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Fast Dissolving Oral Films: An Innovative Drug Delivery System

Pallavi Patil.[1], S. K. Shrivastava[2]

PES's Modern College of Pharmacy (For Ladies) Moshi, Pune- 412 105, Maharashtra, India

Abstract: ***The oral route is most popular route for the administration of therapeutic agents because of the low cost of therapy and ease of administration lead to high levels of patient compliance. The most popular oral solid dosage forms are tablets and capsules. Many patients find it difficult to swallow tablets and hard gelatin capsules particularly pediatric and geriatric patients and do not take their medicines as prescribed. Difficulty in swallowing or dysphasia is seen to afflict nearly 35% of the general population. In some cases such as motion sickness, sudden episode of allergic attack or coughing, fear of choking and an unavailability of water, the swallowing of tablet or capsules may become difficult. To overcome these difficulties, several fast-dissolving drug delivery systems have been developed. Oral fast dissolving film is relatively a new dosage form in which thin film is prepared using hydrophilic polymers, which rapidly dissolves on 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 application.***

Keywords: Fast dissolving films, Oral strips, Film forming polymer, solvent casting, Tensile strength.

1. Introduction

Among the different routes, the most agreeable route for the patients is oral route. Most of the pharmaceutical companies have directed their search activity in developing viable dosage alternatives from oral route for pediatrics, geriatric, noncompliant or nauseous patients. Research in the oral drug delivery segment has led to evolution of dosage forms from simple conventional tablets/capsules to modified release tablets/capsules to oral disintegrating tablet to wafer to the recent development of fast dissolving oral films. 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. It is an ultrathin strip (50-150 microns thick) of postage stamp size with an active agent and other excipients developed on the basis of transdermal patch technology. These evolved from the confectionery and oral care markets over past decade in the form of breath strips and became a novel and widely accepted dosage form by consumers for delivering vitamins and personal care products. These fast dissolving oral films have persistent to extend in sales and launched as patient compliant and convenient products effectively addressing issues for pharmaceuticals as well as nutraceuticals that have been traditionally administered as oral solid dosages. 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 oromucosal absorption. Today, fast dissolving oral films are a well proven and worldwide accepted technology for the systemic delivery of active pharmaceutical ingredients (APIs).

1.1 Special features of Mouth dissolving films

- Thin elegant film
- Available in various size and shape
- Un obstructive
- Excellent mucoadhesion
- Fast disintegration
- Rapid release
- Can be administered without water

1.2 The ideal characteristics of a drug to be selected

- The drug should have pleasant taste.
- The drug should have low dose up to 40 mg.
- The drugs have smaller and moderate molecular weights are preferable.
- The drug should have good stability and solubility in water as well as in saliva.
- It should be partially unionized at the pH of oral cavity.
- It should have the ability to permeate oral mucosal tissue.

1.3 Advantages

- Ease of administration to pediatric, geriatrics, bedridden patients and psychiatric patients who refuse to swallow tablets.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, which enhances bioavailability of drugs.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage; improved clinical performance through a reduction of unwanted effects.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.
- The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- Useful in cases where a rapid onset of action required such as in motion sickness, sudden episodes of allergic attack or coughing, bronchitis or asthma.

- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

1.4 Disadvantages

- Drugs which are unstable at buccal pH cannot be administered.
- Drugs which irritate the mucosa cannot be administered by this route.
- Drug with small dose requirement can only be administered.
- Taste masking- Most drugs have bitter taste, and need taste masking.
- Special packaging- OFDFs are fragile and must be protected from water so it needs special packaging.

1.5 Properties of the Oral Films

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 other region of oral cavity)
Dissolution	Maximum sixty second	Disintegrstion in few mins, forming gel	Maximum 8 - 10 hours
Site of action	Systemic or local	Systemic or local	Systemic or local

2. Formulation Ingredients

2.1 Formulation consideration:

From the regulatory prospective all the excipients used in the formulation and development of oral films and they are regarded as safe (GRAS listed) and should be approved for use in oral pharmaceutical dosage forms. The area of oral thin films is 1-20cm^2 (depend on dose and drug loading containing drug).

2.1.1 Drug (1-25%)

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

2.1.2 Water Soluble Polymers (40-50%)

To obtain the desired film properties, polymers can be used alone or in combination. Generally water-soluble polymers are used as film formers as they achieve rapid disintegration, good mouth feel 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 K-90, polyethylene glycols, pullulan, gelatin, carboxmethylcellulose cekol 30, hydroxy propyl methyl cellulose E-3 and K-3, methyl cellulose A-3, A-6 and A-15, pectin, sodium alginate hydroxypropylcellulose, maltodextrins and eudragit RD10.

