**Review Article**

**ORAL STRIPS an Overview**

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**Abstract**

 Pediatric and geriatric patients, have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take solid preparations due to fear of choking. Even with fast dissolving tablets there is a fear of choking due to its type & appearance. Hence oral strip drug delivery is a better alternative in such cases. The oral films are formulated using polymers, flavors, colors and sweeteners. The oral films are manufactured using solvent casting method, rolling method, extrusion method and solid dispersion method. The films are evaluated for dimensions, disintegration, dissolution, tensile strength and folding endurance. It has many applications like taste masking, immediate release and sustained release formulation.

**Key words**

Topoisomerase II inhibitors, Benzazole derivatives, Molecular modeling, Docking ADME prediction.
Introduction
Among the delivery routes the oral route is the most acceptable from patient compliance aspect. Most of the pharmaceutical dosages are administered orally in the form of pills, granules, powders & liquids etc. Generally pills are designed for swallowing intact or chewing to deliver a precise accurate dose to patients. Some patient’s particularly pediatric and geriatric patients have difficulty in swallowing or chewing solid dosage form. Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking [1].

To overcome this problem, several fast dissolving drug delivery systems have been developed. Fast dissolving drug delivery was pioneered by scientists at Wyeth Laboratories in the UK during the late 1970 [2]. Fast dissolving drug delivery system can be manufactured by a variety of technologies, including direct compression, wet granulation & freeze drying. All the fast dissolving systems actually don not dissolve as their name suggest but some of them use different disintegrating mechanism e.g. use of high levels of disintegrates or effervescent agents, which carry out disintegration of tables rapidly in the month [3].

Even with these differences, most of the existing fast-dissolving drug delivery systems are in the form of solid tables and designed to dissolve in the patient’s mouth within a few seconds or minutes, without the need to drink or chew [4]. The fear of taking solid tables and the risk of choking for certain patient population still exist despite their short disintegration or dissolution times. For findings the way from all these difficulties many researchers have directed their research activity in reformulating existing drugs into new dosage forms. One such relatively new dosage form is the oral strip. This system was based upon the technology of the transdermal patch [5].

Oral strip is a thin film that is prepared using hydrophilic polymers, that rapidly dissolves when placed on the tongue or in the buccal cavity. Oral strip was already popular amongst people in early 2000 year with the introduction and widespread use of Listerine pocket strips, a new launch in mouthwash. Technology Catalyst forecast the market for drug products in oral thin film formulations to be valued at $500 million in 2007 and could reach $2 billion by 2010 [6]. However only a few products consisting bitter molecules have been able to be commercialized because of the complexity associated with the OS.

Consumers have now been exposed to this concept through the introduction of multiple breath freshening product introduction over the past 2 year. Today, oral thin film (OTF’s) is a proven and accepted technology for the systemic delivery of APIs for Over-The-Counter medication and is in the early to mid-development stages for prescription drugs.

NEED OF QUICK DISSOLVING ORAL STRIPS
In the most the cause a fast dissolving drug delivery system is a tablet that dissolves or disintegrates in the oral cavity without the need for water or chewing [3].The main difference between the Quick dissolving or Oral strips drug delivery system & most conventional fast dissolving dosage forms is that is not a tablet. One of the primary objectives in developing Oral Strips was to
identity & satisfy an unmet need of general & specific population (i.e pediatrics, geriatric, bedridden, nauseous or non-compliant patient) and to improve compliance and dosing ease for the medication. This fast dissolving action is mainly due to the large surface area of the film which wets quickly when exposed to the moist oral environment. The oral strip offers a giant leap forward in drug administration by providing a new & easy way of thinking medication. The OS technology continues to be viewed for ODT products that would afford a superior barrier to generic entry & product differentiation to OTC brands.

