IJRAR.ORG E-ISSN: 2348-1269, P-ISSN: 2349-5138

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYTICAL REVIEWS (IJRAR) | IJRAR.ORG

An International Open Access, Peer-reviewed, Refereed Journal

SUBLINGUAL DRUG DELIVERY SYSTEM: A DETAILED REVIEW

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Abstract:

The current composition is concentrated on ideal characteristics, patented technologies, significant features and formulating styles including the use of super disintegrates, which achieve rapid-fire onset of action, better patient compliance and increased bioavailability. Sublingual tablets dissolve presently, releasing the medicine, within many seconds without the need of water and chewing. The ideal behind this review was to summaries the benefits of sublingual expression, medium of action, advantages of route of administration, factors affecting permeability of medicine, colorful in vitro evaluation parameters and commercially available sublingual lozenge forms. Different sublingual technologies address medicinal diligence and patient requirements to enhanced lifecycle and applicable dosing for pediatric, senior, psychiatric cases also cases with dysphagia. Accordingly, numerous scientific ways including snap drying, molding, spray drying, sublimation, direct contraction, mass extrusion, melt granulation system etc. have been employed for development of sublingual tablets. Due to its better stability and bioavailability, the sublingual route could be considered as a promising volition to oral and parenteral routes.

Keywords*: Sublingual tablets; Patient compliance; Sublingual formulation; Scientific techniques; sublingual drug delivery*

1. INTRODUCTION:

Lately there has been interest in exploiting the oral depression as a gate for delivering medicines to the systemic rotation. Oral mucosal medicine delivery is an indispensable system of systemic medicine delivery that offers several advantages over both injectable and enteral styles. Because the oral mucosa is largely vascularized, medicines that are absorbed through the oral mucosa directly enter the systemic rotation, by passing the gastrointestinal tract and first- pass metabolism in the liver. The oral route of administration is considered as the most extensively accepted route. The unique terrain of the oral depression offers its eventuality as a point for medicine delivery.

The nonstop stashing of slaver results in rapid-fire junking of released medicine and this may ask that the oral depression be confined to the delivery of medicines, which have a short systemic rotation. About 60 of all lozenges forms available are the oral solid lozenge form. The target spots for original medicine delivery in the oral depression include the following Buccal, Sublingual, Periodontal region, Tongue, Gum. Other desirable targeting spots conterminous to oral depression include pharynx, larynx, adenoids and tonsils. Within the oral depression, delivery of medicines via the membranes of the oral depression is classified into three orders

i. **Sublingual delivery** which is systemic delivery of medicines through the mucosal membranes lining the bottom of the mouth to the systemic rotation;

ii. **Buccal delivery** which is medicine administration through the mucosal membranes lining the cheeks and the area between the epoxies and upper and lower lips to the systemic rotation.

iii. **Original delivery** which is medicine delivery to periodontal, gingival, delivery for the original treatment of ulcers, bacterial and fungal infections and periodontal complaint[1].

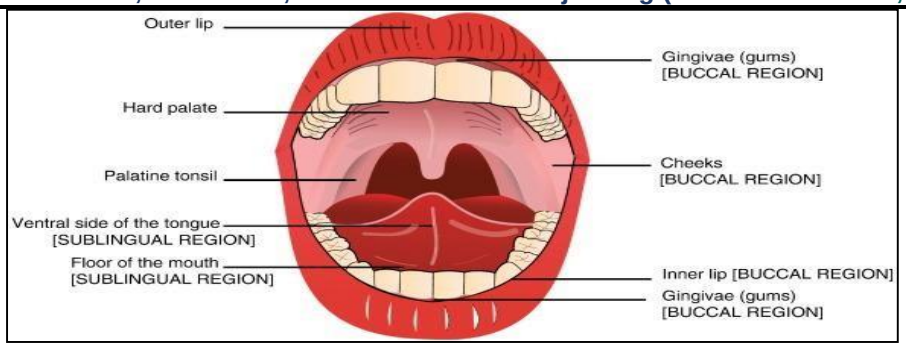


Fig.1., anatomy of oral cavity [2]

2. DIFFERENCE BETWEEN BUCCAL & SUBLINGUAL DELIVERY

Table 1: difference between sublingual and Buccal drug delivery

Sublingual drug delivery	**Buccal drug delivery**
Relatively permeable	Less permeable
Rapid absorption of low M.W. lipophilic compounds	Does not give rapid onset
Not for retentive systems	Highly suited for retentive systems Good for poorly permeating molecules, peptides or proteins
Dosage form comes in: SL sprays SL fast dissolving tablets	Dosage forms comes in: Adhesive tables Ashe patches
Sublingual (SL): Delivery through the mucosa of the ventral surface of the tongue and floor of the mouth under the tongue	Buccal: Delivery through the Buccal mucosa, the epithelial lining of the cheeks, the gums, the upper lips, and lower lips

