Bodde et al. [1990] investigated the relationship between structure and adhesion for mucoadhesive polymers. Their study was based on an assumption that bioadhesion should possess two properties: (i) optimal polarity to make sure the polymer is "wetted" by the mucus, and (ii) optimal fluidity to allow for the mutual adsorption and interpenetration of polymer and mucus to take place. They studied acrylic polymer films, designed for buccal drug delivery. The films were made either through mixing or copolymerization of poly(butyl acrylate) and poly(acrylic acid). In both cases satisfactory mucoadhesion was found within a range of compositions optimized for surface polarity and the fluidity of polymer film.

Shojaei and Li et al. [1995] designed and formulated a series of novel copolymers of acrylic acid and poly ethyleneglycol monomethylether monomethacrylate [P(AA-co-PEG)]. The addition of PEG into the polymer increased the potential for hydrogen bond formation since the lone pair electrons of oxygen in the repeat unit(\(\text{CH}_2\text{CH}_2\text{O}\)) of PEG served as hydrogen bond acceptor. The surface properties of PAA for mucoadhesion were also improved by the PEG incorporation. Using these copolymers, a patch device was prepared for buccal acyclovir delivery and the feasibility of such delivery was proven in vitro with the incorporation of sodium glycocholate as the permeation enhancer.

Nair M.K. and Yie W. Chien et al. [1996] prepared the two prolonged release dosage form for the treatment of oral candidiasis. These dosage forms contain the antifungals, chlorhexidine and clotrimazole, for therapy against Candida albicans, and also benzocaine and hydrocortisone to combat the pain and inflammation secondaly to a candidal infection. Release studies demonstrated that only chlorhexidine and clotrimazole could be delivered in a controlled manner from the mucoadhesive patches. On the other hand, release of all four drugs could be controlled from the mucoadhesive tablets.
Parodi et. al.[1996] prepared A buccoadhesive system for the delivery of oxycodone hydrochloride to the oral mucosa from a colloidal solution of gelatin used as a bioadhesive agent. An in vitro method for measuring the adhesion of release system to a substrate was developed by employing a modified balance. The in vitro release of the buccoadhesive formulation was studied by a USP paddle dissolution apparatus and the results were fitted to an empirical equation.  

Ileango R. et. al [1997] investigated the possibility of obtaining a slow release, relatively constant effective levels of glibenclamide from buccal strips using chitosan. Suitable chitosan-based buccal strips were prepared and to characterized. it using different in vitro methods. Chitosan-based strips of glibenclamide showed suitability over Eudragit-based glibenclamide buccal strips for controlled release behaviour.  

Khanna R. and et. al [1997] prepared Mucoadhesive buccal films of clotrimazole for local delivery of the drug to the oral cavity were formulated by the solvent casting technique. The films were evaluated on the basis of their physical characteristics, bioadhesive performance, release characteristics, surface pH, folding endurance and stretchability. A combination of Carbopol-934P and hydroxypropyl cellulose-M in the ratio of 1:5 and using ethanol (95%) as the solvent was found to give satisfactory results. The film exhibited an in vitro adhesion time of 4 hours and maintained the concentration of clotrimazole in the dissolution medium (isotonic phosphate buffer pH 6.6) above the MIC of Candida albicans (T>MIC, d) for upto 4 hours.  

Khoda Y. et.al. [1997] prepared Solid dispersion films with a highly water-soluble medicine, lidocaine hydrochloride (LDC), water-insoluble ethylcellulose (EC) and water-soluble hydroxypropyl cellulose (HPC). The release profiles of LDC from the solid dispersion films of different composition, and the suppression mechanism of the release in the LDC-EC-HPC system were studied. The release rate of LDC from the solid dispersion film as drug-reservoir was well controlled at EC/HPC composition ratio of 5/5. The mechanism of controlled release was speculated that
there was a little release of HPC together with LDC, and the retained HPC was swelled in the film by the permeating fluid. Then, the release of LDC occurred via diffusion into the swelled HPC phase, causing a marked decrease in the release rate. The film for clinical use, which had the 30% LDC solid dispersion film, adhered almost completely to the buccal mucosa. These observations will provide useful information on clinical application of the LDC-EC-HPC solid dispersion film.12

