Review Article
Volume 9:3,2020
DOI: 10.37421/aim.2020.9.293

Alternative and Integrative Medicine

ISSN: 2327-5162 Open Access

Challenges of Inappropriate Antibiotic Prescription in Dentistry and Threat of Antimicrobial Resistance in Developing Countries-Medicinal Plants to the Rescue

Onoriode Oyiborhoro*

Department of Biochemistry, Faculty of Basic Medical Sciences, University of Medical Sciences, Ondo State, Nigeria

Abstract

Studies have revealed that Dentists across the globe are widely involved in the inappropriate prescription of broad spectrum antibiotics, a practice that is believed to contribute significantly to the current problem of antimicrobial resistance. The factors responsible for the inappropriate prescription of antibiotics by Dentists vary from country to country but the aim of such prescriptions appears to be universal-prevention of possible post-operative infections and complications. In developing countries, Dentists face some unique challenges that make such inappropriate prescription of antibiotics almost inevitable. Some of such challenges include an epileptic power supply and lack of potable water, both of which facilitate the poor infection control practices prevalent in these countries. The invasive nature of minor procedures such as simple tooth extractions and frequent use of poorly sterilized metal-based reusable equipment contribute to an increased risk of transmission of infections in dental practice. In the search for alternative antimicrobial drugs, medicinal plants have been observed to be potential sources of safer and cheaper agents, when compared to synthetic antibiotics. Interestingly, extracts from medicinal plants have long been applied for the treatment of oral infections and maintenance of oral health in many parts of the world, including developing countries, where they are widely distributed. Surprisingly, a very limited number of these extracts, if any, have found their way into the clinics as refined agents such as tablets, for the prophylactic control of post-operative infections in dentistry, especially in developing countries. This is largely due to lack of confidence on the part of Dentists and poor co-ordination among research institutions, pharmaceutical companies and regulatory bodies in these nations. This review therefore seeks to reawaken the interest of all parties concerned, on the need to harness the potentials of medicinal plants in solving the problem of inappropriate antibiotics prescription in dentistry.

Keywords: Antibiotics; Antimicrobial resistance; Dentistry; Medicinal plants; Developing countries

Introduction

The global community is currently grappling with a severe threat of antimicrobial resistance, resulting in part, from the inappropriate prescription and widespread abuse of synthetic broad spectrum antibiotics [1]. This global threat of antimicrobial resistance calls for urgent attention, especially in developing countries, where there is high prevalence of infectious diseases, widespread poverty and lack of standardized infectious disease control mechanism, even in tertiary health institutions. Some of the factors that have been identified to contribute to widespread antimicrobial resistance in developing countries include indiscriminate sale and purchase of antibiotics, inadequate patient education, limited diagnostic facilities, non-human use of antimicrobials, poor drug regulatory mechanisms and very importantly, inappropriate prescription practices by healthcare professionals [2].

Among other factors, the widespread inappropriate prescription, especially of broad spectrum antibiotics by healthcare providers, including Dentists, is a major contributor to the high prevalence of antimicrobial resistance across the globe [3]. However, the problem of inappropriate prescription of broad spectrum antibiotics in most developing countries can be attributed to several factors (Figure 1). In the first instance, there is acute shortage of modern diagnostic facilities and qualified laboratory personnel for effective and accurate detection of microbial strains responsible for most of the infections that are prevalent in these countries. Consequently, bed-side diagnosis of such specific causative microbial agents is completely lacking, even though this is highly essential for prescription of appropriate antibiotics to which identified organisms are susceptible. In most cases, doctors in developing countries are left with no other option than to prescribe broad spectrum antibiotics to which the suspected organisms are likely going to be susceptible. Ordinarily, such broad spectrum antibiotics might not be among the first choice of antibiotics, if antimicrobial susceptibility tests and results are readily available.

Secondly, even when facilities for rapid detection of antibiotic susceptibility patterns are made available, mostly by international donors and non-governmental organizations, shortage of basic amenities such as steady electricity and pipe-borne water supply often hinder the optimum utilization of such facilities for the benefit of patients. Also, there are poor infection control mechanisms in most hospital environments in developing countries. Consequently, simple procedures that should ordinarily not require prescription of antibiotics are usually done under the cover of broad spectrum antibiotics, even in immune-competent individuals, with a view to preventing acquisition of nosocomial infections. This practice contributes massively to widespread resistance of bacteria to conventional synthetic antibiotics, especially in sub-specialties such as dentistry where most procedures, including simple extractions are invasive, even in the midst of poor infection control practices.

***Corresponding author:** Onoriode Oyiborhoro, Department of Biochemistry, Faculty of Basic Medical Sciences, University of Medical Sciences, Ondo State, Nigeria, Tel: +2348168257357; E-mail: doconos2013@gmail.com*

***Received date:** May 23, 2020; **Accepted date:** June 4, 2020; **Published date:** June 11, 2020*

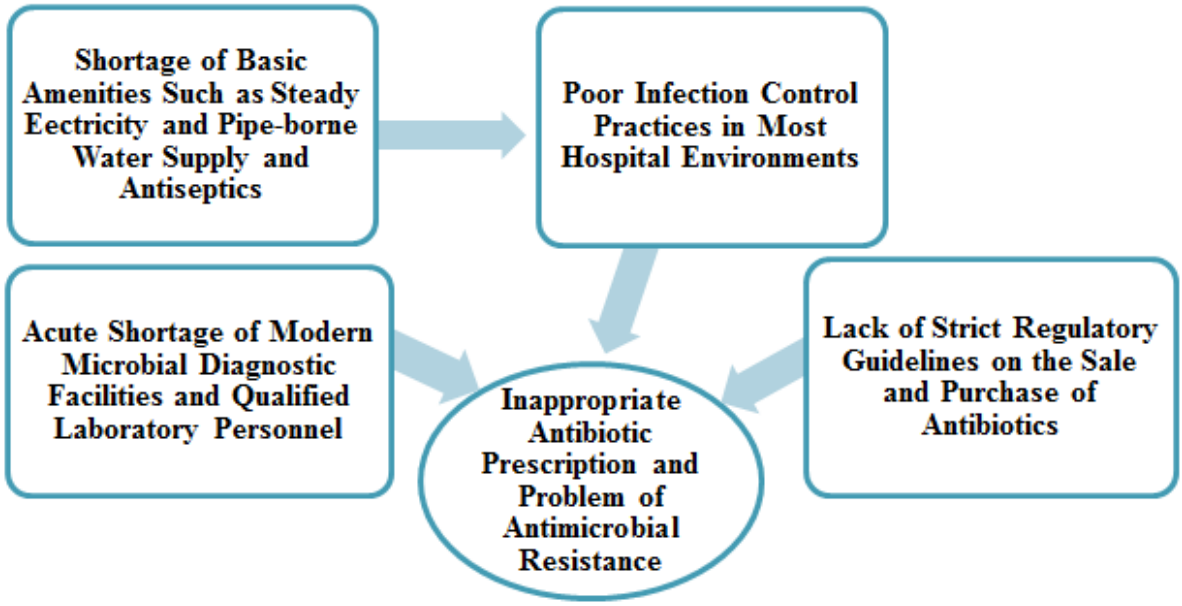

Figure 1: Factors contributing to the problem of inappropriate antibiotics prescription and antimicrobial resistance in developing countries.

