An Overview on: Sublingual Route for Systemic Drug Delivery

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ABSTRACT
Oral mucosal drug delivery is an alternative and promising method of systemic drug delivery which offers several advantages. Sublingual literally meaning is "under the tongue", administrating substance via mouth in such a way that the substance is rapidly absorbed via blood vessels under tongue. Sublingual route offers advantages such as bypasses hepatic first pass metabolic process which gives better bioavailability, rapid onset of action, patient compliance , self-medicated. Dysphagia (difficulty in swallowing) is common among all ages of people and more in pediatric, geriatric, psychiatric patients. In terms of permeability, sublingual area of oral cavity is more permeable than buccal area which is in turn is more permeable than palatal area. Different techniques are used to formulate the sublingual dosage forms. Sublingual drug administration is applied in field of cardiovascular drugs, steroids, enzymes and some barbiturates. This review highlights advantages, disadvantages, different sublingual formulation such as tablets and films, evaluation.

Key Words: Sublingual delivery, techniques, improved bioavailability, evaluation.

INTRODUCTION
Drugs have been applied to the mucosa for topical application for many years. However, recently there has been interest in exploiting the oral cavity as a portal for delivering drugs to the systemic circulation. Notwithstanding the relatively poor permeability characteristics of the epithelium, a number are offered by this route of administration. Foremost among these are the avoidance of first-pass metabolism, ease of access to the delivery site, and the opportunity of sustained drug delivery predominantly via the buccal tissues.

Oral mucosal drug delivery is an alternative method of systemic drug delivery that offers several advantages over both injectable and enteral methods. Because the oral mucosa is highly vascularised, drugs that are absorbed through the oral mucosa directly enter the systemic circulation, by passing the gastrointestinal tract and first-pass metabolism in the liver. For some drugs, this results in rapid onset of action via a more comfortable and convenient delivery route than the intravenous route. 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.

The oral route of administration is considered as the most widely accepted route. The unique environment of the oral cavity offers its potential as a site for drug delivery. Because rich blood supply and direct access to systemic circulation, the oral mucosal route is suitable for drugs, which are susceptible to acid hydrolysis in the stomach or which are extensively metabolized in the liver. The continuous secretion of saliva results in rapid removal of released drug and this may desire that the oral cavity be restricted to the delivery of drugs, which have a short systemic circulation. The mucin film, which exists on the surface of the oral mucosa may provide an opportunity to retain a drug delivery system in contact with the mucosa for prolonged periods if it is designed to be mucoadhesive. Such system ensures a close contact with absorbing membrane, thus optimizing the drug concentration gradient across the biological membrane and reducing the differential pathway. The oral mucosa may be potential site for controlled or sustained drug delivery. Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphagia patients turned the manufacturer to the parenterals and liquid orals. But the liquid orals (syrup, suspension, emulsion etc) have the problem of accurate dosing mainly and parenterals are painful drug delivery, so most patient incompliance.

The target sites for local drug delivery in the oral cavity include the following: Buccal, Sublingual,
Periodontal region, Tongue, Gum. Other desirable targeting sites adjacent to oral cavity include pharynx, larynx, adenoids and tonsils. Within the oral cavity, delivery of drugs via the membranes of the oral cavity is classified into three categories:

i) **Sublingual delivery**
which is systemic delivery of drugs through the mucosal membranes lining the floor of the mouth to the systemic circulation;

ii) **Buccal delivery**
which is drug administration through the mucosal membranes lining the cheeks and the area between the gums and upper and lower lips to the systemic circulation.

iii) **Local delivery**
which is drug delivery to periodontal, gingival, delivery for the local treatment of ulcers, bacterial and fungal infections and periodontal disease. Sublingual administration of the drug means placement of the drug under the tongue and drug reaches directly into the blood stream through ventral surface of the tongue and floor of the mouth. The drug solutes are rapidly absorbed into the reticulated veins which lies underneath the oral mucosa, and transported through the facial veins, internal jugular vein, and brachiocephalic vein and then drain in to systemic circulation. The sublingual route usually produces a faster onset of action than orally ingested tablets and the portion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes. The main mechanism for the absorption of the drug in to oral mucosa is via passive diffusion into the lipoidal membrane. The absorption of the drug through the sublingual route is 3 to 10 times greater than oral route and is only surpassed by hypodermic injection. For these formulations, the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity. Sublingual absorption is mostly rapid in action, but also short acting in duration. Nitroglycerine, for example, is an effective antiangiial drug but is extensively metabolized when taken orally (>90%). It is rapidly absorbed through the sublingual mucosa, and its peak plasma level is reached within 1-2 min. Because of its short biological half life (3-5 min.), however the blood concentration of nitroglycerine declines rapidly to a level below the therapeutic concentration within 10-15 min. In terms of permeability, the sublingual area of the oral cavity is more permeable than the buccal (cheek) area, which in turn is more permeable than the palatal (roof of the mouth) area. The differences in permeability are generally based on the relative thickness, the blood supply, and degree of keratinization of these membranes. In addition to the differences in the permeability of the various mucous membranes, the extent of drug delivery is also affected by the physicochemical properties of the drug to be delivered.

