Review Article

Sublingual Tablets and the Benefits of the Sublingual Route of Administration

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ABSTRACT

Purpose: Sublingual drug delivery can be an alternative and better route when compared to oral drug delivery as sublingually administered dosage forms bypass hepatic metabolism. A rapid onset of pharmacological effect is often desired for some drugs, especially those used in the treatment of acute disorders. Sublingual tablets disintegrate rapidly and the small amount of saliva present is usually sufficient for achieving disintegration of the dosage form coupled with better dissolution and increased bioavailability.

Approach: Published articles from PubMed and other standard sources were utilized to review and compile an overview of sublingual tablets and the benefits of the sublingual route of administration.

Findings: Sublingual tablets were found to have better characteristics when compared to conventional dosage forms. Sublingually administered tablets achieved better bioavailability, rapid onset of action and better dissolution properties due to fast disintegration. The addition of super-disintegrants facilitated rapid disintegration and this approach can be used to treat acute disorders or emergency conditions.

Conclusion: Sublingual tablets or any sublingual dosage form can be used to achieve a rapid onset of action, better patient compliance and increased bioavailability. The sublingual route of administration can be used for drugs which undergo extensive first pass metabolism or degradation in the GIT. Drugs administered sublingually tend to have better bioavailability which correlates to dose reduction when compared to conventional oral tablets.

Key words: *Sublingual tablets; Easy self-medication; Fast disintegration; Increased bioavailability.*

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INTRODUCTION

The sublingual route is a preferable route for the local and systemic administration of certain drugs.[1] This route has quite a few distinct advantages over oral drug delivery due to presence of rich supply of blood vessels, rapid onset of action, enhanced bioavailability, avoidance of the hepatic first pass metabolism, effects of food, amplified patient compliance, and easy self-medication. In the recent years, a number of novel drug delivery systems are taking advantage of sublingual drug delivery and have been successfully introduced in the market.[2]

Sublingual delivery of a drug and its further absorption depends on the permeability of the sublingual membrane, the physicochemical properties of a drug, and the design of the dosage form. This review article focuses on the physicochemical properties and the formulation design because aperceptive of these elements enables the assortment of suitable drug molecules for sublingual delivery and optimization of the final formulation.[3]

Anatomical structure of the oral mucosa

The oral cavity is separated into four regions from which absorption of drugs can take place the sublingual, buccal, gingival, and palatal regions.[4] These regions

vary from each other in their histological formation and biochemical composition and the ability to retain dosage forms long enough to facilitate complete drug absorption. The sublingual membrane present on the floor of the mouth under the tongue is commonly used for both local and systemic drug delivery.[5]

The mucosal lining consists of three distinct layers. The outermost layer is the epithelial membrane composed of stratified squamous epithelial cells and acts as a protective barrier. The basement membrane is the innermost layer of the epithelial membrane. Below the epithelium lies the *lamina propria* followed by the submucosa. The *lamina propria* is a hydrated and less dense layer of connective tissue composed of collagen and elastic fibers. The oral submucosa has a rich supply of blood vessels.[6]

Following absorption through the mucous membrane in the sublingual area, the drug directly diffuses into the venous blood which drains by means of the internal jugular vein, the subclavian vein, and the brachiocephalic vein directly into the superior vena cava through a general trunk. The venous return from these regions enters the systemic circulation, bypassing the hepatic metabolism, unlike oral administration. The direct flow of the drug into the systemic circulation results in better bioavailability of the drug and aswiftcommencement of therapeutic effect.[7]

Drug Absorption through the Sublingual Region

The salivary pH is in the range of 5.5 to 7.0 and the saliva consists of mucus and enzymes such as amylase and carboxylesterase and forms a cohesive gelatinous film on all surfaces of the oral cavity. Mucoadhesion occurs due to the cohesiveness of the sublingual membrane leading to drug absorption. The epithelial membrane in the sublingual region is 100-200µm thick and is non-keratinised.[8]

