ABSTRACT
Oral diseases are major health problems with dental caries and periodontal diseases among the most important preventable global infectious diseases. Oral health influences the general quality of life and poor oral health is linked to chronic conditions and systemic diseases. The association between oral diseases and the oral micro biota is well established. The development of dental caries involves acidogenic and aciduric Gram-positive bacteria (mutans streptococci, lactobacilli and actinomyces). Periodontal diseases have been linked to anaerobic Gram-negative bacteria (Porphyromonas gingivalis, Actinobacillus, Prevotella and Fusobacterium). Several agents are commercially available these chemicals can alter oral micro biota and have undesirable side-effects such as vomiting, diarrhoea and tooth staining. Hence, the search for alternative products continues and natural phytochemicals isolated from plants used as traditional medicines are considered as good alternatives. In this review, plant extracts or phytochemicals that inhibit the growth of oral pathogens, reduce the development of bio films and dental plaque, influence the adhesion of bacteria to surfaces and reduce the symptoms of oral diseases.

Keywords: Periodontal diseases, oral pathogens, dental caries, dental plaque, periodontitis

INTRODUCTION
The relationship between the microorganisms found in dental plaque and the common dental disease of periodontitis has undergone numerous phases historically. Early in the 19th century, it was felt that, like the situation with diseases such as tuberculosis, a specific bacterial species was responsible for the disease processes. The criteria by which a given bacterial species was associated with disease historically has been through the application of Koch's Postulates. These criteria were developed by Robert Koch in the late 1800's. The criteria are as follows:
1. A specific organism can always be found in association with a given disease.
2. The organism can be isolated and grown in pure culture in the laboratory.
3. The pure culture will produce the disease when inoculated into a susceptible animal.
4. It is possible to recover the organism in pure culture from the experimentally infected animal.

However, the concept that a specific bacterial species was responsible for periodontal diseases fell out of favor for several reasons. First, despite numerous attempts, a specific bacterial agent was not isolated from diseased individuals. Rather, the organisms found associated with disease were also found associated with health. Good experimental animal model systems of periodontal disease were not available to test the pathogenicity of specific microorganisms (this, in fact, remains problematic today). Further, in the mid 1900's, epidemiological studies indicated that the older an individual was, the more likely they were to have periodontal disease. This led to the concept that the bacterial plaque itself, irrespective of the specific bacteria found in plaque, was associated with disease. This concept, known as the Non-Specific Plaque Hypothesis, held that all bacteria were equally effective in causing disease. Several important developments caused a change in this thinking. First, it was realized that organisms that are found as part of the "normal" bacterial flora (i.e., found in health), may function as pathogens under certain conditions. These organisms may be altered, or increase significantly in numbers relative to other non-pathogenic species, to function as pathogens: This type of bacterial pathogen is referred to as an endogenous pathogen, in contrast to an organism that is not normally found in healthy states which is termed an exogenous pathogen. Secondly, tremendous advances were made in the 1960's and 1970's in techniques used to culture anaerobic microorganisms (bacterial species that cannot grow in the presence of oxygen). These advances were related to the anaerobic culturing conditions as well as the nutrients required in media to grow anaerobic species, which are typically very fastidious in their nutrient requirements. The growth of anaerobic microorganisms, and examination of their properties using in vitro and in vivo model systems, has now led us back to the understanding that different microorganisms have varying potential to cause disease. Thus, the current concept of the processes involved in the development of periodontal diseases fall under the Specific Plaque Hypothesis. The Specific Plaque Hypothesis states that disease results from the action of one or several specific pathogenic species and is often associated with a relative increase in the numbers of these organisms found in plaque.

Other species that have been implicated as pathogens, including Fusobacterium nucleatum, Prevotella intermedia, Eikenella corrodens, Campylobacter rectus, Bacteroides forsythus, and the oral spirochetes of the genus Treponema. It is important to note that the disease processes involve not only pathogenic microorganisms, but also a susceptible host. Further, many microorganisms function to the benefit of the host, by inhibiting the growth of potential pathogenic species. One example of such an interaction is Streptococcus sanguis, which produces hydrogen peroxide that is lethal for Actinobacillus actinomycetemcomitans. Despite tremendous increases in our understanding of the pathogenic properties of specific plaque microorganisms and the role of specific microorganisms in the disease process, current therapy in periodontics is largely non-specific. The treatments that we utilize (e.g., oral hygiene measures, debridement by scaling and root planning, or even the currently available mouthwashes) are oriented towards reducing the accumulation of plaque on the teeth. Future developments in periodontics will involve the development of therapies which prevent the colonization or growth of specific microorganisms that are known to function as pathogens in this environment.