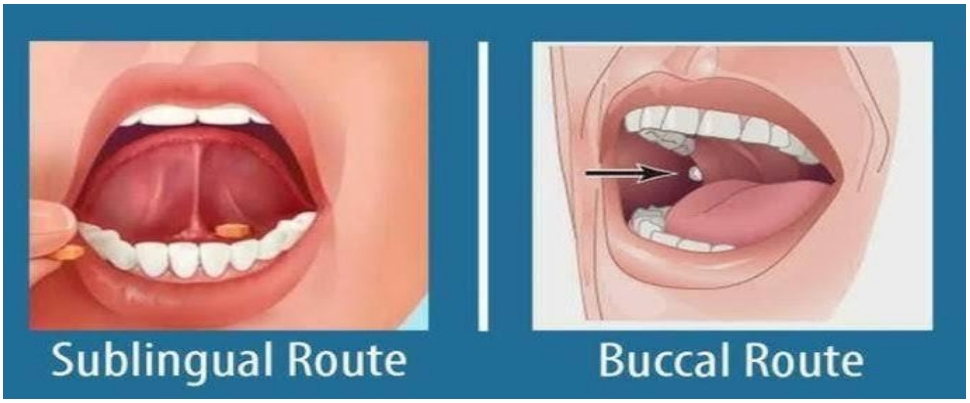


Fig 2. diagrammatic representation of Buccal and sublingual rout

3. SUBLINGUAL DRUG DELIVERY SYSTEM

Sublingual region means under the lingo also called pharmacological route of administration through which medicines diffused into the blood sluice through apkins of sublingual region. By this route direct contact of medicines with oral mucosa which leads the medicine to come directly into systemic rotation which leads to enhance bioavailability and permeability of expression. Dysphagia (difficulty in swallowing) which is a common problem of all age groups, children, and senior persons with uncooperative or persons on reduced liquid input have difficulties in swallowing etc. It's promising approach for prostrating this type of problems.

The medicine goes to hepatic first pass metabolism which results to increase bioavailability of medicine drug.

Sublingual medicine delivery is satisfying approach to remove these problems. The medicine percolated by this area is 5 to 10 times advanced than other delivery system and easy to surpass hypodermic injection. So, low slaver is substantially applicable which affect in tablet breakage in this area.

i. Some medicines suffer expansive first pass metabolism which results in poor bioavailability of its oral lozenge forms, that kind of medicines are suitable for sublingual lozenge form.

ii. medicines which are n't given in parenteral medication are given by sublingual route of administration. The immersion of the medicine through the sublingual route is 3 to 10 times lesser than oral route and is only surpassed by hypodermic injection. For these phrasings, the small volume of slaver is generally sufficient to affect in tablet decomposition in the oral depression. Sublingual immersion is substantially rapid-fire in action, but also short amusement in duration. In terms of permeability, the sublingual area of the oral depression is more passable than the buccal(impertinence) area, which in turn is more passable than the palatal (roof of the mouth) area. Sublingual products have been developed for multitudinous suggestions ranging from migraines (for which rapid-fire onset of action is important) to internal illness (for which case compliance is important for treating habitual suggestions similar as depression and schizophrenia.)[3]



Fig.3. sublingual drug delivery

3.1. Advantages of sublingual drug delivery:

1. Ease of administration to cases who refuse to swallow a tablet, similar as pediatric, senior cases and psychiatric cases.
2. Water is not needed for swallowing the lozenge form, which is accessible point for cases who are traveling and do not have immediate access to water.
3. The large contact face area of the oral depression contributes to rapid-fire and expansive medicine immersion.
4. It can lead to bettered patient compliance as the elimination of associated with injections reduces.
5. Good mouth feels property helps to change the introductory view of drug as “better lozenge”, particularly for pediatric cases.
6. Pregastric immersion can affect in bettered bioavailability and as a result of reduced lozenge, bettered clinical performance through a reduction of unwanted goods.
7. Provides advantages of liquid phrasings in the form of solid lozenge form. [4]

3.2. Disadvantages of sublingual drug delivery

1. Taste masking is a major problem associated with sublingual spray form.
2. It is not applicable for medicines that bear high blood situations or large boluses.
3. Sublingual delivery is not well suited to sustained- delivery systems as it interferes with eating, drinking and talking. [5]

4. DEVELOPMENT OF SUBLINGUAL TABLET FORMULATIONS:

For optimal sublingual expression development, it's necessary to understand the medium of medicine immersion, physicochemical and mechanical parcels of the medicine, function of the excipients in the expression, and taste- masking ways for better case compliance. Following sublingual administration, the medicines are absorbed across the mucous membrane by one of the following mechanisms. [7]

- Passive prolixity
- Active or carrier- intermediated transport
- Endocytosis.

