IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
August 2017 Vol.:10, Issue:1

Challenges Face by Pharmaceutical Industry for the Development of Oral Film Dosages Form

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Kure Sapna R., Deshpande Renuka R., Bhusnure O.G[1]*, Sachin B.Gholve

1. Channabasweshwar Pharmacy College, Dept of Quality Assurance, Latur (MS), India

2. Channabasweshwar Pharmacy College, Dept of Pharmaceutics, Latur (MS), India

3. Channabasweshwar Pharmacy College, Dept of Pharmacology, Latur (MS), India

Submission: 25 July 2017
Accepted: 3 August 2017
Published: 30 August 2017

Keywords: Fast dissolving oral films Oral mucosa Permeability Solvent casting and disintegration.

ABSTRACT

Fast dissolving oral films (FDOFs) are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improves the efficacy of APIs by dissolving within the minute in the oral cavity after the contact with less saliva as compared to fast dissolving tablets, without chewing and no need of water for administration. The oral thin-film technology is still in the beginning stages and has bright future ahead because it fulfills all the need of patients. Eventually, film formulations having drug/s will be commercially launched using the oral film technology. Oral fast dissolving film is relatively a new dosage form in which thin film is prepared using hydrophilic polymers, which rapidly dissolves on the tongue or buccal cavity. The film overcomes the danger/fear of choking. An ideal film should have the properties like pleasant taste, high stability, ease of handling and administration, no water necessary for the application.

HUMAN JOURNALS
www.ijppr.humanjournals.com

INTRODUCTION

The oral route is the most preferred route by medical practitioners and manufacturer due to the highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphasia patients turned the manufacturer to the parenteral and liquid orals. However, the liquid orals (syrup, suspension, emulsion) have the problem of accurate dosing mainly and useful in patients such as pediatric, geriatrics, bedridden, parenteral are painful drug delivery, so most patient in compliance. Fast dissolving oral film, a novel drug delivery system for the oral delivery of the drugs is an ultra-thin film prepared using hydrophilic polymers that rapidly dissolves on the top or the floor of the tongue or buccal cavity. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates in a matter of seconds and dissolves to release medication for oral mucosal absorption. Today, fast dissolving oral films are a well proven and worldwide accepted technology for the systemic delivery of active pharmaceutical ingredients (APIs).[1]

MECHANISM OF ACTION

The delivery system is simply placed on a patient's tongue or any oral mucosal tissue instantly wet by saliva due to presence of hydrophilic polymer and other Excipients, the film rapidly hydrates and dissolves to release the medication for oral mucosal absorption

FLOW CHART FOR THE DEVELOPMENT OF ORAL SOLID DOSAGE FORM.

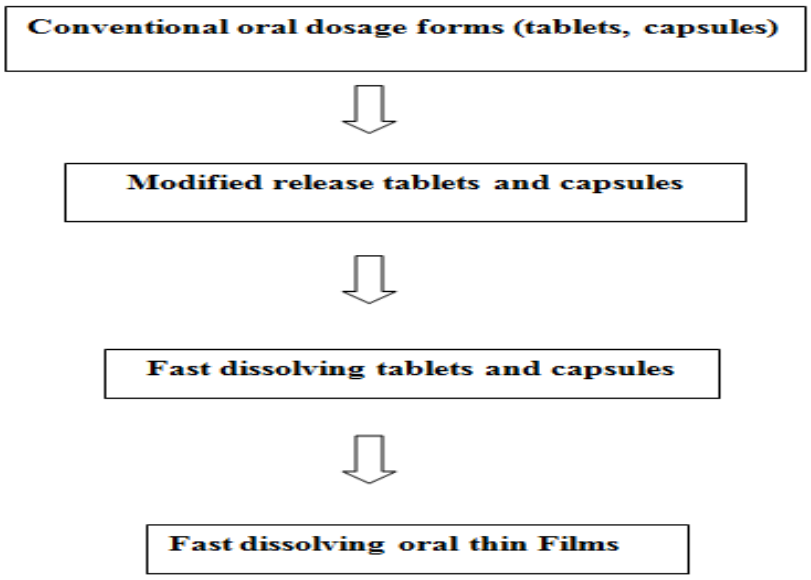

Fig. 1: Different Layers of the oral mucosa.

