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Dental Inserts

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Dental Inserts

Insert means the dosage form to place or introduce into the body. The insert mainly used for dental cavity are called as dental insert.

The mouth is a naturally dirty field, besides its high content of microflora, its high moisture content (96%) and appropriate temperature (37 ºC) increases the incidence of bacteria. (Dolan, Matulka, & Burdock, 2010). Development of bacteria is a concern for dentist as it is associated with failure of dental procedures especially dental implants. Anaerobic gram positive cocci, and anaerobic gram negative rods are amongst the most common strains involved in dental surgery infections. The use of prophylactic antibiotics to combat these strains becomes a general practice in dental implants and procedures. High dose of systemic antibiotics are used to achieve adequate concentrations in the blood to prevent the growth and dissemination of bacteria at the site of implant surgery. The adverse effects associated with the use of systemic antibiotics makes it unappealing, hence the local application of an antibiotic medicated implant will be advantageous. Main advantages of dental inserts are localized action, reduced frequency of administration, reduced side effects and sustained action. Some of the disadvantages of dental inserts are it requires technical person for the administration and drug loss through saliva.

Basic information of Teeth

Humans usually have 20 primary (deciduous, "baby" or "milk") teeth and 32 permanent (adult) teeth. Teeth are among the most distinctive (and long-lasting) features of mammal species. The human teeth function to mechanically break down items of food by cutting and crushing them for swallowing and digesting. The adult human teeth show a morphology mainly differentiated by the shape of their upper surface (crown) and the number of the teeth roots. Individual tooth morphology is associated with the purpose of each tooth type (cutting, shredding or grinding the food)

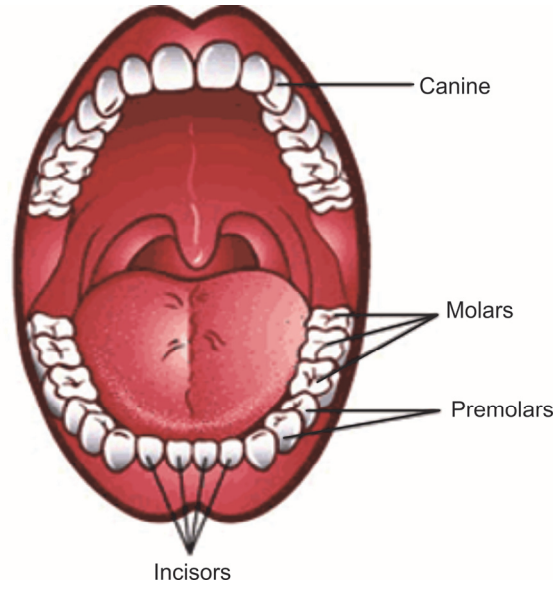

Fig. 1.1 Types of teeth.

(a) Incisors: The 8 incisors are the very front human teeth with flat surfaces, a straight sharp horizontal edge for cutting and biting the food and one long, single, conical root.

(b) Canines: The 4 canine teeth are very strong, pointed corner teeth for tearing and shredding, placed laterally to each lateral incisor. They are larger and stronger than the incisors. The canine tooth morphology is characterized by the large, conical crown which projects beyond the level of the other teeth and one single root, longer than all other teeth types. The upper canine teeth are sometimes called eye teeth.

(c) Premolars: The 8 premolars, used for the chewing food and are placed lateral to and behind the canine teeth, with a flat upper surface and 1-2 roots. Their crown has two pyramidal eminences or cups.

(d) Molars: The 12 molars are the teeth placed at the back. Molar teeth have different tooth morphology with large and flat upper surface and 2-4 roots. Molar is one of types of teeth with largest permanent teeth, used for the final chewing and grinding of the food before swallowing. ('mola' is the latin word for mill).

The roots of teeth are embedded in the maxilla (upper jaw) or the mandible (lower jaw) and are covered by gums. Teeth are made of multiple tissues of varying density and hardness.

Anatomy

Dental anatomy is a field of anatomy dedicated to the study of tooth structure. The development, appearance and classification of teeth fall within its field of study, though dental occlusion. Dental anatomy is also a taxonomic science as it is concerned with the naming of teeth and their structures. This information serves a practical purpose for dentists, enabling them to easily identify teeth and structures during treatment.

The anatomic crown of a tooth is the area covered in enamel above the cemento enamel junction (CEJ) or "neck" of the tooth. Most of the crown is composed of dentin (dentine in British English) with the pulp chamber inside. The crown is within bone before eruption. After eruption, it is almost always visible. The anatomic root is found below the CEJ and is covered with cementum. As with the crown, dentin composes most of the root, which normally has pulp canals. A tooth may have multiple roots or just one root (single-rooted teeth). Canines and most premolars, except for maxillary first premolars, usually have one root. Maxillary first premolars and mandibular molars usually have two roots. Maxillary molars usually have three roots. Additional roots are referred to as super numerary roots.

Tooth Development

Tooth development is the complex process by which teeth form from embryonic cells, grow and erupt into the mouth. Although many diverse species have teeth, their development is largely the same as in humans. In human teeth, to have a healthy oral environment, enamel, dentin, cementum, and periodontium all must develop during appropriate stages of fetal development. Primary teeth start to form in the development of

the embryo between the sixth and eighth weeks and permanent teeth begin to form in the twentieth week. Tooth development is commonly divided into the following stages: bud stage, cap, bell, and finally maturation.

The tooth bud (sometimes called the tooth germ) is an aggregation of cells that eventually forms a tooth. It is organized into three parts: the enamel organ, the dental papilla and the dental follicle. The enamel organ is composed of the outer enamel epithelium, inner enamel epithelium, stellate reticulum and stratum intermedium. These cells give rise to ameloblasts, which produce enamel and the reduced enamel epithelium. The growth of cervical loop cells into the deeper tissues forms Hertwig's Epithelial Root Sheath, which determines a tooth's root shape.

The dental papilla contains cells that develop into odontoblasts, which are dentin-forming cells. Additionally, the junction between the dental papilla and inner enamel epithelium determines the crown shape of a tooth. The dental follicle gives rise to three important cells: cementoblasts, osteoblasts, and fibroblasts. Cementoblasts form the cementum of a tooth. Osteoblasts give rise to the alveolar bone around the roots of teeth. Fibroblasts develop the periodontal ligaments which connect teeth to the alveolar bone through cementum.

