Chapter 1

Bucco Adhesive Systems: An Explored Strategy for Potential Drug Delivery

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Abstract

Mucoadhesive formulations are well known for the delivery of drugs via the mucosal membrane of oral (sublingual, buccal and gingival), rectum, nose, eyes, and vagina. Among the various drug delivery approaches, the buccal mucosa delivery system offers several benefits like easy accessibility, patient compliance, a relatively large surface area of absorption for drug molecules, reduced gastric irritation and simple delivery devices. Moreover, the drugs penetrate the mucous membrane by simple diffusion and are carried in the blood, which is richly supplied with the salivary glands and their ducts, into the systemic circulation via the jugular vein. This noteworthy background supported delivery of different classes of drugs through buccal drug delivery systems. This book chapter discuss the researchers carried out for buccoadhesive dosage forms of the drugs such as antifungal, antiemetic, antibiotics, antihistamines, non-steroidal anti-inflammatory drugs, drugs used for lungs related disorders, drugs acting on cardiovascular system, central nervous systems including antidepressants, drugs for migraine, antiparkinson's, antipsychotic, antiepileptic, neuromodulator, muscle relaxant, anti-diabetic, anaesthetic drugs, antiviral, anticholinergic, anticonvulsant, anticancer, diuretics, antiseptic, statins, beta blockers and corticosteroids. Mucoadhesive drug delivery system thus proves to be an inevitable system for both immediate and sustained release of the drug. Further advances in buccal adhesive technology for effec-

tive local and systemic action also have the potential for reducing the dose and side effects.

Keywords

Mucoadhesive; Buccal; Sustained; Formulation; Dosage Forms

Introduction

Buccal drug delivery is associated with the administration of the desired drug through the buccal mucosal membrane which lines the oral cavity. Among the various drug delivery routes, buccal mucosal delivery proves to be one of the promising approaches due to its successful application for both local and systemic action. Mucus is a translucent and viscid secretion which forms a thin and a continuous gel blanket that is adherent to the mucosal epithelial surface. It is secreted by the goblet cells directly onto the epithelial surfaces or by special exocrine glands with mucus cells such as acini. The mucosa of the buccal cavity is the most easily accessible transbuccal site, which encompasses a rich blood supply. Systemic circulation can be achieved through the internal jugular vein that bypasses the drug from the first metabolism in hepatic region, and thus leading to increased bioavailability. Administration of retentive dosage forms like implants for chronic therapy can also be adopted due to the presence of smooth muscle and immobile mucosa. Large surface area for absorption, reduced gastric irritation, rapid onset of

action, increased patient compliance and the ease of drug administration are the significant advantages of the buccal delivery system. Mucoadhesion has reflected a state in which a bioadhesive substrate adheres and interacts with mucus layer. Underlying mechanism involves complex phenomenon of wetting (swelling), adsorption and interpenetration of the polymer chains. Owing to the rheology of mucoadhesion, mucoadhesive polymers are used which can undergo either matrix or hydrogel formation. Mucoadhesive polymers can be either water soluble or water insoluble polymers which should have the capability of forming swellable networks when joined by cross-linking agents. The polymers for buccal drug delivery used should be nonirritant to the mucous membrane and preferably from the non-covalent bond with the epithelial surface. For drugs exhibiting low flux through this route permeation enhancers are used to overcome the issues related to low drug bioavailability. Also, tags along enzyme inhibitors may be used, which protects the drug from degradation.

Mucoadhesive formulations are distinguished for their delivery to the mucosa of sublingual, buccal, gingival, rectal, nasal, ocular and vaginal. Among them, the buccal mucosal dosage forms and delivery devices present several benefits compared to the other routes due to its simplicity, cost-effectiveness, easy handling and administration for all patients. In general, drugs penetrate the

mucous membrane by simple diffusion and are carried through the salivary glands and their ducts, the richly supplied blood vessels into the systemic circulation via the jugular vein. Active transport, pinocytosis, and passage through aqueous pores usually play insignificant roles in the absorption of drugs across the oral mucosa.

The different types of buccal dosage forms include small tablets/pills, patches or films, gels, and microparticles. The challenges and limitations related to conventional dosage forms have been significantly overcome by the buccal drug delivery systems for different drugs. The objective of this article is to display the comprehensive review on buccal dosage forms of various categories of drugs as depicted in Figure 1. The impact of buccal adhesive dosage forms in treating the diseases with high efficiency, immediate onset, prolonged effect, improved half-life, and bioavailability, reduced first pass metabolism and gastric related side effects for each category of drug as reported by the researchers have been highlighted.

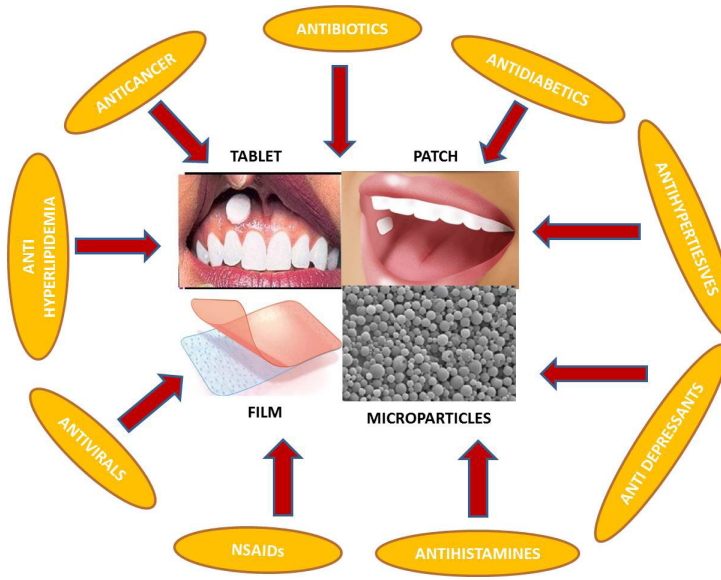

Figure 1: Category of drugs administered as buccal adhesive dosage forms.

Anti Hyperlipidemia Drugs

A significant number of drugs belonging to the class of statins have been developed as buccal drug delivery systems. Statins lower blood cholesterol by inhibiting HMG-CoA reductase found in the liver that plays a key role in the synthesis of cholesterol. Most of the anti-hyperlipidemia drugs undergo extensive first-pass metabolism in the liver, as a result of which the availability of the drug in systemic circulation is very low and variable. These drugs also exhibited unexpected adverse drug reactions for high or repeated dosing. The buccal drug delivery presented

an easy and safe method of drug absorption because drug utilization can be promptly aborted in situations of toxicity by evacuating the dosage form from the buccal cavity.

