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FORMULATION & EVALUATION OF HERBAL BUCCAL TABLET

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1.0 ABSTRACT

This project was aimed to formulate and characterize mucoadhesive buccal tablets of aceclofenac, utilizing different proportions of three polymers carbopol 934, hydroxypropyl methylcellulose, and sodium carboxy methyl cellulose. Twelve batches of buccoadhesive aceclofenac were prepared by the direct compression method. The compressed tablets were then evaluated for physicochemical parameters such as hardness, thickness, weight variation, drug content, friability, swelling index, surface pH, and ex vivo mucoadhesion. In vitro dissolution test was conducted for 12 h according to Indian Pharmacopeia 2018, using the rotating paddle method in phosphate buffer of pH 7.4. Physiochemical parameters like weight variation (231.25–268.75 mg), hardness (8.32–11.56 kg), friability (0.04–0.2%), diameter (9.00 mm), thickness (3.8–4.05 mm), and drug content ((97.67–102.25%) were within the acceptable limit as per Indian Pharmacopeia 2018. The swelling index was reported to be in the range of 112.93–450.19%, at 8 h. The surface pHs of all the batches were in between 6.72 to 6.96. The mucoadhesive strengths (40.5– 50 g) varied with the change in polymer concentrations especially of carbopol 934. The dissolution profile of all the batches varied greatly, with a maximum release of 109.41% (in batch 12 at 6 h) to a minimum release of 44.82% (in batch 3 at 12 h). Among them, only batch 1 ensured sustained and effective drug release (88.34% at 12 h) with appropriate swelling index (112.93%) and mucoadhesive strength (40 g). Fourier Transform Infrared Spectroscopy analysis showed no evidence of drug excipients interaction. Hence, the results concluded that buccal mucoadhesive aceclofenac tablets can be formulated. Furthermore, the property of the tablet not only depends on the concentration but also the behavior of the polymers used. Buccal tablets were prepared using mucoadhesive polymers like Chitosan, HPMC K4M, Na CMC & amp; Sod. alginate by direct compression technique. Buccal tablets were characterized for number of parameters like Hardness, weight uniformity, thickness, % friability, swelling index, mucoadhesive strength, surface pH, drug–excipient interaction study, drug content uniformity and In vitro drug release study. . The continuous secretion of saliva and its subsequent swallowing can lead to substantial drug depletion from the dosage form and hence low bioavailability. Therefore, other transmucosal routes such as nasal, rectal, vaginal, ocular and oral mucosae are being considered as alternatives to conventional oral dosage forms for drug delivery to avoid the above disadvantages associated with conventional oral delivery (i.e., tablets, capsules, syrups, etc.). Of these routes of delivery, the buccal oral mucosa has emerged as one of the target sites for administration of drugs in a wide variety of dosage forms, particularly for those drugs targeted for local delivery in the oral cavity and systemic absorption.

2.0 KEYWORDS*:* Insomnia, Buccal Tablet, Lavender oil, Anxiety, Nutmeg, Stress.

3.0 INTRODUCTION

- Insomnia is technically defined as difficulty falling asleep, staying asleep, or nonrestorative sleep causing daytime impairment or distress despite adequate opportunity and circumstance to sleep occurring at least three times per week for at least one month. Herbs had been used by all cultures throughout history.
- It was an integral part of the development of modern civilization. Traditional medicinal systems consist of many drugs with sedative effect to pursue proper sleep. Nutmeg shown proved properties for sedation.
- It is the reason to use Nutmeg as prophylaxis for treating Insomnia. The western history of nutmeg dated back for 17th century when Nathaniel court hope an English spice merchant succeeded in establishing a rout to run one of ten volcanic islands in the Banda Sea. The evergreen nutmeg tree can reach 20m in height and continues to be cultivated in the original location as well as West Indies
- Buccal delivery system is defined as drug administration through the mucosal membrane lining the cheeks (buccal mucosa). Buccal drug delivery was introduced by Orabase in 1947. In recent year delivery of therapeutic agents through various transmucosal routes has gained significant attention. Buccal delivery of drug provides an attractive alternative to the oral route of drug administration, particularly in overcoming deficiencies associated with the latter mode of dosing.
- Negligible side effect as compares to allopathic, synthetic or semi- synthetic medicine Early relief with new formulations of herbal needed Nutmeg is a well culturally accepted traditional Indian spice we will introduce in the form of buccal tablet.
- To develop an herbal remedy for insomnia. To control the market for synthetic adversely affecting medicines. To develop herbal buccal fast drug realizing and effective medication. To use easily available Herbal Active ingredient. Cost-beneficial or budget-friendly
- Mucoadhesive drug delivery system is a distinct advantage over the traditional dosage forms such as, tablet, gels and solution etc. In the Mucoadhesive buccal patch for systemic drug delivery of drug like flavonoid which is isolated from the leaves of Psidium guajava in which system avoid first pass effect of hepatic metabolism. The buccal patch shows desired physicochemical and mechanical properties. The various evaluation parameter are used to evaluate the Mucoadhesive buccal patch. In-vitro drug release study shows that buccal patch deliver the drug like Quercetin to oral mucosa for the period of 7:30 hrs and also exhibit the stability study under desired condition. HPMC K15 buccal adhesion patch shows satisfactory physico-chemical properties.
- The ratio of hydrophilic polymer carbopol 940 to HPMC K15 had significant Mucoadhesive characteristics like swelling index, ex-vivo mucoadhesion strength and in-vitro drug release is observed between drug release and permeation study in-vitro. So it can conclude that the HPMC K15 and Carbopol 940 could be good carrier in buccal delivery of Quercetin. Keywords: Carbopol 940, mucoadhesive buccal patch, HPMC K15, Psidium Guajava, Quercetin.
- The oral cavity is viewed as a convenient and easily accessible site for the delivery of therapeutic agents. Sobero, the discoverer of nitroglycerine, noted absorption of drugs through oral cavity as early as 1847 and Walton and Lacey first reported systemic studies of oral cavity absorption in 1935. Since then, substantial efforts have been focused on drug absorption from a drug delivery system in the particular region of oral cavity.
- Since the early 1980s there has been renewed interest in the use of bioadhesive polymers to prolong contact time in the various mucosal routes of drug administration. The ability to maintain a delivery system at a particular location for an extended period of time has great appeal for both local as well as systemic drug bioavailability.
- Drug absorption through a mucosal surface is efficient because mucosal surfaces are usually rich in blood supply, providing rapid drug transport to the systemic circulation and avoiding degradation by gastrointestinal enzymes and first pass hepatic metabolism. Conventional Dosage Form The conventional type of buccal dosage forms are buccal tablets, troches and lozenges, and mouth washers.
- These tablets should be designed not to disintegrate but to slowly dissolve, typically over a 15 to 30 minutes period to provide for effective absorption. Troches and lozenges are two other types of tablets used in oral cavity where they are intended to exert a local effect in the mouth or throat.
- The present study demonstrated that the Methanolic extract of the aerial part of Psidium Guajava Linn and to isolate the flavonoid Quercetin showed significant Antibacterial activity and formulation as Antiulcer activity, Mucoadhesive Buccal patch. The mouth ulcer are small painful inside lining of mouth. The usually developed on the inside of the lips and cheeks and under the edge of tongue. Studies were carried out with a view to select suitable polymer composite using in combination with polymers.
- The Psidium Guajaval is a most common plant usually used as a various treatment which is mention in the literature review. Psidium guava has been found most important rich chemical constituent Quercetin as flavonoid which is responsible to cure a mouth ulcer. However no specific formulation for mouth ulcer has been reported as mucoadhesive herbal buccal patch. Therefore the aim of the research project is to develop a formulation easily palatable, absorbable oral formulation rendering
- The mucosa of the mouth is very different from the rest of the gastrointestinal tract and morphologically

is more similar to skin. Although the permeability of skin is widely regarded as poor, it is not generally appreciated that the oral mucosa lacks the good permeability demonstrated by the intestine. These differences within the gastrointestinal tract can largely be attributed to the organization of the epithelia, which serve very different functions. A simple, singlelayered epithelium lines the stomach, small intestine, and colon, which provides for a minimal transport distance for absorbents. In contrast, a stratified or multilayered epithelium covers the oral cavity and esophagus and, in common with skin, is composed of layers with varying states of differentiation or maturation evident on progression from the basal cell layer to the surface. Drugs have been applied to the oral mucosa for topical applications for many years. However, recently there has been interest in exploiting the oral cavity as a portal for delivering drugs to the systemic circulation. Not withstanding the relatively poor permeability characteristics of the epithelium, a number of advantages are offered by this route of administration. Foremost among these are the avoidance of first-pass metabolism, ease of access to the delivery site, and the opportunity of sustained drug delivery predominantly via the buccal tissues.

