Fast Dissolving Oral Films: A Review with Future Prospects

Keywords: Fast Dissolving Oral Films, Low Dose, High Solubility, High Permeability, Better Patient Compliance.

ABSTRACT
Recently, fast dissolving oral films have started gaining fame and acceptance as new drug delivery systems, which aim to enhance safety and efficacy of a drug molecule to achieve better patient compliance. It is a robust form of drug delivery system where the film is placed on the top or the floor of the tongue. When put on the tongue, this film dissolves instantaneously, releasing the drug which dissolves in the saliva. Some drugs are absorbed from the mouth, pharynx, and esophagus as the saliva passes down into the stomach. In such case is enhancing drug bioavailability, no risk of choking, providing good mouthfeel. Fast dissolving drug delivery system to overcome this problem difficulty in swallowing tablets/capsules etc. This review article discusses oral mucosa, formulation components, a method of preparation, evaluation and future prospects of fast dissolving oral films.
1. INTRODUCTION

Among the various routes of drug delivery, the oral route of drug administration is most preferred. Almost 90% of the drugs are administered to the body via oral route for the treatment of various disorders and diseases as it is regarded as the safest, most convenient and most economical method of drug delivery and have the highest patient compliance [1-4]. The drug is either dissolved or swallowed, which then enters into the systemic circulation to produce the desired effect [5-6]. Despite great advancement in drug delivery the oral route of drug administration is considered as the most important method of administration of a drug for systemic effect because of self-medication, ease of administration and avoidance of pain compared to parenteral route [7-10].

1.1. Anatomy of oral cavity

The structure and anatomy of oral cavity is studied for understanding the environment provided for delivering drugs [Fig. 1]. The oral mucosa allows direct access of drug to the systemic circulation and avoids first pass metabolism. The epithelium of the oral cavity is quite similar to that of the skin, with slight differences with regard to keratinization, protective and lubricant mucous which is spread across its surface [11]. The permeability of oral mucosa is 4–1000 times greater than that of the skin. The oral cavity is divided into two regions: outer being the oral vestibule bounded by the lips and cheeks; the hard and soft palates, the floor of the mouth and tonsils [12]. Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. [13].

1.2. Fast dissolving drug delivery system (FDDS)

Fast dissolving drug delivery system is a new generation delivery system also known as fast-dissolving/disintegrating film for the oral delivery of the drugs which came into existence in the late 1970's as an alternative to tablets, capsules, syrups and other formulations for pediatric and geriatric patients who experience difficulties in swallowing traditional solid dosage forms which combines both the advantages of conventional tablet and of liquid formulation [14]. FDDS is easy to administer and provides better patient compliance in the elderly, pediatric, mentally retarded, nauseated and uncooperative patients [15]. This delivery system consists of the solid dosage forms that dissolve quickly i.e. within a matter of seconds.
in the oral cavity without the administration of water. The delivery system consists of a very thin oral strip which is simply placed on the patient’s tongue or any other oral mucosal tissue and instantly gets wetted by saliva [16]. The film rapidly hydrates onto the site of application. It then rapidly dissolves and disintegrates to release the medication for oro-mucosal absorption. Fast dissolving oral thin films are widely accepted by patients and also to the caregiver for their ease-of-delivery, portability and accurate dosing [17]. The robustness of the film depends upon the type and amount of polymer used and general dissolution time for orally dissolving film is 5–20 min. as per pharmacopoeia [18, 19]. They also provide quick onset of action within few seconds as the oro-mucosal absorption of the drug occurs directly from the site of administration to the systemic circulation avoiding the first-pass metabolism to produce the desired effect [20].

Figure 1: Anatomy of the oral cavity (http://baldaivirtuves.info/human-anatomy-mouth/human-anatomy-mouth-anatomy-mouth-oral-cavity-human-anatomy-library-physiology/)

1.3. Advantages of fast dissolving oral films [21]

Advantages offered by FDOFs over other oral formulations are listed below-

- Rapid disintegrating and dissolution in the oral cavity are possible because of availability of larger surface area which improves the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.
• Most ODTs are fragile and brittle, which need a special package for protection during storage and transportation. But the films are flexible; they are not as fragile as ODTs, easy transportation, handling, and storage.

• Precision in the administered dose is ensured from every strip.

