Review Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2015, Volume 3, Issue 5
ISSN: 2321–3647(online)

Orally Disintegrating Strips (ODS) Convenience of Liquid Dosage Form and Dose Accuracy of Solid Dosage Form

Pushpendra kumar Vishwakarma[*1], Pravin Deshkar[1], Nimesh Lal[1], Swati Dhudkewar[1]
1. Unijules Life science Ltd. 1505/1 Universal square, Shanti Nagar, Nagpur-440002 Maharashtra, India.

ABSTRACT

Administration of drugs via the oral mucous membrane has been considered as a promising alternative to the oral route. When rapid onset of action is required in terms of better patient compliance over other conventional solid dosage forms "Buccal route" has been preferred. The area covered by tongue are more permeable than other regions of buccal cavity. By last few years group of researchers are focusing on an innovative drug delivery system called "Orally Disintegrating Strips" (ODS). The large surface area of the Strip allows fast dissolving action and provides new solution for forbearing suffering from dysphagic situation. Oral Disintegrating strips are still in initial phase with a great future ahead as it fulfills the current needs of patients. ODS provides an alternate platform for the drugs that undergo the effect of stomach environment and First pass metabolism. This review article suggests the advantages of ODS over the traditional used medication treatment & the scope associated with business prospective.

Keywords: Oral Disintegrating Strips, films, B-Thyn12, Filzeal,DXThyn-DS, Bioavailability

*Corresponding Author Email: kumaer_v@hotmail.com
Received 20 April 2015, Accepted 04 May 2015

Please cite this article as: Vishwakarma P *et al*., Orally Disintegrating Strips (Ods) Convenience of Liquid Dosage Form and Dose Accuracy of Solid Dosage Form. American Journal of Pharmacy & Health Research 2015.

INTRODUCTION

The administration of drugs can be achieved through various routes to have a systemic pharmacological action. Oral route is most common method to administer the drug, in which the drug is swallowed and enters the systemic circulation through small intestinal membrane. Administration of drugs through parenteral route is not commonly used. Probably 90% of the drugs have been used to get systemic pharmacological action are administered by oral route. Various sites of the body have been reported for absorption of the drugs between mouth and rectum through orally administered drug. Generally, as fast the absorption of drugs would takes place in alimentary canal, the more rapid pharmacological effect can be obtained. It has been estimated that approximately 25% of the people are unable to swallow the capsules and tablets. Because of this, large number of population do not take the prescribed medicines by their doctors and resulting in high incidence of non-compliance and ineffective therapy. Pediatrics and Geriatrics patient are most common population experiencing the dysphagic situation. But it also applies to people like bedridden or busy and working patients, travelling with no access to water. In such cases administration of drugs through oral cavity is preferred. For many years Active Pharmaceutical Ingredients (API's) for topical application have been applied to mucosa. However, medical practitioners started taking interest for delivering drugs to the systemic circulation through the oral cavity. The most widely accepted route of drug administration is oral route and its unique environment provides potential as a site for drug delivery. It has been known for centuries that administration through oral cavity (buccal and sublingual administration) drug solutes are rapidly absorbed. This absorption takes place through the reticulated vein, which lies underneath the oral mucosa and transported through the facial veins, internal juglar vein, and brachiocephalic vein. Absorbed drugs then drained into the systemic circulation. Therefore the administration of drugs through oral cavity can be utilized to bypass the hepatic first-pass metabolism of drugs. The regions of oral mucosal cavity offers higher absorption of drugs in systemic circulation. The oral mucosa is rich in blood supply and more permeable. The administration through oral cavity has been highly acceptable in dysphagic patients. Additionally the oral mucosa is potentially tolerant to allergens due to virtual lack of Langerhans cells. Not all drugs, however, can be administered through the oral mucosa because of the characteristics of the oral mucosa and the physicochemical properties of the drug[1]. The mucous membrane of oral cavity can be potential site for sustained and controlled drug delivery system. Due to highest patient acceptability and convenience oral route is most preferred route of administration by

medical practitioner and manufacturer. Oral solid dosage forms are about 60% of all available dosage forms. The dysphagia patients, less bioavailability, and long onset of time makes the manufacturer and medical practitioner to have a choice of parenteral and liquid orals. But due to problem of accurate dosing in liquid orals (i.e. syrup, suspension, emulsion etc.) and painful delivery in parenteral drugs keeps patients incompliance[2]. In the oral cavity the local sites for drug delivery would be Tongue, Sublingual, Periodontal region, Gum and Buccal.

Structural Features of Oral Cavity

The oral cavity begins from vermillion border (border between skin and lips). Buccal region is that part of the oral cavity and is surrounded by other different regions like anteriorly and laterally with lips and the cheeks, posteriorly and medially with teeth and/or gums, and above and below by the reflections of the mucosa from the lips and cheeks to the gums. The roof of the mouth is made up of hard palate. Blood supply to buccal mucosa is achieved by Maxillary artery. The surface area covered by oral cavity is about 100cm. [3,4] Out of which one third is the surface occupied by buccal mucosa, which is lined with thick layer of epithelium of about 0.5mm.

Structure: The outermost layer present in oral mucosa is called a stratified squamous epithelium (Figure.1)under this layer a basement membrane, a lamina propria, and innermost layer called submucosa is present. The topmost layer of oral mucosa stratified squamous epithelia is similar to the rest of the epithelium present in the body. The squamous epithelium is composed of mitotically active basal cell layer. For turning over completely the epithelium of oral mucosa takes around 5-6 days. [5]The thickness of oral mucosa varies largely throughout the oral cavity. The thickness of buccal

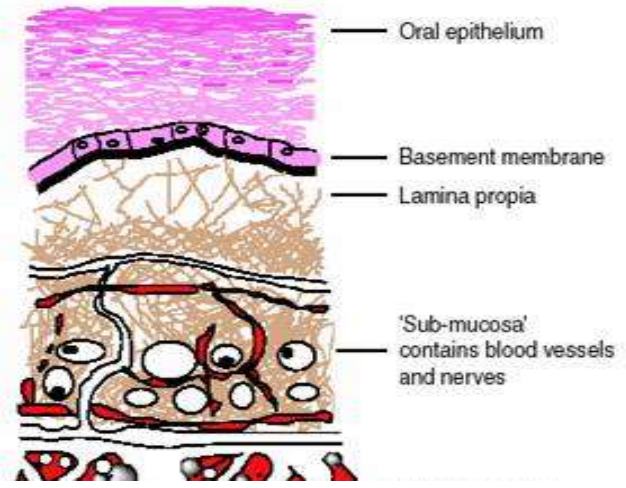

Figure 1: Oral mucosa membrane

Mucosa has been estimated about 500-800µm. whereas the thickness of hard palate, soft palate, ventral tongue, gingiva, and floor of the mouth is about 100-200µm. The composition mucosal layers of oral cavity varies too with different sites, as mucosal layers of gingiva and hard palate is composed of keratin similar to that of epidermis which is composed of ceramides and acylceramides which produces barrier function. The mucosal layers of buccal region, sublingual and soft palate are free from keratin which relatively impermeable to water. [6-8]The layers of sublingual and buccal region also composed of bipolar lipids (neutral) like cholesterol sulfate and glucosyl ceramides. It has been found that the non-keratinized epithelia layers is considerably more permeable to water than that of the keratinized epithelia layers.[5-8]

