BUCCAL DRUG DELIVERY SYSTEM
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INTRODUCTION

- Administration of drug via buccal mucosa (linings of cheek and area between upper and lower lips) to the systemic circulation.
- Potential route for typically large, hydrophilic and unstable proteins, oligonucleotides, and polysaccharides.
- For local and systemic drug delivery.
- Most buccal formulations are designed to provide sustained release of active ingredients.
Lists of drug delivered via buccal route

- acyclovir
- carbamazapine
- buprenorphine
- chlorpromazine
- danazol
- diclofenac sodium
- diltiazem
- metronidazole
- nifidipine
- Melatonin
- Nicotine
- Omeprazole
- Pentazosine
- Propranolol
- Pindolol
- Morphine sulphate
- Ergometrine tartrate

- Nitrates that are used *to relieve the pain* of an angina attack include:
  - Sublingual nitroglycerin
  - Buccal nitroglycerin
  - Sublingual isosorbide dinitrate
  - Chewable isosorbide dinitrate
Marketed products

- **Striant®**, developed by Columbia Labs, is a testosterone extended-release buccal tablet that delivers testosterone systemically for hormone replacement in hypogonadal men.

- **Asftach®** is a buccal tablet containing triamcinolone acetonide for treatment of apththous ulcers, and contains a bioadhesive layer and a dissolvable lactose nonadhesive backing layer.

- **DentiPatch®** has been developed by Noven, which is a lidocaine extended-release buccal patch that adheres to the gingival tissue to provide for local analgesia, and was approved in the United States in May 1996.
ADVANTAGES OF BUCCAL DRUG DELIVERY

- Ease of administration.
- Termination of therapy is easy.
- Permits localization of drug to the oral cavity for a prolonged period of time.
- Can be administered to unconscious patients.
- Offers an excellent route, for the systemic delivery of drugs with high first pass metabolism, thereby offering a greater bioavailability.
- A significant reduction in dose can be achieved thereby reducing dose related side effects.
- Drugs which are unstable in the acidic environment are destroyed by enzymatic or alkaline environment of intestine can be administered by this route.
- Drugs which show poor bioavailability via the oral route can be administered conveniently.
• It offers a passive system of drug absorption and does not require any activation.

• The presence of saliva ensures relatively large amount of water for drug dissolution unlike in case of rectal and transdermal routes.

• Systemic absorption is rapid.

• This route provides an alternative for the administration of various hormones, narcotic analgesic, steroids, enzymes, cardiovascular agents etc.

• The buccal mucosa is highly perfused with blood vessels and offers a greater permeability than the skin.
LIMITATIONS OF BUCCAL DRUG DELIVERY

- Drugs, which irritate the oral mucosa, have a bitter or unpleasant taste, odour, cannot be administered by this route.
- Drugs, which are unstable at buccal pH cannot be administered by this route.
- Only drugs with small dose requirements can be administered.
- Drugs may swallow with saliva and loses the advantages of buccal route.
- Only those drugs, which are absorbed by passive diffusion, can be administered by this route.
- Eating and drinking may become restricted.
- Swallowing of the formulation by the patient may be possible.
- Over hydration may lead to the formation of slippery surface and structural integrity of the formulation may get disrupted by the swelling and hydration of the bioadhesive polymers.
Within the oral mucosal cavity, delivery of drugs is classified into three categories:

(i) sublingual delivery,
(ii) buccal delivery,
(iii) local delivery,

Within the oral mucosal cavity, the buccal region offers an attractive route of administration for systemic drug delivery. The mucosa has a rich blood supply and it is relatively permeable.
STRUCTURE OF ORAL MUCOSA

- Epithelium
- Lamina Propria
- Submucosa
The oral mucosa is composed of an outermost layer of stratified squamous epithelium. Below this lies a basement membrane, a lamina propria followed by the submucosa as the innermost layer.

**A. Buccal Epithelium**

The buccal epithelium is composed of 40 to 50 layers of non-keratinized stratified squamous cells. It is 500 to 800 μm in thickness with varying degrees of maturity.

The uppermost superficial layer of cells is comprised of flattened compact differentiated cells of about 150 μm in thickness.

**PERMEABILITY**

oral mucosae is leaky epithelia intermediate between that of epidermis and intestinal mucosa.

permeability is 4-4000 times greater than that of skin.
• **B. Lamina Propria**

  The lamina propria consists of collagen fibrils, a supporting layer of connective tissue, blood vessels, and smooth muscle. The structure of the lamina propria is not dense and it is not a barrier to drug permeation.

• **C. Submucosa**

  The submucosa is a relatively dense connective tissue that contains a few accessory salivary glands, *mucus acinus*. Mucus acini are surrounded by myoepithelial cells that aid in the secretion of saliva.
APPROACHES OF BUCCAL DRUG DELIVERY

1) MATRIX TYPE.
   - CONVENTIONAL BUCCAL TABLETS.
   - NOVEL BUCCAL ADHESIVE TABLETS.

2) RESERVIOR TYPE.
   - BUCCAL PATCHES

3) BUCCAL FILMS.

4) BUCCAL MUCOADHESIVE HYDROGEL.

5) BUCCAL SPRAY.

6) FAST DISSOLVING BUCCAL TABLETS.

7) BUCCAL WAFERS.

8) BUCCAL MICROSPHERE.
DESIGN OF BUCCAL DOSAGE FORM

1) MATRIX TYPE:  
1) CONVENTIONAL BUCCAL TABLETS.
2) NOVEL BUCCAL ADHESIVE TABLETS

Hydrophilic and Hydrophobic matrices have been used. For moderately water soluble drugs, hydrophilic matrices of HPMC are widely used to control release.