2.1.3 Plasticizer (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 brittleness of the strip as a result improves its flexibility. Choice of plasticizer depends upon 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 plasticizer may lead to blooming, film cracking, splitting and peeling of the strip

2.1.4 Surfactants

They are used as solubilizing and wetting agents making the film to dissolve rapidly within seconds. Sodium lauryl sulphate, tween 80, benzalkonium chloride are some of the widely used surfactants. In recent times Polaxamer 407 has been majorly used as wetting and solubilizing agent

2.1.5 Saliva Stimulating agent

The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving strip formulations. These agents are used alone or in combination between 2-6% w/w of the strip. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants.

2.1.6 Flavoring Agents

Flavoring Agents can be selected from the synthetic flavor oil, oleo resins, extracts derived from various parts of the plant like leaves, fruits, and flowers. Any flavor can be added such as essential oil or water soluble extracts of menthol, intense mints such as peppermint, sweet mint, spearmint, wintergreen, cinnamon, clove, sour fruit flavor such as lemon, orange or sweet confectionary. Flavors such as vanillin, chocolate or fruit essence like apple, raspberry, cherry, pineapple.

2.1.7 Coloring agents

FDC approved natural coloring agents and natural juice concentrates are most commonly used. The concentration should not exceed 1%w/w. Pigments like titanium dioxide, silicon dioxide are also used as prominent coloring agents for oral films

2.1.8 Few categories of drug that can be formulated as oral fims

Category of drugs	*Examples*
5HT3 antagonists	Alosetron, ondansetron, granisetron, palonosetron, ramosetron and tropisetron.
Anti-migraines	Almotriptan, dihydroergotamine mesylate, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan.
Anti-epileptics	Carbamazepine, clonazepam, diazepam, divalproex sodium, fosphenyloin, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, phenyloin, pregabalin, primidone, tiagabine, topiramate, valproate s o d i u m ,
Statins	Atorvastatin, cerivastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin and Simvastatin
Dopamine D1 and D2 antagonists	Amisulpride, bromperidol, cabergoline, domperidone, fenoldopam, haloperidol, metoclopramide, metopimazine, pergolide mesylate, prochlorperazine, quetiapine, ropinirole hydrochloride, sulpiride, tiapride and zotepine.
Selective serotonin reuptake inhibitors	Fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram and alaproclate.

2.1.9 List of few polymers used in formulation of oral films

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

2.1.10 Various flavors used in formulation

Fruit	Apple,raspberry,cherry,strawberry,pineapple
	Peppermintnoil.cinnamon oil,spearmint
Sour	Citreous flavor,root bear,raspberry
Sweet	Vanilla,fruit,berry
Bitter	Walnut,wild cherry,chocolate,mint,anise
Salt	Butterscootch,maple,vanilla,mint,anise,apricoat,pe

3. Manufacturing Methods

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

1. Solvent casting method
2. Hot melt extrusion method
3. Semisolid casting method
4. Rolling method
5. Solid dispersion extrusion

1. Solvent casting method
In this method water soluble polymer and plasticizer are dissolved in the distilled water. The solution is stirred up for 2 hrs in the magnetic stirrer and kept aside to remove all the air bubbles entrapped. Meanwhile, the excipients and API are dissolved and stirred well for 30 min, after the completion of stirring both the solutions are mixed together. Finally the solution is casted on a suitable flat surface to form a film. The film is dried and carefully removed.

2. 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 method:

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

3. 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 film forming polymer should be 1:4. A gel mass is obtained on addition of suitable amount of plasticizer. By the means of heat controlled drums, finally the gel mass is casted in to the films or ribbons

4. Rolling Method
In rolling method a solution or suspension of drug with film forming polymer is prepared and subjected to the roller. The solution or suspension should have specific rheological consideration. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cutted in to desired shapes and sizes. ble flat surface to form a film. The film is dried and carefully removed.