These and other factors are worsened by unrestricted availability, unauthorized sale and indiscriminate purchase of antibiotics, especially broad spectrum antibiotics, facilitated by lack of appropriate and strict regulatory mechanisms in most developing countries [2]. The implication of this is that pharmacies, patent medicine dealers and even market stalls, are oftentimes involved in unauthorized prescription and sale of antibiotics to the unsuspecting public [4]. All relevant regulatory agencies must wake up to their responsibilities of curtailing the problem of antimicrobial resistance arising from antibiotic abuse.

Literature Review

Dental caries as an infectious disease

Dental caries is the most common infectious disease affecting humans, while caries-induced toothache is believed to be the most common reason why patients visit the dentist [5-7]. The infectious nature of dental caries was established long ago through the non-specific and specific plaque hypotheses, both of which identified presence of bacteria as a pre-requisite for caries development and progression. Among other factors such as refined sugars, susceptible tooth and time, the non-specific plaque hypothesis of dental caries suggested that in the presence of high concentration of refined sugars, bacterial colonization of surfaces of affected teeth was responsible for caries formation, without reference to specific species of plaque bacteria. Proponents of this hypothesis believed that all species of oral bacteria were potentially cariogenic and prevention of the dental caries should therefore be focused on mechanical removal of plaque bacteria through effective brushing of tooth surfaces [8].

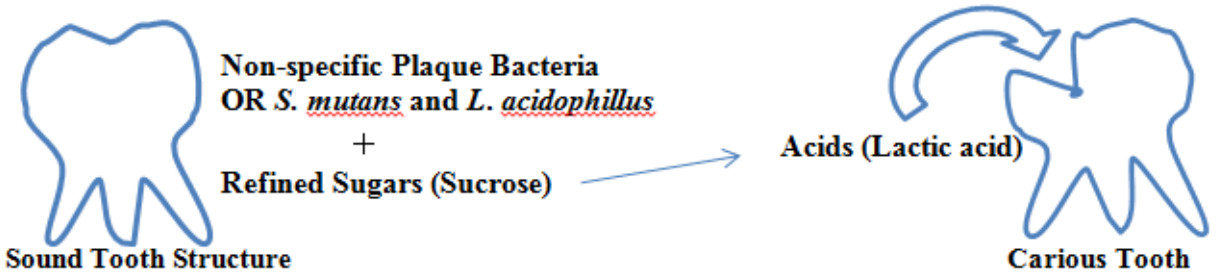

Figure 2: Schematic representation of the role of bacteria and refined sugars in caries formation.

In contrast to the non-specific plaque hypothesis, the experiments that led to the establishment of the specific plaque hypothesis of dental caries were able to demonstrate the role of specific organisms, including *Streptococcus* and *Lactobacillus* species in the development and progression of dental caries [9]. This hypothesis therefore suggests that use of antibiotics targeted against these organisms could potentially prevent and treat dental caries, as against the previous non-specific mechanical plaque removal of the non-specific plaque hypothesis. However, a major setback for the specific plaque hypothesis was the observation that withdrawal of antibiotics resulted in recurrence of disease, while prolonged treatment was associated with development of resistance overtime [8].

Under both hypotheses, pathogenic oral bacteria act on refined sugars, especially sucrose, to produce acids such as lactic acid which demineralizes dental hard tissues (enamel and dentine), leading to caries formation (Figure 2) [9]. Cariogenic *Streptococcus mutans* and *Lactobacillus acidophilus* were further observed to thrive in the presence of synthesized acids (aciduric) hence, perpetuates the disease, unless the process is reversed through

reduction in the consumption of refined sugars, tooth re-mineralization, excavation of carious lesion/restoration of tooth structure and reduction in the population of pathogenic oral bacteria by use of antibiotics [10,11]. Apart from their inappropriate use for treatment of dental caries, broad spectrum antibiotics are also currently prescribed inappropriately for the prevention of possible post-operative and hospital acquired infections, following simple dental procedures such as simple tooth extractions, deep scaling and cavity restorations. Considering the contribution of such inappropriate prescription and use of antibiotics in dentistry to the current global threat of antimicrobial resistance, there is need for development of newer and safer alternative antimicrobial agents and medicinal plants are ideal sources of such agents, from an historical perspective.

Medicinal plants as potential sources of antimicrobial agents in dentistry

Across the globe, extracts from numerous medicinal plants have been studied and observed to possess significant antimicrobial activities against cariogenic oral bacteria such as *Streptococcus mutans* and *Lactobacillus acidophilus*. Similar studies have revealed inhibitory effects of these extracts against multi-species oral biofilms which are believed to promote formation and development of dental caries and other common oral pathologies.

In an elaborate study on the antimicrobial activity of 27 medicinal plants against pathogenic oral organisms, study observed significant activity in extracts from plants such as Ginkgo biloba, *Pinus virginiana*, *Albizia julibrissin*, *Juniperus virginiana*, *Rosmarinus officinalis* and *Tanacetum vulgare*, among others [12]. The compound allicin has been isolated from garlic or *Allium sativum* (Liliaceae), a popular medicinal plant across the globe. Allicin is known to possess strong antimicrobial activity against isolated pathogenic oral organisms, even at Minimum Inhibitory Concentrations (MIC) values as low as 1.1 mg mL^{-1} [13].

Also, the ethyl acetate extract of the leaves of *Harungana madagascariensi*, a popular plant of African origin, has been tested for antimicrobial activity against cariogenic organisms, including *Streptococcus mutans, Lactobacillus acidophilus* and Actinomyces and observed to kill all three organisms. The antimicrobial activity of this extract was further observed to be enhanced by poly (D, L–lactide-co-glycolide) nanoparticles [14]. Other studies also revealed significant antimicrobial activities of commercially available and freshly prepared aqueous propanone extracts of beverages such as green tea, unfermented cocoa and seeds of red grape against isolated *Streptococcus mutans* [15]. These extracts were also observed to inhibit the adhesion of *Streptococcus mutans* to glass surfaces, suggesting some anti-biofilm activities hence their capacity to prevent formation of plaque and dental caries. The high polyphenol content of these beverages also suggest that other high polyphenol-containing foods and beverages including red wines could also possess significant antimicrobial activities against cariogenic oral bacteria.