STRUCTURAL FEATURES OF ORAL MUCOSA

- **STRUCTURE:** The oral mucosa is composed of an outermost layer of stratified squalors epithelium (Figure 2). Below this lies a basement membrane, a lamina propria followed by the submucosa as the innermost layer. The epithelium is similar to stratified squamous epithelia found in the rest of the body in that it has a mitotically active basal cell layer, advancing through a number of differentiating intermediate layers to the superficial layers, where cells are shed from the surface of the epithelium[2.] The oral mucosal thickness varies depending on the site: the buccal mucosa measures at 500-800 µm, while the mucosal thickness of the hard and soft palates, the floor of the mouth, the ventral tongue measure at about 100-200 µm. The composition of the epithelium also varies depending on the site in the oral cavity. The mucosa of the soft palate the sublingual and the buccal regions, however, are not keratinized[3] which is relatively impermeable to water and only have small amounts of ceramide[4, 5]. They also contain small amounts of neutral but polar lipids mainly cholesterol sulfate and glucosylceramide. The figure1 given below shows the layer of oral mucosa from outside to innermost.

- **PERMEABILITY:** The oral mucosa, in general, is intermediate between that of the epidermis and intestinal mucosa in terms of permeability. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin[6]. There are considerable differences in permeability between different regions of the oral cavity

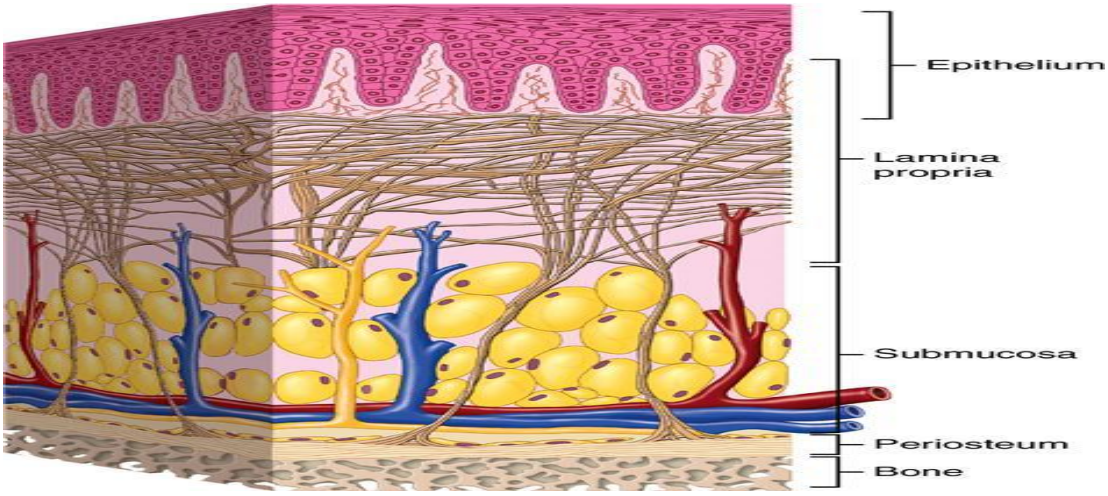

Fig. 2: Structure of the oral mucosa.

