INTRODUCTION AND REVIEW OF LITERATURE

Periodontal disease is a chronic infectious disease of the oral cavity and one of the main causes of tooth loss in humans. This chronic inflammatory disease that affects the supportive tissues of the teeth has a complex etiology ***(Hinricks, 2012).***

The microbial biofilm is the primary cause in the initiation and progression of periodontal diseases. The bio- film may contain large number of bacterial species but current data suggest that only a small number of Gram-negative, anaerobic or capnophilic bacterial species are implicated in the pathogenesis of periodontal diseases.Since the late 1990s, Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola ("the red-complex"), have been recognized as important periodontal pathogens. Other pathogens include Fuso-bacterium nucleatum, Prevotella intermedia, Cambylobacter rectus and Eubacterium nodatum ***(Haffajee & Socransky, 1994).***

Studies carried out by ***slot in 2010*** have identified other microorganisms that may play a role in the pathogenesis of periodontitis such as Herpes simplex virus (HSV), Epstein-Barr virus (EBV) and Cytomegalovirus ***(Slots, 2010).***

Bacteria may give rise to periodontal destruction processes both directly and indirectly by activation of the host immunologycal and inflammatory reactions ***(Genco et al., 1974; Page et al., 1981).***

It is now known that the immune and inflammatory responses are critical to the occurance of periodontitis and are modified by a number of host-related factors, both intrinsic (e.g., genetics) and induced (e.g., pollutants) ***(Page et al., 1979; Taubman et al., 2007).***

Page et al suggested that the interaction between the pathogenic bacteria and a host's defense systems could lead to the development of a periodontal pocket, loss of connective tissue, and bone resorption ***(Page et al., 1982).***

It is not surprising that the root surface itself has also been shown to harbor numerous bacteria that may provide a source for subgingival bacterial repopulation ***(Adriaense et al., 1988; Giuliana et al., 1997).*** Pathogens such as Prevotellaintermedia, Porphyromonas gingivalis, Fusobacterium nucleatum, Bacteroides forsythus, Pepto streptococcus micros and Streptococcus intermedius were found in up to 53.8% of periodontally diseases roots. The root is a bacterial reservoir from which periodontal pathogenic bacteria can recolonize previously treated pockets and contribute to the failure of therapy or the recurrence of disease.(***Giuliana et al., 1997).***

Recently, periodontitis has been classified by ***caton et al*** based on a multi-dimenstional staging and grading system where staging depends on initial severity of periodontal disease on peresentation and complexity in its management while grading depends on the rate of progression of the periodontal disease as well as the response to the anticipated treatment. Staging includes four categories based on the amount of clinical attachment level, probing depth, amount of bone loss, present of vertical infra-bony defects, presence of furcation involvement, tooth mobility and tooth loss due to periodontitis. Grading involves three grades based on the rate of progression of the disease, general health status and other exposure factors such as smoking ***(Caton et al., 2018).***

periodontitis is associated with bone resorption. ***Goldman and Cohen in 1958*** classified bony defects as suprabony, when the base of the pocket was present coronal to the alveolar crest and intrabony when the base of the pocket was present below the alveolar crest. Intrabony defects are of two types; infrabony defects and craters. Infrabony defect are bony defects whose infrabony component affects primarily one tooth, while in craters the defect affects two adjacent root surfaces to similar extent. Intrabony defects have been classified according to the morphology in terms of residual bony walls, width of the defect, and in terms of their topographic extension around the tooth. According to the number of remaining osseous walls, the intrabony defects have

been classified into one wall, two wall or three osseous wall defects ***(Goldman & Cohen, 1958).***