Amish et al. (2012) had used a different set of natural gums such as xanthan gum, tamarind gum, gellan gum and chitosan as mucoadhesive polymers for preparation of bilayered buccal tablets of Rosuvastatin calcium [1]. The tablets were formulated by wet granulation method using ethyl cellulose & magnesium stearate as a backing layer. A sustained release of drug was obtained with the optimized composition of HPMC K4M and chitosan, which also supported as a natural permeation enhancer. Shah Viral et al. (2012) had also performed the experimental trials of similar tablets, wherein direct compression method was adopted that also authenticated the drug release based on the chitosan composition [2].

Atorvastatin calcium bilayered buccal tablet was developed by Ashaet al. (2010) using carbopol 934P, sodium carboxymethylcellulose (SCMC) and hydroxyl ethyl cellulose (HEC) and sodium alginate as polymers, and ethyl cellulose as a backing layer. The swelling index of the tablets was found to be proportional to SCMC content. Tablets containing carbopol and SCMC in the ratio of 3:2 showed maximum drug release without disintegration for up to 6 hours [3].

Simvastatin buccal tablets were developed by Agaiah et al. (2011) using carbopol 934, SCMC and HPMC

through direct compression method. The tablets containing SCMC exhibited better adhesion than the formulation containing HPMC K4M because of the high viscosity of SCMC polymer [4]. Shalini et al. (2012) had worked on buccal patches using Eudragit RS-100 and the variable amount of polymer composite of polyvinyl alcohol (PVA), PVP, HPMC and ethyl cellulose for formulation. The Eudragit-HPMC patch showed better swelling index, wherein the release of drug was retarded with the increase in the amount of polymer [5].

Muthukumaran et al. (2011) developed a bilayered buccal tablet with good swelling index and bioadhesion strength by direct compression method for the drug Gemfibrozil (lipid-lowering fibrates) [6]. Carbopol 934, hydroxypropyl methylcellulose (HPMC) and polyvinylpyrrolidone (PVP) were used as the polymers, while ethyl cellulose was used as a backing layer. Similar formulation experiment was also carried out by Doijad et al. (2011) using same method and polymers [7], but with a different backing layer containing a mixture of magnesium stearate, saccharin sodium, and tartrazine. The tablets containing 1:2 ratio of carbopol 934 and HPMC composition exhibited optimized quality.

Antibiotic Drugs

Antibiotics include broader range of anti-microbial or anti-bacterial agents which reduce the infections by either destroying or inhibiting the bacterial growth. The con-

ventional oral dosage forms of these drugs impart several stability issues both *in vitro* (storage shelf life) and *in vivo* (acidic pH of stomach and other metabolic degradation) leading to reduced half-life. Hence, buccal drug delivery systems could be an alternative approach to circumvent the challenges related to antibiotics administration.

A modified approach of buccal dosage form was reported by Sang Min et al. (2005) using the particulate drug delivery system [8]. Enrofloxacin microspheres were prepared through interpolymer complexation and solvent casting method using chitosan and polyacrylic acid (PAA). The mucoadhesion properties of chitosan was improved by conjugation with PAA. Swelling and dissolution studies of chitosan –PAA microspheres was found to be dependant on the pH of the medium.

Clarithromycin buccal tablets were formulated by Margret et al. (2009) and Pranjal et al. (2012) [9,10]. The former used polymers carbopol 974P, HPMC K15M and HPMC K4M to prepare the tablets, which exhibited controlled release for 12 hours. Combination of HPMC K4M with carbopol 974P showed optimum results compared to the individual polymers. The latter researcher used polymers SCMC, carbopol 974P and sodium alginate, wherein the formulation containing higher proportion of carbopol prolonged the drug release (85.63%) up to 10 hours.

Ananta et al. (2010) developed Ciprofloxacin hydrochloride buccal film using different concentration of poly-

mers HPMC and PVA [11]. The films exhibited desired flexibility and mucoadhesive properties, along with required *in vitro* and *ex vivo* release performance. Triclosan buccal patch was formulated by Mario et al. (2012) using low amiliated pectin (AMP) and carbopol [12]. The patch prepared with AMP carbopol in the ratio of 80:20 (w/w) showed optimal swelling and erosion properties, due to *in situ* interpolymer complex formation.

Antiviral Drugs

Acyclovir, the most effective antiviral drug against herpes simplex infection was formulated as a buccal patch by Ankita et al. (2011). HPMC K4M, HPMC K15, and PEG were used as the polymers while SCMC, PVP K30, and Eudragit RL100 were used as backing membrane materials. In this case, an inclusion complex of Acyclovir was prepared with hydrophilic polymer hydroxypropyl beta-cyclodextrin in the molar ratio of 1:1 and loaded in the patch. The incorporation of inclusion complex enhanced the percentage of drug release substantially, thereby increasing the bioavailability of the drug [13].

Antifungal Drugs

Antifungal drugs are used to treat fungal infections such as ringworm infection, candidiasis, cryptococcal meningitis, etc. These drugs can be preferably administered for the local effect as needed for the treatment of oral candidiasis.

Nyastatin bilayered buccal tablet was prepared by Juan Manuel et al. (2002) using lactose, carbomer, and HPMC as polymers [14]. A quick release of drug from lactose layer was observed followed by the sustained release for up to 6 hours approximately. The ratio of 9:1 of carbopol and HPMC showed required *in vitro* mucoadhesion. Metronidazole benzoate buccal films were prepared by Amal et al. (2007) using chitosan and poly-caprolactone [15]. The double-layered film exhibited maximum mechanical strength and tensile property with sustained drug release for over 6 hours.

Fluconazole buccal film was reported by Soad et al.(2009) using polymers HPMC, HEC, SCMC, chitosan, Eudragit and Sodium alginate either alone or in combination [16]. They ensured optimum Fluconazole release in the buccal region for the prolonged duration of time (>300 min). Ketoconazole bilayered buccal tablets were prepared by Dattatreya et al. (2009) through direct compression method using HPMC K4M and carbopol 934P as polymers, while ethyl cellulose and β-CD were used as backing material and penetration enhancer, respectively [17]. Addition of β-CD to the matrix increased the flux by increasing the solubility of ketoconazole, thus improving the diffusion of the drug.

In situ gel for buccal administration was developed for Itraconazole by Jayaraj Kumar et al. (2010) using the polymers poloxamer 188 and carbopol 934 [18]. Increase

in the concentration of poloxamer 188 decreased the gelation temperature, whereas carbopol 934 increased the gelation temperature and also showed permeation enhancing the effect. Bazigha et al. (2012) prepared Miconazole mucoadhesive buccal film by the solvent casting method using chitosan as polymer [19]. Formulation containing drug at 0.524mg/cm2 concentration, 10% w/w polypropylene glycol and 2%w/w chitosan was considered as optimum with the required *in vitro* drug release.