- Sodium carboxy methyl cellulose (CMC), Hydroxy propyl methyl cellulose (HPMC), sodium alginate and guar-gum as mucoadhesive polymers.
- The carbopol-934 is used as a primary polymer because of its excellent mucoadhesive property and secondary polymers like HPMC, SCMC, and guar-gum were used.
• Ideal buccal adhesive system:
  • - maintain it’s position in mouth.
  • - release the drug in controlled manners.
  • Provide drug release in unidirection.

Example..mucoadhesive buccal tablet of diltiazem HCL.

  Ex. verapamil buccal tablets, sumatriptan succinate buccal tablets.
ii) RESERVOIR TYPE

- Contains cavity for drug and additives separate from adhesive.
- Impermeable backing - controls direction, reduces patch deformation, and disintegration.
BUCCAL ADHESIVE PATCHES.

- Buccal adhesive patches are modified release dosage form that have potential to provide controlled drug delivery from 1 to 24 hrs.
- They adhere to buccal mucosa for extended period of time.
- They consist of solid matrix (non-dissolvable or slowly dissolvable).
- They may be
  - Unidirectionally.
  - Bidirectionally.
  - Multidirectionally.
(a) bidirectional release from adhesive patch by dissolution or diffusion;
(b) unidirectional release from patch embedded in an adhesive Shield
(c) bidirectional release from a laminated patch;
(d) unidirectional release from a laminated patch.
BUCCAL FILMS.

- Thin film drug delivery has emerged as an advanced alternative to the traditional dosage form.
- Placing the strip on or under the tongue or along the inside of the cheek.
- As the strip dissolves, the drug can enter the bloodstream, buccally or sublingually.
- Buccal mucosa preferred over sublingual mucosa.
- It consists of
  - film forming polymer
  - Plasticizer
  - API
  - Stabilizing and thickening agents
  - E.g. buccal film of salbutamol

MARKETED PRODUCT: ONSOLIS (FANTANYL BUCCAL SOLUBLE FILM) WHICH IS USED IN MANAGEMENT OF SEVERE PAIN OF CANCER.
MUCOADHESIVE HYDROGEL

- These are hydrophilic matrices that are capable of swelling when placed in aqueous media.
- Hydrogels, which release the drug by swelling and thereby allowing drug transport through the spaces in the polymer network, are being widely studied for their use in bioadhesive gels. Polyacrylic-based hydrogels have also been extensively studied. An example of a commercially available device is the OTS (oral transmucosal system, TheraTech), which has been used to deliver glucagon-like insulintropic peptide. Example: chitosan glutamate buccal hydrogel with local anaesthetics activity.
• **MUCOADHESIVE HYDROGEL** mainly used for local action.

• Various polymers are used to prepare mucoadhesive hydrogel such as chitosan and its derivatives.

• To obtain mucoadhesive hydrogel, two properties have to be optimised.
  
  1) polarity of polymer surface.
  
  2) molecular mobility of polymer.
BUCCAL SPRAYS.

- GENEREX BIO TECHNOLOGY have introduced insulin spray, which is used for type-1 diabetes patients.
Generex Biotechnology has completed a proof-of-concept study on buccal delivery of heparin using their oral spray platform technology,

This technology is being used to develop a formulation for buccal delivery of insulin for the treatment of diabetes.

Buccal spray delivers a mist of fine droplets onto mucosal membrane probably onto mucin layer.

The solvent either is absorbed through membrane or it is diluted by saliva.

The drug substance that in solvent and not immediately absorbed is deposited as a thin film onto mucin layer.

E.g. estradiol spray.
Fast Dissolving buccal Tablets.

- Fast dissolving buccal tablets for administering a medicament includes active ingredients, a lubricant and water soluble sugar such as sorbitol, combined such that buccal tablets dissolves in about one minute.

It includes:
- buccally absorbable active ingredients
- a lubricant (mg stearate, sds)
  - soluble, directly compressible excipients (spray dried sorbitol)
- such rapid delivery is useful for delivering a bolus dose to achieve a rapid rise in blood level.
- This is covered by patent (U.S. Patent no-5,073,374)
• **BUCCAL WAFERS:** Buccal wafers are rapidly dissolving oral film.

- **ORA-VESCENT:** This drug delivery system have been designed to promote drug absorption through oral mucosa (buccal)

• This may enable more rapid absorption of drug that have a long Tmax.

• In case where the patient is vomiting frequently. Or in migraine gastric transit may be so severely compromised. In such circumstance this delivery may be advantageous.

• However this technology is protected by patent.

• **Mechanism by means of CO2 release.**

• **EX.** An ORA-VESCENT fentanyl buccal tablet.
BUCCAL MICROSPHERE

- Bioadhesive microspheres offer unique carrier system for many pharmaceuticals and can be tailored to adhere to any mucosal tissue. The bioadhesive microspheres can be used not only for controlled release but also for targeted delivery of the drugs to specific sites in body.

- Recent advances, development of polymeric drug delivery systems for protein/peptide drugs.

- Bioadhesive microspheres exhibit a prolonged residence time at site of application or absorption and facilitate an intimate contact with underlying absorption surface and thus contribute to improved and/or better therapeutic performance of drugs.

- E.g. Bioadhesive polymer grafted starch microsphere bearing isosorbide dinitrite for buccal delivery. (chemical abstracts)