- **Ali J et.al. [1998]** prepared Buccoadhesive erodible tablets of trimcinolone acetonide using different bioadhesive polymers along with excipients like mannitol and PEG-6000. In vitro release characteristics were evaluated using a 'flow-thru assembly' which simulated the conditions of the human buccal cavity. The bioadhesive performance and the surface pH of the tablets was satisfactory. The optimized formulation containing 8.0 mg of triamcinolone acetonide, 2.5 mg of mannitol, 7.5 mg of PEG-6000, 2.0 mg of magnesium stearate along with carbopol-934P (CP-934P) and sodium carboxy methyl cellulose-DVP (SCMC-DVP) in the ratio of 1:4 was found to release the drug for a period of over 8 h without getting dislodged. Maximum in vitro drug release was found to be 79.08% in 8 h study. In vivo evaluation of placebo buccoadhesive tablets revealed adequate comfort, taste, non-irritancy during the period of study.13

- **Jhonston et. al.[1998]** Evaluated bioadhesive properties of several different mucoadhesive buccal patches. The patches consisted of custom coformulations of silicone polymers and Carbopol 974P. The contact angle of water was measured for each of the test formulations, using an ophthalmic shadow scope. The corresponding work of adhesion between the water and the patches (W1), and between the patches and freshly-excised rabbit buccal mucosa (W2) was then calculated, using a modification of Dupre's equation. The bioadhesive strength between the patches and excised rabbit buccal mucosa was assessed. The results of the contact-angle measurements indicated that the contact angle decreased with an increase in the amount of Carbopol in the formulation. Additionally, the calculated values of both W1 and W2 increased with an increase in the amount of Carbopol in the buccal-patch
formulations. A correlation (r not equal to 0.9808) was found between the measured contact angle and the calculated values for W2. The direct measurement of the force required to separate a buccal patch from excised rabbit buccal mucosa with the INSTRON demonstrated that the adhesive strength increased with an increase in the amount of Carbopol. This preliminary study has shown that the measurement of contact angles alone may provide a useful technique for estimating the work of adhesion, and may serve as a convenient and rapid screening procedure to identify potential mucoadhesive buccal-patch formulations.\textsuperscript{14}

- **Varshosaz J. et al[2002].** Prepared buccoadhesive controlled-release tablets for delivery of nifedipine by direct compression of carboxymethyl cellulose (CMC) with carbomer (CP), which showed superior bioadhesion properties compared to polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA), hydroxypropylmethyl cellulose (HPMC), and acacia in a modified tensiometry method in vitro. The tablets containing 30 mg of nifedipine and various amounts of CMC and CP showed a zero-order drug release kinetic. The adhesion force was significantly affected by the mixing ratio of CP:CMC in the tablets.\textsuperscript{15}
Kok K. et al. [1999] Studied the suitability of an SCMC (sodium carboxymethyl cellulose/polyethylene glycol 400/carbopol 934P) and HPMC (hydroxypropylmethyl cellulose/polyethylene glycol 400/carbopol 934P) films as drug vehicle for buccal delivery. The mechanical and in vitro bioadhesive strength properties of the films were investigated using texture analyzer equipment, while swelling behavior was studied in different media, namely, distilled water and simulated saliva solution. In addition, the in vivo bioadhesion of the film was studied by estimating the film residence time on buccal mucosa of human volunteers. Increased in carbopol 934P content was found to elevate the elasticity, softness and bioadhesive strength but decrease the strength and degree of swelling of both SCMC and HPMC films. SCMC films swelled more extensively in distilled water while HPMC films in simulated saliva solution.16

Johnston et.al [1999] evaluated the gum from Hakea gibbosa (Hakea) as a sustained release and mucoadhesive component in unidirectional buccal tablet. Flat faced core tablet containing a novel gum and chlorpheniramine maleate were formulated using direct compression technique and were coated with cutina® on all but one face. It was concluded that, such tablet formulations containing a polysaccharide bioadhesive gu, Hakea, may represent an improved buccal delivery system for a variety of water soluble, low molecular weight drug substance. 17