Because of the diverse structures and functions of the different oral mucosa[7] For the better absorption of APIs in oral region permeation enhancer play an important role. So if we want

to absorb the drug mostly in mouth as drug released from formulation then there is the need of permeation enhancer Some example of permeation enhancer given;

- Aprotinin[8]
- 23-lauryl ether[10]
- Azone [11]
- Benzalkonium chloride[12]
- Cetylpyridinium chloride[13]
- Cyclodextrin [14,15]
- Dextran sulfate[18]
- Menthol[22]
- Sodium glycodeoxycholate[19]

FORMULATION INGREDIENTS

DRUG (1-25%)

Several class of drugs can be formulated as mouth dissolving films including antiasthmatic (Salbutamol sulfate), antiulcer (Omeprazole), expectorants, antitussives, NSAID'S (Valdecoxib, Meloxicam).

WATER SOLUBLE POLYMERS (40-50%)

Generally, water-soluble polymers are used as film formers as they achieve rapid disintegration, good mouthfeel and mechanical properties to the films. The strength of the film depends on the type of polymer and the amount in the formulation. By increasing the molecular weight of polymer film bases, disintegration rate of the polymer decreases Polymers frequently used as film formers are water-soluble grades of cellulose ethers, polyvinyl alcohol, polysaccharides, polyvinylpyrrolidone K90, polyethylene glycols, pullulan, gelatin, carboxymethyl cellulose cekol 30, hydroxy propyl methyl cellulose E-3 and K-3, methylcellulose A3, A-6 and A-15, pectin, sodium alginate, hydroxypropyl cellulose, maltodextrins and eudragit RD10.

PLASTICIZERS (0-20%)

Plasticizer enhances mechanical properties such as tensile strength and elongation to the film by reducing the glass transition temperature of the polymer. It also reduces the brittleness of

the strip as a result improves its flexibility. Choice of plasticizer depends upon the type of solvent used and its compatibility with the polymer. Some of the commonly employed plasticizers are phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, low molecular weight polyethylene glycols, castor oil, citrate derivatives like tributyl, triethyl, acetyl citrate, triacetin, and glycerol. Improper use of the plasticizer may lead to blooming; film cracking, splitting and peeling of the strip[8].

SURFACTANTS

Surfactants are used as wetting, solubilizing, or dispersing agent so that the film is being dissolved within seconds and release active agent immediately. Commonly employed are poloxamer 407, benzethonium chloride, sodium lauryl sulfate, tweens, benzalkonium chloride, etc. Out of these most predominantly used surfactant is poloxamer.

SWEETENING AGENTS

Some of the commonly employed sweeteners are dextrose, sucrose, fructose, glucose, isomaltose, polyhydric alcohols (sorbitol, mannitol), etc. Artificial sweeteners like saccharin, cyclamate, aspartame (first generation) and acesulfame K, sucralose, alitame, neotame (second generation) can also be used.

SALIVA STIMULATING AGENTS

Saliva stimulating agents are used to increase the rate of production of saliva that would help in the faster disintegration of the rapid dissolving strip formulations. Examples of salivary stimulants are citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid. Among these, the most preferred one is citric acid.[22]

FLAVOURING AGENTS

The quantity of flavorings agent required to mask the taste depends on the flavor type and its strength. Commonly employed are fruity flavors (vanilla, cocoa, coffee, chocolate, citrus), flavor oils (peppermint oil, cinnamon oil, oil of nutmeg). Flavors can also be chosen from oleoresins, synthetic flavor oils and extract derived from various parts of the plants like fruits, flowers etc.

COLOURING AGENTS

Generally, incorporated coloring agents are FD&C colors, natural colors. Pigments such as titanium dioxide or a full range of colors are available, including FD & C colors, EU Colors, Natural Colors and custom Pantone-matched colors.

MANUFACTURING METHODS

To manufacture fast dissolving oral films, following methods are generally employed:

a. Semisolid casting.

b. Rolling.

c. Solvent casting.

d. Solid dispersion extrusion.

e. Hot melt extrusion.