- From marketing perspective – it grant of marketing exclusivity to the new dosage form would help to gain more revenue.
- Compared to other Oral Disintegrating Tablets – The product is robust.
- Patient point of view – Oral Strips offers ease off administration & improved compliance.
- Manufacturing perspective – Dosage form is cost effective with affordable end product.
- Clinical aspect – Improved bioavailability which in turns help in reduction of dose [7]

Advantages and Disadvantages: - [8]

Advantages :
This dosage form enjoys some distinctive advantages over the oral formulation such as
- Availability of larger surface area.
- Convenient dosing
- No water needed
- No risk of chocking
- Easy to handle, transport and store
- Improved patient convenience
- Improved oral bioavailability of molecule that undergoes first pass effect.
- Reduction in the dose leads to decrease side effects associated with drug
- Taste masking
- Not expensive as prepared with simple method

Disadvantages:-
- The low flux that in turn results in low drug bioavailability
- Difficulty in retaining dosage form for long periods of time (as there is constant salivery secretion within oral cavity).
- Accidental swallowing of dosage forms & salivary scavenging.
- High dose cannot be incorporated into the strip.

ORAL STRIPS FORMULATION CONSIDERATION:

Drug: - The Oral Strips technology has the potential for delivery of variety of APIS. Drug or APIs which can be incorporated in strip delivery are as follows-
1. Which are possible to milled and micronized or to transform them in the form of nano crystals or particles depending upon the ultimate release profile desired.
2. Which require taste masking
3. Those which undergo first pass effect

Water soluble APIs are present in the dissolved state in the OS or in the solid solution form; the water insoluble drugs
are dispersed uniformly in the strip. The distribution of water insoluble molecules in water miscible polymer becomes important from the large scale manufacture point of view [9].

It is always useful to have micronized API which will improve the texture of the film, it disperse uniformly in the Oral Strip and also show better dissolution characteristics. To incorporate unpleasant tasted API in the form of Oral Strip various methods can be used to improve the palatability of the formulation [10].

For example:

1. Among the techniques employed, the simplest method involves the mixing and co-processing of bitter tasting API with excipients with pleasurable taste. This is often termed as obscuration technique.

2. Barrier technologies that can be used to mask the bitter taste include complexation, polymeric coating, conversion into microparticles/microcapsules, coated particles or coated granules. However, in the cases where the drug is encapsulated, the instantaneous release of medicament will not be achieved. Depending on the material employed in encapsulation and the manufacturing technique, the rate of drug release varies. Hence, the issue of palatability and drug response needs to be balanced to achieve maximum advantage of the developed OS formulation [9].

3. Complexation technology involves use of cyclodextrins, resins which surround the bitter API and prevents the direct contact with saliva. Matrixing of the bitter drug or coating of drug with water insoluble polymer has been used widely for taste masking of drugs. The bitter taste of paracetamol was masked with the use of lipidic excipients like hard fat and lecithin [11,12]. Particulate technology has studied widely for the taste masking of APIs. Microparticulates of Famotidine and Eudragit EPO were prepared by spray drying technique. The results rendered a good taste masked product which did not affect the bioavailability of the drug confirming the potential of the developed technology. MonosolRx technology utilizes particulate technology approach for preparation of taste masked product to be incorporated in the OS. The limitation of barrier technologies is the dose of the API since the dose of the drug will ultimately decide the amount of microparticles or complex powder to be accommodated in the OS [9].

4. Due to low solubility of ondansetron base than its salt form, base was used to prepare orally disintegrating tablets. The conversion of the salt of the base can be done in situ by addition of buffering agent in the OS. These agents alter the pH of the saliva and thus convert the salt form of the drug into the low soluble base form leading to taste masking of drug.
5. Recently a novel salting out technology was developed for the taste masking of API. The technology involved coating of drug substance with salting out layer consisting of salt and water soluble polymer. The salt reduced the dissolution of water soluble polymer and drug from the system resulting into taste masking of the drug. As the concentration of salt decreases in the system, the polymer and drug was released and resulted into immediate release of the drug. This salting-out taste-masking system generates lag time with subsequent immediate release. The technology was successfully utilized for the taste masking of paracetamol using as model drug [13].