Shine S. et.al. [2000] investigated the buccal absorption of triamcinolone acetonide mucoadhesive gels in rabbits. The enhancing effect of sodium deoxycholate as an enhancer on the buccal absorption of triamcinolone acetonide from the mucoadhesive gels was evaluated in rabbits. Thus, 2 mg/kg of triamcinolone acetonide was administered from the mucoadhesive gels containing an enhancer (enhancer group) or not (control group) via the buccal routes and compared with intravenous routes (1 mg/kg, i.v. group). AUC of the control, enhancer and i.v group were 2374+/−915, 3778+/−1721 and 3945+/−2085 h ng/ml, respectively, and the absolutive bioavailability of enhancer or i.v to control group were 159.14 or 332.35%, respectively. The average C(max) of control and enhancer group were 263+/−159 and
362+/−201 ng/ml, and the mean T(max) of the control group and enhancer group were 5.00+/−1.67 and 4.33+/−0.82 h, respectively, but there was no significant difference. As the triamcinolone acetonide gels containing sodium deoxycholate as an enhancer was administered to rabbits via the buccal routes, the relative bioavailability showed about 1.59-fold compared with the control group. Buccal administration of triamcinolone acetonide gels containing sodium deoxycholate as an enhancer to rabbits showed a relatively constant, sustained blood concentration with minimal fluctuation.

- **Allemandi et. al. [2002]** designed mucoadhesive tablet with a potential use in the treatment of oral candidosis. A 2-layered tablet containing nystatin was formulated. Lactose CD (direct compression), carbomer (CB), and hydroxypropylmethylcellulose (HPMC) were used as excipients. Tablets were obtained through direct compression. Properties such as in vitro mucoadhesion, water uptake, front movements, and drug release were evaluated. The immediate release layer was made of lactose CD (100 mg) and nystatin (30 mg). The CB:HPMC 9:1 mixture showed the best mucoadhesion properties and was selected as excipient for the mucoadhesive polymeric layer (200 mg). The incorporation of nystatin (33.3 mg) in this layer affected the water uptake, which, in turn, modified the erosion front behavior. Nystatin showed a first-order release. The polymeric layer presented an anomalous kinetic (n = 0.82) when this layer was individually evaluated. The mucoadhesive tablet formulated in this work releases nystatin quickly from the lactose layer and then in a sustained way, during approximately 6 hours, from the polymeric layer. The mixture CB:HPMC 9:1 showed good in vitro mucoadhesion. A swelling-diffusion process modulates the release of nystatin from this layer. A non-Fickian (anomalous) kinetic was observed.

- **Mortada L. M. et.al. [2003]** prepared and evaluated mucoadhesive patches containing 10mg miconazole nitrate. The patches were prepared with ionic polymers, sodium carboxymethyl cellulose (SCMC) and chitosan, or non-ionic polymers, polyvinyl alcohol (PVA), hydroxyethyl cellulose (HEC) and hydroxypropylmethyl cellulose (HPMC). Convenient bioadhesion, acceptable elasticity, swelling and
surface pH were obtained. Patches exhibited sustained release over more than 5h and the addition of polyvinyl pyrrolidone (PVP) generally enhanced the release rate. Optimum release behaviour was shown with patches containing 10% w/v PVA and 5% w/v PVP. Study of the in vivo release from this formulation revealed uniform and effective salivary levels with adequate comfort and compliance during at least 6h. On the contrary, in vivo release of the commercial oral gel product resulted in a burst and transient release of miconazole, which diminished sharply after the first hour of application. Storage of these patches for 6 months did not affect the elastic properties, however, enhanced release rates were observed due to marked changes in the crystal habit of the drug.  

- **Dugger et al. [2003]** developed buccal aerosol spray using polar and nonpolar solvent which provides biologically active compounds for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar composition comprises formulation with aqueous polar solvent, active compound, flavouring agent and propellant. The non polar compositions comprise formulation with non polar solvent, active compound, propellant.  

- **Martina Lee et al., [2003]**, A physically cross-linked palmitoyl glycol chitosan hydrogel has been evaluated as a controlled release system for the delivery of hydrophobic drugs via the buccal route. All gels were mucoadhesive but less so than the control CP tablets. Denbufylline was detected 0.5 h after dosing with the GCP12 formulation and delivery was sustained for at least 5 h after dosing. In comparison delivery from the CP tablets was not sustained and was first detected 1 h after dosing.  