Non-Steroidal Anti-Inflammatory Drugs (NSAID'S)

Various non-steroidal anti-inflammatory drugs are preferably subjected to buccal mucosal absorption and permeation to avoid the commonly reported gastric irritation side effects. Application of these drugs through buccal route is one of the worthy options due to the immediate therapeutic effect of the drug with less first pass metabolic reactions.

Aceclofenac with a short biological half-life (3-5 hours) is one of the commonly recommended drugs of choice as standard anti-inflammatory medication, especially intended for sustained drug release profile to avoid the frequent oral administration. Yadav et al. (2009) formulated a novel drug delivery system for Aceclofenac as buccal adhesive microspheres using ethyl cellulose as polymer material and chloroform as solvent through emul-

sion solvent evaporation method [20]. The formulation released the drug continuously over an extended period of time of 12 hours. Rajesh et al. (2012) also conducted a study with a similar approach based on microcapsules fabricated through orifice ionic gelation technique by a uniform coating of drug particles with sodium alginate, methylcellulose and carbopol [21]. Sodium alginate-methyl cellulose particles provided faster release than sodium alginate-carbopol microcapsules and also exhibited maximum bioadhesive property in both acidic & alkaline pH. Buccal patches were formulated by Amit khairnar et al. (2009) and Prasanth V.V et al. (2012) by solvent casting technique [22,23]. The former used polymers HPMC, Carbopol 934P, PVA, PVP-K30 & Eudragit L-100 in various proportions. The latter researcher used polymers such as gelatin, poly sodium carboxymethyl cellulose, and PVA. Among the eight formulations studied, the preparation containing 4.5% gelatin, 5.5% poly sodium carboxymethyl cellulose, 5% propylene glycol was observed to be ideal for required drug release, folding endurance and mucoadhesive time.

Diclofenac sodium was formulated into various buccal dosage forms such as tablets, patches, and films. The buccal patch was prepared by Panigrahi et al. (2005) using PVA, HEC, and chitosan as bioadhesive polymers [24]. The results indicated a high drug release from PVA patches than the HEC patch, while physical characteristics of both the patches showed a promising adhesion strength.

Similarly, the buccal film was formulated by Doshi et al. (2011) using solvent casting method with polymers PVA and HPMC [25]. In this case, the HPMC based film was found to have higher residence time, bioadhesive strength and release profile compared to PVA films. The buccal tablet was formulated by Edavalath et al. (2011) using carbopol 974P, HPMC K4M and sodium alginate by direct compression method [26]. In this study, numerical optimization technique was applied to find the best formulation using Design Expert Software. The results concluded carbopol 974P as the suitable bioadhesive polymer and HPMC K4M as the rate controlling polymer for required drug release profile. The tablets containing 50 mg drug, 40 mg HPMC and 35 mg carbopol 934P was found with optimum quality standards and stability.

Buccal tablets ofPiroxicam were prepared using HPMC K4M and carbopol 934 as polymers by Velmurugan et al. (2010) [27]. The tablets containing 1:3 ratio of Piroxicam & HPMC K4M exhibited sustained drug release for more than 6 hours and satisfactory bioadhesive properties. Ketoprofen buccal film was prepared by Rita Lala et al. (2011) using polycarbophil & sodium alginate as polymers [28]. The results showed an increase in the mucoadhesive force with increase in polymer concentration and good correlation between ex vivo and in vivo studies. Santosh Kumar et al. (2011) developed a buccal patch of Flurbiprofen with PVA, SCMC, and HPMC as polymers by solvent casting technique [29]. Bioadhesion force and drug release profile were higher for the patches containing

PVA & HPMC along with β-CD (cyclodextrin) compared to other formulations. Celecoxib has been developed as the buccal gel by Yara Peluso et al. (2012) using chitosan polymer [30]. The influence of penetration enhancer was studied and also measures were taken to increase the drug retention at the site.

Antiemetic Drugs

Antiemetic drugs are used to prevent nausea and vomiting, especially to treat the side effects of opium analgesics, general analgesics and chemotherapeutic agents for cancer. These drugs are usually water soluble and rapidly absorbed after oral administration. But, they have short or moderate biological half-life (<5 hours) and are usually administered in repeated doses three or four times daily in order to maintain effective concentrations throughout the day. Buccal route of administration is highly preferred for these drugs for immediate onset and also extended the duration of action.

Domperidone buccal tablets were prepared by Balamurugan et al. (2008) and Gurpreet et al. (2011) by direct compression method [31,32]. The former had trialed the tablets with different ratio of polymers such as HPMC K4M, Eudragit15LV, carbopol 934P and chitosan. The optimum mucoadhesive performance and *in vitro* drug release profile was exhibited by the tablet containing chitosan and HPMC in the ratio of 1:1. Taro gum along with PVP-K30 was used by the latter researcher for the buccal

tablet preparation. The polynomial equation analysis indicated the dominating effect of polymers on mucoadhesive and tensile strength. The in vitro drug release followed first-order kinetics and showed linearity with Higuchi model.

Ondansetron hydrochloride buccal tablet was formulated by Nisreen et al. (2009) using the polymers carbopol, SCMC, Sodium alginate and HPMC [33]. *In vitro* release and permeation studies revealed that the polymer complexed drug had maximum release and permeation, while the stability was maintained up to 6 hours. A similar preparation was reported by Kotagale et al. (2010), wherein the effect of pH modifiers was studied for the tablets prepared with polymers carbopol 934, sodium alginate and gelatin [34]. Increase in the concentration of citric acid decreased the pH, bioadhesion, water uptake and *in vitro* release, and vice versa. Hence, pH modifiers were used to optimize the controlled drug release profile.

Metoclopramide buccal tablet was formulated by Yadav Deepak et al.(2011) through direct compression method using the polymers used were carbopol 934P, chitosan, HPMC K4M and HPMC K15M [35]. A formulation containing Carbopol 934P and HPMC K4M in the ratio of 1:1 showed required bioadhesive force and maximum drug release of 96.10% for 10 hours with Korsemeyer Peppas kinetic.

Anti-Histamine Drugs

Anti-histamine drugs inhibit the action of histamine by preventing its interaction with the histamine receptors, to treat peptic ulcers / gastric reflux disease and to relieve allergies caused due to intolerance reactions. The bioavailability of anti-histamine drugs like Ranitidine following the conventional oral administration is only about 50% which might be due to colonic degradation by colonic bacteria. Hence, buccal mucoadhesive delivery provides a possibility to avoid the first pass effect and pre-systemic elimination in the gastrointestinal tract and liver.