Eruption

Tooth eruption in humans is a process in tooth development in which the teeth enter the mouth and become visible. Current research indicates that the periodontal ligaments play an important role in tooth eruption. Primary teeth erupt into the mouth from around six months until two years of age. These teeth are the only ones in the mouth until a person is about six years old. At that time, the first permanent tooth erupts. This stage, during which a person has a combination of primary and permanent teeth, is known as the mixed stage. The mixed stage lasts until the last primary tooth is lost and the remaining permanent teeth erupt into the mouth.

There have been many theories about the cause of tooth eruption. One of the theories proposes that the developing root of a tooth pushes it into the mouth. Another, known as the cushioned hammock theory, resulted from microscopic study of teeth, thought to show a ligament around the root. It was later discovered that the "ligament" was merely an artifact created in the process of preparing the slide. Currently, the

most widely held belief is that the periodontal ligaments provide the main impetus for the process.

The onset of primary tooth loss has been found to correlate strongly with somatic and psychological criteria of school readiness.

The periodontium is the supporting structure of a tooth, helping to attach the tooth to surrounding tissues and to allow sensations of touch and pressure. It consists of the cementum, periodontal ligaments, alveolar bone, and gingiva. Of these, cementum is the only one that is a part of a tooth. Periodontal ligaments connect the alveolar bone to the cementum. Alveolar bone surrounds the roots of teeth to provide support and creates what is commonly called an alveolus, or "socket". Lying over the bone is the gingiva or gum, which is readily visible in the mouth.

Periodontal Ligaments

The periodontal ligament is a specialized connective tissue that attaches the cementum of a tooth to the alveolar bone. This tissue covers the root of the tooth within the bone. Each ligament has a width of 0.15–0.38mm, but this size decreases over time. The functions of the periodontal ligaments include attachment of the tooth to the bone, supports the tooth, formation and resorption of bone during tooth movement, sensation, and eruption. The cells of the periodontal ligaments include osteoblasts, osteoclasts, fibroblasts, macrophages, cementoblasts, and epithelial cell rests of Malassez. (Xiong, Gronthos, & Bartold, 2013). Consisting of mostly Type I and III collagen, the fibres are grouped in bundles and named according to their location. The groups of fibres are named alveolar crest, horizontal, oblique, periapical, and interradicular fibres. The nerve supply generally enters from the bone apical to the tooth and forms a network around the tooth toward the crest of the gingiva. When pressure is exerted on a tooth, such as during chewing or biting, the tooth moves slightly in its socket and puts tension on the periodontal ligaments. The nerve fibres can then send the information to the central nervous system for interpretation.

Alveolar Bone

The alveolar bone is the bone of the jaw which forms the alveolus around teeth. Like any other bone in the human body, alveolar bone is modified throughout life. Osteoblasts create bone and osteoclasts destroy it, especially if force is placed on a tooth. As is the case when movement of teeth is attempted through orthodontics, an area of bone under compressive force from a tooth moving toward it has a high osteoclast

level, resulting in bone resorption. An area of bone receiving tension from periodontal ligaments attached to a tooth moving away from it has a high number of osteoblasts, resulting in bone formation.

Gingiva

The gingiva ("gums") is the mucosal tissue that overlays the jaws. There are three different types of epithelium associated with the gingiva: gingival, junctional, and sulcular epithelium. These three types form from a mass of epithelial cells known as the epithelial cuff between the tooth and the mouth. The gingival epithelium is not associated directly with tooth attachment and is visible in the mouth. The junctional epithelium, composed of the basal lamina and hemidesmosomes, forms an attachment to the tooth. The sulcular epithelium is non-keratinized stratified squamous tissue on the gingiva which touches but is not attached to the tooth.

Common Problems of Teeth

Plaque

Plaque is a biofilm consisting of large quantities of various bacteria that form on teeth. If not removed regularly, plaque buildup can lead to periodontal problems such as gingivitis. Given time, plaque can mineralize along the gingiva, forming tartar. The microorganisms that form the biofilm are almost entirely bacteria (mainly streptococcus and anaerobes), with the composition varying by location in the mouth. *Streptococcus mutans* is the most important bacterium associated with dental caries.(Krzyściak, Jurczak, Kościelniak, Bystrowska, & Skalniak, 2014)

Certain bacteria in the mouth live off the remains of foods, especially sugars and starches. In the absence of oxygen they produce lactic acid, which dissolves the calcium and phosphorus in the enamel. This process, known as "demineralisation", leads to tooth destruction. Saliva gradually neutralises the acids which cause the pH of the tooth surface to rise above the critical pH, typically considered to be 5.5. This causes 'remineralisation', the return of the dissolved minerals to the enamel. If there is sufficient time between the intakes of foods then the impact is limited and the teeth can repair themselves. Saliva is unable to penetrate through plaque, however, to neutralize the acid produced by the bacteria.

Caries (cavities)

Dental caries (cavities), described as "tooth decay", is an infectious disease which damages the structures of teeth. The disease can lead to pain, tooth loss, and infection. The largest increases in the prevalence of caries have been associated with diet changes. Today, caries remains one of the most common diseases throughout the world. Tooth decay is caused by certain types of acid-producing bacteria which cause the most damage in the presence of fermentable carbohydrates such as sucrose, fructose, and glucose.(Forssten, Björklund, & Ouwehand, 2010) The resulting acidic levels in the mouth affect teeth because a tooth's special mineral content causes it to be sensitive to low pH.

Common Diseases of Teeth

Dental Fear

Dental fear is the fear of dentistry and of receiving dental care. However, it has been suggested that use of the term dental phobia should not be used for people who do not feel that their fears are excessive or unreasonable, and instead resemble individuals with posttraumatic stress disorder caused by previous traumatic dental experiences.

Dental Plaque

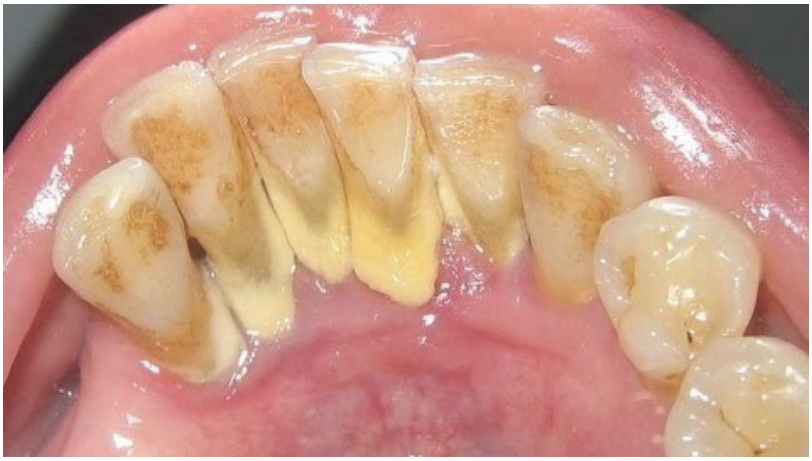

Fig. 1.2 Plaque infected teeth.