Cholesterol, cholesterol esters and glucosyl ceramides present in the epithelial cells of the sublingual membrane render it permeable to drug absorption unlike other regions of the oral cavity. The increased blood supply and the relative thinness and high permeability of the sublingual mucosa allow fast absorption and increased bioavailability of certain drugs after sublingual administration. Hence, the sublingual region is a very suitable site for achieving effective concentrations of drugs which are clinically effective in a short time duration when a rapid onset of action is required.[9]

The sublingual region is constantly washed by saliva and by movements of the tongue and is not suitable for extended retention of a dosage form.[10]

Commercially available sublingual tablets

In recent times, only a small number of sublingual tablets are commercially available for drug administration. These drugs are used for the emergency treatment of angina pectoris, hypertension, treating cancer pain, migraine; etc.[11]Table 1 below lists some of the approved sublingual tablets which are commercially available.

Potential drug candidates for sublingual delivery

The literature is full of studies that have demonstrated the enhanced potential of several drugs when administered through the sublingual route. However, the potential offered by sublingual administration has not been commercially applied for drug delivery.[12] The following examples illustrate superior therapeutic effects of drugs which were administered sublingually compared to oral administration.

- In a comparative effectiveness study of sublingual captopril, nifedipine, and prazosin, it was reported that sublingual captopril could be a better alternative to sublingual nifedipine in treating

Table 1: Commercially available sublingual tablets

Active ingredient	Brand name	Manufacturer
Asenapine	Saphris	Merck
Buprenorphine hydrochloride	Subutex	Sun pharma
Ergoloid mesylates	Ergomes	Cipla
Ergotamine tartrate	Ergomar	Rosedale pharmaceuticals
Fentanyl citrate	Abstral	Galena Biopharmaceuticals
Isosorbide dinitrate	Imdur	Astrazeneca
Nitroglycerin	Nitrostat	Pfizer
Zolpidem tartrate	Intermezzo	Purdue pharma

emergencies occurring due to hypertension due to lesser side effects.[13]

- Sublingual administration of verapamil exhibited significantly higher maximum plasma concentration of the drug (C_{max}), a faster absorption rate, and greater bioavailability as compared to its oral administration. It was also shown to produce a rapid and significant ventricular rate reduction.[14]
- The drug furosemide showed to offer a therapeutic advantage when administered sublingually over the oral route of administration.[15]
- Sublingually administered midazolam was found to be more effective in the emergency treatment of acute febrile and afebrile (epileptic) seizures in children when compared to rectal administration of diazepam.[16]
- A research study proposed the office-based treatment of opiate addiction using sublingual administration of buprenorphine and naloxonebecause of useful results shown by sublingual tablets of buprenorphine and naloxone in the treatment of opiate addiction.[17]
- A sublingual formulation of zolmitriptan exhibited a faster rate of absorption and higher drug exposure as compared to subcutaneous injection and was found to be highly efficient for the treatment of migraine and cluster headaches.[18]
- In a randomized, double-blind clinical research study, 40mg of sublingually administered piroxicam was found to be as effective as a 75 mg intramuscular injection of diclofenac in the emergency treatment of acute renal colic.[19]
- A research study proposed sublingual epinephrine as an alternative to self-injected epinephrine for the treatment of anaphylaxis as the sublingually administered epinephrine resulted in rapid absorption of the drug and a higher peak plasma concentration in animal models when compared to self-injected epinephrine.[20]
- Estrogens have been shown to produce coronary and peripheral vasodilation, vascular resistance reduction, and improvement of endothelial function in menopausal women with cardiovascular disease. Sublingually administered estrogens have been shown to exhibit faster drug absorption (i.e., shorter T_{max} higher C_{max}) than orally administered forms.[21]
- Vaccines are used for prophylactic treatment and preclinical studies conducted on vaccines have shown that sublingual vaccines can be highly immunogenic and may protect against the influenza virus and *Helicobacter pylori*.[22]