Sublingual products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia).

### Advantages
- Ease of administration to patients who refuse to swallow a tablet, such as pediatric, geriatric patients and psychiatric patients.
- Convenience in administration of drug and accurate dosing as compared to liquid formulations.
- Water is not required for swallowing the dosage form, which is convenient feature for patients who are traveling and do not have immediate access to water.
- Good mouth feel property helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
- Fast dissolution of medicament and absorption which will leads to rapid, onset of action.
- Some drugs are absorbed from the mouth pharynx and esophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- It provides advantages of liquid formulations in the form of solid dosage form.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

### Disadvantage
- Since sublingual administration of drugs interferes with eating, drinking, and talking, this route is generally considered unsuitable for prolonged administration.
- Although this site is not well suited to sustained-delivery systems.
- Sublingual medication cannot be used when a patient is uncooperative or unconscious.
- The patient should not smoke while taking sublingual medication, because smoking causes vasoconstriction of the blood vessels. This will decrease the absorption of the medication.

### Sublingual glands
Salivary glands which are present in the floor of the mouth underneath the tongue. They are also known as sublingual glands. They produce mucin in turn produces saliva. The interior area of the mouth remains lubricated due to production of the saliva by the glands, which is necessary for chewing and food swallowing. The fluid which is produced by the glands gets mix with the food, so the food gets easily chewed. Due to low secretion of the saliva it
can create problem in swallowing the food and potential for food lodge in the throat increases.
The absorption is transfer of the drug from its site of administration into systemic circulation, so it can be said that absorption is directly proportional layer thickness. The absorption of the drug follows in this way Sublingual > Buccal > Gingival > Palatal. Due to high permeability and rich blood supply, the sublingual route can produce rapid onset of action so the drug with short delivery period can be delivered and dose regimen is frequent. The drug gets diluted in the saliva and from there the drug is adsorbed across the oral cavity.

For example: Glyceryl nitrate-a potent coronary vasodilator which is used for rapid symptomatic relief of angina. After administration its gets pharmacologically active after 1-2 minutes. Oral spray was found to provide rapid relief of symptom with first class metabolism. The extent of first class metabolism when compared to the sublingual spray decreased to 48% with sublingual tablets and 28% with the oral dose. Nitrate which appears in the plasma concentration can be maintained for 24 hours when administrated sublingually.

The Mechanism of Sublingual Absorption
The absorption potential of the buccal mucosa is influenced by the lipid solubility and therefore the permeability of the solution (osmosis), the ionization (pH), and the molecular weight of the substances. For example, absorption of some drugs via the buccal mucosa is shown to increase when carrier pH is lowering (more acidic) and decrease with a lowering of pH (more alkaline). The cells of the oral epithelium and epidermis are also capable of absorbing by endocytosis (the uptake of particles by a cell as if by hollowly wrapping itself around it. These engulfed particles are usually too large to diffuse through its wall). It is unlikely that this mechanism is used across the entire stratified epithelium. It is also unlikely that active transport processes operate within the oral mucosa. However, it is believed that acidic stimulation and uptake into the circulatory system.

The mouth is lined with a mucous membrane which is covered with squamous epithelium and contains mucous glands. The buccal mucosa is similar to the sublingual mucosal tissue. The salivary glands consist of lobules of cells which secrete saliva through the salivary ducts into the mouth. The three pairs of salivary glands are the Parotid, the Sub mandibular and the Sublingual which lies on the floor of the mouth. The more acid the taste the greater the stimulation of salivary output, serving also to avoid potential harm to acid sensitive tooth enamel by bathing the mouth in copious neutralizing fluid. With stimulation of salivary secretion oxygen is consumed and vasodilator substances are produced, and the glandular blood flow increases, due to increased glandular metabolism.