Dental plaque is a biofilm or mass of bacteria that grows on surfaces within the mouth. It is a sticky colourless deposit at first, but when it forms tartar, it is often brown or pale yellow. It is commonly found between the teeth, on the front of teeth, behind teeth, on chewing surfaces, along the gumline, or below the gumline cervical margins. Dental plaque is also known as microbial plaque, oral biofilm, dental biofilm, dental plaque biofilm or bacterial plaque biofilm.

Progression and build-up of dental plaque can give rise to tooth decay – the localized destruction of the tissues of the tooth by acid produced from the bacterial degradation of fermentable sugar – and periodontal problems such as gingivitis and periodontitis. Plaque control and removal can be achieved with correct daily or twice-daily tooth brushing and use of interdental aids such as dental floss and interdental brushes. (Tarannum, Faizuddin, Swamy, & Hemalata, 2012)

Dental biofilms may become acidic causing demineralization of the teeth (also known as dental caries) or harden into dental calculus (also known as tartar).

Table 1.1 Steps involved in Formation of Dental plaque.

Steps in plaque Formation	Description
Association	Dental pellicle forms on the tooth, and provides bacteria surface to attach
Adhesion	Within hours, bacteria loosely binds to the pellicle
Proliferation	Bacteria spreads throughout the mouth and begins to multiply
Micro colonies	Micro colonies are formed. Streptococci secrete protective layer
Biofilm Formation	Micro colonies form complex groups with metabolic advantages
Growth	The plaque develops a primitive circulatory system

Components of Plaque

Different types of bacteria are normally present in the mouth. These bacteria, as well as leukocytes, neutrophils, macrophages, and lymphocytes, are part of the normal oral cavity and contribute to the individual's health. Approximately 80–90% of the weight of plaque is water. (Verkaik et al., 2011)While 70% of the dry weight is bacteria, the remaining 30% consists of polysaccharides and glycoproteins.

Dental Calculus

Calculus or tartar is a form of hardened dental plaque. It is caused by precipitation of minerals from saliva and gingival crevicular fluid in plaque on the teeth. This process of precipitation kills the bacterial cells within dental plaque, but the rough and hardened surface that is formed provides an ideal surface for further plaque formation. This leads to calculus buildup, which compromises the health of the gingiva. Calculus can form both along the gumline, where it is referred to as supragingival, and within the narrow sulcus that exists between the teeth and the gingiva, where it is referred to as subgingival.

Calculus formation is associated with a number of clinical manifestations, including bad breath, receding gums and chroni-cally inflamed gingiva. Brushing and flossing can remove plaque from which calculus forms; however, once formed, it is too hard. Calculus build up can be removed with ultrasonic tools or dental hand instruments (such as a periodontal scaler).

Composition of Plaque

Calculus is composed of both inorganic (mineral) and organic (cellular and extracellular matrix) components. The mineral proportion of calculus ranges from approximately 40–60%, and consists primarily of "calcium phosphate" crystals.(Jin & Yip, 2002)

The organic component of calculus is approximately 85% cellular and 15% extracellular matrix. Cell density within dental plaque and calculus is very high, consisting of an estimated 200,000,000 cells per milligram. The cells within calculus are primarily bacterial, but also include at least one species of archaea and several species of yeast. The organic extracellular matrix in calculus consists primarily of proteins and lipids (fatty acids, triglycerides, glycolipids, and phospholipids), as well as extracellular DNA. Trace amounts of host, dietary, and environmental micro debris are also found within calculus, including salivary proteins, plant DNA, milk proteins, starch granules, textile fibres, and smoke particles.

Calculus Formation

The processes of calculus formation from dental plaque are not well understood. Supragingival calculus formation is most abundant on the buccal (cheek) surfaces of the maxillary molars and on the lingual surfaces of the mandibular incisors. These areas experience high salivary flow because of their proximity to the parotid and sublingual salivary

glands. Subgingival calculus forms below the gumline and is typically darkened in colour by the presence of black-pigmented bacteria, whose cells are coated in a layer of iron obtained from heme during gingival bleeding. Dental calculus typically forms in incremental layers that are easily visible using both electron microscopy and light microscopy. These layers form during periodic calcification events of the dental plaque, but the timing and triggers of these events are poorly understood. The formation of calculus varies widely among individuals and at different locations within the mouth. Many variables have been identified that influence the formation of dental calculus, including age, gender, ethnic background, diet, location in the oral cavity, oral hygiene, bacterial plaque composition, host genetics, access to professional dental care, physical disabilities, systemic diseases, tobacco use, and drugs and medications.

Tooth Decay

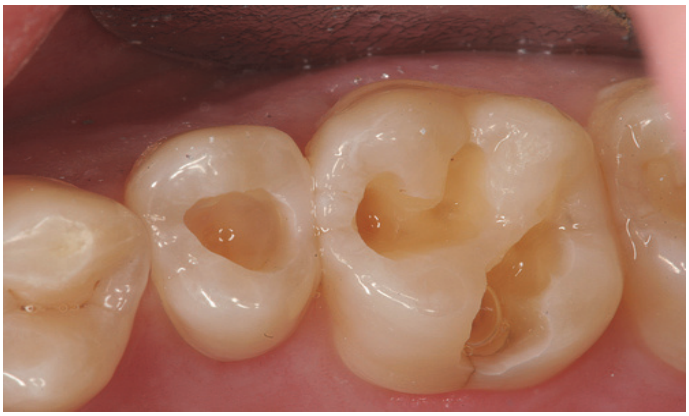

Fig. 1.3 Tooth decay.