A. SEMISOLID CASTING

In this method, at first, a solution of water-soluble film forming polymer is prepared. Then the resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate) which was prepared in ammonium or sodium hydroxide. The ratio of the acid insoluble polymer to the film forming polymer should be 1:4. A gel mass is obtained by addition of the suitable amount of plasticizer. By the means of heat controlled drums, finally, the gel mass is cast into the films or ribbons.

B. ROLLING

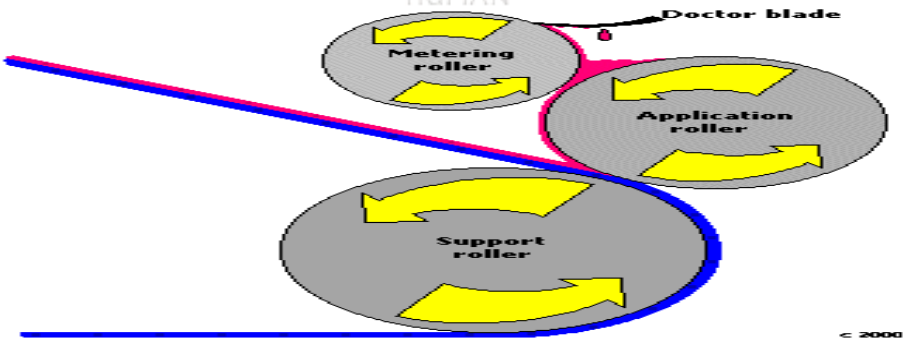

Fig. 3: Three roller coating film forming the unit.

Solvents mainly used in this method are water and mixture of water and alcohol. By the means of high shear processor, active agent and other ingredients are dissolved in the small portion of the aqueous solvent. Water soluble hydrocolloids are dissolved in water to form the homogenous viscous solution. Then the resultant solution or suspension containing drug is rolled on a carrier. Finally, the obtained film is cut into desired shapes and sizes.[20]

C. SOLVENT CASTING

In this method water, soluble polymers are dissolved in water and the drug along with other ingredients is dissolved in suitable solvent. Then both the solutions are mixed, stirred, finally cast into the Petri plate and dried.[18]

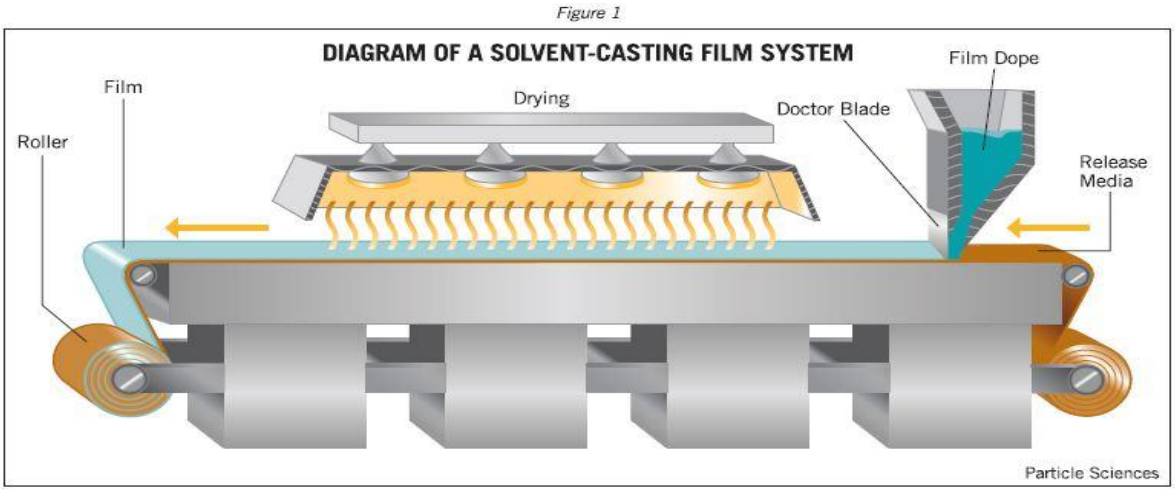

Fig. 4: Solvent Casting Technique.

