Chapter 1

Introduction And Literature Review
The continuous progress of periodontitis-affected teeth eventually leads to the loss of or damage to their function\(^5\). The bacterial flora of the gingival crevice is important in the etiology of periodontal disease\(^6-8\) is established. In healthy condition, gingival and teeth 2mm gap between the normal is between 0. During periodontitis, and other bacterial collagenase enzymes, respectively pathologically deepened sulcus depth is usually exceeding 5mm. The state concerning infectious disease at the site of poly morph nuclear cells brought about by the anti-inflammatory response are possible.

And can help to prevent tooth loss. A recent study has several important systemic diseases and periodontal infections exciting evidence. Theoretically, periodontal disease, systemic health effects by one or more of several methods can be envisaged:
Deep and adjacent tissue (facial, aircraft, sinus infection or brain) direct extension of infection to the periodontium.

Circulating inflammatory mediators in the periodontium passage from distant sites (atherosclerosis) has an impact on the work.

Distant sites (endocarditis, thrombosis / atherosclerosis) in the systemic circulation, oral bacteria to cause infection penetration.

Diseases (pulmonary or gastrointestinal infection) promote or exacerbate the remote mucosal sites, oral bacteria, spread their products or host products.

**Causes of periodontal disease:**

Periodontal disease is marked by bacterial overgrowth. The Bacteriodes gingivalis, Bacteriodes melaninogenicus subspecies intermedius and Fusobacterium nucleatum included. In juvenile periodontitis, including microflora Capnocytophage and Actinobacillus actinomycetemcomitans.

**Treatment of periodontal diseases:**

Systemic antibiotic therapy is also important to note that the clinical efficacy established that, superimposed infections, patient non-compliance etc. Increased levels of the toxic side effects of systemic administration of high doses to Periodontitis are a condition of localized disease because it is responsible for local drug treatments. Gingivitis and plaque buildup and accumulation, lower. Superior effects, the drug was used as a chlorhexidine pocket irrigation, however, reduce the signs of periodontal disease were observed.

Deep and adjacent tissue (facial, aircraft, sinus infection or brain) direct extension of infection to the periodontium. Circulating inflammatory mediators in the periodontium passage from distant sites (atherosclerosis) has an impact on the work. Distant sites (endocarditis, thrombosis / atherosclerosis) in the systemic circulation, oral bacteria to cause infection penetration. Diseases (pulmonary or gastrointestinal infection) promote or exacerbate the remote mucosal sites, oral bacteria, spread their products or host products.

Tetracycline hydrochloride absorption and active for 5 minutes, irrigation, root dentin and gingival crevicular fluid concentrations of free 8mcg/ml average end (GCF) will be introduced gradually in the 3 weeks of
tetracycline sufficient retention occurs. Periodontitis has been evaluated locally or other drugs, minocycline, doxycycline, ofloxacin and is fluorbiprofen metronidazole\(^{29}\). Basic periodontal pocket with a controlled drug release from the target device. By controlling the length of cellulose acetate hollow fibers tetracycline treatment of periodontal disease, in the first possibility was examined by Goodson et al. Placed into the periodontal pocket \(^{34}\) in the clinical signs and improvement of spirocheate numbers were generated by the fiber. Similarly, tetracycline treatment of periodontal disease site \(^{35}\) hallows fiber filled in an excellent condition.

