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SUBLINGUAL DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT:

The study explores the efficacy and advantages of sublingual drug delivery as an alternative to traditional oral and parenteral routes, particularly for patients suffering from dysphagia. Sublingual administration leverages the high permeability and vascularization of the oral mucosa, allowing for rapid absorption and onset of pharmacological effects while bypassing first-pass metabolism. The research highlights the anatomical structure of the oral mucosa, detailing the varying absorption capabilities of the sublingual, buccal, gingival, and palatal regions. It discusses the formulation requirements for sublingual tablets, emphasizing the importance of drug properties such as taste, molecular weight, and stability. Furthermore, the paper addresses the advantages of sublingual delivery, including enhanced patient compliance and suitability for emergency situations, while also acknowledging its limitations. The review presents commercially available sublingual medications and concludes that sublingual drug delivery is particularly beneficial for short-acting medications, thereby improving therapeutic outcomes for patients with swallowing difficulties.

KEY WORDS: Dysphagia, Oral Mucosa, Sublingual Gland, Direct Compression.

INTRODUCTION:

Medications have been used for topical application on the mucosa for many years. However, there has been a growing interest in utilizing the oral cavity as a means to deliver drugs into the systemic circulation. The sublingual route for drug delivery has developed as a method to achieve a rapid pharmacological effect.

Dysphagia, or difficulty in swallowing, is a prevalent issue across all age groups, particularly among the elderly, children, and individuals who may be mentally challenged, uncooperative, nauseated, or who are following restricted liquid intake or diets, as they struggle with these dosage forms.

Sublingual medications are placed under the tongue, allowing them to enter the systemic circulation directly through the ventral side of the tongue and the floor of the mouth. The drug is quickly taken up by the network of veins located beneath the oral mucosa and is then carried through the facial veins, the internal jugular vein, and the brachiocephalic vein before entering systemic circulation.

Given that the sublingual region of the oral cavity has the highest permeability within the buccal cavity, the sequence of permeability in this area starts with the sublingual region, followed by the buccal area (cheeks), and lastly the palatal region. This ranking is primarily determined by the relative thickness and the degree of blood supply to each specific area.

The sublingual method typically leads to a quicker onset of effects compared to tablets taken orally, as the portion absorbed via the sublingual blood vessels avoids the first-pass metabolism in the liver.

Sublingual tablets are generally small and flat, lightly compressed to retain softness. These tablets need to dissolve rapidly to allow for quick absorption of the active pharmaceutical ingredient (API), and they are formulated to dissolve in a small amount of saliva; once the tablet is placed under the tongue, the patient should refrain. Sublingual formulations have been created for various purposes, including migraine treatment (where quick relief is crucial) and mental health conditions (where adherence is key for managing long-term issues like depression and schizophrenia).

The sublingual method offers 3 to 10 times the absorption of medication compared to the oral route and only to hypodermic injection in this regard. The sublingual method is particularly suitable for medications with a short duration of action.

The majority of medications that are delivered sublingually are classified as antianginal medications. The goal of providing an instant pharmacological effect led to the development of systemic drug delivery via the sublingual route.

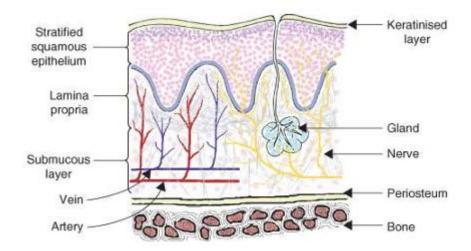
ORAL MUCOSA:

The oral mucosal lining offers an improved pathway for the local and systemic delivery of different medications and for treating certain diseases. This method of drug administration presents several distinct benefits over enteral and parenteral methods due to its rich blood supply, rapid onset, enhanced bioavailability, evasion of first-pass metabolism and food interactions, increased patient adherence, and ease of self-administration.

The absorption of drugs in the oral mucosa is influenced by (a) the permeability of the oral mucous membrane and the structure of the tissues beneath,

(b) the physicochemical characteristics of the drugs, and (c) the design of the formulation. This review emphasizes the last two aspects, as grasping these factors allows for the identification of drug candidates appropriate for oral mucosal administration and enhances drug delivery.

ANATOMICAL STRUCTURE OF THE ORAL MUCOSA:

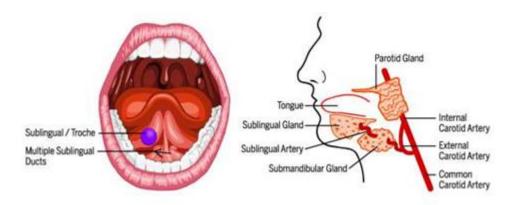


There are four distinct parts of the mouth cavity that can absorb drugs: the sublingual, buccal,

gingival, and palatal regions. The histological and biochemical characteristics of the mucosal membrane, as well as its ability to retain the dosage form f or a prolonged amount of time

order to facilitate complete drug absorption, differ across these regions. The buccal membrane along the cheeks and the sublingual membrane on the flo or of the mouth under the tongue are commonly used for systemic drug distribution. The mucosal lining is composed of three distinct layers. The topmos t layer is the epithelial membrane, a protective barrier composed of stratified squamous epithelial cells. The innermost layer of the basement membrane is where the epithelium gets resupplied.