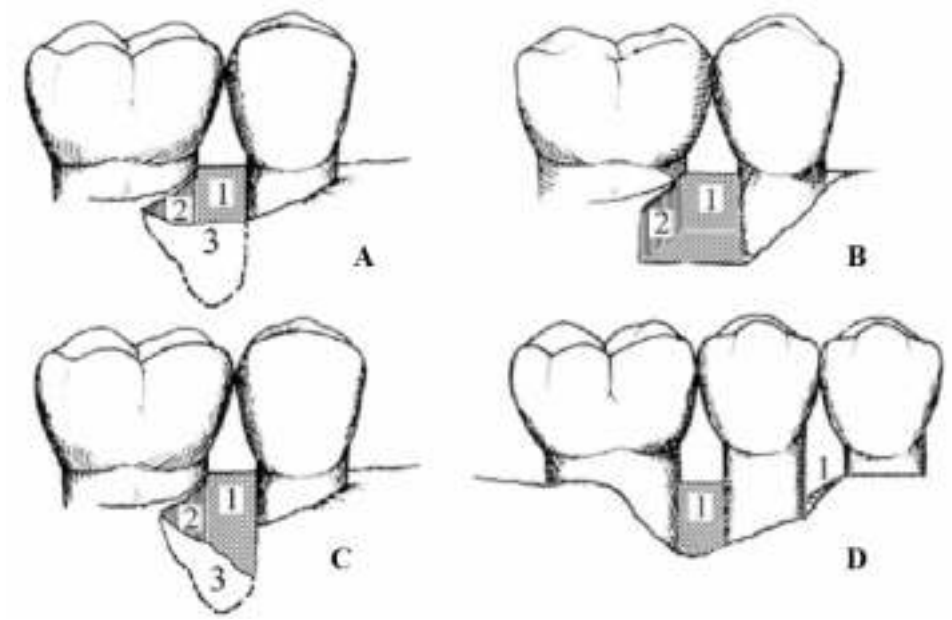

Fig. (1): Classification scheme for intrabony defects. ***(Reynolds et al., 2010).*** A: 3 wall defect,B:2 wall defect, C:2 and half wall defect, D:1 wall defect

The disease progression model points to a periodic phenomenon, with periods of quiescence, when no periodontal destruction occurs and periods of exacerbation when destruction of the periodontal structures occurs. Periodontal destruction characterized histologically by acute inflammation, with a significant increase in the number of neutrophils ***(Goodson et al., 1982; Lindhe et al., 1983).***

Periodontitis clinical signs include changes in the morphology of gingival tissues, gingival bleeding as well as true periodontal pocket formation. This condition provides a

good environment for the growth and proliferation of anaerobic pathogenic bacteria ***(Sunil et al., 2004).***

Graves & Cochran in 2003 suggested that bone loss that occur in response to bacterial inflammatory reaction depends on two factors. First, the concentration of inflammatory mediators present in the gingival tissue that must be sufficient to activate pathways leading to bone loss. Second, the inflammatory mediators that must penetrate the gingival tissues and reach within a critical distance to the alveolar bone (***Graves & Cochran, 2003).***

Proinflammatory cytokines, such as interleukin1 (IL-1), IL-6, IL-11, and IL -17, tumor necrosis factor-alpha (TNF-α). The kinins, such as bradykinin and various chemokines also have a stimulatory effect on bone resorption. This is the opposite of the expression of anti-inflammatory cytokines and other mediators, such as interleukin 4 (IL-4) ,IL-10,IL -12, IL-13, and IL-18, as well as interferon-beta (IFN-b) and interferon -gamma (IFN-γ), which serve to inhibit bone resorption ***(Lerner, 2006).***

Bone resorption and formation are regulated by the total amount of the receptor activator of nuclear factor kappa B-ligand (RANKL) expressed by various cells, as well as the RANKL receptor RANK on osteoclast precursor cells and the soluble decoy receptor osteoprotegerin (OPG). When RANKL expression is enhanced relative to OPG, RANKL is available to

bind RANK on osteoclast precursors, tipping the balance to favor activation of osteoclast formation and bone resorption. When OPG concentrations are high relative to RANKL expression, OPG binds RANKL, inhibiting it from binding to RANK which leads to reduced formation of osteoclasts and apoptosis of preexisting osteoclasts ***(Boyle et al., 2003).***

