

Overview on Sublingual Tablets

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ABSTRACT

The demand for fast disintegrating tablets has been growing during the last decade, due to the characteristics of fast disintegrating sublingual tablets for the potential emergency treatment. The sublingual course is a quick onset of activity and preferred patient consistency over orally ingested tablets. Sublingual from the Latin for "under the tongue", alludes to the pharmacological course of the organization by which drugs diffuse into the blood through tissues under the tongue. Sublingual drug delivery can be an alternative and better route when compared to oral drug delivery as sublingually administered dosage forms bypass hepatic metabolism. 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.

Keywords: Sublingual Tablets, Better Bioavailability, Fast Disintegration, Tongue, Mucus.

INTRODUCTION

Sublingual from the Latin for under the tongue refers to the pharmacological route of administration by which drugs diffuse into the blood through tissues under the tongue [1].

Advantages [2]

- 1) Rapid onset of action is achieved as compared to the oral route.
- 2) The liver is bypassed and also drug is protected from metabolism due to digestive enzymes of the middle gastrointestinal tract
- 3) Improved patient compliance due to the elimination of associated pain with injections; administration of drugs in unconscious or incapacitated patients; the convenience of administration as compared to injections or oral medications
- 4) Low dosage gives high efficacy as hepatic first-pass metabolism is avoided and also reduces the risk of side effects.

- 5) The large contact surface of the oral cavity contributes to rapid and extensive drug absorption. Due to rapidity in action, these sublingual dosage forms are widely used in emergency conditions e.g. asthma. Rapid absorption and higher blood levels due to high vascularization of the region and therefore particularly useful for the administration of antianginal drugs.
- 6) They also present the advantage of providing fast dissolution or disintegration in the oral cavity, without the need for water or chewing

Disadvantages [3]

- 1) Since the sublingual administration of drugs interferes with eating, drinking, and talking, this route is generally considered unsuitable for prolonged administration.
- 2) Although this site is not well suited to sustained-delivery systems.

- 3) Sublingual medication cannot be used when a patient is uncooperative.
 - 4) The patient should not smoke while taking sublingual medication, because smoking causes vasoconstriction of the vessels. This will decrease the absorption of the medication.
 - 5) Various types of sublingual dosage forms are available but tablets, films, and sprays are in trends these days. For the preparation of these dosage forms, different methods are described depends upon the feasibility and advantages over the others.
 - 6) One disadvantage, in any case, is tooth staining and brought about by long term utilization of this technique with acidic or generally burning
- 2) **Binding to the Oral Mucosa:** systemic availability of drugs that bind to oral mucosa is poor.
 - 3) **pH and pKa of the Saliva:** As the mean pH of the saliva is 6.0, this pH favors the absorption of drugs that remain unionized. Also, the absorption of the drugs through oral mucosa occurs if the pKa is greater than 2 for acid and less than 10 for a base.
 - 4) **Lipophilicity of the Drug:** For a drug to be absorbed completely through the sublingual route, the drug must have slightly higher lipid solubility than that required for GI absorption is necessary for the passive permeation.
 - 5) **The Thickness of the Oral Epithelium:** As the thickness of the sublingual epithelium is 100-200 μm which is less as compared to buccal thickness. So the absorption of drugs is faster due to thinner epithelium and also the immersion of drugs in a smaller volume of saliva.

FACTORS AFFECTING THE SUBLINGUAL ABSORPTION [4]

- 1) **Solubility in Salivary Secretion:** In addition to high lipid solubility, the drug should be soluble in aqueous buccal fluids *i.e.* biphasic solubility of the drug is necessary for absorption.

