

SUBLINGUAL DRUG DELIVERY SYSTEM

LIST OF CONTENTS

- 1. Sublingual tablets**
- 2. Fast-disintegrating sublingual tablets**
- 3. Bioadhesive sublingual tablet**
- 4. Thin film drug delivery**
- 5. Lipid matrix sublingual tablet**
- 6. Sublingual immunotherapy**
- 7. Sublingual vitamin tablet**
- 8. Market preparation**
- 9. References**

SUBLINGUAL DRUG DELIVERY SYSTEM

1. SUBLINGUAL TABLETS

They are to be placed under the tongue and produce immediate systemic effect by enabling the drug absorbed directly through mucosal lining of the mouth beneath the tongue.

The drug absorbed from stomach goes to mesenteric circulation which connects to stomach via portal vein. Thus, absorption through oral cavity avoids first-pass metabolism. The tablets are usually small and flat, compressed lightly to keep them soft. The tablet must dissolve quickly allowing the API to be absorbed quickly. It's designed to dissolve in small quantity of saliva. After the tablet is placed in the mouth below the tongue, the patient should avoid eating, drinking, smoking and possibly talking in order to keep the tablet in place. Swallowing of saliva should also be avoided since the saliva may contain dissolved drug. Bland excipients are used to avoid salivary stimulation.

Advantages:

1. First pass - The liver is by-passed thus there is no loss of drug by first pass effect for sublingual administration, Bioavailability is higher.
2. Rapid absorption - Because of the good blood supply to the area absorption is usually quite rapid.
3. Drug stability - pH in mouth relatively neutral so a drug may be more stable.

Disadvantages:

1. Holding the dose in the mouth is inconvenient. If any is swallowed that portion must be treated as an oral dose and subject to first pass metabolism.
2. Only small doses can be accommodated easily.

Glyceryl Trinitrate - a potent coronary vasodilator which is used for the rapid symptomatic relief of angina. It has been found impressively effective when administered sublingually; pharmacologically active after only 1 - 2 minutes.

Some of the drug like desoxycortisone acetate, morphine, captoprill, nifedipine and 17-B Oestradiol gives impressive absorption when given sublingually, it has also been shown that the sublingual administration of 17-B Oestradiol requires only 1/4 of the oral dose.

SUITABILITY OF API FOR PREPARATION OF SUBLINGUAL TABLET

- ❖ Many drug properties could potentially affect the performance of sublingual tablets.
For example, the solubility,
crystal morphology,
particle size,
hygroscopicity,
compressibility and
bulk density of a drug can significantly affect the final tablet's characteristics, such as tablet strength and disintegration.
- ❖ Some drugs undergoes extensive first pass metabolism which results in poor bioavailability of its oral dosage forms that kind of drugs are suitable for sublingual dosage form.
- ❖ Drugs that are unstable in parenteral preparation are suitable for sublingual dosage form.

EVALUATION

- ❖ Surface pH of the tablet
- ❖ Uniformity of weight
- ❖ Content uniformity
- ❖ Hardness
- ❖ Thickness
- ❖ Diameter
- ❖ Disintegration time
- ❖ Wetting time and
- ❖ Friability

Wetting Time (WT): The tablet was placed at the center of 2 layers of absorbent paper fitted into a rectangular plastic dish (11 cm × 7.5 cm). After the paper was thoroughly wetted with distilled water, excess water was completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch.

2. FAST-DISINTEGRATING SUBLINGUAL TABLETS

- ❖ Tablets that disintegrate or dissolve rapidly in the patient's mouth are convenient for young children, the elderly and patients with swallowing difficulties, and in situations where potable liquids are not available.

- ❖ Only the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity.
- ❖ The medication can then be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingual mucosa.
- ❖ The sublingual route usually produces a faster onset of action than orally ingested tablets and the portion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes.

HOW TO PREPARED

To formulate rapidly-disintegrating or dissolving tablets. Direct compression, one of these techniques, requires the incorporation of a superdisintegrant into the formulation, or the use of highly water-soluble excipients to achieve fast tablet disintegration. Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture- and heat-labile medications. However, the direct compression method is very sensitive to changes in the type and proportion of excipients and in the compression forces, when used to achieve tablets of suitable hardness without compromising the rapid disintegration characteristics. Extremely fast tablet disintegration would be required to enhance the release of drug from tablets for rapid absorption by the sublingual mucosa blood vessels.