- **Repka et.al [2003]** used hot-melt extrusion technology to prepare muco-adhesive matrix films containing clotrimazole (CT) intended for local drug delivery applications for the oral cavity. The film system's formulation contained hydroxypropyl cellulose and poly (ethylene oxide) as polymeric carriers, the bioadhesive polycarbophil, and other excipients. The CT formulation was processed at a temperature range of 125–130°C utilizing a Killion extruder (Model KLB-100) equipped with a 6-inch flex-lip die. The extruded films demonstrated excellent
content uniformity and a post processing drug content of 93.3%. The results of study indicated that HME was a viable technique for the preparation of muco-adhesive films.  

- **Pramod Kumar T.M. et al. [2004]**, concluded that Carbopole and HPMC are suitable for developing buccoadhesive core-in-cup system of Terbutaline sulphate. These two polymers act in a complimentary fashion in that carbopole increases the bioadhesion while HPMC helps in sustaining the release. Thus, the variation in their ratios could be adjusted to obtain the desired release profiles. Formulations containing a higher proportion of carbopole exhibited high mucoadhesive strength, swelling index and faster release. Thus, the study revealed that the buccoadhesive formulation showed good mucoadhesive properties with sustain release of Terbutaline sulphate.  

- **Miller-Nazila Salamat et al. [2005]**, show that advantages associated with buccal drug delivery have rendered this route of administration useful for a variety of drugs. This review highlights the use of mucoadhesive polymers in buccal drug delivery. Starting with a review of the oral mucosa, mechanism of drug permeation, and characteristics of the desired polymers, this article then proceeds to cover the theories behind the adhesion of bioadhesive polymers to the mucosal epithelium. Additionally, we focus on the new generation of mucoadhesive polymers such as thiolated polymers, followed by the recent mucoadhesive formulations for buccal drug delivery.  

- **Cappello Brunella et al. [2006]**, Developed a tablet for the buccal delivery of the poorly soluble drug carvedilol (CAR), based on poly(ethyleneoxide) (PEO) as bioadhesive sustained-release platform and hydroxypropyl-β-cyclodextrin (HPCD) as modulator of drug release. As first, PEO tablets loaded with CAR/HPCD binary systems with different dissolution properties were tested for CAR and HPCD release features and compared to PEO tablets containing only CAR. When the drug was incorporated as CAR/HPCD freeze-dried product, all CAR content was released from the tablet in about 10 h, displaying a constant release regimen after a transient. The effect of HPCD incorporation on the release mechanism, was rationalized on the basis of the interplay of different physical phenomena: erosion and swelling of the tablet, drug dissolution, drug counter-diffusion and complex formation. In the second part of the study, the potential of HPCD-
containing PEO tablets as buccal delivery system for CAR was tested. It was found that the incorporation of HPCD in the tablet did not alter significantly its good adhesion properties. The feasibility of buccal administration of CAR was assessed by permeation experiments on pig excised mucosa.26

- **Govender et.al [2008]** prepared and characterized monolayered multipolymeric films (MMFs) comprising of a hydrophilic drug and polymers of opposing solubilities. Films were prepared by emulsification and casted by a new approach using a silicone-molded tray with individual wells. MMFs comprising of drug with Eudragit® 100 (EUD100) and Chitosan (CHT), i.e. films with drug and polymers of opposing solubilities were successfully prepared. It was found that maximum swelling of the films occurred after 1 h and 28.26% of the films eroded during the 8-h test period. 27

- **Singh et.al [2008]** formulated and evaluated buccal bioadhesive films of clotrimazole for oral candidiasis. The film was designed to release the drug at a concentration above the minimum inhibitory concentration for a prolonged period of time so as to reduce the frequency of administration of the available conventional dosage forms. The different proportions of sodium carboxymethylcellulose and carbopol 974P (CP 974P) were used for the preparation of films. Carbopol was used to incorporate the desired bioadhesiveness in the films. The films were prepared by solvent casting method and evaluated for bioadhesion, in vitro drug release and effectiveness against Candida albicans. In vitro drug release from the film was determined using a modified Franz diffusion cell while bioadhesiveness was evaluated with a modified two-arm balance using rabbit intestinal mucosa as a model tissue. Films containing 5% CP 974P of the total polymer were found to be the best with moderate swelling along with favorable bioadhesion force, residence time and in vitro drug release. The microbiological studies revealed that drug released from the film could inhibit the growth of C. albicans for 6 h. The drug release mechanism was found to follow non-Fickian diffusion.28
Boateng et. al. [2009] designed solvent cast films from three polymers, carboxymethyl cellulose (CMC), sodium alginate (SA) and xanthan gum by drying the polymeric gels in air. Three methods, (a) passive hydration, (b) vortex hydration with heating, and (c) cold hydration, were investigated to determine the most effective means of preparing gels for each of the three polymers. Different drying conditions [relative humidity- RH (6-52%) and temperature (3-45°C)] were investigated to determine the effect of drying rate on the films prepared by drying the polymeric gels. Glycerol was used as a plasticizer. Vortex hydration with heating was the method of choice for preparing gels of SA and CMC, and cold hydration for xanthan gels. CMC films prepared at 45°C and 6% RH produced suitable films at the fastest rate while films containing equal quantities of glycerol and CMC possessed an ideal balance between flexibility and rigidity.  