SUBLINGUAL GLANDS:



Salivary glands are located beneath the tongue on the floor of the mouth. Another name for them is sublingual glands. They create mucin, which leads to the production of saliva. Because saliva is produced by the glands and is essential for chewing and swallowing food, the inside of the mouth stays moisturized. When the glands create fluid, it mixes with the meal, making it easier to chew.

Low salivary production can make it difficult to swallow meals and increase the risk of food getting stuck in the throat. It is possible to say that absorption is exactly proportional to layer thickness since it involves the transport of the medication from the site of administration into the systemic circulation. This is how the medication is absorbed, buccal > gingival > palatal > sublingual. The sublingual route can cause a rapid beginning of effect due to its high permeability and robust blood supply, allowing for frequent dosing regimens and the introduction of drugs with short delivery periods.

SUITABILITY OF DRUG FOR PREPARATION OF SUBLINGUAL TABLET:

- No bitter taste.
- Dose lowers than 20 mg, e.g. nifedipine.
- Small to moderate molecular weight.
- Good stability in water and saliva.

- Partially no ionized at the oral cavities pH.
- Sublingual dosage forms are appropriate for medications that are unstable when administered parenterally.
- Should have lower bio availability.
- Drugs that are not appropriate for sublingual tablets are frequently dosed.
- Ability to permeate oral mucosa.

ADVANTAGES:

- Compared to the oral method, a rapid commencement of action is attained.
- The intermediate gastrointestinal tract's digestive enzymes prevent the liver from being metabolized and shield the medication from doing so.
- Better patient compliance since injection-related pain is eliminated; pharmaceuticals can be administered to patients who are unconscious or incapable of doing so; and administering drugs is more convenient than using injections or oral pills.
- > Because hepatic first pass metabolism is prevented and side effect risk is decreased, low dosage results in great efficacy.
- The mouth cavity's vast contact surface aids in the quick and thorough absorption of drugs.
- > These sublingual dose forms are frequently utilized in emergency situations because of their quick action.
- Because of the region's strong vascularization, there is rapid absorption and increased blood levels, making it especially helpful for administering antianginal medications.
- > They also have the benefit of quickly dissolving or disintegrating in the mouth without the need for chewing or water.

DISADVANTAGES:

- Sublingual medication administration is generally regarded as inappropriate for extended administration since it disrupts speech, eating, and drinking.
- ➤ However, sustained-delivery methods are not a good fit for this site.
- Sublingual medication cannot be given to a patient who is not cooperative. Because
 - The patient should abstain from smoking while taking sublingual medication
 - Since smoking causes the capillaries to contract.

This will decrease the absorption of the drug Although there are many other kinds of sublingual dosage forms, tablets, films, and sprays are now popular. Various techniques are given for the creation of these dosage forms, depending on their viability and relative benefits.

PREPARATION OF SUBLINGUAL TABLETS:

DIRECT COMPRESSION:

The direct compression process is widely used in the commercial manufacture of sublingual tablets. Because it uses materials that are easily combined and don't need further granulation procedures before lubrication and compression, it is an easy and economical process. Direct compression-made sublingual tablets have a respectably quick disintegration rate and good mechanical strength.

A super disintegrant, lubricant, and directly compressible soluble excipients are all included in the formulation of the directly compressible sublingual tablet. Additionally, it could include buffers, surface-active agents, sweeteners, flavors, dry binder, and microcrystalline cellulose. Because of their high water solubility, sweetness, agreeable mouthfeel, and effective flavor masking, sugar-based excipients are frequently utilized as bulking agents.

ADVANTAGES:

- Low labor input.
- Dry process.
- Fewest processing steps.

DISADVANTAGES:

- > During handling of dry materials static charge may form which may present uniform distribution of drug.
- > Direct compression diluents may interact with the drug. For example, amine drug with Lactose produce discoloration of tablet.

COMMERCIALLY AVAILABLE SUBLINGUAL TABLETS:

DRUG	CATEGORY	DOSE
Fentanyl citrate	Opioid Analgesic	50mg, 100mg
Buprenorphine	Opioid Analgesic	2mg, 8mg
Lorazepam	Anti-anxiety	1mg, 2mg
Zolpidem tartrate	Sedative/Hypnotic	5mg, 10mg
Isosorbide dinitrate	Vasodilator	2.5mg, 5mg, 10mg
Nitroglycerine	Anti-anginal	0.3mg, 0.4mg, 0.6mg

CONCLUSION:

The sublingual method of drug delivery offers a highly efficient option for rapid systemic absorption, especially advantageous for individuals who struggle with swallowing. By utilizing the distinctive anatomical and physiological characteristics of the oral mucosa, sublingual medications improve patient adherence and deliver a quick onset of action, making them particularly suitable for medications with a short duration of action and has proven effective for various drugs including antianginal medications.