Radiographic evaluation:

Radiographs provide information about the quality localization of the bone defect and the pattern of the bone resorption, changes in the bony trabeculae, condition of the lamina dura, length and shape of the root and the crown root ratio. Some etiological factors like calculus and faulty restoration can also be seen in radiographs ***(White & Pharoah, 2014).***

Radiograph should be precise in order to assess the bony defect. Two Dimensional radiographs can be insufficient for the detection of intrabony alveolar defects due to the obstruction of spongious bone changes by cortical plate ***(Clinical Applications of Cone-Beam Computed Tomography in Dental Practice, 2006).***

In their 2005 study, ***Mengel*** and coworkers investigated the use of cone beam compeuted tomograhy (CBCT) in the diagnosis of periodontal defects .It was demonstrated that all intrabony defects could be measured in three planes in the

CBCT scans with great accuracy true to scale ***(Mengel et al., 2005).***

Similar results were found by ***Noujeim*** and coworkers when using the CBCT system to detect simulated interradicular lesions of varying depth in comparison with intraoral radiography ***(Noujeim et al., 2007).***

Grimard et al in 2009 had found that proximal osseous defects and furcation defects on the facial and lingual surfaces of multi-rooted teeth could be identified with a high degree of accuracy by their radiographic appearances using CBCT ***(Grimard et al., 2009).***

Treatment of periodontitis:

In 2000 ***pihlstrom*** realized that appropriate therapy for patients with periodontitis varies considerably with the extent and pattern of attachment loss, local anatomical variations, type of periodontal disease, and therapeutic objectives ***(Pihlstrom, 2000).***

The periodontal treatment aims to stop gingival inflammation, eliminate bleeding, reduce periodontal pocket depth, arrest destruction of soft tissue and bone ***(Sathwara & Sathwara, 2014).***

In his study in 1996 and 1999 ***Cobb*** illustrated that mechanical therapy is usually the first mode of treatment

recommended for most periodontal infections. The term mechanical therapy refers to both supragingival and subgingival scaling as well as root planning. Mechanical therapy consists of debridement of the roots by the meticulous use of hand or power-driven scalers to remove plaque, endotoxin, calculus and other plaque-retentive local factors ***(Cobb, 1996, 1999).***

The American Academy of Periodontology World Workshop consensus report states that ultrasonic and sonic instrumentation have shown similar clinical effects as manual scaling and root planning ***(Loos et al., 1987; Laurell, 1990).***

In 2001 Drisko suggested that in most periodontitis cases, simply performing a thorough periodontal debridement under local anesthesia will stop disease progression and result in improvement in the clinical signs and symptoms of active disease ***(Drisko, 2001).***

Not all patients respond well to therapy nor are they able to maintain a stable periodontium over extended periods of time following successful periodontal therapy. There are many factors that influence therapeutic outcomes usually include poor compliance with oral hygiene regimens and failure to return for regular maintenance care ***(Wilson, 1996).***

Other risk factors influencing nonsurgical treatment outcomes include the presence of persistent deep pockets and

molars with furcation involvement, periodontal surgical therapy constitutes a key aspect of the treatment of patients having such periodontal diseases ***(Wennstorm et al., 2008)***. It is mainly performed to gain access to roots and alveolar bone, to enhance visibility, increase scalling and root planning effectiveness, eliminate or reduce periodontal pockets and restore the periodontal tissues lost through the disease ***(Reddy, 2008).***

In 1996, Kaldahl et al., have shown that surgical treatment of pockets ≥5 mm by flap and osseous surgery results in greater pocket reduction than nonsurgical scaling and root planing. Surgical debridement in general has been shown to provide better access to plaque and calculus removal in deep pockets and furcations than a closed scaling and root planing approach ***(Kaldahl et al., 1996).***

Antimicrobial therapy:

Comprehensive mechanical debridement of sites with deep periodontal pockets is difficult to occur. It alone may fail to eliminate the pathogenic microflora because of their location within the gingival and dental tissues or in other areas inaccessible to periodontal instruments. As an adjunctive approach, systemic or local administration of antimicrobial therapy is done because of the microbial etiology of periodontitis ***(Cobb, 1996).***

Systemic administration of antimicrobial drugs have been used as adjuncts to surgical and nonsurgical mechanical therapies in the treatment of a range of periodontal diseases ***(Greenstein, 2006).***

Almost all available antibiotics have been tested for use in the treatment of periodontitis, such as amoxicillin, azithromycin, clindamycin, doxycycline, metronidazole, tetracycline and a combination of metronidazole and amoxicillin ***(Feres et al., 2001; Sigusch et al., 2001; Ramberg et a., 2001; Rooney et al., 2002; Carvalhoet al., 2004; Carvalho et al., 2005; Xajigeorgiou et al., 2006; Haas et al., 2008; Haas et al., 2012; Aimetti el al., 2012).***

There are many disadvantages of systemic antibiotics which include adverse drug reactions, uncertain patient compliance and lower concentration of the drug at gingival crevicular fluid ***(Slots & Rams, 1990; Goodson, 2000; Guerrero et al., 2007; Kim et al., 2010).***

Local administration of antibacterial agents in the form of mouth washes, dentifrice or gels is an effective measure in controlling supragingival plaque. Delivery of antimicrobials using local delivery and controlled release systems at the target site produces more constant and prolonged concentration profiles ***(Divya & Nandakumar, 2006).*** These devices utilizes the control release technologies to deliver sustained therapeutic concentrations for at least three or more number of days

following a single application ***(Saarangi et al., 2013).*** The drug will be released over time either by degradation of a polymer backbone or diffusion through polymer matrix or by a combination of the any two mechanisms ***(Kaur et al., 2015).***

Local application into periodontal pocket could be useful, both in terms of raising drug concentration directly in the gingival crevicular fluid, and avoiding any systemic side effects ***(Schwach-Abdellaoui et al., 2000).***

On their research ***Kim et al. (2002)*** noted that the FDA has approved the use of a gelatin chip that contains chlorhexidine, an ethylene vinyl acetate fiber that contains tetracycline, and a minocycline polymer formulation as adjuncts to scaling and root planning. The FDA has also approved doxycycline in a bio-absorbable polymer gel as a stand-alone therapy for the reduction of probing depths and gain of clinical attachment ***(Kim et al., 2002).***

For more than 45 years chlorhexidine (CHX) have been successfully used in periodontal therapy due to a high potency, lowest side effects and no bacterial resistance formation .Slow releasing devices for a long-term therapy have been developed and clinically established with different effects ***(Schiott et al., 1970; Eickholz, 2006; Da Rocha et al., 2015; Greenstein & Tonetti, 2000).***

Local antibiotics that are commercially available as controlled release devices suffer from several potential problems, including insufficient spectrum of antimicrobial activity in some periodontal polymicrobial infections, risks of producing an antibiotic resistant microbiota, and high acquisition costs***(Slots, 2002).***

Herbal drugs and periodontal therapy:

Herbal and natural products of folk medicine have been used for centuries in every culture throughout the world. "Let food be your medicine and let medicine be your food" was advised by Hippocrates, over two millennia ago. It's still true today that "you are what you eat. Natural phytochemicals isolated from plants used in traditional medicine are considered nowadays as good alternatives to synthetic chemicals." (***Zhu & Woerdenbag, 1995; Park et al., 2003; Chung et al., 2006; Prabhu et al., 2006).***

The development of traditional medicinal systems incorporating plants as means of therapy can be traced back to the Middle Paleolithic age some 60,000 years ago as found from fossil studies. In recent times, developed countries are turning to the use of traditional medicinal systems that involve the use of herbal drugs. It has been noted that 25% of all drugs prescribed today come from plants ***(Solecki & Shanidar, 1975; Farnsworth & Morris, 1997; Raskin & Ripoll, 2004).***

