Biopharmaceutics of Nonoral medication

Buccal or sublingual administration

- Certain tablets are intended to be placed beneath the tongue or in the cheek pouch and retained in the mouth.
- This regions are vascular and allow rapid absorption of certain drugs in a manner consistent with pH partition theory.
- Buccal or sublingual route appears ideal for lipid soluble drugs that are metabolized in the gastrointestinal tract or liver during absorption.
This because the blood supply draining the buccal cavity empties directly into the systemic circulation and bypasses the liver.

In general, buccal or sublingual tablets are designed to disintegrate and dissolve slowly in the mouth to minimize the possibility of swallowing part of the dose.

Exceptions include nitroglycerine and isosorbide dinitrate, which should dissolve within seconds to provide prompt relief for acute angina episodes.
This mode of therapy is most used for certain drugs such as:-

- Certain hormones (methyltestosterone, testosterone, estradiol) methadone, mepridine, lidocaine, chlorpheniramin and barbiturates.

The pH of saliva is about 6. Increasing the pH of fluids in the cavity promotes the absorption of weak bases but reduces the absorption of weak acids.
• The buccal absorption of flubiprofen which is a weak acid was greater at pH 5.5 where the acid was less dissociated.
Some important differences exist between gastrointestinal and buccal absorption of drugs:

1. **Clindamycin**, which is well absorbed from the GIT, is absorbed poorly, from the buccal cavity over the pH range of 4.0 to 8.5.

2. A higher degree of lipid solubility required for good absorption from the buccal cavity than from the GIT.
The slow absorption of **buprenorphine** after buccal administration is due to the following phenomenon:

- The storage compartment in the buccal membrane. In this compartment the drug may repartition into the oral cavity or be slowly absorbed into systemic circulation.

Sublingual **nitroglycerin** remains the treatment of choice in the acute management of angina pectoris.
The advantages are:

- A lack of tolerance, ease of administration, rapid consistent, and complete absorption

The low and variable absorption of sublingual nitroglycerin may be related to:

1. The patient's inability to maintain the dose in the mouth without swallowing.
2. The inadequate moisture in the mouth (dry mouth).
The sublingual mucosa should be sufficiently moist to facilitate the dissolution of nitroglycerin sublingual tablets.

Nicotine gum was developed as substitution therapy to help people to stop smoking.

The preparation consists of nicotine bound to an ion exchange resin and incorporated into a gum base.

The resin is expected to release almost all its nicotine over 20 to 30 min of chewing.
- It was found that the nicotine is well absorbed from buccal cavity during gum chewing and is helpful to people who are trying to stop smoking.

- **Buccal spray** has been applied to nitroglycerin and some patients may find it easier to use the spray than to open a bottle and remove a small sublingual tablet.

- Because dry mouth can delay the dissolution of sublingual nitrate tablets, the aerosol droplets may be better absorbed in some patients.
lorazepam as preanesthetic agent is more rapidly absorbed after sublingual administration than after IM injection, with the additional advantages of no pain or discomfort on administration.

Alprazolam is widely used prescribed as an anxiolytic agent and for the treatment of panic disorder.

Sublingual administration may be a useful alternative for panic disorder patients who cannot swallow tablet or for those who don’t have access to water or some other liquid to facilitate swallowing.
Alprazolam absorption following sublingual administration is at least as rapid as after oral administration on an empty stomach.

Sublingual administration, however, may prove to be preferred to oral administration of alprazolam after a meal, when gastric emptying is prolonged and the rate of absorption is reduced.

Oral clonidine and captopril have been found useful in treatment of hypertensive emergencies who require immediate reduction in blood pressure.
Both oral and buccal nifedipine have been reported to lower blood pressure within 1h in patients with dangerously elevated pressure.
Although buccal nifedipine appears to be useful for reducing elevated blood pressure, doubts have been raised as to whether the effects are the result of buccal absorption or, alternatively, the result of swallowing the material contained in the soft gelatin capsule followed by gastrointestinal absorption.

To clarify this question, the sublingual absorption of nifedipine was investigated in healthy human subjects and compared with oral administration.
The relative bioavailability of nifedipine after sublingual compared with oral administration was only 17% so the therapeutic results obtained with sublingual administration of nifedipine are probably due to swallowing the drug.

The absorption of methyltestosterone was compared in healthy subjects after administration of 10 mg and 25 mg tablets and an aqueous solution containing 10 mg of methyltestosterone as well as after 5 and 10 mg sublingual tablets.
The sublingual tablets produced significantly higher *methyltestosterone* level in the serum per mg of dose than did the other dosage forms.

These results clearly demonstrate the potential advantage of sublingual administration and the avoidance of presystemic metabolism.

Similar findings have been reported with *isosorbide dinitrate*. 
An interesting technique for the administration of a bronchodilator aerosol, fenoterol, in children with asthma, ranging from 3 months to 9 years.

Rapid and effective bronchodilatation was obtained in most patients simply by directing the jet of the aerosol onto the buccal mucosa.

This technique could be useful in the treatment of young children who cannot use an aerosol dosage form in the recommended manner.
The peripheral vasoconstriction effects of ergotamine intramuscularly and sublingually were compared in normal subjects.

It was concluded that the two forms at the appropriate doses should be equally effective in the treatment of migraine.