Non-antibiotic approaches for oral applications

P.V. Araújo¹, A. Gala-Garcia¹, R.T.R.C. Peixoto¹, R.D. Sinisterra² and M.E. Cortés¹

¹Restorative Dentistry Department, Faculty of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil
²Chemistry Department, Institute of Exact Science, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

New promising non-antibiotic agents are being widely studied due to the limited range of synthetic antimicrobial drugs available and the worldwide increased resistance in bacterial pathogens, causing treatment failures in human and animal infectious disorders. This chapter will discuss the use of some alternative approaches that can potentially be used in antimicrobial treatment of oral diseases. Among several non-antibiotic applications to the treatment and prevention of bacterial diseases, the use of photodynamic therapy (PDT) associated to a photosensitizer and the use of natural products such as acriflavin, propolis, Aloe vera has received considerable investigation in dental research. Both of them appear to be efficient for treatment of localized and superficial oral infections, such as caries, periodontal diseases and root canal infections.

Keywords: Non-antibiotic; photodynamic therapy; essential oils; dental caries; periodontal disease

1. General remarks

The emergence of multiple antibiotic resistant organisms in the general community is a potentially serious threat to public health. A paradigm shift in the treatment of infectious disease is necessary to prevent antibiotics becoming obsolete and, where appropriate, alternatives to antibiotics ought to be considered [1]. There are already several non-antibiotic approaches to the treatment and prevention of infections, including the use of natural products or photodynamic therapy (PDT). These non-antibiotic approaches have received considerable investigation in dental research. PDT leads to the production of cytotoxic reactive oxygen species, which can cause rapid oxidation of cellular constituents and cell death, upon irradiation with light corresponding to an absorption maximum of a photosensitizer [2]. This therapy appears to be efficient for treatment of localized and superficial infections, like oral infections such as caries, periodontal diseases and root canal infections. Besides that, natural products have been recently investigated more thoroughly as promising agents for the prevention of oral diseases, especially plaque-related diseases and inflammation control [3]. The increasing resistance to available antimicrobials has attracted the attention of the scientific community regarding a search for new cost-effective drugs of natural or synthetic origin. Essential oils in general demonstrate antimicrobial activity against cariogenic microbes and fungal filaments as well. This chapter will discuss the use of some alternative approaches that can potentially be used in antimicrobial treatment of oral diseases and highlight the real effectiveness of these agents.

2. Photodynamic Therapy

Photodynamic therapy (PDT) is an established treatment for localized tumors, involving the application and retention of an applied photosensitizing agent in malignant tissues and a substantial body of work has shown that this photodynamic approach can also be used to kill bacteria [4]. The concept of PDT was initiated in 1900 when Raab [5] described the antimicrobial action of acridine and light on Paramecium species. The use of PDT in dental research has received considerable investigation. According to Wilson [6] several species of oral bacteria, in the presence of an appropriate photosensitizing agent, can be killed by light from a low-power laser. Susceptible species include the plaque-forming and cariogenic-species S. sanguis, S. mutans, S. sobrinus, L. casei. and A. viscosus. Various methodologies using substrates as bacterial suspensions, human dental plaque samples, collagen matrix that resembled demineralized dentine or extracted carious teeth have been used to demonstrate the bactericidal effect of PDT against cariogenic bacteria [7].

PDT can be defined as the administration of a nontoxic drug or dye known as a PS either systemically, locally, or topically to a patient bearing a lesion (frequently but not always cancer), followed after some time by the illumination of the lesion with visible light (usually long wavelength red light), which, in the presence of oxygen, leads to the generation of cytotoxic species and consequently to cell death and tissue destruction [8].