Furthermore, extracts from four Brazilian medicinal plants, including *Cocos nucifera*, *Ziziphus joazeiro*, *Caesalpinia pyramidalis* and *Aristolochia cymbifera* were studied for activity against isolated pathogenic oral organisms. Extracts from all four plants showed activity against test organisms, with the ethanol extract of *Aristolochia cymbifera* producing the highest activity, with Minimum Inhibitory Concentrations (MIC) ranging between 0.1 to 4.0 mg mL^{-1} [16]. In South Africa, extracts from the plants *Annona senegalensis* and *Euclea natalensis* also showed activity against isolated oral pathogens, although at higher MIC values greater than 25 mg mL^{-1} [17]. Studies in India have also suggested that extracts from some medicinal plants of Indian origin, including *Aleo barbadensis* (aleo vera), *Zingiber officinale* (ginger), *Azadirachta indica* (neem), *Ocimum sanctum* (tulsi) and *Emblica officinalis* (amla) could also function as potential sources of antimicrobial agents against cariogenic *Streptococcus mutans* [18]. For example, bioactive compounds such as carvacrol, ursolic and eugenol have been isolated from *Ocimum sanctum* and observed to possess strong antimicrobial effects [19].

The compound eugenol is widely used in both medical and dental practice, due to its observed antibacterial, anti-inflammatory, anti-oxidant, anticancer and analgesic properties. Previous studies had revealed that eugenol could significantly inhibit the acid-producing capacity of *Streptococcus mutans*, as well as synthesis of water-insoluble glucans by glycosyl transferases. Results from these studies also demonstrated the ability of eugenol to suppress the adhesion of *Streptococcus mutans* to saliva-coated hydroxyapatite crystals, while reducing the occurrence and severity of dental caries in rats.

Other bioactive compounds of plant origin that have been studied for activity against *Streptococcus mutans*, *Lactobacillus acidophilus* and Actinimyces species include the isoprenylflavones artocarpin and artocarpesin, both of which were isolated from the plant *Artocarpus heterophylus*. Results obtained revealed activity against these organisms, with MIC values of between 3.13 and 12.5 µg mL^{-1} [20].

Screening of medicinal plants for antimicrobial activities in Kenya has also revealed strong inhibitory effects of methanol and acetone extracts of *Vernonia adoensis* stem bark against some isolated pathogenic oral organisms, with diameters of zones of inhibition ranging between 9 mm and 16 mm [21]. Finally, the plant *Spilanthes oleracea*, popularly known as toothache plant is an important medicinal plant in India, Brazil and several tropical countries of Africa, where it is widely applied for treatment of toothaches and other oral infections. Studies on plant samples of Nigerian origin were able to demonstrate potent antimicrobial activities of methanol and chloroform extracts of *Spilanthes oleracea* leaves and flowers against a group of isolated oral bacteria, including *Streptococcus mutans*, *Lactobacillus acidophilus*, *Pseudomonas aeruginosa* and *Streptococcus pyogens* [22]. At the highest concentration of 20 mg/mL, these extracts produced diameters of zones of inhibition ranging between 21 mm and 29 mm in Agar Well Diffusion studies, as against the 34 mm produced by 10 µg/mL concentration of standard ciprofloxacin.

Inappropriate antibiotics prescription in dentistry and antimicrobial resistance

Among authorized healthcare providers, Dentists have a significant role to play in minimizing the problem of inappropriate prescription of broad spectrum antibiotics, since they are believed to prescribe approximately 10% of all common antibiotics, oftentimes, inappropriately [23]. In an ideal situation and standard practice, dental procedures like simple tooth extractions and cavity restorations could be done in immune-competent individuals without prescription of broad spectrum antibiotics, especially when such procedures are done under strictly sterile conditions. This however, is not usually the case, as most Dentists, especially in developing countries, continue to prescribe broad spectrum antibiotics after simple dental procedures, for reasons previously highlighted [24]. For example, a typical routine post-operative prescription after a simple tooth extraction in most dental clinics in Nigeria includes 500 mg Amoxicillin, 6 hourly for 5 days; 400 mg Metronidazole, 6 hourly for 5 days and 1 g Paracetamol, 8 hourly, for 3 days.

In Jeddah, studies have also revealed poor compliance or adherence of Dentists to professional guidelines on antibiotic prescription, even among prescriptions made for children [25]. These and other similar practices have contributed immensely to the current global threat of antimicrobial resistance and urgent steps need to be taken, in order to reverse the trend. For example, studies in the past have observed significant resistance of pathogenic oral organisms isolated from active carious lesions to some antibiotics commonly prescribed in dentistry, including Amoxicillin and Metronodazole [24,26].

Although rampant in developing countries, the problem of inappropriate prescription of antibiotics by Dentists is not limited to developing nations of the world. In technologically advanced societies where simple dental procedures are expected to be done under strictly sterile conditions that

should eliminate the inappropriate prescription of antibiotics, Dentists are still responsible for a reasonably high proportion of inappropriate antibiotic prescriptions in countries such as Germany and the United Kingdom [27,28]. Some of the reasons that have been put forward as being responsible for the inappropriate prescription of antibiotics by Dentists in Europe include lack of follow-up time by practitioners, especially during weekends and holidays, when such prescriptions are intended to cover for their absence and consequent lack of follow-up in the clinics [27]. In England, dental prescriptions have been observed to account for about 5% of all antimicrobial prescriptions, even when such prescriptions are not completely approved for treatment of oral infections [28]. Similar to Nigeria, most Dentists in England were found to commonly prescribe Amoxicillin (61.2% of prescriptions) for 5 or 7 days and Metronidazole (29.9% of prescriptions) for 5 days, in 65.2% of patients [29].

According to an article published in the Journal of American Dental Association (JADA), approximately 10% of all antibiotics prescribed for outpatients in the US was made by Dentists, amounting to about 24.5 million courses of antibiotics, with some regions having dental antibiotics prescription rate as high as 99.5 per 1000 people [30]. These findings suggest a global trend in the inappropriate prescription of common antibiotics, especially Amoxicillin and Metronidazole, by Dentists, a situation that is most likely responsible for the high resistance of pathogenic oral bacteria to these antibiotics [31].