PERIODONTITIS
Periodontitis is now seen as resulting from a complex interplay of bacterial infection and host response, often modified by behavioral factors. Advances in research over recent years have led to a fundamental change in the periodontal disease model. The prevailing model of periodontal disease in the 1960s suggested that all individuals are susceptible to severe periodontitis; that gingivitis progresses to periodontitis with consequent bone and tooth loss, and that the susceptibility to periodontitis increases with age. All aspects of this model are under strong challenge from the results of more recent research. The belief in universal susceptibility has given way to the current view that only some 20% of any population suffer
from severe generalized periodontitis, even though moderate
disease affects a majority of adults. Risk factors, such as smoking,
have a profound effect on the predisposition to periodontal disease.3
There is now a clear association between smoking and periodontal
diseases, independent of oral hygiene, age, or any other risk factor.
Smokers have shown there is no difference between smokers and
non-smokers in amounts of plaque accumulation, or in the
prevalence of the principal bacteria which are considered
pathogenic for periodontitis. What smoking appears to do is
suppress the vascular reaction which follows gingivitis. In effect this
is a masking effect on the signs of inflammation. Smoking may also
be a factor in the interaction between periodontal disease and
polymorph nuclear leukocyte defect in the peripheral blood. There is
also some evidence that smoking is associated with osteoporosis;
the link with dental alveolar bone loss is currently under study.
In human periodontitis, there is no simple, direct pathogen-disease
link. More than 500 bacteria have been identified within periodontal
pockets. Moreover, it is impossible to accurately associate the
complex microbiota in a periodontal lesion, in a given patient, with
the bacterial species that may have contributed to development of
that lesion. Much evidence suggests, however, that a finite set of
pathogenic microbiota, sometimes working alone, or in
 combinations, cause periodontal diseases in humans.5 Most
pathogens associated with periodontal lesions are Gram-negative
 anaerobic rods, while some pathogens are also Gram-positive
facultative and anaerobic cocci and rods, and Gram-negative
 facultative rods. Due to this mixed variety of pathogens, and their
variability in sensitivity to antibiotics, simplistic antimicrobial
colonization therapy is impractical. Three pathogens have an especially
strong association with the presence of progressive periodontal
disease: Actinobacillus actinomycetemcomitans, spirochetes of acute
 necrotizing gingivitis, and Porphyromonas gingivalis. One potential
virulence factor recently ascribed to P. gingivalis and A.
actinomycetemcomitans, which is shared by a number of respiratory
and enteric pathogens, is the ability to enter mammalian cells.6 These
pathogens are very often the cause of continued loss of
periodontal attachment despite diligent conventional mechanical
periodontal therapy, as well as causing refractory periodontitis,
localized juvenile periodontitis, and other types of early-onset
periodontitis. Patients who suffer from these conditions may benefit
from antibiotic therapy. Evaluation of the patient’s periodontal
status requires obtaining a relevant medical and dental history and
conducting a thorough clinical and radiographic examination, with
evaluation of extra oral and intraoral structures.1 A medical history
should be taken and evaluated to identify predisposing conditions
that may affect treatment. Patient medical and oral health
conditions include, but are not limited to, diabetes, hypertension,
and pregnancy. Factors which may also play a role in treatment
outcome are smoking, substance abuse and medications. Adult
periodontitis is defined as inflammation of the gingiva and the
adjacent dental attachment apparatus. The disease is characterized
by loss of clinical attachment due to destruction of the periodontal
ligament and loss of the adjacent supporting bone. As mentioned
previously, dental plaque bacteria play a key role in what is now
understood to be the complex process by which the common types
of oral diseases occur: dental caries and periodontal diseases.5 As
with other infectious diseases, there is a balance between the host
immune responses on one hand and the microbial pathogenesis on
the other hand. In health, host immune responses are sufficient to
hold in check the pathogenic potential of both the normal resident
microbial flora and exogenous microbial pathogens. Infectious
diseases such as periodontal disease occur when this equilibrium is
disturbed. Clinical features may include combinations of the
following signs and symptoms: edema, erythema, gingival bleeding
upon probing and/or suppuration.13 Adult periodontitis with slight
to moderate destruction is characterized by a loss of up to 1/3 of the
supporting periodontal tissues; a loss of over 1/3 of the periodontal
supporting tissues is seen in advanced adult periodontitis.
Radiographic evidence of bone loss is apparent in advanced adult
periodontitis, and may be evident in adult periodontitis with slight
to moderate destruction. Adult periodontitis with slight to
moderate or advanced loss of periodontal supporting tissues may be
localized, involving one area of a tooth’s attachment, or more generalized,
involving several teeth or the entire dentition.14 A patient may
simultaneously have areas of health and adult periodontitis with slight,
moderate, and advanced destruction.