Chlorohexidine load ETHYL cellulose films were evaluated for their effectiveness periodontitis \(^{36}\). Minocycline ETHYL cellulose film containing the drug-loading, semi-synthetic tetracycline was prepared and evaluated\(^{37-39}\). Acrylic strips with various antimicrobial agents have been fabricated and evaluated\(^{40-42}\). Examples of chemical treatment with an antibiotic Periodontitis has been evaluated locally or other drugs, minocycline, doxycycline, ofloxacin and is fluorbiprofen metronidazole\(^{29}\). Basic periodontal pocket with a controlled drug release from the target device. By controlling the length of cellulose acetate hollow fibers tetracycline treatment of periodontal disease, in the first possibility was examined by Goodson et al. Placed into the periodontal pocket \(^{34}\) in the clinical signs and improvement of spirocheate numbers were generated by the fiber. Similarly, tetracycline treatment of periodontal disease site \(^{35}\) hallows fiber filled in an excellent condition. Solution invaded territory irrigating, and are systemically administering antibiotics. So, to overcome this deficiency, periodontal pockets in the administration of medication directly to the research has been carried out. It was systemically\(^{43}\) periodontal pockets as they will produce in the local administration of tetracycline systemic dose of 1/1000, it was reported that the same effect can bring. Syringeable into the polymer drug solubilized dispersed in the N, N-dimethyl pyrrolidone (NMP), triacetin as biocompatible formulations contain SOLVENTS is dissolved. These systems are easily disposable syringes with needles gauge No.22 using the site (periodontal pocket) can be administered to. When the polymer solution containing the drug
Local drug delivery systems:

Local antibiotics in treatment of systemic therapy offer many advantages. These systems are site specific. The sub-gingival sites direct placement in the antibacterial agent(s), including

Systemic agents:

Conventional treatment of any response\textsuperscript{44, 45} does not show. In these cases, antibiotics can lead to antibiotic treatment is of great interest due. The minimal inhibitory concentrations of gingivitis pathogens\textsuperscript{46} product and suspended production of more than one concentration of gingival fluid, systemic administration of antibiotics has resulted in changes in vegetation that plaque is shown. Comprehensive evaluation of common systemic antibiotics tetracycline, Periodontitis has been evaluated locally or other drugs, minocycline, doxycycline, ofloxacin and is fluorbiprofen metronidazole\textsuperscript{29}. Basic periodontal pocket with a controlled drug release from the target device. By controlling the length of cellulose acetate hollow fibers tetracycline treatment of periodontal disease, in the first possibility was examined by Goodson et al. Placed into the periodontal pocket\textsuperscript{34} in the clinical signs and improvement of spirocheate numbers were generated by the fiber. Doxycyclin, metronidazole and ciprofloxacin and erythromycin and clindamycin is less. Pharmaceuticals in the local (semisolid) drug delivery system\textsuperscript{47, 48} the ointments, pastes, creams and Drug Administration of the traditional state interests, etc., many drugs do not reach a sufficient concentration of the body at the target site, because most of the drugs were dissolved prematurely disabled and are.

**TYPES OF DIFFERENT SEMI SOLID FORMULATIONS**

1. Creams\textsuperscript{50}:

Occlusive effect of therapeutic or prophylactic creams is not required where the proposed solution or dispersion of medicaments applied to the skin are used to. Oil in water type creams shaving cream, hard creams and foundation creams include oil in water (W / O) creams and emollient creams include cold creams.
2. Ointments\textsuperscript{50, 51}: -

Ointments skin or mucous membranes follow a particular purpose, are semisolid preparations, the general basis of the non-aqueous solution or dispersion of one or more medicaments. Anhydrous ointments are often basic and animal, vegetable or mineral origin, fats, oils and waxes include non-fat and artificial, including the bases. At the pharmacological effects Minimum requirements for dental pastes are as follows. It should be non-toxic, pleasant and convenient to use. It should confirm to national standards for its abrasively to enamel and dentine. Its business should be stable during shelf life. It should be economic costs. Paste tube can cause damage that is excessive force; usually without application of force application will emerge from a collapsible tube. The sauce, to distinguish it from a normal situation, loss of sensation, or physical storage required. The enamel and dentine will ensure national standards for it’s abrasively of ointments are intended to produce medicaments, or near, the application site has been used as a vehicle, they are applied as protective emollients and skin.