6. The OS technology offers advantages in certain critical clinical situations. For drugs that are projected as local anesthetic or pain killer, the OS has demonstrated improved clinical benefits. Certain pathologies require instantaneous release of the medicament for prompt relief. For instance, in the case of migraine a rapid clinical effect is desired by the individual. Regiospecific delivery of the medicament would be required in the cases of sore throat, cough, allergy and other local oral manifestations. Breath strips also offer superior consumer compliance. Similarly, cases of motion sickness need immediate attention. Also since OS technology does not require water during administration as compared to the regular tablet dosage forms; it is very handy during travel. This dosage form can also be used for natural extracts and nutraceuticals including vitamin B12, chromium picolinate, melatonin and possibly [14].

**STRIP FORMING POLYMERS:**

**Ideal properties of polymer:**

1. The polymer employed & degradation product should be non-toxic, non-irritant and devoid of leachable impurities.
2. It should have good wetting and spreading property.
3. The polymer should exhibited sufficient peel, shear and tensile strengths.
4. The polymer should be readily available and should not be very expensive.
5. It should have good shelf life
6. They should not aid in causing secondary infection in the oral mucosa or dental regions.
7. Polymer should have local enzyme inhibition action along with penetration enhancing property.

A variety of polymers are available for preparation of OS. The polymers can be used alone or in combination to obtain the desired strip properties. Various polymers can be employed to modulate the disintegration property of the oral strip. This is especially used in case of slowly disintegrable oral bioadhesive strips or patches that need to be retained in intact form for longer duration in the oral cavity. The bioadhesive polymer used in such formulations imparts the adhesive property to the strip such that it adheres to
buccal mucosa to deliver the drug for prolonged period. Bioadhesive polymer should ideally adhere quickly to the buccal mucosa and should have sufficient mechanical strength. Mucoadhesive polymers include polycarbophil, cellulose derivatives like hydroxypropyl methylcellulose, poly(acrylic acid) derivatives, sodium carboxymethyl cellulose, hydroxyethyl cellulose, hyaluronic acid, xanthan gum, locust bean gum, guar gum, carrageenan, sodiumalginate, chitosan, poly (ethylene oxide), poly (ortho esters), poly (hydroxybutyrate), poly (cyano acrylates), polyphosphazenes, poly (vinyl alcohol) etc. Second generation mucoadhesive polymers include thiolated polymers. They are multifunctional polymers consisting of hydrophilic macromolecules having free thiol groups on the polymer backbone. The polymer forms disulfide bonds with cysteine-rich subdomains of mucus glycoproteins. Corium International has developed a new class of adhesive hydrogels (Corplex™) (www.coriumgroup.com). The polymer has properties of both hydrophobic pressure sensitive adhesives and hydrophilic bioadhesives. This is prepared by non-covalent (Hydrogen bond) cross-linking of film forming hydrophilic polymer (like polyvinyl pyrrolidone) with a short-chain plasticizer (typically; polyethylene glycol) bearing complementary reactive hydroxyl groups at the chain ends.

**Examples:**
There are a number of marketed products available that are based on mucoadhesion phenomena. Oramoist® is a Timed Release oral disk that adheres to the roof of the mouth and has a moisturizing effect for about 4 hrs [15]. It is recommended for dry mouth syndrome (xerostomia). Compeed® is another formulation that is intended to treat cold sore (www.compeed.com). This system is similar to transdermal formulation wherein the patch has to be applied onto the affected area. The disadvantage is that since it does not contain bio disintegrating ingredients, the patch has to be removed after use. Canker Cover® is a tablet-like patch that is used in the treatment of canker sore (www.cankercover.com). It adheres to the canker sores and lasts for 8–12 h. It forms a clear gel patch after application. The patch once applied needs careful manipulation using water for its removal and at times may cause pain. Striant® is a bioadhesive delivery system for testosterone replacement therapy (www.striant.com). It is a small monoconvex tablet that rapidly adheres to the buccal mucosa, gets hydrated due to saliva to form gel like form that remains in the region of where the gummeets the upper lip above the incisor teeth for a period of 12 h. Dentipatch® is trans-oral anesthetic patch [16].