D. SOLID DISPERSION EXTRUSION

Firstly solid dispersion is prepared by extruding immiscible components with drug and then shaped into films by the means of dies.[19]

E. HOT MELT EXTRUSION.

In hot melt extrusion method at first drug is mixed with carriers in solid form. Then the mixture is molten by the means of extruder having heaters. Lastly, the melt is shaped into films by the dies**.**

EVALUATION TESTS:

- **MORPHOLOGY STUDY**

The morphology of the films is studied using Scanning Electron Microscopy (SEM), at a definite magnification.[5]

- **ORGANOLEPTIC EVALUATION**

For this purpose in-vitro methods of utilizing taste sensors and specially designed apparatus are being used. These in-vitro taste assessment apparatus are adapted for high-throughput taste screening of oral pharmaceutical formulations.

- **THICKNESS**

It can be measured by micrometer screw gauge at different locations. It is crucial to determine uniformity in the thickness of the film as this is directly related to the accuracy of dose in the strip.

EVALUATION TEST PARAMETERS

A.MECHANICAL PROPERTIES :

Three mechanical properties namely tensile strength, tear resistance, elastic modulus and percentage elongation are calculated.

1. TENSILE STRENGTH

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by formula

Tensile strength = Load at Failure X 100 /Strip thickness X Strip Width.

2. TEAR RESISTANCE

Principally very low rate of loading 51 mm (2 in.)/min is employed and is designed to measure the force to initiate tearing. The maximum stress or force (that is generally found near the onset of tearing) necessary to tear the specimen is noted as the tear resistance value in newtons (or pounds /force).

3. YOUNGS MODULUS

It is calculated by formula,

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

Young's modulus = Slope × 100/Film thickness × cross-head speed.

The hard and brittle film demonstrates a high tensile strength and Young's modulus with small elongation.

4. FOLDING ENDURANCE

It is determined by folding the films of uniform cross-sectional area and thickness at the same place repeatedly until it breaks. The number of times the film could be folded at the

same place without breaking gives the value of folding endurance. Typical folding endurance for the film is between 100-150.

B. ORGANOLEPTIC EVALUATION

1. Swelling index:

The studies of the swelling index of the film are conducted in the simulated salivary fluid. The film sample is weighed and placed in a pre-weighed stainless steel wire sieve. The mesh containing the film is submerged into 50ml of the simulated salivary medium contained in a mortar. Increase in weight of the film is determined at each interval until a constant weight is observed. The degree of swelling is calculated using the formula:

$$SI = wt - wo / wo$$

Where SI = swelling index,

Wt. = weight of the film at time "t", and

wo = weight of the film at t = 0

2. Transparency :

The transparency of the films can be determined using a simple UV spectrophotometer. Cut the film samples into rectangles and placed on the internal side of the spectrophotometer cell. The determine transmittance of films at 600 nm. The transparency of the films was calculated as follows

Transparency = (logT600)/b = - €c Where T600 is the transmittance at 600 nm and b is the film thickness (mm) and c is concentration.[21,22]

3.Assay/ Content uniformity :

This is determined by any standard assay method described for the particular API in any of the standard pharmacopeias. Content uniformity is determined by estimating the API content in an individual strip. Limit of content uniformity is 85–115 percent.

4.Disintegration time :

The disintegration of orally fast dissolving films requires USP disintegration apparatus. The disintegration time limit of 30 seconds or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips. Disintegration time will vary

depending on the formulation but typically the disintegration range from 5 to 30 seconds. Although, no official guidance is available for oral fast disintegrating films strips.[23]

5.Dissolution test :

Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopeia. The dissolution medium will essentially be selected as per the sink conditions and highest dose of the API. Many times the dissolution test can be difficult due to tendency of the strip to float onto the dissolution medium when the paddle apparatus is employed.[23]

SOME OF THE EXAMPLES OF MARKETED FAST DISSOLVING ORAL FILMS.