3. Pastes\textsuperscript{50, 51}: -

Pastes one or more drug substances intended for topical application which is a semisolid dosage form. Powder absorbs some of the liquid hydrocarbon is less greasy than ointments because of Pastes. The protective absorbents, antiseptics, used as is, or broken surface to soothe skin, they often spread rather thickly on the dressings are applied. Pastes are usually high percentage of insoluble powders (at concentrations of 20% to 60%) included. As well as local anesthetics, spermicidal, and dermatological agents to a vehicle is being used as a prison for lubrication of gloves and instruments are used, patch testing in the film formers, and electrocardiograph leads to the expression of the terminal growth is for. Enter the internal organs used as a lubricant for catheters or devices are required to be sterile juice. Interest of the transparent or translucent solutions or hydrophobic bases is semisolid or solid preparations. Pastes the water, they remain in place after application and effective in the absorption of serous secretion. And permeability due to their inertia, pastes hairy parts of the body are not suitable for application. as it usually is less oily preparation area contain powerful medicament healthy skin and lead to the spread of the sensitivity of the reaction.
The local impact of a dental paste is designed for adhesion to the mucous membrane. The therapeutic and cosmetic dental pastes default paste formulations are divided into two types. The therapeutic "treatment of medical disease" and "curative" as the Oxford Dictionary is defined by the American Heritage Dictionary. Therapeutic dental paste for treatment of certain oral disease by clinical trials has tested and prescribed by a doctor is usually the active ingredient of the drug.

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- The sauce, to distinguish it from a normal situation, loss of sensation, or physical storage required.
- The enamel and dentine will ensure national standards for its abrasively.

4. Gels

Gels are often oily and none usually is applied externally. The word 'gel' but some oily suspensions for oral use (e.g., aluminum hydroxide gel) has been applied in the pharmacy. As well as local anesthetics, spermicidal, and dermatological agents to a vehicle is being used as a prison for lubrication of gloves and instruments are used, patch testing in the film formers, and electrocardiograph leads to the expression of the terminal growth is for. Enter the internal organs used as a lubricant for catheters or devices are required to be sterile juice. Interest of the transparent or translucent solutions or hydrophobic bases is semisolid or solid preparations. Continuous structure, a characteristic feature is the presence of solid-like properties. In a typical polar gel, natural or synthetic polymer, a hydrophilic matrix is created in three dimensions.
OBJECTIVE OF THE WORK

Effective antibiotics to local administration, local administration support systemically administered antibiotics are required. Ciprofloxacin hydrochloride antimicrobial agents belong to a group is a Fluoroquinolone.

It is reported to periodontal therapy or ciprofloxacin. Other fluoroquinolones (ciprofloxacin) e.g., ofloxacin and periodontopathic microorganisms and periodontal disease has been reported to be active against topical chemotherapy. In less greasy popular pastes, ciprofloxacin or ofloxacin as the formulations have been established Dental preparations available in the market, product, cost effectiveness, popularity, ease of packaging and transport are due. Production, cost effectiveness, popularity, ease of packaging and transport. In this context, for the treatment of dental infections and diseases. There are very few semisolid formulations and medicated dental pastes and the need for research into the development of

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PROFILES OF DRUGS AND POLYMERS USED IN THE STUDY

CIPROFLOXACIN HYDROCHLORIDE\textsuperscript{54-60}:  

Ciprofloxacin hydrochloride belongs to fluoroquinolone groups of antimicrobial agents with a wider spectrum of activity.

Chemical structure:

\begin{center}
\includegraphics[width=0.5\textwidth]{ciprofloxacin.png}
\end{center}

Routes of administration and dosage\textsuperscript{61}:

Ciprofloxacin hydrochloride as the 30 to 60 minutes by intravenous infusion, severe infections, hydrochloride is given by mouth as the mouth; ciprofloxacin hydrochloride eye drops are available of.

OFLOXACIN\textsuperscript{62-67}:

Ofloxacin belongs to fluoroquinolone groups of antimicrobial agents with a wider spectrum of activity.

