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REVIEW ARTICLE

A Comprehensive Review on Buccal Drug Delivery System

Namita S. Bhosale*, Aniket S. Gudur, Rishi Ramesan, Dipasha D. Rane, Pranil D. Arolkar, Afrin S. Darwajkar, Pratiksha P. Mestry, Vijay A. Jagtap
Yashwantrao Bhonsale College of Pharmacy, Charathe – Vazarwadi, Tal - Sawantwadi, Dist – Sindhudurg --416510 Maharashtra.
*Corresponding Author E-mail: **namitasbhosale@gmail.com**

ABSTRACT:
This analysis focuses primarily on the several benefits of the buccal drug delivery system (BDDS) over the traditional and systemic formulation. Bypassing first pass metabolism, it aids in improving bioavailability. The formulation of this medication delivery system maintains contact with the mucosal surface, improving absorption and lengthening the resident time. Although not all medications can be administered with this approach, the majority of medications can. Because the degree of mucoadhesion is a crucial phenomenon for the buccal medication delivery system, bio adhesive polymers play a significant role in this drug delivery method. The paper discusses the advantages and disadvantages of the buccal drug delivery system, the anatomy of the oral mucosa, the mechanism of drug penetration, the use of natural polymers and permeation enhancers in the buccal drug delivery system. This evaluation also addresses currently on the market products used as buccal medication delivery systems and their potential future applications.

KEYWORDS: Buccal drug delivery system, Bioavailability, Natural polymer, Bio adhesive, Permeation enhancer.

INTRODUCTION:
The most popular and practical method for drug delivery has been oral. The oral route of administration has drawn more attention in the pharmaceutical industry due to its ease of administration, greater dosage form design flexibility compared to other routes, and the long-held belief that drugs administered orally are just as effectively absorbed as foods consumed on a daily basis. Most pharmaceuticals intended for oral administration are of the instant release variety, which are intended for immediate drug release for quick absorption. The latter releases the drug into the bloodstream only through the hepatic system, so the amount in the blood stream may be significantly less than the amount that was included in the tablet's formulation. Additionally, a common side effect of many soluble tablet drugs is liver damage. Other approaches to drug distribution into the body were looked into to get around some of these restrictions. Those are: -

1. Trans Dermal Drug Delivery System.
2. Trans Mucosal Drug Delivery System.

Transmucosal drug delivery system:
It offers the advantage of avoiding the hepatic-gastrointestinal first pass elimination associated with oral administration when medications are delivered through the absorptive mucosa in a variety of readily accessible body cavities, such as the buccal, ocular, nasal, rectal, and vaginal mucosae.
Different types:

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- Buccal Drug Delivery System.
- Ocular Drug Delivery System.
- Vaginal Drug Delivery System.
- Rectal Drug Delivery System.
- Nasal Drug Delivery System.
- Gastro Intestinal Drug Delivery System.

Buccal drug delivery system:

The mouth's mucosa resembles skin more morphologically and differs greatly from the remainder of the gastrointestinal system. The oral mucosa does not exhibit the good permeability shown by the intestine, despite the fact that skin permeability is typically acknowledged to be poor. The arrangement of the epithelia, which has widely distinct activities, is largely responsible for these variations throughout the gastrointestinal tract. The stomach, small intestine, and colon are lined with a straightforward, single-layered epithelium, allowing for the shortest possible transport distance for absorbents. In contrast, the mouth cavity and oesophagus have stratified or multi-layered epithelium covering them. Like skin, these layers have varied degrees of differentiation or maturation that become apparent as they move up from the base layer. For many years, drugs have been topically applied to the oral mucosa. However, there has recently been interest in using the oral cavity as a conduit for distributing medications throughout the body. This route of delivery has a lot of benefits despite the epithelium's generally low permeability features. The ability to administer drugs sustainably, mostly through the buccal tissues, and the simplicity of access to the delivery site are among their top benefits. If necessary, delivery can also be stopped rather quickly. Fast cellular regeneration occurs after local stress and damage, therefore the strength of the epithelium required to endure mastication also supports the drug delivery mechanism well. Indeed, improving permeability and dosage form retention at the point of application are unquestionably the two most difficult problems to solve in oral mucosal drug administration. Continuous saliva production and swallowing might result in significant medication depletion from the dose form and consequently limited bioavailability[1].