4.1. Mechanism of sublingual absorption:

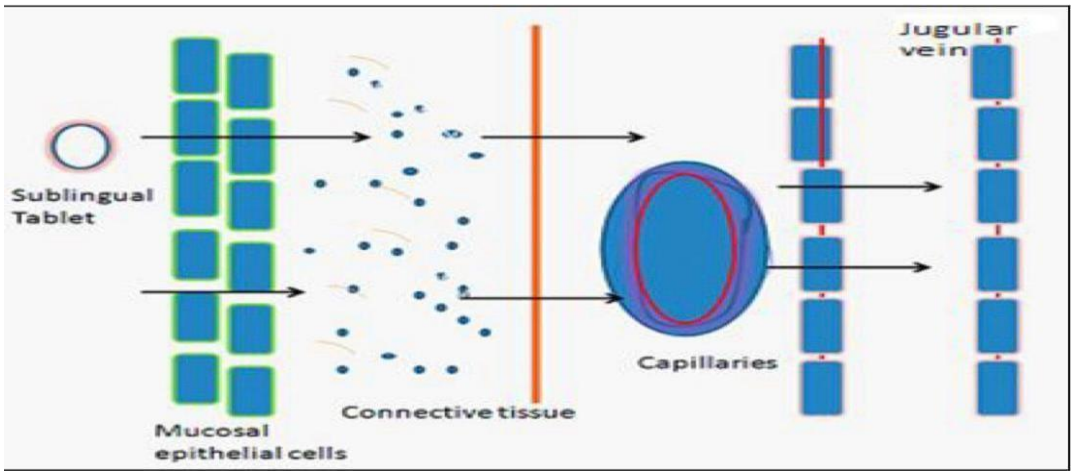


Fig 4., mechanism of absorption through sublingual mucosa [7]

The mucosal filling consists of three distinct layers. The remotest sub caste is the epithelial membrane, which consists of stratified scaled epithelial cells and has a defensive hedge function. The inmost sub caste of the epithelial membrane is called the basement membrane that replenishes the epithelium. Below the epithelium lies the lamella propria followed by the submucosa. The lamella propria is a doused and less thick sub caste of connective towel containing collagen and elastic fibers. The oral submucosa is also plushily supplied with blood vessels. The following immersion through the mucous membrane in the sublingual region, the medicine incontinently diffuses into venous blood. The venous blood from the sublingual region of the oral depression drains into a common box, which also drains via the internal jugular tone, the subclavian tone, and the brachiocephalic tone directly into the superior vena cava. therefore, venous return from these regions enters the systemic rotation, bypassing the pre-systemic medicine elimination, unlike in oral administration. [9]

It's believed that further acidic medium of the salivary glands, with arrangement of vasodilatation, makes easier immersion with uptake in blood sluice. Mouth area is lined with whole filling of mucous membrane which is place under a cover of scaled epithelium and have mucous glands. The salivary glands have lobules of cells through this slaver buried by salivary tubes in mouth. Three types of salivary glands are parotid, submandibular and sublingual gland which is located on the bottom of the mouth. The further acidic taste is, lesser stashing of salivary enzymes affair which help to avoid prospective detriment to acid - sensitive tooth(enamel) by bathing the mouth in abundant negating fluid. The sublingual roadway peregrination ahead to salivary glands and inventories to the neighboring muscles and to the mucous sub caste of the mouth, lingo and epoxies. [11]

4.2. Physicochemical properties of drugs.[7]

Table 2 lists the physicochemical parcels of some commercially available medicines administered sublingually. These parcels of the medicines grease their immersion by unresisting prolixity through the oral mucosa.

Table 2. physiochemical properties of sublingually administered drug:

Drug	Molecular weight	Largest dose**	Water solubility	pKa	Log P
Nitro-glycerine	227	0.6mg	1.8mg/ml	-5.6	0.94
Fentanyl citrate	336*	0.8mg	0.025mg/ml(citrate)	8.4	2.9
Buprenorphine	467.6	2-8 mg	Insoluble in water	8.24, 10.0	4.9
Asenapine maleate	285.8*	10mg	3.7mg/ml	8.6	4.9
Nicotine	162.234	4mg	Slightly soluble	8.21	0.99
Ergotamine tartrate	583.68*	2mg	Insoluble in water	6.3	2.4

*Molecular weight of the base

**largest dose for sublingual tablet

5. **FORMS**: [20]

Pharmaceutical medications for sublingual administration are manufactured in the form of:

1. **Sublingual tablets:** tablets which fluently melt in the mouth, dissolve fleetly and with little or no residue. Nitro- glycerin tablets are an illustration; the anti-emetic ondansetron is another.
2. **Sublingual strips:** analogous to tablets in that they fluently melt in the mouth and dissolve fleetly. Suboxone is an illustration of drug that comes in a sublingual strip.
3. **Multi-purpose tablets:** Answerable tablets for either oral or sublingual (or buccal) administration, frequently also suitable for medication of injections, Hydrostat(hydromorphone) and a number of brands of morphine tablets and cells.
4. **Sublingual drops:** a concentrated result to be dropped under the lingo, as with some nicocodeine cough medications,
5. **Sublingual spray:** spray for the lingo; certain mortal and veterinary medicines are allocated as similar.
6. **Lozenges:** goods a metered and case- controlled- rate combination of sublingual, buccal, and oral administration, as with the Acted fentanyl.
7. **Effervescent buccal or sublingual tablets:** this system drives the medicine through the mucous membranes important faster (this is the case in the stomach with carbonated or bouncy liquids as well) and is used in the Fentora fentanyl buccal tablet.

Fig 5., Sublingual forms

sublingual films **sublingual tablets** **sublingual drops**







6. DRUGS FOR SUBLINGUAL DRUG DELIVERY SYSTEM:

Sublingual medicine administration is applied in the field of cardiovascular medicines, steroids, some barbiturates and enzymes. It has been a developing field in the administration of numerous vitamins and minerals which are set up to be readily and completely absorbed by this system. Sublingually absorbed nutrition, which avoids exposure to the gastric system and liver, means direct nutritive benefits, particularly important for victims of gastro - intestinal difficulties similar as ulcers, hyperactive gut, coeliac complaint, those with compromised digestion, the senior and invalids. exemplifications of medicines administered by this route include antianginal like nitrites and nitrates, anti-hypertensive like nifedipine, anesthetics like morphine 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}[15]

6.1. Ideal Properties of Drug in Sublingual Drug Delivery System: [15]

- medicine should not bitter in taste.
- Cure should be lower than 20 mg, e.g., Nifedipine.
- Small to moderate molecular weight.
- Good stability in water and slaver.
- witnessing first pass effect e.g., ketotifen fumarate.
- medicine should not ionize at the pH of oral depressions.
- numerous medicine parcels that potentially affect the performance of sublingual tablets like solubility, demitasse morphology, flyspeck size, hygroscopicity, bulk viscosity, and compressibility of medicine.
- Parenterally unstable medications of the medicine are suitable for sublingual lozenge form

6.2. Excipients used in sublingual dosage forms: [16]

i) Binders
ii) Fillers
iii) Disintegrants and super disintegrants
iv) Antiadherants
v) Lubricant
vi) sweeteners and sugar-based excipients
vii) flavoring agents

7. SUBLINGUAL FORMULATION: [17]

7.1. Fast Disintegrating Sublingual Tablets:

The tablets which disintegrate or dissolve fleetly in case's mouth are accessible for the senior cases or youthful children with swallowing difficulties and in situations where drinkable liquids are n't available. Fast disintegrating tablet means a solid lozenge form that contains cure and disintegrates fleetly without water when kept under the lingo. It offers bettered convenience and are constantly preferred over conventional solid oral lozenge forms. Sublingual tablet led to notable enhancement over current treatment options for specific cases. The European medicinal agency commission of medicinal products for mortal use (CHMP) described

sublingual tablets as having-great advantage for children. The size, disintegrating time and taste play important part in marketable eventuality of expression. A fast- disintegrating time reduces any choking hazard and will also make it harder to resolve out the cure.

7.2. Bio tenacious Sublingual flicks:

This is rearmost conception of sublingual film grounded on collaborative fusions conforming of water answerable carrier covered with small patches of substances and bio tenacious polymer. With this it's possible to gain a rapid-fire dissolution in combination with bio tenacious reduction of medicine in the oral depression.

7.3. Sublingual Spray:

This are expression in which medicine is dissolved or dispersed in a detergent and filled in the vessel with metered stopcock and on deposit a suitable cure of medicine delivered through stopcock in a sublingual area.

7.4. Lipid Matrix Sublingual Tablets:

Lipid matrix sublingual tablets is lozenge form using creation in sublingual and liposomal technologies to produce a drug that put forward briskly and more complete immersion than other traditional oral routes of medicine delivery.

7.5. Sublingual Vitamin Tablets:

The sublingual vitamin that all croakers offer is vitamin B12 (cyanocobalamin). Vitamin- B12 is veritably helpful in our body's metabolism only taken by mouth.

7.6. Sublingual immunotherapy

It's a type of immunotherapy that have liquid drops of allergen excerpts delivered by in sublingual form. Sublingual immunotherapy is veritably important helpful in case of Seasonal Antipathetic Conjunctivitis (SAC) and imperishable Antipathetic Conjunctivitis (PAC).

