Literature Review

1. Medlicott et al discusses the pathogenesis of periodontal diseases and the biopharmaceutical consideration of the active moiety delivery in treatment of the periodontal disease. They concluded that, for the improvement of the use of intrapocket delivery systems, antimicrobial aims must be clearly defined. Presently, the delivery systems may be directly administered to the infectious site within the periodontal pocket for a range of time periods. It was found that a period of 1 to 3 days was sufficient to alleviate the signs and symptoms of periodontal disease, but they are not preventing recolonisation and reoccurrence of the condition. Even if the treatment was lengthened same effect was observed. The decrease in microbial activity needs to be investigated during the treatment, to ensure whether the cessation is due to therapy or due to better oral hygiene.  

2. Kristmundsdottir et al summarizes the formulation and evaluation of a steroidal solution for treatment of oral disease, its advantages over local creams of steroids and its possible reduced side effects. The study showed results favorable to the use of the solution. The solution prepared was quite compatible in handling as it was easy to use. The formulation showed much better activity than the more potent formulations. Due to this the side effects are reduced to a larger extent and the distress situation is dealt with.

3. Li et al studies the invtro activity of two antibacterial monomers against oral pathogens and their compatibilities with each other. The monomers studied were 2-methacryloxyethyl dodecyl methyl ammonium bromide (MAE-DB) and 2-methacryloxyethyl hexadecyl methyl ammonium bromide (MAE-HB). The kinetics involved were studied by time kill method. The Toxicological study was also carried out on the monomers. From the data it was concluded that unpolymerized monomers are more effective against the bacteria. Their cytotoxicity was less than the one used for reference on the human gingival fibroblast.

4. Yoshihiko et al in the article have taken the reference of their previous findings. Based on their earlier reports they confirm the antibacterial activity of chitosan when used in chewing gum against the bacteria present in the oral saliva. The acceptance of such dosage form in various age groups is also elaborated. The test was carried out on human volunteers of various age groups. The double blind study was carried out over a specified
period, and the volunteers were asked to chew in total eight pieces of the gum. From the
data collected of the salivary samples from the volunteers it was concluded that indeed
inclusion of chitosan in gum helps in inhibiting the bacteria of oral cavity.  

5. Assimopoulou et al discuss the antioxidant activity of various resins and their bioactive
triterpenes. The study revealed that P. Lentiscus showed significant antioxidant activity in
oil substrate. The study also concluded that the antioxidant property of the resins were
dependent on the nature of the oil used as substrate. The antioxidant activity was studied
on various oil substrates like corn oil, lard and olive oil. 

6. Silva et al have discussed regarding the presence of H.pylori in the oral cavity of subjects
suffering from periodontal disease. The study concluded that, patients with both gastric
disease and periodontal disease showed the presence of H.Pylori in the oral cavity. 
H.pylori was found only in the supragingival plaque and not in the subgingival samples. 
Samples collected were subjected to polymerase chain reaction and then studied. From
the study a connection between the oral hygiene and presence of H. pylori was
observed. 

7. Thuille et al, in their study showed the bactericidal activity of various Herbal extracts on
the common pathogens. The study was carried out under same conditions for all the
extracts to determine the effect of solvents on the said activity. From the study the MIC
of all extracts was determined. It was observed that during MIC determination, the role of
solvents is also of prime importance as presence of alcohol as the solvent will add to the
bactericidal effect. 

8. More et al, The study reports the use of plants from the family Fabaceae, Ebenaceae,
Bombaceae and Anonnaceae for treating oral diseases. The study was performed on the
extracts of the medicinal plants and their antimicrobial activity against oral pathogens
was determined. The MIC and MBC of the extracts against five microorganisms was
found. The study aims to study the various medicinal plants used in South Africa. Those
Plants were used as chewing sticks against the bacteria present in oral cavity. Those
bacteria are responsible for dental problems. Thus their antimicrobial activity was
studied.

9. Knuth Kim et al, The literature details the anatomy physiology of the oral cavity. It also
explains the various delivery systems which can be utilized to deliver drug to the oral
cavity. The reasons for development of buccal/mucosal delivery systems for delivery of drug to oral cavity are also elaborated. Various delivery systems like buccal adhesive tablets, patches, dental plasters are also explained. Hydrogels are hydrophilic natural or synthetic crosslinked polymers that have the ability to swell in an aqueous environment without dissolution. Hydrogels have the advantage of their structure which can provide them with properties similar to biological tissues and yet maintain mechanical integrity. The property of flexibility, when hydrogels are swollen, provides in some cases a superior drug delivery device. The article focuses on vaginal and oral drug delivery systems using hydrogels. The oral cavity, gastric retention, intestinal, colonic, and rectal delivery are explained in detail in the review.  

