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Review on Sublingual Tablet

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Abstract: Objective: As sublingually given dose forms avoid hepatic metabolism, sublingual medication delivery can be an alternate and superior method to oral drug delivery. For some medications, particularly those prescribed for the treatment of acute diseases, a quick onset of pharmacological activity is frequently required. Sublingual pills dissolve quickly, and the major saliva available is typically enough to achieve dosage form disintegration along with enhanced dissolving and increased bioavailability.

Findings: Comparing sublingual pills to traditional dosage forms, it was discovered that the former had superior qualities. Due to their rapid breakdown, tablets taken sublingually had more bioavailability, a quicker onset of action, and improved dissolving characteristics. Rapid disintegration was made possible by the addition of super-disintegrants, and this method can be applied to the treatment of urgent or acute disorders.

Conclusion: To make sure a quick onset of action, higher patient compliance, and increased bioavailability, sublingual tablets or any sublingual dosage form might be used. Drugs that undergo significant first pass metabolism or degradation in the GIT can be administered sublingually. When compared to normal oral tablets, drugs given sublingually typically have improved bioavailability, which leads to dose reduction.

Keywords: Bioavailability, Sublingual, Disintegration.

I. INTRODUCTION

Sublingual drug delivery developed out of the need to give a quick onset of pharmacological impact. Dysphasia (difficulty swallowing) affects people of all ages, but it is particularly prevalent in the elderly, children, and patients who are intellectually impaired, recalcitrant, queasy, or on restricted liquid intake/diets [1,2]. Sublingual translates as below the tongue. Sublingually administered medications penetrate the ventral surface of the tongue and the floor of the mouth, directly entering the systemic circulation. The medication quickly enters the reticulated vein beneath the mouth mucosa, travels through the internal jugular vein, face veins, and braciocephalic vein, and is subsequently emptied into the systemic circulation. The most permeable portion of the buccal cavity, given the oral cavity, is the sublingual region. Sublingual, buccal (cheek), and palatal areas have lower buccal cavity permeability than one another [3].

Solid drugs can be taken orally as tablets, powders, capsules, cachets, or capsules. Even in the case of prolonged action preparations, which technically include the equivalent of numerous conventional doses of medication, these dosage forms are known together as solid unit dosage forms because they contain an amount of medication that is administered as a single unit [4]. The medication that the stomach absorbs travels to the portal vein-connected mesenteric circulation. Therefore, oral absorption prevents first pass metabolism. The sublingual pills are typically tiny, flat, and lightly crushed to maintain their softness. To enable the medicine to be absorbed, the tablets need to disintegrate fast. After the tablet is placed in the mouth beneath the tongue, the patient should refrain from eating, drinking, smoking, and possibly talking in order to keep the tablet in place. It is designed to disintegrate in small amounts of saliva. The need for quick start of pharmacological activity led to the development of sublingual systemic drug delivery [5]. Short-acting medications are perfect candidates for the sublingual method. However, not all compounds are permeable and accessible to oral mucosa. The majority of medications supplied via the sublingual route are absorbed by simple diffusion; in this case, the sublingual area behaves like a litmus paper rapidly soaking up the substances. The majority of medications that are taken orally come into the antianginal drug category. In order to give an early beginning of pharmacological impact, systemic drug delivery via the sublingual route was developed. When compared to pills taken orally, the sublingual route typically results in a quicker beginning of action, and the part absorbed through the sublingual blood vessels skips the hepatic first pass metabolic process [6].

Children frequently experience difficulties swallowing due to their immature neurological and muscular systems, but these issues can be readily resolved with the aid of fast-dissolving sublingual pills. The oral route of drug administration is thought to be the most common one because it has advantages over other routes such being the most natural, simple, convenient, and safe way to deliver pharmaceuticals, having more design freedom in dose forms, being simpler to produce, and being less expensive.

Sublingual tablets could be manufactured successfully by choosing the right pharmaceutical excipients in the right quantity, in combination with the best manufacturing procedures [7]. Sublingual drug delivery developed out of the need to give a quick onset of pharmacological impact. Dysphasia (difficulty swallowing) affects people of all ages, but it is particularly prevalent in the elderly, children, and patients who are intellectually disabled, uncooperative, queasy, or on restricted liquid intake or diets [8, 9,10]. Sublingual is a term for below the tongue. The medication that the stomach absorbs travels to the portal vein-connected mesenteric circulation. Therefore, oral absorption prevents first pass metabolism. The sublingual pills are typically tiny, flat, and lightly crushed to maintain their softness. To enable fast API absorption, the tablets must disintegrate quickly. After the tablet is inserted in the mouth behind the tongue, the patient should refrain from eating, drinking, smoking, and possibly talking in order to keep the tablet in place. It is designed to disintegrate in small amounts of saliva. The need for quick start of pharmacological activity led to the development of sublingual systemic drug delivery [11,12,13,14].