Sublingual tablet formulation development

For the development of an optimal sublingual tablet formulation, it is important to consider the mechanism of absorption of a drug, physicochemical properties; function of the excipient used in formulation development, taste masking techniques used etc.[23]

Mechanism of drug absorption from the sublingual region

After sublingual administration of a dosage form, the drug is absorbed by *Passive diffusion, Active transport or Endocytosis*.[24]

Passive diffusion is a spontaneous process. Molecular weight, solubility of the drug, concentration gradient, temperature, surface area of the membrane, and the proximity of the drug molecule to the membrane determine the rate of drug diffusion into the tissues.[25] A drug molecule is absorbed by passive diffusion when it exists in its unionized form in the saliva. Various physical models have been illustrated to explain the process of drug absorption from saliva through the lipid bilayer of the mucous membrane directly into the systemic circulation. The rate of absorption of a drug across the mucous membrane is directly related to its partition coefficient. Some amino acids like, glutamic acid, L-ascorbic acid, nicotinic acid, and thiamine, are transported through a specific carrier-mediated process.[26]

Lipids which are present in the sublingual mucous membrane act as the main barrier for the permeability of hydrophilic drugs. However, well-hydrated connective tissues provide resistance to hydrophobic

drug molecules. Hence, the potential transport path across the sublingual mucous membrane may be either polar or non-polar. Polar molecules cross via the ionic channels present in the intercellular spaces of the epithelium, or the aqueous pores present in the epithelial cells whereas the non-polar molecules pass through the lipid regions of the epithelium. For this reason, it is important to understand the hydrophobic or hydrophilic nature of a drug during the process of formulation development. This process appears to be the most useful index for evaluating the suitability of a drug molecule for absorption across the sublingual region.[27]

Physicochemical properties of the drug

The physicochemical properties of the drugs facilitate their absorption by passive diffusion through the sublingual membrane. Table 2 lists the physicochemical properties of some commercially available drugs administered sublingually.

For efficient absorption through the sublingual membrane, the drug must be lipophilic enough to be able to partition through the lipid bilayer, but not so lipophilic such that once it is in the lipid bilayer, it will not partition out again. Satisfactory oral absorption of drugs has been observed over a wide range of log P (octanol/water partition coefficient) values of 1 to 5. As the log P value increases beyond 5, the salivary solubility of the drug is usually not enough to provide adequate concentration for the drug to diffuse through the lipid bilayer.[28] According to the diffusive model of absorption, the flux across the lipid bilayer is directly proportional to the concentration gradient. Therefore, lower salivary solubility results in lower absorption rates and vice versa. In general, a drug which has been formulated for sublingual should ideally have a molecular weight of less than 500 (as free base) to facilitate its diffusion.[29]

Because drugs diffuse through the lipid bilayer in an unionized form, based on the pH-partition theory, the pK_a of drugs also plays a very important role in the transport of a drug across the sublingual membrane. The oral cavity, unlike the gastrointestinal tract, has a narrow pH range which lies between 5.0 to 7.0. Hence, when a basic drug administered in its salt form, it predominantly exists as a free unionized base if the pH is raised above its pKa value and this increase in the unionized fraction of the drug considerably increases its bioavailability. For this reason, the inclusion of a suitable buffer during the formulation of an ionizable drug makes it possible to control the pH of aqueous saliva in a range which is most appropriate for the optimal the absorption of such drugs. The drugs which do not contain ionizable groups are not affected by changes in pH.[30]

Unlike the gastrointestinal tract, the absorptive surface of the oral cavity is much smaller; therefore, large doses cannot be administered via this route.[31] Thus, only potent drugs, which require small doses to obtain the desired therapeutic effect, can be administered through this route. In addition to these critical attributes of the drug, it is highly desirable that the drugs intended for sublingual delivery must be adequately taste masked to achieve patient compliance.[32]

Table 2: Physicochemical properties of a few sublingually administered drugs.