BioErodible Muco Adhesive (BEMA™) technology, which is designed to deliver either local or systemic levels of drugs across mucosal tissues. It consists of a small, bioerodible polymer film for application to the mucosal membranes (inner lining of cheek). As compared to the OS, most of the above marketed disk formulations have higher thickness. Hence this might cause inconvenience to the individual when the system is residing in the buccal cavity. Additionally there is a risk of inadvertent detachment of the system leading to loss of clinical response.
Thus, Oral mucosal patches can be categorized into three types namely patches with a dissolvable matrix, patches with a non dissolvable backing, and patches with a dissolvable backing. Patches with a dissolvable matrix are designed to release drug into the oral cavity. The mucoadhesive layer (either in drug matrix or attached to drug matrix) would prolong the duration of drug matrix in the oral cavity. Hence, in comparison to other dosage forms, these systems are longer acting and can potentially deliver more drug quantities. Patches with non-dissolvable backing are usually designed for systemic delivery. Being closed systems the formulations are protected from saliva, the drug concentrations are controlled and drug is continuously delivered for few hours. However, the disadvantages with these patches are that they use only a small mucosal area and the backings have to be removed by the patient after drug administration. Patches with dissolvable backing have the advantage of the entire patch being dissolved in the oral cavity. Patches with dissolvable backings are shorter acting as compared to those with non-dissolvable backing membranes.

**Plasticizers:**
Plasticizer is a vital ingredient of the OS formulation. It helps to improve the flexibility of the strip and reduces the brittleness of the strip. The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer [17, 18]. 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 are some of the commonly used plasticizer excipients. Typically the plasticizers are used in the concentration of 0–20% w/w of dry polymer weight. However inappropriate use of plasticizer may lead to film cracking, splitting and peeling of the strip [19]. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug [20].

**Examples:** Various plasticizers were studied for their plasticization effect on the gelatin strips. In these studies it was observed that malic acid was found to be better plasticizer as compared to citric acid, oleic acid and tartaric acid as it did not crystallize out when the strips were dried. Amongst the different grades of polyethylene glycol (PEG); PEG 300 was found to be better plasticizer for gelatin as compared to higher molecular weight PEG. This is because lower molecular weight PEG formed visually superior films and had low water vapor permeation rate. When sugars like mannitol and sorbitol were tested as plasticizers for gelatin strips, sorbitol was found to be better as compared to mannitol since mannitol crystallizes out from the gelatin strip [21].

Maltodextrin can also be plasticized and converted into OS with incorporation of glycerin and propylene glycol as plasticizer in the concentration range of 16–20% w/w. In this case, glycerin was found to be better than propylene glycol when the strips were manufactured by solvent casting as well as hot melt extrusion methods. However, PEG has miscibility problems with maltodextrins and do not act as good plasticizers [22].
Certain drug molecules themselves can act as plasticizer. For example, Ibuprofen interacted with Eudragit RS 30 D and played the role of a plasticizer. In this case, the glass transition temperature of Eudragit RS 30 D decreased and smooth film formation was observed due to the hydrogen bonding between the drug and the polymer. Also, the dissolution rate of ibuprofen decreased when its concentration in the formulation was increased [23].

MECHANISMS OF PLASTICIZATION:
The mechanism proposed of how the plasticization takes place namely internal plasticization (involving chemical interaction). Formulators prefer to adopt the latter mechanism as it does not involve chemical interactive alterations in the product. An example of internal plasticization is where PEG 4000 was used as plasticizer for phenobarbital where the drug release was reduced to considerable extent. Cellulosic hydrophilic polymers were easily plasticized with hydroxyl containing plasticizers like PEG, propylene glycol, glycerol and polyols. In contrast, less hydrophilic cellulosic polymers were plasticized with esters of citric acid and phthalic acid [9]. Glycerol acts as a better plasticizer for polyvinyl alcohol while diethylene glycol can be used for both Hypromellose as well as polyvinyl alcohol films [24].