Ranitidine hydrochloride buccal film was prepared by Alagusundaram et al. (2009) and Alka et al. (2011) through solvent casting technique using the polymers HPMC and PVP [36,37]. The former used the polymer HPMC E15 in combination with carbopol 934P and proved that high concentration of carbopol had a positive effect on *in vivo* mucoadhesive strength. The physicochemical characteristics and *in vitro* release studies of the formulation containing 2% HPMC and 1% PVP was found to be optimum.

Famotidine buccal patches were developed by Manish et al. (2010) using the polymers HPMC, SCMC, and PVA through solvent casting method [38]. The patches exhibited 72.58% to 91.9% drug release in 20 minutes. The increased amount of HPMC and SCMC influenced with higher modulus elasticity and increased bioadhesive property.

Loratadine buccal tablet was prepared by Borgaonkar et al. (2011) by direct compression method using polymers HPMC K4M, chitosan and sodium alginate [39]. The mucoadhesive strength of tablets was 4.00 to 7.00g and force of adhesion increased with increase in polymer concentrations. A formulation containing 30% HPMC K4M was found to be promising, which released 99% drug within 8 hours.

Drugs Acting on Cardiovascular Diseases

Beta Blockers

Beta blockers include the category of drugs that target the β-receptors of cardiac tissue. They are widely used for the management of cardiac arrhythmia, myocardial infarction, angina pectoris and hypertension. These drugs are well absorbed from the gastrointestinal tract but their half-life and bioavailability are low (around 25%) due to extensive first-pass metabolism. Hence, buccal dosage forms are more preferable for this class of drugs.

Bilayered buccal tablets of Carvedilol prepared by direct compression method were evaluated by Hirlekar et al. (2009) and Wadageri et al. (2012) [40,41]. The formerly used polymers such as carbopol 974P, SCMC, and PVP K-30, while the latter used HPMC K4M and carbopol 934P. The results revealed that with an increase in the con-

centration of carbopol 934P, the swelling index and viscosity increased, thereby controlling the drug release. The effect of methyl-β-cyclodextrin (MβCD) was also studied and postulated that MβCD increased the concentration of drug in saliva, which aided in higher permeability of drug across the buccal mucosa.

Various studies have also been reported for buccal patches of Carvedilol. Vamshi Vishnu et al. (2007) used HPMC and hydroxyl propyl cellulose (HPC) as polymers and propylene glycol as a plasticizer for developing the buccal patches [42]. Fourier transform infrared spectroscopy (FTIR) study showed no evidence of interaction between polymer and drug, and also the X-ray diffraction (XRD) study concluded the drug in its original crystalline state.Arpita et al. (2010) [43] formulated patches using HPMC K15M and carbopol 940 as polymers, which showed satisfactory physicochemical properties and good correlation in drug release and drug permeation studies by *in vitro* methods. In other research reports, buccal patch has been reported by Navneet et al. (2011) and Amanpreet et al. (2012) with the use of chitosan and pectin-chitosan composite materials, respectively [44,45]. Chitosan showed good mucoadhesiveness, swelling characteristics and maintained a satisfactory residence time and drug release for 8 hours. In case of the pectin-chitosan composite, the interpolymer complexes were observed with sufficient bioadhesion strength, *in vitro* drug release and increased bioavailability.

A propranolol hydrochloride buccal patch was prepared by Vishnu et al. (2007) using Eudragit L-100 as base matrix and carbopol 934 & PVP K30 as polymers [46]. The full factorial design was employed for the experimental optimization study and the results concluded that Eudragit alone could provide the required swelling property. However, an addition of carbopol 934 increased bioadhesion but decreased drug release, while PVP K30 increased the drug release and swelling index but decreased the mucoadhesive strength. Another type of buccal film was developed by Angela et al. (2012) using polymers like gelatin and chitosan [47]. Addition of mannitol in the formulation increased the water uptake ability and exhibited drug release. Also, mucoadhesion strength was proportional to the chitosan concentration.

Vishnu et al. (2007) and Deelip et al. (2009) had used the polymers sodium alginate and carbopol 934P for developing the buccal tablets of Propranolol [48,49]. The swelling index was found to be directly proportional to sodium alginate and inversely proportional to carbopol 971P. Mucoadhesion and *in vitro* drug release was maintained for 12 hours and the mechanism of drug release followed zero-order kinetics. Bilayered buccal tablets of Propranolol were prepared by Shukla et al. (2010) using ethyl cellulose as backing membrane and HPMC K4M, xanthan gum and acrypol 934P as polymers [50]. The type and amount of polymer in each blend mixture and the type of diluents used were the fundamental factors affecting the drug release.

Metroprolol tartarate bilayer buccal tablets were developed by Manohar et al. (2010) by direct compression method using SCMC, gum karaya, xanthan gum and locust bean gum [51]. Combination of xanthan gum and locust bean gum in the ratio of 2:1 exhibited complete drug release in 45 minutes, but poor drug permeation. Incorporation of 1% sodium lauryl sulfate improved the drug permeation across porcine buccal mucosa. Naga Raju et al. (2011) also developed another buccal tablet by using polymers carbopol 934P, sodium alginate and HPMC K4M [52]. The release and bioadhesion of a tablet could be controlled by changing polymer type and concentration. Tablets containing drug (50 mg), mannitol (98.7 mg), magnesium stearate (4.4 mg) and talc (4.4 mg) were identified as optimum formulation. Similarly, Metroprolol succinate buccal tablet was prepared by Rajendra et al. (2011) by direct compression method using polymers carbopol 934, SCMC and cross-linked tamarind seed polysaccharide (TSP) [53]. The tablets containing the ratio of 1:2 carbopol 934P and TSP exhibited more sustained release of a drug, which could be controlled by partially crosslinking the matrix. Metroprolol succinate buccal patch was prepared by Navneet et al. (2012) using polymers CMC and chitosan [54]. Patches with 5% chitosan demonstrated optimal characteristics and the in vivo drug delivery in rabbits showed superior bioavailability over the conventional oral administration.

Atenolol buccal patch was prepared by Surya et al. (2010) by the solvent casting method using carbopol 934P, SCMC, and HPMC as polymers [55]. It was confirmed that the proportional amount of various hydrophilic polymers influenced the drug release. Labetalol hydrochloride buccal tablet was prepared by Ganesh et al. (2011) by direct compression method using xanthan gum as a polymer [56]. They showed a significant increase in oral bioavailability than the pure drug suspension.

Calcium Channel Blockers

Calcium channel blockers are used to decrease the blood pressure in patients with hypertension and also help to reduce the occurrence of other cardiovascular diseases.