More worrisome is the fact that some of these antibiotics are components of the first line of choice of antibiotics for more serious complications of oral infections such as Acute Necrotizing Ulcerative Gingivitis (ANUG) and Ludwig's Angina. Frequent and inappropriate exposure of immune-competent dental patients to these antibiotics exposes them to a grave danger of developing resistance to these antibiotics, such that they become ineffective when required for management of life-threatening systemic infections in the future [32]. Apart from systemic complications of oral infections, dental patients with inappropriate exposures to common antibiotics are also at risk of developing resistance to antibiotics used for treatment of other infections such as respiratory, gastrointestinal and urinary tract infections. Such increased risk of resistance arises as a result of cross-resistance, where organisms begin to development resistance to a completely new set of antibiotics, as a result of resistance to other antibiotics to which they were previously inappropriately exposed. Indeed, most of these infections have been observed to be leading causes of morbidity and mortality in developing countries [33].

Considering the high prevalence of oral infections, especially dental caries and periodontal diseases, coupled with widespread inappropriate prescription of antibiotics by Dentists, the fight against the global threat of antimicrobial resistance cannot be won without the cooperation of Dentists across the globe. According to the Faculty of General Dental Practice (FGDP), UK Guidelines on Antimicrobial Prescribing for General Dental Practitioners, all antibiotics should be prescribed only for the appropriate clinical case and in the correct dosage, frequency and duration. The guideline further recommends that Amoxicillin and Metronidazole should only be prescribed as an adjunct to the treatment of dentoalveolar infections in order to limit the spread of infection. Also, Metronidazole should be the drug of choice for Acute Necrotizing Ulcerative Gingivitis (ANUG) and Pericoronitis, while duration of treatment should be limited to 5 days for Amoxicillin and 3 days for Metronidazole [29].

There were no indications that antibiotics should be prescribed for cavity restorations and simple tooth extractions, as commonly practiced in most developing countries such as Nigeria. It is however, worthy of note that Dentists are faced with some unique challenges that make the inappropriate prescription of broad spectrum antibiotics almost inevitable, especially in developing countries. For example, dental patients are particularly at risk of hospital acquired infections as a result of direct contact with several hospital equipment, dental instruments and other restorative materials which are introduced directly into the oral cavity during oral examination and treatment [34]. The risk of acquiring such infections is even increased in developing countries where most dental procedures are carried out in environments that are not sterile enough to prevent both direct and cross infections. The situation is worsened by the fact that majority of these procedures are surgical or invasive, with direct contact between surgical instruments and the bloodstream (Figure 3).

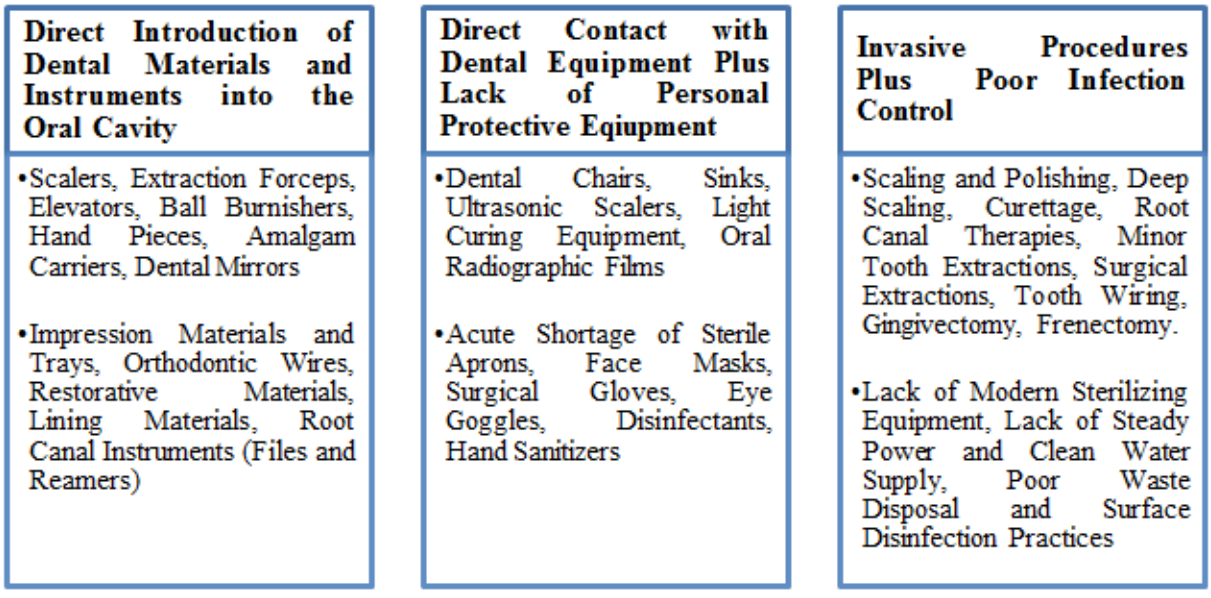

Figure 3: Factors contributing to increased risk of direct and cross infection in dental practice in developing countries.

In attempting to minimize possible perioperative and postoperative infections in dental practice, most Dentists in developing countries prescribe broad spectrum antibiotics on a prophylactic basis, even after minor procedures such as simple tooth extractions and cavity restorations [24]. There is therefore the need to urgently address the situation and search for alternative ways of preventing common nosocomial and post-operative infections in dentistry, especially in developing countries. Here in lies the importance of medicinal plants with antimicrobial activities, especially in developing countries of tropical West Africa and other continents such as Asia, blessed with abundance of medicinal plants and herbs.

Use of medicinal plants with antimicrobial activities in oral health care products

Improvements in scientific research and better collaboration between research institutions and the industry have led to substantial transformation of crude extracts of medicinal plants into several important home care products such as perfumes, body creams, hair creams, aftershaves surface disinfectants and insecticides. In the area of dental care, crude extracts of medicinal plants with potent antimicrobial activities against pathogenic oral bacteria have also been applied in several forms such as chewing sticks, herbal toothpastes, mouth washes, mouth sprays and herbal tablets for the prevention and treatment of oral infections and maintenance of oral health. Although a large number of stems of medicinal plants have long been used as chewing sticks in many African cultures, fewer number of herbal toothpastes and more limited number of herbal tablets have been developed from these plants, leaving room for more improvements (Figure 4).