The long serum half-life of ofloxacin methylated and can contribute. Ofloxacin in the position 4 position of nitrogen and quinolone nucleus contains 11 carbon link oxazin ring. This ring results in an increase in heat.
Chemical Structure:

The gastro-enteritis, gonorrhea, lower respiratory tract infections, skin infections, spotted fever, typhoid fever, urinary tract infection, is used. It is also used in the treatment of surgical infections. Ofloxacin leprosy can be treated. Fluoroquinolones such as ofloxacin or ciprofloxacin hydrochloride and is used to treat eye infections. Fluoroquinolones such as ciprofloxacin hydrochloride and ofloxacin is a mouth infection.

**KAOLIN**

- **Chemical name:** Hydrated aluminum silicate.
- **Empirical formula and molecular weight:** The USP 25 describes kaolin as a native aluminum hydrated silicate, Powdered and freed from gritty particles by elutriation. The BP 2001 similarly describes light kaolin but additionally states that it contains a suitable dispersing agent. Typical molecular weight is 258.16.
- **Functional category:** Adsorption; suspending agent; tablet and capsule diluents.
- **Description:** Kaolin occurs as a white to grayish-white colored, unctuous powder free from gritty particles. It has characteristics earthy or clay like taste.
- **Specific gravity:** 2.6
- **Viscosity:** 300 mPas (300 cps) for a 70% w/v aqueous suspension.
- **Solubility:** Practically insoluble in diethyl ether, ethanol (95%), water, other organic solvents, cold dilute
Applications:

It is also used as the vehicle stalled. In topical preparations, sterilized KAOLIN is used. Theoretically, KAOLIN anti-diarrheal preparations have been used. The KAOLIN abrasive or polishing agent in the pastes is used as formulations.

GLYCERIN:\n
- **Chemical name:** Propane-1,2,3-tiol
- **Empirical formula:** \( \text{C}_3\text{H}_8\text{O}_3 \)
- **Molecular weight:** 92.09.
- **Functional category:** Antimicrobial preservatives; emollient; humectants; plasticizers; solvent; sweetening agent; tonicity agent.

Applications:

In topical formulations and cosmetics, glycerin is used mainly for its humectants and emollient properties. In parenteral preparations, glycerin is used as a solvent. In oral solutions, glycerin solvent, sweetening agents, antimicrobial preservatives, which are used as film coatings. Glycerin also topical formulations such as creams and emulsions are used. Uses different amounts of glycerin are given below. glycerin is used mainly for its humectants and emollient properties. In parenteral preparations, glycerin is used as a solvent. In oral solutions, glycerin solvent, sweetening agents, antimicrobial preservatives, which are used as film coatings.

- **Description:** Glycerin is a clear, odorless and colorless, viscous, hygroscopic liquid; it has a sweet taste, approximately 0.6 times as sweet as sucrose.

- **Melting point:** 17.8°C

METHYL PARABEN:\n
- **Chemical name:** Methyl 4-Hydroxybenzoate
- **Empirical formula:** \( \text{C}_8\text{H}_8\text{O}_3 \)
- **Molecular weight:** 152.15
- **Functional category:** Antimicrobial preservative.
Applications:

Preservatives, it kill mold and mildew as it is used, and to create a broad-spectrum antimicrobials are used synergistically with bactericides. In cosmetics, it is the most frequently used antimicrobial preservatives.

Description: Colorless crystalline or white crystalline powder. Parabens are phytoestrogens found in plants such as blue berries.

- **Antimicrobial properties:** Methyl paraben exhibit antimicrobial activity between pH 4-8. Preservative efficiency decreases with increasing pH owing to the formation of the phenolate anion.

**PROPYL PARABEN**

- **Chemical name:** Propyl 4-Hydroxybenzoate
- **Empirical formula:** \( C_{10}H_{12}O_3 \)
- **Molecular weight:** 180.20
- **Functional category:** Antimicrobial preservative.
- **Description:** White, crystalline, odorless and tasteless powder.

- **Antimicrobial properties:** Propyl paraben exhibit antimicrobial activity between pH 4-8. Preservative efficiency decreased with increasing pH owing to the formation of the phenolate anion.