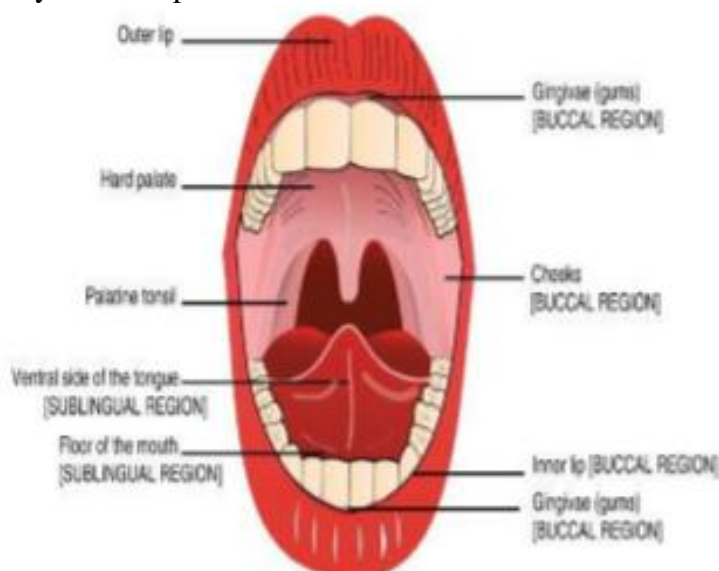


Fig. 1. Sublingual Route of Drug Administration

THE ANATOMICAL STRUCTURE OF THE ORAL MUCOSA

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

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 [4].

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. Oral submucosa has a

rich supply of blood vessels. Following absorption through the mucous membrane in the sublingual area, the drug directly diffuses into the venous blood which drains utilizing 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 as with commencement of therapeutic effect [4].

Table 1: Thickness and Surface Area of Oral Cavity Membranes

Oral Cavity Membrane	Thickness	Surface Area
Buccal Mucosa	500-600	5.2
Sublingual Mucosa	100-200	26.5
Gingival Mucosa	200	-
Palatal	250	20.1

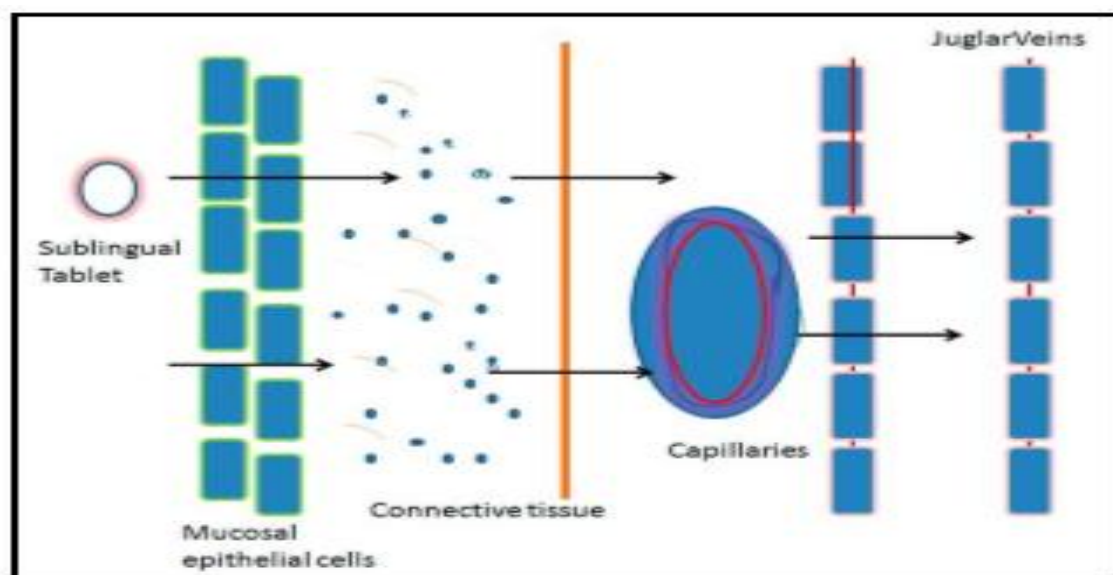


Fig. 2. Mechanism Showing Sublingual Absorption of Drugs

Sublingual drug administration is applied in the field of cardiovascular drugs, steroids, some barbiturates, and enzymes. It has been developing field in the administration of many vitamins and minerals which are found to be readily and thoroughly absorbed by this method.