PERIODONTITIS ASSOCIATED WITH SYSTEMIC CONDITIONS
A number of systemic factors have been documented as capable of
affecting the periodontium and/or treatment of periodontal disease.
Systemic etiologic components may be suspected in patients who
exhibit periodontal inflammation or destruction which appears
disproportionate to the local irritants. Periodontal therapy may be
modified based on the current medical status of the patients.
Periodontal organisms may be the source of infections elsewhere in
the body. Therefore, those infections may also affect systemic
health.6 The therapeutic goal is to achieve a degree of periodontal
health consistent with the patients overall health status. Achieving
this goal, however, may be directly affected by the degree of control
of the systemic condition. The systemic and psychological status of
the patient should be identified, therefore, to reduce medical risks
that may compromise or alter the periodontal treatment.

The human oral cavity is a complex biological system in which
members of a diverse microbial community interact with themselves
as well as with different host structures and components. It has been
reported that this cavity is colonized by approximately 500 bacterial
species most of which are still poorly characterized. The bacterial
flora of this human cavity includes a wide range of bacterial cell
types as well as important fungi such as Candida albicans, while
some of them are classified as opportunistic pathogens capable of
causing severe infections in compromised patients. Although
complex, the interactions among the members of the oral flora
develop according to reproducible temporal and spatial patterns,
a process that results in co-aggregation-mediated interactions and the
formation of multi-species microbial biofilms known as dental
plaque.15 These cell arrangements allow microorganisms to prosper
in a hostile environment, which is the case for the significant clinical
bacterial pathogens that prosper in the human host. These cell
structures are the result of specific microbial-microbial and
microbial-host interactions, which play a role in the ability of
microbial cells to evade the host response and resist antimicrobial
agents. Furthermore, there is evidence that bio films play a
significant role in the horizontal transfer of genetic material among
members of these cell aggregates a process that facilitates their
adaptation to different ecological niches. Most of the knowledge
available to date with regard to the microbial and host factors and
processes involved in these interactions has been obtained with
classical techniques based on the utilization of molecular genetic
and molecular biology. Although these approaches have produced
important and novel information, they have provided a rather
narrow picture of these complex interactions. In contrast, a holistic
view of the genetic blueprint of a bacterial cell can be readily
obtained once its entire genome is sequenced with automated
methods and annotated in databases that contain comparative
sequences. This genome-wide approach, which uses tools such as
genomics and bioinformatics, is based mainly in the comparative
analysis of gene content and structure among different bacterial cells
and gene expression under different physiological conditions using
DNA arrays. Whole-genome comparisons and transcriptome
analysis have the benefit of providing wider and more
comprehensive information regarding the genome structures and
gene expression patterns that will facilitate the understanding of the
evolution and adaptation of bacterial pathogens, and the complex
mechanisms by which they interact with their hosts. For example,
the application of DNA microarrays and global transcriptional
analysis has facilitated the study of the interaction between the
pathogenesis and the analysis of gene expression under different environmental
conditions, respectively, of important bacterial pathogens such as
Escherichia coli and Pseudomonas aeruginosa. These studies have provided
novel and important information with regard to lateral gene transfer and the role of
pathogenicity factors or pathogenicity factors. For example, the virulence attributes
of bacteria to particular hosts and the complex mechanisms by which they interact
with their hosts. For example, the application of DNA microarrays and global transcriptional
analysis has facilitated the study of the interaction between the
pathogenesis and the analysis of gene expression under different environmental
conditions, respectively, of important bacterial pathogens such as
Escherichia coli and Pseudomonas aeruginosa. These studies have provided
novel and important information with regard to lateral gene transfer and the role of
pathogenicity factors or pathogenicity factors.