Tooth decay is a breakdown of teeth due to acids made by bacteria. It can lead to a hole in the tooth, called a cavity. If not treated, tooth decay can cause pain, infection, and tooth loss. The cause of caries is acid from bacteria dissolving the hard tissues of the teeth (enamel, dentin and cementum). The acid is produced from food debris or sugar on the tooth surface. Simple sugars in food are these bacteria's primary energy source and thus a diet high in simple sugar is a risk factor. If mineral breakdown is greater than build up from sources such as saliva, caries results. Caries is also associated with poverty, poor cleaning of the mouth, and receding gums resulting in exposure of the roots of the teeth.

Prevention of dental caries includes regular cleaning of the teeth, a diet low in sugar, and small amounts of fluoride.

Signs & Symptoms

The appearance of a chalky white spot on the surface of the tooth, indicating an area of demineralization of enamel. This is referred to as a white spot lesion, an incipient carious lesion or a "microcavity". As the lesion continues to demineralize, it can turn brown but will eventually turn into a cavitation. Before the cavity forms, the process is reversible, but once a cavity forms, the lost tooth structure cannot be regenerated. A lesion that appears dark brown and shiny suggests dental caries were once present but the demineralization process has stopped, leaving a stain. Active decay is lighter in color and dull in appearance.

Once the decay passes through enamel, the dentinal tubules, which have passages to the nerve of the tooth, become exposed, resulting in pain that can be transient, temporarily worsening with exposure to heat, cold, or sweet foods and drinks. A tooth weakened by extensive internal decay can sometimes suddenly fracture under normal chewing forces. When the decay has progressed enough to allow the bacteria to overwhelm the pulp tissue in the centre of the tooth, a toothache can result and the pain will become more constant. Death of the pulp tissue and infection are common consequences. The tooth will no longer be sensitive to hot or cold, but can be very tender to pressure.

Dental caries can also cause bad breath and foul tastes. In highly progressed cases, an infection can spread from the tooth to the surrounding soft tissues. Complications such as cavernous sinus thrombosis and Ludwig angina can be life-threatening.

Causes

Four things are required for caries formation: a tooth surface, caries-causing bacteria, fermentable carbohydrates (such as sucrose), and time. This involves adherence of food to the teeth and acid creation by the bacteria that makes up the dental plaque. However, these four criteria are not always enough to cause the disease and a sheltered environment promoting development of a cariogenic biofilm is required. The caries disease process does not have an inevitable outcome, and different individuals will be susceptible to different degrees depending on the shape of their teeth, oral hygiene habits, and the buffering capacity of their saliva. Dental caries can occur on any surface of a tooth that is

exposed to the oral cavity, but not the structures that are retained within the bone.

Prevention

Dietary modification

Oral Hygiene

Gingivitis

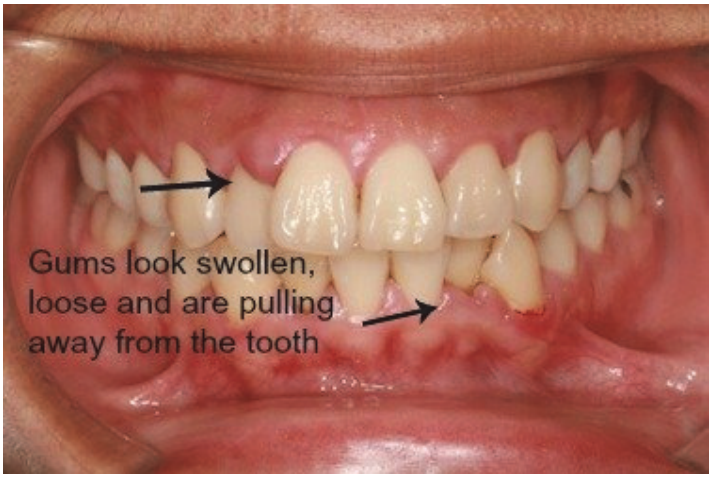

Fig. 1.4 Teeth infected with gingivitis.

Gingivitis ("inflammation of the gum tissue") is a non-destructive disease that occurs around the teeth. Gingivitis is reversible with good oral hygiene; however, without treatment, gingivitis can progress to periodontitis, in which the inflammation of the gums results in tissue destruction and bone resorption around the teeth.

Signs & Symptoms

The symptoms of gingivitis are somewhat non-specific and manifest in the gum tissue as the classic signs of inflammation:

- Swollen gums
- Bright red or purple gums
- Gums that are tender or painful to the touch
- Bleeding gums or bleeding after brushing and/or flossing
- Bad breath

The stippling that normally exists in the gum tissue of some individuals will often disappear and the gums may appear shiny when the gum tissue becomes swollen and stretched over the inflamed underlying connective tissue. The accumulation may also emit an unpleasant odour. When the gingiva are swollen, the epithelial lining of the gingival crevice becomes ulcerated and the gums will bleed more easily even with gentle brushing, and especially when flossing.

Causes

The cause of plaque-induced gingivitis is bacterial plaque, which acts to initiate the body's host response. This in turn, can lead to destruction of the gingival tissues, which may progress to destruction of the periodontal attachment apparatus. The plaque accumulates in the small gaps between teeth, in the gingival grooves and in areas known as plaque traps: locations that serve to accumulate and maintain plaque. Examples of plaque traps include bulky and overhanging restorative margins, claps of removable partial dentures and calculus (tartar) that forms on teeth. Although these accumulations may be tiny, the bacteria in them produce chemicals, such as degradative enzymes, and toxins, such as lipopoly-saccharide or lipoteichoic acid (LTA), that promote an inflammatory response in the gum tissue. This inflammation can cause an enlargement of the gingiva and subsequent formation. Early plaque in health consists of a relatively simple bacterial community dominated by Gram-positive cocci and rods.(Palmer & Jr, 2014) As plaque matures and gingivitis develops, the communities become increasingly complex with higher proportions of Gram-negative rods, fusiforms, filaments, spirilla and spirochetes. Later experimental gingivitis studies, using culture, provided more information regarding the specific bacterial species present in plaque.

Risk Factors

Risk factors associated with gingivitis include the following:

- Age
- Osteoporosis
- Low dental care utilization (fear, financial stresses, etc.)
- Poor oral hygiene
- Overly aggressive oral hygiene such as brushing with stiff bristles
- Mouth-breathing during sleep
- Medications that dry the mouth

- Cigarette smoking
- Genetic factors
- Pre-existing conditions

Classification

There are two primary categories of gingival diseases, each with numerous subgroups.