5. Solid dispersion extrusion
Solid dispersion extrusionSolid dispersion refers to the dispersion of two or more active ingredients in an inert carrier in the presence of amorphous hydrophilic polymers in solid state. The API is dissolved in suitable solvent and incorporated into PEG. The drug and solvents are immiscible in nature. Solid dispersions are then shaped into films by means of dies

4. Evaluation Tests

A. Mechanical properties

1. **Thickness test**
   A micrometer screw gauge is used to measure the strip thickness. In order to obtain uniformity of film, thickness is measured at 5 different locations. The thickness of the film should be less than 5%
2. **Tack test**
   Tack is the tenacity with which the film adheres to the accessory that has been pressed into contact with strip. This test also determines the dryness.
3. **Tensile strength**
   Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by formula

$$\text{Tensile strength} = \frac{\text{Load at Failure X 100}}{\text{Strip thickness X Strip Width}}$$

4. **Percentage elongation**
   It is calculated by formula

$$\% \text{ Elongation} = \frac{\text{Increase in length of strip x 100}}{\text{Intial length of strip}}$$

5. **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:

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

   Hard and brittle strips demonstrate a high tensile strength and Young's modulus with small elongation. Typical Young's modulus value for film is 0.30 ± 0.07MPa

6. **Tear resistance**:
   Tear resistance of plastic film or sheeting is a complex function of its ultimate resistance to rupture. The maximum stress or force (that is generally found near the Onset of tearing) required to tear the specimen is recorded as the tear resistance value in Newton (or pounds-force).

7. **Folding endurance**:
   To determine folding endurance, a strip of film is cut and repeatedly folded at the same place till it broke. 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 film is between 100-150.

B. Organoleptic evaluation

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

1. **Swelling index:**
   The studies of swelling index of the film are conducted in 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 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. **Surface of PH**
   Surface pH of the film was determined by placing the film on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on film. The change in the colour of pH paper was observed and report.
3. **Contact Angle:**
   Contact angle are measured by Goniometer at room temperature. Take a dry film and place a drop of distilled water on the surface of the dry film. Images of water droplet were recorded with in 10 sec of deposition by means of digital camera. The contact angle was measured on both side of drop and average is taken
4. **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
   b is the film thickness (mm)
   c is concentration

5. **Uniformity of drug content:**
   This parameter can be determined by dissolving known weight of film by homogenization in 100 ml of simulated saliva of pH 6.8 for 30 min with continuous shaking. Content uniformity is determined by estimating the API content in individual film. Limit of content uniformity is 85-115%.
6. **Moisture content**
   Initially the prepared film was weighed and placed in the desiccators containing cadmium chloride. After 3 days the film was reweighed to obtain the percentage of moisture loss

$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final Weight}}{\text{Initial weight}} \times 100$$

7. **Disintegration test:**
   Disintegrating time is defined as the time (seconds) at which a film breaks when brought in contact with water or saliva. The disintegration time limit of 30 s or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral film. Pharmacopoeial disintegrating test apparatus may be used for this study. Typical disintegration time for film is 5-30 s.
   a. **Slide frame method:** one drop of distilled water was dropped by a Pipette onto the oral films. Therefore the films were clamped into slide frames and were placed planar on a Petri dish. The time until the film dissolved and caused a hole within the film was measured.
   b. **Petri dish methods:** 2 mL of distilled water was placed in a Petri dish and one film was added on the surface of the water and the time measured until the oral film was dissolved completely.
8. **In-vitro Dissolution test**
   By this method cumulative drug release and cumulative percentage of drug retained were calculated. In-vitro drug dissolution was performed using USP paddle type apparatus. The studies were carried out at 37°C with stirring speed of 75 rpm in 900 ml phosphate buffer (pH 6.8). 5 ml of samples were withdrawn at predetermined time intervals of 2, 4, 6, 8, 10 min and replaced with the same volume of buffer. The samples were collected and the concentration was determined at appropriate wavelength using UV-visible spectrophotometer.

Few marketed Preparations of oral films:

Oral Film	*Active Ingredient*	*Manufacture/Marketed*	*Category*
Triaminic	Diphenhydrramine HCL	Novartis	Anti allergic
Listerine	Cool mint	Pfizer	Mouth freshers
Theraflu	Dextrmetharphan HBR	Novartis	Anti allergic
Dextromethorphan	Dextrrometharphan	Hughes medical corporation	Anti-tussive agent
Ondansetron Rapidfilms®	Ondansetron	labtec pharma	Post operavtive nausea and vomiting
Caffeine films	Caffeine	Dow chemical company	CNS stimulant
Donepezil	Donepezil	Labtec GmbH	Anticholinesterase

5. Conclusion

Oral fast dissolving films have emerged as revolutionary trend and extensive research activities involving various categories of drug are going on in this field. This technology covers vast category of patients specially geriatrics, pediatrics. Also it offers plenty of advantages over other dosage forms like enhanced bioavailability, and faster action. Most important application in Emergency cases and for moving patients. So it can be concluded that the oral films with so many advantages and high patient compliance have glowing futuristic opportunities.