Drug	Molecular weight	Largest dose*	Water solubility	pK_a	Log p
Asenapine maleate	285.5	10 mg	3.7 mg/ml	8.6	4.9
Buprenorphine	467.6	2-8 mg	Insoluble in water	8.24, 10.0	4.9
Ergotamine tartrate	583.68	2mg	Insoluble in water	6.3	2.4
Fentanyl citrate	336	0.8 mg	0.025 mg/ml (citrate)	8.4	2.9
Nicotine	162.234	4mg	Slightly soluble	8.21	0.99
Nitroglycerin	227	0.6mg	1.8 mg/ml	-5.6	0.94

**Largest dose for a sublingual tablet*

Functions of excipients used

The quantity and type of disintegrants used during formulation also play a significant role in achieving rapid disintegration. Effervescent agents are used to facilitate disintegration. The inclusion of water-soluble excipients, such as saccharides, helps to achieve rapid dissolution by enhancing the wettability of the tablet matrix. However, the process of manufacturingand certain critical process specifications can also affect the disintegration and dissolution of sublingual tablets.[33]

Taste masking techniques

Some drugs may have a bitter or unpleasant taste. When such drugs are dissolved in the saliva for mucosal absorption, they may also interact with the taste buds in the mouth and produce a bitter and unpleasant taste which may be unacceptable to patients. Patient acceptability of a formulation is improved by various physicochemical approaches that prevents the interaction of the drug with the taste buds and thus eliminates the negative sensory response.[34]

Sweeteners, flavors, and other taste-masking agents are essential components for formulations containing drugs with an unpleasant taste. Sugar-based excipients quickly dissolve in saliva and produce endothermic heat of dissolution. They create a pleasant feeling in the mouth and are most suitable for sublingual tablets along with other flavors. The coating of bitter drugs is not an option for drugs to be dissolved in saliva.[35]

To address this critical patient compliance concern, suitable taste-masking strategies should be studied in the formulation development stage and should be incorporated in the product design. The technologies that are reported in the literature for the evaluation of taste include the electronic tongue, measurement of the frog taste nerve response, the spectrophotometric method, and a human taste panel.[36]

Characteristics of sublingual tablets

Due to the short residence time in the mouth, fast disintegration and dissolution is very important for the absorption of a drug following sublingual administration. For this reason, sublingual tablet formulations need to be designed in such a way that they disintegrate and dissolve rapidly in saliva, without the usage of any additional water to achieve this goal.[37]

The physical and mechanical characteristics of a tablet, such as size, hardness, porosity, and wettability, play a crucial role in its disintegration time. A smaller sized tablet with low hardness and high porosity will disintegrate more rapidly than a larger or harder tablet.[38] However, a tablet which is highly porous coupled with low hardness is more friable and prone to self-disintegration, and this presents problems during packaging and handling. During formulation development, all approaches to increase the mechanical strength of sublingual tablets should be probed, without compromising disintegration and dissolution properties of the sublingual tablet.[39]

Following sublingual administration, the patient is advised to abstain from swallowing the tablet and avoid eating, drinking, or chewing to facilitate absorption of the drug through the sublingual membrane. Even swallowing saliva needs to be avoided, to prevent ingestion through the gastrointestinal tract where the drug absorption maybe inefficient or the drug may undergo degradation. Because these aspects pose some inconvenience to the patient, they should be taken into account at the formulation development stage to improve patient compliance.[40]

Sublingual tablets promote rapid absorption and higher bioavailability with a fast onset of action. If the dissolution of the drug is incomplete, contact time with the sublingual membrane is short, and/or permeation is too low, part of the formulation may be swallowed and consequently not be absorbed through the sublingual membrane, with subsequent effects on the bioavailability of the drug. Many sublingual tablets may be compromised by the possibility that the patient may swallow the active pharmaceutical ingredient before it has been released and absorbed through the sublingual membrane into the systemic circulation.[41]