Applications:

Preservatives, it kills mold and mildew as it is used, and to create a broad-spectrum antimicrobials are used synergistically with bactericides. In cosmetics, it is the most frequently used antimicrobial preservatives.

**PROPYLENE GLYCOL**

- Used as a emulsifier and as a carrier for flavors in ethanol as vehicle selection, the lack of volatility in the food industry to provide a more uniform taste.
LITERATURE REVIEW

Subhas G\textsuperscript{69} (2010), reported that the Periodontal diseases regardless of sex and age of the population is the main cause of loss of teeth in adulthood. Various treatment modalities are available to the dental profession. Police with automatic scaling plaque control instructions and prevent the most common initial periodontal disease control is practiced by the general dentist. Root planning and soft tissue curettage procedures for the treatment of moderate type of periodontal disease, it is added. In some cases, it has had limited success, and therefore, in the periodontal pocket, or local drug delivery by topical application of antibacterial drugs have been tried in local programs. Topical drug delivery and controlled release of drugs have been identified as a local drug delivery. Periodic use of local drug delivery to reduce bleeding,

Swati R, Sandeep W, et al\textsuperscript{70} (2010), developed Ornidazole cut to inject without Poloxamer 407 (Pluronic F-127), using the periodontal pocket for the direct placement of controlled release characteristics of biocompatible and biodegradable in situ gel formulation syringeable. Ornidazole special periodontal disease is responsible for the anaerobic gram-negative, facultative bacteria to work on. Ornidazole Metronidazole is very low compared to the periodontal pathogens. In vitro drug release of the formulation containing 20% Pluronic F-127 completely drug within 8 hours of release. In vitro antibacterial activity, isolation, characterization and identification of bacterial strains collected from patients with periodontal disease from dental plaque samples were carried out. Ornidazole jail antibiotic assay of E.coli, S.aureus and coagulase negative Staphylococcus spp was introduced to was different. Marketing formula with antibacterial inhibition in vitro studies have shown a higher zone. Study results Pluronic F-127 polymer in situ gel formulation for the development of periodontal disease is promising, indicating that.

Jongjan M, Juree, et al\textsuperscript{72} (2010), formulated Zink oxide containing gel for the treatment of periodontitis, and so for all practical purposes. ZnO as the gel-forming agent and xanthan gum as was used main compound studied. Effects of clove oil and eugenol prepared juice viscosity, pH and including antimicrobial activity were evaluated in terms of their gel properties were studied. The preparation added in jail. Xanthan gum, ZnO, clove oil and eugenol increase in the viscosity of the prepared gel
was increased. Systems, including clove oil, eugenol antimicrobial activity tended to be higher than that.

Nagaraju R, Udupa N, et al\textsuperscript{79} (2003), formulated Poly (caprolactone), a biodegradable, polymer tinidazole of using dental implants. Clinical study was conducted to evaluate the usefulness of periodontal therapy. Low drug concentration is desirable in the saliva, was found. A high concentration of drug in the oral cavity mucus commencal normal flora can suppress and even cause some adverse effects on the growth of opportunistic organisms may create a cover. Tinidazole implants were able to open up and make sure that the clinical efficacy of implants in the gingival crevicular fluid of various periodontopathic organisms maintains an effective concentration.

Venkatesh, Udupa N\textsuperscript{81} (2002) prepared and evaluated Daniel poly (lactide-co-glycolide) (75:25) co-polymer with Ciprofloxacin and tinidazole in the interest of the biodegradable. Prepare a mixture of in vitro release syringeability, for drug content uniformity was evaluated. Juice prepared in drug content was found to be uniform and easily extruded through a syringe with a 22 gauge needle may be. The motion equations and SEM studies of drug candidates with a first-order kinetics, and the spread of drugs in the treatment of the data is published by the signal from the. In vivo studies indicate patients

Karnik A and vania P\textsuperscript{84} (2001), demonstrated that the Periodontitis is inflammation of the gum, which is a result of poor oral hygiene. Recommended for the treatment of periodontitis is the most powerful antibiotic Doxacycline hydrochloride tetracycline belongs to the class. Because of the sustained release of DOX DOX stable gel-SOL archiving static injection purpose of this work. Currently available too inconvenient DOX injection every 4-5 hours that can be induced, so we tried to develop DOX is an injection of a novel gel-SOL.DOX.