- Buccal drug delivery system is known as administration of particular drug through mucosal membrane. The ease of administration of drug and prevention of achieved drug degraded in the Gastro-intestinal tract (GIT) and by passing first pass metabolism, increases the bioavailability, hence buccal cavity is alluring site for drug delivery. It leads to bioadhesion in which materials binds with biological substrate (mucosal membrane). There are four regions where the drug can be administrated mainly those are: palatal, sublingual, buccal, and gingival. The buccal delivery system leads to the delivery system in which drugs takes places within/through the mucosa to show local/systematic pharmacological action. This system is used for the treatment of diseases takes places in buccal cavity and also for the systematic diseases.
- This system is considered as a possible alternative to drug administration as it has more advantages over peroral routes. Buccal mucosa avoids enzymatic decomposition in gastrointestinal tract and firstpass metabolism of drug as the buccal mucosa are highly vascularized with an abundant blood supply and is relatively permeable which allows drug to be absorbed directly into the systemic circulation.
- The mucosal drug administration aims to achieve a site-specific release of drug on the mucosa, whereas thetrans-mucosaldrug administration involves drug absorptionthroughthe mucosal barrier to reach the systemic circulation. Difficulties associated with parenteral delivery and poor oral availability provided the impetus for exploring alternative routes for the deliveryofsuch drugs. These include routessuch as pulmonary, ocular, nasal, rectal, buccal, sublingual, vaginal, and transdermal.
- The ability to maintain a delivery system at a particular location for an extended period of time has great appeal for both local as well as systemic drug bioavailability. (5)However, some drugs, such as proteins and peptides, when administrated by oral route are susceptible to the first-pass metabolism in the liver and the enzymatic degradation in the gastrointestinal tract. Alternatively, other routes have been proposed as potential sites for drugs administration, including the buccal mucosa. The polymers can be used alone or in combination to obtain the desired film properties.
- Among the various transmucosal routes, buccal mucosa has excellent accessibility, an expanse of smooth muscle and relatively immobile mucosa, hence suitable for administration retentive dosage forms. Direct access to the systemic circulation through the internal jugular vein bypasses drugs from the hepaticfirst pass metabolism leading to high bioavailability.
- The oral cavity comprises the lips, cheek, tongue, hard palate, soft palate and floor of mouth. The oral cavity is lined by relatively thick, dense and multilayered mucous membrane of highly vascularized nature. The mucous secreting region comprises soft palate, floor of mouth underside of tongue and labial and buccal mucosa which have normally non keratinized epithelium. Transmucosal routes of drug delivery offer distinct advantages over per oral administration for systemic drug delivery. The transmucosal delivery of drug can involve the mucosallining of buccal, sublingual, nasal, vaginal, rectal and ocular. Among that oral mucosa is perhaps most convenient and preferred route for drug delivery.

There are four potential areas for drug delivery in the oral cavity, namely

- Buccal
- Sublingual
- Palatal
- Gingival Buccal drug delivery specifically refers to the delivery of drugs within/through The buccal mucosa to affect local/systemic pharmacological actions

Need for Study

Local drug delivery to mouth includes any system that is applied to the oral mucosal membrane to treat conditions of the mouth such as periodontal disease gingiv it is, oral candidiasi and other chronic lesions or topical bacterial fungal infections.

The oral cavity can be cited as one of the best sites for the delivery of drugs. Mucosal and trans mucosal (local effect and systemic effect, respectively) drug administration can be achieved through this route. The effect of the former is such that a site-specific release of

the drug on the mucosa is achieved, and in the latter, the drug reaches the systemic circulation by the way of mucosal barrier and gets absorbed. On account of irritation and impairment, the oral mucosa is less sensitive than the nasal epithelium. In trans mucosal drug administration, the sublingual and buccal mucosa work as absorption sites that has two curative goals.

The strong interaction between polymer and mucosal lining of the tissue allow sincreased contact time, modification of tissue-membrane permeability and localization of drug delivery which results in this improved bioavailability of drugs through mucoadhesive buccal delivery systems. The buccal region of oral cavity is an attractive site for the delivery of drugs owing to the ease of the administration. Buccal drug delivery involves the administration of desired drug through the buccal mucosal membrane lining of the oral cavity.

There are different methods for the evaluation of buccal drug delivery system. These includes weight variation, dimension, hardness, drug content, dissolution, uniformity of content, swelling index, mucoadhesive property for tablets, films and patches and viscosity for gel.

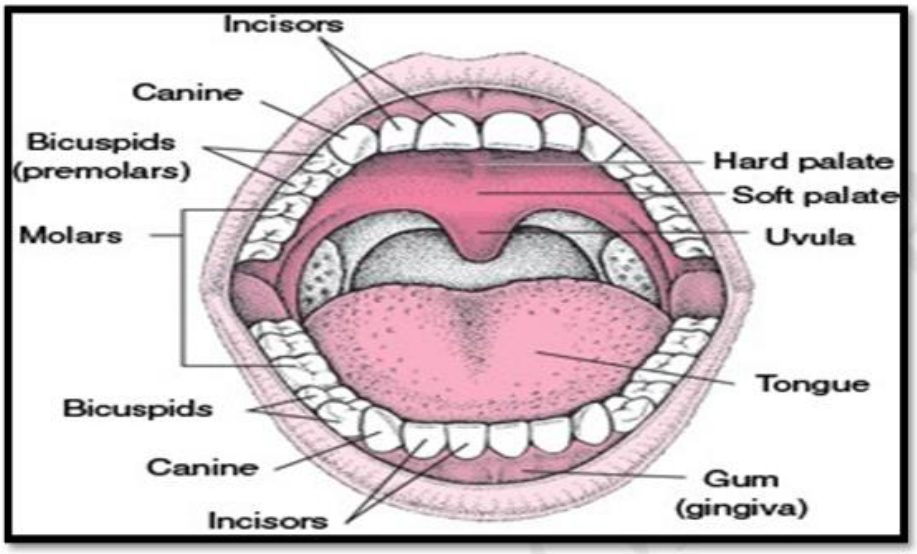

Fig. No. 1: Oral cavity of Buccal Drug.

DRUG DETAIL

1. Drug name: Nutmeg (Myristica fragrans)

Biological name:- It is obtained from kernel of dried ripe seeds of Myristica fragrans belonging to family myristicaceae.

Fig No. 2: Nutmeg.

2. Drug name: - Lavender oil

Biological name: -It is extracted from lavendula angustifolia (also known as lavendulan officinalis, spica and vera) Family :-Labiatae.

Fig No. 3: Lavender oil.

Fig No. 4: Magnesium Stearate.

3. Drug name: - Magnesium Stearate

Magnesium stearate is an additive that is most frequently used as a lubricant. Magnesium stearate is capable of forming films on other tablet excipients during prolonged mixing, leading to a prolonged drug liberation time, a decrease in hardness, and an increase in disintegration.

Magnesium stearate is an additive that's primarily used in medication capsules. It's considered a "flow agent." It prevents the individual ingredients in a capsule from sticking to each other and the machine that creates the capsules. It helps improve the consistency and quality control of medication capsules.

4. Drug Name: Starch

Foods that are high in starch are a good source of nutrition. They are broken down into glucose, which is the body's main fuel, particularly for our brain and muscles, after they are ingested. B vitamins, iron, calcium, and folate are all essential nutrients found in starchy foods. Starch is widely used as a binder in the wet granulation process of massing and screening which is an important step in the production of tablets, capsules, and other solid dosage forms. The sole aim of starch in terms of dietary function is to turn glucose into energy for our body. Glucose is the only carbohydrate that our body can use. Glucose circulates in our bloodstream, where it is absorbed by cells and used as a source of energy. Food starches are commonly used as thickeners and stabilisers in foods like puddings, custards, soups, sauces, gravies, pie fillings, and salad dressings, as well as in the production of noodles and pasta. Starch is made up of long chains of sugar molecules that are connected together. Starch's primary role is to help plants store energy. In an animal's diet, starch is a source of sugar. Amylase, an enzyme contained in saliva and the pancreas that breaks down starch for energy, is used by animals to break down starch.

Starch is a tasteless, fluffy white powder that is insoluble in cold water, alcohol, and other solvents. Starch is a polysaccharide made up of 1,4 linkages between glucose monomers. The chemical formula of the starch molecule is $(C_6H_{10}O_5)_n$. Starch is made up of long chains of sugar molecules that are connected together. The linear polymer amylose is the most basic form of starch, while amylopectin is the branched form. The primary role of starch is to help plants in storing energy. In an animal's diet, starch is a source of sugar. Amylase, an enzyme contained in saliva and the pancreas that breaks down starch for energy, is used by animals to break down starch.

Fig. No. 5: Starch Powder.

Fig. No. 6: Lactose Powder.

5. Drug Name; Lactose

Lactose is a sugar that is naturally found in milk and milk products, like cheese or ice cream.