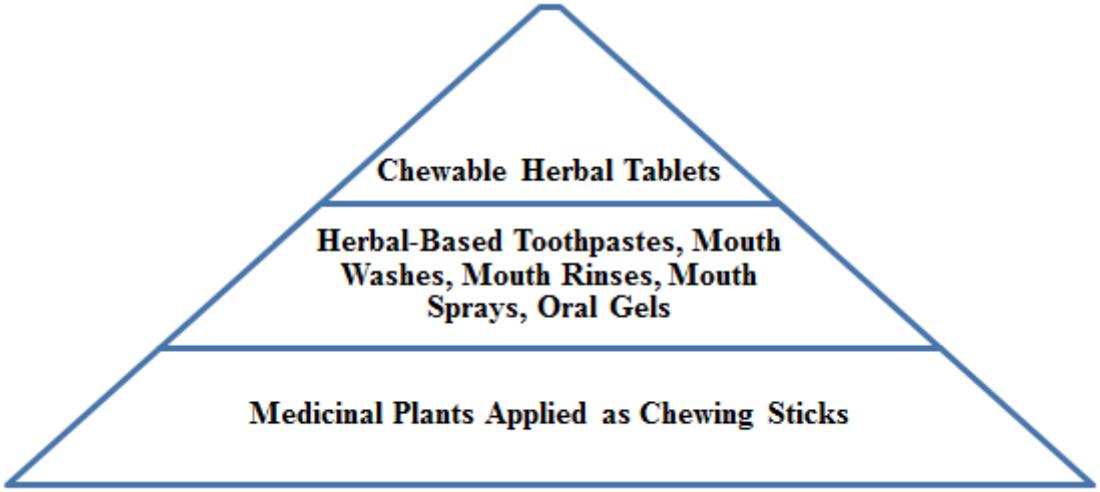

Figure 4: Pyramid showing the different modes of application of medicinal plants and their extracts for oral health care.

Medicinal plants as chewing sticks

The pharmacological properties of medicinal plants, including their antimicrobial, anti-inflammatory, anti-nociceptive and analgesic properties have long been harnessed for the prevention and treatment of oral infections and diseases either in their crude or purified forms. For example, the use of stems of medicinal plants as chewing sticks (plant-based toothbrushes) is a common traditional oral care practice among Africans. Studies had previously observed that use of such chewing sticks could prevent the formation of dental plaque hence, reduce the incidences of dental caries and gingivitis among users [35].

Jatropha curcas: The plant *Jatropha curcas* of the family Euphorbiaceae is a tropical and sub-tropical plant that has its origin from Central America. The stem of *Jatropha curcas* is commonly used as a chewing stick for the prevention of oral infections and maintenance of oral health, while extracts from different parts of the plant have been reported to possess strong antimicrobial activities against oral pathogens [36,37].

Rhus vulgaris and *Lantana trifolia*: Researchers in Uganda had also identified eight plants that are commonly used as chewing sticks in rural settlements and studied them for antibacterial activities against cariogenic *Streptococcus mutans*. Results obtained revealed that aqueous extracts of *Rhus vulgaris* and *Lantana trifolia*, the two most commonly used plants possess strong antimicrobial effects against *Streptococcus mutans*, with mean diameters of zones of inhibition of 24.33 ± 0.29 mm and 14.17 ± 0.29 mm, respectively. The former result compared favourably with the 30.67 ± 0.29 mm obtained for standard benzyl penicillin [38].

Salvadora persica (Miswak): Studies on extracts from *Salvadora persica* had also revealed strong antimicrobial activity against isolated *Streptococcus mutans*, *Lactobacillus acidophilus*, *Porphyromonas gingivalis*, *Haemophilus influenza* and *Staphylococcus aureus*, while regular chewing of this plant twice daily was found to reduce the chances of developing dental caries and gingivitis [39,40]. Extracts of *Salvadora persica* were also observed to function better as disinfectants for dental root canals during Root Canal Therapies (RCTs), when compared with sodium hypochlorite, the most commonly used agent for RCTs [41].

Disthemonanthus benthamianus Baill and *Zanthoxylum zanthoxyloides* Lam: In Nigeria, *Disthemonanthus benthamianus* (Caesalpiniaceae) and *Zanthoxylum zanthoxyloides* (Rutaceae) are two important medicinal plants commonly used as chewing sticks. The ethanol and aqueous extracts of both plants have been shown to possess strong antimicrobial activities against several oral pathogens, including *Pseudomonas aeruginosa*, *Candida albicans* and methicillin-resistant strains of *Staphylococcus epidermidis* [42].

Limitations of use of conventional toothpastes for oral care

Some of the active components of conventional toothpastes include synthetic agents such as fluoride, chlorhexidine and triclosan [43]. Fluoride is usually absorbed systemically from sources such as water, milk, salt or fluoride supplements and incorporated into dental hard tissues such as enamel and dentine during tooth development, with minimal topical effects on erupted teeth [44,45]. Topical fluorides are obtained from toothpastes, mouthwashes and gels and are mainly involved in the inhibition of plaque bacteria and reduction in enamel demineralization with consequent prevention of caries formation [46]. The use of systemic and topical fluoride has therefore been observed to produce significant anti-cariogenic effects [47]. However, the specific amount of fluoride-containing water, milk and salt required to produce desired anti-cariogenic effects is usually difficult to ascertain [48]. Also, there are limited scientific methods for assessing the effectiveness of systemic and topical fluorides in preventing and controlling dental caries [49].

Furthermore, presence of fluoride in conventional toothpastes has been associated with some negative side effects. For example, studies in children have revealed adverse effects of fluoride on cognitive development, especially when ingested in high concentrations [50]. Similar studies on fluoridated water consumed by iodine-deficient children suggest that fluoride levels as low as 0.9 ppm in water could lead to development of intellectual deficits [51]. The situation is even worse in fluoridated toothpastes, where presence of flavouring agents makes them to become very appealing to children, whose swallowing reflexes are yet to fully develop. Consequently, children exposed to fluoridated toothpastes have the tendency to swallow excess amounts of fluoride, which predisposes them to neurotoxicity of fluoride [52]. Other possible negative effects of excess fluoride consumption

in children and adults include dental fluorosis, skeletal fluorosis, renal complications, fetal defects and hypersensitivity of the gastrointestinal tract [53]. Use of chlorhexidine for oral care has been associated with dry mouth, irritation of the oral tissues, pigmentation of enamel and tongue and alterations in the sense of taste; while triclosan binds poorly to dental tissues [54].

Extracts of edible medicinal plants as components of toothpastes and mouthwashes

Apart from being applied in their crude and natural forms as chewing sticks for the control of dental caries and gingivitis, antimicrobial components of medicinal plants have also been formulated into herbal toothpastes, with some advantages over conventional chemical based toothpastes. In contrast to synthetic chemical agents, most of the medicinal plants with antimicrobial activities against cariogenic bacteria also function as important vegetables and spices in many local African cultures.

The plant *Syzygium aromaticum* (clove) is an important aromatic spice in countries like India, Indonesia, Southern China and Nigeria, where it is commonly used for preparation of local dishes and soups [54]. Similarly, *Dennettia tripetala*, popularly called pepper fruit, is an important fruit in Western Cameroon, Ivory Coast and Nigeria [55]. The pungent spicy nature of *Dennettia tripetala* also makes it suitable as a condiment, with phytochemicals such as saponins, flavonoids, tannins, alkaloids, terpenoids and glycosides identified to be responsible for its pharmacological activities [54]. Also, fresh leaves of *Spilanthes oleracea* (toothache plant) is widely consumed as a vegetable in soups or used as a flavouring agent in salads or spices in stews [56].