EVALUATION

- ⊠ Surface pH of the tablet
- ⊠ Tablet weight variation
- ⊠ Content uniformity
- ⊠ Hardness
- ⊠ Thickness
- ⊠ Diameter
- ⊠ Disintegration time
- ⊠ Wetting time and
- ⊠ Friability

3. BIOADHESIVE SUBLINGUAL TABLET

The new sublingual tablet concept presented is based on interactive mixtures consisting of a water-soluble carrier covered with fine drug particles and a bioadhesive component. With this approach, it is possible to obtain rapid dissolution in combination with bioadhesive retention of the drug in the oral cavity.

Bioadhesion is usually defined as the bond formed between two biological surfaces or between a biological and a synthetic surface. The term

mucoadhesion is used when the mucus or mucosal surface is involved in these adhesive bonds.

Problem associated with sublingual tablet formulations is that there is always a risk that the patient will swallow part of the dose before the active substance has been released and absorbed locally into the systemic circulation. This could result in an unwanted prolongation of the pharmacological effect. Addition of a bioadhesive component is a well-known method of increasing the possibility of a more site-specific release. However, this concept is normally applied to non-disintegrating tablets or discs to achieve extended release of the active substance and, consequently, such a system will not be suitable for a fast acting formulation. Therefore, it would be of interest to study a disintegrating tablet which releases the drug quickly, but which also has bioadhesive properties which could prevent the drug from being swallowed.

EVALUATION

- ✧ Bioadhesion
- ✧ Tablet weight variation,
- ✧ Content uniformity,
- ✧ Hardness,
- ✧ Thickness,
- ✧ Diameter
- ✧ Disintegration time,
- ✧ Wetting time and
- ✧ Friability

Bioadhesion mechanisms

The mucus layer is often involved in the adhesion of a bioadhesive polymer and is present as either a gel layer adhering to the mucosal surface or a solution or suspension of various substances. The mucus layer mainly consists of mucin glycoproteins, inorganic salts, proteins, lipids and water, with the composition varying depending on its source. The electronic theory involves an electronic transfer between the two materials causing a double layer of electrical charge, which results in attraction forces. The adsorption theory involves adhesion between the mucosa and the adhesive material by van der Waals interactions, hydrogen bonds and related forces. The wetting theory involves interfacial tensions between the two materials. Penetration of polymer chains into the mucus network and vice versa, causing a mechanical bond, is referred to as the diffusion theory. The importance of water content and movement of water into the bioadhesive material from the mucosa, i.e. dehydration of the mucosa, has also been suggested as a mechanism for adhesion.

Evaluation of the bioadhesive properties of a material

One common in vitro method of evaluating bioadhesion is based on the fracture approach, i.e. directly evaluating the force required to separate the formulation from the mucosa, after keeping them in contact under a specified force for a specified time. The tensile stress can then be determined by dividing the maximum force of detachment by the total surface area involved in the adhesive interaction. This method has been used for evaluating the bioadhesive properties of both pure materials and formulations.

Measurement of bio-adhesive strength

Bio-adhesive strength of the tablets was measured on a modified physical balance using the method described by Gupta et al. The method used bovine cheek pouch as the model mucosal membrane and IPB pH 6.6 as the moistening fluid. The surface of the mucosal membrane was first blotted with a filter paper and then moistened with 25/L1 of IPB pH 6.6. The weight, in g, required to detach the tablets from the mucosal surface gave the measure of bio-adhesive strength.

4. THIN FILM DRUG DELIVERY

Thin film drug delivery is a process of delivering drugs to the systemic circulation via a thin film that dissolves when in contact with liquid, often referred to as a **dissolving film** or **strip**. Thin film strips are typically designed for oral administration, with the user placing the strip on or under the tongue or along the inside of the cheek. As the strip dissolves, the drug can enter the blood stream enterically, buccally or sublingually.