Phototoxicity mechanisms are initiated by the absorption of light by a given photosensitizer. After absorption of light, part of the energy is transferred to the triplet state in the photosensitizer molecule. Either charge (type I reaction) or energy (type II reaction) is transferred to a substrate or to molecular oxygen to generate reactive oxygen species. In photodynamic action, singlet oxygen (¹O₂) is considered to play a major role. This highly reactive oxygen initiates further oxidative reactions in the proximate environment, such as the bacterial cell wall, lipid membranes, enzymes, or nucleic acids [9].
The specificity of PDT is aided by the fact that singlet oxygen is the dominant bactericidal molecule which has a short life span and a limited diffusion distance of 100nm [9]. The advantages of this approach are that bacteria can be irradiated in very short periods of time (seconds or minutes) and damage to adjacent host tissues and disruption of the normal microflora can be avoided [6].

Some authors use the term photodynamic antimicrobial chemotherapy (PACT) when PDT is applied as an antimicrobial approach [10,11]. PACT, as a treatment of localized infection, will only be useful if it can be tolerated by the patient. It has been shown that human cells (keratinocytes and fibroblasts) can survive PACT conditions that are lethal to microorganisms. The differences in susceptibility are likely to be due to differences in cell size, and structure. Human cells are between 25 and 50 times larger than bacterial cells and thus require more damage to induce cell death. The former also have a nuclear membrane which may provide an additional barrier to photodynamic killing. The low toxicity of human cells on exposure to PACT that is lethal to microorganisms indicates that PACT has potential for in vivo use [10].

PDT has two main advantages over conventional antibiotic treatments. First, the bactericidal activity is confined to areas which have been treated using the photosensitizer and light, avoiding disruption of the indigenous microflora at sites distant from the infected area. Second, the development of resistance to $^{1}O_2$ by bacteria is unlikely due to its non-specific mode of action [12].

Various classes of chemical compounds, including phenothiazines, phthalocyanines, and porphyrines, with phototoxic properties have been successfully tested as photoactivating agents against Gram-positive and Gram-negative bacteria [6]. Although most PDT applications are associated with a laser light, non-laser light sources have also been used. Studies developed in the last decade clearly indicate that the use of the visible-light isolated from a hand held photopolymerizer unit (non-laser light source) does not induce any thermal or photochemical damage to the retina. There is also the complete absence of visual damage to the patient or to the technician due to UV-A or UV-B irradiation presented in lower doses in the light spectrum. In addition to that, the cost of use of HHP is lower than of laser light [13].

According to Williams et al. [14] the energy dose is the most important factor in killing bacteria. Wilson et al. [15] describes that the energy dose could be calculated from the equation: exposure time (s) multiplied by the laser output power (mW). By increasing the power, the energy dose applied to the bacteria could be increased without altering exposure time, as it is important for clinical convenience to have a short exposure time. Besides that, it is necessary that the photosensitizer have an absorption spectrum near to emission spectrum of the lamp source [16]. Therefore, taking into consideration these parameters, it is possible that various combinations of different light sources and PS could be effective in lethal photosensitization of bacteria.

As the chemical antibacterial agents are difficult to maintain at a therapeutic concentration in the oral cavity and can be rendered ineffective by resistance development in the target organisms, PDT could be considered an alternative antimicrobial approach. Bacteria and other microbes can be sensitized to light through prior treatment with a chemical photosensitizing agent.

Dental caries is a disease which, after demineralization of the enamel has occurred, progresses slowly down into the dentine. The lesion consists of an advancing zone of demineralization behind which is a zone of partially demineralized dentine infected with bacteria [17]. The difficulties in determining the amount of tissue removal necessary clinically and the inadequacies of most restorative materials currently available in effectively achieving a long-term seal means that an effective means of disinfecting both the infected and affected tissue is highly desirable before completion of treatment. If bacteria in infected but only partly demineralized tissue could be killed, even more tissue could be retained [18].

As reported by Zanin et al. [19], dental caries may be a disease well suited to photosensitization therapy. If bacteria within carious lesions could be eradicated in vivo by photosensitization, there would be beneficial consequences for dental health. Caries are often localized infections, and the photosensitizer could be applied to the lesion by means of a localized injection and light could then be delivered via an optical fiber upon the localized region. Infected or damaged dentine could be better preserved, thereby making patient treatment easier (for both dentist and patient) by enabling lesions to be restored with minimal tissue removal, and improving the long-term prognosis for the repaired tooth.