Diltiazem hydrochloride buccal tablets were formulated by various researchers using direct compression method. Alka et al. (1995) have used polymers carbopol 934, HPC-L, HPMC K4M and PVP K-30 for manufacturing the buccal tablets [57]. A good correlation was observed between *in vitro* drug release and *in situ* release with the correlation coefficient of 0.74. The drug release followed a first order kinetics. Manivannan et al. (2008) used the polymers SCMC, HPMC, sodium alginate and guar gum for the preparing the buccal tablets [58]. The 4:1 ratio of drug and polymer showed significant swelling properties with optimum release profile. Madhuri et al. (2012) formulated the tablets using carbopol 971P and 974P [59]. The tablets

containing the drug-polymer ratio of 1:0.25 showed moderate drug release for 8 hours and the increase in the concentration of carbopol 971P increased the mucoadhesive strength and *in vitro* residence time.

Lercanidipine hydrochloride buccal tablet was developed by Shrikant et al. (2008) using PEO and HPMC as polymers [60]. Formulations containing a high concentration of PEO supported the maximum mucoadhesion strength and drug release.

Verapamil hydrochloride buccal tablet was formulated by Margret et al. (2009) using the polymers carbopol 934P, HPMC K4M, HEC and SCMC [61]. A formulation containing 45 mg of carbopol 934P and 95 mg of HEC was considered as an optimized formulation with respect to bioadhesive strength and *in vitro* drug release. A buccal patch of Verapamil was designed by Subhashet al. (2009) using solvent casting method with polymers chitosan and PVP K-30 [62]. The drug release rate increased with the inclusion of PVP K-30, which also influenced the modified release kinetics.

Varshosaz (2002) had developed buccal tablets of Nifedipine with the polymers CMC, Carbomer, PVP, PVA and HPMC by direct compression method [63]. Increase in the percentage of CMC caused the significant decrease in the drug release rate, and the presence of carbomer was proved to be necessary for required bioadhesion. A linear relationship was obtained between the mean *in vitro* release pattern and *in vivo* release.

ACE Inhibitors & Angiotensin receptor blockers

Angiotensin Converting Enzyme (ACE) inhibitors and angiotensin receptor blockers are other categories of potential drugs used in the treatment of hypertension. Certain molecules exhibit low half-life, bioavailability, and stability through conventional oral administration, which paved way for the development of buccal dosage forms.

Lisinopril buccal tablet was prepared by Guda et al. (2010) using carbopol 934, HPMC and HEC [64]. Formulation with the ratio of 2:4 carbopol 934 and HPMC K4M showed significant swelling properties with optimum release profile. Enalapril maleate film was prepared by Semalty et al. (2010) by solvent casting technique with SCMC, HPMC, HEC and PVP K-30 as polymers [65]. Films containing 20mg of Enalapril maleate in SCMC and HEC exhibited good swelling, residence time and controlled drug release for more than 10 hours. Perindopril buccal tablets were prepared by Bhanja et al. (2010) [66] with polyethylene oxide (PEO) and carnauba wax polymer by direct compression method followed by sintering technique at various temperatures, which helped in the controlled release of the drug. Tablets with 4 mg of drug exhibited sustained drug release for 8 hours with desired therapeutic concentrations.

Valsartan buccal tablet was formulated by Anilkumar et al. (2012) using guar gum and pectin as polymers by direct compression method [67]. The results revealed guar

gum as better polymer compared to pectin for drug release, which showed a sustained effect for 23 hours. Losartan potassium bilayered tablet was prepared by Praveen (2012) using polymers carbopol 934P, HPMC K4M, and HPMC K15M, while ethyl cellulose was used as a backing layer [68]. The tablets containing HPMC K4M and carbopol 934P extended the drug release for up to 10 hours and bioadhesive time up to 11 hours.

Diuretics

Furosemide is a loop diuretic drug used for treating renal failure and heart disorders, which was developed as bilayer buccal tablets by Ravi Krishna et al. (2011) [69]. Polymers such as carbopol 941NF, carbopol 971P, Methocel K4M, K15M, and SCMC were used. The combination of SCMC and carbopol 971P improved the release and permeation rate of a drug from the tablets when compared to carbopol alone. Formulations containing HPMC K4M and drug in the ratio of 1:1 were also identified as a stable buccal adhesive tablet with maximum drug release.

Drugs Acting on Central Nervous System

Targeting of drug to the central nervous system (CNS) is a challenging scenario in drug delivery applications. However, when the drugs acting on CNS are administered through buccal route, the immediate release and absorption of drugs into systemic circulation facilitate timely

onset of action. Several researchers have reported the significant improvement in the therapeutic efficacy of CNS drugs given as buccal dosage forms.

CNS Stimulants

Bioadhesive dosage form of Caffeine (anhydrous) as CNS stimulant was designed by Gaurav et al. (2011) using a combination of bioadhesive polymers such as SCMC, HPMC and carbopol 934P in different ratios [70]. The formulation containing SCMC and Carbopol 934P exhibited greater swelling index than those containing SCMC and HPMC. *In vitro* release studies showed that the formulation consisting of 3:1 ratio of SCMC and Carbopol 934P released Caffeine for over a period of 8 hours. The dissolution profile before and after storage was identified to be similar, hence proving the good stability.

Nicotine can cause both stimulation and depression depending on the mood of patients and the dose used. It is commonly used to facilitate smoking cessation and avoid the withdrawal syndromes. Buccal patches of Nicotine were formulated by Rana et al. (2011) using the polymers xanthan gum or carbopol 934 with ethyl cellulose as backing layer [71]. Mucoadhesion and *in vitro* release studies indicated that the interaction to be stronger between drug and xanthan gum. The non-medicated carbopol patch showed a significant decrease in mucoadhesion strength and no effect on xanthan patches. The *in vitro* release studies showed a reasonable fast initial release profile followed

by controlled drug release over 10 hours. Nicotine buccal tablets consisting of sodium alginate and nicotine-magnesium aluminum silicate complex were formulated by Sopaphan et al. (2011) through direct compression method [72]. Tablets containing the complex at pH 9 showed remarkably higher permeation rate than those containing complexes prepared at acidic and neutral pH levels. A Larger amount of sodium alginate decreased the drug release and permeation rate but increased the mucoadhesion property of the tablets.

Anti Depressants

Antidepressant drugs are specifically used to treat conditions such as anxiety disorders, eating disorders, chronic pain and dysmenorrhea.

