper then above it an aluminum foil was wrapped 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°C/60% relative humidity (RH) and 40°C/75% RH. After 3 months, the films were evaluated for drug content, disintegration time, and physical appearance observation.

Swelling property

Film swelling studies is conducted using simulated saliva solution. Each film sample is weighed and placed in a reweighed stainless-steel wire mesh. The mesh containing film sample is submerged into 15ml medium in a plastic container. Increase in the weight of the film was determined at preset time interval until a constant weight was observed 20.

The degree of swelling was calculated using parameters $w_t - w_0 / w_0$, w_t is weight of film at time t , and w_0 is weight of film at time zero.

Packaging

A variety of packaging options are available for fast-dissolving films. Single packaging is mandatory for films, which are pharmaceutical products; an aluminum pouch is the most commonly used packaging format. APR-Labtec has developed the Rapid card, a proprietary and patented packaging system, which is specially designed for the Rapid films. The rapid card has same size as a credit card and holds three rapid films on each side. Every dose can be taken out individually

Patented approaches

XGel¹

XGel™ film provides unique product benefits for healthcare and pharmaceutical products: It is non-animal derived, approved on religious grounds, and is suitable for vegetarians; the film is genetically modified organism (GMO) free and continuous production processing 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.

Soluleaves¹

This 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. For pharmaceutical uses, this method of administration is especially useful for pediatric or elderly 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 as well as delivering nutritional products. Soluleaves™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 min.

Wafertab¹

Wafertab™ is a drug delivery system that incorporates pharmaceutical actives into an ingestible filmstrip. The 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 the body of a premanufactured XGel™ film, 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.

Foamburst¹

It is a special variant of the Soluleaves™ technology where 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.

Micap¹

Micap plc signed an option agreement in 2004 to combine its expertise in microencapsulation technology with the Bio Progress water soluble films. The developments will be aimed at providing new delivery

mechanisms for the \$1.4 billion global market for smoking cessation products (SCPs).

APPLICATIONS OF OTF IN DRUG DELIVERY SYSTEMS⁶

- Oral mucosal delivery via sublingual, buccal, and mucosal routes by use of oral thin film could become preferential delivery method for therapies requiring rapid drug absorption, including those used to manage pain, allergies, sleep, and central nervous system disorders.
- Topical applications: The use of dissolvable films may be feasible in delivery of active agents such as analgesic or antimicrobial agents in the wound care and other applications.
- Gastroretentive delivery system: Dissolvable films are being considered in the dosage form for which water soluble and poorly soluble molecules of various molecular weight are contained in
- film format. Dissolution of film could be triggered by pH or enzyme secretion of gastrointestinal tract (GIT) and could potentially be used for treatment of gastrointestinal disorder.
- Diagnostic devices: Dissolvable films may be loaded with sensitive reagent to allow controlled release when exposed to a biological fluid or to create isolation barriers for separating multiple reagents to enable a timed reaction within a diagnostic device.

Clinical and regulatory aspects⁷

In the US Food and Drug Administration (US FDA), if the product is bioequivalent to that of the existing oral product the drug, an Abbreviated New Drug Application (ANDA) route is followed. There is no clinical studies associated on this generic approval processes (section 505 (j) of the Food, Drug, and Cosmetic Act). The example of such case would be a comparative bioequivalence between an orally disintegrating tablet (ODT) formulation and orally dissolving film (ODF) product. However, developed oral film product may exhibit different pharmacokinetic profile compared to the existing marketed product. The ODF is categorized as 'new dosage form' and the section 505 (b) (2) approval process needs to be followed. In this case a new clinical study would be required. The advantage of new clinical study is that it would award 3 years of marketing exclusivity to the product. In Europe, marketing authorization approval is essential as per the European Medicine Evaluation Agency guidelines. Either of the two modes, that is, decentralization procedure or