Araújo et al. [20] evaluated the current status of the photodynamic therapy (PDT) against cariogenic microorganisms by means of a systematic review. In total, 19 studies were reviewed. All but one in vitro studies assessed showed significant killing of microorganisms demonstrating the bactericidal effect of PDT against cariogenic bacteria. The results among all the studies evaluated were difficult to be compared, because of their heterogeneity regarding photosensitizer, light source, exposure time and photosensitizer incubation period before the irradiation. Based on the studies included in that systematic review, it was not possible to achieve a clinical protocol to apply the PDT in vivo and the authors concluded that further works are necessary to make this treatment clinically accessible and to determine the efficacy of PDT on carious dentin in vivo.

Considering the importance to establish the safety of the antimicrobial photodynamic therapy on dental pulp cells, once this tissue has limited remodeling potential, Diniz et al. [21] evaluated the effects of antimicrobial PDT (aPDT) directly applied on human primary pulp cell cultures. The analysis of cell viability showed that laser irradiation had no effect on cell viability. The photosensitizer used, methylene blue (MB), when applied in the lower concentrations (0.0125 and 0.025 mg/ml) caused a slight cytotoxicity, whereas higher MB concentration (0.050mg/ml) caused severe...
The cytotoxic effects of aPDT showed to be dye-concentration dependent. As higher the concentration of MB, greater was the reduction in cell viability. When MB was at minimal dose (0.0125 mg/ml), the percentage of cell death was considered slightly cytotoxic. In contrast, aPDT with MB concentrations of 0.025 and 0.050 mg/ml reduced cell viability in a severe mode. It was concluded that aPDT associating MB at low concentration (0.0125mg/ml) and red laser may represent a low-risk therapy for restorative dentistry applications. On the other hand, taken into consideration that this is an in vitro study with direct exposure of a cell monolayer to aPDT, which is an extreme experimental condition, one can conclude that the physiology of dental pulp in vivo could minimize aPDT effects. Therefore, aPDT with MB at 0.025 mg/ml might also be used to treat dentin caries. Antimicrobial PDT protocols using MB concentrations above 0.025 mg/ml and red laser irradiation, as described herein, may be harmful for dental pulp cells.

Araújo et al. [22] evaluated the antimicrobial effect of photodynamic therapy (PDT) in carious lesions in vivo by culture and real-time PCR methods (Figure 1 shows the clinical protocol of PDT in carious lesions in vivo). Ten teeth with deep active carious lesions were selected and five portions of carious dentin were removed for each tooth. Two increments were used as control, to represent the superficial and deep dentin, respectively. Methylene blue at 100mg/L was placed in contact with the cavity for five minutes, before being irradiated with a halogen light source for one minute. Then, after PDT, other three portions were removed. The samples were processed in laboratory and the number of viable colony forming units (CFU) was obtained. The Streptococcus mutans DNA was isolated from carious dentin samples removed before and after PDT and amplification and detection of DNA were performed with Real-Time PCR. The cavities were then restored with glass ionomer cement. Although PDT may not affect the number of S. mutans DNA copies immediately after the treatment, clear reduction of the number of CFU was found. As the samples were collected immediately after the application of PDT, there could not have given sufficient time to occur any damage to nucleic acids. There are two basic mechanisms that have been proposed to account for the lethal damage caused to bacteria by PDT: (a) DNA damage and (b) damage to the cytoplasmic membrane, allowing leakage of cellular contents or inactivation of membrane transport system and enzymes [23]. The authors concluded that more studies are need to bring new information on the application of PDT in the treatment of caries disease in order to improve the currently used conventional treatment, enabling one more way to avoid the cavity to be restored to be at a risk of suffering further recurrence of caries through reducing the number of viable microorganisms in the restoration.