are completely sequenced and annotated, a process that is near completion for several of them. However, there are investigators who have not waited until the genomes of oral bacteria were completely annotated and published, and have already started these types of analyses with some oral pathogens18. Streptococcus mutans, a major pathogen of dental caries, has been detected in heart valves and isolated from the blood of patients with infective endocarditis (IE), suggesting its close relationship with infective endocarditis. S. mutans is classified into four serotypes (c/d/e/f/k) based on the chemical composition of its cell surface serotype-specific rhamnose–glucose polymers (RPGPs), which form a backbone of rhamnose polymers with side chains of glucose polymer. Serotype c is reported to be the most prevalent in oral isolates at approximately 70–80 %, followed by e, f and k. In our previous study, four S. mutans strains isolated from the blood of patients with bacteremia after tooth extraction or IE were characterized; however, none of those strains were classified as serotype c. The serotype-specific RPGPs of S. mutans were demonstrated to play important roles in streptococcal adherence to human monocytic and fibroblastic cells, and speculated to be its most efficient cytokine-stimulating components. In addition, the hydrophile nature of RPGPs is known to be associated with the resistance to phagocytosis by human polymorphonuclear leukocytes. Further, RPGPs were shown to possess properties allowing them to bind directly to human platelets and trigger their aggregation in a dose-dependent manner. In our previous study, serotype k strains featured a drastic reduction in the amount of glucose side chains and were shown to be less susceptible to phagocytosis by human polymorphonuclear leukocytes than the parent strain. However, the virulence of each serotype of S. mutans in blood remains to be elucidated. Recently, the association of cardiovascular diseases and periodontitis has received attention because of results showing that periodontopathic bacterial DNA could be detected in the diseased cardiovascular tissues. We previously reported that not only periodontopathic bacterial species, but also several streptococcal species, were detected in cardiovascular specimens, such as heart valve and atheromatous plaque, and S. mutans was the most frequently detected. In the present study, detection of S. mutans in additional specimens, as well as serotype determination of S. mutans-positive specimens was carried out18. The main diseases of the teeth include plaque, caries and pyorrhoea. Proper dental care is necessary for eliminating tooth decay and periodontal diseases. The people living in Indian subcontinent largely depend on the traditional systems for the treatment of toothache, caries and other diseases related to teeth. The traditional herbal products are often used in dental care as a component of dental powder, such as essential oils, have been reviewed previously. Medicinal plants have been used as traditional treatments for numerous human diseases for thousands of years and in many parts of the world. In rural areas of the developing countries, they continue to be used as the primary source of medicine. About 80% of the people in developing countries use traditional medicines for their health care. The natural products derived from medicinal plants have proven to be an abundant source of biologically active compounds, many of which have been the basis for the development of new lead chemicals for pharmaceuticals. With respect to diseases caused by microorganisms, the increasing resistance in many common pathogens to currently used therapeutic agents, such as antibiotics and antiviral agents, has led to renewed interest in the discovery of novel anti-infective compounds. As there are approximately 500 000 plant species occurring worldwide, of which only 1% has been phytochemically investigated, there is great potential for discovering novel bioactive compounds. There have been numerous reports of the use of traditional plants and natural products for the treatment of oral diseases. Many plant-derived medicines used in traditional medicinal systems have been recorded in pharmacopoeias as agents recommended for the alleviation of toothache. Cinnamomum verum bark is an astringent and is thus useful for checking the bleeding of gums. The essential oil of C. verum has antimicrobial and antibacterial properties. Accacia nilotica bark and ash of almond kernel can be pulverized together and mixed with common salt to make a highly effective preparation to contain pyorrhoea and for strengthening of gums by making them strong. Use of clove oil is recommended for the alleviation of toothache.