References

[1] Priya Y D, Chaudhary Y A, Murthy T E G K, Seshagiri B. Approaches for taste masking of bitter drugs: a Review. Journal of Advances in Drug Research. 2011; (2): 58-67.
[2] Parul Saini, Anoop Kumar, Pankaj Sharma, Sharad Visht, Fast Disintegrating Oral Films: A Recent Trend of Drug Delivery International Journal of Drug Development & Research, October-December 2012 **,** 4**(** 4) **,** 80-94.
[3] Banker. G.S.,"Film coating theory and practice", J. Pharm. Sci.1966, 55, 81- 89.
[4] Chien. M J, Tirol. G, Charles. B, Corniello. C, Waston. G, Sanchez. I., "Castable edible pharmaceutical films", Dow Chemical Company, West Haven,USA. 2007, 1-7.
[5] Thakur Smriti. Mouth dissolving films: a review, International Journal of Pharma and Bio Sciences ,2013 Jan; 4(1), 899 – 908.
[6] Naga Sowjanya Juluru, Fast dissolving oral films: a review,International Journal of Advances in Pharmacy, Biology and Chemistry Vol. 2(1), Jan- Mar, 2013, 108-112.
[7] R. Gowri, N. Narayanan, S. Revathy, P. Prabhavathy, et.al, Melt in Mouth Films- an effective alternative drug delivery system, International Journal of Biological & Pharmaceutical Research. 2013; 4(9): 645-650.
[8] Rathi Varun, Senthil V, Kammili lavanya, Hans Ritu. Brief review on oral film technology, International Journal of Research in Ayurveda and Pharmacy , 2 (4), 2011, 1138-1147.
[9] Priyanka Nagar, Iti Chauhan, Mohd Yasir Insights into Polymers: Film Formers in Mouth Dissolving Films**,** Drug Invention Today, 2011, 3(12), 280-289.
[10] Mitali M Vaidya, Nilesh M Khutle, Parag Side,oral fast dissolving drug delivery system: a modern approach for patient compliance, World Jounal of Pharmaceutical Research 2 (3), 558-577.
[11] Bhupinder Bhyan, Sarita Jangra, Mandeep Kaur, Harmanpreet Singh, International Journal of Pharmaceutical Sciences Review and Research, August 2011, 9(2), 50- 57.
[12] Arun Arya, Amrish Chandra1, Vijay Sharma and Kamla Pathak . Fast dissolving oral films: an Innovative Drug Delivery System and Dosage form, International Journal of ChemTech Research, 2 (1), Jan-Mar 2010, 576-583.
[13] Deepak Heer, Geeta Aggarwal and S.L. Hari Kumar, Recent Trends of fast dissolving drug delivery system - an overview of formulation technology, Pharmacophore 2013, Vol. 4 (1), 1-9.
[14] 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
[15] World Health Organization Working document QAS/08.257, Feb 2008, (http:// www.who. int/medicines/ services/ expert committees/ pharmprep/ PediatricMedicinesPharmDevelopment_ QAS08_257_29022008.pdf).
[16] American Standard of Testing and Materials, ASTM D1004 - 08 Standard Test Method for Tear Resistance (Graves Tear) of Plastic film and Sheeting.
[17] Shinde, A.J., K.C. Garala and H.N. More, 2008. Development and characterization of transdermal therapeutics system of tramadol hydrochloride, Asian J. Pharmaceutics, 4, 265-269.
[18] Aggarwal Jyoti et.al, Fast dissolving oral films : Novel approach to drug delivery, International research journal of pharmacy,2011, 2(12), 69-74.
[19] S raju.et al, Flash release oral films of metoclopramide hydrochloride for pediatric use:Formulation and in-vitro evaluation, journal of chemical and pharmaceutical research, 2011, 3(4),636-646.
[20] Mahammad Rafi Shaik, formulation and characterization of domperidone oral thin films, International Journal of Pharma Sciences 3(1),2013: 126-128.
[21] Naga Sowjanya Juluru et.al, Fast Dissolving Oral Films: A Review International Journal of Advances in Pharmacy,Biology and Chemistry,2(1), Jan- Mar, 2013, 108- 112**.**
[22] Shinde, A.J., K.C. Garala and H.N. More, 2008. Development and characterization of transdermal therapeutics system of tramadol hydrochloride, Asian J. Pharmaceutics. 4: 265-269.
[23] Gisel E.G. Oral motor skills following sensori motor intervention in the moderately eating impaired child with cerebral palsy. Dysphagia. 1994; 9:180.192.
[24] Anderson O. et al. Problems when swallowing tablets. Tidsskr NorLaegeforen. 1995; 115: 947. 949.