Product	Manufactured by	Indication
Caffeine films	Dow chemical company	CNS Stimulant.
Dextromethorphan fast dissolving films	Hughes medical corporation	Anti-tussive agent.
Chloraseptic® Relief stripsTM	Innocent Inc	Minor irritation, pain, and sore throat.
Folic acid fast Dissolving films	Huges Medical Corporation	Anaemia.
Diphenhydramine Hydrochloride films	MonoSolRX	Antiasthmatic.
Triaminic Thin Strips®	Novartis Pharmaceuticals	Nasal decongestant.
Methylcobalamin Fast Dissolving films	Hughes medical corporation	Diabetic /peripheral neuropathy.

CONCLUSION

OFDFs are not well defined in the literature but no doubt a revolutionary and an innovative drug delivery system for all the population groups, specifically geriatric, pediatric patients and patients with swallowing difficulties. OFDFs are also having great potential of delivering the medicinal agent systemically as well locally and have several advantages over many dosage forms even over the fast disintegrating tablets. This explains the extensive research activities going on this technology.

ADVANTAGES:

- Fast dissolving film combines all the advantages of tablets (accurate dose, self-administration) with those of liquid dosage forms (easy swallowing, quick bioavailability). The administration of drugs by the oral route has several advantages over another route of administration such as,

- No special set up required for industry.
- No need of water or a spoon for administration and without chewing.
- Dose accuracy in comparison to syrups
- Rapid onset of action
- The drug enters the systemic circulation with reduced hepatic first pass effect
- Lower doses
- Minimal side effects
- Delivery can also be terminated relatively easily if required.
- Site specific action and local action.
- Noninvasive.
- Patent life extension

CHALLENGES FACE BY PHARMACEUTICAL INDUSTRY FOR THE DEVELOPMENT OF ORAL FILM DOSAGES FORM

Following are some of the challenges in formulating fast dissolving oral film and trying to elaborate and solve these problems. These challenges are directly related to patient compliance.

These include -

1) Insolubility of drug

2) Taste masking of bitter and obnoxious drug

3) Reduction in drying time of film

4) High dose incorporation in film

5) Co-administration of drugs

6) Stability of film against humidity and temperature

7) Need special packaging

8) Dose uniformity.

1. Insolubility of drug: Solubility plays a rate limiting parameter to get desired concentration of drug of orally administered formulation in the systemic circulation. The problem of solubility is the main challenge for the formulation of oral film of BCS class II drugs having low solubility and high permeability.[24]

2. Taste masking of bitter and obnoxious drug: Taste masking becomes a prerequisite for better drugs used in fast dissolving oral film to improve the patient compliance especially in the pediatrics and geriatric population. Taste is an important parameter in case of fast dissolving oral film. The oral film has to remain in contact with oral mucosa until it completely dissolves in saliva in an oral cavity. For this, a taste of bitter drugs should be masked. So, taste masking becomes a prerequisite for better drugs used in fast dissolving oral film to improve the patient compliance especially in the pediatrics and geriatric population.[25]

3. Reduction in drying time of film: Drying time plays an important role in oral film formulation and also in case of the rate of production of the oral film in industries. Generally, hot air oven is not used for drying of oral film of thermo labile drugs. So, the oral film is dried at room temperature, However, it takes more time to dry (about one day).

Panchal M. S.et.al. (2012) has reported that time taken by formulation for drying was found to be 24 hours at room temperature for the formulation of mouth dissolving film of Ropinirole hydrochloride prepared by using Pullulan polymers[26] ·35°C temperature for 12 hours was used by Jadhav S. D. et.al. (2012) for drying fast dissolving oral film of Sertraline hydrochloride[26.]