The sublingual artery travels forward to the sublingual gland, it supplies the gland and branches to the neighboring muscles and to the mucous membranes of the mouth, tongue and gums. Two symmetrical branches travel behind the jaw bone under the tongue to meet and join at its tip. Another branches meets and anastomoses with the sub mental branches of the facial artery. The sublingual artery system stems from the lingual artery – the body’s main blood supply to the tongue and the floor of the mouth – which arises from the external carotid artery. The proximity with the internal carotid artery allows fast access to its route supplying the greater part of the cerebral hemisphere.

Drugs for sublingual administration
Sublingual drug administration is applied in the field of cardiovascular drugs, steroids, some barbiturates and enzymes. It has been a developing field in the administration of many vitamins and minerals which are found to be readily and thoroughly absorbed by this method. Sublingually absorbed nutrition, which avoids exposure to the gastric system and liver, means direct nutritional benefits, particularly important for sufferers of gastro-intestinal difficulties such as ulcers, hyperactive gut, coeliac disease, those with compromised digestion, the elderly and invalids – the nutritional benefit is independent of gastro-intestinal influences. Examples of drugs administered by this route include antianginal like nitrites and nitrates, anti hypertensive like nifedipine, analgesics likemorphine and bronchodilators like fenoterol. Certain steroids like estradiol and peptides like oxytocin can also be administered e.g. fentanyl citrate, apomorphine, prochlorperazine dimaleate (PRO), and hydrazine HCl (HYD).

Sublingual formulation
Sublingual tablets
They are to be placed under the tongue and produce immediate systemic effect by enabling the drug absorbed directly through mucosal lining of the mouth beneath the tongue. The drug absorbed from stomach goes to mesenteric lining of the mouth beneath the tongue. The drug absorbed from stomach goes to mesenteric lining of the mouth beneath the tongue. Thus absorption through oral cavity avoids first pass metabolism. The tablets are usually small and flat, compressed lightly to keep them soft. The tablet must dissolve quickly allowing the API to be absorbed quickly. It is designed to dissolve in small quantity of saliva. After the tablet is placed in the mouth below the tongue, the patient should avoid eating, drinking, smoking and possibly talking in
order to keep the tablet in place. Swallowing of saliva should also be avoided since the saliva may contain dissolved drug. Bland excipients are used to avoid salivary stimulation. Various techniques can be used to formulate rapidly disintegrating or dissolving tablets. Direct compression is one of these techniques which require incorporation of a superdisintegrant into the formulation, or the use of highly water-soluble excipients to achieve fast tablet disintegration. Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat-labile medications.

a) Fast disintegrating sublingual tablets (FDT)
FDT is defined as a solid dosage form that contains medicinal substances and disintegrates rapidly (within few seconds) without water when kept on the tongue. The drug is released, dissolved, or dispersed in the saliva, and then swallowed and absorbed across the GIT (14). FDTs also are also called as Orodispersible tablet, mouth-dissolving, quick-dissolving, fast-melt, and freeze-dried wafers. Tablets that disintegrate or dissolve rapidly in the patient’s mouth are convenient for young children, the elderly and patients with swallowing difficulties and in situations where potable liquids are not available. Direct compression is one of the techniques which require the incorporation of a superdisintegrant into the formulation, or the use of highly water-soluble excipients to achieve fast tablet disintegration. Compared to conventional dosage form the drug dissolution, its absorption as well as onset of clinical action and its bioavailability may be significantly greater (15-17). Though chewable tablets are available in the market, they are not same as the new FDTs. Patients for whom chewing is difficult or painful can use these FDTs. It can be used easily in infants and in children who have lost their primary teeth and who do not have full use of their permanent teeth (18).

Recent market studies indicate that more than half of the patients prefers FDTs than other conventional dosage forms and most patients would ask their doctors for FDTs (70%), purchase FDTs (70%), or prefer FDTs than regular tablets or liquids (>80%) (20). The US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines, in the „Orange Book“ an FDT as “a solid dosage form containing medicinal substances, which disintegrates rapidly in saliva, usually within a few seconds, when placed upon the tongue” (21). The implication of these dosage forms is emphasized by the term “Orodispersible Tablet”, by the European Pharmacopoeia which defines it as a tablet that can be placed in oral cavity where it disperses rapidly before swallowing (22). FDTs has been developed for numerous indications ranging from migraines (in which quick onset of action is necessary) to mental illness (in which patient compliance is necessary for treating chronic indications such as mental depression and schizophrenia) (23).

