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Buccal film: A Novel Approach for Enhanced Drug Delivery

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ABSTRACT: Novel Drug Delivery System is helpful in improving patient compliance,safety,efficacy,one such new way of administrating drugs is in the form of buccalfilms.Buccal films dissolves in the buccal cavity at a faster rate which helps to deliver the drug to produce rapid therapeutic action by reducing first pass metabolism.

Key words: Colouring agent, sweetening agent, surface PH,folding endurance.

I. INTRODUCTION:

Fast-dissolving buccal film drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. They are usually used for pharmaceutical and neutraceutical products. It is the newest frontier in drug delivery technology that provides a very convenient means of taking medications and supplements. There are multiple fast-dissolving over the counter and prescribed products on the market worldwide, most of which have been launched recently. There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology.

Now the main question arises that what are fast dissolving buccal films. A fast-dissolving buccal film drug delivery system, in most cases, is a film containing active ingredient that dissolves or disintegrates in the saliva remarkably fast, within a few seconds without the need for water or chewing. Some drugs are absorbed well from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. Fast dissolving buccal films use a dissolving film to administer drugs via absorption in the mouth (buccally or sublingually) and/or via the small intestines (enterically). A film is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity, delivering the drug to the systemic circulation via dissolution when contact with liquid is made. Fast dissolving buccal films drug delivery has emerged as an advanced alternative to the traditional tablets, capsules and liquids often associated with prescription and over the counter medications. Similar in size, shape and thickness to a postage stamp, 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. Different buccal delivery products have been marketed or are proposed for certain diseases like trigeminal neuralgia, meniere's disease, diabetes and addiction. Improved patient compliance is a primary benefit of the fast-dissolving drug delivery systems. Other benefits of fast-dissolving films include ease of swallowing [1], no water necessary for administration, and accuracy of dosage. This fast-dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist oral environment. These additional, superior benefits allow patients to take their medication anytime and anyplace under all circumstances. The fast dissolving buccal film drug delivery system offers a giant leap forward in drug administration by providing a new and easy way of taking medication. Many fast-dissolving tablets are soft, friable, and/or brittle (such as the lyophilized dosage forms) and often require specialized and expensive packaging and processing. These tablets are either very porous or inherently soft-molded matrices, or tablets compacted at very low dissolution/disintegration time. The delivery system is simply placed on a patient's tongue or any oral mucosal tissue [2].

Instantly wet by saliva, the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oral mucosal absorption or with formula modifications, will maintain the quick-dissolving aspect but allow for gastrointestinal absorption to be achieved when swallowed.

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Formulation of fast dissolving buccal film involves the application of both aesthetic and performance characteristics such as strip-forming polymers, plasticizers, active pharmaceutical ingredient, sweetening agents, saliva stimulating agent, flavoring agents, coloring agents, stabilizing and thickening agents. From the regulatory perspectives, all excipients used in the formulation of oral drug strips should be approved for use in oral pharmaceutical dosage forms. In recent application of fast dissolving buccal films it has been made possible that vaccines can be provided to infants in impoverished area against rotavirus [3].

FDA approved fast dissolving buccalfilms[4-6]

SL . NO	DRUG	YEAR	USE	COMPANY
01	Suboxone® (Buprenorphine and Naloxone	31/08/2010	Sublingual film indicated for maintenance treatment of opioid dependence and should be used as part of a complete treatment plan to include counselling and psychosocial support.	Reckitt Benckiser Pharmaceuticals Inc.
02	Zuplenz	January 2010	Prevention of postoperative, highly and moderately emetogenic cancer chemotherapyinduced, and radiotherapy-induced nausea and vomiting.	PharmFilm® technology
03	Ondansetron	23rd March 2010	Prevention and treatment of Chemotherapy and Radiotherapy Induced Nausea and Vomiting ("CINV") in adults as well as children aged equal or above 6 months, and the prevention and treatment of Post Operative Nausea and	APR Applied Pharma Research s.a. ("APR") and Labtec GmbH ("Labtec")

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			Vomiting (PONV) in adults and children aged equal or above 4 years	
04	Zelapar	October 2005	Treatment for Perkinson's disease	Valeant Pharmaceuticals International Inc.