8. FACTORS AFFECTING SUBLINGUAL ABSORPTION: [19]

a) **Thickness of oral epithelium**:
   a. As the consistence of sublingual epithelium is 100 - 200 µm which is less as compared to buccal consistence. So the immersion of medicines is briskly due to the thinner epithelium and also the absorption of medicine in lower volume of slaver.

b) **Lipophilicity of medicine:**
   a. For a medicine to be absorbed fully through sublingual route, the medicine must have slightly advanced lipid solubility than that needed for GI immersion is necessary for unresistant saturation.

c) **pH and pKa:**
   a. It is of the slaver as the mean pH of the slaver is 6.0, this pH favors the immersion of medicines which remain unionized. Also, the immersion of the medicines through the oral mucosa occurs if the pKa is lesser than 2 for an acid and lower than 10 for a base.

d) **oil painting to water partition measure:**
   a. It composites with favourable oil painting to - water partition portions are readily absorbed through the oral mucosa. An oil painting -water partition measure range of 40 - 2000 is considered optimal for the medicines to be absorbed sublingually.
   b. **Solubility in salivary stashing:** In addition to high lipid solubility, the medicine should be answerable in waterless buccal fluids i.e. biphasic solubility of the medicine is necessary for immersion.

e) **List to oral mucosa**: Systemic vacuity of medicines that bind to oral mucosa is poor.

9. METHODS OF PREPARATION OF SUBLINGUAL FORMULATION: [17]

Although several technologies are available to manufacture sublingual tablets, generally contraction molding, direct contraction, and indurate drying have been generally used for marketable manufacture of sublingual tablets. The contraction molding process has been used since the early nineteenth century for the medication of nitro- glycerin tablets. Presently, the direct contraction and indurate- drying styles are generally exploited for marketable manufacture of sublingual tablets.

9.1. Compression molding:

The phrasings for the contraction molding process generally contain answerable excipients to conduct quick and complete dissolution, and taste modifiers for patient compliance. Molded tablets have also been prepared directly from a molten matrix, in which the medicine is dissolved or dispersed (heat molding), or by sinking the detergent from a medicine result or suspense at room pressure (no vacuum lyophilization). The contraction molding process involves moistening of the expression mix with a detergent (generally hydro- alcoholic), followed by putrefying into tablets under low pressure. The wettish tablets are eventually dried. Several patented technologies are also available for marketable manufacture of contraction moldered tablets.

a) Takeda (Osaka, Japan) has developed an admixture containing a combination of beans and sugars. This admixture, after blending with the medicine and wetting down with a suitable quantum of water, can be contraction moldered. The tablets manufactured from this personal admixture are reported to have sufficient mechanical strength and parade rapid-fire decomposition

b) Novartis Consumer Health (Basel, Switzerland) has filed a patent operation for tablets prepared by allocating the medicine result or suspense into molds, sinking the detergent from the molds by heating under reduced pressure, or microwave oven radiation, and also sealing the dried units directly in the earth.

9.2. Direct contraction:

The direct contraction system is generally used for marketable manufacture of sublingual tablets. It's a simple and cost-effective process, as it employs constituents that can be mixed well and do n't bear farther granulation way previous to lubrication and contraction. Sublingual tablets manufactured by the direct contraction system parade good mechanical strength and nicely fast decomposition.

The directly compressible sublingual tablet expression contains directly compressible answerable excipients, a super disintegrant, and lubricant. It may also contain microcrystalline cellulose, dry binder, buffers, face active agents, sweeteners, and flavors. Sugar-grounded excipients are extensively used as bulking agents because of their high waterless solubility, agreeableness, affable feeling in the mouth, and good taste masking. Several new approaches of incorporating disintegrants and other answerable and/ or undoable excipients to gain rapid- fire dissolution and acceptable mechanical strength are reported.

a) One illustration is the Flash tab technology of multiparticulate actives (carpeted chargers and uncoated or coated microgranules). In these tablets, the contemporaneous presence of a disintegrant with a high lump or disintegrating force, defined as “disintegrating agent,” and a substance with a low swelling force (bounce, cellulose, and direct- contraction sugar), defined as “swelling agent” ,was claimed as the crucial factor for the rapid-fire decomposition of a tablet. The tablet manufactured by this technology is reported to have acceptable mechanical strength.

9.3. Indurate drying:

The process of snap drying (lyophilization) is precious, time- consuming, and produces tablets of poor mechanical strength. For these reasons, it is not generally used to manufacture sublingual tablets. It's a process of choice for products that are unstable or are heat sensitive.

The process involves lowering the temperature of the product in a waterless medium to below indurating, followed by applying a high- pressure vacuum. To prize the water in the form of a vapor, which is collected as ice on a condenser, a gradational temperature rise is applied during the drying process. The product temperature at the ice sublimation interface and the expression collapse temperature are critical to gain a snap- dried cutlet of quality structure. This process retains the physical structure and preserves the material for storehouse or transport.