• Pharmaceutical companies and consumers alike have embraced OTFs as a practical and accepted an alternative to traditional OTC medicine forms such as liquids, tablets, and capsules. OTFs offer fast, accurate dosing in a safe, efficacious format that is convenient and portable, without the need for water or measuring devices [22].

• Oral strip technology provides an alternate route for drugs with first pass metabolism [23].

• This dosage form is preferable for patients suffering from dysphagia, repeated emesis, motion sickness, and mental disorders as they are unable to swallow the large quantity of water.

• OTFs are typically the size of a postage stamp and disintegrate on a patient’s tongue in a matter of seconds for the rapid release of one or more APIs. The formulation of dissolvable films is customarily facilitated through aqueous polymer matrices that span a wide molecular weight (MW) range, thereby providing flexibility to achieve certain physical properties.

• From a commercial perspective, thin film drug delivery technology offers an opportunity new business opportunity like product differentiation, product promotion, patent extensions and lifecycle management.

1.4 Disadvantages of fast dissolving oral film [24]

• Drugs which are unstable at buccal pH cannot be administered.

• Drugs which irritate the mucosa cannot be administered by this route.

• A drug with small dose requirement can only be administered.

• Taste masking- Most drugs have the bitter taste, and need taste masking.
• Special packaging- OFDFs are fragile and must be protected from water so it needs special packaging.

1.5 Comparison between Fast Dissolving Oral Films and Fast Dissolving Tablets [25, 26]

The difference between the two dosage forms is listed in table 1.

Table 1: Comparison between Fast Dissolving Oral Films and Fast Dissolving Tablets

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Fast Dissolving Oral Film</th>
<th>Fast Dissolving Tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Large surface area gives greater dissolution.</td>
<td>Less surface area gives lesser dissolution than FDOF.</td>
</tr>
<tr>
<td>2.</td>
<td>Fast dissolving oral films are flexible and durable.</td>
<td>Fast dissolving tablet is brittle and less durable than FDOF.</td>
</tr>
<tr>
<td>3.</td>
<td>Only low dose can be incorporated in the formulation.</td>
<td>High dose can also be incorporated in the formulation.</td>
</tr>
<tr>
<td>4.</td>
<td>Fast dissolving films are of thickness 0.015-.05 inches.</td>
<td>Fast dissolving tablet is of the same size of a conventional tablet.</td>
</tr>
<tr>
<td>5.</td>
<td>Patient compliance is more.</td>
<td>Patient compliance is less than FDOF.</td>
</tr>
</tbody>
</table>

2. Formulation Components of FDOFs

2.1 Active Pharmaceutical Ingredient [27]

The film composition contains 1-30% w/w of the active pharmaceutical ingredient. Always use low dose active pharmaceutical ingredients because high dose of drug are difficult to incorporate in fast dissolving film. A number of drugs can be used as fast dissolving oral film including anti-histamine, anti-diarrheal, anti-depressants, vasodilators, anti-asthmatic, anti-emetic, etc. [28]. Dimenhydrinate can also be incorporated into ODFs for taste masking. Common examples of drugs incorporated into ODFs are salbutamol sulfate, rizatriptan benzoate, verapamil, ondansetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, indomethacin, etc. [29].

2.2 Film-Forming Polymers

Polymers are the most important ingredient of the fast dissolving oral film. Robustness of the film depends on the amount of polymer added in the oral strip. Generally, 45% w/w of
polymer is used which is based on total weight of dry film. The selection of polymer is one of the most important and critical parameters for the successful development of oral films because of their tensile strength which depends upon the type and amount of polymer used [30]. Mainly hydrophilic polymers are used in the oral strip as they rapidly disintegrate in the oral cavity as they come in contact with saliva [31]. Currently, both natural & synthetic polymers are used for the preparation of fast dissolving film.