Harish et.al [2009] formulated and evaluated in situ oral topical gels of clotrimazole based on the concept of pH triggered and ion activated systems. A pH triggered system consisting of carbapol 934 P and ion triggered system using gellan gum along with HPMC. It was observed that, the formulation containing gellan gum showed better sustained release compared to carbapol based gels.  

Vaidya V.M. et al., [2009], formulated buccal tablets of Terbutaline sulphate prepared by direct compression method. Carbopole934P, chitosan, HPMC K4M, and HPMC K15M were used as a polymers. They found that decreasing the content of carbopole 934P result in decrease in adhesion force.  

Ahmed Mohammed G et al., [2010] developed a new oral drug delivery system utilizing both the concepts of controlled release and mucoadhesiveness, in order to obtain a unique drug delivery system which could remain in stomach and control the drug release for longer period of time. Gastro-retentive beads of captopril were prepared by orifice ionic gelation method in 1:1 and 9:1 ratio of alginate along with mucoadhesive polymers viz; hydroxy propyl methyl cellulose, carbopol 934P, chitosan and cellulose acetate phthalate. The prepared beads were subjected for
various evaluation parameters. The alginate-cellulose acetate phthalate beads showed the better sustained release as compared to all other alginate polymer combinations.\textsuperscript{32}

- **Dhakar Ram Chand et al., [2010]** formulated and evaluated mucoadhesive microspheres of Rosiglitazone Maleate for treatment of diabetes type-2 by combine the potential advantages of mucoadhesion with controlled drug delivery using various ratio of polymers. Mucoadhesive microspheres were prepared by emulsification solvent evaporation techniques. Microspheres were found discrete, spherical and free flowing. The work has demonstrated that among all the formulations of microspheres, particularly those of formulation containing sodium carboxy methyl cellulose are promising candidates for the sustained release of Rosiglitazone Maleate in the gastrointestinal tract.\textsuperscript{33}

- **Choudhary Arpita et al., [2010],** Carvedilol patches were prepared using HPMC K15 and Carbopol 940. The patches were evaluated for their thickness, folding endurance, weight and content uniformity, swelling behaviour, mucoadhesive strength and surface pH. In vitro release studies were conducted for carvedilol-loaded patches in phosphate buffer (pH, 6.8) solution. The patches exhibited drug release in the range of 77.05 to 97.20\% in 8 hours. Data of in vitro release from patches were fitted into kinetic models (Higuchi and Korsmeyer-Peppas models) to explain release profiles. The optimized formulation (patch V) showed first order release followed by zero order.\textsuperscript{34}

- **Paola Mura et.al [2010] developed** mucoadhesive film for topical administration in the oral cavity of flufenamic acid, a poorly soluble anti-inflammatory drug. Drug and β-cyclodextrin (HPβCD) were complexed to improve drug dissolution and release rate. Buccal films were prepared utilising chitosan as mucoadhesive polymer, KollicoatIR® as film-forming polymer and glycerol as plasticiser. Different combinations of these components were used and the obtained films were characterised for weight, thickness, swelling, mucoadhesive and mechanical properties. The film containing chitosan 2\%, glycerol 7.5\% and KollicoatIR® 1\% showed the best properties for the development of the film formulation.\textsuperscript{35}

- **Patel K.R. et al., [2010],** formulated the mucoadhesive patch containing carvedilol using different mucoadhesive polymers like Chitosan, HPMC, HPC, and Na-CMC alone
and in combination with PVP. These patches show satisfactory mucoadhesive characteristic. Incorporation of PVP in the patches enhanced the permeability of carvedilol.36