In lactose intolerance, digestive symptoms are caused by lactose malabsorption. Lactose malabsorption is a condition in which your small intestine cannot digest, or break down, all the lactose you eat or drink. Not everyone with lactose malabsorption has digestive symptoms after they consume lactose. Only people who have symptoms are lactose intolerant. Most people with lactose intolerance can consume some amount of lactose without having symptoms. Different people can tolerate different amounts of lactose before having symptoms. Lactose intolerance is different from a milk allergy. A milk allergy is an immune system disorder.

Lactose, or milk sugar, is a disaccharide sugar composed of galactose and glucose subunits and has the molecular formula C12H22O11. Lactose makes up around 2–8% of milk (by mass). The name comes from lact (gen. lactis), the Latin word for milk, plus the suffix -ose used to name sugars. The compound is a white, water-soluble, non-hygroscopic solid with a mildly sweet taste. It is used in the food industry.

Lactose is a disaccharide derived from the condensation of galactose and glucose, which form a β-1→4 glycosidic linkage. Its systematic name is β-D-galactopyranosyl-(1→4)-D-glucose. The glucose can be in either the α-pyranose form or the β-pyranose form, whereas the galactose can have only the β-pyranose form: hence α-lactose and β-lactose refer to the anomeric form of the glucopyranose ring alone. Detection reactions for lactose are the Woehlk and Fearon's test. the different lactose content of different dairy products such as whole milk, lactose free milk, yogurt, buttermilk, coffee creamer, sour cream, kefir, etc. Lactose is hydrolysed to glucose and galactose, isomerised in alkaline solution to lactulose, and catalytically hydrogenated to the corresponding polyhydric alcohol, lactitol. Lactulose is a commercial product, used for treatment of constipation.

Fig No. 7: Gum Tragacanth.

6. Drug Name: Gum tragacanth

Gum Tragacanth is a viscous, odorless, tasteless, water-soluble mixture of polysaccharides obtained from sap that is drained from the root of the plant and dried. The gum seeps from the plant in twisted ribbons or flakes that can be powdered. It absorbs water to become a gel, which can be stirred into a paste. The major fractions are known as tragacanthin, highly water-soluble as a mucilaginous colloid, and the chemically related bassorin, which is far less soluble but swells in water to form a gel. The gum is used in vegetable-tanned leatherworking as an edge slicking and burnishing compound, and is occasionally used as a stiffener in textiles. The gum has been used historically as a herbal remedy for such conditions as cough and diarrhea. Powders using tragacanth as a basis were sometimes called diatragacanth. As a mucilage or paste, it has been used as a topical treatment for burns. It is used in pharmaceuticals and foods as an emulsifier, thickener, stabilizer, and texturant additive. It is the traditional binder used in the making of artists' pastels as it does not adhere to itself the same way other gums (such as gum arabic) do when dry. Gum tragacanth is also used to make a paste used in floral sugarcraft to create lifelike

flowers on wires used as decorations for cakes, which air-dries brittle and can take colorings. It enables users to get a very fine, delicate finish to their work. It has traditionally been used as an adhesive in the cigarrolling process used to secure the cap or "flag" leaf to the finished cigar body.

In the Middle East, and in Turkey in particular, gum tragacanth is used in paper marbling to make size on which to float and shape the pigments, just as carrageenan is used in the West.

Gum tragacanth is also used in incense-making as a binder to hold all the powdered herbs together. Its water solubility is ideal for ease of working and an even spread, and it is one of the stronger gums for holding particles in suspension. Only half as much is needed, compared to gum arabic or something similar.

Tragacanth is a natural gum obtained from the dried sap of several species of Middle Eastern legumes of the genus Astragalus, including A. adscendens, A. gummifer, A. brachycalyx, and A. tragacantha. Some of these species are known collectively under the common names "goat's thorn" and "locoweed". The gum is sometimes called Shiraz gum, shiraz, gum elect or gum dragon. The name derives from the Greek words tragos (meaning "goat") and akantha ("thorn"). Iran is the biggest producer of this gum.

Uses

It is used as a demulcent, emollient, thickening, suspending emulsifying agent.

Mucilage of tragacanth is used a binding agent in tables and excipient in the pills.

Powder of treacanth is used as an adhesive, in lotions for external use in spermicion eles, scabluzer in icecrem sances.

4.0 LITERATURE REVIEW

4.1 Ajda Ota Front Pharmacol. et al. (2017)

Recent formulation approaches to oral delivery of herbal medicines Jong Chan Byeon, Jung Bin Ahn, Woo Suk Jang, Sang-Eun Lee, Jin-Seok Choi, Jeong-Sook Park Journal of pharmaceutical investigation The well-known anticancer agent, paclitaxel, is a naturally occurring diterpenoid from Taxus brevifolia. It is an effective antineoplastic agent that has been widely used for the treatment of various cancers, including breast, ovarian, and lung cancers. One of the major limitations for the therapeutic use of herbal medicines is low solubility. Moreover, despite their potential efficacy, herbal medicinal products have been widely criticized due to a lack of standardization and poor apparent quality. In the case of herbal extracts, many compounds could be degraded in the highly acidic pH of the stomach. Other ingredients could be metabolized in the liver before reaching the systemic circulation. In addition, herbal extracts are often poorly compressible and very hygroscopic powders with poor powder flowability. As herbal drugs have much potential, several researchers are trying to develop novel drug delivery systems, such as solid dispersion, fast-dissolving tablets, sustained—and extended-release formulations, microparticles, microcapsules, nanoparticles, and mucoadhesive systems. This review provides an overview of existing pharmaceutical systems of herbal medicines and recent techniques to overcome the drawbacks of conventional formulations that result in reduced.

4.2 Kiran wadkar et al. (2007)

Owing to the ease of the administration, the oral cavity is an attractive site for the delivery of drugs. The main difficulty for administration via the buccal route is an effective physiological removal mechanism of the oral cavity that takes way the formulation from the buccal site and decreases the bioavailability of drugs. The use of mucoadhesive polymers in buccal drug delivery shows assessing buccal drug permeation and absorption, however some studies bring an in vivo performance. This review points to the use of polymers in the manufacture of drug delivery systems (hydrogels, films and tablets) and shows the results of their in vivo performance tests An overview of polymeric dosage forms in buccal drug delivery: State of art, design of formulations and their in vivo performance evaluation

4.3 DK Patelet et. al. (2012)

Owing to the ease of the administration, the oral cavity is an attractive site for the delivery of drugs. The main difficulty for administration via the buccal route is an effective physiological removal mechanism of the oral cavity that takes way the formulation from the buccal site and decreases the bioavailability of drugs. The use of mucoadhesive polymers in buccal drug delivery shows assessing buccal drug permeation and absorption, however some studies bring an in vivo performance. This review points to the use of polymers in the manufacture of drug delivery systems (hydrogels, films and tablets) and shows the results of their in vivo performance tests.

4.4 Krishnapurasrinivasan et. al. (2006)

Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance. Over the past three decades, orally disintegrating tablets (ODTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance. ODTs are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue. Products of ODT technologies entered the market in the 1980s, have grown steadily in demand, and their product pipelines are rapidly expanding. New ODT technologies address many pharmaceutical and patient needs, ranging from enhanced life-cycle management to convenient dosing for paediatric, geriatric, and psychiatric patients with dysphagia. This has encouraged both academia and industry to generate new orally disintegrating

formulations and technological approaches in this field. The aim of this article is to review the development of ODTs, challenges in formulation, new ODT technologies and evaluation methodologies, suitability of drug candidates, and future prospects.

4.5 Paul C. Chikezie et. al. (2015)

Tablets are cheapest formulation and easy to administrate to patients. Tablets are most patient compliance formulation since years. Ayurvedic tablets called 'Vati', formulate using different plants part which richest with active ingredient.[1] Many different vati's are used for the treatment of various disorders effectively. Vati is easy to formulate and evaluate compare to other formulations and highly patient compliance. Vati has more self-llife and easy to store with higher production rate.[2,3] Khaskhas biological name is Vetiveria zizanioides (L.) belongs to Poaceae family. The dry roots are used for formulation and contain sesquiterpenes 3-4%, sesquiterpenols 18-25% and sesquiterpenones 7-8%. Vetiveerol, Vetivone, Khusimol, Khusimone, Vetivenate, Zizaene, Prezizaene, and Vetivene are important chemical constituents present in khas-khas. Khaskhas slows acetylcholine and adrenergic effects on body and relax the CNS. It widely used to treat insomnia and inducing sleep into patients. It has many more uses like in mouth ulcer, epilepsy, Tablets are cheapest formulation and easy to administrate to patients. Tablets are most patient compliance formulation since years. Ayurvedic tablets called 'Vati', formulate using different plants part which richest with active ingredient.[1] Many different vati's are used for the treatment of various disorders effectively. Vati is easy to formulate and evaluate compare to other formulations and highly patient compliance. Vati has more self-llife and easy to store with higher production rate.[2,3] Khas-khas biological name is Vetiveria zizanioides (L.) belongs to Poaceae family. The dry roots are used for formulation and contain sesquiterpenes 3-4%, sesquiterpenols 18-25% and sesquiterpenones 7-8%. Vetiveerol, Vetivone, Khusimol, Khusimone, Vetivenate, Zizaene, Prezizaene, and Vetivene are important chemical constituents present in khas-khas. Khaskhas slows acetylcholine and adrenergic effects on body and relax the CNS. It widely used to treat insomnia and inducing sleep into patients. It has many more uses like Evaluation of efficacy and safety of "test drug" in patients suffering from primary insomnia-a randomized, double-blind, placebo-controlled, comparative, interventional, multi.