b) Bioadhesive sublingual tablets
The new sublingual tablet concept presented is based on interactive mixtures consisting of a water soluble carrier covered with fine drug particles and a bioadhesive component. With this approach, it is possible to maintain rapid dissolution in combination with bioadhesive retention of the drug in the oral cavity. Bioadhesion is usually defined as the bond formed between two biological surfaces or between a biological and a synthetic surface. Problem associated with sublingual tablet formulation is that there is always a risk that the patient will swallow part of the dose before the active substance has been released and absorbed locally into systemic circulation. This could result in an unwanted prolongation of the pharmacological effect. Addition of a bioadhesive component is a well-known method of increasing the possibility of a more site-specific release. However, this concept is normally applied to non-disintegrating tablets or disc to achieve extended release of the active substance and, consequently, such a system will not be suitable for a fast acting formulation. Therefore, it would be of interest to study a disintegrating tablet which releases the drug quickly, but which also has bioadhesive properties which could prevent the drug from being swallowed.

Bioadhesion mechanisms
The mucus layer is often involved in the adhesion of a bioadhesive polymer and is present as either a gel layer adhering to the mucosal surface or a solution or suspension of various substances. The mucus layer mainly consists of mucin glycoprotein,
inorganic salts, proteins, lipids and water with the composition varying depending on its source. The electronic theory involves an electronic transfer between the two materials causing a double layer of electric charge, which results in attraction forces. The adsorption theory involves adhesion between the mucosa and the adhesive material by van der waals interaction, hydrogen bonds and related forces. The wetting theory involves interfacial tensions between the two materials. Penetration of the polymer chains into the mucus network and vice versa, causing a mechanical bond, is referred to as the diffusion theory. The importance of water content and movement of water into the adhesive material from the mucosa, i.e. dehydration of the mucosa, has also been suggested as a mechanical for adhesion.

**Measurement of bio-adhesive strength**

Bio-adhesion strength of the tablets was measured on a modified physical balance. The method used bovine cheek pouch as the method mucosal and IPB ph 6.6 as the moistening fluid. The surface of the mucosal membrane was first blotted with a filter paper and then moistened with 25/L 1 of IPB pH 6.6. the weight in grams is required to detach the tablets from the mucosal surface gave the measure of bio-adhesive strength.

c) **Lipid matrix sublingual tablets**

Such tablets are formulated using advances in sublingual and liposomal technology to create a dosage form that offers a faster and more complete absorption than traditional oral routes of administration. The lipid matrix sublingual tablet is a bioavailable, quick, convenient and consistent dosage form for many nutraceuticals that are often taken orally. For e.g., Glutathione MB12(methylcobalamin) melatonin.

d) **Sublingual vitamin tablet**

Vitamin D i.e. cholecalciferol is a natural precursor of calcium regulating hormone calcitriol. Vitamin D is thus used in hypocalcaemia/ hyperparathyroidism. Because of its incomplete absorption from GI tract, local intestinal degradation and hepatic metabolism, it is given sublingually.

2) **Thin film drug delivery**

Thin film drug delivery is a process of delivering drugs of the systemic circulation via thin film that dissolves when in contact with liquid, often referred to a dissolving films or strips and dissolve within 1 min when placed in the mouth without drinking or chewing. Such dissolving film or strip are typically designed for oral administration, with the user placing the strip on or under the tongue or along the inside of the cheek. Thin film’s ability to dissolve rapidly without the need for water provides an alternative to patients with swallowing disorders and to patients suffering from nausea, such as those patients receiving chemotherapy.

The first developed fast-dissolving dosage form consisted in tablet form, and the rapid disintegrating properties were obtained through a special process or formulation modifications. More recently, fast-dissolving films are gaining interest as an alternative to fast-dissolving tablets to definitely eliminate patients’ fear of choking and overcome patent impediments. Fast-dissolving films are generally constituted of plasticized hydrocolloids. Problems are caused by foaming during the film formation due to the heating of the material or solvent evaporation, the flaking during the slitting and the cracking in the cutting phase. The films should be stable to moisture, facilitate the handling, have to be flexible and exhibit a suitable tensile stress and do not stick to the packaging materials and fingers.

Film can be prepared by five method: 1) Solvent casting. 2)Semisolid casting. 3)Hot melt extrusion. 4)Solid dispersion extrusion. 5) Rolling.