PDT might also be used to control specific pathogenic microorganisms. According to the literature, periodontopathic germs (particularly Prevotella intermedia, Porphyromonas gingivalis, Fusobacterium nucleatum, and Actinobacillus actinomycetemcomitans) can be significantly reduced by low energy laser light if the cells are marked beforehand with photosensitive dyes [24].
Periodontitis is an inflammatory disease of the gingival tissue induced by bacteria residing in the plaque biofilm on the subgingival tooth surface. Periodontal disease is one of the most common diseases of the oral cavity and is the major cause of tooth loss in adults. Bacteria are the primary etiologic factor of periodontal diseases; however, recent evidence also lists yeast and herpes viruses as putative pathogens [25]. Meanwhile, our understanding of the pathogenic process has been hindered by the fact that it is usually the result of a polymicrobial infection including indigenous organisms with little pathogenic potential [26]. The body’s immune system fights the bacteria as the plaque spreads and grows below the gum line. Bacterial toxins and the body’s natural response to infection start to break down the bone and connective tissue that hold teeth in place. If not treated, the bones, gums, and tissue that support the teeth are destroyed.

The inflammation leads to pocket formation in the gum tissue, attachment loss, bone destruction, and ultimately, possible tooth loss. In industrialized nations, periodontitis affects 30–50% of the adults, 10% of them with severe symptoms. Due to its high prevalence, the disease imposes a serious public health concern. While specific microbial species are believed to play a role in the disease process, periodontal therapy today remains targeted toward removal of the plaque mass as opposed to elimination of specific pathogens. Scaling and root planning (SRP) have routinely been shown to be effective in treatment of chronic periodontitis without the concomitant use of systemic or local antimicrobials [27].

However, mechanical instrumentation has limitations and even with therapy, some patients still have attachment loss probably due to the persistence of periodontal pathogens and subsequent recolonization. Thus, the advent of other options to improve the effectiveness of periodontal therapy is needed due to limited access to furcation areas, concavities, grooves, distal sites of molars and deep pockets found during conventional periodontal therapy. The increase in bacterial resistance due to the use systemic antibiotics could also justify the appearance of other adjuvants for established periodontal treatment [28].

In this context, photodynamic therapy (PDT) appears as a method for microbial reduction, with minimal side effects. The procedure could be beneficial in areas of difficult access, reducing the need for flaps, treatment time and the risk of bacteremia. Balata et al. [29], in a randomized controlled clinical trial, evaluated the effects of PDT as an adjunct to full-mouth ultrasonic debridement in the treatment of severe chronic periodontitis. Twenty-two subjects were recruited. At least two teeth (one with a PD ≥7 mm and another with a PS ≥5 mm) were randomly assigned (by coin toss) to one of the treatments: with (test group) or without PDT (control group). PDT was performed on only one side of the mouth and the initial step was subgingival irrigation with 0.005% methylene blue dye. Two minutes after applying the photosensitizer, the low power laser – AsGaAl (Photon Lase III – PL7336, DMC, São Carlos –SP, Brazil) was applied in a 90 degree angle with the gingival surface and with no contact with the tissues (660 nm, 100 mW, 9 J, 90 seconds per site, 320 J/cm², diameter tip 600 μm). After treatment, the patients were included in a supportive periodontal therapy program, in which they received weekly supragingival plaque control during the first month attachment level (CAL). All parameters were collected before, 1, 3 and 6 months after treatment. Despite the existent biological plausibility in PDT, the results showed that PDT does not provide additional clinical benefit to non-surgical periodontal therapy.

A randomized controlled clinical study compared the effects of PDT alone without sub gingival SRP to sub gingival SRP in subject with aggressive periodontitis. At three months following the therapy, both treatment yielded comparable outcomes in terms of reduction of bleeding on probing and probing depth (PD), gains in clinical attachment level (CAL), thus suggesting a potential clinical benefits of PDT [30].