Advantages:

The oral mucosa has a plentiful supply of blood. Drugs enter the systemic circulation through the deep lingual or face vein, internal jugular vein, and brachiocephalic vein after being absorbed from the oral cavity by the oral mucosa. Following buccal delivery, the drug enters the bloodstream directly, skipping the first pass effect.

- It is more easily accessible for administration and removal of dose forms and is highly vascularized.
- No first-pass hepatic impact.
- Simple administration.
- No pre-systemic metabolism in the gastrointestinal tract.
- Easy accessibility for patients.
- A swath of smooth muscle and mucosa that is largely immobile and appropriate for administering retentive dose forms.
- Avoid exposing the medications to the digestive fluids.
- Faster cellular healing and accomplishment of a localised region on the buccal mucosa's smooth surface.
- Low enzyme activity, suitable for medications or excipients that irritate or cause moderate, reversible harm to the mucosa. The oral mucosa is frequently exposed to a wide range of various foreign substances. In order to prevent irreparable damage from drugs, dosage forms, or additives utilised therein, a strong membrane has evolved.
- Non-invasive drug administration technique.
- The ability to incorporate a pH modulator, an enzyme inhibitor, or a permeability enhancer in the formulation.

Disadvantages:

- The buccal membrane has a lower permeability than the sublingual membrane, in particular; (170 cm2).
- Drugs are continuously diluted at the site of absorption by saliva (0.5-2 L/day), resulting in low drug concentrations at the surface of the absorbing membrane.

Limitations in buccal absorption:

- The absorptive membrane's surface area is significantly less.
- This route cannot be used to give medications that are unstable at buccal pH.
- Only medications with a low dose requirement can be given.
- Only medications that are absorbed through passive diffusion can be given via this route.
- This swelling and hydration of the buccal adhesive polymers may result in the creation of a slippery surface and may undermine the structural integrity of the formulation[14].

ANATOMY OF BUCCAL MUCOSA:

Epithelium:

About 40–50 layers of stratified squamous epithelial cells make up the epithelium. The cuboidal-shaped basal cells, which have a layer beneath them and undergo continuous mitosis before rising to the surface, give rise to the epithelial cells. The cells differentiate as they move through the intermediate layers to the surface, growing bigger, flatter, and encircled by an exterior lipid

matrix (membrane-coating granules). The tissue's permeability to drugs is determined by this exterior lipid matrix.

Basement membrane:
Between the connective tissues of the lamina propria and the sub mucosa and the basal layer of epithelium, the basement membrane (BM), a continuous layer of extracellular materials, serves as a border. The BM is composed of three layers: the lamina lucida, lamina densa, and a sublayer of fibrous material.

The functions of the BM include providing:
1) The adhesion of the epithelium to the supporting connective tissues.
2) Epithelium mechanical support.
3) A physical obstruction to the movement of some big molecules and cells.

Connective tissue:
If present, the lamina propria and sub mucosa make up the connective tissues. The lamina propria is a continuous strip of connective tissue that supplies the oral mucosa with blood vessels and nerve fibres. Lingual, frontal, and retromandibular veins are primarily responsible for vascular drainage from the oral mucosa. These veins evade first-pass metabolism because they open into the internal jugular vein.

Permeability barriers:
The buccal mucosa's permeability falls between that of the intestinal mucosa and the skin's epidermis. Epithelium makes up roughly the outer one-third of the epithelium, where it acts as the main barrier to drug diffusion. Both keratinized and nonkeratinized epithelia share this trait. Keratinization is therefore unlikely to provide significant buccal penetration resistance. Membrane Coating Granules (MCG) are spherical or oval organelles that range in size from 100 to 300 nm. They can be found in both keratinized and non-keratinized epithelia, although their compositions are different in each. The permeability barrier is created by the way MCGs release their contents into the intercellular space.

FACTORS AFFECTING BUCCAL ABSORPTION:

The oral cavity is a complicated environment for drug delivery because of a number of interrelated and independent factors that lower the absorbable concentration at the site of absorption.

1. Membrane Factors:
This includes the degree of keratinization, the amount of absorbable surface area, the mucus layer of the salivary pellicle, the intercellular lipids of the epithelium, the basement membrane, and the lamina propria. The thickness of the absorptive membrane, blood supply, lymph outflow, cell renewal, and enzyme content all work together to slow the rate and amount of medication absorption into the bloodstream.