Novel buccal dosage forms

The novel buccal dosage forms consist of buccal adhesive tablets, patches, films, semisolids (ointments and gels) and powders.

A. Buccalmucoadhesive tablets

Buccalmucoadhesive tablets are dry dosageforms which gets moistened when come in contact with buccal mucosa.

Example: a double layer tablet, consisting of adhesive matrix layer of HPC and polyacrylic acid with an inner core of cocoa butter containing insulin and a penetration enhancer (sodium glycocholate).

B. Patches and Films

Buccal patches consists of two laminates, with an aqueous solution of the adhesive polymer being cast onto an impermeable backing sheet, which is then cut into the desired oval shape.

C. Semisolid Preparations (Ointments and Gels)

Bioadhesive gels or ointmentshave not patient acceptability as like other solid bioadhesive dosage forms, and most of the dosage forms are used only for localized drug therapy within the oral cavity.

D. Powders

HPC and beclomethasone in powder form when sprayed on to the oral mucosa of rats, a significant increase in the residence time relative to an oral solution is seen, and 2.5% of beclomethasone is retained on buccal mucosa for over 4 hrs. [7]

Some commonly used film[8-11]

SL.NO	NAME OF THE POLYMER	CHARACTERISTICS
01	Pullulan	Water soluble, neutral, non-toxic, non immunogenic, biodegradable, non-mutagenic, non-carcinogenic, impermeable to oxygen, high adhesion and film forming abilities, non ionic polysaccharide and is blood compatible
02	Lycoat NG 73	Easily dispersible in cold water, lumps free dispersion, gives homogenous solution, simple cooking by heating will develop its film forming ability and can be used alone as film forming polymer to formulate buccal films
03	Maltodextrin	Film forming polymers and can be used to form the buccal film by film casting method as well as extrusion method. It can form a homogenous film
04	Hydroxypropyl Cellulose	Non-ionic, water soluble, thermoplastic polymer, can be used to prepare flexible films because of it gives low surface and interfacial

International Journal of Pharmaceutical Research and Applications
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		[4]
05	Hydroxypropyl methyl cellulose	Extensively used film former, available in different grades, E3, E5 and E15 etc. it has high glass transition temperature, it forms tough and flexible films from aqueous solutions. Lipophilics contents can be incorporated in films formulated by HPMC
06	Polyvinyl pyrrolidone	Water soluble, good wetting characteristics, non-ionic, pH-stable, resist the temperature, used to form films readily and it is colorless. Forms films with rapid and easy disintegration

Formulation aspects for BuccalFilm[12]

Active Pharmaceutical Ingredient

Active pharmaceutical substance can be from any class of pharmaceutically active substances that can be administered orally or through the buccal mucosa. Like antiulcers, antiasthmatics, antitussive, antihistaminic, antiepileptic, expectorants, antianginal etc. For the effective formulation, dose of drug should be in mgs (less than 20 mg/day). Usually 5%w/w to 30%w/w of active pharmaceutical ingredients can be incorporated in buccal film. High dosage of molecules is difficult to incorporate into film.

Ideal Characteristics of Drug to be selected:-

- No Bitter Taste
- Dose lower than 20mg
- Low molecular weight
- Good stability in water and saliva
- Ability to permeate oral mucosal tissue

Mucoadhesive agents

Different situations for buccalmucoadhesion are possible depending on the dosage form. In the case of dry or partially hydrated formulations, polymer hydration and swelling properties probably play the main role. The polymer hydration and consequently the mucus dehydration could cause enhance in mucouscohesive characteristics that support mucoadhesion. Swelling should help polymer chain flexibility and interpenetration between polymer and mucin chains. The spreading coefficient and the capability to form physical or chemical bonds with mucin increase when fully hydrated dosage forms. So that depending on the type of formulation, polymers with different characteristics have to be considered. The polymers most commonly used in buccal dry or partially hydrated dosage forms include polyacrylic acid (PAA), polyvinyl alcohol (PVA), sodium carboxymethyl cellulose (NaCMC), hydroxypropyl methylcellulose (HPMC), hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC) and sodium alginate. Their peculiarity depends in the mucoadhesion mechanism: such substances are able to identify and bind some specific sugar residues on mucosal surface without altering the structure of the recognized ligand.