Kargill B and Kadir T\textsuperscript{85},(2001), investigated the A kind word, the root of the antibacterial effect sterile paper were collected. Fresh mixed ornidazole and sterile saline were placed in the root canals. One week later, root canal, bacterial content together again. Microbiological analysis was performed. Our result is based on the anti-bacterial activity of microorganisms in the ornidazole causes significant changes that appear.
Reinhardt R, Maze G, et al\textsuperscript{87} (1995), determined 4-day period, lactic acid glycolic bioerodible tetracycline gel system (with high viscosity and low viscosity gel) to treat periodontitis sites with a simple placement of tetracycline levels in gingival fluid crevicuau. Over 90% of the sites of interest in the gingival crevicular fluid per ml were more than 100 MCG tetracycline.

Giordano J, and Loasche W\textsuperscript{88} (1995), evaluated the local delivery antimicrobial agents and the effect of systemic antimicrobials. 20% metronidazole, the first weeks after the film containing 20% chlorohexidine or edit films. Plus scaling and root planning, local delivery antimicrobial agents in the treatment of refractory primary teeth can lead to reduced surgical needs.

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Polson A, Garrett S, et al\textsuperscript{90} (1995), compared 5% sanguinarine chloride polymer delivery system efficiency of 10% doxycycline hyclate contained within. Polymer delivery system to improve the diagnosis and treatment of periodontal health maintained significantly better than using the sub-gingival treatment with doxycyclin established.

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Drisko C, and Charles M\textsuperscript{93} (1995), evaluated the Results showed that treatment resulted in improvement in clinical parameters.

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Subuski D, Asthon P, et al\textsuperscript{95} (1994), evaluated Due to the sustained release of tetracycline and ciprofloxacin. Polylactic acid (PLA) and poly vinyl alcohol (PVA) membrane made of hydrophilic lipophilic membrane composed of effectiveness was examined. Results of both drugs in the first 24 hours of the hydrophilic membrane (PVA), compared to the lipophilic membrane (PLA), provided that a long sustained release stated. The art Polylactic acid (PLA), observed over a period of 14 days provided sustained drug release.

Zaremba KA, Famili P, et al\textsuperscript{97} (1994), evaluated the Local efficacy of 25\% tetracycline in conjunction with conventional treatment is applied. Clinical parameters improved treatment results suggested sites.

Lowenguth RM, and Gandini L\textsuperscript{99} (1993), evaluated ETHYLENE VINYL ACETATE with fiber containing 25\% tetracycline hydrochloride effectiveness of periodontal treatment. Pocket depth reduction and treatment in the control group compared with no treatment is given at 2 months post-treatment level of the test resulted in connections. Gingival crevicular fluid analysis within the tetracycline concentration tetracycline fiber therapy achieved mainly restricted to sites that showed. Local delivery of tetracycline to measure the local juvenile periodontitis was noted most effective.

Kazakos G, Cobb C, et al\textsuperscript{100} (1993), evaluated Antimicrobial effects of tetracycline monolithic fiber rich. The fibers used in a ten day period adversely affect the epithelial lining and the antimicrobial effects of the fibers are not confirmed.

Okada K, Wolff L, et al\textsuperscript{104} (1992), studied using biodegradable polymer containing minocycline showed that the device that the device maintained an effective antibacterial concentration of 1 mcg/ml for 14 days.

Brasswell L, Offenbacher SFM, et al\textsuperscript{105} (1992), evaluated Slow-release resorbable polymers for the treatment of periodontitis in patients subgingivel minocycline. Probing depth and attachment level was significantly improved treatment sites.