4.6 Agarwal SS, Singh VK. Immunomodulators et.al (2015)

The mean total sleep time and sleep efficiency were significantly improved in drug Test drug compared to placebo. Test drug tablet was significantly effective in reducing time to sleep onset, total number of awakenings, wake time after sleep onset and severity of insomnia. Sleep quality was also significantly improved. Stoppage of treatment for seven days did not show rebound of insomnia. No significant post treatment change in any of the lab investigations was observed in both the groups. Conclusion Test drug is safe and effective for the treatment of primary insomnia without rebound insomnia effect.

4.7 Dhaval A. Chandarana1, Keyur S. Patel, Samir C. Patel, Deepa R. Patel, Shailesh T. Prajapati et.al (2003)

The aim of the study was to formulate and evaluate mucoadhesive buccal tablets of carvedilol to avoid the first-pass metabolism.

4.8 Hiral Koradia, Khushbu Chaudhari et.al (2007)

The objective of this study was to develop buccoadhesive controlled release dosage form of Mirtazapine. The unidirectional buccal tablets of Mirtazapine were prepared by direct compression method using Carbopol 934P and HPMC K4M as a buccoadhesive controlled release agents. FTIR studies showed that the drug and excipients were compatible. A 32 full factorial design was applied to systematically optimize the formulation. The formulations were evaluated for pre and post compression parameters, swelling studies, ex vivo buccoadhesive strength and in vitro drug release studies. The results indicated that the concentration of Carbopol 934P (X1) and concentration of HPMC K4M (X2) significantly affected the cumulative drug release in 1 h and 6 h (%) (R1, R2), Swelling Index (%) at 6 h (R3) and buccoadhesive strength (R4). The results of ex vivo permeability through sheep buccal mucosa suggested good permeability of drug from optimized formulation. The formulation remained stable during stability study. The prepared unidirectional buccal tablets provided low drug release in initial time point (1 h) and complete drug release in 6 h, optimum swelling and good bioadhesive strength which indicates a potential alternative drug delivery system of Mirtazapine.

4.9 Malla Reddy College of Pharmacy, Department of Pharmaceutics, Maisammaguda, Dhulapally, et.al (2021)

The aim of present study was to formulation and evaluation of Mucoadhesive buccal tablets of Resperidone. Mucoadhesive buccal tablets of Resperidone were prepared by direct compression method using polymers such as Karaya gum, tamarind gum, carbopol, and Sodium carboxy methyl cellulose. The Buccal tablets were evaluated for various physical, drug content uniformity, in-vitro drug release and drug-excipient interactions (FT-IR). FT-IR spectroscopic studies indicated that there were no drug-excipient interactions. The formulation F9 (containing 30mg of Carbopol) were found to be best formulation, which showed maximum drug release within 8 h. These formulations have showed good bioadhesion strength (18 gm).

4.10 Formulation and Evaluation of Mucoadhesive Herbal Buccal Patch of Psidium Guava L.
K.G. Bhutkar M.C.E. Society's Allana College of Pharmacy, Pune, Maharashtra, India. et.al (2015)
Mucoadhesive drug delivery system is a distinct advantage over the traditional dosage forms such as, tablet, gels and solution etc. In the Mucoadhesive buccal patch for systemic drug delivery of drug like **m**flavonoid which is isolated from the leaves of Psidium guajava in which system avoid first pass effect of hepatic metabolism. The buccal patch shows desired physicochemical and mechanical properties. The various evaluation parameter are used to evaluate the Mucoadhesive buccal patch. Invitro drug release study shows that buccal patch deliver the drug like Quercetin to oral mucosa for the period of 7:30 hrs and also exhibit the stability study under desired condition. HPMC K15 buccal adhesion patch shows satisfactory physico-chemical properties. The ratio of hydrophilic polymer carbopol 940 to HPMC K15 had significant Mucoadhesive characteristics like swelling index, ex-vivo mucoadhesion strength and in-vitro drug release is observed between drug release and permeation study in-vitro. So it can conclude that the HPMC K15 and Carbopol 940 could be good carrier in buccal delivery of Quercetin.

4.11 BVP Deepthi, K Kartheswari, G Akhila, Hadia Huma, Uma Ruqiya Basharath and Dr. JVC Sharma et.al (2013)
In the present study, an attempt was made to prepare buccal tablets of Ivabradine HCL (an anti-anginal drug), in order to overcome bioavailability problems, to reduce dose dependent side effects and frequency of administration. Buccal tablets containing the drug were prepared by direct compression method using combinations of polymers (such as sodium CMC, HPMC K200M and karaya gum). Estimation of Ivabradine HCL was carried out spectrophotometrically at 292 nm. The Buccal tablets were evaluated for various physical and biological parameters, drug content uniformity, in-vitro drug release, drug- excipient interactions (FTIR). IR spectroscopic studies indicated that there are no drug-excipient interactions. The formulations F9 (containing 30mg of HPMC K200M) were found to be promising, which showed maximum drug release within 8 h. These formulations have displayed good bioadhesion strength (4.66 gm respectivel.

4.12 Formulation and evaluation of buccal tablets: a review MS. Dhotre Bhagyashree Gopalrao, Ms. Syeda Farheen F. Rajeshbhaiyya Tope College of Pharmacy, Nipani-Bhalgaon, Aurangabad et.al (2023)
Buccal tablets were prepared using mucoadhesive polymers like Chitosan, HPMC K4M, Na CMC & Sod. alginate by direct compression technique. Buccal tablets were characterized for number of parameters like Hardness, weight uniformity, thickness, % friability, swelling index, mucoadhesive strength, surface pH, drug–excipient interaction study, drug content uniformity and In vitro drug release study. The continuous secretion of saliva and its subsequent swallowing can lead to substantial drug depletion from the dosage form and hence low bioavailability. Therefore, other transmucosal routes such as nasal, rectal, vaginal, ocular and oral mucosae are being considered as alternatives to conventional oral dosage forms for drug delivery to avoid the above disadvantages associated with conventional oral delivery (i.e., tablets, capsules, syrups, etc.). Of these routes of delivery, the buccal oral mucosa has emerged as one of the target sites for administration of drugs in a wide variety of dosage forms, particularly for those drugs targeted for local delivery in the oral cavity and systemic absorption.

4.13 Dasari Nirmala, Vaddi Harika, Muvvala Sudhakar Malla Reddy College of Pharmacy, Department of Pharmaceutics, Maisammaguda, Dhulapally, Secunderabad - 500100 Affiliated by Osmania University et.al (2021)
The aim of present study was to formulation and evaluation of Mucoadhesive buccal tablets of Resperidone. Mucoadhesive buccal tablets of Resperidone were prepared by direct compression method using polymers such as Karaya gum, tamarind gum, carbopol, and Sodium carboxy methyl cellulose. The Buccal tablets were evaluated for various physical, drug content uniformity, in-vitro drug release and drug-excipient interactions (FT-IR). FT-IR spectroscopic studies indicated that there were no drug-excipient interactions. The formulation F9 (containing 30mg of Carbopol) were found to be best formulation, which showed maximum drug release within 8 h. These formulations have showed good bioadhesion strength.

4.14 Margret Chandira*, B.Jayakar Department of Pharmaceutical sciences, Vinayaka missions college of Pharmacy, Vinayaka mission University, Salem, Tamilnadu et.al (2017)
Medicinal plants have curative properties due to the presence of various complex chemical substance of different composition, which arefound as secondary plant metabolites in one or more parts of these plants. Ipomoea digitata Linn., Convolvulaceae is a annual extensive perennial climber with large ovoid and tuberous roots herb indigenous to India and widely used in the treatments of hypolipodemic, hypogycemic, for debility, to increase secretion of milk, to increases milk, poor digestion, tuberculosis, enlarged liver etc. It was also found to have alterative, aphrodisiac, cholagogue, demulcent, diuretic, rejuvenative actions. The present paper deals with formulation and evaluation of anti-diabetic activity of tablets prepared from aqueous extract of the selected plant. A solid pharmaceutical dosage formulation using a novel dry plant extract (tuberous roots) using various excipients viz., carbopol, ethylcellulose, MCC, dibasic calcium phosphate and PEG-4000 by direct compression was reported to be statically significant as anti-diabetic activity. The present communication also deals with the evaluation of

formulated tablets (weight variation, friability, hardness and disintegration time).