The performing tablets are generally light and have largely pervious structures that allow rapid- fire dissolution or decomposition. The snap- drying process may affect in a product with an

unformed structure, leading to an enhanced dissolution rate. still, tablets manufactured by snap drying process have poor stability at a advanced temperature and moisture. [18]

10. EVALUATION OF SUBLINGUAL DRUGS: [15]

1. General Appearance

The general appearance of a tablet, its visual identity and over all" fineness" is essential for consumer acceptance. Include in are tablet's size, shape, color, presence or absence of an odor, taste, face texture, physical excrescencies and thickness and legibility of any relating marking.

2. Size and Shape

The size and shape of the tablet can be dimensionally described, covered and controlled.

3. Wetting Time

Using this test, the time needed for humidity to access the tablet fully is measured and conceivably represents the time needed to release medicine in the presence of nanosecond volumes of slaver.

4. Uniformity of Weight

procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined collectively and inclusively on a digital importing balance. The average weight of one tablet was determined from the collaborative weight.

5. Frangibility

It's measured of mechanical strength of tablets. Roche friabilator can be used to determine the frangibility.

6. Tablet Hardness

Hardness of tablet is defined as the force applied across the periphery of the tablet in the order to break the tablet. The resistance of the tablet to dicing, bruise or breakage under condition of storehouse metamorphosis and running before operation depends on its hardness. Hardness of the tablet of each expression is determined using Monsanto Hardness tester.

7. In- Vitro Dispersion Time

In- vitro dissipation time can be measured by dropping a tablet in a teacup containing 50 ml of Sorenson's buffer pH 6.8.

8. In- Vitro Disintegration Test

The test can be carried out on 6 tablets using the outfit specified in I.P. 1996 distilled water at 37ºC ± 2ºC was used as a decomposition media and the time in alternate taken for complete decomposition of the tablet with no palable mass remaining in the outfit measure in seconds.

11. COMMERCIALLY AVAILABLE SUBLINGUAL TABLETS:

Table 4., drugs available as sublingual tablets [7]

Drug	Manufacturer
Nitro-glycerine	Pfizer
Isosorbide dinitrate	Multiple manufacturer
Fentanyl citrate	Galena biopharma
Buprenorphine hydrochloride	Multiple manufacturers
Ergotamine tartrate (ergo mar)	Rosedale therapeutics
Ergoloid mesylates	Watson
Asenapine (saphris)	Merck sharp and dohme
Buprenorphine hydrochloride and naloxone hydrochloride	Multiple manufacturer
Zolpidem tartrate (intermezzo)	Purdue pharma

Table 5., Some marketed sublingual tablets [3],[6]

Brand name	drug	category	strength
Abstral	Fentanyl citrate	Opioid analgesic	50, 100, 200, 300, 400,600, 800microgram
Subutex	Buprenorphine	Opioid analgesic	2 and 8 mg
Avitan	Lorazepam	Antianxiety	1, 2 mg
Edular	Zolpidem tartrate	Sedatives/hypnotics	5, 10 mg
Isordil	Isosorbide dinitrate	vasodilators	2.5, 5, 10 mg
Nicorette microtab	Nicotine bitartrate		2mg
Saphris	Asenaphine	Antipsychotic agent	5, 10 mg
Prohealth melatonin	Melatonin	Hormone	2 mg

12. POTENTIAL DRUG CANDIDATES FOR SUBLINGUAL DELIVERY [20]

The following exemplifications illustrate superior remedial operation when medicines were administered via the sublingual route as compared to oral administration.

a) Captopril, nifedipine, prazosin: In a relative effectiveness study of sublingual captopril, nifedipine, and prazosin, it was reported that sublingual captopril may be a better volition to sublingual nifedipine in treating hypertensive extremities grounded on lower side goods. Another study has shown that sublingually administered captopril and nifedipine are effective in the treatment of hypertensive extremities; still, for severe forms of hypertension, this study recommends sublingual nifedipine.

b) Verapamil: Sublingual administration of verapamil has displayed significantly advanced maximum tube attention of the medicine(Cmax), a faster immersion rate, and lesser bioavailability as compared to its oral

administration. It has also been shown to produce a rapid-fire and significant reduction in ventricular rate.

c) Furosemide: Sublingual administration of furosemide was shown to offer a remedial advantage over the oral route of administration.

d) Buprenorphine and naloxone: The sublingual tablets of buprenorphine and naloxone have shown useful results for the treatment of drowsy dependence.

e) Zolmitriptan: Zolmitriptan is used for the treatment of migraine and cluster headaches.

f) Piroxicam: In a randomized, double-eyeless clinical trial, comparing 40 mg of sublingual piroxicam with a 75 mg intramuscular injection of diclofenac for the exigency treatment of acute renal bellyache, sublingual piroxicam was set up as effective as the intramuscular diclofenac.

g) Epinephrine tone: fitted epinephrine is used for the treatment of anaphylaxis. In a study, sublingual epinephrine redounded in rapid-fire immersion and advanced peak tube attention in

beast models when compared to tone- fitted epinephrine. The study proposed sublingual epinephrine as a volition to tone- fitted epinephrine.

h) Estrogens: Estrogens in menopausal women with cardiovascular complaint have been shown to produce coronary and supplemental vasodilation, reduction of vascular resistance, and enhancement of endothelial function. Sublingual estrogens have displayed briskly medicine immersion (i.e., shorter Tmax advanced Cmax) than orally administered forms.