Dental implants have become an indispensable established therapy in dentistry in order to replace missing teeth in different clinical situations. In the last decades, increasing evidence raised on the presence of peri-implant inflammations representing one of the most frequent complications affecting both the surrounding soft and hard tissues which can lead to the loss of the implant. In addition to medication and manual treatment (e.g. with curettes, ultrasonic and air polishing systems) innovative techniques such as laser-supported and photodynamic therapy methods are recently described as conservative therapy options [31]. Basetti et al. [32] conducted a prospective randomized clinical trial, and after manual debridement by titanium curettes and glycine air powder treatment half of the patients received adjunctive photodynamic therapy and the other half received minocycline microspheres into implant pockets. After 12 months of follow-up, the number of periopathogenic bacteria and level of IL-1β decreased significantly in both groups without significant differences between them. In a study by Deppe et al. [33], regarding to the effectiveness of phototherapy on a moderate and severe peri-implantitis, both clinical attachment and bleeding index were significantly reduced suggesting that severe cases still resulted in bone resorption. As a recommendation, photodynamic therapy has to be considered as an additional treatment option. Due to the fact that it is a relatively new approach, the data is rare and there are no long-term-studies available. Further evaluations and prospective clinical trials are needed for evaluation [31].

The success of endodontic treatment is based on the effective decontamination of the root canal system, whereas microbial agents are essential for the development and maintenance of pathological processes that damage the pulp and periapical region [34].

Xu et al. [35] suggested that PDT can be used as an adjunct to endodontic disinfection without damaging the cells of periapical region in their evaluation of the in vitro effects of methylene blue at 50 μg/mL and irradiation with diode
light amplification by stimulated emission of radiation (LASER) at 665 nm for 5 min on human gingival fibroblasts and osteoblasts.

Oliveira et al. [36] reviewed the dental literature, describing the main factors involving antimicrobial effects of PDT combined with conventional endodontic treatment in the total disinfection of the root canal system. A literature search was performed using the following index databases: PubMed, ISI Web of Knowledge and MedLine, between 2000 and 2014, looking for studies regarding antimicrobial action of PDT and its application to endodontic therapy. The authors concluded that PDT is presented as an important auxiliary tool to antimicrobial substances commonly used in endodontic treatment. However, this therapy presents different challenges regarding its susceptibility to different microorganisms, according to their physiology. Thus, for PDT to be employed with maximum effectiveness is important that further studies be performed in order to determine appropriate parameters for energy dosage used, photosensitizer concentration, time of preradiation, and exposure.

After comparing the antimicrobial effects of PDT against Enterococcus faecalis in root canals, Garcez et al. [37] suggested that the use of an optical fiber/diffusor, when used for endodontic treatment, had better results than when laser light was used directed to access of the pulp cavity.

Soukos et al. [38] conducted a study to investigate the effect of PDT on endodontic pathogens in planktonic phase as well as on Enterococcus faecalis biofilms in experimentally infected root canals of extracted teeth. Strains of microorganisms were sensitized with methylene blue (25 μg/ml) for five minutes followed by exposure to red light of 665 nm with an energy florescence of 30 J/cm2. Methylene blue fully eliminated all bacterial species with the exception of Enterococcus faecalis (53% killed). The same concentration of methylene blue in combination with red light (222 J/cm2) was able to eliminate 97% of Enterococcus faecalis biofilm bacteria in root canals using an optical fiber with multiple cylindrical diffusers that uniformly distributed light at 360°. Hence, PDT may be developed as an adjunctive procedure to kill residual bacteria in the root canal system after standard endodontic treatment.

Lethal photosensitization of a wide range of bacteria responsible for caries, periodontal diseases and root canal infections has been demonstrated. With the recognition that each of these diseases is associated with a specific organism, or group of organisms, increasing interest is being shown in the use of antimicrobial agents to supplement these rather crude mechanical procedures. In all of the above-mentioned oral infections, the topical application of antimicrobial agents is an important part of disease prevention and/or treatment. PDT could provide an alternative to such agents as a means of killing bacteria in these situations, as access of the photosensitiser and light to the disease lesion presents no great difficulty in any of the three diseases [6]. PDT is proposed as a potential, low-cost approach to the treatment of oral infection and efforts should be undertaken to make this treatment clinically accessible to be used in vivo [20].