Venlafaxine is clinically recommended for the treatment of anxiety and major depressive disorders, for which buccal tablets were prepared by V.Prasad et al. (2010)using the polymers Carbopol 934P, HPMC K4M, SCMC and HPMC K15M [73]. HPMC K4M and drug in the ratio of 1:1 showed optimum physical properties. The drug release increased with increase in the concentration of HPMC K4M and HPMC K15M with the maximum release of 99.51%. Buccal patch was prepared using solvent casting technique by Varinder et al. (2011)with chitosan and pectin as polymers [74]. The incorporation of PVP-K30 enhanced the drug release rate. Patches containing 1:4 ratio of chitosan and pectin exhibited higher bioadhe-

sive strength with sustained drug release. Venlafaxine gel was prepared by Pankaj et al. (2012) using cress seed mucilage in addition with different ratio of carbopol 934 [75]. Different concentration of carbopol 934P had significant effect on gel vicosity, strength and mucoadhesive property. They have also experimented Venlafaxine microsphere using linseed mucilage by spray drying technique. The formualtion containing 1:2.5 ratio of drug and polymer showed maximum mucoadhesion, swelling index and marked increase in bioavailability.

Bilayered buccal tablet of Paraxetine hydrochloride was prepared by Manasa et al. (2011) using the polymers sodium alginate and carbopol 971P [76]. Both the polymers in the ratio of 5:1 showed maximum percentage of *in vitro* drug release for 12 hours without disintegration. Swelling index was found to be directly proportional to sodium-alginate content and inversely proportional to the carbopol 971P content.

Drugs used for Migraine

Drugs which are used for the treatment of a chronic neurologic disorder migraine have been successfully designed as buccal dosage forms for required onset and duration of action. Sumatriptan succinate patch and tablet was formulated by Supriya et al. (2008) and Saleem et al. (2011), respectively [77,78]. The patches were prepared by solvent casting technique using the polymers gelatin and PVP K-30. A 3^2 full factorial design was employed to study the effect of independent variables. The bilayered

patch containing 35% w/w chitosan, 1% PVP K-30 and 3% polymethylsiloxane exhibited required mucoadhesive strength, 98% of drug release within 2 hours and 12% of drug permeation occurred through the buccal mucosa. The tablet was prepared by direct compression method using polymers HPMC K4M and sodium alginate. They showed good swelling for up to 7 hours maintaining the integrity of formulation. Mucoadhesive strength was observed between 4.86 to 11.88, which was enhanced by increase in the polymer concentation. As the concentration of chitosan increased, significant increase in permeation flux and decrease in swelling index and mucoadhesion was observed.Zolmitriptan film was prepared by Raghavendra Rao et al. (2011) using polymers HEC and chitosan [79]. The *in vitro* drug release was extended for up to 10 hours with diffusion rate limited process and zero order kinetics.

Anti-Parkinson Drugs

Parkinsons disease is a degenerative disorder of the central nervous system and treated with specific dopamine level regulating drugs. Anti-Parkinson drugs namely, Rasagiline mesylate and Ropinirole drugs have been administrated through buccal mucosa to treat the symptoms of this chronic disease.

Rasagiline mesylate buccal film was formulated by Rama et al. (2010) using the polymers carbopol 940P and sodium alginate by 3^2 fractional design to explore the effect of the individual polymers [80]. Carbopol had a more

pronounced effect than sodium alginate on mucoadhesive strength. A good relationship was established between the experiment and predicted values which confirmed the practicability and validity of the model. Ragavendra Rao et al.(2012) formulated Ropinirole buccal patch by solvent casting technique using HPMC K4M, carbopol 934P, carbopol 940P and PVP as polymers [81]. Formulations containing HPMC K4M and carbopol 940 retarded the drug release in a controlled manner for the prolonged period of more than 8 hours. The release of drug from the films followed zero order kinetics and diffusion rate limited mechanism. Addition of hydrophilic polymer carbopol 940P significantly improved the bioadhesion of films but decreased the drug release rate.

Antipsychotic Drugs

An antipsychotic drug Respiridone was formulated as the buccal patch by Manasa et al. (2010) using HPMC, chitosan, PVA and PVP as polymers [82]. The tensile strength of patch was enhanced by the presence of PVA, which formed effective cross-linking and higher viscosity. Drug release was highest in the formulation containing HPMC-chitosan combination and the mechanism of drug release was both diffusion and dissolution controlled.

Antiepileptic Drugs

Phenytoin is used to prevent and control seizures and it works by reducing the spread of seizure activity in the brain. Phenytoin sodium bilayer oral Bucco adhesive pol-

ymeric film was developed by Bahri Najafi et al. (2012) [83]. One layer contained various ratios of polymer carbopol 934, SCMC, HPMC and PEG 400 as a plasticizer, whereas the other layer contained cellulose acetate phthalates which acted as water resistant material for the unidirectional release of the drug. A formulation containing 60% HPMC, 20% SCMC and 20% Carbopol had zero order drug release kinetics with the good swelling profile, adhesion strength and appropriate residence time.

Oxcarbamazepine is primarily used in the treatment of epilepsy and also recommended as a mood-stabilizing agent. Bilayered buccal tablet of Oxcarbazepine was formulated by Konda et al. (2012) using polymers HPMC, SCMC, carbopol 934P and PVP along with ethyl cellulose as backing material [84]. The formulation containing the combination of carbopol, HPMC K4M and PVP showed optimum drug release for a period of 12 hours, with zero-order kinetics and non-fickian diffusion mechanism.

Neuromodulators

Novel mucoadhesive tablets of Oxytocin were prepared as cores in cup fashion by Pulak Kumar et al. (2008) [85]. Adhesive cups were prepared with the mucilage isolated from Dispyrosperegrina fruit (DPM) and compared with other polymers such as HPMC, carbopol 934P and microcrystalline cellulose (MCC). sodium taurocholate and sodium thioglycollate were used as permeation enhancers since the formulation prepared without permea-

tion enhancer showed poor permeability. The force of adhesion and bond strength of cups prepared with DPM was greater, but the swelling property was lesser than the other polymers. Retention time increased with increase in amount of mucoadhesive material.

Drugs for Lung Related Disorder

The lungs related disorders include asthma, chronic obstructive pulmonary disease (COPD) and emphysema, which commonly causes the inflammation and narrowing of the airway of lungs with mucous accumulation and difficulty in breathing. Drugs have been administered through different modes like conventional oral tablets, capsules, intra nasal spray, nebulizer, metered dose inhalers. But, these drugs usually experiences extensive first pass metabolism which also has only a short half-life with a narrow therapeutic index. In some cases, comparative bioavailability studies have shown inadequate therapeutic response for a sustained release formulation. However, the development of a buccal bioadhesive formulation with controlled release patterns provided a single day dosing and ensured good patient compliance by reducing the repeated acute asthma attack.

