The objective of our review is to compile the recent advancements and literatures regarding the fast dissolving film i.e. Oral dissolving film could reach $2 billion by 2010. However only a few products thin film formulations to be valued at $500 million in 2007 and Technology Catalysts forecasts the market for drug products in oral listerine pocket strips, a new launch in the mouthwash range. The early 2000 year with the introduction and widespread use of this dosage form. (ODFT) was already popular among the people in re-instruct the populace about the technique of administration of form of breath-freshening strips, no further efforts were needed to ODFT derived products were readily popular in the market in the proper way to administer the product like giving instructions to the patients. The ODT in market was accompanied by educating the mass about the ease of acceptability of this dosage form by pediatric as well as geriatric patients. The ODT technology continues to be viewed as an alternative for ODT products that would afford a superior barrier to generic entry and product differentiation to over-the-counter brands. From the marketing perspective, a patented ODF technology would be beneficial. The grant of marketing exclusivity to the new dosage form would help to gain more revenue. As compared to the other ODTs such as tablets; the product is robust. From the patient point
of view OS offers ease of administration and improved compliance. The manufacturing of this dosage form is cost-effective with affordable end products. From clinical aspect, the improved bioavailability can be advantageous in reducing the dose of the formulation. This would lead to product with minimized side effects. The product can be a substitute with more clinical advantage. However, not all drugs can be incorporated into this dosage form. The disadvantage of ODFT is that high dose cannot be incorporated into the strip. Hence researchers have proven that the concentration level of active can be improved up to 50 percent per dose weight. Novartis Consumer Health’s Gas-X® thin strip has a loading of 62.5 mg of simethicone per strip 7.

**Formulation considerations**

Formation of oral Strip (OS) involves the intricate application of aesthetic and performance characteristics such as taste masking, fast dissolving, physical appearance, mouth-feel etc. The excipients used in formulation of OS are given below as per their categories. From the regulatory perspectives, all excipients used in the formulation of OS should be generally regarded as Safe (i.e. GRAS-listed) and should be approved for use in oral pharmaceutical dosage forms.

**Strip forming polymers**

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. The film obtained should be tough enough so that there won’t be any damage while handling or during transportation. The robustness of the strip depends on the type of polymer and the amount in the formulation 8. The various polymers available, pullulan, gelatin and hypromellose are most commonly used for preparation of OS. Pullulan is a natural polymer obtained from non-animal origin and does not require chemical modification. Modified starches are also used for preparation of OS. Due to low cost of this excipient it is used in combination of pullulan to decrease the overall cost of the product. About 50 to 80 percent; w/w of pullulan can be replaced by starch in the production of OS without loss of required properties of Pullulan. Combination of microcrystalline cellulose and maltodextrin has been used to formulate OS.

**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. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of strip. The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer 9,10. 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 percent; w/w of dry polymer weight 11. However, inappropriate use of plasticizer may lead to film cracking, splitting and peeling of the strip. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug.

**Sweeteners agents**

Sweeteners have become the important part of the food products as well as pharmaceutical preparations. Saccharin, cyclamate and aspartame are the first generation of the artificial sweeteners followed by acesulfame-K, sucralose, alitame and neotame which fall under the second generation artificial sweeteners. Acesulfame-K and sucralose have more than 200 and 600 time sweetness. Neotame and alitame have more than 2000 and 8000 time sweetening power as compared to sucrose. Rebiana which is a herbal sweetener, derived from plant Stevia rebaudiana (South American plant) has more than 200 - 300 time sweetness 12.

**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.

**Flavoring agents**

It was observed that age plays a significant role in the taste fondness. 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, 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.

**Coloring agents**

Pigments such as titanium dioxide or FD & C approved coloring agents are incorporated (not exceeding concentration levels of 1 percent; w/w) in OS when some of the formulation ingredients or drugs are present in insoluble or suspension form.

**Quality control tests**

**Thickness**

It 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.

**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-coat and dry print-free. Although for these tests are primarily used for paint films most of the studies can be adapted intrinsically to evaluate pharmaceutical OS as well 11. 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.

**Tensile strength**

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks 14. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below:

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

**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. 15

\[
\% \text{Elongation} = \frac{\text{Increase in length of strip} \times 100}{\text{Strip thickness}}
\]
Appetite suppressant fucus vesiculous and guarana extract, gar cinia cambogia Cambogia helps to reduce the food intake by supplements

Donezepil Rapidfilm® Donepezil Hydrochloride 5 mg and 10 mg. Treatment of mild to moderately severe dementia of the Alzheimer’s type.

Chloraseptic® Relief Strips** Benzocaine 3 mg, BHT, corn starch, erythritol, FD&C Red 40, hydroxypropyl methylcellulose, malic acid, menthol, monosodium glycyrhrizinate, cherry flavors, polyethylene oxide, sucralose

Chloraseptic® Kids Benzocaine 2 mg & menthol, grape flavor, BHT, corn starch, erythritol, FD & C Blue 1, FD & C Red 40, hydroxypropyl methylcellulose, malic acid, menthol, monosodium glycyrhrizinate, polyethylene oxide, sucralose

Sore Throat Relief Strips

Suppress™ Cough strips with Dextromethorphan hydrobromide 2.5 mg, Asulfame potassium, FD&C Blue 1, glycerin, menthol, natural and artificial flavors, pectin, with

Initial length of strip

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)

Young’s modulus

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

\[
\text{Young’s modulus} = \frac{\text{Slope} \times 100}{\text{Strip thickness} \times \text{Cross-head speed}}
\]