2. Environmental factors:
A. Saliva: Also known as the salivary pellicle or film, saliva coats the whole buccal mucosa lining. The salivary film is 0.07 to 0.10 mm thick. The rate of buccal absorption is influenced by the film's thickness, composition, and motion.
B. Minor salivary glands: The buccal mucosa's epithelium or deep epithelial region is home to these glands. On the buccal mucosa's surface, they continuously release mucus. Despite the fact that mucus aids in the retention of mucoadhesive dose forms, it may act as a barrier to medication penetration.

3. Buccal tissue movement:
The buccal portion of the oral cavity exhibits fewer active motions. To maintain the dosage form in the buccal region for extended periods of time and to withstand tissue movements during talking and, if possible, during eating or swallowing, mucoadhesive polymers must be included[2].

COMPOSITION OF BUCCAL PATCHES:

Table 1.

Active ingredient	Drug of choice and compatibility.
Polymers (Adhesive layer)	Polyvinyl pyrrolidone, polyvinyl alcohol, carbopol, hydroxyethyl cellulose, and other mucoadhesive polymers.
Diluents	Because of its excellent aqueous solubility, flavouring properties, and direct compression-suitable physico-mechanical properties, lactose DC is chosen as a diluent. Another illustration is starch and microcrystalline starch.
Sweetening agents	Aspartame, mannitol, sucralose, etc.
Flavouring agents	Vanillin, clove oil, menthol, etc.
Backing layer	Polyvinyl alcohol, ethyl cellulose, etc.
Penetration enhancer	Cyanoacrylate etc.
Plasticizers	Propylene glycol, PEG-100, PEG-400, etc[1].

METHODS OF PREPARATION:

1) Solvent casting: In this process, the medication and all patch excipients are co-dispersed in an organic solvent and coated on a release liner sheet. A thin coating of the protective backing material is laminated onto the sheet of coated release liner after the solvent has evaporated to create a laminate. To create patches with the specified size and geometry, it is die-cut.

2) Direct milling: This eliminates the need for solvents in the manufacturing of patches. Direct milling or kneading are typically used to mechanically combine the drug and excipients without the use of any liquids. The finished material is rolled on a release liner until the

necessary thickness is reached after the mixing process. Following that, the backing material is laminated as previously said. The solvent-free approach is favoured since there is no chance of residual solvents and no associated solvent-related health risks, even though there are only slight or even no changes in patch performance between patches made using the two processes[3].

NATURAL POLYMERS:

Table 2.

Name	Xyloglucan
Composition	All vascular plants' major cell walls contain this hemicellulose, however the enzymes necessary for xyloglucan processing are only found in Charophyceae algae. It is the most prevalent hemicellulose in the primary cell wall of many dicotyledonous plants. A hemicellulose, xyloglucan has side chains with xylose, galactosyl, and fucosyl substituents[4].
Extraction	The glucose, xylose, and galactose contents of the xyloglucan component powder isolated from defatted TKP employing 95% ethanol in precipitation procedure with protease enzyme application for 3 hours were comparable to the commercial xyloglucan standard[5].

Table 3.

Name	Pectin
Biological source	A refined polysaccharide substance known as pectin can be found in a variety of plant sources, including the inner peel of citrus fruits, apples, raw papayas, etc.
Composition	Depending on the amount of carbohydrate connections, pectin is a polysaccharide with a variable molecular weight ranging from 20,000 to 400,000. L-rhamnose and D-polygalacturonate residues are joined together to form the molecule's central structure. D-galactose, L-arabinose, D-xylose, and L-fructose are four neutral sugars that make up the side chains of the pectin molecule. Pectin is very water soluble and appears after extraction as a coarse or fine yellowish powder that forms thick colloidal solutions. Although the parent substance, protopectin, is insoluble, pectinic acids are easily produced by hydrolysis of it (also known generically as pectins)[6].
Extraction	Endo-xylanase treatment of apple pomace produced the highest pectin output (19.8%) and extremely high DM (73.4%). GalA content in endo-cellulase-treated pectin was high (70.5%), which was one of its distinguishing characteristics. With both enzymatic preparations used simultaneously, a 10.2% extraction yield and a pectin with a high galacturonic acid content (74.7%) were produced[7].

Table 4.