1) **Solvent casting method**

Film is 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.

2) **Semisolid casting**

Solution of water soluble film forming polymer is mixed with solution of acid insoluble polymer which forms homogenous viscous solution. The ratio should be 1:4. For e.g. cellulose acetate phthalate, cellulose acetate butyrate. It is then sonicated which is coated on non-treated casting film.

3) **Hot Melt Extrusion**

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

4) **Solid Dispersion Extrusion**

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

5) **Rolling**

Solution or suspension drug is rolled on the 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.

Evaluation

Hardness and thickness
The test is done as per the standard methods. The hardness of three randomly selected tablets from each formulation is determined by placing each tablet diagonally between the two plungers of tablet hardness tester (with the nozzle) and applying pressure until the tablet broke down into two parts completely and the reading on the scale is noted down. The thickness of three randomly selected tablets from each formulation is determined in mm using a vernier caliper (Pico India). The average values is calculated.

Drug Content
Randomly ten tablets are selected from formulation, finely powdered and powder equivalent mg of drug is accurately weighed and transferred to 100 ml volumetric flasks containing solution of desired pH. The flask is shaken to mix the contents thoroughly. The volume is made up to the mark with solution and filtered. One ml of the filtrate is suitably diluted and drug content is estimated using a double beam UV-visible spectrophotometer. This procedure is repeated thrice and the average value is calculated.

Wetting time (WT)
It is useful for quality control and provides supportive evaluation of these sublingual tablets. Unlike the disintegration test, the wetting test uses minimal water, which may be more representative of the quantity of moisture available sublingually. Using this test, the time required for moisture to penetrate the tablet completely is measured and possibly represents the time required to release drug in the presence of minute volumes of saliva. The tablet was placed above absorbent paper fitted into a petri dish. After the paper is thoroughly wetted with distilled water, excess water is completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet is then recorded using a stopwatch.

Disintegration test
A relatively simple method with rigorous conditions is developed. Each individual tablet is dropped into 10-ml glass test tube (1.5-cm diameter) containing 2ml distilled water, and the time required for complete tablet disintegration is observed visually and recorded using a stopwatch. The visual inspection is enhanced by gently rotating the test tube at a 45° angle, without agitation, to distribute any tablet particles that might mask any remaining undisintegrated portion of the tablets. In the USP disintegration test for sublingual tablets, the disintegration apparatus for oral tablets is used without the covering plastic disks, and 2 minutes is specified as the acceptable time limit for tablet disintegration.

Water absorption ratio
A piece of tissue paper folded twice is placed in a small Petri dish containing 6 ml of water. A tablet is put on the tissue paper and allowed to completely wet. The wetted tablet is then weighted. Water absorption ratio, R was determined using following equation:

\[ R = 100 \times \frac{W_a - W_b}{W_a} \]

where, \( W_a \) = Weight of tablet after water absorption
\( W_b \) = Weight of tablet before water absorption.

In vitro disintegrating test
Disintegration times for sublingual tablets is determined using USP tablet disintegration apparatus with desired medium. The volume of medium was 900 ml and temp was 37± 2 °C. The time in seconds taken for complete disintegration of the tablets with no palatable mass remaining in the apparatus is measured.

In vitro dissolution test
In-vitro release rate of sublingual tablets will be carried out using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus (Paddle method). A aliquot sample of the solution is withdrawn from the dissolution apparatus. The samples are replaced with fresh dissolution medium of same quantity. The samples are filtered through Whatman filter paper No 40 and analyzed in UV spectrophotometer. The percentage drug release is calculated using an equation obtained from the calibration curve.

Test for film
Tensile Strength
Tensile strength is the maximum stress applied to a point at which the film specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the film as given below:

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

Percent Elongation
A film sample stretches when stress is applied and it is referred to as strain. Strain is basically the deformation of film divided by original dimension of the sample. Elongation of film increases as the plasticizer content increases.
Percent Elongation

\[ \frac{L - L_0}{L_0} \times 100 \]

where,

\( L = \) Increase in length of film
\( L_0 = \) Initial length of film.

Young's Modulus

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

\[
\text{Young's Modulus} = \frac{\text{Slope} \times 100}{\text{Film thickness} \times \text{Cross-head speed}}
\]

Folding Endurance

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

Thickness

The thickness of the polymer films was measured by using screw gauge. The thickness of each strip at six different areas was determined and standard deviation was calculated.