Composition of Oromucosal cells:

Mucosal cells of oral cavity are made up of proteins and carbohydrates, because of its adhesive nature it allows cells to move relative one another with less friction.[9] The synthesis and secretion of mucus in other parts of the body takes place by goblet cells, whereas in oral cavity is done by minor and major salivary glands. Mucus also plays an important role in bioadhesion of mucoadhesive drug delivery system.[10]It has also been found that about 70 % of total mucin is present in saliva, and is produced by minor salivary glands.[11] There are 3 pairs of salivary glands present in oral cavity (Sublingual, submandibular and parotid). Saliva is composed of both organic (1%) and inorganic materials. Salivary amylase is the digestive enzymes present in saliva. Which is responsible for metabolism of starch in oral cavity. The chemical composition of saliva is similar to that of blood plasma. The pH of saliva lies between 5-7. A healthy adult is capable of producing about 1-2 litres of saliva every day and that much of saliva is available to hydrate the orally administered dosage forms. Moreover, because of water rich environment of mouth makes manufacturer to add the hydrophilic agents as a vehicle for oral drug delivery system.

Permeability:

The permeability of oral mucosa is intermediate between the skin and the intestinal membrane. It has been found that the permeability of oral mucosa is 4-4000 time more than that of the epidermis. There is quite a lot difference in permeability of different regions of oral cavity. This difference is due to the various structure and function of different regions of oral cavity. For enhancing the absorption of drugs from oral dosage forms in oral cavity permeation enhancer has been used. The permeation enhancers are as follows:

1. Aprotinin
2. Cetylpyridinium chloride

3. Cyclodextrin
4. Menthol
5. Sodium glycodeoxycholate
6. Sodium taurodeoxycholate
7. Azone
8. 23-lauryl ether
9. Dextran sulfate

Oral absorption pathway

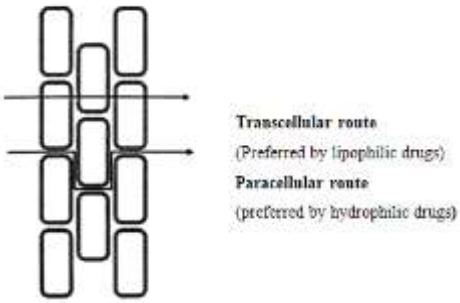

Figure 2 Absorption pathways in oral cavity

There are various barriers in oral cavity which inhibits the rate and extents of drug absorption such as saliva, mucus, membrane coating granules, basement membrane etc. Microscopic studies with visible tracers like dextran and protein suggests that mostly the absorption of drug molecules takes place across stratified squamous epithelium by two pathways (figure 2)

1. Transcellular pathways
2. Paracellular pathways

However, rate of absorption depends upon the physicochemical properties of the drug molecules. This phenomenon suggests that the drug molecules uses one or both pathways for absorption. One is predominant over the other on the basis of physicochemical properties of the molecules.[12,13]

Factors affecting the oral absorption of drug molecules[14]

1. **Drugs solubility in saliva**

   The drugs administered orally should be soluble in saliva in addition to highly lipid soluble. Solubility of molecules in both lipid and water is important for oral absorption.

2. **Oral mucosa binding capacity**

   The drugs incorporated in oral dosage form should have less binding capacity with oral mucosa. As more the binding capacity, less the systemic availability of drug molecules.

3. **Acid dissociation constant (pKa) and pH of saliva**

   As pH of saliva ranges from 5-7 facilitates the maximum absorption of drugs which keeps the molecules unionized. If pKa of acidic drugs is more than 2and for basic drugs less than 10, then there would be greater absorption of drug molecule through oral mucosa.

4. **Hydrophobicity of drugs**

   The drugs to be absorbed through oral cavity should be little more lipid soluble than required in GIT absorption.

5. **Oral epithelium's thickness**

   As the thickness of epithelium layers varies from region to region throughout the cavity, the maximum absorption of drug molecules takes place through soft palate, ventral tongue, gingiva, and floor of the mouth.

Orally Disintegrating Strips(ODS)

Orally Disintegrating Strips(ODS) can be defined as the orally administered dosage forms which employs film forming polymers (generally are hydrocolloids), Plasticizers, and API's with other additives. When ODS are placed on the tongue, it quickly hydrates, adheres and dissolves in oral cavity and facilitates the rapid local and systemic action. The transition of oral drug delivery system has been taken place from conventional tablets/capsules to modified released tablets to orally disintegrating tablets to wafer to latest and modern dosage form called Orally Disintegrating Strips (ODS). Basically ODS can be considered as thin strips of stamp size with API's. Pediatrics and Geriatrics have shown equal acceptability to this dosage form. This is due to the ODS portability and convenience of dosing. Various Marketing research firms have done forecast for emerging market of ODS such as Root analysis and Technology Catalysts forecasts the market for drug products in ODS valued of $500 million in 2007, $2 billion in 2012, and $15 billion in 2015 and continuous upward global growth trends by 2025.

This ODS dosage forms gives some distinct advantages over other conventional oral formulations.[15]

1. ODS are more durable, quick dissolving and stable than other oral dosage forms.
2. Since every film is manufactured in such a way that it distributes the absolute amount of drugs over the film and enables to enhance the dosage accuracy compare to liquid formulations.
3. Due to inherent ease of administration and intuitive nature of the ODSimproves patient compliance and accurate dosing of the drugs.

4. ODS has the ability to dissolve rapidly without the need of water, ODS provides an alternate way to the patients who are unable to swallow and suffering from nausea, such as those patients receiving chemotherapy.
5. Continuous administration of drugs become possible by ODS and also for the drugs with a short biological half-life.
6. ODS quickly disintegrates and dissolves in the oral cavity in few seconds due to Accessibility of larger surface area.
7. The large surface area of ODS (1-20 cm^2) allows rapid hydration by saliva then rapidly disintegrates, dissolves and crosses the oral mucosa directly and enters the systemic circulation without undergoing first-pass hepatic metabolism and increases the bioavailability of drugs.
8. By taking ODS the first pass effect can be bypassed and due to which dose of drugs can significantly reduce which can prompt to decrease in side effects associated with the molecule.
9. ODS also avoids the risk, pain and inconvenience of parenteral shots.
10. ODS also prevents the drug molecule from the acidic environment of stomach.
11. For manufacturing of ODS No special set up required.
12. The delivery of ODS can be terminated any time when required
13. Because of Noninvasive ODS provides higher acceptability.
14. ODS can also be an alternate for Patent life extension.

Disadvantages of ODS

1. Only small doses can be incorporated in ODS.
2. In ODS dose uniformity is a technical challenge.
3. ODS are moisture sensitive and expensive packing is required.

Mechanism of action

The delivery system of ODS are very simple, it has to be placed on a patient's tongue or anywhere in oral cavity. Instantly, hydrophilic polymers added in ODS will wet the Strips by saliva, the film rapidly hydrates and start dissolving to release the API's incorporated in films. Thereafter drug molecules are freely available for absorption in oral cavity.