4.15 Chakshu Walia & Akansha Arya et.al (2023)
The buccal drug delivery system is defined as the system which drug is administrated in the buccal mucosa and involves placing a drug between gums and cheek, where it dissolves and is absorbed into your blood with systematic circulation. Both sublingual and buccal drugs, films, and sprays in the market. The review provides the knowledge about buccal delivery system its description, components and structure of buccal mucosa, anatomy & physiology of oral cavity, mucus layer of several parts, advantages and disadvantages and mechanism of mucoadhesion. The details about barriers, mucus and saliva, the several polymers used in Mucoadhesive drug delivery system, theories of buccal drug delivery, adhesion and evaluation which takes places in these types ofdrug delivery and the several commercially available dosages forms in the market.

All these details are described and demystified in this review article.

4.16 Sabnam Gupta et.al (2021)
The buccal region within the mucosal cavity of the mouth provides an alternative route over an oral drug administration for systemic as well as local drug delivery. As the buccal mucosa hasanabundant blood supply and is relatively permeable, it can be considered as most accessible and desired location for both local and systemic drug delivery. The buccal method for medication delivery greatly helps in avoiding issues in the gastrointestinal environment, such as increased first-pass metabolism and medication degradation. Buccoadhesive systems offer varieties of advantages such as convenience in administration and termination of therapy in case of emergency, higher patient compliance, better bioavailability, rapid absorption, etc. This current review highlights the bucco-adhesive drug delivery system, its advantages and limitations, mechanisms and theories of mucoadhesion, different buccoadhesive dosage forms, and bioadhesive polymers. It also highlights the current status on mucoadhesive drug delivery methods for the buccal cavity or bucco-adhesive systems.

4.17 A. Puratchikody et.al (2011)
The major hindrance for the absorption of a drugtaken orally is extensive first pass metabolism or stability problems within the GI environment like instability in gastric pH and complexation with mucosal membrane. These obstacles can be overcome by altering the route of administration as parenteral, transdermal or trasmucosal. Among these trasmucosal has the advantage of ease of administration, patient compliance and are economic too. The mucosa of the buccal cavity s the most easily accessible transmucosal site. Buccal transmucosal delivery helps to bypass first- pass metabolism by allowing direct access to the systemic circulation through the internal jugular vein. The buccal transmucosal route has been researched for a wide variety of drugs. Several methodologies have been considered so far, to design and manipulate the release properties towards the invention of buccal mucosal delivery systems. This article aims at reviewing the numerous techniques that has been designed till date for optimizing buccal transmucosal drug delivery.

4.18 N.G. Raghavendra Rao et.al (2013)
The buccal region of the oral cavity is an attractivetarget for administration of the drug of choice, particularly in overcoming deficiencies associated with the latter mode of administration. Problems such as high firstpass metabolism and drug degradation in the gastrointestinal environment can be circumvented by administering the drug via the buccal route. Moreover, rapid onset of action can be achieved relative to the oral route and the formulation can be removedif therapy is required to be discontinued. It is also possible to administer drugs to patients who unconscious and less co-operative. To prevent accidental swallowing of drugs adhesive mucosal dosage forms were suggested for oral delivery, which included adhesive tablets, adhesive gels, adhesive patches and many other dosage forms with various combinations of polymers, absorption enhancers. Natural polymers have recently gained importance in pharmaceutical field.

Mucoadhesive polymers are used to improve drug delivery by enhancing the dosage form's contact time and residence time with the mucous membranes. Mucoadhesion may be defined as the process where polymers attach to biological substrate or a synthetic or natural macromolecule, to mucus or an epithelial surface.

When the biological substrate is attached to a mucosal layer then this phenomenon is known as mucoadhesion. The substrate possessing bioadhesive polymer can help in drug delivery for a prolonged period of time at a specific delivery site. The studies of Mucoadhesive polymers provide a good approach of mucoadhesion and some factors which have the ability to affect the mucoadhesive properties of a polymer. Both natural and synthetic polymers are used for the preparation of mucoadhesive buccal patches. In addition to this, studies have been conducted on the development of controlled or slow-release delivery systems for systemic and local therapy of diseases in the oral cavity.

4.19 Azizur Rahman & Juber Akhtar et.al (2017)
Objective was designed to prepare, develop and evaluate fast dissolving films (FDFs) for oro-buccal drug delivery of chlorpromazine. Background: The drug delivery through or o-buccal mucosais very interesting one but it partially lacked oro-buccal delivery products in the market. Methods: FDFs of chlorpromazine were prepared by solvent casting method using polymers PVA, HPMCE-5, HPMCE-15 and were evaluated for film specific parameters. FDFs were also evaluated for

dissolution and percentage drug release by in vitro and ex vivo dissolution or drug permeation study. Results: The prepared films DPF1, DHF2, DHF3, DHPF4 and DHPF5 were of smooth surface without bubbles and cracks; flexible and non-sticky; uniform in weight without any significant weight variation; around to neutrals urface pH; unchanged folding endurance; 84-95%mg drug content variation. Thickness of DPF1 was less compared to DHF2, DHF3, DHPF4 and DHPF5. DPF1 showed excellent elasticity and undergone disintegration in less time. Chlorpromazine was rapidly released in vitro from all formulations and release was found to be maximum 97.2%over a period of150s in DPF1. Chlorpromazine was significantly more rapidly released ex vivo from DPF1 and release was found to be 85.10% over a period of 150s. Conclusion: The prepared FDFs of chlorpromazine were in accordance to the standard range of film specific parameters and comply it. FDF of chlorpromazine prepared with the polymer PVA is better than other prepared films with other polymers for oro-buccal drug delivery of chlorpromazine in buccal cavity for the treatment of either psychosis or emesis.

4.20 Vaishali A. Chaudhari et.al (2014)

Among the various routes of administration, oral route is the most suitable, convenient and widely accepted. Drug action scan be improved by developing new oral drug delivery systems such as the mucoadhesive buccal drug delivery system. Here the oral cavity is an attractive site for drug delivery due to ease of administration and avoids possible drug degradation in the gastrointestinal tract as well as first pass hepatic metabolism. Mucoadhesion is currently explained by six theories: electronic, adsorption, wettability, diffusion, fracture and mechanical. Several in vitro and in vivo methodologies are proposed for studying its mechanisms. The aim of present study was to review the mechanisms and theories involved in mucoadhesion, as well as to describe the most-used methodologies and polymers in mucoadhesive drug delivery systems.

4.21 Tarun Virmani & Charan Singh et.al (2015)

Buccal delivery of drugs provides an attractive alternate to the oral route of drug administration, particularly in disadvantages associated with the latter mode of dosing. Problems such as first pass metabolism and drug degradation in the harsh gastro intestinal environment can be circumvented by administering drug via buccal route. Moreover, the oral cavityis easily accessible for selfmedication and can be promptly in case of toxicity just by removing the dosage form from buccal cavity. It is also possible to administer drug for those who cannot be dosed orally via this route.

4.22 MANOJ KUMAR P et.al (2016)

Being an alternate method of systemic drug delivery, oral mucosal drug delivery proves to be advantageous over both injectable and enteral methods. Because of the mucosal surface usually being rich in blood supply, it enhances drug bioavailability, thereby enabling rapid drug transport to the systemic circulation. Moreover, in most cases, it avoids degradation by first-pass hepatic metabolism. The drug absorption takes place faster as it is in contact with the absorption surface. The drug delivery system helps the drug to remain at the same place of application longer for once or twice daily dosing. For some drugs, the alternate way of administration results in novel methods of action as opposed to the above-said procedure. The characteristics of the oral mucosa as well as physicochemical properties of the drug pose as a hindrance to the oral mucosal administration of some drugs. Commercial availability of drug is restricted, although most of the drugs are qualitatively assessed for oral transmucosal delivery. The clinical benefit produced by an oral transmucosal dosage for misgoodeven though the production of this dosage form is expensive. Transmucosal products are the recent drug delivery strategies. Delivery through transmucosal productsbenefits the absorption 4 times than that of the skin. Considering the availability of products, only some drugs are used for oral transmucosal delivery. Hence, new drugs have to beprocessed and developed to meet the limited transmucosal drug delivery. The present paper intends to emphasize the importance of oral transmucosal drug delivery and also highlights on the latest advancement in the field.