A sublingual tablet is designed to promote the retention of the active pharmaceutical ingredient under the tongue, to prevent its swallowing, and to minimize inter and intra individual variability. This approach used a formula which incorporated ordered mixtures of fine active ingredient particles and bio-adhesive polymers which were attached to coarser excipient carrier particles.[42]Tablets formulated following the above method have the potential to rapidly disintegrate and release the drug, which adhere to the sublingual mucosa, and thus prolong the contact time at the absorption site. Directly compressible sublingual tablets developed using this approach led to the bio-adhesive retention of the active pharmaceutical ingredient in the oral cavity and optimal exposure of the drug to the salivary fluid in the mouth which results in complete and rapid sublingual absorption.[43]

Manufacturing techniques used in sublingual tablet Formulation

Direct compression

The direct compression method is most commonly used for commercial manufacture of sublingual tablets. It is a simple, cost-effective and efficient process, as it employs ingredients that can be blended well and do not require further granulation steps prior to lubrication and compression. Sublingual tablets manufactured using direct compression exhibit good mechanical strength and fast disintegration.[44]

The directly compressible sublingual tablet formulation contains directly compressible and water soluble excipients, a super disintegrant, and lubricants. It may also contain microcrystalline cellulose, a dry binder, buffers, surface-active agents, sweeteners, and flavors. Sugar-based excipients are widely used as bulking agents because of their high aqueous solubility, sweetness, pleasant feeling in the mouth, and good taste-masking.[45] Nearly all sublingual formulations incorporate some saccharide-based materials. The choice of a specific disintegrant and its quantity are critical for achieving quick disintegration and dissolution rates. If required during formulation development, effervescent agents are used to increase the disintegration and dissolution rates of certain sublingual tablet formulations.[46]

Several novel approaches of incorporating super disintegrants and other soluble and/or insoluble excipients to obtain rapid dissolution and adequate mechanical strength are reported in literature.[47] One example is the *Flashtab technology*® of multiparticulate actives (coated crystals and uncoated or coated microgranules). In these sublingual tablet formulations, the simultaneous presence of a disintegrant with a high swelling or disintegrating force, defined as "disintegrating agent," and a substance with a low swelling force (starch, cellulose, and direct-compression sugar), defined as "swelling agent," was claimed to be the key factor for achievingrapid disintegration of the formulation. The tablet manufactured by this technology was reported to have adequate mechanical strength.[48]

Daiichi (Tokyo, Japan) developed a fast disintegrating formulation of moderate strength, using a combination of starch or cellulose, and one or more water-soluble saccharides. Erythritol was found to be the best sugar for this type of formulation, showing rapid disintegration that was not affected by the hardness of the tablet, good palatability coupled with sweetening, and a refreshing sensation in the mouth because of the occurrence of endothermic heat of dissolution.[49]

Compression molding

Tablets manufactured by the compression molding process exhibit rapid disintegration and dissolution, which is usually within 5–10 seconds. These formulations pose special challenges during handling and packaging, because of their poor mechanical strength, they may require special packaging for the purpose of shipping.[50] Alternatively, the mechanical strength of the formulations may be increased by using a suitable binder. However, the level of binder should be optimized to avoid any adverse effects on disintegration and dissolution of the formulation.