Table 2: List of polymers used in oral thin films [32, 33]

<table>
<thead>
<tr>
<th>Group</th>
<th>Class</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural</td>
<td>Carbohydrate</td>
<td>Pullulan, pectin, sodium alginate, maltodextrin, Sodium starch glycolate (SSG)</td>
</tr>
<tr>
<td>Natural</td>
<td>Proteins</td>
<td>Gelatin</td>
</tr>
<tr>
<td>Natural</td>
<td>Resin</td>
<td>Polymerized rosin (novel film former)</td>
</tr>
<tr>
<td>Synthetic</td>
<td>Cellulose derivatives</td>
<td>Hydroxypropyl methylcellulose (E3, E5, E15, K3, K15, K50), Methylcellulose (A3, A6, A15), Carboxy methylcellulose seckol- 30, Sodium carboxymethyl cellulose, Microcrystalline cellulose, Croscarmellose sodium (CCS).</td>
</tr>
<tr>
<td>Synthetic</td>
<td>Vinyl polymer</td>
<td>Poly vinyl pyrrolidone (K-90, K-30), Poly vinyl alcohol, poly ethylene oxide</td>
</tr>
<tr>
<td>Synthetic</td>
<td>Acrylic polymer</td>
<td>Eudragit (RD-100, 9, 10, 11, 12 and RL-100)</td>
</tr>
</tbody>
</table>

2.3 Plasticizer

Plasticizer helps to improve the flexibility and reduces the brittleness of the strip by reducing the glass transition temperature of the polymer. The selection of plasticizer depends on its compatibility with the polymer and the type of solvent used in the formulation [34, 35]. Commonly used plasticizers are glycerol, propylene glycol, low molecular weight polyethylene glycols (PEGs), phthalate derivatives like dimethyl, diethyl, and dibutyl phthalate, citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil. The plasticizers concentration of 0–20 % w/w of dry polymer weight is used by avoiding the film cracking, splitting and peeling of the strip [36, 37]. The use of certain plasticizers may
also affect the absorption rate of the drug [38]. The properties of plasticizer are important to decrease the glass transition temperature of the polymer in the range of 40-60ºC for a non-aqueous solvent system and below 75 ºC for aqueous systems [39]. 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 [40]. Glycerol acts as a better plasticizer for polyvinyl alcohol while diethylene glycol can be used for both Hypromellose as well as polyvinyl alcohol films [34].

2.4 Surfactants [41, 42]

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

2.5 Sweetening agents [43, 44]

Sucrose is the most commonly used sweeteners in FDOFs. Sucrose is very soluble in water and being colorless does not impart any undesirable color to the final formulation. Some of the commonly employed sweeteners are dextrose, sucrose, fructose, glucose, isomaltose, polyhydric alcohols (sorbitol, mannitol), etc. Artificial sweeteners like saccharin, cyclamate, aspartame (first generation), sucralose, alitame and neotame (second generation) can also be used.

2.6 Saliva stimulating agents [45]

Saliva stimulating agents are used to increase the rate of production of saliva that would help in the faster disintegration of the rapid dissolving strip formulations. Examples of salivary stimulants are citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid.

2.7 Flavouring agents [43]

Flavours used in the formulation must be non-toxic, soluble, stable and compatible with the excipients. The quantity of flavouring agent required to mask the taste depends on the flavour type and its strength.
Table 3: Preferred flavours as per the type and taste of the drug [46]

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preferred Flavour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td>Cherry, maple, pineapple, orange, raspberry, banana-vanilla, butterscotch,</td>
</tr>
<tr>
<td></td>
<td>coconut-custard, fruit-cinnamon, strawberry, vanilla</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Apricot, cherry, cinnamon, grape, honey, lime, peach-orange, peach-rum, raspberry,</td>
</tr>
<tr>
<td></td>
<td>wild cherry</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Banana-pineapple, banana-vanilla, cinnamon-peppermint, orange, peach-orange,</td>
</tr>
<tr>
<td></td>
<td>grenadine-strawberry,</td>
</tr>
<tr>
<td>Decongestants &amp; Expectorants</td>
<td>Anise, apricot, butterscotch, cherry, coconut-custard, custard-mint-strawberry,</td>
</tr>
<tr>
<td></td>
<td>grenadine-peach, strawberry-lemon, gooseberry, orange-lemon, coriander, pineapple,</td>
</tr>
<tr>
<td>Electrolyte-solutions</td>
<td>Cherry, grape, lemon-lime, raspberry, wild cherry syrup,</td>
</tr>
<tr>
<td>geriatrics</td>
<td>grenadine-strawberry, lime, port-wine, cherry-wine, wild-strawberry.</td>
</tr>
<tr>
<td>Salt taste drugs</td>
<td>Butterscotch, maple</td>
</tr>
<tr>
<td>Bitter taste drugs</td>
<td>Wild cherry, walnut, chocolate-mint, licorice</td>
</tr>
<tr>
<td>Sweet taste drugs</td>
<td>Fruit, berry, vanilla</td>
</tr>
</tbody>
</table>

2.8 Colouring agents [47]

Generally incorporated colouring agents have FD&C approved colours, natural colours, pigments such as titanium dioxide etc. The colouring agents should not exceed concentration levels of 1%w/w.