Salbutamol sulphateis used to relief bronchospasm and considered as a pioneer drug for treating asthma. Salbutamol was designed as buccal patch dosage form by Panigrahi et al. (2004) and Rajesh Singh et al. (2009) through solvent casting process using PVA, HPMC, chitosan and PVP as polymers [86,87]. The results concluded

that the patch containing PVA exhibited prolonged zero-order drug release and bioadhesion compared to HPMC. The favorable extension of drug release occurred due to the presence of chitosan and PVP, where both acts as rate controlling polymer in the mucoadhesive patch. Salbutamol bilayered buccal tablet was also reported using polymer xanthan gum, which showed constant drug release in the range of 78.66-99.78% till 8 hours with first order kinetics. Studies done by Prasanth et al. (2009) and Ayrivan et al. (2011) involved the addition of PEG-400 and propylene glycol (PG) as plasticizers which increased the swelling index of the patches [88,89]. The former used Eudragit L-100, HPMC, PVA and Carbopol 934 as polymers to optimize each plasticizer for maintaining good integrity and bioadhesion. The latter used the same polymers along with SCMC, PVP occluding Eudragit L-100. Around 36 formulations with varying composition were studied for each plasticizer and the results concluded the similar strategy.

Raghavendra Rao N G et al. (2010) developed buccal patches of Montelukast sodium using HEC, SCMC, Eudragit RL-100 and PVP K-30 for the treatment of chronic asthma attacks [90]. The *in vitro* residence time was between 3.20-5.59 hours and the *in vitro* release studies exhibited 68.83-92.22% drug release in 8 hours with zero order kinetics with diffusion rate-limited mechanism.

Terbutaline sulphate was formulated Vaidya et al. (2009) as buccal tablets through direct compression method using polymers carbopol 934P, Chitosan, HPMC K4M

and HPMC K15M [91]. Mannitol was also added to accelerate the drug release from the polymeric matrices. Good correlation was observed between *in vitro* drug release and drug permeation studies. Decrease in the content of carbopol 934P showed significant decrease in the adhesion force of the tablets.

Theophylline is one of the potent drugs of choice for treating chronic obstructive pulmonary disease (COPD) as the common lung diseases which causes severe difficulty in breathing. Theophylline buccal tablets were developed by Harikrishna et al. (2010) through direct compression technique using the polymers Carbopol 974P and Polycarbophil [92]. Incorporation of more than one polymer and increase in polymer percentage increased the bioadhesion proportionately. The *in vitro* drug release patterns showed prolonged release following the korsemeyer-peppas kinetics model.

Triamcinolone acetate (TAA) is a potent corticosteroid used for the treatment of asthma, inflammation, rhinitis, and ulcers. The buccal films of TAA were formulated by Myung et al. (2011) and Avinash et al. (2011) through solvent casting technique wherein TAA was solubilized in the matrix polymers HPMC, Poloxamer, and carbopol 934 [93,94]. Increase in the percentage of carbopol and HPMC resulted in the proportionate increase in the percentage of moisture loss (PMA). HPMC helped in the extension of drug release up to 10 hours, while carbopol had very little effect on this extension. The flux was controlled by adjusting the amount of TAA loaded in the film

whereas poloxamer concentration did not affect the rate of drug release.

Anti-Diabetic Drugs

Hypoglycemic drugs treat diabetes mellitus by lowering the blood glucose levels in the body. The conventional oral anti-diabetic drugs lacks complete bioavailability and long term effect in the blood circulation. Hence, sustained release dosage forms are highly prefered to maintain the therapeutic concentration for chronic therapy and reduce the dosing frequency. Buccal delivery systems provide required efficacy of several anti-diabetic drugs.

Novel microcapsules of Glipizide were reported by Choudary et al. (2003) through orifice ionic-gelation process using the polymers SCMC, methyl cellulose, sodium alginate, carbopol and HPMC [95]. They exhibited good mucoadhesive property and extended drug release, which depend on the composition of the coating. *In vivo* evaluation of the alginate-carbopol microcapsules confirmed the sustained drug release for 14 hours. Glipizide buccal film was formulated by Mona et al. (2008) by solvent casting technique using HPMC, SCMC, carbopol 934P and eudragit RL-100 as polymers [96]. The films containing 5 mg Glipizide in 4.9% HPMC and 1.5% SCMC displayed required swelling, residence time and drug release.

Glibenclamidebuccal films were developed by Goudanavar et al. (2010) and Indira Prasanna et al.(2011) using solvent casting technique [97,98]. The former used

the polymers HPC, PVP and ethyl cellulose wherein the films exhibited satisfactory physical and mechanical properties. To improve the release of drug from these films, experimental optimization was carried out with different composition of the ingredients. The latter researcher used the polymers HPMC, carbopol and PVP, wherein the formulation containing 750 mg HPMC, 20 mg carbopoland polyvinylpyrrolidone was found with optimum results. Good correlation was observed between *in vivo* and *in vitro* study.

Glimepride buccal patch was formulated by Patel et al. (2012) using polymers carbopol 934P, HPMC and ethyl cellulose [99]. Formulations containing maximum amount of swellable and hydrophilic polymer (HPMC K100M and Carbopol 934P, respectively) showed higher swelling index and sustained the drug release for 24 hours based on diffusion followed with zero order kinetics.Rosiglitazone maleate buccal tablets was formulated by Basanta et al. (2012) by employing direct compression method with the polymers carbopol 934P and HPMC [100]. Formulations containing carbopol 934P and HPMC in 1:1 ratio showed required bucco adhesive force and maximum drug release (99%) in 8 hours through non-fickian diffusion mechanism.

Anesthetic Drugs

Local anesthetic drugs are those that bring reversible loss of consciousness in a local region. Most of the oral cavity diseases are associated with the sudden inflamma-

tory process. Hence, topical administration of the local anesthetic drugs would be recommended for the immediate response. Lidocaine is an amide local anesthetic, commonly recommended for this purpose. A double-layered buccal tablet of Lidocaine was prepared by Nahid et al. (2011) using infrared hydraulic press [101]. The first layer was impermeable membrane prepared by compression of Kollidon SR, magnesium stearate, aerosol and talc blend, while the second layer was designed by compression of a mixture of drug, mucoadhesive polymer carbopol 934P and cellulose derivative polymer HPMC. The *in vivo* mucoadhesion performance of the tablets showed very good adherence to buccal mucosa for 6 hours with no sign of irritation. A novel type of Lidocaine buccal patches was developed by Cristina et al. (2012) using solvent casting method [102]. Lidocaine (30%)/Comperitol (70%) solid dispersion in the form of microspheres was embedded inside the patch either alone or together with free Lidocaine. The system allowed controlled and bimodal release of the drug, wherein a prompt release was also obtained by the addition of plasticizers. The drug release was accelerated and completed in 3 hours when lidocaine was loaded on HPMC rather than carbopol.