II. ORAL CAVITY OVERVIEW

The outermost layer of stratified squamous epithelium makes up the oral mucosa. A basement membrane, a lamina propria, and the sub mucosa make up the layers below this. In terms of permeability, the oral mucosa falls somewhere between the intestinal mucosa and the epidermis. Because distinct areas of the oral cavity have varied structures and functions, there are significant variances in the permeability between them [15].

III. SUBLINGUAL GLAND

A sublingual glands, which are also referred to as sublingual glands, are located on the oral cavity's floor, or beneath the tongue. These glands create mucin and aid in saliva production, both of which are critical for breakdown. Additionally, it offers lubrication to make chewing and swallowing of food easier. It is important to recognize the sublingual glands' role in lubrication and binding. As food is chewed, a gland secretion mixes with it, making the substance slick and simple to swallow. The masticated meal may easily pass through the throat and into the digestive tract since it contains saliva. Low saliva production increases the likelihood that food will become lodged in the throat and can significantly increase the difficulty of swallowing. These glands not only lubricate, but also support the promotion of healthy dental hygiene [16]. The lipid solubility, which affects the permeability of the solution (also known as osmosis), the ionization, and the drug's molecular weight all have an impact on absorption. Endocytocis is the mechanism through which the medication is absorbed by the oral epithelial cells. It Is doubtful that the stratified epithelium as a whole exhibits the same process. However, it's thought that acidic stimulation of the salivary glands and the ensuing vasodilatation make it easier for substances to be absorbed and transported through the circulatory system. A mucous membrane that Is lined with mucous glands and covered in squamous epithelium lines the inside of the mouth. Comparable to buccal mucosa is the sublingual mucosal tissue [17,18].

IV. PERMEABILITY

The intestinal mucosa and the epidermis are both relatively leaky epithelia, as is the mouth mucosa. The buccal mucosa's permeability is thought to be 4–4000 times larger than the skin's. Sublingual mucosa is more permeable than buccal mucosa, and the degree of keratinization of these tissues decreases in that order, with buccal mucosa being thicker and less keratinized than sublingual mucosa [19].

V. FACTORS AFFECTING ON SUBLINGUAL ABSORPTION[20]

1) *Drug Lipophilicity:* Passive permeation requires a medicine to have a little higher lipid solubility than that needed for GI absorption in order for it to be entirely absorbed through the sublingual route.
2) *Binding To Oral Mucosa:* Drugs that bind to oral mucosa are not widely available.
3) *pH Of The Saliva:* The average pH of saliva is 6.0, which facilitates the absorption of unionized medicines.
4) pKa OF THE SALIVA: If the pKa is greater than 2 for an acid and less than 10 for a base, the medicines are absorbed through the mouth mucosa.
5) *Solubility Of Salivary Secretion:* The medicine should also be soluble in aqueous buccal fluids, or biphasic solubility, in addition to high lipid solubility, as this is important for absorption.
6) *Partition Coefficient of Oil To Water:* Through the oral mucosa, substances with favorable oil to water partition coefficients are easily absorbed. The best oil-water partition coefficient range for sublingual medication absorption is thought to be 40–2000.

7) *Oral Epithelium Thickness:* As opposed to buccal thickness, the sublingual epithelium has a thickness of 100–200 µm. As a result of the thinner epithelium and the drug's immersion in a smaller volume of saliva, the absorption of medicines is accelerated.

VI. ADVANTAGES [21,22,23]

1) Compared to taking a medication orally, there is a quicker commencement of action.
2) Drug administration in unconscious or incapacitated patients; improved patient compliance since injection-related pain was eliminated; convenience of delivery compared to injections or oral meds.
3) Bypassing the liver and shielding the medication from metabolism are the middle gastro intestinal tract's digestion enzymes.
4) As hepatic first pass metabolism is avoided and the potential of side effects is decreased, low dosage results in high efficacy.
5) Additionally, they offer the benefit of quick dissolution or disintegration in the oral cavity without the need for chewing or drinking.
6) The mouth cavity's vast contact surface increases the rate and extent of medication absorption. These sublingual dose forms are frequently utilized in emergency illnesses, such as asthma, due to their quick action.
7) Due to the high amount of vascularization in the area, administration of antianginal medicines is made particularly useful due to the rapid absorption and increased blood levels.