3. Manufacturing Methods [48-50]: There are five methods which are used alone or in a combination with the following process for the manufacture of the fast dissolving oral films.

i) Solvent casting

ii) Semisolid casting

iii) Hot melt extrusion

iv) Solid dispersion extrusion
v) Rolling

3.1 Solvent-casting method

The OTF is preferably formulated using the solvent casting method, whereby the water-soluble ingredients are dissolved to form a clear viscous solution. The API and other agents are dissolved in smaller amounts of the solution and combined with the bulk. This mixture is then added to the aqueous viscous solution. The entrapped air is removed by vacuum. The resulting solution is cast as a film and allowed to dry, which is then cut into pieces of the desired size.

Advantages:

- Better uniformity of thickness and better clarity than extrusion.
- Film has fine gloss and freedom from defects such as die lines.
- Film has more flexibility and better physical properties.
- The preferred finished film thickness is typically 12-100 μm, although various thicknesses are possible to meet API loading and dissolution needs.

Disadvantages:

- The polymer must be soluble in a volatile solvent or water.
- A stable solution with a reasonable minimum solid content and viscosity should be formed.
- Formation of a homogeneous film and release from the casting support must be possible.

3.2 Hot Melt Extrusion

In the present method, the mass is prepared first under the control of temperature and steering speed. Afterward, the film is coated and dried in a drying tunnel, once again the temperature, air circulation, and line speed is controlled. Then follows a slitting and in the last step the films are punched, pouched and sealed.
Advantages:

- Without the use of any solvent or water.
- Fewer processing steps.
- Compressibility properties of the API may not be of importance.
- A better alternative for poorly soluble drugs.
- More uniform dispersion because of intense mixing and agitation.
- Less energy compared with high shear methods.

Disadvantages:

- Thermal degradation due to use of high temperature
- Flow properties of the polymer are essential to processing
- A limited number of available polymers
- All excipients must be devoid of water or any other volatile solvent

3.3 Semisolid Casting

In this method solution of a water-soluble film-forming polymer are mixed to a solution of the acid insoluble polymer to form homogenous viscous solution (e.g. cellulose acetate phthalate, cellulose acetate butyrate). After sonication, it is coated on non-treated casting film. On drying the thickness of the film is about 0.381-1.27 cm. The ratio of the acid insoluble polymer to film-forming polymer should be 1:4.

3.4 Solid Dispersion Extrusion

Solid dispersions are prepared by immiscible components and drug. Finally, the solid dispersions are shaped into films by means of dies.

Precautions while preparing solid dispersions: The selected solvent or dissolved drug may not be miscible with the melt of the polyethylene glycol and polymorphic form of the drug precipitated in the solid dispersion may get affected by the liquid solvent used.
3.5 Rolling Method

In this 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 gives desired shape and size.

4. Evaluation Parameters of FDOFs [52-59]

4.1 Thickness

As the thickness of a film is directly concern with drug content uniformity so it is necessary to ascertain uniformity in the thickness of the film. It can be measured by micrometer screw gauge or calibrated digital Vernier Calipers at different strategic locations. The thickness of the film should be in the range 5-200 μm.

4.2 Dryness test/tack tests

About eight stages of the 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 OFDF. 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.

4.3 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:

\[
Tensile\ strength = \frac{load\ of\ breakage}{Strip\ thickness \times Strip\ Width}
\]
4.4 Percent elongation

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

\[
\% \text{Elongation} = \frac{\text{Increase in length} \times 100}{\text{Original length}}
\]

4.5 Young’s modulus

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

\[
\text{Young’s modulus} = \frac{\text{Force at corresponding strain}}{\text{cross-sectional area}} \times \frac{1}{\text{corresponding strain}}
\]

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

4.6 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 Newton’s (or pounds-force).

4.7 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.

4.8 Organoleptic 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.

4.9 Surface pH of the film

Surface pH of the films was determined by placing the film on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on films. The change in the colour of pH paper should be observed.