13. RECENT DEVELOPMENTS:

1) Nitro- glycerine: delivering sublingual aerosol expression (nitro- glycerine in forces) in a metered - cure scattering pump, Nitro lingual spray, was developed. It delivers nitro- glycerine by scattering onto or under the lingo in the form of spray driblets, which eventually increase the immersion and hence the bioavailability of nitro- glycerine. The rapid-fire onset of action is always needed in case of hypertension. [3][9]

2) Nanofiber: As we know that the nanofiber is a new conception of medicine delivery systems and the operations of nanofiber in colorful fields are yet to be explored. Nanofiber in medicine delivery system is a point of interest for experimenters. Nanofiber due to its high face area to volume rate can release the huge quantum of medicine incontinently. farther depending on the polymer used in the nanofiber can also control the release of medicine for extended period of time. Vrbata et al., makes nanofiber with Sumatriptan succinate and naproxen, both these medicines are used in migraine treatment. The nanofiber exhibition moment release and high permeability of the medicine through sublingual mucosa. The medicine lading capacity was 40 to the nanofiber volume. Nanofiber can also be used to give the sustained and controlled release of medicine through sublingual point. Sharma et al., makes a nanofiber using biodegradable polymer Poly(vinyl alcohol) and sodium alginate for sublingual delivery of insulin. In vitro release study demonstrated insulin release follows first order kinetics after original burst release. The nicorandil loaded nanofiber also shows the prolonged time of action. [6]

3) Nanoparticles: Nanoparticles are used in sublingual medicine delivery to ameliorate the immersion, uptake, and accumulation of medicines across natural walls. Nanoparticles can be made from a variety of accoutrements, including lipids, natural and synthetic polymers, and cold-blooded accoutrements. Nanoparticles can be used for sublingual medicine delivery because

* Fast onset of action

* Useful for certain medicines

* Controlled release

14. FUTURE PROSPECTS:

Sublingual medicine delivery systems have promising prospects, with the request value anticipated to grow to$ 5.9- 6.06 billion by 2028. This growth is driven by the adding fashion ability of these delivery options, inventions, and investments.

Some implicit areas of operation for sublingual medicine delivery include

- Pain operation sublingual opioids can be useful for treating advance pain in cancer cases.
- habitual conditions sublingual medicine delivery systems may have a part in treating habitual conditions.
- Oncology sublingual medicine delivery systems may have operations in oncology.

15. CONCLUSION:

Sublingual medicine delivery has been used for expression of numerous medicines with view point of rapid-fire medicine release and quick onset of action. Sublingual products were developed to overcome the difficulty in swallowing conventional tablet, among pediatric, senior and psychiatric cases with dysphagia. The target population has expanded to those who want accessible dosing without water anywhere, anytime.

The eventuality for similar lozenge forms is promising because strong request acceptance and patient demand. Peak blood situations of utmost products administered sublingually are achieved within 10 - 15 twinkles, which is generally important faster than when those same medicines are ingested orally. The percent of each cure absorbed is generally advanced than that achieved by means of oral ingestion. colorful types of sublingual lozenge forms are available in request like tablets, flicks and sprays.

When a case requires immediate pain relief, the sublingual route of administration is an effective way to give pain relief. lately numerous medicines have been formulated for sublingual medicine delivery with an ideal of rapid-fire medicine release and confining the region of medicine release to mouth. Compared to generally used tablets, capsules and other oral lozenge forms, sublingual immersion is generally important briskly and more effective. Sublingual tablets are accessible for youthful children, the senior and cases with swallowing difficulties, and in situations where drinkable liquids are not available.

16. CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this investigation**.**

17. ACKNOWLEDGMENTS:

The authors would like to thank Kasturi shikshan sanstha college of pharmacy, Shikrapur, Pune for their kind support during preparation of review article.