VII. DISADVANTAGES [24]

1) While sustained delivery techniques are not a good fit for this site.
2) Sublingual administration is often viewed as being undesirable for continuous administration since it interferes with speaking, eating, and drinking.
3) Patient resistance prevents the administration of sublingual medicine.
4) Because smoking constricts the blood vessels, the patient shouldn't smoke when taking sublingual medication. The medication's absorption will be reduced as a result.
5) There are many different sublingual dose forms, but tablets, films, and sprays are currently popular. Different approaches are presented depending on their viability and advantages over the alternatives for the manufacture of these dosage forms.
6) Anyhow, one drawback of this procedure with acidic or generally burning medication and filler is teeth discoloration, which results from prolonged uses.

VIII. PHYSIOLOGICAL CRITERIA OF DRUG FOR SUBLINGUAL DRUG DELIVERY: [25,26,27,28,29,30,31]

Physiological properties of drug	Accepted range
Dose	Less than 20 mg
Taste	Not particularly bitter
Stability	Excellent stability in saliva and water
Molecular weight	Moderate
pka	• More than 2 for acidic drug • Less than 10 for basic drug
Log p	1.60 to 3.30
Lipophilicity	Lipophilic

IX. EVALUATION PARAMETERS

In addition to some specialized tests, evaluation parameters for the tablets listed in the pharmacopoeias must be evaluated. After being formulated according to a rule, the quality of the blend's physicochemical qualities often determines the quality of the tablet.

A. *Pre-Compression Study*

The flow and compressibility of the directly compressible tablet blends were tested for pre-compression investigations [32].

1) *BULK DENSITY (BD):* 2 g of the blend from each formulation was added to a 10 mL measuring cylinder after being lightly shaken to break up any agglomerates that may have formed. The volume is noted as the bulk volume [32].
   BD= Weight of powder/ Bulk volume
2) *TAPPED DENSITY (TD):* Following the determination of BD, a tapped density device was installed on the measurement cylinder. The powder was tapped 500 times to get the tapped volume. The tapping was repeated 750 more times after that, and the volume was recorded (the difference between the two volumes should be less than 2%). If it is greater than 2%, tapping is repeated another 1250 times, with the constant volume of taps being logged [32].
   TD= Weight of powder/ Tapped volume
3) *ANGLE OF REPOSE (θ):* According to the funneling procedure, the mixture was poured through the funnel's walls while it was fixed in place so that its bottom tip was exactly 2 cm above a hard surface. The mixture was poured up until the point at which the surface of the upper tip of the pile contacted the lower tip of the funnel [32].
   $\theta = \tan^{-1} h/r$
   (Where, θ= repose angle, h= height of heap and
   r= radius of base of heap)
4) CARL's INDENX (CI): [32]
   CI= (TD-BD) ×100 / TD
5) HAUSNER's RATIO (HR): [32]
   It is a figure that indicates how well a powder flows.
   HI= TD/BD

B. Post Compression Studies

1) *WEIGHT VARIATION TEST:* Twenty tablets were randomly chosen from each formulation, and their individual weights were precisely measured using an electronic scale. The acceptability of weight variation was then assessed.

The weight variation test's acceptable upper limit according to U.S.P. [33]

AVG. WEIGHT OF TABLET	ACCEPTABLE % CHANGE
80 mg or less	10
Less than 250 mg but more tan 80 mg	7.5
250 mg or more	5

2) *FRIABILITY TEST:* A friabilator was used to assess the friability of 20 tablets from each batch for 4 minutes at a speed of 25 RPM. The percentage weight reduction was then determined once the tablets had been dusted off and weighed again [34].
   % Friability= (initial wt. – wt. after friability) * 100/ initial wt.
3) *HARDNESS TEST:* Uses a hardness tester to assess the diametrically opposed crushing strength of tablets from each formulation [34].
4) *THICKNESS TEST:* Using a verniercalipers, the thickness of the tablets from each formulation was measured [35].

X. RAPID STABILITY TEST ON IMPROVED FORMULATION

Were transported in accordance with the recommendations of the International Conference on Harmonization (ICH). Tablets were kept at 45 °C ± 2 °C and 75 % ± 5 % RH in the final pack. The corresponding samples were taken out and assessed for post compression studies at the end of the 1st, 2nd, 3rd, and 6th M, which lasted up to 6 months [36].