- ❖ The sublingual delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.
 - All tablet dosage forms, softgels and liquid formulations primarily enter the blood stream via the gastrointestinal tract, which subjects the drug to degradation from stomach acid, bile, digestive enzymes and other first pass effects. As a result, such formulations often require higher doses and generally have a delayed onset of action.
 - Conversely, sublingual thin film drug delivery can avoid these issues and yield quicker onsets of action at lower doses.
- ❖ Thin film is more stable, durable and quicker dissolving than other conventional dosage forms.
- ❖ Thin film enables improved dosing accuracy relative to liquid formulations since every strip is manufactured to contain a precise amount of the drug.
- ❖ Thin film not only ensures more accurate administration of drugs but also

can improve compliance due to the intuitive nature of the dosage form and its inherent ease of administration. These properties are especially beneficial for pediatric, geriatric and neurodegenerative disease patients where proper and complete dosing can be difficult.

- ❖ Thin film's ability to dissolve rapidly without the need for water provides an alternative to patients with swallowing disorders and to patients suffering from nausea, such as those patients receiving chemotherapy.
- ❖ Thin film drug delivery has the potential to allow the development of sensitive drug targets that may otherwise not be possible in tablet or liquid formulations.
- ❖ From a commercial perspective thin film drug delivery technology offers an opportunity to extend revenue lifecycles for pharmaceutical companies whose drug patent is expiring and will soon be vulnerable to generic competition.

Evaluation

- ♣ Uniformity of content
- ♣ Uniformity of weight
- ♣ Uniformity of thickness
- ♣ Surface pH
- ♣ Folding endurance
- ♣ % Flatness
- ♣ % Elongation
- ♣ Tensile strength
- ♣ Module of elasticity
- ♣ In-vitro dissolution diffusion

5. LIPID MATRIX SUBLINGUAL TABLET

Lipid Matrix Sublingual Tablet is formulated using advances in sublingual and liposomal technology to create a dosage form that offers a faster and more complete absorption than traditional oral routes of administration.

The Lipid Matrix Sublingual Tablet is a bioavailable, quick, convenient, and consistent dosage form for many specialty nutraceuticals that are often taken orally.

Examples Include: Glutathione MB12 (Methylcobalamin) Melatonin

A True Sublingual Tablet + Lipid Matrix Technology:

- Not a Lozenge, Troche, or Tablet Triturate: A True Sublingual Tablet!
- Rapid Dissolve Formula
- Liposomal Drug Delivery
- Bioavailable & Avoids First Pass Effect
- Convenient & Consistent Dosing Application
- Single or Combination Drug Delivery

THE DESIGN OF A SUBLINGUAL TABLET WITH RAPID OROMUCOSAL ABSORPTION FOR ADMINISTRATION OF A POTENT DRUG

For a tablet containing a potent drug, three formulation aspects are of special interest. Firstly, incorporation of the necessarily small amounts of a very potent drug could result in poor dose homogeneity, especially if direct compression is desired. Secondly, disintegration should be fast to facilitate rapid drug dissolution. Thirdly, some bioadhesive properties are desirable to avoid swallowing the drug. However, these bioadhesive properties should not hinder the fast drug release.

6. SUBLINGUAL IMMUNOTHERAPY

Sublingual immunotherapy, or SLIT, is a form of immunotherapy that involves putting drops of allergen extracts under the tongue.

SLIT is usually delivered one of two ways: drops (or tablets) of allergen extract are placed under the tongue, then either swallowed or spat out. Most studies have looked at swallowing the extract, which seems to work better. Immunotherapy by the oral route (swallowed and not kept under the tongue for any period of time), causes too many gastrointestinal side effects (nausea, vomiting, diarrhea), and therefore is not used.

Generally, SLIT is administered daily, or multiple times per week, over a period of year.

Sublingual monomeric allergoid in tablets given to pediatric patients with allergic rhinitis and/or asthma due to grass pollen.

7. SUBLINGUAL VITAMIN TABLET

The only Sublingual vitamin that all doctors recommend is vitamin B12 (Cyanocobalamin). you must have enough of it for your bodies metabolism.

Recommended to be taken once a day.

8. MARKET PREPARATION

- ✧ **TENORMIN SUBLINGUAL TABLET (ISOPROTERENOL)**
- ✧ **MICROTAB SUBLINGUAL TABLET (NICOTINE)**
- ✧ **NASCOBAL SUBLINGUAL TABLET (VITAMIN B₁₂)**
- ✧ **SUBUTER SUBLINGUAL TABLET (BUPRENORPHINE)**
- ✧ **NITROQUICK SUBLINGUAL TABLET (NITROGLYCERIN)**