Name	Chitosan
Biological source	Found in the shells of many different creatures, such as insects and fungus, as well as crustaceans like lobsters, crabs, and shrimp.
Composition	At least 50% of the free amine form of chitin, or deacetylated chitin, is present in chitosan, which has a heterogeneous chemical structure composed of both 1-4 linked 2-acetamido-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-glucopyranose[8].
Extraction	The debris from shrimp shells is first cleaned and dried. The dry shrimp shell scraps are powdered. This powder is demineralized using 2N HCL at a 1:15 ratio at room temperature for two hours at 150 RPM. The resulting powder is deproteinized using 2N NaOH in a 1:20 ratio at 150 RPM at 50°C. After the acquired chitin has been deacylated with 50% NaOH for 1 hour at 121°C and 15 psi, chitosan has been produced[9].

Table 5.

Name	Gelatin
Biological source	The collagen found in the skin, bones, and connective tissues of animals like cattle, poultry, swine, fish, and horses is partially hydrolyzed to create the protein gelatin, which is used in food production.
Composition	Proline and four hydroxyproline residues, as well as glycine (nearly one in three residues, organised every third residue), are abundant in gelatin[10].
Extraction	The sodium hydroxide solution was applied to the fish skins and left on for 40 minutes. The fish skin was then treated with acid after being washed with sodium hydroxide, first with sulphuric acid 0.2% (v/v) and then with citric acid solution 1% (w/v). The skins were rinsed in cold water after the acid solutions were drained. The last stage of gelatin extraction took place in distilled water at 45°C for 18 hours. The freeze-drying technique was used to get rid of any remaining water in the gelatin extract. To eliminate additional water, the extracts were filtered through two layers of clothing and heated to 70°C. The filtrate was dried at 50°C in a hot air oven[11].

EVALUATION PARAMETERS:

Physical parameters:

1) Surface pH
2) Thickness measurement
3) Swelling study
4) Water absorption capacity test

Performance parameters:

1) Drug content uniformity
2) Permeation study of buccal patch
3) Mechanical strength
4) In-vitro release study
5) Stability study

Physical parameters:

1) Surface pH:

On an agar plate, buccal patches are allowed to swell for two hours. A pH paper is placed on the surface of the swollen area to measure the surface pH.

2) Thickness measurement:

Using a screw gauge/micrometer, the thickness of each film is measured five separate places (the centre and the four corners) (figure 1).

Figure 1. Screw Gauge

3) Swelling study:

Buccal patches are weighed separately (W1), placed separately in 2% agar gel plates, incubated at 37°C 1°C, and checked for any physical changes. Patches are taken from the gel plates every hour until three hours, after which extra surface water is gently wiped away with filter paper. The swelling index (SI) is then computed using the formula after the swelled patches are reweighed (W2).

$$\% SI = \frac{\text{Weight of the swollen tablet} - \text{Initial weight of the tablet}}{\text{Initial weight of the tablet}} \times 100$$

4) Water absorption capacity test: Circular Patches with a surface area of 2.3cm2 are stored in an incubator that is kept at 37°C 0.5°C and allowed to swell on the surface of agar plates made in simulated saliva (2.38 g Na_2HPO_4, 0.19 g KH_2PO_4, and 8g NaCl per litter of distilled water adjusted with phosphoric acid to pH 6.7). Samples are weighed (wet weight) at various time intervals (0.25, 0.5, 1, 2, 3 and 4 hours), dried for 7 days in a desiccator over anhydrous calcium chloride at room temperature, and then the final constant weights are recorded. The formula is used to compute water uptake (%).

$$\text{Measured water absorption capacity} = \frac{We - Wo}{Wo}$$

Performance parameters

1) Drug content uniformity:

Three film units of each formulation were taken in separate 100ml volumetric flasks, 100ml of PH 6.8 phosphate buffer was added, and the mixture was agitated continuously for 24 hours to determine the drug content uniformity. The solutions were filtered, appropriately diluted, and UV spectrophotometer analysis was performed at 276nm (Sysronic) (figure 2).

Figure 2. UV Spectrophotometer

2) Permeation study of buccal patch:

Phosphate buffer with a pH of 6.8 is placed in the receptor compartment, and the hydrodynamics in the receptor compartment are maintained by magnetic bead stirring at 50 rpm. Samples are taken at regular intervals and their drug content is examined.