Sweeteners:
Sweeteners have become the important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The sweet taste in formulation is more important in case of pediatric population. Natural sweeteners as well as artificial sweeteners are used to improve the palatability of the mouth dissolving formulations.

classification of Sweeteners:
Natural sweeteners - e.g. sucrose, dextrose, fructose, glucose, liquid glucose & maltose.
Artificial sweeteners - These are further classified into 2 types
First Generation - Sacchrin, cyclamate, aspartate.

The sweetness of fructose is perceived rapidly in the mouth as compared to sucrose and dextrose. Fructose is sweeter than sorbitol and mannitol and thus used widely as a sweetener. Polyhydric alcohols such as sorbitol, mannitol, isomalt and maltitol can be used in combination as they additionally provide good mouth-feel and cooling sensation. Polyhydric alcohols are also less carcinogenic and do not have bitter after taste which is an important aspect in formulating oral preparations. The sweetness property of most of the polyols is less than half of that of sucrose except xylitol and maltitol which have similar sweetness as that of sucrose (scale of 0.8–1.0). However it should be noted that the use of natural sugars in such preparations need to be restricted in people who are on diet or in the case of diabetic patients. Due to this reason, the artificial sweeteners have gained more popularity in food and pharmaceutical preparations. The artificial sweetener is preferred over natural sugars because lower concentration is required and multiple uses don't result in dental caries in individuals [25]. But the disadvantage of these artificial sweeteners is the after taste effect. This disadvantage of artificial sweeteners can
be reduced by mixing or blending the natural and artificial sweetener. The flavor quality of these artificial sweeteners is different than the natural sweeteners and may not be acceptable to the patients who are accustomed to the natural sugars. The amalgamation of sweeteners may lead to synergism and improvement in the taste of the formulations [26]. Aspartame was used for the preparation of oral strips of valdecoxib. For the oral strip of piroxicam, maltodextrin was employed as sweetening agent [27]. Generally sweeteners are used in the concentration of 3 to 6 %w/w either alone or in combination.

**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. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them. These agents are used alone or in combination between 2 to 6%w/w of weight of the strip. Other OS ingredients such as sweeteners also act as salivary stimulants. Food grade sugars as well as synthetic sugars are useful salivary stimulants along with acidulate. Glucose, fructose, xylose, maltose, lactose are few examples of such sweeteners [25]. The stimulation of salivation can be measured by comparing the amount of resting flow and stimulated flow at equal time under same conditions. The stimulant action of sweeteners is dependent on the sweetness value. Fructose has the sweetness value of 1.1 as compared to 0.7 of glucose and 1.0 of sucrose.

**Flavoring agents:**
Perception for the flavors changes from individual to individual depending upon the ethnicity and liking. It was observed that age plays a significant role in the taste fondness. The selection of flavor is also dependant on the type of drug to be incorporated in the formulation. For example, mint flavor is generally added in products used for gastric related ailments like indigestion. The acceptance of the oral disintegrating or dissolving formulation by an individual by enlarge depends on the initial flavor quality which is observed in first few seconds after the product has been consumed and the after taste of the formulation which lasts for at least about 10 min [28].

Flavoring agents can be selected from synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Flavors can be used alone or in the combination. Peppermint oil, cinnamon oil, spearmint oil, oil of nutmeg are examples of flavor oils while vanilla, cocoa, coffee, chocolate and citrus are fruity flavors. Apple, raspberry, cherry, pineapple are few examples of fruit essence type. The amount of flavor needed to mask the taste depends on the flavor type and its strength. Preferably up to 10%w/w flavors are added in the OS formulations. Cooling agents like monomethyl succinate can be added to improve the flavor strength and to enhance the mouth-feel effect of the product [29].

**Coloring agents:**
Pigments such as titanium dioxide or FD&C, EV colors, natural colors and custom pantone matched approved coloring agents are incorporated (not exceeding concentration levels of 1%w/w) in OS [30, 31].
Stabilizing and thickening agents:
The stabilizing and thickening agents are employed to improve the viscosity and consistency of dispersion solution or suspension before casting. Natural gums like xanthan gum, locust bean gum, carrageenan and cellulose derivatives can be used in the concentration up to 5%w/w as thickening agents and stabilizing agents [32].