mutual recognition process can be adopted. The Ministry of Health, Labor and Welfare is responsible for product approval in Japan.[46] Many of the regulatory agencies lay special emphasis on the taste and palatability aspects, especially if the product is intended to target the pediatric population. Oral mucosa irritation testing is carried out in both animal models and humans. In case of animal studies, the most appropriate model is hamster cheek pouch, it is a reliable model for predicting irritation criteria prior to testing in humans. In clinical trials, the clinical endpoint is significant. Primary and secondary outcome measures are to be noted. The objective is to demonstrate the superiority and advantage of newly developed OS as against the existing traditional conventional dosage forms. The ICH has laid guidance on product development. According to the ICH Q8 guideline on pharmaceutical development, companies may choose either an empirical approach or a more systematic approach towards product development. This document is an integral part of regulatory document for USA, EU, and Japan. Clinical study protocol should define a clear objective; different problems should be tackled in separate well-defined studies. The planned study should have sufficient resolution power to pick up critical adverse health effect (including supporting rationale). Calculation of the study size(s) is dependent on type of study (e.g., effects on soft tissues and/or on hard tissues). Specification of all endpoints should be determined. Description of usage pattern(s) (single/multiple application) is to be included. Follow-up during a relevant period after treatment (e.g., single application with follow-up periods of 1, 3, 6, and 12 months; multiple applications with longer follow-up, etc.) should be mentioned. There should be an inclusion of confounders and effect modifiers along with description of subject source(s), selection criteria, and methodology with appropriate analytical details. Due to the modified drug dissolution characteristics, clinical effect and drug bioavailability may be very different than conventional dosage forms. Being a noninvasive delivery system, it bypasses the first-pass effect to a large extent which can alter the clinical profile. The safety profiles can be improved as toxic metabolites that result from hepatic metabolism can be lowered in the case of drug being majorly absorbed from buccal mucosa. Another aspect is its faster onset of action which leads to rapid signs of clinical end-point.

Since every strip ideally contains precise amounts of the drug and the dosage form is independent of physiological variability of gastrointestinal tract, the intersubject variability in clinical response is fairly reduced. On the other hand, the absorption of drugs through oral mucosa would be much rapid than the

conventional counterparts that have to disintegrate and then solubilize the active, there is a possibility of dose dumping phenomena. Its clinical implications need to be studied. Due to this rapid response characteristic, the safety aspects of dosage form should be closely monitored.

Marketed Films¹:

Table 1. List of marketed fast dissolving films

S.No	Product	Manufactured By
1	Dextromethorphan HBr (cough suppressant), Diphenhydramine Citrate (cough and cold), Breath Strips	MonoSol Rx
2	Donepezil rapid dissolving films, Ondansetron rapid dissolving films	Labtec Pharma
3	Lifesaving rotavirus vaccine to infants	Johns Hopkins undergraduate biomedical engineering students
4	Methyl cobalamin fast dissolving films, Diphenhydramine HCl fast dissolving films, Dextromethorphan fast dissolving films, Folic Acid 1mg fast dissolving films, Caffeine fast dissolving films	Hughes medical corporation
5	Altoid cinnamon strips, Boots vitamin c strips, Cool shock peppermint strips, Benzocaine films, Caffeine films	Dow chemical company
6	Listerine Pocket Paks Breath Freshening Strips	Pfizer Warner-Lambert consumer healthcare division
7	Energy strips - Caffeine 20 mg, Acetylsalicylic Acid (ASA), Ondansetron HCl, Dexamethasone, Nitroglycerine, Risperidone Vitamin B12, melatonin, folic acid, biotin	ODF Technologies Inc.
	Benzocaine, Diphenhydramine HCl, Dextromethorphan	

Table 02: Few marketed preparations of oral films¹:

Oral film	Active Ingredient	Manufacture/Marketed	Category
Triaminic	Diphenhydramine HCL	Novartis	Anti-allergic
Listerine	Cool mint	Pfizer	Mouth fresheners
Theraflu	Dextromethorphan HBR	Novartis	Anti-allergic
Dextromethorphan	Dextromethorphan	Hughes medical corporation	Anti-tussive agent
Ondansetron Rapidfilms	Ondansetron	Labtec pharma	Post-operative nausea and vomiting
Caffeine Films	Caffeine	Dow chemical company	CNS stimulant
Donepezil	Donepezil	Labtec GmbH	Anticholines terase

Table 03: List of few polymers used in formulation of oral films¹:

Pullulan	Locust bean gum
Hydroxyl Propyl Methyl Cellulose (Hypromellose)	Polyvinyl pyrrolidone (PVP)
Modified starches	Polyvinyl alcohol
Polyethylene oxide	Carrageenan
Xanthan gum	Hydroxyl Ethyl Cellulose

Table 04: Various flavours used in formulation¹:

Fruit	Apple, raspberry, cherry, strawberry, pineapple, peppermint and oil, cinnamon oil, spearmint
Sour	Citric flavour, root bear, raspberry
Sweet	Vanilla, fruit, berry
Bitter	Walnut, wild cherry, chocolate, mint, anise
Salt	Butterscotch, maple, vanilla, mint, anise, apricot

Table 05: Properties of Oral films¹:

Property	Flash release	Mucoadhesive melt release	Mucoadhesive sustained release
Area (cm ²)	2-8	2-7	2-4
Thickness (μm)	20-70	50-500	50-250
Structure	Film single layer	Single or multilayer system	Multilayer system
Excipients	Soluble, Highly hydrophilic polymer	Soluble, hydrophilic polymer	Low/non-soluble polymer
Drug phase	Solid solution	Solid solution/ Suspended drug particle	Suspension or solid solution
Application	Tongue (upper plate)	Gingival or buccal region	Gingival (or another region of oral cavity)
Dissolution	Maximum Sixty second	Disintegration in few mins, forming gel	Maximum 8-10hours
Site of action	Systemic or local	Systemic or local	Systemic or local

CONCLUSION

Fast dissolving oral films have several advantages over the conventional dosage forms. So, they are of great importance during the emergency cases such as allergic reactions and asthmatic attacks whenever immediate onset of action is desired. They are the most acceptable and accurate oral dosage form which can bypass the hepatic system and show more therapeutic responses.

REFERENCES:

1. Rajni Bala, Pravin Pawar and Sandeep Arora: Orally dissolving strips: A new approach to oral drug delivery system, Int J Pharm Investig ,3(2): 67-76, (2013).
2. Arun Arya, Amrisha Chandra, Vijay Sharma and Kamla Pathak: Fast Dissolving Oral Films: An Innovative Drug Delivery System and Dosage Form. International Journal of ChemTech Research ,2 (1): 576-583, (2010).
3. M.D. Nehal Siddiqui, Garima Garg and Pramod Kumar Sharma: A Short Review on "A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents". Advances in Biological Research, 5 (6): 291-303, (2011)
4. Deepthi*, B. Venkateswara Reddy, and K. Navaneetha : Formulation and Evaluation of Fast Dissolving Oral Films of Zolmitriptan , American Journal of Advanced Drug Delivery,(2):153-163,(2014).
5. Alka Tomar , Kiran Sharma, Nitesh S Chauhan, Ashu Mittal, Umakant Bajaj : Formulation and evaluation of fast dissolving oral films of dicyclomine as potential route of buccal delivery international journal of drug delivery research, Int. J. Drug Dev. & Res ,4(2): 408-417,(2012).
6. Ali MS, Vijendar C, Sudheer Kumar D and Krishnaveni J: Formulation and Evaluation of Fast Dissolving Oral Films of Diazepam, J Pharmacovigilance, 4(3):1-2(2016).
7. Mahaveer Singh and Hemant R. Jadhav: "Fast Dissolving Oral Films", book chapter in 'Current Advances in Drug Delivery Through Fast Dissolving/Disintegrating Dosage Forms', Edited by Prof. Vikas A Saharan, Bentham Science, 318-356. (2017)

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