Use of medicinal plants with antimicrobial activities as components of important dishes in many cultures suggest that these plants and their important phytochemicals are potentially safe and less toxic as components of herbal toothpastes, when compared to the synthetic chemical constituents of conventional toothpastes. Consequently, extracts and bioactive components of medicinal plants have also been applied in the formulation of herbal toothpastes, where they function as important antibacterial agents in the prevention and control of dental caries as well as maintenance of oral health. For example, extracts from *Salvadora persica* (miswak) have been successfully incorporated into commercial herbal toothpastes such as Sarkan toothpaste, QualiMeswak toothpaste, Epident toothpaste and Siwak-F toothpaste in the United Kingdom, Switzerland, Egypt and Indonesia, respectively [57].

Apart from chewing sticks and herbal toothpastes, the antimicrobial agents of medicinal plants are also important constituents of mouthwashes, mouth sprays and gels, for the control of several oral infections. Some of these products have been successfully registered and patented in countries such as the United States, United Kingdom and Australia. For example, the company A. Vogel Australia Pty. Ltd. markets the Dentaforce herbal mouth wash and mouth spray which are produced from *Spilanthes oleracea* extracts and used for the treatment of gingivitis and periodontal diseases [56].

Majority of the herbal oral healthcare products have been studied for antimicrobial activities and observed to possess strong antimicrobial effects against oral pathogens, including cariogenic *Streptococcus mutans* and *Lactobacillus acidophilus*. Using Agar Well Diffusion and Broth Dilution techniques, studied the antimicrobial activities of herbal toothpastes formulated from extracts of *Syzygium aromaticum*, *Dennettia tripetala* and *Jatropha curcas* latex against isolated organisms such as *Streptococcus mutans*, *Lactobacilus acidophilus*, *Candida albicans*, *Streptococcus pyogens* and *Staphylococcus epidermidis* [54]. Results obtained revealed potent antimicrobial effects against the test organisms, with diameters of zones of inhibition and MIC ranging between 4.0 mm and 18.3 mm and 2.5 mg/mL and 20.0 mg/mL respectively.

Extracts of medicinal plants as components of chewable herbal tablets for oral care

Attempts have also been made in the past to develop extracts from medicinal plants with antimicrobial activities against oral pathogens into chewable herbal tablets, with advantages of better taste and compliance, when compared to conventional synthetic agents. The development of chewable tablets from aqueous extracts of guava has previously been described, using methods, with 1 g of each tablet comprising crude extracts, 10% solution of PVP K 30, mannitol, aerosil, magnesium stearate, papermint and menthol [58,59]. Assessment of the antimicrobial activity of crude extracts used for tablet formulation revealed significant activity against isolated *Streptococcus mutans*, with diameters of zones of inhibition of 12.50 ± 0.71 mm, as against the 13 mm produced by the standard antibiotic, kanamycin. Formulated herbal tablets also exhibited bactericidal activities against *Streptococcus mutans*, with 32 × MIC reducing total colony counts to zero within 2 to 3 hours, in time kill studies. These findings suggest that chewable herbal tablets could be used for treatment of dental caries [59].

These findings further indicate that if properly harnessed, the antimicrobial components of medicinal plants can be enhanced to serve as replacements for synthetic antibiotics such as amoxicillin and metronidazole in the prophylactic management of nosocomial and post-operative infections in dentistry. Consequently, the introduction of herbal tablets and their widespread acceptance could potentially eliminate the inappropriate prescription of synthetic antibiotics and reserve them for treatment of more serious cases with systemic manifestations, as indicated in the 2019 guidelines on antibiotics prescription in dentistry. Unfortunately, herbal tablets are rarely available in the dental clinics, especially in developing countries, where they are mostly needed, due to the poor infection control practices.

Discussion

If the fight against antimicrobial resistance is to be won, a holistic assessment of all factors contributing to the problem must be done, in addition to the increased search for new antimicrobial agents. Social factors such as widespread poverty, lack of access to potable water and constant electricity supplies and corruption within the health sector are some of the factors contributing to the poor infection control in hospitals and lack of modern diagnostic facilities in the healthcare system of most developing countries. Consequently, there is increased risk of transmission and poor diagnosis of nosocomial infections within the hospital environment, especially in sub-specialties such as dentistry, where there is frequent direct contact between surgical instruments and patients' bloodstream. Dentists in developing countries are quite aware of these challenges and are faced with two options of either prescribing broad spectrum antibiotics inappropriately; or obeying the guidelines on the prescription of antibiotics in dentistry and exposing their patients to increased risks of contracting infections. Current practices suggest that the former option is being implemented, which unfortunately, has compounded the problem of antimicrobial resistance, not only in developing countries but also in advanced nations of the world where antibiotics are also inappropriately prescribed by Dentists for various other reasons.

Conclusion

There is currently an unprecedented global increase in the level of confidence and use of medicinal plant extracts for treatment of infectious diseases hence, medicinal plants with antimicrobial effects appear to be the solution to the rising problem of antimicrobial resistance, especially in dentistry. Developing countries are important reservoirs of medicinal plants with antimicrobial effects, even in the presence of poor infection control practices. These countries are therefore positioned to benefit largely from the potentials that are inherent in such medicinal plants. Over the years, extracts from these plants have been applied in different forms for maintenance of oral health and treatment of dental diseases, with the potential of functioning as alternatives to synthetic antibiotics in the prophylactic management of post-operative oral infections. However, the success of medicinal plants as

antidotes to the problem of antimicrobial resistance, especially in dentistry, would require establishment of guidelines and modernization of scientific methods and protocols used for the transfer of bioactive antimicrobial agents of medicinal plants from the forests and gardens to the clinics. Research institutions must also partner with indigenous pharmaceutical companies, in order to increase the confidence of Dentists in the prescription of drugs of medicinal plant origin for treatment of oral diseases.

Acknowledgement

The author acknowledges the contribution of Enoh F. Akpojotor, who typed most of the manuscript.