[25] Kahrilas P.J. Anatomy, physiology and pathophysiology of dysphagia. Acta. Otorhinolaryngol Belg. 1994; 48: 97.117.
[26] Sastry S.V, Nyshadham J.R, Fix J.A. Recent technological advances in oral drug delivery . a review. Pharmaceutical Science & Technology Today April 2000; 3(4).
[27] Vondrak B, Barnhart S. Dissolvable Films for Flexible Product Format in Drug Delivery, Pharmaceutical Technology Supplement. April 2008.
[28] Gisel E.G. Oral motor skills following sensori motor intervention in the moderately eating impaired child with cerebral palsy. Dysphagia. 1994; 9:180.192.
[29] Anderson O. et al. Problems when swallowing tablets. Tidsskr NorLaegeforen. 1995; 115: 947. 949.
[30] Sastry S.V, Nyshadham J.R, Fix J.A. Recent technological advances in oral drug delivery . A review. Pharmaceutical Science & Technology Today April 2000; 3(4).
[31] Zhang H, Zhang J, Streisand J.B. Oral mucosal drug delivery: clinical pharmaco-kinetics and therapeutic applications, Clin. Pharmacokinet. 2002; 41 (9): 661.680.
[32] Barnhart S.D, Sloboda M.S. The Future of Dissolvable Films. Drug Delivery Technol. 2007;7 (8): 34.37.
[33] Meathrel B, Moritz C. Dissolvable Films and Their Potential in IVDs. IVD Technol. 2007; 13 (9): 53.58.
[34] Corniello C. Quick dissolving strips: from concept to commercialization. Drug Del. Technol. 2006; 6(2): 68.71.
[35] Frankhauser C, Slominski G, Meyer S. Disintegrable oral films, U.S. Patent 2007/ 0202057, Aug. 30, 2007.
[36] Sakellariou P, Rowe R.C. Interactions in cellulose derivative films for oral drug delivery, Prog. Polym. Sci. 1995; 20: 889.942.
[37] Banker G.S. Film coating theory and practice, J. Pharm. Sci. 1966; 55: 81.89.
[38] Rowe F.C, Forse S.F. The effect of polymer molecular weight on the incidence of film cracking and splitting on film coated tablets. J. Pharm. Pharmacol. 1980; 32 (8):583.584.
[39] Rowe R.C, Forse S.F. The effect of film thickness on the incidence of the defect bridging of on film coated tablets. J. Pharm.Pharmacol. 1980; 32(9):647.648.
[40] Rowe R.C, Forse S.F. The effect of plasticizer type and concentration on the incidence of bridging of intagliations on film-coated tablets. J.Pharm.Pharmacol. 1981; 33(3):174.175.
[41] Singh P, Guillory J.K, Sokoloski T.D, Benet L.Z, Bhatia V.N. Effect of inert tablet ingredients on drug absorption I. Effect of polyethylene glycol.
[42] Cilruzo F and Cupone EI: Diclofenac fast-dissolving film: suppression of bitterness by a taste-sensing system. Drug Dev. Ind. Pharmacy. 2010: 1-8.
[43] Gavaskar Basani, Kumar Subash Vijaya, Guru Sharan and RaYMadhusudan: Overview on fast dissolving films, International Journal of Pharmacy and Pharmaceutical Sciences 2009; 2: 2933.
[44] Arya A and Chandra A: Fast Dissolving Oral Films: An Innovative Drug Delivery System and Dosage Form. International Journal of Chem Tech Research 2010; 2: 576-583.
[45] Borsadia BB and Osborne JA: Quick dissolving films-A novel approach to drug Delivery. Drug delivery technology 2005: 41-48.
[46] Shimoda H and Taniguchi K: Preparation of fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy. European Journal of Pharmaceutics and Biopharmaceutics 2009; 73: 361-365.
[47] Liang CA and Chen HL: Fast dissolving intraoral drug delivery systems. Expert Opinion Therapy Patents; 2001; 11: 981- 986.
[48] Koland M and Charyulu N: Fast dissolving sublingual films of ondansetron hydrochloride: Effect of addivites on in vitro drug release and mucousal permeation, Journal of Young Pharm 2010; 2: 216-221.
[49] Singh S and Gangwar S: Formulation and evaluation of rapidly disintegrating film of levocetrizine hydrochloride. Der Pharmacia Lettre 2010; 2: 434-439.