Plasticizers

It is a necessary ingredient of the oral films. The selection of plasticizer depends upon its compatibility with the polymer and also the type of solvent used in the casting of film. It improves the flexibility of the film and reduces the brittleness of the film. They are used in the concentration of 1 - 20%w/w of dry polymer weight. Examples include: Glycerol, Propylene glycol, Low molecular weight polyethylene glycols, Citrate derivatives like triacetin, acetylcitrate, Phthalate derivatives like dimethyl, diethyl, dibutyl derivatives, Castor oil etc.

Sweetening Agents

Sweetening agents are important in food and all pharmaceutical products which are disintegrate or dissolved in oral cavity. The standard source of sweetener is sucrose, dextrose, fructose, glucose, liquid glucose and maltose. The sweetness of fructose is accepted rapidly in the mouth as compared to sucrose and dextrose. But use of natural sweeteners has major issue to diabetic patients. Due to this reason, intake of the artificial sweeteners has more popularity in food and pharmaceutical preparations. Saccharin,

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cyclamate and aspartame are the first generation of the artificial sweeteners followed by acesulfame-K, sucralose, alitame and neotame which fall under the second generation artificial sweeteners.

Saliva Stimulating Agents

Addition of this agent in formulation is important because it increase rate of production of saliva so that film undergoes fast disintegration and rapid dissolution takes at buccal cavity. Usually acids which are used in the preparation of food can be utilized as salivary stimulants. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them. These agents are used individually or in combination between 2 to 6%w/w of weight of the film.

Cooling Agent

Monomethyl succinate is used as cooling agents which helps to improve the flavour strength and to improve the mouthfeel effect of the film. Other cooling agents such as WS3, WS23 and Utracoll II can also be used in conjunction with flavors.

Flavoring Agent

It was observed that flavoring agent plays a major role in the taste fondness. Synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers are used for selection of flavoring agent. Depending of flavoringagents strength, need of amount of flavoring agent to m mask taste.

Coloring Agent

Pigments like as Titanium dioxide or FD&C approved colouring agents are incorporated (not exceeding concentration levels of 1%w/w) in buccal film formulation when some of the formulation ingredients or drugs are present in insoluble or suspension form.

Surfactants

Surfactants are used as solubilising or wetting agent. Film gets dissolved rapidly within seconds by use of surfactant and immediately drug is released. Solubility of poorly soluble drugs in buccal can be improved by using surfactant. For examples are Polaxamer 407, sodium lauryl sulphate, benzalkonium chloride, benzethonium chloride, tweens and spans etc.

Stabilizing and thickening agents

Addition of stabilizing and thickening agents are important to improve the viscosity and consistency of dispersion or solution of the film preparation before casting. Natural gums like xanthan gum, locust bean gum, carragenan and cellulosic derivatives are few examples of stabilizing and thickening agents. They are used in the concentration up to 5%w/w.

Manufacturing methods of Buccal film

Buccal film formulation is mainly prepared by following three methods

1. Solvent Casting Method
2. Hot Melt Extrusion Method
3. Direct Milling Method

1. Solvent Casting Method

In solvent casting method, required quantity of polymer is added and dissolved in distilled water. Active pharmaceutical ingredient in small quantity added in this solution. Plasticizer is added in solution and stirred well. Solution is then casted on petridish and kept in hot air oven for drying at 400C. After drying removed it from petriplate by cutting with blade and allowed to keep in desicator for 24hours. Henceforth cut in required size and shape.

Steps involved in Solvent Casting Method

Step 1: Preparation of casting solution
Step 2: Deaeration of solution
Step 3: Transfer of appropriate volume of solution into the mould
Step 4: Drying the casting solution
Step 5: Cutting the final dosage form to contain desired amount of drug.