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. The disintegration time of prepared films was measured in triplicate.

Uniformity of drug content

The film of area 1x1 cm² was cut and dissolved in 6.8 phosphate buffer solution and made up to 100 mL in a volumetric flask. Then 1 mL was withdrawn from the solution and diluted to 10mL. The absorbance of the solution was taken at 276 nm and concentration was calculated. By correcting dilution factor, the drug content was calculated. The test was performed in triplicate.

In-vitro dissolution studies

Dissolution study was carried out in USP paddle type apparatus using 300 mL of stimulated salivary fluid (pH 6.8) as a dissolution medium at 50 rpm. Temperature of the dissolution medium was maintained at 37±0.5°C. Samples of 5mL were withdrawn at every 4 minute interval, filtered (through 0.45μ) and replaced with 5mL of fresh dissolution medium. The samples were suitably diluted and estimated spectrophotometrically at 276 nm by using ELICO-164 double beam UV-Visible spectrophotometer. The dissolution experiments were conducted in triplicate. Dissolution rate was studied for all designed formulations and dissolution parameters were calculated.

CONCLUSION

Sublingual drug delivery have been used for formulation of many drugs with view point of rapid drug release and quick onset of action. Sublingual products were developed to overcome the difficulty in swallowing conventional tablet, among pediatric, geriatric and psychiatric patients with dysphagia. The target population has expanded to those who want convenient dosing without water anywhere, anytime. The potential for such dosage forms is promising because strong market acceptance and patient demand. Peak blood levels of most products administered sublingually are achieved within 10-15 minutes, which is generally much faster than when those same drugs are ingested orally. Sublingual absorption is efficient. The percent of each dose absorbed is generally higher than that achieved by means of oral ingestion. Various types of sublingual dosage forms are available in market like tablets, films and sprays.
Table 1:

<table>
<thead>
<tr>
<th>Superdisintegrant</th>
<th>Commercially available</th>
<th>Mechanism of action</th>
<th>Special comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross linked Cellulose</td>
<td>Crosscarmellose®</td>
<td>Swells 4-8 folds in &lt; 10 seconds. Swelling and wicking both</td>
<td>Swells in two dimensions. Direct compression or Granulation. Starch free.</td>
</tr>
<tr>
<td></td>
<td>Ac-Di-Sol®, Nynex ZSX®, Primellose®, Solutab®, Vivasol® L-HPC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cross linked PVP</td>
<td>Crosspovidone M®. Kollidon®. Polyplasdone®</td>
<td>Swells very little and returns to original size after compression but act by capillary action</td>
<td>Water insoluble and spongy in nature so get porous tablet</td>
</tr>
<tr>
<td>Crosslinked starch</td>
<td>Explotab® Primogel®</td>
<td>Swells 7-12 folds in &lt; 30 seconds.</td>
<td>Swells in three dimensions and high level serve as sustain release matrix</td>
</tr>
<tr>
<td>Crosslinked algic Acid</td>
<td>Algic acid NF</td>
<td>Rapid swelling in aqueous medium or wicking action</td>
<td>Promote disintegration in both dry or wet granulation.</td>
</tr>
</tbody>
</table>

Table 2: Marketed Products of Sublingual Tablet

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Category</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstral Fentanyl Citrate</td>
<td>Opioid Analgesic</td>
<td>50, 100, 200, 300, 400, 600, 800 µg</td>
</tr>
<tr>
<td>Subutex Buprenorphine</td>
<td>Opioid Analgesic</td>
<td>2 and 8mg</td>
</tr>
<tr>
<td>Avitan Lorazepam</td>
<td>Antianxiety</td>
<td>1, 2 mg</td>
</tr>
<tr>
<td>Edular Zolpidem tartrate</td>
<td>Sedatives/ Hypnotics</td>
<td>5, 10 mg</td>
</tr>
<tr>
<td>Isordil Isosorbide dinitrate</td>
<td>Vasodilators</td>
<td>2.5, 5 10mg</td>
</tr>
<tr>
<td>Suboxone Buprenorphine hydrochloride</td>
<td>Narcotic + Opioid antagonist</td>
<td>2/0.5, 8/2 mg</td>
</tr>
<tr>
<td>Nitrostat Nitroglycerine</td>
<td>Antianginal</td>
<td>0.3 mg, 0.4 mg, or 0.6 mg</td>
</tr>
</tbody>
</table>

Fig. 1:
REFERENCES