Figure 3: How to use ODS

Formulation Consideration of ODS[9-11]

Depending upon drug loading and dosing capacity of ODS, it has surface area of 1-20cm^2. 30mg of drugs can be incorporated at once in ODS. Mechanical property of ODS depends on the formulation consideration and it has been reported as important factor for ODS. All excipients used in the formulation pf ODS should be Generally Regarded as Safe (i.e. GRAS-listed). Approved for use in oral dosage forms.(Table 1)

1. Drugs

The ODS technology has potential to for delivery of several classes of API's. However, since the size of ODS has limitation high dose of API's cannot be incorporated in ODS. Generally, API's 5-30%w/w and multivitamins up to 10% w/w of ODS weight can be incorporated with dissolution time less than 59 sec.[16,17]The distribution of the drugs in ODS varies on the basis of their solubility. The water soluble drugs are incorporated in dissolved states or in the solid solution form and water insoluble drugs dispersed uniformly over the film. For large scale manufacturing the distribution of insoluble drugs in water miscible polymers is important. On the basis of desired release profile drugs can be added as micronized, milled or in the form of nanoparticles.[18]

Ideal characteristics of drugs.

1. Drugs should not be of bitter taste, or it if it is having bitter taste then should be masked.
2. Drugs should be stable in saliva and water.
3. Dose of the drugs should be less as possible or not more than 40 mg.
4. Drugs should be partially unionized at 5-7 pH.
5. Drugs should be able to permeate the oral mucosa.

The list of Drugs which has been incorporated in ODS. (Table 2)

2. Water soluble Polymers

Large numbers of polymers are available for preparation of ODS. The desired Strips can be obtained either by using polymers alone or in combination. The prepared ODS should be tough enough to handle the mechanical stress while transportation. The type and amount of the polymers used in the formulation is responsible for robustness of ODS. ODS should have property to disintegrate and release the API's within seconds. Water soluble polymers are the agents providing the platform and is most essential part of ODS.[19-24]

Ideal properties of water soluble polymers.

1. It should be non-toxic, non-irritant, and devoid of leachable properties.
2. It should be able to easily hydrate and spread.
3. It should exhibit sufficient peel, shear and tensile strengths.
4. It should be non-expensive and easily available.
5. It should have good shelf life.
6. It should not aid in causing secondary infections in oral cavity.

3. Plasticizers

Plasticizers is an important content of ODS formulation. Plasticizers are responsible for improving the flexibility and brittleness of ODS. By reducing the glass transition temperature plasticizers significantly improve Stripsproperty.[25,26]The commonly used polymers are Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, Citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil. However inappropriate use of plasticizer may results to cracking splitting and peeling of the films. [27,28,29] It has also been found that the absorption rate of drugs can be affected by use of certain.[30]

4. Surfactants

Surfactants are also known as wetting or solubilizing or dispersing agents. It is added in the formulation so that Stripscan dissolve and release the API's instantly. Some common examples of surfactants are sodium lauryl sulfate, benzalkonium chloride, tweens etc. One of the most important surfactant is polaxamer 407.[31]

5. Sweetening agents

Sweeteners have become an important part of ODF formulation, and intended to be disintegrate and dissolve in oral cavity. Natural and Synthetic sweeteners are used to improve the palatability of oral dosage forms. The sweet taste is important in development of formulation for pediatric patients. Commonly used sweeteners are sucrose (derived from cane or beet in the form of liquid or dry state), dextrose, fructose, glucose, liquid glucose, maltose Saccharin, cyclamate and

aspartame, acesulfame-K, sucralose, alitame and neotame, Rebiana (herbal sweetener, derived from plant *Stevia rebaudiana*). Some sweeteners are added in formulation to produce good mouth feel and cooling sensations are polyhydric alcohols such as sorbitol, mannitol, isomalt and maltitol and can be used in combination.[32]

6. Saliva stimulating agents

These agents are used in the ODS formulation to increase the rate of saliva production in oral cavity. Which will help the Strips to disintegrate and dissolve instantly. Generally, acids which are used in food preparations are utilized as saliva stimulants. Commonly used stimulants are Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid.[33]

Flavoring, coloring, stabilizing and thickening agents

It has been observed that age plays an important role in taste fondness. The younger generations like flavors such as fruit punch, raspberry etc. whereas geriatric patients like mint or orange flavors. Selection of flavors also depends on the type of drugs incorporated in ODS. for example Peppermint oil, cinnamon oil, spearmint oil, oil of nutmeg , vanilla, cocoa, coffee, chocolate and citrus, apple, raspberry, cherry, pineapple etc.[34]Pigments such as titanium dioxide or FD&C approved coloring agents are incorporated in ODS formulations (not exceeding concentration levels of 1%w/w).[35,36]Stabilizing and thickening agents are incorporated in film formulation to improve the viscosity and consistency of dispersion of ODS. for example, xanthan gum, locust bean gum, carragenan and cellulosic derivatives.[37]

PRODUCTION AND MANUFACTURING OF ODS

Manufacturing and production of ODS can be done by using any of the process mentioned below,[38, 39]

1. Solvent casting
2. Semisolid casting
3. Hot melt extrusion
4. Rolling process

1. Solvent casting

In solvent casting process of ODS production excipients are dissolved in water, then water soluble polymer and at last drugs are added in it and stirred till proper mixing to make homogenous solution. Homogenized solution then casted in petri dish and allowed to dry.