4.23 Vyas Heli Rajeshkumar et.al (2022)

Nowadays, extensive research is being done on the d esign and production of a new drug delivery system to improve safety, efficiency and compliance issues. The only delivery system that complements all of the above-mentioned methods is Buccal Film Technology. If planning of any appropriate drug delivery, buccal drug delivery system is considered to be the best amongst all. A buccal drug delivery system directly enters systemic circulation. It uses a jugular vein pass to deliver drugs from hepatic first pass metabolism, which boosts their bioavailability. All in all, the buccal mucosa has excellent accessibility, muscle elasticity, and smooth mucosa which is why it is ideal for controlling the final dose forms. Buccal films release drugs orally in a slow and predetermined dose that provide swell defined benefits in addition to standard dosage forms for the prevention and treatment of certain diseases. Buccal films share certain features like reduced size, volume, dynamic control, which is why they taste better and more acceptable forms than other buccal drug delivery systems such as gels, pills, lozenge, micro particles, etc. is more appropriate than the others. In addition, certain factors such as non-irritability, natural flexibility, painless management, easy drug withdrawal choose the buccal drug delivery system as a promising method for further research. It is very expensive and there are no medicines to be swallowed, which is why it is so convenient and friendly to pediatric patients and Geriatrics patients. This article provides a detailed review of the introduction, benefits, limitations, buccal film types, composition, preparation methods, estimates and sales arrangements

and their capabilities of these formulation forms as pharmaceutical formulation forms.

4.24 Karigar Asif & Savaliya Pratik et.al (2011)
This review highlights the several advantages of buccal drug delivery system (BDDS) over the conventional and systemic formulation majorly. It helps to enhance bioavailability through bypassing the first pass metabolism. On this drug delivery system, the formulation keeps in contact with the mucosal surface resulting in better absorption and prolonged resident time. Though all drugs are not suitable for this drug delivery system yet is useful for most of the drugs. Bioadhesive polymers roles a major part in this drug delivery system because the extent of Mucoadhesion is a very important phenomena for the buccal drug delivery system. This review covers merits and demerits of buccal drug delivery system, anatomy of oral mucosa, mechanism of drug permeation, polymers and permeation enhancer used in buccal drug delivery system. This review also covers available marketed product as buccal drug delivery system and future aspects of buccal drug delivery system.

4.25 Sarath Chandran C et.al (2013)
Oral route is the most convenient route of drug delivery because of several advantages. But due to some reason such as high first pass metabolism, drug degradation in the GIT etc, certain drugs are not an ideal candidate for conventional route. So in order to retain the patient compliance and also to achieve controlled release, mucodhesive system may be a better choice. The property and existence of such system mainly depends on the polymeric platform, and its interaction with the drug. Several other excepients such as permeation enhancers, plasticizer, etc are also used in order to modify the release pattern and to improving the stability of the formulation. This article briefly describes the basis, requirement, and the standards of an ideal muco adhesive buccal drug delivery.

5.0 PLAN OF WORK
Buccal tablets were prepared by direct compression method. Tablet ingredients were screened through a 0.150-mm sieve before mixing to achieve a uniform particle size distribution. Then, 1 mg of RIS and required amounts of polymer and LM were weighed carefully and mixed with a cubic mixer for 15 minutes.

Pre-formulation Study of Pre-compression Parameters
Bulk Density: It is the ratio of mass to bulk volume. It is required to decide appropriate packing of dosage forms. An accurately 10 gm of sample was weighed and transferred to a 50 ml measuring cylinder. The volume was noted. The Bulk density was obtained by dividing weight of the sample in grams by final volume in cm3 and it was determined by equation given below:
Bulk density = Mass / Bulk volume

Tapped Density: Accurately weighed quantity of powder was carefully poured in to graduated 50 ml measuring cylinder through large funnel. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. This is expressed in gm / ml and determined by the following formula: Tapped density = Weight of the powder / Tapped volume

Fig No. 8: Monsanto Hardness Tester.

Fig No. 9: Prizer Hardness Tester.

Angle of Repose: A funnel was kept vertically in stand at a specified height above a paper placed on horizontal surface. The bottom was closed and 10 gm of sample powder was filled in funnel. The funnel was opened to release the powder on paper to form a smooth conical heap.[1,3] The height of heap was measured using the scale. A border of heap was marked circularly and its diameter was measured at four points. The angle of repose was calculated using following formula:

Tan θ = h / r Where; θ= angle of repose r=radius of the base h=height from tip of funnel to the surface of graph paper.

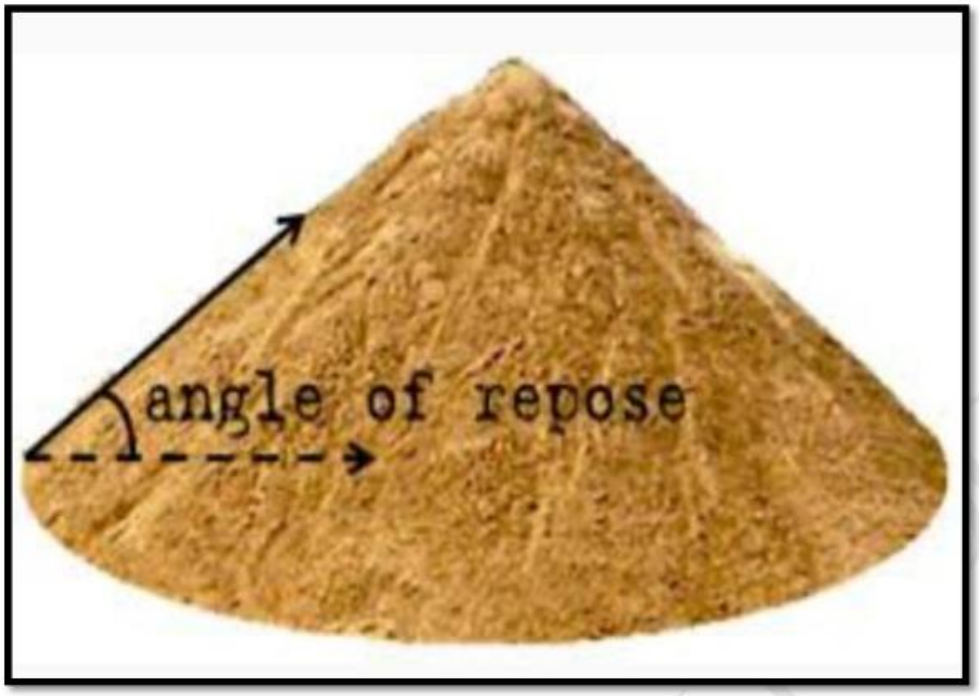

Fig No. 10: Angle of Repose.

Friability test

Friability of a tablets can determine in a laboratory by Roche Friabilator. The friabilator consists of plastic chamber that rotates at 25rpm, dropping the tablets through a distance of six inches in the Friabilator, which is then operated for 100 revolutions. The tablets are Reweigh Reweighed.

Compress tablets loss less than 0.5% to 1.0% of the tablet Weight are considered acceptable.

Fig No 11: Friabilator.

Disintegration Test

This test was a time required for the tablet to separate into particles, the disintegration test measure only the time required under a given set of acondition for a group of tablet to disintegrate into particles. This test was performed to identify the disintegration of tablet in a specific time period.

Fig No. 12: Disintegrator Tester.

Dissolution Test

In general, a single tablet is placed in a small wire mesh basket and immersed in the dissolution medium (as specified in the monograph) contained in a 1000 ml flask at 37°± 0.5°c. generally, it is rotated at 50 rpm unless otherwise specified.

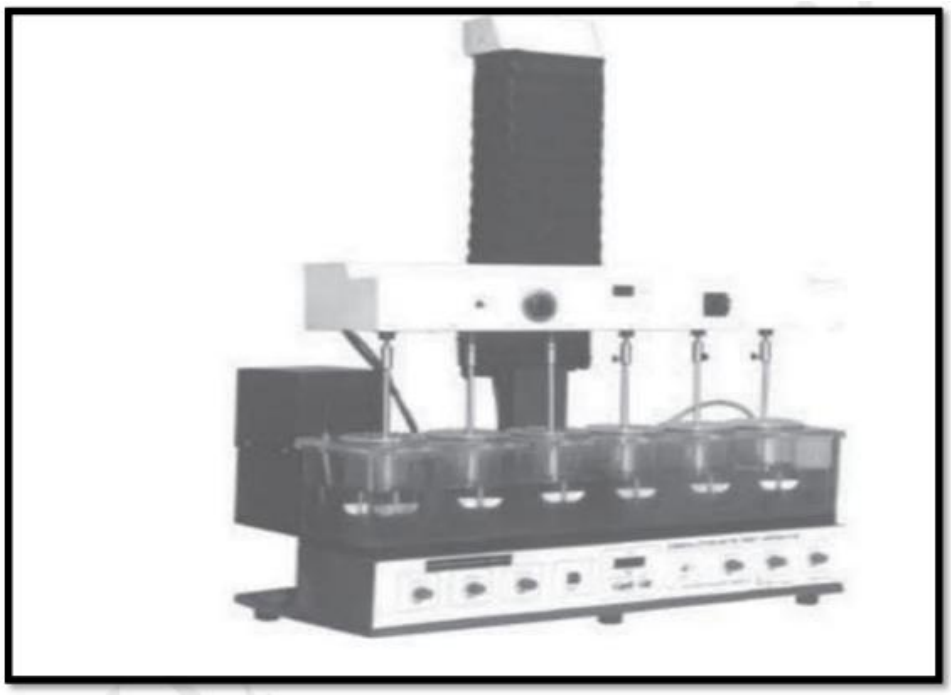

Fig No. 13: Dissolution Apparatus.