4. Dose incorporation in the film: Dose of the drug in oral film formulation can be increased by increasing area of the container. The only area should be increased keeping the thickness of formulation solution constant so that volume of solution needed for the formulation is also increased which help in the incorporation of high dose and reduction in drying time also.[27]

5. Co-administration of drugs: Use of more than one drug i.e. co-administration of drugs is a very difficult task in oral film formulation. Because it may affect disintegration time as well as dissolution rate of formulation.[27]

6. Stability of film against humidity and temperature: Fast dissolving oral film consists of about 45% of polymer, which is hydrophilic in nature. In the humid atmosphere, the film will absorb water and are liquefied due to the dissolution of the film in water. Therefore, the stability of film against humidity is very difficult and challenging task. Amorphous drugs often have higher dissolution rates than their crystalline forms, but lower physical stability during storage. Addition of crystallization inhibitors such as hydrophilic polymers to the amorphous drug to form a film formulation is the best method to prevent drug crystallization[28.]

7. The need of special packaging: In the pharmaceutical industry, it is vital that the package selected adequately preserve the integrity of the product. A variety of packaging options is available for fast dissolving films. An aluminum pouch is the most commonly used packaging material. APR- Labtec developed the Rapid card, patented packaging system designed for the Rapid films. The rapid card has the same size as a credit card and holds three rapid films on each side. Every dose can be taken out individually[29.]

8. Dose uniformity: Film, which is to be made in a container, has to cut into desired area containing a required dose of the drug. So, to get a uniform dose in all films which cut into the desired area is a challenging task.

REFERENCES

1. Vollmer. U and Galfetti. P., "Rapid film: Oral thin films as an innovative drug delivery System and dosage", Drug Dev Report. 2006, 64-67.
2. Shojaei, A.H., 1998. Buccal Mucosa as A Route for Systemic Drug Delivery: A Review. J. Pharmacy and Pharmaceutical Sci., 1(1): 15-30.
3. Harris, D. and J.R. Robinson, 1992. Drug delivery via the mucous membranes of the oral cavity. J. Pharmaceutical Sci., 81: 1-10.
4. Wertz, P.W. and C.A. Squier, 1991. The cellular and molecular basis of barrier function in oral epithelium. Crit. Rev. Ther. Drug Carr. Sys., 8: 237-269.
5. Squier, C.A., P.Cox, and P.W. Wertz, 1991 Lipid content and water permeability of skin and oral mucosa. The J. Investigative Dermatol 96: 123-126.
6. Galey, W.R., H.K. Lonsdale and S. Nacht, 1976 The in vitro permeability of skin and buccal mucosa to selected drugs and tritiated water, J. Investigative Dermatol., 67: 713-717.
7. Harris, D. and J.R. Robinson, 1992. Drug delivery via the mucous membranes of the oral cavity. J. Pharmaceutical Sci., 81: 1-10.
8. Aungst, B.J. and N.J. Rogers, 1988. Site dependence of absorption-promoting actions of Laureth-9, Na salicylate, Na EDTA and Aprotinin on rectal, nasal and buccal insulin delivery. Pharmaceutical Res 5(5): 305-308.
9. Oh, C.K. and W.A. Ritschel, 1990. Biopharmaceuticals aspects of buccal absorption of insulin. Methods and Findings in Experimental and Clinical Pharmacol, 12: 205-212.
10. Wolany, G.J.M., J.Munzer, A. Rum melt and H.P. Merkle, 1990.Buccal absorption of Sandostatin (octreotide) in conscious beagle dogs Proceed. Intern. Symp. Control. Rel. Bioact. Mater., 17: 224-225.

