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Dental Caries, Etiology, and Remedy through Natural Resources

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Abstract

Caries and oral mucosal and periodontal diseases are the major cause of oral health problems. They are prevalent in all ages and demographic and socioeconomic groups. Irrespective of geographic location in the world, both males and females are affected from the condition. Dental caries' etiology has four main factors: bacteria, time, susceptible tooth surface, and fermentable carbohydrates. Due to the high prevalence of oral disease and increased microbial resistance against antibiotics, there is a need for alternative methods. Therefore, the search for viable alternative products is of paramount importance. Phytochemicals isolated from plants, which are used in traditional medicines, are considered to be safe and effective alternatives compared to synthetic chemicals. This situation diverted efforts toward finding natural products as the potential medicine for treating dental caries. The chapter will focus on the etiology of dental caries and different remedies using the natural resources for prevention and treatment of the disease. A wide variety of secondary metabolites in medicinal plants having in vitro antimicrobial activities provide a hope for novel drug compounds.

Keywords: dental caries, etiology, natural resources, bacteria

1. Introduction

1.1. Dental caries

Oral diseases, a major health issue in the world [1], are economically affecting people of developed countries as 10% of the health expenditure is related to dental care. Even though there is an improvement in oral health in most of the developed countries, there are still dentally disadvantaged people, usually with low socioeconomic status [2].

1.2. Prevalence in the world

Caries and oral mucosal and periodontal diseases are the major oral health problems in developing countries [3]. They are prevalent in all ages and demographic and socioeconomic groups. Irrespective of geographic location in the world, both males and females are affected from the condition. Dental caries is most prevalent in Latin America, South Asia, and the Middle East and least common in China [4]. Dental caries increase with age due to denture use and poor hygiene. The presentation of caries varies among people, but the risk factors and developmental stages are the same [5]. According to a survey by the National Health and Nutrition Examination Survey (NHANES) in the United States (1992–2004), conducted among adults between 20 and 64 years old, there was a decline in cases up to 97% in the 1990s, but still the prevalence is high, affecting 92% of people. In developing countries, this percentage rose to 96% [6]. Oral diseases like tooth loss, oropharyngeal cancers, dental caries, oral mucosal and periodontal diseases, and HIV/AIDS-related oral diseases are the main public health problems globally [1, 7]. Out of total 291 diseases and injuries evaluated in global burden of disease, untreated tooth decay has the highest rate of prevalence between 70 and 90% of populations [8], and it is also one of the most common reasons for tooth extraction.

2. Etiology of dental caries

Caries is a chronic, multifactorial disease, which causes destruction and demineralization of hard tissues of teeth by acid production occurring from bacterial fermentation of food [9]. **Figure 1** represents the common factors involved in caries formation.