Carr's Index: It is also one of the simple method to evaluate flow property of a powder by comparing the bulk density and tapped density. Carr's index is an indication of the compressibility of a powder.[1,2] It is expressed in percentage and determined by the following formula:

% Car's consolidation index = Tapped density – Bulk density / Tapped density x 10

Hausner Ratio: A small index like percentage compressibility index has been defined by Hausner. Values less than <1.25 indicates good flow, where as greater than 1.25 indicates poor flow.[1,2] Added glidant normally improves flow of the material under study.

Hausner's ratio can be calculated by;

Hausner's ratio = Tapped density / Bulk density x 100

6.0 AIM AND OBJECTIVE

AIM

Herbal Buccal Tablet - Alterative Treatment For Insomnia

Innovationsaim to make drug delivery more patient-friendly, convenient, and non-invasive. This can lead to better adherence to medication regimens, especially for patients who have difficulty swallowing pills or need frequent dosing.

OBJECTIVE

1. To develop an herbal remedy for insomnia.
2. To control the market for synthetic adversely affecting medicines.
3. To develop herbal buccal fast drug realizing and effective medication.
4. To use easily available Herbal Active ingredient.
5. **Cost**-beneficial or budget-friendly.

1. **Enhanced Bio availability**: Improve the absorption and availability of drugs by utilizing the highly permeable and vascularized buccal mucosa, which can bypass the gastrointestinal tract and liver metabolism, leading to more efficient drug delivery.
2. **Precise Drug Targe ting**: Develop systems that can target specific areas within the oral cavity or systemic circulation, allowing for localized treatment of oral conditions or targeted delivery to specific tissues or organs.
3. **Minimization of Side Effects**: Design delivery systems that minimize systemic side effects by delivering drugs directly to the target site, reducing exposure to non-target tissues and organs.
4. **Improved Patient Compliance**: Createpatient-friendly and convenient delivery methods that enhance compliance with medication regimens, leading to better treatment outcomes.
5. **Rapid Onset ofAction**: Achieve faster onset of drug action by delivering drugs directly into the bloodstream through the buccal mucosa, leading to quicker therapeutic effects compared to oral ingestion.
6. **Long-Term Stability**: Ensure the stability of drug formulations within the buccal delivery system to maintain drug efficacy over time and under various storage conditions.
7. **Reduced Dosage Frequency**: Develop sustained or controlled-release formulations that allow for less frequent dosing while maintaining the rapeuticefficacy, thus improving patient convenience and adherence.
8. **Compatibility with Various Drug Types**: Create delivery systems that are compatible with A wide range of drug molecules, including small molecules,

peptides, proteins, and vaccines, expanding the scope of applications for buccal drug delivery.

9. **MinimalInvasiveness**: Design delivery systems that are minimallyinvasive and comfortable for patients, reducing the need for needles or invasive procedures commonly associated with other routes of drug administration.

7.0. MATERIALS AND METHOD

7.1 Material procurement

Nutmeg powder and lavender oil (helps to reduce insomnia) are collected from the local market. Magnesium stearate, gum tragacanth (as a mucoadhesive), starch (as a binder), and lactose (as a diluent) these all ingredient was collected from college laboratory.

7.2 Method

Buccal tablets were prepared by direct compression method. Tablet ingredients were screened through a 0.150-mm sieve before mixing to achieve a uniform particle size distribution. Then, 1 mg of RIS and required amounts of polymer and LM were weighed carefully and mixed with a cubic mixer for 15 minutes.

7.3. Materials: Carrageenan and Carrageen Were gifts from BASF. Ibuprofen (Batch Number:026H1368) And Glycerol (Batch Number: RB12720) Were all Purchased from Sigma-Aldrich (Dillingham, UK) And Used as Received.

7.4. In Vitro Methods: Now Days, Most of The In Vitro Studies Examining Drug Transport Across Buccal Mucosa Have Used Buccal Tissues from Animal Models. Animals Are Sacrificed Immediately Before the Startof An Experiment. Buccal Mucosa with Underlying Connective Tissue Is Surgically Detached from The Oral Cavity, The Connective Tissue Is Then Carefully Removed and The Buccal Mucosal Membrane Is Isolated. The Membranes Are Then Placed and Stored In Ice-Cold (4°C) Buffers (Usually Krebs Buffer) Until Mounted Between Side-By-Side Diffusion Cells for The In Vitro Permeation Experiments. It Is Also Called as Buccal Absorption Test. For Kinetic Drug Absorption Measurement This Method Can Be Polymer Characterization Can Be Done by Evaluating There Mucoa dhesive Strength Both In Vivo And In Vitro Technique.

7.5. Quantitative Methods: These Are Also Called Macroscopic Methods. The Majority of The Quantitative Bio And mucoadhesion Measurement Methods Found in The Literature Are Based on Measuring the Force Required to Break the Adhesive Bond Between the Model Membrane and The Adhesive. Depending On the Directionin Which the Adhesive Is Being Separated from The Substrate, Peel, Shear, And Tensile Forces Can Be Measured.

7.6. Viscometric Method: A Simple Visco metrical Method 30 Is to Quantify Mucin– Polymer Bioadhesive Bond Strength. Viscosities Of 15 % W/W Porcine Gastric Mucin Dispersion Were Measured with Brookfield's Viscometer. In Absence or Presence of Selected Neutral, Anionic and Cationic Polymer, Viscosity Components and The Forces bioadhesion Were Calculated.

7.7. Fluorescent Probe Method: In This Method the Membrane Lipid Bilayer Dand Membrane Proteins Were Labeled with Pyrenean Fluorescein Isothiocyanate, respectively. The Cells Were Mixed with The Mucoadhesive Agentsand Changesin. Fluorescence Spectra Were Monitored. This Gave a Direct Indication of Polymer Binding and Its Influence on Polymer Adhesion.

7.8. Colloidal Gold Staining Method: The Technique Employs Red Colloidal Gold Particles, Which Were Adsorbed on Mucin Molecules to Form Mucin–Gold Conjugates, Which Upon Interaction with Bioadhesive Hydrogels Develops a Red Color on The Surface. This Can Be Quantified by Measuring At 525 Nm Either the Intensity on The Hydrogel Surface or The Conjugates.

7.9. Direct Staining Method: Tisa Novel Technique to Evaluate Polymer Adhesion to Human Buccal Cells Following Exposure to Aqueous Polymer Dispersion, Both In Vitro And In Vivo. Adhering Polymer Was Visualized by Staining With 0.1 % W/V Of Either Alcian Blue or Eosin Solution; And the Uncompelled Dye Was Removed by Washing With0.25M Sucrose. The Extent of Polymer Adhesion Was Quantified by Measuring the Relative Staining Intensity of Control and Polymer Treated Cells by Image Analysis.

7.10. Ex Vivo Methods: Ex-Vivo Studies Examining Drug Transport Across Buccal Mucosa Uses Buccal Tissues from Animal Models. Immediately After Sacrificing the Animals the Buccal Mucosal Tissue Is Surgically Removed from The Oral Cavity. The Membranes Are Stored in Krebs Buffer at 4 °C Until Mounted in The Diffusion Cells for The Ex Vivo Permeation Experiments. Preservation Of the Dissected Tissue Is an Important Issue That Will Affect the Studies. There Is No Standard Means by Which the Viability or The Integrity of The Dissected Tissue Can Be Assessed.

7.11. Rolling method: Inrolling method a solution or suspension containing drug is rolled on a carrier. Solvent is mainly water and mixture of water and alcohol. Film is dried on the rollers and cut into desired shapes and sizes detachment of the film from the mucosal surface was recorded.

7.12. Hot melt extrusion method: Hot Melt Extrusion Process Includes the Medication and Other Excipients to Be Molten. The Material Is Then Pressed Through an Aperture to Produce a More Homogeneous Substance in Various Shapes Such as Granules, Tablets, Or Films. It Is Utilized in The Administration of Transdermal Drugs.

8. Evaluation of Buccal Tablet

Hardness

Hardness (diametric crushing strength) is a force required to break a tablet cross the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The hardness was tested by using Monsanto hardness tester.