In a review on traditional medicinal plant extracts and natural products for prevention and treatment of oral diseases, ***Palombo (2011)*** noted that there exists a need for alternative prevention and treatment options for oral diseases that are safe, effective and economical in the wake of high incidence of oral disease, increased resistance by bacteria to antibiotics, adverse effects of some antibacterial agents currently used in dentistry and financial considerations in developing countries. Herbal dentifrices are available and have been evaluated in clinical trials for controlling plaque and gingivitis in both developed and developing countries ***(Mandel, 1998; Goldstein & Epstein, 2000; Davies et al., 2010; Palombo, 2011; Surathu and Kurumathur, 2011; Oke et al., 2011; Maldupa et al., 2012).***

Plants and natural products from time immemorial has been used for their pharmacological applications as antiulcerative, wound healing, anti-inflammatory, antimicrobial and antioxidant properties. Ocimum sanctum has been used for its antiulcerative property, Alo vera, basil and black pepper have been used for their antibacterial properties and anti-inflamatory property. Many plants have tried for their anti-oxidant property like green tea and broccoli. Capsicum has been used also for its analgesic properties ***(Cowan, 1999; Colvard et al., 2006; Dharmani & Palit, 2006; Petti et al., 2009).***

Many plants and natural products have been tested in periodontal treatment. Aloe vera have the strong anti-bacterial,

anti-viral and anti-neoplastic properties. Aloe vera gel was applied as an adjunct to scaling and root planning in periodontitis significantly better results was obtained ***(Virdi et aL., 2012; Dheepika & Maheswari, 2014).***

Tulsi has also proven to be very effective in counteracting halitosis. It is suitable for gingivitis and periodontitis due to its anti-inflammatory property (***Sen, 1993).***

Moreover, Green tea inhibit the growth of Prophrymonas gingivalis (P.G), Prevotella intermedia. Green tea also inhibits the activity of P. gingivalis-derived collagenase ***(Sakanaka et al., 1996; Sakanaka & Okada, 2004).***

Eucalyptus, neem leaf and bloodroot also possess antibacterial and anti- inflammatory properties and can help in improving oral health status. Other individual herbs, herbal combinations such as mixture of menthol, chamomile, peppermint oil, sage oil, clove oil, caraway oil, echinacea extract and myrrh tincture exhibit properties to reduce severity of periodontitis symptoms and can improve the oral hygiene ***(Pai et al., 2004; Nagata et al., 2008; Mundinamane et al., 2011).***

Turmeric:

The turmeric (Curcuma longa) plant, a herb belonging to the ginger family, is cultivated extensively in south and south east tropical Asia. The rhizome of this plant is also referred to

as the root and is the most useful part of the plant for medicinal purposes. The most active component of turmeric is curcumin, which makes up 2 to 5% of the spice. Curcumin is an orange–yellow crystalline powder practically insoluble in water ***(Aggarwal et al., 2006).***

Curcumin was first isolated in 1815 and its chemical structure was determined by Roughley and Whiting in 1973. It has a melting point at 176–177°C,forms a reddish-brown salt with alkali and is soluble in ethanol, alkali, ketone, acetic acid and chloroform. Turmeric contains protein (6.3%), fat (5.1%), minerals (3.5%), carbohydrates (69.4%) and moisture (13.1%). The essential oil (5.8%) obtained by steam distillation of rhizomes has a-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpines (53%) ***(Chattopadhyay et al., 2004).***

Although extraction and separation of curcumin from turmeric powder was reported way back in 1815, more improved and advanced extraction methods are still being reported.Solvent extraction followed by column chromatography has been the most commonly employed method reported for separating curcumin from turmeric, and several polar and non-polar organic solvents have been used, including hexane, ethylacetate, acetone, methanol ***(Marczylo et al., 2009; Kim et al., 2013; Paulucci et al., 2013).***