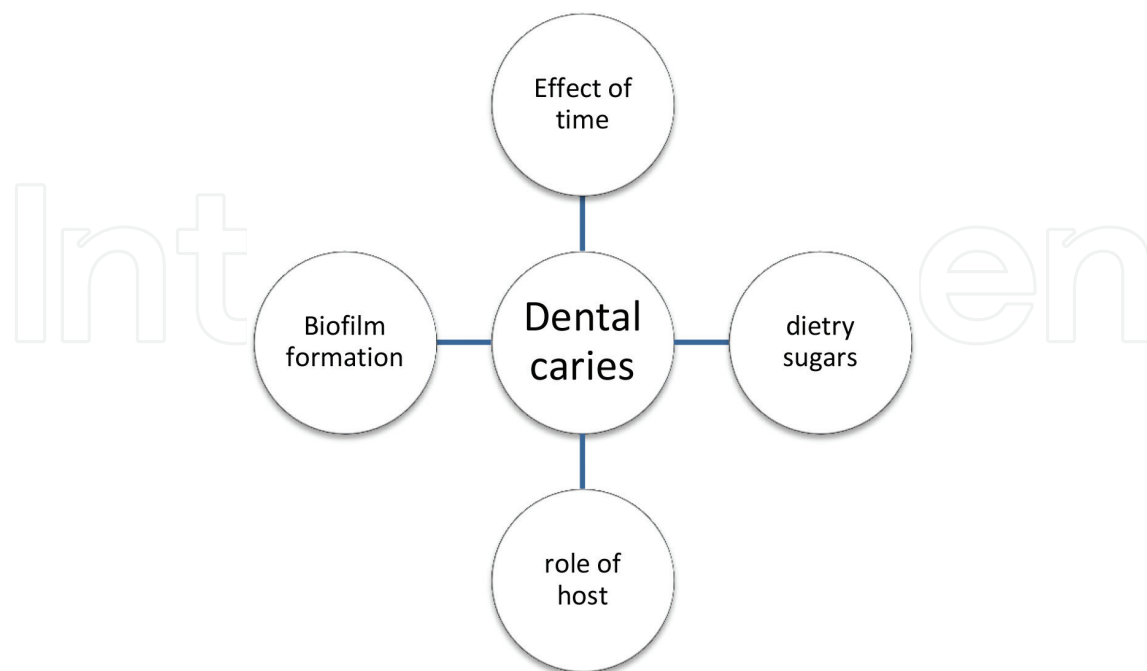


Figure 1. Common factors causing dental caries.

2.1. Dental plaque and biofilm

Biofilms are usually associated with the etiopathogenesis of periodontal diseases [10]. In order to survive in a niche, the ability of microbes to adhere to tooth surface and multiply in protected environments like tooth cervices and periodontal pockets is very important. This accumulation of microbes on the tooth surface is called *plaque*, which can be defined as “a structure entity in which the microbes are embedded in a highly organized intercellular matrix,” These microbes are involved in different metabolic, physical, and molecular interactions. This consortium provides advantages to the participating microbes for resistance to antimicrobial agents, increased pathogenicity, growth, and host defenses [11]. Four stages involved in the biofilm formation are summarized in **Figure 2**.

The primary colonizers of tooth form the biofilm by auto-aggregation and co-aggregation resulting in different morphological structures. The microenvironment moves from aerobic to facultative anaerobic [10]. The bacteria multiply and in matured biofilm occur. Quorum sensing is another important characteristic seen in biofilm-associated bacteria, which actually involves the regulation of specific gene expression. This occurs by means of accumulation of different signaling compounds that facilitate the intercellular communication. This gives biofilm their unique characteristics [12].

2.2. Microbiology of dental caries

The interaction between bacteria and its surrounding epithelium is acute element in bacterial infections. If left untreated pain, infection, and tooth loss depending on the severity will occur. Dental plaque is a sticky substance that sticks to the surface of the teeth. It is considered as complex biofilm that is also the main cause of dental caries [13]. Dextran, produced

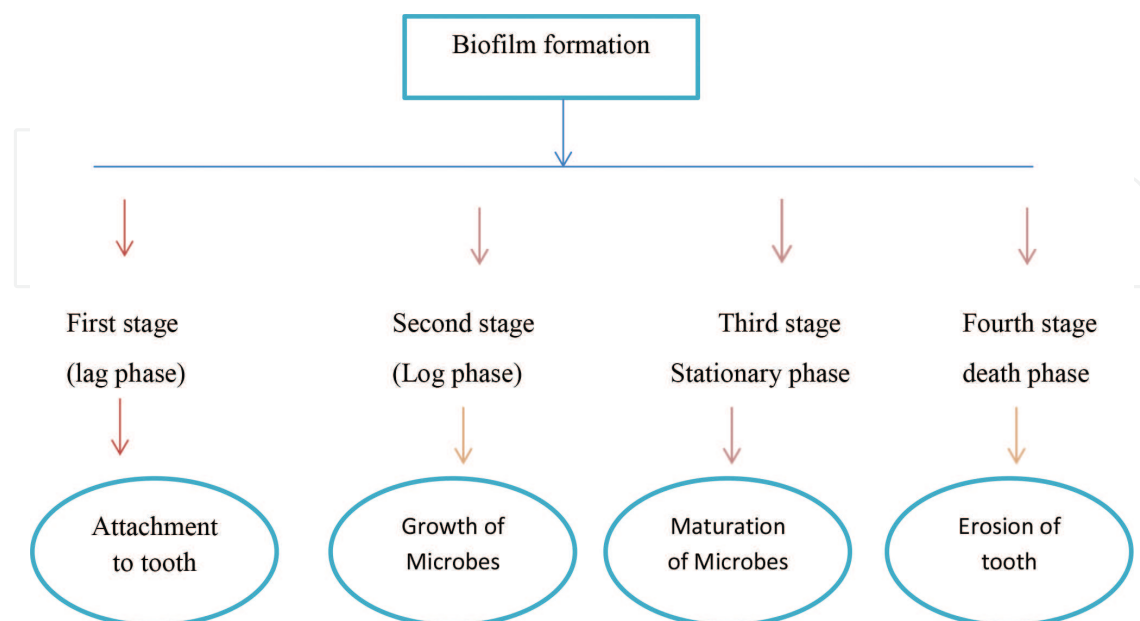


Figure 2. Stages of biofilm formation.