Bjorn Klinge, Jinta Korn K, et al\textsuperscript{106} (1992), evaluated 10\% metronidazole paste was applied twice daily for four weeks in 6 beagle dogs on one side of the mandible and other side a placebo paste was used. At the end of the study metronidazole treated sites showed improved parameters.
Stoltze K and Michale S\textsuperscript{107} (1992), treated 14 patients with periodontal pockets with 25\% metronidazole dental gel. The results indicated that high concentration of metronidazole could be obtained in periodontal pockets without inducing plasma concentrations.

Reinhardt R, Maze G, et al\textsuperscript{87} (1995), determined 4-day period, lactic acid glycolic bioerodible tetracycline gel system (with high viscosity and low viscosity gel) to treat periodontitis sites with a simple placement of tetracycline levels in gingival fluid crevicuar. Over 90\% of the sites of interest in the gingival crevicular fluid per ml were more than 100 MCG tetracycline.

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Zaremba KA, Famili P, et al\textsuperscript{97} (1994), evaluated the Local efficacy of 25\% tetracycline in conjunction with conventional treatment is applied. Clinical parameters improved treatment results suggested sites.

Lowenguth RM, and Gandini L\textsuperscript{99} (1993), evaluated ETHYLENE VINYL ACETATE with fiber containing 25\% tetracycline hydrochloride effectiveness of periodontal treatment. Pocket depth reduction and treatment in the control group compared with no treatment is given at 2 months post-treatment level of the test resulted in connections. Gingival crevicular fluid analysis within the tetracycline concentration tetracycline fiber therapy achieved mainly restricted to sites that showed. Local delivery of tetracycline to measure the local juvenile periodontitis was noted most effective.

Kazakos G, Cobb C, et al\textsuperscript{100} (1993), evaluated Antimicrobial effects of tetracycline monolithic fiber rich. The fibers used in a ten day period adversely affects the epithelial lining and the antimicrobial effects of the fibers are not confirmed.

Okada K, Wolff L, et al\textsuperscript{104} (1992), studied using biodegradable polymer containing minocycline showed that the device that the device maintained an effective antibacterial concentration of 1 mcg/ml for 14 days.

Brasswell L, Offenbacher SFM, et al\textsuperscript{105} (1992), evaluated Slow-release resorbable polymers for the treatment of periodontitis in patients subgingivel minocycline. Probing depth and attachment level was significantly improved treatment vel sites.
Bjorn Klinge, Jinta Korn K, et al\textsuperscript{106} (1992), evaluated 10\% metronidazole paste was applied twice daily for four weeks in 6 beagle dogs on one side of the mandible and other side a placebo paste was used. At the end of the study metronidazole treated sites showed improved parameters.

Stoltze K and Michale S\textsuperscript{107} (1992), treated 14 patients with periodontal pockets with 25\% metronidazole dental gel. The results indicated that high concentration of metronidazole could be obtained in periodontal pockets without inducing plasma concentrations.

Stoltze K Michale S\textsuperscript{108} (1992), treated One of 12 patients with 25\% metronidazole gel. Gingival crevicular fluid (GCF) after application 4, 8, 12, 24 and at 36 hours was collected and analyzed for drug content. GCF concentration results in 92\% of patients at 12 hours were maintained about Mike that shown, only 8\% of patients maintained a 36-hour drug in GCF.

Stabholze A, Soskole WA, et al\textsuperscript{110} (1991), evaluated Sustained release in patients with periodontitis, no device used and the deep periodontal pocket containing chlorohexidine found to be beneficial in the treatment.

Osterrwaal PJM, Mikx FHM, et al\textsuperscript{115} (1990), compare Irrigation with 1\% and 10\%, respectively, 21 hours and 66 hours, with the fibers of the ethylene VINYL ACETATE 1\% and 10\% and tetracycline irrigation solution D, 10 day period in GCF 1.5 mg per ml of tetracycline to maintain the average concentration.

Minabe A, Takeruchi K, et al\textsuperscript{119} (1989), developed Periodontal pockets, tetracycline release kinetics of the insertion device installed Minabe then from 17 to 180 MCG / ml 10 days at a tetracycline concentration of collagen strips