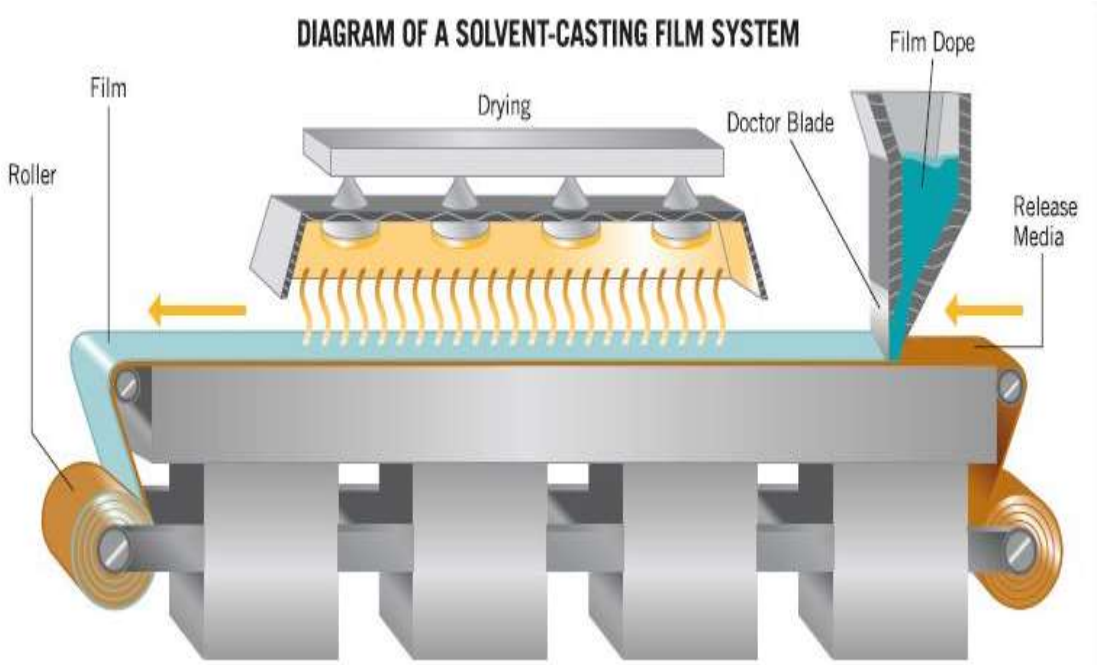

Figure 4: Solvent casting method

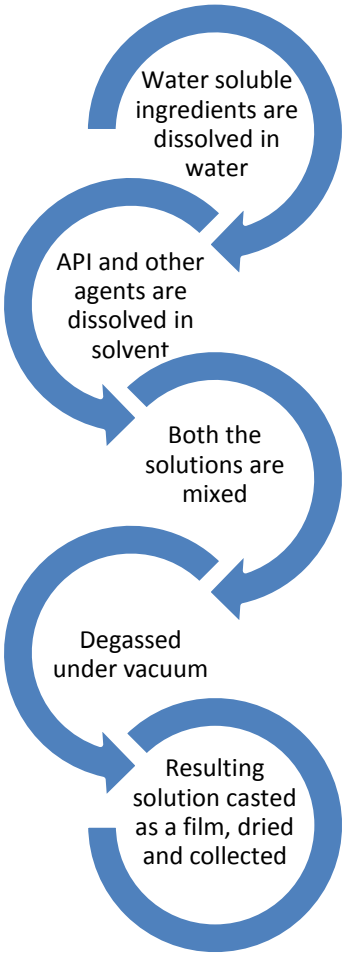

Figure 5: Flowchart of manufacturing process.

2. Semisolid casting

In this process of ODS production, water soluble polymers are mixed to acid insoluble polymers to form viscous homogenous solution. It is coated on non-treated casting film after sonication. The ratio of 1:4 should be maintained (Acid insoluble polymer to water soluble polymer.)[38,39]

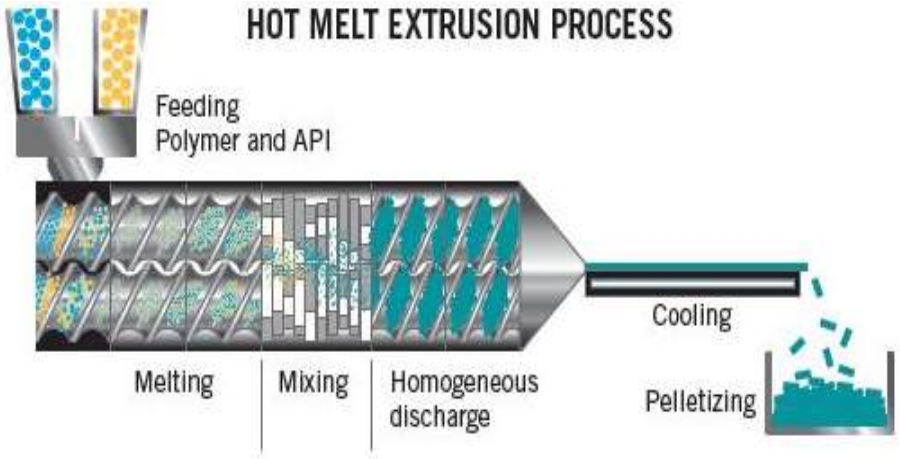

Figure 6: Semisolid casting method

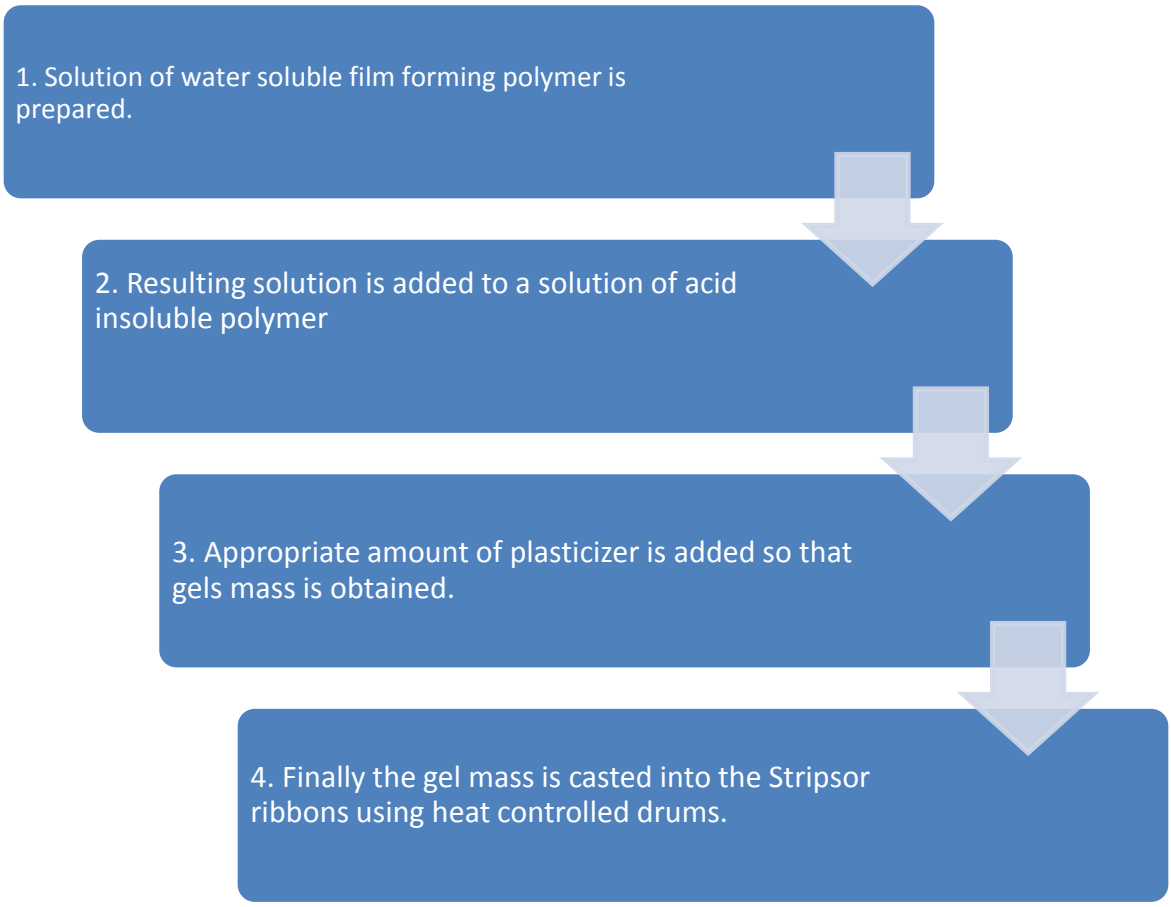

Figure 7: Hot melt extrusion process

3. Hot melt extrusion

In this process of ODS production, drugs are mixed with carrier in solid form followed by extruders, where heaters melt the mixture and finally shapes into Strips with the help of dies.