3) Mechanical strength:

Tensile strength and elongation at break are two mechanical characteristics of the films (patches) that are measured using a tensile tester. A film strip that is 60 x 10 mm in size, has no visible flaws, and is cut, then it is placed between two clamps that are 3 cm apart. The strips are dragged apart by the top clamp moving at a rate of 2 mm/sec until the strip break, and the force and elongation of the film at the point of the trip break are recorded. Clamps are used to secure the patch during the test without crushing it. The formula 36, where M is the mass in gm, g is the acceleration due to gravity in cm/sec2, B is the specimen's width in cm, and T is its thickness in cm, is used to compute the tensile strength and elongation at break values. Tensile strength (kg/mm2) is the force at break (kg) divided by the specimen's initial cross-sectional area (mm2) (figure 3).

Figure 3. Tensile Tester

4) In-vitro release study:

The drug release from the bilayered and multi-layered patches is investigated using the United States Pharmacopeia (USP) XXIII-B rotating paddle method. The phosphate buffer with a pH of 6.8 served as the dissolving media. At a speed of 50 rpm and a temperature of 37°C + 0.5°C, the release is carried out. With the use of an instant adhesive, the glass disc is connected to the buccal patch's supporting layer. The disintegration vessel's bottom receives the disc. At predefined intervals, samples (5 ml) are removed and replaced with new media. Following the proper dilution, the samples were filtered using Whatman filter paper and examined for drug content. Using a glass diffusion cell of the Keshary-Chien/Franz type, buccal permeation through the buccal mucosa of sheep and rabbits is tested in vitro at a temperature of 37°C 0.2°C. Mounted between the donor and receptor compartments is fresh buccal mucosa. The buccal patch should be applied with the compartments clamped together and the core facing the mucosa. The buffer is positioned inside the donor chamber (figure 4).

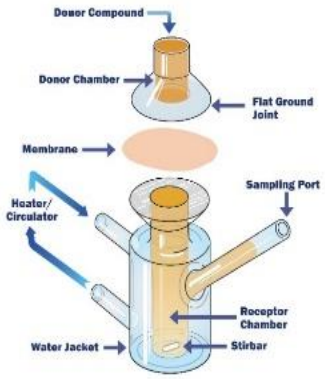

Figure 4. Franz Diffusion Cell

5) Stability study:

Human saliva is used to conduct stability research on bi-layered and multi-layered patches that have been optimised. Humans are used to collect the saliva (age 18-50years). A temperature-controlled oven set at 37°C 0.2°C is used to incubate buccal patches for six hours. Each buccal patch is placed in a separate Petri dish with 5ml of human saliva. It is necessary to use dose formulations with improved bioavailability at set intervals of time (0, 1, 2, 3, and 6 hours). Improved transmucosal and transdermal medication delivery techniques would be extremely important since they completely eliminate the discomfort element associated with parenteral routes of drug administration. Buccal adhesive systems have a plethora of benefits, including ease of accessibility, ease of administration and withdrawal, resiliency, minimal enzymatic activity, affordability, and high patient compliance. Adhesion of buccal adhesive drug delivery devices to mucosal membranes increases the gradient of drug concentration at the site of absorption, improving the bioavailability of medications administered systemically. Additionally, buccal adhesive dosage forms have been utilised to treat local conditions at the mucosal surface, such as mouth ulcers, in order to lessen the overall dose needed and decrease any potential side effects from systemic medication administration. Researchers are currently searching for new drug transport mechanisms outside of conventional polymer networks. Currently, the most successful oral dosage forms on the market are solid dosage forms, liquids, and gels. Future developments in vaccine design and administration of tiny proteins/peptides will influence buccal adhesive medication delivery[12].

INSTRUMENTATION:

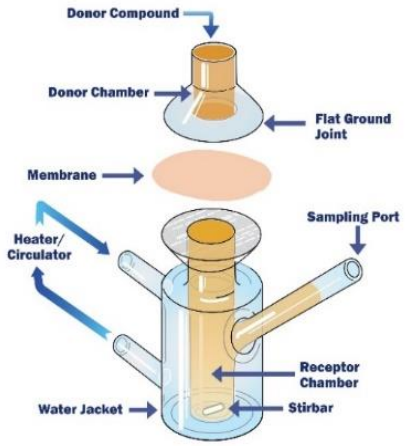

Figure 5. Franz Diffusion Cell

Franz type cell, also known as a side-by-side cell, has a fixed volume receptor chamber, controlled temperature, a port to sample the receptor fluid, and stirred receptor fluid (Side-by-Side Cells allow stirring of both the donor and receptor chambers) (figure 5).