I. Dental plaque-induced gingival diseases.
    1. Gingivitis associated with plaque only
    2. Gingival diseases modified by systemic factors
    3. Gingival diseases modified by medications
    4. Gingival diseases modified by malnutrition

II. Non-plaque-induced gingival lesions
    1. Gingival diseases of specific bacterial origin
    2. Gingival diseases of viral origin
    3. Gingival diseases of fungal origin
    4. Gingival diseases of genetic origin
    5. Gingival manifestations of systemic conditions
    6. Traumatic lesions
    7. Foreign body reactions
    8. Not otherwise specified

Treatment

The focus of treatment is to remove plaque. Therapy is aimed at the reduction of oral bacteria and may take the form of regular periodic visits to a dental professional together with adequate oral hygiene home care. Thus, several of the methods used in the prevention of gingivitis can also be used for the treatment of manifest gingivitis, such as scaling, root planning, curettage, mouth washes containing chlorhexidine or hydrogen peroxide, and flossing.(Bamadi, 2013) Interdental brushes also help remove any causative agents.

Complications

- Recurrence of gingivitis
- Periodontitis

- Infection or abscess of the gingiva or the jaw bones
- Trench mouth (bacterial infection and ulceration of the gums)
- Swollen lymph nodes
- Associated with premature birth and low birth weight

Periodontitis

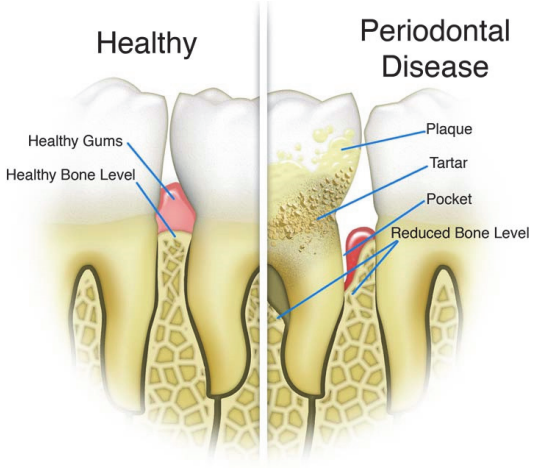

Fig. 1.5 Comparison of healthy teeth and periodontal teeth.

Periodontal diseases are inflammatory conditions affecting the physiological structural organs supporting the teeth. The gingiva become detached from the tooth to from periodontal pockets, providing an ideal ecological niche for proliferation of anaerobic bacteria their by providing a host response which may lead to local inflammation. The resulting tooth mobility is eventually reflected clinically tooth loss.

Periodontal disease is a term used to collectively designate several specific disease of the gingiva and of the tissues supporting the teeth (periodontitis). Gingivitis, a moderate stage of the disease, caused by an accumulation of supragingival plaque, is characterized by swelling, light bleeding, and redness of the marginal gingiva. Periodontitis, a more severe stage of periodontal disease, result in the resorption of the alveolar bone and detachment of the periodontal ligaments supporting the tooth. Progression of periodontitis results in loss of tooth support structure so that teeth become mobile and cannot function properly. In some cases if treatment is not instituted support structure degenerate to a point where

repair is not possible and tooth extraction is required. The role of bacteria in the aetiology of these diseases has been well established.

Pathogenesis of Periodontitis

The periodontium consist of four distinct structures that support the teeth in the oral cavity, namely the gingiva, alveolar bone, cementum and periodontal ligament. In healthy state a shallow gingival sulcus exists between gingiva and the teeth. This is generally less than 3mm deep but deepens with disease progression. Damage to the periodontium results from the direct toxic effects of subgingival bacteria and destructive effects of the host inflammatory response a loss of attachment of the periodontal ligament from tooth root surface and epical migration of the junctional epithelium occurs so that a periodontal pocket is formed. Clearance of the subgingival infection and elimination of the periodontal pocket are considered as priority in treatment of periodontitis.

The Periodontal Pocket

The periodontal pocket is lined with an epithelium on one side and tooth cementum on the other. No actual space exists as these two tissues as these rest against each other. Lack of attachment is demonstrated by insertion of a periodontal probe and changes in the attachment level or pocket depth has been monitored to asses disease progression. Pocket depths ranging from 4 to 12 mm are generally observed at decreased sites.(Choi, Lee, Choi, & Joo, 2015)

The periodontal pocket is naturally irrigated with gingival crevicular fluid (GCF). Healthy sites are associated with small volumes (0.04µl) and low flow rates (0.03µl/min) and examination of the protein concentrations show it to be similar to extracellular fluid and it is thought to represent a normal extracellular transdute. In contrast, at diseased sites there is increased fluid production and the protein composition is similar to that of serum, indicating that an exudate is formed at these sites. The volume and fluid flow rate, however, depends on the degree of inflammation at individual sites. Volume of about 0.5µl and flow rates of 0.5µl/min and 20µl/hr (0.33µl/min) have been reported.

Treatment

The goal of periodontitis treatment is to thoroughly clean the pockets around teeth and prevent damage to surrounding bone.

Nonsurgical treatments If periodontitis isn't advanced, treatment may involve less invasive procedures, including:

Scaling: Scaling removes tartar and bacteria from your tooth surfaces and beneath your gums. It may be performed using instruments, a laser or an ultrasonic device.

Root planning: Root planning smoothes the root surfaces, discouraging further build-up of tartar and bacteria, and removes bacterial by-products that contribute to inflammation and delay healing or reattachment of the gum to the tooth surfaces.

Antibiotics: Topical or oral antibiotics can help control bacterial infection. Topical antibiotics can include antibiotic mouth rinses or insertion of gels containing antibiotics in the space between your teeth and gums or into pockets after deep cleaning. However, oral antibiotics may be necessary to completely eliminate infection-causing bacteria.

Surgical treatments: If you have advanced periodontitis, treatment may require dental surgery, such as:

Flap surgery (pocket reduction surgery): Your periodontist makes tiny incisions in your gum so that a section of gum tissue can be lifted back, exposing the roots for more effective scaling and root planing. Because periodontitis often causes bone loss, the underlying bone may be recontoured before the gum tissue is sutured back in place. After you heal, it's easier to clean these areas and maintain healthy gum tissue.

Soft tissue grafts: When you lose gum tissue, your gumline recedes. You may need to have some of the damaged soft tissue reinforced. This is usually done by removing a small amount of tissue from the roof of your mouth (palate) or another donor source and attaching it to the affected site. This can help reduce further gum recession, cover exposed roots and give your teeth a more pleasing appearance.