Surfactants:
Surfactants are used as solubilising or wetting or dispersing agent so that the film is getting dissolved within seconds and release active agent immediately. Some of the commonly used are sodium lauryl sulfate, benzalkonium chloride, bezthonium chloride, tweens etc. One of the most important surfactant is polaxamer 407 that is used as solubilizing, wetting and dispersing agent [33].

MANUFACTURING METHOD [34]
One or combination of the following processes can be used to manufacture the mouth dissolving films.

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

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

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

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

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

Rolling Method:
In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cutted in to desired shapes and sizes.

Evaluating parameters [35,36,37,38,39,40]

1. Thickness
The thickness of strip can be measured by micrometer screw gauge at different strategic locations. This is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of dose in the strip.

2. Dryness test/tack tests
About eight stages of film drying process have been identified and they are set-to-touch, dust-free, tack-free (surface dry), dry-to-touch, dry-hard, dry-through (dry-to-handle), dry-to-recoat and dry print free. Although these tests are primarily used for paint films, most of the studies can be adapted intricately to evaluate pharmaceutical OS as well. The details of evaluation of these parameters can be checked elsewhere and are beyond the scope of this review. Tack is the tenacity with which the strip adheres to an accessory (a piece of paper) that has been pressed into contact with the strip. Instruments are also available for this study.

3. Mechanical properties
Mechanical properties of films are evaluated Instron using a TA.XT2 texture analyzer equipment equipped with a 5kg load cell. Films are held between two clamps positioned between 3cm. During measurement the strips were pulled at rate of 2mm/sec. The force and elongation were measured when film breaks. Three mechanical properties namely tensile strength, elastic modulus and % elongation are calculated.

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

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

ii) Percent elongation
When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases.

\[
\%\text{elongation} = \frac{\text{Increase in length of strip} \times 100}{\text{Initial length of strip}}
\]

iii) Tear resistance
Tear resistance of plastic film or sheeting is a complex function of its ultimate resistance to rupture. Basically 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) required to tear the specimen is recorded as the tear resistance value in Newtons (or pounds-force).

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

\[
\text{Young's modulus} = \frac{\text{Slope} \times 100}{\text{Strip thickness} \times \text{Crosshead speed}}
\]

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

4) Folding endurance
Folding endurance is determined by folding the films of uniform cross sectional area and thickness until it breaks.

5) Morphology study
The morphology of the films is studied using scanning electron microscopy (SEM), at a definite magnification.
6) **Swelling property**

Film swelling studies is conducted using simulated saliva solution. Each film sample is weighed and placed in a preweighed stainless steel wire mesh. The mesh containing film sample is submerged into 15ml medium in a plastic container. Increase in the weight of the film was determined at preset time interval until a constant weight was observed. The degree of swelling was calculated using parameters $wt-w/wo$, where $wt$ is weight of film at time $t$, and $wo$ is weight of film at time zero.

7) **Contact angle**

Contact angle measurements is performed at room temperature with a goniometer (AB Lorentzen and Wettre, Germany). A drop of double distilled water was placed on the surface of the dry film. Images of the water droplet were recorded within 10 seconds of deposition by means of digital camera. Digital pictures were analyzed by imageJ 1.28v software (NIH, USA) for angle determination. A minimum of five measurements, taken at different positions of the film, was carried out. The contact angle was measured on both sides of the drop and averaged.

8) **In vitro disintegration time**

In vitro disintegration time is determined visually in a glass dish of 25ml distilled water with swirling every 10 sec. The disintegration time is the time when the film starts to break or disintegrates.

9) **In vitro dissolution studies**

The in vitro dissolution study is carried out in simulated saliva solution pH 6.4 phosphate buffer using USP paddle apparatus at 37±0.5°C. Samples are withdrawn at regular time interval interval and analyzed by UV-Visible spectrophotometer.