10. Abdellaoui et al have elaborated information regarding the refractory subjects who require treatment repeatedly and the line of treatment used previously for the purpose as well as the recent developments in treatment to avoid the various side effects of the systemic therapy are shared. Approaches to improve drug action to the most remote area of the cavity can be sustained and controlled release and site specific delivery. It also concludes the possible disadvantages of using delivery devices.

11. Bär et al, in their literature provides a faster method for detection of the MIC and MBC of antibiotics using fluorescence spectroscopy. The method is different from conventional methods as it determines the ratio of live to dead bacteria. The investigation gave a comparative data of the bactericidal efficiency of various antibiotics. Escherichia coli and Pseudomonas aeruginosa were used as reference strains. The study revolved around a kit developed for fast determination of bactericidal activity of antibiotics. The kit utilizes two colour fluorescence assay for bacterial viability testing.

12. Takahashi Nobuhiro, In the article the author has given the description of the cariogenic bacteria in the oral cavity. The vast diversity of the microbial system in the oral cavity leads to a changing microbial community in the cavity thus altering the pathology of the oral cavity periodically. The changes in pH and nitrogenous environment leads to better adapting pathogens which are more resistant. Thus environment governed by the metabolic activity of microbes changes the healthy oral cavity to a more pathogenic one.

13. Rathbone et al, have given an insight on the use of the oral cavity as a potential route for delivery of drugs to systemic circulation. Alongwith the various advantages associated
with this route of drug delivery, the disadvantages related to the amount of drug to be delivered, movements of the oral cavity and patient compliance are elaborated for considering the design of the dosage form. The article emphasizes on the need to develop a used friendly oral mucoadhesive system.  

14. Sterer et al, in their article the herbal plants are considered for their antibacterial and malador treating activity. The antibacterial activity was analysed statistically. The article gives an insight on the novel delivery system involving mucoadhesion and sustained release of the herbal formulation. A mucoadhesive tablet was developed and tested in human volunteers against placebo tablets. The reduction in unpleasant odor of breath formed the basis of the study.

15. Nakano et al discuss the microdata of the various areas of the mouth including the tongue and subgingival cavity. The cause for oral malodor is due to the formation of sulphur by the oral pathogens. Knowledge of these sulphur producing bacteria and the mechanism involved can help in the formulation of suitable delivery systems to combat oral malodor. Various bacteria were tested for their methyl mercaptan producing ability in the broth. The foul smell from human breath was judged by smelling the expelled air from the mouth and then rated by judges. It was concluded that targeting METase enzyme will be a potential platform for development of the future dosage forms.

16. Squier et al in the article the authors have given a detailed explanation of the oral mucosa in normal as well as in disease condition. They have explained how the physiological state of the oral mucosa can alter the release of the drug and the different behavior of the delivery devices in pathological conditions. In disease state the oral mucosa becomes thin. The thickness of oral epithelium and the rapid healing factors affect the use of delivery devices meant for adhesion.

17. Khanna Rajesh et al, The study was carried out for the treatment of oral Candidiasis. The tablets prepared were evaluated using a modified form of the flow through cell apparatus. Different polymers were utilized for mucoadhesive properties. From the study it was found that the mucoadhesive strength of the polymers depend on the concentration of the polymers added. The apparatus gave a good correlation between the in vivo and in vitro adhesion studies.
18. Roskos K.V. et al, The paper discusses regarding the development of non erodible devices containing acrylic and ethylcellulose strips. As they were non erodible, there was a need to remove the device, thus biodegradable devices were evaluated for the anaerobic pathogens. The release rate of drugs from these devices was evaluated from a specially devised flow through cell. Adhesion test was carried out using Micro load cell to test adhesion of polymer on hard tissue substrates.29

19. Morales et al, in the literature describes different aspects of formulating mucoadhesive buccal films. The polymers used were tested for their mucoadhesive properties, and permeation characteristics for formulations. The formulation contains the mucoadhesive polymers such as carboxymethyl cellulose, hydroxyethyl cellulose etc., these polymers have a backing layer to direct drug release towards the buccal mucosa. The article explains the various methods for preparation of the films like casting method and hot melt extrusion. The evaluation of adhesion and permeability enhancement are also discussed.30