The formulations for the compression molding process typically consist of soluble excipients to impart arapid and complete dissolution, and taste

modifiers for patient compliance. Molded tablets can also be prepared directly from a molten matrix, in which the drug is dissolved or dispersed (heat molding), or by evaporating the solvent from a drug solution or suspension at normal room pressure which is called no vacuum lyophilization.[51]

The process of compression molding involves moistening of the formulation blend with a suitable solvent which is usually hydro-alcoholic, followed by molding into tablets under low pressure after which the moist tablets are finally dried. The lower compression pressure employed for molding and drying of the moist tablet produces a highly porous tablet structure with enhanced dissolution.[52] The choice ratio and quantity of granulating fluids are critical to the physicochemical properties, performance, and stability of the formulation, and should be optimized. Several patented technologies are also available for the commercial manufacture of compression molded sublingual tablet formulations.[53]

- Takeda (Osaka, Japan) developed a mixture containing a combination of starches and sugars, which after blending with the active pharmaceutical ingredient and wetting with a suitable amount of granulating fluid, can be compression molded. The formulations manufactured from this proprietary mixture were reported to have sufficient mechanical strength and exhibit fast disintegration.[54]
- Novartis Consumer Health (Basel, Switzerland) filed a patent application for tablets prepared by dispensing the drug solution or suspension into molds, evaporating the solvent from the molds by heating under reduced pressure, or microwave radiation, and then sealing the dried units directly in the mold.[55]
- Nippon Shinyaku (Kyoto, Japan) compression-molded and dried a kneaded mixture containing drug and a water-soluble sugar. This process claimed to impart a sufficient physicochemical stability to the tablet, good appearance, and dissolution time of less than 30 s in the sublingual region.[56]

Freeze drying

The process of freeze drying (lyophilization) is expensive, time-consuming, and produces tablets of poor mechanical strength. For these reasons, it is not a method which is used commonly to manufacture sublingual tablets. However, it has certain advantages over other processes, as the tablets made by this process have high porosity, and when placed under the tongue disintegrate and dissolve instantly. It is a process of choice for products that are unstable in nature or are thermolabile.[57]

The process involves of lyophilization involves lowering the temperature of the drug in an aqueous medium to below freezing, followed by the application of a high-pressure vacuum. To extract the water in the form of a vapor, which is collected as ice on a condenser, a gradual temperature rise is applied during the drying process.[58] The product temperature at the ice sublimation interface and the temperature during formulation collapse are critical to obtain a freeze-dried cake of the drug which has optimum specifications. This process helps to retain the physical structure and preserves the material during storage or transport.[59]

The resulting formulations have a low weight and have highly porous structures that allow rapid dissolution or disintegration. The freeze-drying process may result in a product with anamorphous structure, leading to an enhanced dissolution rate. However, tablets formulated using the freeze drying process possess poor stability at elevated temperatures and humidity conditions.[60]

Hot melt Extrusion

In the production of pharmaceutical formulations, a homogeneous and consistent mixing of multiple formulation ingredients is required. In the production of pharmaceutical formulations, which require homogeneous and consistent mixing of multiple formulation ingredients, a twin screw extruder is used because the rotation of the intermeshing screws provides better mixing to produce a homogeneous solid containing finely dispersed drug

particles, or a solid-solution of drug in polymer.[61] This can improve the dissolution rate and bioavailability of poorly-water soluble drug formulations. A uniformly distributed active pharmaceutical ingredient is also a pre-requisite for the production of drug-eluting devices with intra and inter-batch reproducibility of drug-release kinetics.[62]

Melting is accomplished by frictional heating within the barrel, and for twin-screw extruders, as the materials undergo shearing between the rotating screws and between the screws and the wall of the barrel as they are conveyed. The barrel is also heated with heaters mounted on the barrel, or cooled with water. The barrel section temperatures are usually optimized so that the viscosity of the melt is low enough to allow conveying down the barrel and proper mixing, while keeping temperatures low enough to avoid thermal degradation of the materials.[63]

The screws of a twin screw extruder are usually to provide different types of mixing and conveying conditions at various zones in the barrel.[64] During product development, modular screws with multiple elements fitted on a common shaft, allow the tailoring and optimization of the screw design for each product. Sections of the screw can be designed to perform particle-size reduction and conveying functions based on the specifications of the process.[65]But, hot melt extrusion is not exactly a viable process for the formulation of sublingual tablet dosage forms which contain thermolabile active pharmaceutical ingredients.[66]