18. REFERENCES:

1) Nibha, Kumari and SS. Pancholi. “An Overview on: Sublingual Route for Systemic Drug Delivery.” (2012).
2) Parmar K and Patel MB: A review on sublingual spray: novel drug delivery system. Int J Pharm Sci Res 2017; 8(11): 4533-39.
3) Narang, N. & Sharma, J. (2011). Sublingual mucosa as a route for systemic drug delivery. International Journal of Pharmacy and Pharmaceutical Sciences. 3. 18-22.
4) Labhade, S., Malode, C., Rawal, V., & Rupvate, S. (2019). Review on Sublingual Drug Delivery System. Journal of Drug Delivery and Therapeutics.
5) Pawar, Poonam & Ghorpade, Hemant & Kokane, Bhavana. (2018). Sublingual route for systemic drug delivery. Journal of Drug Delivery and Therapeutics. 8. 340-343. 10.22270/jddt. v8i6-s.2097.
6) Amar Deepak, Amit Kumar Goyal, Goutam Rath, Nanofiber in transmucosal drug delivery, Journal of Drug Delivery Science and Technology, Volume 43, 2018, Pages 379-387
7) Ashraf, M. & Sayeed, V.A. (2014). Considerations in developing sublingual tablets-an overview. Pharmaceutical Technology Europe. 26. 33-40.
8) Şenel, S., & Comoglu, T. (2018). Orally disintegrating tablets, fast-dissolving, buccal and sublingual formulations. Pharmaceutical Development and Technology, 23(5), 431.
9) Saha P, Verma S, Das PS. SUBLINGUAL DRUG DELIVERY: AN INDICATION OF POTENTIAL ALTERNATIVE ROUTE. Int J Curr Pharm Sci [Internet]. 2017 Nov. 14 [cited 2024 Nov. 8];9(6):5-7.
10) Chapter 3 - The Spectrum of Pain and Anxiety Control, Editor(s): Stanley F. Malamed, Sedation (Sixth Edition), Mosby, 2018, Pages 14-22,
11) Prajapati ST, Patel PB, Patel CN. Formulation and evaluation of sublingual tablets containing Sumatriptan succinate. Int J Pharm Investig. 2012 Jul;2(3):162-8.
12) Hua S. Advances in Nanoparticulate Drug Delivery Approaches for Sublingual and Buccal Administration. Front Pharmacol. 2019 Nov 5;10:1328. doi: 10.3389/fphar.2019.01328. PMID: 31827435; PMCID: PMC6848967.
13) : Shelke V, Mutha S. Formulation and evaluation of lansoprazole sublingual tablet. J Res Pharm. 2020; 24(2): 264-276
14) Thulluru, Ashok & Mahammed, Nawaz & Madhavi, C & Nandini, K & Sirisha, S & Spandana, D. (2019). Asian Journal of Pharmaceutical Research (AJPRes.) Sublingual Tablets -An Updated Review. Asian Journal of Pharmaceutical Research. 9. 2231-5691. 10.5958/2231-5691.2019.00016.9.
15) MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US);
16) Miner, J. R. (2020). Sublingual analgesia: a promising proposal for the treatment of pain. Expert Opinion on Drug Delivery, 17(2), 123–126.
17) Dey P, Maiti S. Orodispersible tablets: A new trend in drug delivery. J Nat Sci Biol Med. 2010 Jul;1(1):2-5. doi: 10.4103/0976-9668.71663.
18) Kanade TS, Gupta A, Mahajan S, et al. Review on Sublingual Tablets-A Promising Formulation for Instant Action. Int J Pharm Sci. 2023;3(1):1–6. DOI: 10.51626/ijps.2023.03.00012
19) Heleen Kraan, Hilde Vrieling, Cecil Czerkinsky, Wim Jiskoot, Gideon Kersten, Jean- Pierre Amorij, Buccal and sublingual vaccine delivery, Journal of Controlled Release, Volume 190, 2014, Pages 580-592, ISSN 0168-3659.
20) John D. Smart, The basics and underlying mechanisms of mucoadhesion, Advanced Drug Delivery Reviews, Volume 57, Issue 11, 2005, Pages 1556-1568,ISSN 0169- 409X
21) Andreas Bernkop-Schnürch, Mucoadhesive systems in oral drug delivery, Drug Discovery Today: Technologies, Volume 2, Issue 1, 2005, Pages 83-87, ISSN 1740- 6749
22) Hua S (2019) Advances in Nanoparticulate Drug Delivery Approaches for Sublingual and Buccal Administration. Front. Pharmacol. 10:1328.
23) Hua S. Advances in Nanoparticulate Drug Delivery Approaches for Sublingual and Buccal Administration. Front Pharmacol. 2019 Nov 5;10:1328.
24) Guadarrama-Escobar OR, Serrano-Castañeda P, Anguiano-Almazán E, Vázquez-Durán A, Peña-Juárez MC, Vera-Graziano R, Morales-Florido MI, Rodriguez-Perez B, Rodriguez-Cruz IM, Miranda-Calderón JE, Escobar-Chávez JJ. Chitosan Nanoparticles as Oral Drug Carriers. Int J Mol Sci. 2023 Feb 21;24(5):4289.