10) **Determination of dissolution rate by conductivity method**

In the past 5 years several personal care products formulated in quick release film form have entered the marketplace, of which fast-dissolve breath fresheners were first. The fast dissolve oral films completely dissolve in as little as 1 minute. The majority of oral films on the market today contain ionizable components. This work presents a method for higher solution monitoring of the dissolution of fast dissolving oral films by measuring conductivity of the dissolution medium.

Equipment (Fig.no 6) includes the following:
- Variable speed stirrer motor: capable of 250 rpm.
- Analytical balance (medium weight): capable of weighing to the nearest 0.01g and having a range not less than 400g.
- Low-form beaker: 3×800 ml.
- Impeller: 2-inch diameter, 1 blade (stainless steel or monel metal).
- Conductivity probe: capable of measuring conductivity to 0.1 µ siemens (Hann 8033 conductivity meter).
- Laboratory equipment stand.
- Double-sided clear tape: 3/4 inch-wide.
- External stands to hold conductivity probe.
- Scissors
- Stopwatch with a second hand.

Film Preparation

One side of the film is adhered to the double sided tape, and the double sided tape is cut to the dimensions of the film (Figure.no 6).

Test Procedure

- Fill a clean beaker with 300 g ($\pm$0.05g) of the deionized water.
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- Test the conductivity of the water to establish the background value.
- Adhere the film inside the dry, clean 800ml beaker so that the centre section is even with or slightly below the 100 ml line of the beaker. Arrange the Conductivity probe and the impeller in the beaker.
- As quickly as possible pour the 300 ml of the water in the beaker containing the film, impeller and the conductivity probe. When the water completely covers the film, start the timer (approx 3sec). Then restart the impeller stirring at 250rpm.
- Take a data point at every 10 sec for the first minute. The take data as appropriate.

Conclusion
Oral strip is novel dosage form that satisfies an unmet need of general and specific population like pediatrics geriatrics bedridden nauseous or non complaint patients. Due to advances in techniques to improve palatability of dosage forms, dissolution characteristics of drug and release characteristics variety of drugs can be incorporated in the form of oral strips.

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disintegrating film, which cannot be spit out, for an antiemetic or antimigraine agent, U.S. Patent 2008/0213343 A1, Sept 4, 2008.


Table No. 1.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ingredients</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Drug (API)</td>
<td>1-25%</td>
</tr>
<tr>
<td>2</td>
<td>Strip forming polymer</td>
<td>40-50%</td>
</tr>
<tr>
<td>3</td>
<td>Plasticizer</td>
<td>0-20%</td>
</tr>
<tr>
<td>4</td>
<td>Sweeteners</td>
<td>3-6%</td>
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<tr>
<td>5</td>
<td>Saliva stimulating agents</td>
<td>2-6%</td>
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<tr>
<td>6</td>
<td>Flavoring agents</td>
<td>10%</td>
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<tr>
<td>7</td>
<td>Coloring agents</td>
<td>1%</td>
</tr>
<tr>
<td>8</td>
<td>Stabilizing &amp; thicking agent</td>
<td>5%</td>
</tr>
<tr>
<td>9</td>
<td>Surfactant</td>
<td>q.s (if required)</td>
</tr>
</tbody>
</table>
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Fig no 1 Solvent casting method

Fig no 2 Semisolid casting method
**Fig. No. 3 Hot melt extrusion**

1. Drug is mixed with carriers in solid form
2. Extruder having heaters which melts the mixture
3. This melt is shaped into films by the dies

**Fig. No.4 Solid dispersion extrusion**

1. A drug is dissolved in a suitable liquid solvent
2. Above solution is then incorporated into the melt of polyethylene glycol.
3. Finally the solid dispersion is shaped into films by means of dies.
Premixed batch has been blended with drug

This uniform matrix is then fed to the pan through the second metering pumps

The metering roller determines the thickness of the film and applies it to the application roller.

The film is finally formed on the substrate and carried away via the support roll σ.

**Fig no 5 Rolling Method**

**Fig no 6 conductivity Test Apparatus**