Considerations critical to product quality

To develop a sublingual tablet that can impart the desired physicochemical and mechanical properties of the drug at the site of absorption, it is crucial to understand, control, and monitor the following critical to quality attributes: particle size of API, wetting time, disintegration and dissolution, content uniformity, hardness, friability, size and weight variation, stability, texture and taste masking, etc.[67]

Most of these tests are universal quality evaluations of conventional tablet dosage forms and are equally relevant for sublingual tablets.[68] However, the management of ailments and conditions of use for sublingual tablets require a very short residence time in the oral cavity. This critical attribute specifically calls for fast disintegration, dissolution, and absorption of the dosage form resulting in a quick onset of therapeutic response.[69]

The drugs that are administered sublingually generally have low solubility. Therefore, to enhance dissolution, particle size reduction and control over the particle size of the API is very important especially with drugs which have low solubility.[70,71] However, a tighter control on particle size of API is desirable in sublingual drug products to maintain a reproducible quality and performance of the drug product in view of the limited window of dissolution and absorption time.[72]

The conditions that exist in the oral cavity for disintegration and dissolution of sublingual tablets are considerably different when compared to conventional oral tablets. For this reason, the compendial methods used for disintegration and dissolution testing are not suitable for sublingual tablets because the compendial methods for disintegration and dissolution tests were developed to test the *in vitro* performance of tablets developed for disintegration and dissolution in the stomach following oral ingestion.[73] Other specialized tablets, such as modified-release, sustained release or enteric-coated tablets, may also partly release the drug in the stomach. In contrast, sublingual tablets are designed to completely disintegrate and dissolve in the oral cavity under the tongue.[74]

To address this critical difference, various researchers have proposed approaches to test disintegration and dissolution of sublingual tablets. Some of these approaches make use of thephysiological conditions of the oral cavity as a guide in testing disintegration and dissolution of sublingual tablets.[75]

One such disintegration test employs a 10 cm diameter Petri dish filled with 10 ml of water that contains eosin, a water-soluble dye. A 10 cm diameter circular tissue paper is placed in the Petri dish. The

tablet is carefully placed in the center of the dish and the time for the tablet to completely disintegrate into fine particles is noted as the disintegration time. This methodis widely used to test the ability of the sublingual tablets to disintegrate and dissolve in a minimal quantity of water, which is more illustrative of the moisture available under the conditions of use.[76]

Another popular *in-vitro* test method involves a texture analyzer (TA) instrument to accurately determine the disintegration time. In this method, a tablet under constant force is immersed in a defined volume of water and the time for the tablet to disintegrate is determined by measuring the distance the probe travels into the tablet.[77] The time-distance profiles generated by the TA software enable the calculation of the beginning and end of disintegration time. The influences of the applied force, the volume of water, and water temperature are the critical experimental conditions.[78]

The palatability of a sublingual formulation, especially those containing APIs that have an unpleasant taste, is another critical factor for patient compliance as the drug product disintegrates, dissolves, and is absorbed in the oral cavity. Various taste-modifying techniques are reported in the literature including sweeteners, flavoring agents, inclusion and molecular complexes, granulation, salt formation, pro-drug, viscosity modifiers, solid dispersions, and the use of lipoproteins among others.[79]

CONCLUSION

This review illustrates that there are a number of commercially available sublingual formulations which are manufactured using various technologies. The information which is available publicly on sublingual tablets implies that this particular dosage form has a very good potential to enhance drug delivery for the treatment of a number of conditions. In most reported cases and research studies, it has been shown that sublingual dosage forms not only improve patient compliance, but also reduce the time for onset of therapeutic response, and considerably increase the bioavailability of the drug when compared to conventional orally administered tablets.

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