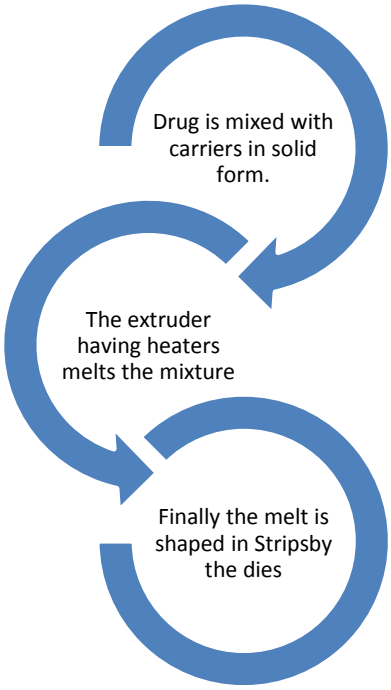

Fig 8: Flowchart of Hot melts extrusion Process

4. Rolling Process

In this process of ODF production premixing has to be done followed by film formation.

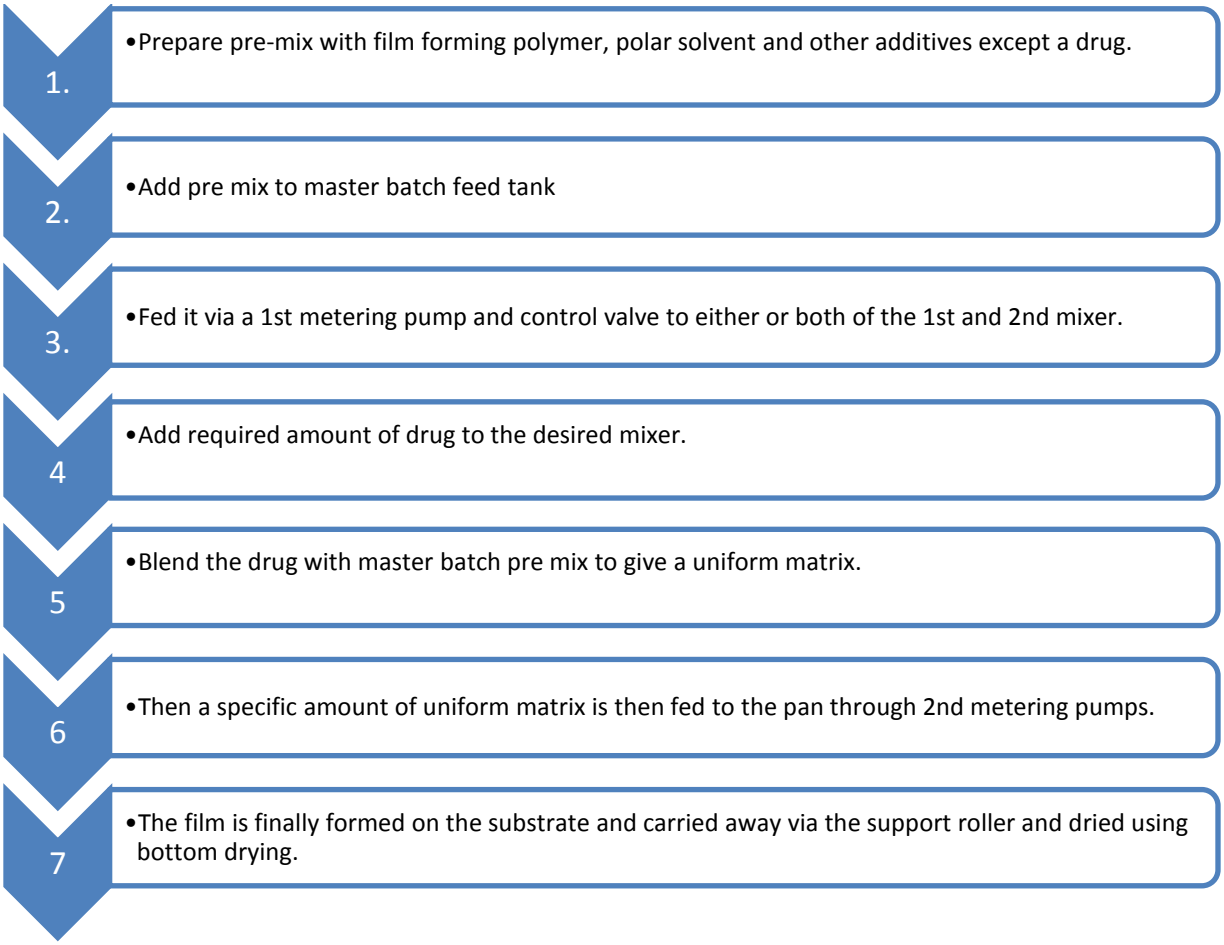

Figure 9: Flow chart of rolling process

Evaluation of Manufactured ODS

1. **Thickness test**: This property can be measured by using micrometer screw gauges at different strategic location. It is important to assure the uniformity and thickness of film because it is directly related to accuracy of dose in films.
2. **Tack Test:** Tack is tenacity, due to which film sticks to a piece of paper that has been touched with film. Eight different stages of film drying has been identified such as 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.[40]
3. **Tensile strength**: This can be defined as the maximum stress applied to a point at which the film breaks. It can be calculated by an equation[41]

   Tensile strength = Load at failure × 100/ Strip thickness × film width
4. **Percent elongation**: Strain can be defined as the stress applied to the Strips lead to deformation. It can be calculated by equation. [42]

   % elongation = Increase in length of film× 100 / Initial length of film

5. **Young's modulus**: Young's modulus or elastic modulus is basically used to measure the stiffness of films. It can be represented as the ratio of applied stress over strain in the region of elastic deformation as follows: Young's modulus= Slope × 100 / Strips thickness × cross – head speed

   Hard and brittle ODS shows a high tensile strength and Young's modulus with small elongation.
6. **Folding endurance**: This property can be determined by folding the film at the same place till its breaks. The number of folding in which film got breakdown become its endurance value.[43]
7. **Disintegrating time**: This property can be defined as the time required to disintegrate the film in oral cavity when comes in contact with saliva. For orally disintegrating tabs. This time is around 30 sec. or less, therefore this CDER guideline can also be used for ODS. The disintegrating time for ODS should be 5-30 secs.[44]
8. **Dissolution test:** This property can be measured by any standard basket or paddled apparatus explained in any pharmacopoeia. The selection of medium are done on the basis of sink condition and highest dose of drugs.[45]

Packaging of ODS[46]

In pharmaceutical it is important to preserve the integrity of pharmaceutical products. Therefore selection of packaging should be adequate. To protect the dosage of ODS during manufacturing and production special care is required. Various types of packaging options are available for ODS. Single packaging is mandatory for ODS. The most important and commonly used packaging for ODS is Aluminum pouch. Some other packaging formats available for ODS are Foil, paper or plastic pouches, Blister card with multiple units.

Ideal characteristics of Packaging material used for ODS

1. It should be capable of protecting products from environmental conditions.
2. It must be FDA approved.
3. It must meet applicable tamper resistant requirements.
4. It must be non-toxic.
5. It must not be reactive with ingredient or other products.
6. They must not impart to the product taste or odour.