11. Kurosaki, Y, S. Hisaichi, L.Hong, T. Nakayama and T.Kimura, 1989. Enhanced permeability of keratinized oral-mucosa to salicylic acid with 1th oral-mucosa to salicylic acid with 1th in hamster cheek pouch. International J. Pharmaceutics, 49(1): 47-55.
12. Kurosaki, Y., S. Hisaichi, T. Nakayama and T. Kimura 1989. Enhancing effect of 1-dodecylazacycloheptan 2-one (Azone) on the absorption of salicylic acid from keratinized oral mucosa and the duration of enhancement in vivo. International J. Pharmaceutics 51(1): 47-54.
13. Siegel, I.A. and H.P. Gordon, 1985. Effects of surfactants on the permeability of canine oral mucosa in vitro. Toxicology Letters, 26(2-3): 153-157.
14. Siegel, I.A. and H.P. Gordon, 1985. Surfactant-induced increase of permeability of rat oral mucosa to non-electrolytes in-vivo. Archives of Oral Biol., 30: 43-47.
15. Siegel, I.A. and H.P. Gordon, 1985. Effects of surfactants on the permeability of canine oral mucosa. "Castable edible pharmaceutical films", Dow Chemical Company, West Haven, USA. 2007, 1-7.
16. http://www. Patent storm.us /patents/6740332/claims.html.
17. Frey. Film Strips and Pharmaceuticals, Pharma Mfg & Package Sourcer. 2006, 92– 93.
18. Mishra. R, Amin. A., Quick API Delivery. Pharmaceutical Technology Europe, pp. 15.
19. Frey. Film Strips and Pharmaceuticals, Pharma Mfg & Package Sourcer. 2006, 92– 93.
20. Anand. V, Kataria. M, Kukkar. V, Saharan. V and Choudhury. P.K., "The latest trends in the taste assessment of pharmaceuticals", Drug Discovery Today 2007, 12, 257- 265.
21.Han Jung H, Floros John, Casting antimicrobial packaging films and measuring their physical properties and antimicrobial activity. Journal of Plastic Film and Sheeting 13; 1997:287-297.
22. Jutaporn Chana-Thaworn, Suphitchaya C, Thawien W, Properties and antimicrobial activity of edible film incorporated with kaim wood extract, LWT - Food Science and Technology. 44; 2011: 284-292.
23. Dixit RP, Puthli SP, Oral strip technology: Overview and future potential. Journal of Controlled Release. 139; 2009: 94–97.
24. Peh. K K and Wong. CF., "Polymeric film as vehicle for buccal delivery: swelling, Mechanical and Bioadhesive properties", J Pharm Pharm Sci.1999, 2, 53-61.
25. Barnhart. S, Rathborne. M, Hadgraft. J, Roberts. M and Lane M., "Thin film oral dosage forms, in Modified release drug delivery technology", Drugs and the pharmaceutical sciences, 2nd edition, 209- 216.
26. Nishimura. M, Matsuura. K, Tsukioka. T, Yamashita. H, Inagaki. N, Sugiyama. T and Itoh. Y., "In vitro and in vivo characteristics of prochlorperazine oral disintegrating film", Int J Pharm. 368:2009, 368: 98-102
27. Wadhwa J., Puri S., Taste masking: A novel approach for bitter and obnoxious drugs, International Journal of Biopharmaceutical & Toxicological Research 2011; 1:1: 47- 60.
28. Panchal M., Patel H., Bagada A., Vadalia K., formulation, and evaluation of mouth dissolving film of Ropinirole hydrochloride by using pullulan polymers, IJPRAS 2012; 1:3: 60-72.
29. Yuvraj G. Jadhav, Upendra C. Galgatte*, Pravin D. Chaudhari Challenges In Formulation Development of Fast Dissolving Oral Films, Indo American Journal of Pharmaceutical Research, Vol 3, Issue 8, 2013, 6391-6407.
30. Gaisford S., Verma A., Saunders M., Royall P., Monitoring crystallization of drugs from fast dissolving oral films with isothermal calorimetric, International Journal of Pharmaceutics 2009; 380: 105-11.
31. Pandya K., Patel K., Patel M., and Patel N., Fast dissolving films: a novel approach to oral drug delivery, Asian Journal of Pharmaceutical Science & Technology 2013; 3:1: 25-31.