20. Senel et al, have described the method for preparation of the buccal tablets. The major advancement in the paper is the use of sodium glycodeoxycholate as penetration enhancer for the drug into the oral mucosa. They also evaluated the changes in histology of the buccal mucosa after application of the buccoadhesive tablet. The changes to the mucosa were found to be reversible. The placebo containing only polymer had no irritation to the applied cavity. Repetitive studies will have to be carried out to ensure the irritation effect.31

21. Han et al gave the importance of manufacturing a robust formulation for buccal delivery. They have compared various batches of the drug which contained varying concentration of polymer ratio and the effect of hydrophilic prodrug on the release profile from the device. They concluded that release was more when more hydrophilic prodrugs were used in the formulation.32

22. Abruzzo et al, The emphasis of the paper was on preparation of a gelatin –chitosan film for buccal delivery of the antihypertensive drug Propranolol Hydrochloride. The method of complex formation is described. The release of the drug was compared statistically. In addition adhesion studies and water uptake studies were carried out. They concluded that gelatin chitosan complex films gave minimum water uptake and maximum residence
time thus specified number of films can be applied to achieve the daily requirement of the said antihypertensive drug.\textsuperscript{33}

23. İkinci et al have discussed the formulation consisted of buccal adhesive tablets of nicotine containing varying concentrations of carbomer 974P and HPMC. The residence time and release rate of the medicament from the various batches were evaluated. It was concluded that the nicotine hydrogen tartarate was released for a period of 8hrs from the formulation and it remained intact except for the formulation containing Carbomer and HPMC in a ratio of 20:80.\textsuperscript{34}

24. Mumtaz et al, The research paper gives information of a novel dissolution apparatus which can be used to study the release of drug from buccal adhesive tablets. Chicken mucosa was utilized for the purpose and the effect of varying concentrations of polymers like PAHD and HPMC were studied for their effect on the release rate of the drug. It was concluded that PAHD gave faster dissolution and more adhesion than HPMC.\textsuperscript{35}

25. Nafee et al in the article describes the formulation of buccal patch of miconazole nitrate for mucoadhesion using various ionic and non ionic polymers. The effect of addition of Polyvinyl pyrrolidone on the release rate of the medicament was studied and found to be increasing with the addition of PVP. The buccal patch showed advantage over the oral gels of the same medicament. The formulation provided a uniform and sustained release of the drug from the patch. The release study in vivo were carried out by examining the saliva of the patient after placing the patch in the buccal cavity.\textsuperscript{36}

26. Burgalassi et al discusses the formulation in which they explored a new property of tamarind gum as mucoadhesive agents. The patch proved to be of better patient compliance and when tested in human volunteers remained intact for 8 hrs without any sensitivity. Various polymers used were tested for their adhesiveness. The formulation of the patch is done in a simple process of compression which could be easily accepted for large scale production.\textsuperscript{37}

27. In the article by Miller et al, emphasizes on the advantages of mucoadhesives in the buccal delivery. It gives a detailed account about the physiology of the oral cavity, the factors affecting the mucoadhesion of polymers in buccal cavity. It gives a description of the desired characteristics of the polymer when used as mucoadhesive in buccal cavity.
The various formulations relate to buccal cavity like, Buccal patches, buccal films, buccal gels ointments are described in the text.\textsuperscript{38}

28. Sandra Kockisch et al, The microspheres prepared for triclosan delivery showed sustained release rate. The release rate of the drug was found to depend on the polymer used in the formation of microspheres. The release of triclosan microspheres was compared using different polymers it was found that microspheres prepared from Gantrez, Carbopol or polycarbophil, the release appeared to obey zero-order kinetics whereas in the case of chitosan-derived vehicles, the release profile fitted the Baker and Lonsdale model. It was conclude that microspheres prepared using of chitosan, are promising candidates for the sustained release of triclosan in the oral cavity.\textsuperscript{39}

29. In the article by Llabot et al, the design of nystatin films on buccal and gastrointestinal mucosae was evaluated for the adhesion test. The effect of plasticizers on the adhesion of the film was evaluated. It was concluded that plasticizer addition increases the adhesion of film by increasing the interlinking and penetrability of polymer to the mucosa.\textsuperscript{40}