XI. CONCLUSION

In accordance to the study, sublingual tablets had better drug delivery for juvenile and geriatric patients as well as greater patient compliance. Many medications, especially those that call for a quick onset of action, have been formulated for sublingual drug delivery. These tablets eliminate the issue with swallowing practical tablets. The target market now includes people who prefer water-free, handy tablets. Through a number of glands located in the sublingual cavity, the medication content of the tablets is absorbed into the bloodstream. Thus, a quick start to action is accomplished.

XII. ACKNOWLEDGMENT

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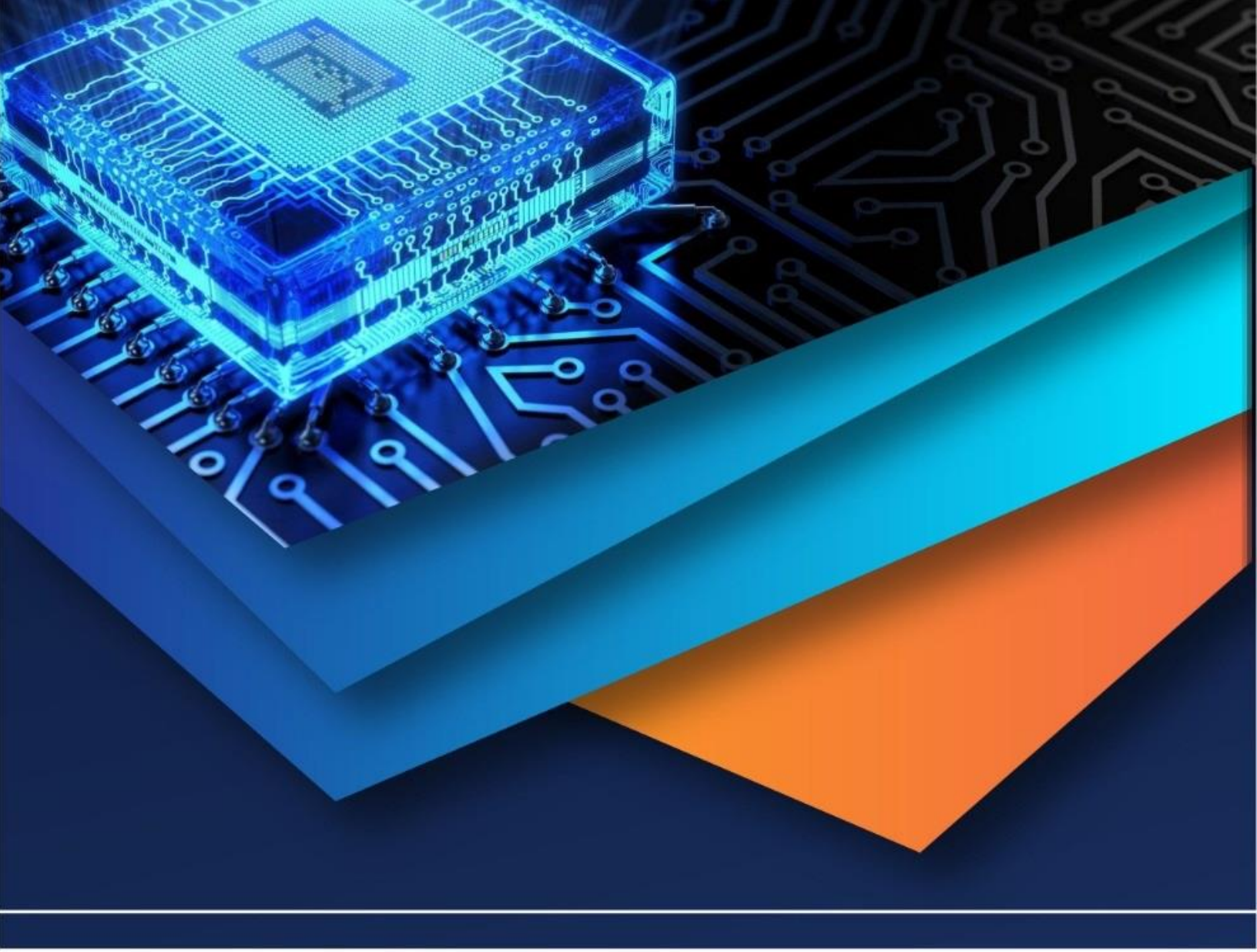

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