Folding endurance

Folding endurance is determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value

Disintegration time

The disintegration time limit of 30 s or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips. Although, no official guidance is available for oral fast disintegrating films strips, this may be used as a qualitative guideline for quality control test or at development stage. Pharmacopoeial disintegrating test apparatus may be used for this study. Typical disintegration time for strips is 5–30 s

Dissolution test

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

Assay/drug content and content uniformity

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

Organoletic evaluation

For evaluation of psychophysical evaluation of the product, special controlled human taste panels are used. In-vitro methods of utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeial methods are being used for this purpose. These in-vitro taste assessment apparatus and methodologies are well suited for high-throughput taste screening of oral pharmaceutical formulations

<table>
<thead>
<tr>
<th>Product category</th>
<th>Ingredients</th>
<th>Indication/applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biofilm Energy boosters</td>
<td>Caffeine, green tea extract and guarana</td>
<td>The product maintains the energy levels.</td>
</tr>
<tr>
<td>Detoxification strip</td>
<td>Green tea extract which is high in polyphenols and rich in anti-oxidants.</td>
<td>Wound healing, regulating body temperature, blood sugar and promoting a healthy digestion</td>
</tr>
<tr>
<td>Male vitality strip</td>
<td>Maca root extract and Siberian ginseng extract, herbs which enhance libido, Cinnamint flavor.</td>
<td>Aphrodisiac</td>
</tr>
<tr>
<td>Appetite suppressant</td>
<td>fucus vesiculous and guarana extract, garcinia cambogia</td>
<td>Cambogia helps to reduce the food intake by suppressing appetite.</td>
</tr>
<tr>
<td>Vitamins and food supplements</td>
<td>Various vitamins, minerals and supplements</td>
<td>It is useful for the people who do not like to pop up the tablets or soluble supplements</td>
</tr>
<tr>
<td>Breath freshener strip, (Antibacterial strip)</td>
<td>Contain mint flavor and antibacterial agent, cetylpyridinium chloride</td>
<td>Mouth freshener</td>
</tr>
<tr>
<td>Saliva promoting strips</td>
<td>Fruit acid extracts, range of flavors</td>
<td>It is used in the dry mouth as a side effect of the other medications.</td>
</tr>
<tr>
<td>Labtec GmbH Ondansetron Rapidfilm®</td>
<td>Ondansetron 4 mg and 8 mg.</td>
<td>It is used in the prevention of chemotherapy and radiation-induced nausea and vomiting and prevention of postoperative nausea and vomiting.</td>
</tr>
<tr>
<td>Donezepil Rapidfilm®</td>
<td>Donepezil Hydrochloride 5 mg and 10 mg.</td>
<td>Treatment of mild to moderately severe dementia of the Alzheimer’s type.</td>
</tr>
<tr>
<td>Paladin Labs (Bioenvelop)</td>
<td>Nicotine</td>
<td>To reduce the smoking habit</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>B6, B12, C; D3 for kids, D3 for adults</td>
<td>Multi vitamin supplement,</td>
</tr>
<tr>
<td>Multivitamin for kids and adults</td>
<td>-</td>
<td>Nutraceuticals</td>
</tr>
<tr>
<td>Teeth whitening</td>
<td>Benzocaine, Caffeine, Melatonin, MentholOmega, Hoodia, Protein, Vinpocetine</td>
<td>Mineral improvement product</td>
</tr>
<tr>
<td>Food supplements</td>
<td>Chromium, Guaraná</td>
<td>Mineral supplements</td>
</tr>
<tr>
<td>Minerals Natural products</td>
<td>Ginseng, Guarana</td>
<td>Aphrodisiac, Appetite reducer.</td>
</tr>
<tr>
<td>Innovien Inc Chloraseptic® Relief Strips**</td>
<td>Benzocaine 3 mg, BHT, corn starch, erythritol, FD&amp;C Red 40, hydroxypropyl methylcellulose, malic acid, menthol, monosodium glycyrhrizinate, cherry flavors, polyethylene oxide, sucralose</td>
<td>Occasional minor irritation, pain, sore throat and sore mouth</td>
</tr>
<tr>
<td>Chloraseptic® Kids</td>
<td>Benzocaine 2 mg &amp; menthol, grape flavor, BHT, corn starch, erythritol, FD &amp; C Blue 1, FD &amp; C Red 40, hydroxypropyl methylcellulose, malic acid, menthol, monosodium glycyrhrizinate, polyethylene oxide, sucralose</td>
<td>Occasional minor irritation, pain, sore throat and sore mouth</td>
</tr>
<tr>
<td>Sore Throat Relief Strips</td>
<td>Dextromethorphan hydrobromide 2.5 mg, Asulfame potassium, FD&amp;C Blue 1, glycerin, menthol, natural and artificial flavors, pectin,</td>
<td>Temporarily suppresses coughs due to minor throat and bronchial irritation</td>
</tr>
</tbody>
</table>
CONCLUSION

Our review concludes that, many of the pharmaceutical companies are switching their product franchise from ODTs to ODFTs. This technology option can also provide a good platform for patent non-infringing product development. ODFT allows brand extension for products. The ODFT is a good tool for product life cycle management for increasing the patent life of existing molecules or products. Compared to some of the complicated and expensive process (like lyophilization) used to manufacture ODTs, the ODFT is relatively easy to fabricate; thus reducing the overall cost of the therapy.

REFERENCES