Bone grafting: This procedure is performed when periodontitis has destroyed the bone surrounding your tooth root. The graft may be composed of small fragments of your own bone, or the bone may be synthetic or donated. The bone graft helps prevent tooth loss by holding your tooth in place. It also serves as a platform for the regrowth of natural bone.

Guided tissue regeneration: This allows the regrowth of bone that was destroyed by bacteria. In one approach, your dentist places a special piece of biocompatible fabric between existing bone and your tooth. The material prevents unwanted tissue from entering the healing area, allowing bone to grow back instead.

Tissue-stimulating proteins: Another technique involves applying a special gel to a diseased tooth root. This gel contains the same proteins found in developing tooth enamel and stimulates the growth of healthy bone and tissue.

Oral Microbiology

The microorganisms found in the human oral cavity have been referred to as the oral microflora, oral microbiota, or more recently as the oral microbiome. Approximately 280 bacterial species from the oral cavity have been isolated in culture and formally named. It has been estimated that less than half of the bacterial species present in the oral cavity can be cultivated using anaerobic microbiological methods and that there are likely 500 to 700 common oral species. The oral cavity is a major gateway to the human body.(Dewhirst et al., 2010) Food enters the mouth and is chewed and mixed with saliva on its way to the stomach and intestinal tract. Air passes through the nose and mouth on the way to the trachea and lungs. Microorganisms colonizing one area of the oral cavity have a significant probability of spreading on contiguous epithelial surfaces to neighboring sites. Microorganisms from the oral cavity have been shown to cause a number of oral infectious diseases, including caries (tooth decay), periodontitis (gum disease), endodontic (root canal) infections, alveolar osteitis (dry socket), and tonsillitis. Evidence is accumulating which links oral bacteria to a number of systemic diseases, including cardiovascular disease, stroke, preterm birth, diabetes and pneumonia.

Anaerobic bacteria in the oral cavity include: Actinomyces, Arachnia, Bacteroides, Bifidobacterium, Eubacterium, Fusobacterium, Lactobacillus, Leptotrichia, Peptococcus, Peptostreptococcus, Propionibacterium, Selenomonas, Treponema, and Veillonella. Genera of fungi that are frequently found in the mouth include Candida, Cladosporium, Aspergillus, Fusarium, Glomus, Alternaria, Penicillium, and Cryptococcus, among others. Bacteria accumulate on both the hard and soft oral tissues in biofilms. Bacterial adhesion is particularly important for oral bacteria.

Fusospirochetes

Spirochetes and fusiform bacilli live as normal flora in the mouth, but in the case of bleeding in the oral cavity, the bacteria can cause infection and diseases to oral cavity:

1. Acute necrotizing ulcerative gingivitis (ANUG)
2. Vincent angina with a membrane covering the throat area

Veillonella

Veillonella are gram-negative anaerobic cocci. It is thought that this species thrives in the acidic environment of caries and is thought to slow the development of dental caries. It converts the acidic products of other species to less acidic products.

Actinobacillus actinomycetemcomitans

Actinobacillus actinomycetemcomitans is considered an oral pathogen due to its virulence factors, its association with localized aggressive periodontitis in young adolescents, and studies indicating that it can cause bone loss.

Lactobacillus

Some *Lactobacillus* species have been associated with dental cavities although these bacteria are normally symbiotic in humans and are found in the gut flora.

Porphyromonas Gingivalis

Porphyromonas gingivalis is a gram-negative, anaerobe that can be found along the gingiva, cheek, and tongue. P. gingivalis possesses fimbriae which it uses to adhere to surfaces rich in initial plaque organism such as oral streptococci and antinomyces naeslundii; however it can also bind to other colonizers such as Fusobacterium nucleatum, treponema denticola, and bacteriodes forsythus. P. gingivalis releases a vast array of enzymes, toxic metabolites and cellular constituents, which are often dentrimental to the host in a variety of ways. Proteases are among the proteinases secreted, and are directly involved in the destruction of host tissues and loss of alveolar bone and supporting periodontal tissues(Silva et al., 2017), which are characteristic of periodontal disease. (Silva et al., 2017)However, the role these proteinases play in adhesion, nutrition, and virulence have not been resolved as they are all interdependent. Apart from protein activity, P. gingivalis has a plethora of destructive enzymes and metabolites – phospholipid A (bone resportion), alkaline and acid phosphatases (alveolar bone breakdown), DNase and RNase, sialidase, volatile sulfur compounds, butyrate and propionate (cytotoxins), and indole in ammonia (cytotoxins). P. gingivalis activity is undeniably crucial to the development and advancement of periodontal disease.

Spirochete-Treponema Denticola

Spirochete *Treponema denticola* is a gram-negative anaerobe associated with subgingival plaque and consequently periodontal disease. T. denticola has the ability to adhere to both host cells and tissues, matrix

proteins, collagen, as well as other bacteria, most notably Porphyromonas gingivalis.(Kreth, Merritt, & Qi, 2009) After adherence to these surfaces its products - peptidases, proteinases, hemolytic and hemagglutinating activities, adhesions, and proteins with pore-forming properties - provoke immune system cells, resulting in cell damage and liberation of harmful factors into the gingiva. These factors result in gingivitis and eventually periodontitis.

Actinomyces Naeslundii

Actinomyces naeslundii is a facultative anerobic pathogen that contributes to gingivitis, mild periodontitis, and root surface tooth decay. A. naeslundii with naeslundi has the ability to adhere to the pellicle of a tooth, epithelial cells, collagen, and basement membrane, as well as the capacity to coaggregate with oral bacteria such as *Streptococcus*, Veillonella, *Prevotella*, *Porphyromons*, *Fusobacterium*, and Capnocytophaga. (Ji, Choi, & Choi, 2015). The diverse capabilities of A. naeslundii with naeslundi make it a key contributor to dental plaque. To attach to the enamel surface of a tooth it produces fimbriae, which are thinner and shorter than flegellum. A. naeslundii is unique in that it has a multitude of metabolic properties, both aerobic and anaerobic, that give it the flexibility that allows it to survive and contribute to the build up of plaque. Following the consumption of carbohydrates, this bacterium produces organic acids that results in the erosion of the enamel surface due to plaque build up. If the plaque is allowed to remain, an immune response will promote the inflammation of the gingiva, also known as gingivitis.