ODS Technologies and Commercialized Products.[47-56]

After breath fresheners Over-the-Counter drugs (OTC) and Nutraceuticals market was the first to move into ODF technology with active molecules such as Herbal and non-herbal extracts and

vitamins. Listrine® was the famous pocketpaks® introduced for bad breath in 2001 by Pfizer. Similarly Theraflu® and Triaminic® brands were introduced by Novartis in ODF form. The detailed information on various type of ODS products is given in Table.3

CONCLUSION

As ODS helps to overcome the current unmet needs of patients, the future holds the significant potential. More commercialization of ODS brands will determine the future acceptance & growth, and can also serve as a better alternative in improving patients compliance. More importantly, oral disintegrating films can be easily carried during travel & can be consumed without water & hence becomes more unique, elegant & needful dosage form. Compare to some of the expensive and difficult process (i.e. Lypophilization) used to manufacture orally disintegrating tablets, the ODS are relatively easy. Therefore, it helps to reduce the overall cost of therapy. ODS are also good tools for product life cycle management and allows brand extension of Products. The ODS technology improves the business potential promises for future in Cosmeceuticals, Nutraceuticals and Pharmaceuticals.

Table 1: ODS composition contains

Contents	Percentage (%)
Drugs	5% to30%w/w
Water soluble polymer	45%w/w
Plasticizers	0-20%w/w
Surfactants	q.s.
Sweetening agent	3 to 6 %w/w
Saliva stimulating agent	2 to 6%w/w
Fillers, colors, flavors etc.	q.s.

Table 2: List of the drugs which has been incorporated in ODS are as follows

Molecule	Therapeutic category	Dose
Nicotine	Smoking Cessation	1.0–15.0 mg
Nitroglycerin derivatives	Vasodilator	0.3–0.6 mg
Zolmitriptan	Antimigraine	2.5 mg
Loratidine	Antihistaminic	5–10 mg
Desloratidine	Antihistaminic	5.0 mg
Diphenhydramine hydrochloride	Antihistaminic	25.0 mg
Loperamide	Antidiarroheal	2.0 mg
Famotidine	Antacid	10.0 mg
Flurazepam	Anxiolytic, Anticonvulsant	15.0–30.0 mg
Chlorpherinamine maleate	Antihistaminic	4.0 mg
Acrivastine	Antihistaminic	8.0 mg
Oxycodone	Opoid Analgesic	2.5–10.0 mg
Diclyclomine	Muscle Relaxant	25.0 mg
Omeprazole	Proton pump inhibitor	10.0–20.0 mg

Cetrizine	Antihistaminic	5.0–10.0 mg
Ketoprofen	Anti–inflammatory	12.5–25.0 mg
Azatidine maleate	Antihistaminic	1.0 mg
Sumatriptan succinate	Antimigraine	35.0–70.0 mg
Chlorhexidine gluconate	Antimicrobial	0.12%
Tiprolidine hydrochloride	Antihistaminic	2.50 mg

Table 3. Commercialized ODS

Product category	Ingredient/s	Indication/applications
Unijules Life science Ltd.		
Filzeal™ DxThyn™/ DxThyn™-DS BThyn™	Tadalafil 20 mg Dextromethorphan 5.5 mg/11mg Methylcobalamine 1500mcg	Erectile dysfunction In cough with Smoking, pollution, acute& chronic RTI Diabetic Neuropathy Diabetic Nephropathy ,CVD, FibromylgiaAlzhiemers Disease, Anemia,Cervical Spondolytis, Megaloblastic anaemia
Novartis Pharmaceuticals[48] Triaminic Thin Strips® Cough &Runny Nose	Diphenhydramine HCl 12.5 mg, acetone, alcohol, FD&C blue #1, FD&C red #40,flavors, hydroxypropyl cellulose, hypromellose, isopropyl alcohol, maltodextrin, microcrystalline cellulose, polyethylene glycol, pregelatinized starch, propylene glycol, purified water, sodium polystyrene sulfonate, sorbitol, sucralose, titanium dioxide	It reduces cough due to minor throat and bronchial irritation as may occur with a cold. It relieves itchy, watery eyes due to hay fever.
Night Time Triaminic Thin Strips® Cold & Cough	Diphenhydramine HCl 12.5 mg, Phenylephrine HCl 5 mg, acetone, FD&C blue #1, FD&C red #40, flavors, hypromellose, maltodextrin, mannitol, polyethylene glycol, polypropylene glycol, purified water, sodium polystyrene sulfonate, sucralose, titanium dioxide.	Antihistamine/cough suppressant, Nasal decongestant. It temporarily relieves cough due to minor throat and bronchial irritation as may occur with a cold. Nasal and sinus congestion. Itchy and runny nose
Triaminic Thin Strips® Long Acting Cough	Dextromethorphan 5.5 mg (equivalent to 7.5 mg Dextromethorphan HBr), acetone, alcohol, dibasic sodium phosphate, FD&C red #40, flavors, hydroxypropyl cellulose, hypromellose, isopropyl alcohol, maltodextrin, microcrystalline cellulose, polacrilin, polyethylene glycol, pregelatinized	It temporarily relieves cough due to minor throat and bronchial irritation as may occur with a cold.

	starch, propylene glycol, purified water, sodium phosphate, sorbitol, sucralose, titanium dioxide.	
Day Time Triaminic Thin Strips® Cold & Cough	Dextromethorphan 3.67 mg (equivalent to 5 mg Dextromethorphan HBr), Phenylephrine HCl 2.5 mg, acetone, alcohol, FD&C blue #1, FD&C red #40, flavors, hypromellose, isopropyl alcohol, microcrystalline cellulose, polacrilin, polyethylene glycol, propylene glycol, purified water, sodium polystyrene sulfonate, sucralose, titanium dioxide	It is used as nasal decongestant
Triaminic Thin Strips® Cold with Stuffy Nose	Phenylephrine HCl 2.5 mg, acetone, alcohol, FD&C blue #1, FD&C red #40, flavors, hypromellose, isopropyl alcohol, maltodextrin, microcrystalline cellulose, polyethylene glycol, propylene glycol, purified water, sodium polystyrene sulfonate, sucralose and titanium dioxide	It temporarily relieves nasal and sinus congestion as may occur with a cold.
Theraflu® Daytime Thin Strips	Dextromethorphan 14.8 mg (equivalent to 20 mg Dextromethorphan HBr), Phenylephrine HCl 10 mg, acetone, alcohol, FD&C red #40, flavors, Hypromellose, mannitol, polyethylene glycol, polystyrene sulfonate, polacrilin and sucralose	It temporarily relieves nasal and sinus congestion as may occur with a cold. It reduces cough due to minor throat and bronchial irritation as may occur with a cold.
Theraflu® Nighttime Thin Strips	Diphenhydramine HCl 25 mg, Phenylephrine HCl 10 mg, acetone, alcohol, FD&C blue #1, flavors, Hypromellose, mannitol, polyethylene glycol, polystyrene sulfonate, polacrilin and sucralose	It is used for nasal congestion, runny nose, sneezing, itchy nose and throat etc.