International Journal of Pharmaceutical Research and Applications
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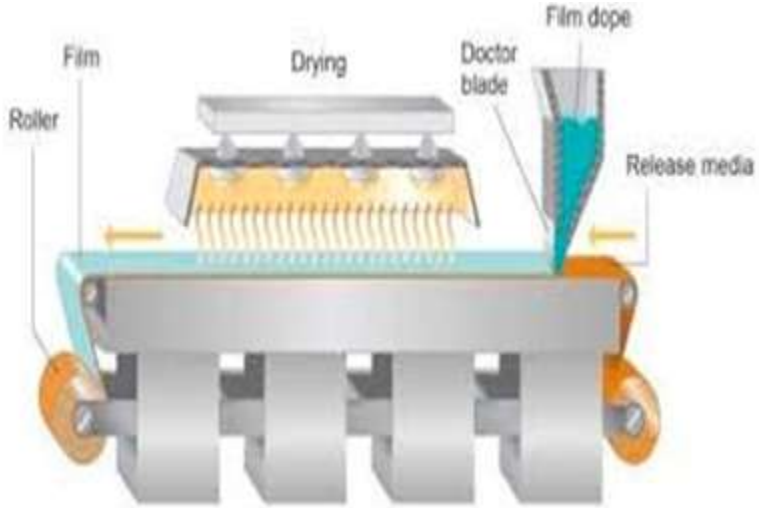


2. Hot Melt Extrusion Method

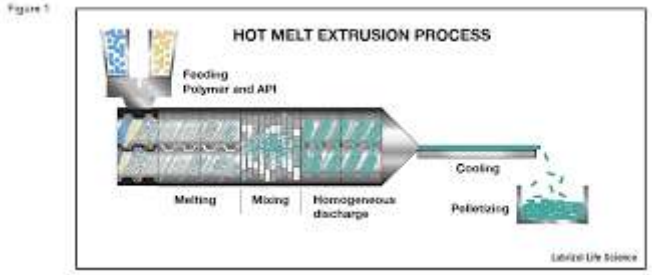
In hot melt extrusion method mixture of drug and other excipients is molten. Then forced through orifice to yield a more homogenous material in different shapes like granules, tablets, or films. It is used for transdermal drug delivery System.

Steps involved in Hot Melt Extrusion Method

Step 1: The drug is mixed with carriers in solid form

Step 2: Extruder having heaters melts the mixture

Step 3: Finally the melted mixture is shaped in films by the dies



Advantages and Disadvantages of Hot Melt Extrusion Method.

Advantages

- Fewer operation units
- Better content uniformity
- An anhydrous process

Disadvantages

Thermal process creates stability problem.

- Flow properties of polymer are important to processing.
- Limited numbers of polymers are available.

3. Direct Milling Method

This method is solvent free method. In this method, drug and excipients are mixed without presence of liquid by direct milling or by kneading. Then resulting material is rolled on release liner til the required thickness is obtained. This method is usually preffered because of there is no possibility of residual solvent and no any association of solvent related health issue.[13]

International Journal of Pharmaceutical Research and Applications
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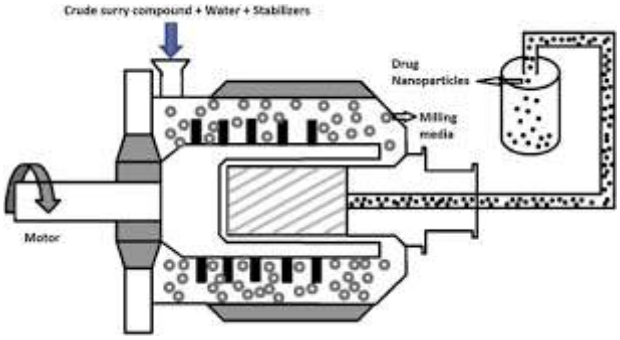

Evaluation Parameters of Buccal film

Weight of the film

Buccal film is weighed by calibrated weighing balance. Individual weight of each film is calculated. Average weight is calculated and analyzed weight of film.

Thickness

Thickness of buccal film is evaluated by calibrated micrometer screw gauge. The thickness is measured at five different points of the film and means value is calculated. This is done to ensure the uniformity in the thickness of the film as it is directly correlated with accuracy of dose in the film and supports the reproducibility of the method used for the formulation.

Tensile strength

The tensile strength is the property of the film that requires a load to cause load deformation failure of film. Film strips in special dimension is held between two clamps positioned at a specific distance. Tensile strength is calculated by applying load at rupture and cross sectional area of fractured film from following equation.