References

1. Llor, Carl, and Lars Bjerrum. "Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem." *Ther Adv Drug Saf* 5 (2014): 229-241.
2. Ayukekbong, James, Michel Ntemgwa and Andrew Atabe. "The threat of antimicrobial resistance in developing countries: causes and control strategies." *Antimicrob Resist Infect Control* 6 (2017): 47.
3. Suchi, Khurana, and Jodalli Praveen "Antibiotics in dentistry. A Boon or Bane." *J Dent App* 2 (2015): 132-137.
4. Hart, Cahmm and Samuel Kariuki. "Antimicrobial resistance in developing countries." *BMJ* 317 (1998): 647-650.
5. Balakrishnan, Mayooran, Robin Sessa Simmonds and John Tagg. "Dental caries is a preventable infectious disease." *Aust Dent J* 45 (2000): 235-245.
6. World Health Organization. "Oral Health Report." (2018).
7. Ekanayake, Lilani, Yuichi Ando, and Hideo Miyazaki. "Patterns and factors affecting dental utilization among adolescents in Sri Lanka." *Int Dent J* 51 (2001): 353-358.
8. Rosier, Bob, Marko De Jager, Egija Zaura and Bastiaan Krom. "Historical and contemporary hypotheses on the development of oral diseases: are we there yet?" *Front Cell Infect Microbiol* 4 (2014): 92.
9. Hoceini, Amina, Nihel Klouche Khelil, Ilhem Ben-Yelles and Amine Mesli, et al. "Caries-related factors and bacterial composition of supragingival plaques in caries free and caries active Algerian adults." *Asian Pac J Trop Biomed* 6 (2016): 720-726.
10. Rathee Manu and Sapra Amit. "Dental Caries." *In: StatPearls Publishing* (2019).
11. Qiu, Wei, Yujie Zhou, Zixin Li and Tu Huang, et al. "Application of Antibiotics/ Antimicrobial Agents on Dental Caries." *Biomed Res Int* (2020).
12. Tichy, Josef and Jan Novak. "Extraction, assay, and analysis of antimicrobials from plants with activity against dental pathogens (*Streptococcus* sp.)." *J Altern Complement Med* 4 (1998): 39-45.
13. Bakri, Issam and CW Ian Douglas. "Inhibitory effect of garlic extract on oral bacteria." *Arch Oral Biol* 50 (2005): 645-651.
14. Moulari, Brice, Hassan Lboutounne, Jean-Pierre Chaumont and Yves Guillaume, et al. "Potentiation of the bactericidal activity of *Harungana madagascariensis* Lam. ex Poir.(Hypericaceae) leaf extract against oral bacteria using poly (D, L-lactide-co-glycolide) nanoparticles: *in vitro* study." *Acta Odontologica Scandinavica* 64 (2006): 153-158.
15. Smullen, Joanne, Greorge Koutsou, Howard Foster and Albert Zumbé, et al. "The antibacterial activity of plant extracts containing polyphenols against *Streptococcus mutans*." *Caries Res* 41 (2007): 342-349.
16. Alviano, Wagner, Daniela Alviano, Cláudio Galuppo Diniz and Angelo Antoniolli, et al. "*In vitro* antioxidant potential of medicinal plant extracts and their activities against oral bacteria based on Brazilian folk medicine." *Arch Oral Biol* 53 (2008): 545-552.
17. More, Garland, Thilivhali Emmanuel Tshikalange, Namrita Lall and Francina Botha, et al. "Antimicrobial activity of medicinal plants against oral microorganisms." *J Ethnopharmacol* 119 (2008): 473-477.
18. Jain, Isha, Pranat Jain, Dakshina Bisht and Amitkumar Sharma, et al. "Use of traditional Indian plants in the inhibition of caries-causing bacteria-*Streptococcus mutans*." *Braz Dent J* 26 (2015): 110-115.
19. Agarwal, Pooja, and Nagesh Lakshminarayan. "Evaluation of the antimicrobial activity of various concentrations of Tulsi (Ocimum sanctum) extract against *Streptococcus mutans*: An *in vitro* study." *Indian J Dent Res* 21 (2010): 357-359.
20. Sato, Masaru, Shuu Fujiwara, Hironori Tsuchiya and Teruhisa Fujii, et al. "Flavones with antibacterial activity against cariogenic bacteria." *J Ethnopharmacol* 54 (1996): 171-176.
21. Muhindi, Stephen, Chrispus Mutuku Ngule and Francis Ramesh. "Phytochemical and antibacterial potential of *Vernonia adoensis* stem bark to curb cariogenic microorganisms." *Am J Phytomedicine Clin Ther* 4 (2016): 19-27.
22. Onoriode, Oyiborhoro and Emmanuel O Oshomoh. "Antibacterial activity of methanol and chloroform extracts of Spilanthes oleracea plant on isolated pathogenic oral bacteria." *J App Sci Environ Manag* 22 (2018): 237-245.
23. Pallasch, Thomas. "Global antibiotic resistance and its impact on the dental community." *J N J Dent Assoc* 71 (2000): 14-15.
24. Onoriode, Oyiborhoro, Emmanuel O Oshomoh and Enoh Akpojotor. "Susceptibility Pattern of Isolated Pathogenic Oral Bacteria to Some Commonly Prescribed Antibiotics in Dental and General Medical Practice." *J Drug Deliv Ther* 9 (2019): 83-89.
25. Al-Johani, Khalid, Sid Goud Reddy, AS Al Mushayt and Azza El-Housseiny. "Pattern of prescription of antibiotics among dental practitioners in Jeddah, KSA: A cross-sectional survey." *Niger J Clin Pract* 20 (2017): 804-810.
26. Dwivedi, Deepak, Tejram Kushwah, Mukesh Kushwah and Vinod Singh. "Antibiotic susceptibility pattern against pathogenic bacteria causing Dental Caries." *South Asi J Exp Biol* 1 (2011): 31-35.
27. Loffler, Christin, Femke Bohmer, Anne Hornung and Hermann Lang, et al. "Dental care resistance prevention and antibiotic prescribing modification-the cluster-randomised controlled DREAM trial." *Implement Sci* 9 (2014): 27.
28. Zahabiyoun Sana, Sahabi Mahasti and Mohammad Javad Kharazi. "Improving Knowledge of General dental Practitioners on Antibiotic Prescribing by Raising Awareness of the Faculty of General Dental Practice (UK) Guidelines." *J Dent* 12 (2015): 171-176.
29. Sturrock, Andrew, D Landes, T Robson and L Bird, et al. "An audit of antimicrobial prescribing by dental practitioners in the north east of England and Cumbria." *BMC Oral Health* 18 (2018): 206.
30. Roberts, Rebecca, Monina Bartoces, Sydney Thompson and Lauri Hicks. "Antibiotic prescribing by general dentists in the United States, 2013." *J Am Dent Assoc* 148 (2017): 172-178.
31. Haque, Mainul, Massimo Sartelli and Seraj Zohurul Haque. "Dental Infection and Resistance-Global Health Consequences." *Dent J* 7 (2019): 22.
32. Sweeney, Louise, Jayshree Dave, Philip Chambers and John Heritage. "Antibiotic resistance in general dental practice-a cause for concern?" *J Antimicrob Chemother* 53 (2004): 567-576.
33. Okeke, Iruka, Ramanan Laxminarayan, Zulfiqar Bhutta and Adriano Duse, et al. "Antimicrobial resistance in developing countries. Part I: recent trends and current status." *Lancet Infect Dis* 5 (2005): 481-493.
34. Laheij, Amga, JO Kistler, Georgios Belibasakis and Hannamari Valimaa, et al. "Healthcare-associated viral and bacterial infections in dentistry." *J Oral Microbiol* 4 (2012): 17659.
35. Akpata, Enosakhare Samuel, and Ezekiel Olabisi Akinrimisi. "Antibacterial activity of extracts from some African chewing sticks." *Oral Surg Oral Med Oral Pathol* 44 (1977): 717-722.