Theraflu® Thin Strips®– Multi Symptom	Diphenhydramine HCl 25 mg, acetone, alcohol, FD&C red #40, flavors, Hypromellose, hydroxyl propyl cellulose, maltodextrin, microcrystalline cellulose, polyethylene glycol, pregelatinized starch, polystyrene sulfonate, sorbitol and sucralose. Titanium dioxide	It temporarily relieves nasal and sinus congestion as may occur with a cold. It reduces cough due to minor throat and bronchial irritation as may occur with a cold.
Biofilm[49] Energy boosters Detoxification strip Male vitality strip Female vitality strip Appetite suppressant Vitamins and food supplements Breath freshener strip (Antibacterial strip) Saliva promoting strips	Caffeine, green tea extract and guarana Green tea extract which is high in polythenols and rich in anti-oxidants. Spearmint flavor Maca root extract and Siberian ginseng extract, herbs which enhance libido, Cinnamint flavor. Botanical ingredients like damiana and passion flower *fucus vesiculosus* and *guarana* extract, *garcinia cambogia* Various vitamins, minerals and supplements Contain mint flavor and antibacterial agent cetylpyridinium chloride Fruit acid extracts, range of flavors	The product maintains the energy levels Green tea has been used as a traditional medicine to help everything from wound healing, regulating body temperature, blood sugar and promoting a healthy digestion It acts as an aphrodisiac and improves the libido in males. It is used to improve general well-being, increase energy and enhance mood These are top selling natural ingredients associated with weight loss. Cambogia helps to reduce the food intake by suppressing appetite It is useful for the people who do not like to pop up the tablets or soluble supplements. It is used as mouth freshener and to stop bad breath It is used in the dry mouth as a side effect of the other medications.
Labtec GmbH[50] Ondansetron Rapidfilm®	Ondansetron 4 mg and 8 mg	It is used in the prevention of chemotherapy and radiation-induced nausea and vomiting and prevention of postoperative nausea and vomiting.
Donezepil Rapidfilm®	Donepezil Hydrochloride 5 mg and 10 mg.	Treatment of mild to moderately severe dementia of the Alzheimer's type

Paladin Labs (Bioenvelop)[51] Smoking cessation Multivitamin for kids and adults Teeth whitening Food supplements Minerals Natural products	Nicotine B6, B12, C; D3 for kids, D3 for adults Benzocaine, Caffeine, Melatonin, MentholOmega, Hoodia, Protein, Vinpocetine Chromium Ginseng, Guarana	To reduce the smoking habit Multi vitamin supplement, Lifestyle improvement product Nutraceuticals Mineral supplements Aphrodisiac, Appetite reducer.
Innozen Inc[54,56,57] Chloraseptic® Relief Strips™	Benzocaine 3 mg, BHT, corn starch, erythritol, FD&C Red 40, hydroxypropyl methylcellulose, malic acid, menthol, monoammonium glycyrrhizinate, cherry flavors, polyethylene oxide, sucralose	Occasional minor irritation, pain, sore throat and sore mouth
Chloraseptic® Kids Sore Throat Relief Strips	Benzocaine 2 mg and menthol, grape flavor, BHT, corn starch, erythritol, FD&C Blue 1, FD&C Red 40, hydroxypropyl methylcellulose, malic acid, menthol, monoammonium glycyrrhizinate, polyethylene oxide, sucralose	Occasional minor irritation, pain, sore throat and sore mouth
Suppress™ Cough strips with Dextromethorphan	Dextromethorphan hydrobromide 2.5 mg, Asulfame potassium, FD&C Blue 1, glycerin, menthol, natural and artificial flavors, pectin, peppermint oil, sucralose, sugar, water	Temporarily suppresses coughs due to minor throat and bronchial irritation associated with cold or inhaled irritants.

Suppress™ Cough strips with menthol	Artificial flavors, ascorbic acid, aspartame, asulfame potassium, carrageenan, diglycerides, fatty acid ester, FD&C yellow 5 (tartrazine), glycerin, menthol, monoglycerides, pectin, sodium alginate, sorbitan monolaurate, sorbitol, spices, starch, water	Temporarily suppresses coughs due to minor throat and bronchial irritation associated with cold or inhaled irritants.
Hughes Medical Co.[52] Methylcobalamin Dextromethorphan Folic Acid Loratidine Caffeine Diphenhydramine HCl	1 mg 2.5 mg–5.5 mg–15 mg 1 mg–5 mg 10 mg–20 mg 2.5 mg 2.5 mg–5 mg	Peripheral neuropathy, Diabetic neuropathy Anti-tussive agent used to prevent cough. Required for formation of healthy red blood cells and used in anemia. It is a non-sedative antihistaminic agent used to treat the allergy It is used as a stimulant It is used as antihistaminic, sedative, hypnotic and antiemetic
Pfizer Inc.[47] Listerine® pocketpaks®	Available in cool mint®, Fresh Citrus, Cinnamon, and fresh burst®. Pullulan is used as a film forming polymer.	These strips dissolve instantly and kill 99% of bad breath germs.
Prestige Brands[53] Little cold sore throat strip Chloraseptic relief strip	Ascorbic acid, pectin Benzocaine, menthol	Cold/allergy Sore throat
BioDelivery Sciences Int.[55] Onsolis™ BEMA™ Buprenorphine	Fentanyl buccal soluble film Buprenorphine	Pain in opioid-tolerant patients Therapeutic alternative for patients with incomplete pain relief or those unable to tolerate the side effects of non-narcotic analgesics

REFERENCES

1. Zhang H, Zhang J, Streisand JB. Oral Mucosal Drug Delivery: Clinical Pharmacokinetics and Therapeutic Applications. Clin Pharmaco 2002;41(20):661 -680
2. Nehal Siddiqui MD, Garg G and Sharma PK. A Short Review on "A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents".Advance in biological Research,2011; 5 (6): 291-203
3. Curatolo W.The lipoidal permeability barriers of the skin and alimentary tract. Pharm.Res. (1987);4 271
4. N.H.F. Ho and W.I Higuchi. J.Pharm.Sci.1971: 60,533. Galey, W.R., Lonsdale, H.K., and Nacht, S., The in vitro permeability of skin and buccal mucosa to selected drugs and tritiated water, J. Invest. Dermat. 1976; 67:713-717.
5. Harris, D. and Robinson JR. Drug delivery via the mucous membranes of the oral cavity. JPharmaceutical Sci.,1992; 81: 1-10.
6. Wertz, P.W. and Squier CA. Cellular and molecular basis of barrier function in oral epithelium. Crit. Rev. Ther. Drug Carr. Sys,1991; 8: 237-269
7. Squier, C.A., Cox. P and Wertz P.W. Lipid content and water permeability of skin and oral mucosa. The J. Investigative Dermatol.1991; 96: 123-126.
8. Squier, C.A. and P.W. Wertz. Structure and function of the oral mucosa and implications for drug delivery. (in eds) M.J. Rathbone, Oral. Mucosal. Drug Delivery, Marcel Dekker, Inc., New York, New York: 1996; pp: 1-26
9. Tabak LA, Levine CMJ, Mandel ID and Ellison SA. Role of salivary mucin in the protection of the oral cavity. J. Oral Pathology and Med.1982; 11: 1-17.
10. Peppas NA and Buri PA. Surface interfacial and molecular aspects of polymer bioadhesion on soft tissues. J. Controlled Release.1985; 2: 257-275.
11. Rathbone M,Drummond B and Tucker I. Oral cavity as a site for systemic drug delivery. Advanced Drug Delivery Reviews,1994 ;13(1-2): 1-22.
12. Sudhakar Y, Kuotsu,Bandyopadhyay AK. Buccal bioadhesive drug delivery - A promising option for orally less efficient drugs, J. Contr. Rel., (2006); 114, 15–40.
13. Wani MS, Parakh R, Dehghan MH, Polshettiwar SA, Pande VV,Chopade VV. Current Status In Buccal Drug Delivery.2007;www.pharmainfo.net as on 28 April
14. Katz M, Barr M. A study of sublingual absorption I. Several factors influencing the rate of adsorption. J Am Pharm Assoc Am Pharm Assoc (Baltim), 1955; 44(7): 419- 423.