4.10 Swelling property

Film swelling studies are conducted using simulated saliva solution. Each film sample is weighed and placed in a pre-weighed stainless steel wire mesh. The mesh containing film sample is submerged into a 15ml medium in a plastic container. Increase in the weight of the film was determined at pre-set time interval until a constant weight was observed.

The degree of swelling was calculated using parameters

$$\alpha = \frac{wt - wo}{wo}$$

wt is a weight of film at time t and wo is a weight of film at time zero.

4.11 Transparency

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

$$\text{Transparency} = \frac{(\log T_{600})}{b} = -c$$

Where T600 is the transmittance at 600 nm and b is the film thickness (mm) and c is concentration.
4.12 Assay/ Content uniformity

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

4.13 Disintegration time

A disintegration of orally fast dissolving films requires USP disintegration apparatus. The disintegration time limit of 30 seconds or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips. Disintegration time will vary depending on the formulation but typically the disintegration range from 5 to 30 seconds. Although, no official guidance is available for oral fast disintegrating films strips.

4.14 Dissolution test

Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopeias. 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 a tendency of the strip to float onto the dissolution medium when the paddle apparatus is employed.

5. Future Prospects

In the pharmaceutical industry, great advancements have been made in oral drug delivery technologies. The market has come a long way from the conventional tablets/capsules to modern-day fast disintegrating and rapidly acting tablets/films. Various limitations such as lower bioavailability of oral solid drugs, the inconvenience of administering injections, inaccurate dosing by liquid formulations are keystone which has turned the focus of pharmaceutical companies to develop novel oral dosage forms that eliminate these limitations. Fast dissolving oral thin films are designed to meet most of these challenges. The concept isn’t new and several over the counter oral thin films are readily available. Good acceptance from the users and an increasing demand of over the counter oral film products has led to the development of prescription drugs into oral thin films. This emerging area is gaining attention from both established and start-up pharmaceutical firms. Companies are utilizing their oral thin film technologies to develop different types of oral thin films (e.g. oral...
dispersible, sublingual, buccal). In addition to the drugs, several hormones and vaccines are also being formulated into oral thin films with the aim of providing improved patient compliance. Some of the key players in this area include MonoSol Rx, Applied Pharma Research/Labtec GmbH, BioDelivery Sciences and NAL Pharma. Many companies are collaborating with these technology providers and utilizing oral thin films as a lifecycle management tool for their branded drugs that have lost patent in other dosage forms. There are not many prescriptions for oral thin films currently available in the market; however, the pipeline holds a wider promise. Despite the uncertainties related to the development, approval and penetration rate, the market is likely to witness stable growth in the coming decade. According to the clinical and regulatory aspects in the US Food and Drug Administration (US FDA), if the product is bioequivalent to that of the existing oral product the drug, an Abbreviated New Drug Application (ANDA) route is followed. There are no clinical studies associated with this generic approval processes (section 505 (j) of the Food, Drug, and Cosmetic Act). The example of such case would be a comparative bioequivalence between an orally disintegrating tablet (ODT) formulation and orally dissolving film (ODF) product. However, developed oral film product may exhibit different pharmacokinetic profile compared to the existing marketed product. The ODF is categorized as “new dosage form” and the section 505 (b) (2) approval processes needs to be followed. In this case, a new clinical study would be required. The advantage of new clinical study is that it would award 3 years of marketing exclusivity to the product. Preclinical toxicity studies are not required if the molecule is the same as that of the approved product. Safety, tolerability, and efficacy features are to be demonstrated in such trials. Oral mucosa-irritation testing is carried out in both animal models and humans. The future looks very promising for the film technology in the time to come as new technologies are rapidly introduced to prepare thin films.

6. CONCLUSION

FDOFs have better patient compliance and may improve biopharmaceutical properties, improve efficacy and better safety, compared with conventional oral dosage forms. After the FDTs, the new products as FDOFs are intended for the application in the oral cavity and they are innovative and promising dosage form especially for use in elder patients. The development of fast dissolving drug products also provides an opportunity for a line extension in a marketplace, for a wide range of drugs (e.g. NSAIDS, antiulcer, antihistamine, Hypnotics & sedatives, antipsychotics, antiparkinsonism, antiemetic, antimigraine and
antidepressants). In future, this system is most acceptable and prescribed due to its quick action *i.e.* within a minute. Because of increasing patient demand, the popularity of these dosage forms will expand the study in future.

7. REFERENCES