3. Natural products

Nowadays, natural products and phytotherapics have been widely used in dentistry. Plants with medicinal properties are useful and an effective source for treatment of various oral disease processes. The phytotherapeutic substances are generally classified into three groups: plant products, animal products and products of mineral origin [39]. In dentistry, they are used as anti-inflammatory substances such as Marticaria recutita Linn, irrigants such as Orange oil, sedative and ansiolitics products such as Arctium lappa and antimicrobial agents such as Acacia nilotica, Propolis and Aloe vera barbadensis [40]. Those products are used in cases of caries, apthous ulcers, lichen planus, alveolar osteitis, endodontic infection, gingivitis, oral infection, dentine tissue regeneration [41]. Natural products associated with minimal percent of antimicrobial [42] and antimicrobial medical devices are also used for implantology [43].

3.1 In cariology

Dental caries is a chronic disease, being considered the main oral health problem worldwide, this condition has a multifactorial etiology, where demographic, socioeconomic, behavioural, and biological risk factors that could be enrolled. The etiological agent of dental caries is Streptococcus mutans, this cariogenic bacteria is also the cause of dental pain and could lead to tooth loss, affecting oral health related quality of life [44]. Many antimicrobial agents in human saliva are known to have bacteriostatic or bactericidal effects against Streptococcus mutans. Studies carried out proved the antimicrobial activity of dentifrice containing Aloe vera have shown inhibition in the growth of organisms such as Streptococcus, S. mutans, S. sanguis and Candida albicans [45]. Clinical studies showed that mouthrinses and dentifrices containing Aloe vera have shown a remarkable reduction in gingivitis and plaque accumulation after its use [46, 47]. Other antimicrobial agents derivatives of plants such as Garlic (Allium sativum), Ginger (Zingiber officinale), Tulsi (Ocimum sanctum) are being proposed to reduce dental caries [48].

3.2 Natural product in Endodontics and oral pathology

Substances are used as antimicrobial irrigant agents because root canal irrigation plays a pivotal role in endodontics treatment. Due to the cytotoxic reactions of most of the commercial intracanal medicaments used, their inability to eliminate bacteria from dentinal tubules, constant increase in antibiotic resistance and side effects caused by synthetic
irrigants, the research has shifted toward developing herbal alternatives and the trend of recent medicine is to use biologic medication extracted from natural plants [49]. Even though chemo-mechanical preparation of root canal is able to reduce the number of bacteria, the intracanal medicament with antibacterial action is required to maximize the disinfection of root canal system [50]. The irrigating substances derive of Calcium hydroxide Ca(OH)2 are not effective in eliminating bacteria from the dentinal tubules. It was reported that Enterococcus faecalis present in dentinal tubules is resistant to Ca(OH)2 over 10 days [51]. Substance derivate of propolis can be used as an intracanal medicament or root canal irrigant, and can act as a maintenance environment for avulsed teeth to keep periodontal ligament cells viable. [52].

An experimental study showed that propolis had similar antibacterial effects that a formulation of 0.5 g of ciprofloxacin plus 0.5 g of minocycline or 0.2% chlorhexidine gel on E. faecalis in deep dentin. Considering the possible tooth discoloration with formulation based on those antibiotics, 0.2% CHX gel or propolis can be used as alternative intracanal medicaments in root canal treatment. In cases of gutta-percha removal procedure, the Orange oil or Narangah is composed mostly of d-limonene. It also has a long chain aliphatic hydrocarbon alcohols, aldehydes like octanal. It is suggested as an alternative to chloroform or xylene for gutta-percha softening and also in dissolving endodontic sealers. On the other hand, the orange oil can allow a better recovery of the periapical tissues to be a biocompatible material.