30. Bromberg et al in the article describe the composite wafer was formulated having varying layers of mucoadhesive polymer as the surface layer, other layers consisted of antimicrobial agents, biodegradable polymers, and matrix polymers. The rapid dissolving property of wafer led to its less residence time in the oral cavity. Thus addition of polymers like ethylcellulose can help in increased residence of the drug and its controlled release can be facilitated.\textsuperscript{41}

31. Jones et al in the article details the viscoelastic properties, mucoadhesion characteristics of various poloxamers and polyacrylic acid containing polymeric systems. The effect of pluronic 407 and C934P, their sol gel transition temperature and their resistance to deformation at 37 degrees were studied. The formulations having 20% composition of pluronic 407 and C934P showed the best results for mucoadhesive drug delivery system in oral cavity.\textsuperscript{42}

32. Southard et al in the article summarizes the need for a delivery system for local application in the oral cavity. The microbial evaluation, clinical testing and human trials were done to verify the results. It was concluded that drug delivery in oral cavity has various advantages over conventional dosage form. It details the importance of sustained release dosage form for the oral cavity and the requirements of a sustained release dosage
form. The sustained release dosage may give more better patient compliance in treating patients with dental diseases.\textsuperscript{43} 

33. Schnu’rch et al have proved the increase in bioavailability of drug from a mucoadhesive system can be achieved by using permeation enhancers. The combination of the drug with GSH and chitosan form a mucoadhesive system which prolongs the residence of drug on the mucosa. Longer residence time helps in sustaining the release of drug in the area. Mucoadhesion is one of the necessary characteristics for prolonging the stay of the drug in the area. Polymers which swell, show mucoadhesive properties are ideal candidates for suataining release of the drug.\textsuperscript{44} 

34. Paraschos et al, The literature gives a detailed method for extraction of the active components of the plant belonging to the anacardiaceae family and its activity against Helicobacter pylori. The activity of the mastic extract without the polymer is studied and concluded that the activity against H.Pylori is enhanced in absence of sticky polymer.\textsuperscript{45} 

35. Benhammou et al have evaluated the phenolic extracts of Pistacia Lentiscus and were studied for their antibacterial and antifungal properties. The microbial assay results concluded that the extracts showed excellent antibacterial and antifungal properties. Thus they can be further evaluated for their use in formulations. The study was carried on various microorganisms like bacteria, yeast and moulds.\textsuperscript{46} 

36. Nagai et al described ‘Hydrogel’ as a swollen or swellable hydrophilic matrix with a limited swelling capacity in water or aqueous media. The drug is released through the spaces between the matrix and the boundary. The authors have compared the effect of various polymers for the adhesive property. They found that HPC alone gave slight adhesion but dissolution was faster and Carbopol had good adhesion but swollen carbapol was too hard. Thus they are to be used in combination. The advantages of buccal delivery over conventional were elaborated and the possibility of using the buccal route for systemic effect was also considered for future work.\textsuperscript{47} 

37. Yajaman et al described the mucosa of the buccal cavity as highly vascularized. The jugular vein bypasses the first pass metabolism. The route can thus be utilized for delivery of drugs which are highly degraded by the first pass metabolism. The article gives a detailed description of the physiology of oral cavity. The in vitro and In vivo evaluation for permeability and residence time are detailed.\textsuperscript{48}
38. Janet A.J. Hoogstraate et al, The article gives a review regarding the buccal route for drug delivery. The physiology of the buccal cavity its advantages and disadvantages. The review covers all points regarding the use of drugs from the said route. The delivery of high molecular weight peptides results in poor bioavailability because of lower permeability. The various cavities available in the mouth for absorption are the floor of the mouth, inside area of the cheeks and the gingival cavity. The permeation through these route is of prime importance for higher bioavailability of the drugs made available for absorption through the oral cavity.49

39. Wong et al in the study involves testing of the bioadhesive properties of polymers like carbopol 974P and Methocel K4M, using texture analyzer equipment and chicken pouch. The parameters measured were work of adhesion and peak detachment force. The variables studied were contact force, contact time and speed of withdrawal of the probe from the tissue. The studies showed that carbopols showed the best values for the parameters taken into consideration. It also claims that some amount of contact force was necessary for good bioadhesion.50

40. Triantafyllou et al, The authors have found the main reason as to which the Chios Mastic Gum leads to anti-inflammatory activity. They concluded that mastic gum inhibits protein Kinase which attenuates production of superoxide and Hydrogen peroxide by NADPH oxidases. This antioxidant property may have direct implication to the anti-inflammatory activity.8