36. Upadhyay, Bhuvaneshwar, Shikha Roy and Ashwani Kumar. "Traditional uses of medicinal plants among the rural communities of Churu district in the Thar Desert, India." *J Ethnopharmacol* 113 (2007): 387-399.
37. Garba, Saidu and SO Okeniyi. "Antimicrobial activities of total alkaloids extracted from some Nigerian medicinal plants." *J Microbiol Antimicrob* 4 (2011): 60-63.
38. Odongo, Charles Okot, Nathan Lubowa Musisi, Paul Waako and Celestino Obua. "Chewing-stick practices using plants with anti-streptococcal activity in a Ugandan rural community." *Front Pharmacol* 2 (2011): 13.
39. Sofrata, Abier, Peter Lingstrom, Mostafa Baljoon and Anders Gustafsson. "The effect of miswak extract on plaque pH." *Caries Res* 41 (2007): 451-454.
40. Lafi, Abdul G Al and H Ababneh. "The effect of the extract of the miswak (chewing sticks) used in Jordan and the Middle East on oral bacteria." *Int Dent J* 45, no. 3 (1995): 218-222.
41. Al-Sabawi, Nawal, Abdul-Khalik K. Al Sheikh Abdal and Mahmoud YM Taha. "The antimicrobial activity of *Salvadora persica* solution (miswak-siwak) as root canal irrigant (a comparative study)." *J Pure Appl Sci* 4 (2007): 69-91.
42. Adebiyi, Akindele Olupelumi, Tian Koekemoer, Abayomi Peter Adebiyi and N Smith, et al. "Antimicrobial and antioxidant activities of crude extracts of two Nigerian chewing sticks." *Pharm Biol* 47 (2009): 320-327.
43. Maripandi, Arjunan, Arun Kumar, and Ali A Al-Salamah. "Prevalence of dental caries bacterial pathogens and evaluation of inhibitory concentration effect on different tooth pastes against *Streptococcus* spp." *Afr J Microbiol Res* 5 (2011): 1778-1783.
44. Sket, Tea, Andreja Kukec and Barbara Artnik. "The history of public health use of fluorides in caries prevention." *Slovenian J Pub Health* 56 (2017): 140-146.
45. Rosin-Grget Kata, Kristina Peros, Ivana Sutej and Kresimir Basic. "The cariostatic mechanisms of fluoride." *Acta Medical Academy* 42 (2013): 179-188.
46. Buzalaf, Marília Afonso Rabelo, Juliano Pelim Pessan, Heitor Marques Honório and Jacob Martien Ten Cate. "Mechanisms of action of fluoride for caries control." *In Fluoride and the oral environment* 22 (2011): 97-114.
47. Kumar, Jayanth, and Mark Eric Moss. "Fluorides in dental public health programs." *Dent Clin North Am* 52 (2008): 387-401.
48. Espelid, Ivar. "Caries preventive effect of fluoride in milk, salt and tablets: A literature review." *Eur Arch Paediatr Dent* 10 (2009): 149-156.
49. Marinho, Valeria CC. "Cochrane reviews of randomized trials of fluoride therapies for preventing dental caries." *Eur Arch Paediatr Dent* 10 (2009): 183-191.
50. Choi, Anna, Guifan Sun, Ying Zhang and Philippe Grandjean. "Developmental fluoride neurotoxicity: A systematic review and meta-analysis." *Environ Health Perspect* 120 (2012): 1362-1368.
51. Fa-Fu, Lin, Hong-Xin Zhao Aihaiti, Lin Jin and Jiang Ji-Yong, et al. "The relationship of a low-iodine and high-fluoride environment to subclinical cretinism in Xinjiang." *Iodine Deficiency Disorder Newsletter* 7 (1991): 24-25.
52. Baez, Ramon, Poul Erik Petersen and Thomas Marthaler. "Basic methods for assessment of renal fluoride excretion in community prevention programmes for oral health." *World Health Organization* (2014).
53. Ullah, Rizwan, Muhammad Sohail Zafar and Nazish Shahani. "Potential fluoride toxicity from oral medicaments: A review." *Iran J Basic Med Sci* 20 (2017): 841-848.
54. Oluwasina, Olugbenga Oludayo, Ifunanya Vivian Ezenwosu, Clement Olusola Ogidi and Victor Olusegun Oyetayo. "Antimicrobial potential of toothpaste formulated from extracts of *Syzygium aromaticum*, *Dennettia tripetala* and *Jatropha curcas* latex against some oral pathogenic microorganisms." *AMB Express* 9 (2019): 20.
55. Etukudo Inyang. "Forest, Our Divine Treasure." *Dorland Publisher* (2000): 24.
56. Paulraj, Jayaraj, Raghavan Govindarajan and Pushpangadan Palpu. "The genus Spilanthes ethnopharmacology, phytochemistry, and pharmacological properties: A review." *Adv Pharmacol Sci* (2013): 1-12.
57. Niazi, Fayez Hussian, Mustafa Naseem, Zohaib Khurshid Sultan and Muhammad Zafar, et al. "Role of *Salvadora persica* chewing stick (miswak): A natural toothbrush for holistic oral health." *Eur J Dent* 10 (2016): 301-308.
58. Shangraw, Rick, Michael Liberman, Liebermans Lachman and JB Schhwartz. "Pharmaceutical dosage forms, tablets." (1989): 367-415.
59. Saraya, S, J Kanta, N Sarisuta and Rungravi Temsiririrkkul, et al. "Development of guava extract chewable tablets for anticariogenic activity against *Streptococcus mutans*." *Mah Univer Jou of Pharma Sci* 35 (2008): 18-23.

How to cite this article: Onoriode Oyiborhoro. "Challenges of Inappropriate Antibiotic Prescription in Dentistry and Threat of Antimicrobial Resistance in Developing Countries-Medicinal Plants to the Rescue". Altern Integ Med 9 (2020) doi: 10.37421/aim.2020.9.293