Tensile strength (N/mm2) = breaking force (N)/ cross sectional area of sample (mm2)

Surface pH of the film

The films are allowed to swell by keeping them in contact with 1 ml of distilled water for 2 h at room temperature, and pH is noted down by bringing the electrode in contact with the surface of the film, allowing it to equilibrate for 1 min.

Folding endurance

Folding endurance is to be determined by repeatedly folding the film at the same place, until it breaks. The number of times, the film could be folded at the same place without breaking gives the value of folding endurance.

Percentage moisture loss

This is used to check integrity of films. Film is cut out and then takes weight. After it is keep in desicator containing fuse anhydrous calcium chloride. After 72 hours it is removed and weighted. Average percentage moisture loss is calculated by below formula.

Percentage Moisture Loss = (Intialweightfilm weight)×100/Initial weight

Drug Content uniformity Buccal film is dissolved in 100 ml of pH 6.8 buffer separately and mixture is suitably diluted. The amount of drug in film is measured absorbance spectrophotometrically at 242 nm. The average drug content is calculated.

In vitro disintegration time

It is determined visually in a petriplate containing 2 ml distilled water with swirling every 10 seconds. The time at which film started to break or disintegrate is recorded as the in vitro disintegration time.

In vitro dissolution study

An in vitro dissolution study is carried out using USP type II apparatus (Basket type apparatus). pH 6.8 buffer (50 mL) is used as a dissolution medium at 50 rpm speed and 370C temperature. At specific time intervals, 1 ml samples were withdrawn and replaced with the equal quantity of fresh dissolution medium. Buccal films are filtered through 0.45 µm Whatman filter paper, and analyzedspectrophotometrically at λmax of active pharmaceutical ingredient. [25, 26] Dissolution kinetics study It is done by determining the best fit mathematical model for formulations. R and k values for different mathematical models are determined putting the dissolution data in respective mathematical models. The model for which the R value is the highest that model is considered as the best fit model for the concerned formulation. The n value for the best fit model is

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recorded and it is used to determine the fickian or non-fickian diffusion pattern the formulation follows.

A. Zero-order kinetic: Qt = Qo + k0t

Where, Qt is amount of drug release at time t K0 is zero order release rate constant. Q0 is amount of drug present initially at t = 0

B. First-order kinetic: ln (100 – Q) = lnQ0 – k1t

Where, Q = amount of drug release at time t Q0 = amount of drug present initially K1 = first order release rate constant

C. Higuchi equation Q = kH t1/2

Where, Q = amount of drug release at time t KH = Higuchi dissolution constant

Swelling index

The initial weight of the film is determined using a digital balance (W0). Then the films are allowed to swell on the surface of petri plate and kept in an incubator maintained at 37 °C. Weight of the swollen film is determined (Wt) at predetermined time intervals for 5 min. The percentage of swelling (% S) is calculated using the following equation.

% S= (Wt-Wo)*100 /Wo

Where Wt is the weight of swollen patch after time t,

W0 is the initial weight of patch at t=0.

Ex-vivo diffusion study

For in vitro release study, goat buccal mucosa membrane is used as a barrier membrane with Phosphate buffer (pH 6.8) as a medium. Drug release from film is evaluated by Franz diffusion cell. Buccal mucosa membrane is mounted between the donor and receptors compartments. The film is placed on the mucosal membrane. The diffusion cell is placed in simulated saliva maintained at 37±2°C.The receptor compartment is filled with 50 mL phosphate buffer (pH 6.8) and hydrodynamics is maintained by stirring with a magnetic bead at 50 rpm. 1 mL sample is withdrawn and replaced with 1 mL fresh medium to maintain the sink condition. The samples are analyzed by U.V. spectrophotometer at specific wavelength.

Stability study

Stability of a pharmaceutical product may be defined as the capability of a particular formulation, in a specific container / closure system, to remain within its physical, chemical, microbiological, therapeutic and toxicological specifications. The stability of all the formulations was carried out at different temperatures as per ICH guidelines. [31] Stability study is carried out storage conditions; one was normal room conditions at 400C/75% RH for 6 months and another at 300C/75% for 24 to 36month. Film is packed in packing material like aluminum foil and then evaluated for the DSC, FTIR, Folding endurance, disintegration time, drug content and in vitro drug release.