In order to know the effect of antibiotic Metronidazole is taken and dental inserts were manufactured by taking different polymers. The amount of antibiotic is choosen based on the minimum inhibitory concentration value studied as per the following procedure:

Minimum Inhibitory Concentration

Label the tube to be inoculated with the name of organism and date, then place the test tubes in the palm of left hand and separate the test tubes to form “V” shape structure. Take inoculating loop in the right hand and sterilize by holding them in the hottest portion of the Bunsen burner flame until the entire wires become red hot and then allow to cool for 15 to 20 seconds. The tubes are uncapped by grasping the first cap with the little finger and the second cap with the next finger and lifting the closures or cotton plugs upward. Following removal of closures or cotton plugs, the necks of the tubes are passed through the flame to avoid

contamination of microorganisms. Insert the sterile inoculating loop into stock culture and remove small amount of microorganisms. The cell laden loop or needle is inserted into the sub culture tube. In the case of a broth medium, the loop or needle is shaken slightly to dislodge the organisms. Incase of agar slant medium, it is drawn lightly over the hardened surface in a straight or zig-zag line. For inoculation of an agar stab tube, a straight needle is inserted to the bottom of the tube in a straight line and rapidly withdrawn along the line of insertion. Re-flame the neck of the tubes. The caps or cotton plugs are replaced. The needle or lop is again flamed to destroy the existing organisms. Incubate all cultures at 37ºC for 24 to 48 hrs.

Manufacturing of Metronidazole Dental Inserts

All the dental inserts containing 10mg of Metronidazole, and 10mg polymer were prepared by direct compression technique using a 16 station tablet compression machine round, concave multi tip punches of 3mm diameter an die set. The effect of various ratios of different polymers on drug release was studied.

In the preparation of dental inserts to retard the release of activbe pharmaceutical; ingredient retardants are used, they include retardents like HPMC K100M, and K200M, Chitosan, Ethyl cellulose, Carnuba wax, Sodium alginate, Carbopol and Eudragit .

For the dental inserts prepared by using the active pharmaceutical ingredient and polymers evaluation tests are to be conducted and the procedure is as following:

Evaluation of Pre compression Blend

Prior to compression, powder blend was evaluated for their characteristic parameters such as **Angle of repose** (Subrahmanyam CVS 2006)

The angle of repose of pre compression blend was determined by the funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a manner that the tip of the funnel just touched the apex of the heap of the powder. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone measured and angle of repose was calculated using the fallowing equation.

$$\text{Tan } \theta = h/r$$

Where, h and r are the height and radius of the powder cone, θ is the angle of repose.

Table 1.2 Angle of Repose values.

S. No	Angle of Repose (θ)	Properties
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Poor flow

Bulk density (Leon lachman 2009, Subrahmanyam CVS 2006)

Density is defined as weight per unit volume. Bulk density, ^{2}b, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of the powder primarily depends on particle size distribution, particle shape and tendency of particles adhere together. Bulk density is very important in determining the size of containers needed for handling, shipping and storage of raw material and blend. It is also important in selecting the blender. 30g of powder blend introduced into a dry 100mL cylinder, without compacting. The power was carefully leveled without compacting and unsettled apparent volume (V^3) was read.

The bulk density was calculated using the formula:

$$\rho_b = M/V_o$$

Where, ρ_b = Apparent bulk density

M = Weight of the sample and

Vo = Apparent volume of powder

Tapped density (Subrahmanyam CVS 2006)

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides a fixed drop of 14 ± 2 mm at a nominal rate of 300 drops per minute, the cylinder was tapped 500 times initially fallowed by an additional tap of 750 times until difference between succeeding measurement is less than 2% and then tapped volume, Vf was measured to the nearest Graduated unit. The density was calculated, in gm per mL, using the formula:

$$\rho_{tap} = M/Vf$$

Where, ρ_{tap} = Tapped density

M = Weight of the sample

Vf = Tapped volume of powder

Powder Compressibility (Subrahmanyam CVS 2006)

The compressibility index (Carr's index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory the less compressible material the more flowable it is.

As such it is measure of the relative importance of inter-particulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities

will be closer in value. For poorer flowing materials, there are frequently greater inter-particle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the compressibility index which is calculated using the following formula:

$$\text{Carr's index} = [(\rho_{tap} - \rho_b)/\rho_{tap}] \times 100$$

Where, ρ_b = bulk density

ρ_{tap} = tapped density

Table 1.3 Carr's Index Values.

S. No	Carr's Index	Properties
1	5-12	Free-flowing
2	13-16	Good
3	18-21	Fair to passable
4	23-35	Poor
5	33-38	Very poor
6	>40	Extremely poor

Hausner's ratio (Subrahmanyam CVS 2006)

It is the ratio of tapped density and bulk density. Hausner found that this ratio was related to interpartical friction and as such could be used to predict powder flow properties. Generally a value less than 1.25 indicates good flow properties, which is equivalent to 20% of Carr's Index.

Hausner's ratio = Tapped density/Bulk density

Evaluation of Dental Insets

Physicochemical Characterization of Dental Inserts

The prepared Metronidazole dental inserts were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content (Indian Pharmacopoeia, 2007).

Weight Variation

The weight variation test is done by taking 20 inserts randomly and weighed accurately. The composite weight divided by 20 provides an average weight of tablet. Not more than two of the individual weight deviates from the average weight by 10 % and none should deviate by more than twice that percentage. The weight variation test would be a satisfactory method of determining the drug content uniformity (Indian Pharmacopoeia, 2007).

The percent deviation was calculated using the following formula:

% Deviation = (Individual weight of each table- Average weight of table) × 100 / Average weight of tables

The average weight of insets in each formulation was calculated and presented with standard deviation.

Table 1.4 Pharmacopoeial Specifications for Tablet Weight Variation.

Average weight of tablets (I.P)	Maximum % difference allowed	Average weight of tablets (U.S.P)
Less than 80 mg	10	Less than 130 mg
80 mg – 250 mg	7.5	130 mg – 324 mg
More than 250 mg	5	More than 324 mg

Thickness: The thickness and diameter of the inserts from production run is carefully controlled. Thickness can vary with no change in weight due to difference in the speed of the tablet compression machine. Hence this parameter is essential for consumer acceptance, insert uniformity and packaging. The thickness and diameter of the tablets was determined using Digital vernier calipers. Ten inserts from each formulation were used and average values were calculated. The average thickness for tablets is calculated and presented with standard deviation (Indian Pharmacopoeia, 2007).