CURE FOR DENTAL DISEASES

Traditional Plant-Based Medicines

Medicinal plants have been used as traditional treatments for numerous human diseases for thousands of years and in many parts of the world. In rural areas of the developing countries, they continue to be used as the primary source of medicine. About 80% of the people in developing countries use traditional medicines for their health care. The natural products derived from medicinal plants have proven to be an abundant source of biologically active compounds, many of which have been the basis for the development of new lead chemicals for pharmaceuticals. With respect to diseases caused by microorganisms, the increasing resistance in many common pathogens to currently used therapeutic agents, such as antibiotics and antiviral agents, has led to renewed interest in the discovery of novel anti-infective compounds. As there are approximately 500 000 plant species occurring worldwide, of which only 1% has been phytochemically investigated, there is great potential for discovering novel bioactive compounds. There have been numerous reports of the use of traditional plants and natural products for the treatment of oral diseases. Many plant-derived medicines used in traditional medicinal systems have been recorded in pharmacopoeias as agents recommended for the alleviation of toothache. Cinnamomum verum bark is an astringent and is thus useful for checking the bleeding of gums. The essential oil of C. verum has antimicrobial and antibacterial properties. Accacia nilotica bark and ash of almond kernel can be pulverized together and mixed with common salt to make a highly effective preparation to contain pyorrhoea and for strengthening of gums by making them strong. Use of clove oil is recommended for the alleviation of toothache.
Plumbagin was identified as the active component of this extract. Tichy and Novak investigated a collection of 27 medicinal and random plants extracts and identified a number that inhibited the growth of oral streptococci. The most active extracts included those from Abies canadensis (Pinaeaceae), Albizia julibrissin (Fabaceae), Cephalium miliar to proporaceae, Ginkgo biloba (GinkgoPacific), Juniperus virginiana (Cupressaceae), Pitsa virginiana (Pinaceae), Rosmarinus officinalis (Lamiaceae), Sassafras albidum (Laureace), Tanacetum vulgare (Asteraceae) and Thujia plicata (Cupressaceae). Bioautography indicated that a number of extracts contained common antimicrobial components, while no extracts possessed chemically different constituents.11

A boiling water extract of Gopa/tis rhizoma (Ranunculaceae) was used as an artificial sweetener in many foods. Its antiangiogenic properties were investigated by adding 0.78–50% xylitol to broth cultures of S. mutans, S. sallivaris and S. sanguis, incubating at 37°C for 18 h and determining the optical density of the cultures. Streptococcus mutans was the only bacterium inhibiting the growth of S. mutans under a range of sucrose concentrations, pH values and in the presence of organic acids in a temperature-dependent manner and also inhibited the growth of cells adhered to a glass surface.22

Alkaloids the alkaloid berberine isolated from C. rhizoma (Ranunculaceae) showed bacteelical activity against oral bacteria, with greatest activity against A. actinomycetem comitans and P. gingivalis. Much less activity was observed against Lactobacillus and Streptococcus species. Berberine also inhibited the collagenase activity of A. actinomycetemcomitans and P. gingivalis.35

Sugar Alcohols xylitol is a sugar alcohol naturally found in plants. It is known to have antimicrobial properties and is used in the oral cavity, including pathogens has been documented. Indeed, there is evidence that commercial mouthwashes containing essential oils are useful in the long-term control of plaque and mild–moderate gingivitis and are preferred to those containing chlorhexidine for long-term daily use. A number of recent studies add to the evidence that essential oils may be suitable additives in products used for the maintenance of oral hygiene or prevention of dental disease.4

The essential oil of Melauxea alternifolia (Myrtaceae), known as tea tree oil (TTO), has been used medicinally for many years. TTO has antimicrobial properties and is used in the superficial treatment of skin infections. In addition to their inhibitory and bactericidal activities, most of the oils were able to inhibit adhesion of S. mutans and P. gingivalis. Essential oils are also capable of enhancing the activity of chlorhexidine.5 When used in combination, the essential oils of cinnamon and manuka were able to significantly reduce the amount of chlorhexidine required to inhibit the growth of oral pathogens. This enhanced activity was also seen against bacterial cultures grown as biofilms. Between 4- and 10-fold reductions of the amount of chlorhexidine required to inhibit biofilm bacteria was observed when used in combination with cinnamon, manuka and Leptospermum morrisii oils.5

CONCLUSIONS

The plant extracts, essential oils and purified phytochemicals have the potential to be developed into agents that can be used as preventative or treatment therapies for oral diseases. While it is encouraging to see a number of clinical trials of such products, further studies of the safety and efficacy of these agents will be important to establish whether they other therapeutic benefits, either alone or in combination with conventional therapies, that can help to reduce the overall burden of oral diseases worldwide. In particular, studies that address issues such as adequate statistical power, blending, standardization of extracts or purified compounds, and quality control would be of great value.

REFERENCES