Muscle Relaxant Drugs

Tizanidine buccal tablets were prepared by Gazzi et al. (2009) by direct compression method using the polymers HPMC and SCMC as either alone or in combina-

tion [103]. The results proved sustained release of the drug through the non-Fickian mechanism. Tizanidine hydrochloride buccal patch was prepared by Mohamed et al. (2012) using the polymers Eudragit RS100 or RL100 and chitosan [104]. Formulations with Eudragit polymer alone exhibited satisfactory physicochemical properties but lacked gradual *in vitro* drug release. The incorporation of chitosan resulted in the formation of a porous structure which exhibited gradual release of the drug.

Anticholinergic Drugs

Oxybutynin hydrochloride is an antispasmodic and anticholinergic agent used for the treatment of overactive bladder. Subhash Chandra Bose et al.(2011) formulated a buccal patch using the polymers HPMC K4M, chitosan, PVP and PVA [105]. Patches containing HPMC K4M and chitosan exhibited greater drug release in the range of 68.3% to 99.9% for 8 hours than the other formulations. *In vitro* release study showed a linear decrease in percentage release of drug with the anproportionate increase in the amount of polymer.

Anti-Cancer Drugs

Fenretidine buccal patch was formulated by Kashppa-Goudet al.(2011) for site-specific chemoprevention of oral cancer [106]. HPMC K4M, Polycarbophil, and Eudragit were used as the polymers for developing the patch by

solvent casting technique. Fenretidine/Eudragit RL oral mucoadhesive patches with 20 wt% and 80+40wt% sodium-deoxycholate solubilizers were reported to provide optimal and continuous drug release.

Anti-Septic Drugs

Mucoadhesive patch for delivery of Cetyl Pyridinium Chloride was prepared by Noha et al. (2003) using PVA, HEC, and Chitosan [107]. Non-ionic polymer PVA showed good mucoadhesive and swelling characteristics, and the medicated PVA patches maintained a satisfactory residence time in a buccal cavity with ensured the zero-order release of drug for 7 hours.

Chlorhexidine has been reported as different buccal dosage forms by various researchers. A novel method of the tablet was prepared by Paolo et al. (2002) using Chlorhexidine loaded chitosan microspheres [108]. The microspheres were prepared by spray-drying method while the tablet was fabricated by direct compression method using the ingredients mannitol and sodium alginate. Tablets comprising the combination of polymers showed high drug release and mucoadhesiveness which may be due to the ionic interactions between the polymers.Chris et al. (2003) formulated Chlorhexidine buccal tablets by direct compression using the polymers SCMC, HEC and Polyacrylic acid (PAA) [109]. Compacts composed of HEC/

Polyacrylic acid exhibited greater *in vitro* retention than those composed of SCMC. In focus of the patient acceptability and in vitro performance, the compacts composed of 25 mg PAA/75mg HEC containing 10 mg Chlorhexidine was suggested as their best product for use in an oral cavity. Another Chlorhexidine buccal tablet was reported by Jafer et al. (2010) by direct compression using a blend of HPMC and chitosan as bioadhesive polymers [110]. Increase in the proportion of HPMC in the blend decreased the drug release rate and increased the adhesion force. Eskandar et al. (2012) had studied the use of mucilage of cardimyxa as a mucoadhesive material in the production of Chlorhexidine buccal tablets by direct compression process [111]. Increasing the tablet hardness and mucoadhesiveness, shortening of disintegration and dissolution times were achieved by using 20% w/w cardia myxa mucilage.

The chlorhexidine diacetate buccal film was prepared by Claudia et al. (2008) through the solvent casting technique [112]. Six different formulations of mono and double layered film were prepared by using polymers HPMC, chitosan, and sodium alginate. The presence of chitosan has no influence on the drug release profile and swelling of films. The alginate-based formulations were identified with fast swelling and good performance for prolonged residence time.

Others Drugs

Several other categories of drugs have been developed as buccal dosage forms for its significant and meritorious applications.

Curcumindisplayed numerous pharmacological activities such as anti-oxidant, anti-inflammatory, antitumor and antimicrobial. Curcumin bilayered buccal tablets were developed by Latheeshjlal et al. (2011) by direct compression method using the polymer HPMC K4M and ethyl cellulose as backing layer [113]. The formulations containing 5% HPMC K4M and 0.1% sodium lauryl sulfate exhibited best mucoadhesive performance and *in vitro* drug release profile. Higher the HPMC content higher mucoadhesion was observed, however, the increase in polymer concentration reduced the drug release. Another novel drug delivery system as polycaprolactone nanoparticle coated mucoadhesive chitosan containing Curcumin was developed by Leticia et al. (2012) [114]. Nanoparticles were prepared by nanoprecipitation method using different molar masses and concentration of chitosan and triblock co-polymer poloxamer (PEO-PPO-PEO). Dynamic light scattering (DLS) studies showed the nanoparticle to be monodisperse. When coated with chitosan, the nanoparticles showed a greater ability to interact with mucin indicating their suitability for mucoadhesive applications.

Carbenoxolone sodium which was used for treating

Aphthous ulcer in oral cavity was formulated as buccal disc by Nathaya et al. (2010) through the direct compression method using pectin polymers [115]. Bioadhesion of the disc decreased when the discs were hydrated. Water movement and buccal hydration played an important role in the bioadhesion of dried pectin disc. Discs prepared from high-degree esterification (DE) pectin showed weaker and more friable characteristic than the low-DE pectin. Decreasing the amount of pectin produced a disc with high dissolution rate and low bioadhesive performance.

Conclusion

Mucoadhesive drug delivery system through buccal region thus proved to be an inevitable approach for local or systemic therapy by both immediate and sustained release effect. The buccal mucosa offered several advantages such as controlled drug delivery, prolonger residence time, faster absorption, immediate onset of action, etc. The mucosa was well supplied with both vascular and lymphatic drainage and hence, first-pass metabolism in the liver and presystemic elimination in the gastrointestinal tract could be avoided. Buccal adhesive systems also offered other innumerable advantages in terms of accessibility, administration and withdrawal, low enzyme activity, economy and high patient compliance. Various formulations including tablets, disc, patches, films, gels, microspheres, nanoparticles were also witnessed. The commonly used mucoadhe-

sive polymers HPMC, carbopol, sodium alginate, sodium carboxy methyl cellulose, xanthan gum and Eudragit are valuable materials offering boundless options for optimization of required quality and standard drug release. Based upon the potential site of absorption / application and adhesive strength, polymer characteristics, biocompatibility and safety, suitable mucoadhesive polymer should be selected and preparation techniques should be adopted. With the right dosage form design and formulation, the permeability through the local environment of the mucosa can be controlled and manipulated in order to accommodate high drug permeation. While considering a formulation development of mucoadhesive drug delivery dosage form, the physiological factors shall be considered at the site of action. Further advances in mucobuccal adhesive technology and sustained local drug release also have the potential for reducing the systemic side effects from ingested or injected therapies.

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