Thickness

Three tablets from each batch of formulation were collected and the thickness of the tablets was measured with the help of venires caliper. The average thickness was calculated.

Friability

Roche friability test apparatus was used to determine the friability of the tablets. Twenty pre-weighed tablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The percentage friability was calculated according to the following formula

The present research was carried out to develop mucoadhesive herbal buccal tablets of Nutmeg and lavender oil to overcome the problem of insomnia. The preparation process was simple, reliable and inexpensive. All the prepared tablet formulations were found to be good without capping and chipping. The mucoadhesive herbal buccal tablets of Nutmeg and lavender oil by using direct compression method. All the prepared tablets were in acceptable range of weight variation, hardness, thickness, friability and drug content as per.

Weight Variation

The weight of tablet is measured to ensure that a tablet contain the proper amount of drug. Randomly selected twenty tablets form each batch were subjected to weight variation test as per Indian Pharmacopoeia 2007. Not more than two individual weight deviates from the average weight by more than 5% percentage deviation.

Uniformity of Content

Drug content uniformity was determined by dissolving the tablets in ethyl alcohol and filtering with whattman filter paper. The filtrate was evaporated and drug residue dissolved in 100ml phosphate buffer pH 6.8. The 5 ml solution was then diluted with phosphate buffer pH 6.8 to 20 ml, filtered through whattman filter paper, and analyzed at 289 nm using UV double beam spectrophotometer.

Swelling Studies

The degree of swelling of bio adhesion polymers is an important factor affecting adhesive. For conducting the study, a tablet was weighed and placed in Petri dish containing 5 ml of phosphate buffer at pH 6.8 for 6 hrs, the tablets were taken out from the petridish and excess water was removed carefully by using filter paper. The swelling index was calculated using the following formula: Swelling index = Wt - Wo / Wo x 100

Wt = weight of swollen tablet at each time interval

Wo = weight of initial tablet

Surface pH

The surface pH of the buccal tablets was determined in order to investigate the possibility of any side effects in-vivo. Since an acidic or alkaline pH may cause irritation to the buccal mucosa, so it was determined to keep the surface pH as close to neutral as possible. A combined glass electrode was used for this purpose. The tablet was allowed to swell by keeping it in contact with 1 ml of distilled water for 2 h at room temperature. The pH was measured by bringing the electrode in contact with the surface of the tablet and allowing it to equilibrate for 1 minute.

Measurement of Adhesion Force

Measurement of adhesion force was determined by using bovine buccal mucosa which was obtained from slaughter house. The underlying tissues were separated and washed thoroughly with phosphate buffer solution (pH 6.8). The membrane was then tied to the bottom of the lower vial using rubber band. The vial was kept in glass bottle which was filled with phosphate buffer solution at 37 ± 1 ºC in such way that buffer just reaches the surface of mucosal membrane and kept it moist. The tablet to be tested was stuck on the lower side of the hanging Glass vial by using adhesive tape and the weight (2 gm) on the right pan was removed. N-vitro Dissolution Studies: The United State Pharmacopeia (USP) type II dissolution apparatus was used to study the release of drug from herbal buccal tablets. The dissolution medium consisted of 900 ml of phosphate buffer (pH 6.8). The release was performed at 37 ± 0.5 ºC, at a rotation speed of 50rpm Samples (5 ml, at each time) were filtered with fresh medium. The samples were filtered through Whatman filter paper no. 41 with appropriate dilutions with phosphate buffer (pH 6.8) and were assayed spectrophotometrically at 289 nm against phosphate buffer as blank.

9.0 RESULTS AND DISCUSSION

Bulk Density: It is the ratio of mass to bulk volume. It is required to decide appropriate packing of dosage forms. An accurately 10 gm of sample was weighed and transferred to a 50 ml measuring cylinder. The volume was noted. The Bulk density was obtained by dividing weight of the sample in grams by final volume in cm3

and it was determined by equation given below: Bulk density = Mass / Bulk volume.

Tapped Density: Accurately weighed quantity of powder was carefully poured in to graduated 50 ml measuring cylinder through large funnel. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. This is expressed in gm / ml and determined by the following formula:
Tapped density = Weight of the powder / Tapped volume
Angle of Repose: A funnel was kept vertically in stand at a specified height above a paper placed on horizontal surface. The bottom was closed and 10 gm of sample powder was filled in funnel.

The funnel was opened to release the powder on paper to form a smooth conical heap. The height of heap was measured using the scale. A border of heap was marked circularly and its diameter was measured at four points. The angle of repose was calculated using following formula:
Tan θ = h/r

Where; θ= angle of repose r=radius of the base h=height from tip of funnel to the surface of graph paper.

Carr's Index: It is also one of the simple methods to evaluate flow property of a powder by comparing the bulk density and tapped density. Carr's index is an indication of the compressibility of a powder. It is expressed in percentage and determined by the following formula: % Car's consolidation index = Tapped density – Bulk density / Tapped density x 10

Hausner Ratio: A small index like percentage compressibility index has been defined by Hausner. Values less than ratio can be calculated by; Hausner's ratio = Tapped density / Bulk density x 100

Hardness: Hardness (diametric crushing strength) is a force required to break a tablet cross the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The hardness was tested by using Monsanto hardness tester.

Thickness: Three tablets from each batch of formulation were collected and the thickness of the tablets was measured with the help of venires calliper. The average thickness was calculated.

Friability: Roche friability test apparatus was used to determine the friability of the tablets. Twenty pre-weighed tablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The percentage friability was calculated according to the following formula: % Friability = Initial weight - final weight / Initial weight x 100

Weight Variation: The weight of tablet is measured to ensure that a tablet contain the proper amount of drug. Randomly selected twenty tablets form each batch were subjected to weight variation test as per Indian Pharmacopoeia 2007. Not more than two individual weight deviates from the average weight by more than 5% percentage deviation.

Formulation code	Bulk Density (gm/cm3)	Tapped Density (g/cm3)	Hausner's Ratio	Compressibility index	Angle of Repose (Θ
F I	0.33± 0.01	0.37± 0.00	1.16± 0.06	18.16± 0.58	27.58 ± 0.84
FII	0.32± 0.00	0.33± 0.00	1.05± 0.05	9.85± 0.89	24.60 ± 1.37
FIII	0.30± 0.00	0.32± 0.00	1.11± 0.02	11.88± 0.78	24.82± 1.45
FIV	0.28± 0.00	0.31± 0.00	1± 0.00	8.2± 0.85	25.51 ± 0.84
FV	0.26± 0.00	0.27± 0.00	1.12± 00	9.99± 0.64	27.07 ± 2.10
FVI	0.23± 0.00	0.25± 0.00	1.03± 0.04	9.33± 1.44	26.06 ± 2.51

Evaluation Post Compression Parameters

Formulation NO	Weight variation (mg)	Hardness (kg/cm)	Thickness (mm)	% Friability	% Drug content
F1	Passes	7.2 ±0.21	4.2±0.16	0.99±0.00	89.01±0.47
F2	Passes	7.9±0.23	4.3±0.2	0.94±0.00	90.30±0.33
F3	Passes	7.7±0.21	4.5±0.12	0.86±0.00	92.04±0.45
F4	Passes	6.8±0.52	4.1±0.11	0.96±0.00	91.43±0.34
F5	Passes	7.2±0.14	4.4±0.15	0.77±0.00	89.88±0.55
F6	Passes	7.8±0.23	4.3±0.02	0.76±0.00	94.2±0.52

SURFACE pH STUDY

Formulation code	Surface pH
F1	6.7 ± 0.04
F2	6.8 ± 0.01
F3	6.8 ± 0.05
F4	**6.9** ±0.00
F5	**6.7** ±0.01
F6	**6.8** ±0.00

Fig No. 14: Tablet Of NutMeg and Lavender oil.

10. 0 CONCLUSION

The present research was carried out to develop mucoadhesive herbal buccal tablets of Nutmeg and lavender oil to overcome the problem of insomnia. The preparation process was simple, reliable and inexpensive. All the prepared tablet formulations were found to be good without capping and chipping. The mucoadhesive herbal buccal tablets of Nutmeg and lavender oil by using direct compression method. All the prepared tablets were in acceptable range of weight variation, hardness, thickness, friability and drug content as per pharmacopeial specification. The surface pH of prepared buccal tablets was in the range of salivary pH, suggested that prepared tablets could be used without risk of mucosal irritation. The buccal tablets showed good swelling up to 6 h in distilled water maintaining the integrity of formulation which is required for bio adhesion. The in-vitro release of Nutmeg was extended for 9 -12 h. Formulations F6 batch shows good in- vitro drug release 89.95%. All the tablets showed good residence time 5 - 6.9 h indicated good adhesive capacity and all the tablets showed good mucoadhesive strength of 11.33 - 21.55g with high force of adhesion. DSC studies of tablet indicated that there was no drug excipient interaction.

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