Nutrition which is absorbed sublingually avoids exposure to the gastric system and liver, which means direct nutritional benefits particularly important for sufferers of gastrointestinal difficulties such as ulcers, hyperactive gut, coeliac disease, those with compromised

digestion. Drugs like cardiovascular drugs such as nitrites and nitrates, analgesics such as morphine, antihypertensive such as nifedipine, bronchodilators such as fenoterol could be administered successfully through sublingual route to show their rapid onset of action. Treatment of angina pectoris, hypertension, and antiatherosclerotic activity could be done effectively with the sublingual dosage form because it offers the fast release of drugs from the formulation and it reaches the systemic circulation directly which bypasses the first-pass metabolism of drugs. Fast disintegrating sublingual tablets could be used for potential emergency treatment. The demand for fast disintegrating sublingual tablets has been increasing day by day because of the swallowing difficulties of geriatric and pediatric patients. Because of easy administration and better patient compliance, fast disintegrating sublingual formulations have become popular as NDDS (Novel Drug Delivery System).

Drugs like lisinopril could be delivered through a sublingual route for the treatment of hypertension which is caused by obesity, stress, decreased physical activity, increased salt intake, and decreased calcium and potassium intake. Treatment of cardiovascular disease could be done effectively because it offers faster disintegration of tablets, faster onset of action, and rapid absorption of drugs by sublingual mucosa blood vessels. Moreover, drug candidates that undergo pregastric absorption when formulated as ODT may show increased oral bioavailability. The sublingual route is mostly useful for the fastest onset of action as in the case of angina pectoris. The use of an ODT formulation of ondansetron has been found to be helpful in the treatment of children as young as 6 months of age suffering from gastroenteritis and dehydration [5].

Types of Sublingual Tablets

- 1) Fast disintegrating sublingual tablets
- 2) Bioadhesive sublingual tablets
- 3) Lipid matrix sublingual tablets
- 4) Sublingual vitamins tablets
- 5) Sublingual immunotherapy.

MATERIALS AND METHODS

Glimepiride RS and acetonitrile were obtained from Alpha Chemika, India; sodium dihydrogen phosphate, phosphoric acid, and methanol obtained were from Merck [5].

Methods of Preparation [2]

Following methods can be used to prepare sublingual tablet

- 1) Direct compression Method
- 2) Compression molding
- 3) Freeze-drying

Direct Compression Method

This is a commonly used method for the preparation of sublingual dosage forms and it is a simple and most economical method. The direct compression method is best suitable for heat-labile drugs. In this method, we are using directly compressible and soluble ingredients, lubricant, and a super disintegrant (*For example: Crospovidone, Microcrystalline cellulose, etc.*), dry binder, sweeteners, and flavors.

Compression Molding

Tablets produced by this method will disintegrate and dissolved rapidly (within 4 to 11 sec). The disadvantage of this method is tablets having poor mechanical strength, to overcome this problem binders are added to formulation blend.

Freeze-Drying

This is costly and consumes more time compared to direct compression; this method produces tablets of poor mechanical strength. Tablets produced by this method will have high porosity and

dissolve instantly. This method is suitable for heat-sensitive drugs.

Table 1. Commercially Available Sublingual Tablets

Active Ingredients	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
Isascorbide Dinitrate	Imdur	Astrazeneca
Nitroglycerin	Nitrostat	Pfizer
Zolpidem tartrate	Intermezzo	Purdue Pharma

CONCLUSION

The review states that a number of sublingual manufacture in various technologies. The study let out that sublingual tablets are proved better for patient compliance and a better way of drug delivery for pediatrics and geriatrics patients. and it also gives the rapid on set of action because of the systemic circulation through capillaries present in the sublingual cavity. these tablets overcome the difficulties in swallowing.

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