Hardness: Insert hardness is defined as the force required to breaking a insert in a diametric compression test. Inserts require a certain amount of

strength, or hardness and resistance to friability, to withstand the mechanical shocks during handling, manufacturing, packaging and shipping. The resistance of the insert to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Ten Inserts were taken from each formulation and hardness was determined using Monsanto hardness tester and the average was calculated. It is expressed in Kg/cm^2 (Indian Pharmacopoeia, 2007).

Friability: Hardness is not an absolute indicator of the strength because some formulations when compressed into very hard tablets lose their crown positions. Therefore, another measure of the insert strength, its friability, is often measured. Tablet strength is measured by using Roche friabilator. Test subjects to number of tablets to the combined effect of shock, abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm for 4 minutes, dropping the tablets to a distance of 6 inches in each revolution (Indian Pharmacopoeia, 2007).

A sample of pre-weighed inserts was placed in Roche friabilator which was then operated for 100 revolutions. The inserts were then dedusted and reweighed.

Percent friability (% F) was calculated as

$$\text{Friability (\%)} = \frac{\text{Initial weight of tablets} - \text{Final weight of tablets}}{\text{Inital weight of tablets}} \times 100$$

$$F\ (\%) = \frac{[W_0 - W]}{W_0} \times 100$$

Where, W_0 is the initial weight of the tablets before the test and

W is the final weight of the tablets after test.

Assay: Twenty inserts of each formulation were taken and amount of drug present in each insert was determined. Powder equivalent to one insert was taken and added in 100 mL of pH 6.8 phosphate buffer followed by shaking for 24 hrs by using rotary shaker. The solution was filtered through a 0.45µ whatman's filter paper, diluted suitably and the absorbance of resultant solution was measured by using UV-Visible spectrophotometer at 236 nm using pH 6.8 phosphate buffer (Indian Pharmacopoeia, 2007).

Swelling and Erosion Analysis

For the determination of swelling index (SI), tablets were weighed and fixed onto 2×2 cm glass slides, which were then immersed in Petri dishes containing 10 mL of PBS (pH 6.6) medium Temperature was kept constant at 37°C±0.5°C during the study. After predetermined times, tablets were removed, and the excess surface water was wiped with filter papers. Swollen tablets were carefully reweighed, and SI was calculated by using Equation 1. (B. Celik, 2017). Throughout the study, photographs of swollen tablets were also taken. After swelling studies tablets were kept at 60°C for 24 hours to completely remove excess water. They were reweighed until constant measurements were achieved, and matrix erosion (ME) was calculated by using Equation 2.

$$SI\ (\%) = 100\ (Wt - W_0) / W_0 \quad \text{.....(1)}$$

$$ME\ (\%) = 100\ (W_0 - Wd) / W_0 \quad \text{.....(2)}$$

Where W_t is the swollen tablet weight at a given time, W_0 is the tablet weight obtained initially, and W_d is the tablet weight after drying. All experiments were performed in triplicate.

Kinetic Analysis of Dissolution Data (Agaiah Goud B *et al.*, 2011, D'Souza A *et al.,* 2013)

To analyze the *in vitro* release data, various kinetic models were used to describe the release kinetics. The zero order rate Eq. (3) describe the systems where the drug release rate is independent of its concentration. The first order Eq. (4) describes the release from system where release rate is concentration dependent. Higuchi (1963) described the release of drugs from insoluble matrix as square root of time dependent process based on fickian diffusion Eq. (5). The Hixon –crowell cube root law Eq. (6) describes the release from systems where there is a change in surface area and diameter of particles or tablets.

$$C = K_0 t \quad \text{.....(3)}$$

Where, K_0 is zero-order rate constant expressed in units of concentration/time and t is the time.

$$\text{Log } C = \text{Log} C_0 - K_1 t / 2.303 \quad \text{.....(4)}$$

Where, C_0 is the initial concentration of drug and K_1 is the first order constant.

$$Q = K_H t^{1/2} \quad \text{.....(5)}$$

Where, K_H is the constant reflecting the design variables of the system.

$$Q_0^{1/3} - Q_t^{1/3} = \mathbf{K_{HC}\, t} \qquad \text{.....(6)}$$

Where, Q_t is the amount of drug remained in time t, Q_0 is the initial amount of the drug in tablet and K_{HC} is the rate constant for Hixson-Crowell rate equation.

The fallowing plots were made using the *in vitro* drug release data.

1. Cumulative % drug release vs. time (zero order kinetic model);
2. Log Cumulative of % drug remaining vs. Time (first order kinetic model);
3. sCumulative % drug release vs. Squa-----*re root of time (Higuchi model);
4. And Log Cumulative of % drug release vs. Log time (Korsmeyer Peppas).

Mechanism of Drug Release

Korsmeyer *et al* (1983) derived a simple relationship which described drug release from a polymeric system Eq. (7)

$$M_t / M_\infty = Kt^n \qquad \text{.....(7)}$$

Where M_t / M_∞ is a fraction of drug released at time t, K is the release rate constant incorporating structural and geometric characteristics of the tablet and n is the release exponent. The n value is used to characterize different release mechanisms. A plot of Log cumulative % drug release vs. Log time was made. Slope of the line was n.

The n value is used to characterize different release mechanisms as in table 1.5, for the cylindrical shaped matrices. Case II generally refers to the erosion of the polymeric chain anomalous transport (Non-Fickian) refers to a combination of both diffusion and erosion controlled drug release.

Table 1.5 Diffusion Exponent and Solute Release Mechanism for Cylindrical Shape.

Diffusion Exponent (n)	Over all solute diffusion mechanism
0.45	Fickian diffusion
0.45<n<0.89	Anomalous (Non-fickian) diffusion
0.89	Case –II transport
n>0.89	Super Case –II transport

In vitro Release Studies

The drug release from dental inserts was studied using the vial bottles at 25 rpm in which 5 ml of 6.8 pH buffer is placed and a temperature of 37ºC along with magnetic stirring was maintained with the help of thermo magnetic stirrer and aliquots of 1 mL were collected at different time intervals up to 5days and analyzed after appropriate dilution by using UV Spectrophotometer at 236nm.

In vivo Studies

In vivo studies are done on volunteers who are selected on the inclusion criteria of studies. Based upon the severity of disease the prepared insert of drug is placed in the formed pocket using surgical procedure. After one week X-rays studies were performed and depth was measured.

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