Uses: Compound absorption into a membrane, finite dosage permeation, and steady-state compound fluxes are all evaluated (either alone or in formulations.)

Considerations:

1) The build-up of the compound in the receptor portion is not a problem if you are employing a highly permeable compound with a big volume receptor chamber because the greater volume lowers the gradient (sink conditions are maintained).
2) The build-up of compound lowers the flux of the chemical if you are employing a highly permeable compound with a tiny receptor chamber because it reduces the concentration gradient (non-sink conditions).
3) The detection of the drug in a big volume receptor chamber can be difficult if you're utilising a low permeability substance[13].

CONCLUSION:

Research on buccal medication administration has grown and advanced significantly during the last few decades. Because it has important benefits such avoiding first pass metabolism in the liver and pre-systemic removal in the gastrointestinal tract, the transmucosal route is growing in popularity. Buccal drug administration offers a viable and alluring alternative for the non-invasive delivery of powerful peptide and protein therapeutic molecules as well as significant potential for the systemic distribution of medications that are ineffective when taken orally. Despite the benefits of administering medications through the buccal mucosa, this route is nevertheless exceedingly difficult. The main challenges are the mucosa's barrier qualities and the small absorption region. The use of substances that combine mucoadhesive, enzyme inhibitory, and penetration enhancer properties, as well as the design of novel formulations, are strategies being researched to overcome these challenges. These approaches not only improve patient compliance but also favour an intimate and prolonged contact of the drug with the absorption mucosa. The use of mucoadhesive for the administration of novel medications and the pursuit of perfect mucoadhesive are expected to present new and unanticipated difficulties. To evaluate and compare various materials and formulations in terms of their capacity to increase medication absorption via the buccal route, standard in vitro and ex vivo biological models must be developed.

REFERENCE:

1. Rao NR, Shravani B, Reddy MS. Overview on buccal drug delivery systems. Journal of Pharmaceutical Sciences and Research. 2013 Apr 1; 5(4):80.
2. Fathima SR, Kumar SN, Rao BN, Ruksana S, Harish P, Joy S, Divya S, Ayesha S. Mucoadhesive Buccal Patches-A Review.
3. Parmar HG, Jain JJ, Patel TK, Patel VM. Buccal patch: A technical note. Int J Pharm Sci Rev Res. 2010; 4(3):2010.
4. Zavyalov AV, Rykov SV, Lunina NA, Sushkova VI, Yarotsky SV, Berezina OV. Plant polysaccharide xyloglucan and enzymes that hydrolyze it. Russian Journal of Bioorganic Chemistry. 2019 Dec; 45(7):845-59.
5. https://ifst.onlinelibrary.wiley.com/doi/abs/10.1111/jfpp.14055#:~:text=The%20xyloglucan%20component%20powder%20extracted,to%20the%20commercial%20xyloglucan%20standard
6. Mohnen D. Pectin structure and biosynthesis. Current Opinion in Plant Biology. 2008 Jun 1; 11(3):266-77.
7. Masuelli M, Blumenberg M. Pectins: extraction, purification, Characterization and applications. BoD–Books on Demand; 2020 Jan 22.
8. Kou SG, Peters LM, Mucalo MR. Chitosan: A review of sources and preparation methods. International Journal of Biological Macromolecules. 2021 Feb 1; 169:85-94.
9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5352841/#:~:text=Chitosan%20extraction%20was%20done%20following,at%20room%20temperature%20%5B23%5D.
10. Karayannakidis PD, Zotos A. Fish processing by-products as a potential source of gelatin: A review. Journal of Aquatic Food Product Technology. 2016 Jan 2; 25(1):65-92.
11. https://www.iosrjournals.org/iosr-jbb/papers/Vol2-issue6/Version-1/I02064049.pdf.
12. Koyi PK, Khan AB. Buccal patches: a review. International Journal of Pharmaceutical Sciences and Research. 2013 Jan 1; 4(1):83.
13. https://www.slideshare.net/laboratoryenterprises/diffusion-testing-fundamentals-introduction?from_m_app=android
14. Sharma N, Jain S, Sardana S. Buccoadhesive drug delivery system: a review. Journal of Advanced Pharmacy Education & Research Jan-Mar. 2013; 3(1):9-12.