Advantages of Buccal Film

- No risk of chocking.
- No need of chewing and swallowing.
- Rapid onset of action and minimum side effects.
- Accurate dosing compared to liquid dosage form.
- Taste masking is possible.
- Good mouth feel and good stability.
- Requires less excipient.
- Ease of transportation, storage and consumer handling.
- More Economical
- Ease of administration to pediatric, geriatric patients. Also to patients who are mentally retarded, disabled or non cooperative.
- Prolongs residence time of dosage form at site of absorption. So improves bioavailability.
- Drug can be protected from degradation in GI tract and acidic environment.
- Buccal film has large surface area that leads rapid disintegration and dissolution in oral cavity. [14]

Disadvantages of Buccal Film

- Saliva is continuously secreted into the oral cavity diluting drugs at the site of absorption resulting in low drug concentrations at the surface of the absorbing membrane. Instinctively swallowing of saliva results in a maximum part of dissolved or suspended released drug being removed from the site of absorption. Moreover, there is risk that the delivery system itself would be swallowed
- Drug characteristics can make boundary for use of the oral cavity as a site for drug delivery. Taste, irritancy, allergy and adverse properties such as discoloration or erosion of the teeth can limit the drug candidate list for buccal route. Conventional type of buccal drug delivery systems did not allow the patient to concomitantly eat, drink or in some during talk. [15]

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II. CONCLUSION:

Fast dissolving buccal films are convenient and novel approach for the drug delivery .Drug reaches systemic circulation at a faster rate to produce expected pharmacological action. This films can be called as promising formulations. To enhance the patient compliance, safety, efficacy and drug delivery.

REFERENCES:

[1]. Slowson M, Slowson S. What to do when patients cannot swallow their medications. Pharm Times. 1985;51:90-6.
[2]. Tripathi KD. Essentials of medical pharmacology. JP Medical Ltd; 2013 Sep 30.
[3]. Thakur M, Sharma I, Moda M, Sharma N. Fast Dissolving Films: A Review.
[4]. Kumar PS. Development and Evaluation of Buccoadhesive Controlled Release Delivery System of Carvedilol (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
[5]. Patel R, Naik S, Patel J, Baria A. Formulation development and evaluation of mouth melting film of ondansetron. Arch Pharm Sci Res. 2009 Oct;1(2):212-17.
[6]. Mahajan A, Chhabra N, Aggarwal G. Formulation and characterization of fast dissolving buccal films: A review. Der Pharm Lett. 2011;3(1):152-65.
[7]. Rao NR, Shravani B, Reddy MS. Overview on buccal drug delivery systems. Journal of pharmaceutical sciences and research. 2013 Apr 1;5(4):80.
[8]. Pathare YS, Hastak VS, Bajaj AN. Polymers used for fast disintegrating oral films: a review. Int. J. Pharm. Sci. Rev. Res. 2013 Jul;21(1):169-78.
[9]. Parissaux X, Joshi AA, Francois A, Lefevre P. Evaluation of a novel modified starch polymer in an easy to formulate thin-film drug delivery system and comparison with some marketed formulations. Young. 2007;1070(804):323.
[10]. Cilurzo F, Cupone IE, Minghetti P, Selmin F, Montanari L. Fast dissolving films made of maltodextrins. European Journal of Pharmaceutics and Biopharmaceutics. 2008 Nov 1;70(3):895-900
[11]. Nagar P, Chauhan I, Yasir M. Insights into Polymers: Film Formers in Mouth Dissolving Films. Drug invention today. 2011 Dec 1;3(12).
[12]. Jagtap VD. Buccal Film—A Review on Novel Drug Delivery System. Int. J. Res. Rev. 2020;7:17-28.
[13]. Jagtap VD. Buccal Film—A Review on Novel Drug Delivery System. Int. J. Res. Rev. 2020;7:17-28.
[14]. Jagtap VD. Buccal Film—A Review on Novel Drug Delivery System. Int. J. Res. Rev. 2020;7:17-28.
[15]. Patel H, Pathak B, Patel T, Vaghela N, Patel D, Surati J, Shah K. A REVIEW ON BUCCAL DRUG DELIVERY SYSTEM. Pharma Science Monitor. 2023 Jul 1;14(3).