In oral pathology propolis has been used as antifungal agent against Candida albicans because is an opportunistic fungal pathogen found as part of the normal microflora and in immunosuppressed patient. Propolis is a resinous substance collected by Apis mellifera from various tree buds that are used to coat hive parts and to seal cracks and crevices in the hive [53]. Recently, numerous biological properties of propolis have been reported including antimicrobial, antiviral, free radical scavenging, and antitumoral activities were reviewed [54]. An in vivo study conducted to evaluate the antimicrobial efficacy of propolis against C. albicans showed excellent effect to control antifungal activity. Although some studies have focused on showing the antifungal activity of propolis extract, few studies have shown their effects on morphology and structure of C. albicans [55, 56]. Concerning the antimicrobial activity of propolis phenols, C. albicans was the most resistant and S. aureus the most sensitive propolis. The reference microorganisms were more sensitive than the ones isolated from biological fluids [57, 58]. However, there is a necessity of identification of target microorganism and factors associated with the infection. The usefulness of these agent in endodontic is limited to studies based on clinical evidence in order to prevent side effect on the periapical area and systemic.

3.3 Natural products for control of inflammation

Natural products can play an important role in the oral diseases treatment, as some of them can be included in mouthrinses or tooth pastes. Among natural products, essential oils are promising therapeutic tools for oral infections. These oils are complex mixtures of volatile compounds obtained from plants, such as the terpenoids, with antioxidant and antimicrobial properties against a wide range of pathogens, including C. albicans and dermatophytes [59]. In dentistry some derivatives of essential oils have been used since the early days of the profession. This fact is due to the antimicrobial and analgesic power offering by terpenic derivatives such carvacrol, terpinen-4-ol, and α-terpineol) [60].

An in vitro study about the activity of eight terpenic derivatives (carvacrol, farnesol, geraniol, linalool, menthol, menthone, terpinen-4-ol, and α-terpineol), a phenylpropanoid (eugenol) and a phenethyl alcohol (tyrosol) were evaluated against oral Candida isolates from patients suffering from denture stomatitis [61]. Leaves and barks of S. terebinthifolius contain tannins, flavonoids, saponins and essential oils. The activity of these oils has been associated to anti-inflammatory properties and might enhance the healing effect provided by the tannins [62].

An important evidence of efficacy of a Schinus terebinthifolius (ST) mouthwash in reducing gingival inflammation levels (GI) and biofilm accumulation (BA) in children with gingivitis was investigated. This was a randomized, controlled, triple blind, and phase II clinical trial, with children aged 9–13 years presenting with biofilm-induced gingivitis. The sample was randomized into experimental (0.3125% ST) and control (0.12% chlorhexidine/CHX) groups. Gingival bleeding and simplified oral hygiene indexes were used to assess the efficacy variables. It was found that both ST and CHX were able to significantly reduce GI levels after 10 days, and there was no significant difference between them. ST mouthwash showed significant anti-inflammatory activity (equivalent to CHX), but it was not able to reduce biofilm accumulation [63].

Although, the enormous benefits related with the use of natural products to treat and prevent oral diseases, various aspects have been associated with their use such as: poor water solubility, limited intestinal absorption and low water stability of phytochemicals generally prevented from achieving a high oral bioavailability and even detectable plasma levels of the parent compound [64].

In conclusion, this review showed the state-of-the-art of PDT and naturals products, which have been used to merge alternative to antibiotic agents, in order to decrease the side effect and to avoid the rising microbial resistance. These alternatives are being developed and despite the fact that natural products have been used widely since antiquity for several purposes, there is an urgent need to standardize their use and to study accurately the actual effective concentrations, as well as toxic, allergenic, irritant and adverse effects of these products. It will be necessary for the dentists to have an understanding of all the technical and scientific knowledge about these substances, to be possible to
have a satisfactory therapeutic result. PDT is proposed as a potential, low-cost approach to the treatment of oral infection and efforts should be undertaken to make this treatment clinically accessible to be used in vivo [20].

References


Palombo EA. Traditional medicinal plant extracts and natural products with activity against oral bacteria; potential application in prevention and treatment of oral diseases. Evid Based Complement Alternat Med. 2011, 680354


Sinha Dakshita J, Sinha Ashish A . Natural medicaments in dentistry. AYU. 2014 35: 2, 113-118