15. Rao NR, Reddy SK, Swapna D, Konasree SD and Enugala S. Formulation and evaluation of rapidly dissolving buccal patches. Int J Pharm & Bio Sci, 2011; 1(3): 145-159
16. Kulkarni N, Kumar LD, Sorg A. Fast dissolving orally consumable Stripscontaining an antitussive and a mucosa coating agent, U.S. Patent 2003/206942, Nov 6, 2003.
17. Ali S, Quadir A. High molecular weight povidone polymer-based Stripsfor fast dissolving drug delivery applications. Drug Del. Technol. 2007; 7 (6) 36–43.
18. Hariharan M, Bogue A. Orally dissolving film strips (ODFS): the final evolution of orally dissolving dosage forms, Drug Del. Technol. 2009;9 (2): 24–29
19. Harwood RJ, Hypromellose. In: R.C. Rowe, P.J. Sheskey (Eds.), Handbook of Pharmaceutical Excipients. Pharmaceutical Press; London, 2006, pp. 346–349.
20. Galichet LY. Starch.In: R.C. Rowe, P.J. Sheskey (Eds.), Handbook of Pharmaceutical Excipients, Pharmaceutical Press; London, 2006, pp. 725–730
21. http://www.accessdata.fda.gov/scripts/fcn/gras_notices/215492E.PDF.
22. Cook W. Pectin. In: R.C. Rowe, P.J. Sheskey (Eds.), Handbook of Pharmaceutical Excipients, Pharmaceutical Press; London, 2006, pp. 507–508.
23. Price JC. Gelatin. In: R.C. Rowe, P.J. Sheskey (Eds.), Handbook of Pharmaceutical Excipients. Pharmaceutical Press; London, 2006, pp. 295–298.
24. Parson D, Carboxymethyl cellulose.In: R.C. Rowe, P.J. Sheskey (Eds.), Handbook of Pharmaceutical Excipients, Pharmaceutical Press; London, 2006, pp. 120–123.
25. Sakellariou P,Rowe RC. Interactions in cellulose derivative Stripsfor oral drug delivery. Prog. Polym. Sci. 1995; 20: 889–942.
26. Banker GS. Film coating theory and practice, J. Pharm. Sci. 1966; 55: 81– 89
27. Rowe RC, Forse SF. The effect of polymer molecular weight on the incidence offilm cracking and splitting on film coated tablets. J. Pharm. Pharmacol. 1980; 32 (8) 583–584.
28. Rowe RC,Forse V. The effect of film thickness on the incidence of the defect bridging of intagliations on film coated tablets. J. Pharm. Pharmacol. 1980; 32 (9): 647–648.
29. Rowe RC,Forse SF. The effectof plasticizer type and concentration on the incidence ofbridgingof intagliationson film-coated tablets,J.Pharm.Pharmacol.1981; 33 (3): 174–175.
30. Singh P, Guillory JK, Sokoloski TD,Benet LZ, Bhatia VN. Effect of inert tablet ingredients on drug absorption I. Effect of polyethylene glycol 4000 on the intestinal absorption of four barbiturates. J. Pharm. Sci,1966;55 (1) 63–68.
31. Wale A and Weller PJ. Handbook of Pharmaceutical Excipients. 2nd edition.1994; 24, 27, 352 448.

32. Prakash I,DuBois GE, Clos JF, Wilkens KL,Fosdick LE. Development of rebiana, a natural, non-caloric sweetener. Food Chem. Toxicol, 2008 ;46: S75–S82.
33. Israel K, Leo M, Salivary stimulant, U.S. Patent 4820506, April 11, 1989
34. Brown D, Orally disintegrating tablets – taste over speed, Drug Del. Technol. 3 (6) (2003)
35. Maibach T. Film comprising nitroglycerin. WO Patent PCT/US2008/053466, Aug 14 2008.
36. Obermeier P, Kohr T,Kramer K, Kolkkers K. Oral, quickly disintegrating film, which cannot be spit out, for an antiemetic or antimigraine agent, U.S. Patent 2008/0213343 A1, Sept 4, 2008.
37. Sau-hung S, Robert S, Lori D. Fast dissolving orally consumable films, U.S. Patent 6,596,298, July 22, 2003
38. 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.
39. 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. International Journal of Pharmaceutical Sciences 2009: 98–102
40. Sward G. Drying time. In: G. Sward (Ed.), Paint Testing Manual– physical and chemical examination of paints varnishes lacquers, and colors,13th Ed., American Society for Testing and Materials. pp. 268
41. Felton L, O'Donnell P,McGinity J. Mechanical properties of polymeric Stripsprepared from aqueous dispersions, In: Aqueous polymeric coatings for pharmaceutical dosage forms, 3rd edition, J. McGinity, L. Felton (Eds), Vol. 176, Drugs and the pharmaceutical sciences, pp. 108.
42. Fulzele SV,Sattuwar PM,Dorle AK. Polymerized rosin: novel film forming polymer for drug delivery, Int J Pharm, 2002; 249: 175–184
43. Shinde AJ,Garala KC, More HN. Development and characterization of transdermal therapeutics system of tramadol hydrochloride, Asian J. Pharm. 2008; 265–269
44. Barnhart S. Thin film oral dosage forms, In: Modified release drug deliverytechnology, M. Rathborne, J. Hadgraft, M. Roberts, M. Lane (Eds) vol. 183, 2nd edition, Drugs and the pharmaceutical sciences, pp. 209–216
45. Nishimura M, Matsuura K, Sukioka T, Yamashita H,Inagaki N, Sugiyama T, Itoh Y. In vitro and in vivo characteristics of prochlorperazine oral disintegrating film. Int. J Pharm. 2009; 368: 98–102.

46. Ghodake PP, Karande KM, Osmani RA, Bhosale RR, Harkare BR and Kale BB. Mouth dissolving films: An innovative vehicle oral drug delivery. Int J Pharma Res & Rev. 2013; 2(10): 41-47
47. http://www.listerine.com/product-pocket-paks.jsp.
48. http://www.triaminic.com.
49. http://www.biofilm.co.uk.
50. http://www.labtec-pharma.com/index.php?article_id=24.
51. http://www.bioenvelop.com/english/prd_technology.html.
52. http://www.monosolrx.com/index.html.
53. http://www.snoreeze.com/the-snoreeze-range/snoreeze-oral-strips.
54. http://www.aridispharma.com/oral.html.
55. http://www.bdsi.com/
56. http://www.meldexinternational.com/pages/content/index.asp?PageID=50.
57. http://www.technology-catalysts.com/pdf/ODT5_brochure.pdf.