by the dietary sucrose fermentation by *Streptococcus mutans*, is responsible for the stickiness of plaque. As a result of fermentation, *S. mutans* produce lactic acid, which ultimately starts enamel decalcification. This plays a role in initiation of enamel caries. In fact, the development of dental plaque depends on the result of interaction between the plaque adhesion to the tooth surface and the physical shear forces involved in dislodging and removal of plaque [14]. If the dental plaque is not removed properly, tooth decay will flourish [15]. The mature dental plaque is embedded in a matrix of bacteria and host polymer that includes proteins, DNA secreted by cells, and polysaccharides [16–19]. This provides the protection of bacteria against host defenses and predators, from desiccation and enhanced resistance against antimicrobial compounds [20]. *Streptococcus mutans*, *S. mitis*, *S. constellatus*, *S. sanguis*, *S. salivarius*, *S. anginosus*, *S. gordonii*, *S. intermedius*, and *S. oralis* are some of the primary acid-tolerant bacteria that are associated with dental plaque [21]. Accumulation of plaque in gingival and subgingival regions shifts the microflora from gram positive to gram negative. This can cause the periodontal diseases [22]. Dental caries is linked with high blood pressure, diabetes, heart diseases, and sometimes multiple sclerosis along with continuous pain that gets aggravated by cold, heat, sugar, and drinks [23, 24].

Four main factors are associated with dental caries etiology. These factors are bacteria, time, susceptible tooth surface, and fermentable carbohydrates [25, 26]. Along with these factors, there are certain behavioral and sociodemographic factors that are likely to increase the risk of caries. These include poor oral hygiene, age, improper tooth brushing habits, plaque, and sugar-containing drinks [27].

The oral cavity of human is considered as a complex ecosystem which has both acid-producing and acid-tolerant bacteria. Almost 700 different bacterial species have been known for human oral cavity [28–30], and nearly 200–300 species have been identified for dental plaque [31] using different culture-dependent and culture-independent techniques. *S. mutans* is considered as the main organism responsible for human dental caries. Certain factors like ability to form biofilms, tolerance of frequent and rapid environmental fluctuations, and metabolizing carbohydrates are considered to be responsible for the virulence of these bacteria [32, 33]. In addition, the *mutans* is also associated with bacterial endocarditis, inflammation of heart valves. Synthesis of the extracellular polysaccharides by *S. mutans* from sucrose through glucosyltransferases (GTFs) is considered another important virulence factor that causes caries in humans [34]. This not only facilitates the adhesion and accumulation of the organism on the tooth surface but also provides protection against host immune defenses along with provision of increased resistance against antibiotics and gene expression [35]. This combination of virulence properties allow the *mutans* to colonize the surface of tooth and modify the nonpathogenic to highly cariogenic dental biofilm that ultimately leads to caries formation [36].

3. From synthetic to herbal products

The second primary cause of death in the world is infectious diseases. Treatment of these diseases is problematic today because of severe side effects of different antimicrobials and the

growing resistance against all the lifesaving drugs due to their continuous use [37, 38]. The issue becomes much worst with almost 70% of bacteria that cause common infections in hospitals develop resistance to at least one of the common antibiotic that is used for treatment [39, 40]. Even the antibacterial agents can enhance the development of resistant bacterial strains [41]. Different antibiotics like erythromycin and penicillin are effective against dental caries in humans and animals, but because of their adverse effects, they are not recommended in clinical application [42]. Chlorohexidine, penicillin, cephalothin, ampicillin, methicillin, and digluconate are some of the other antibiotics that have effect on dental caries [22]. Recently, resistance has also been observed in cariogenic bacteria against these antibiotics. The development of resistant strains and the associated side effects of these medicines have resulted in diversion of research toward screening of natural products (plants) for anticaries activity as some plants have shown potential against dental caries-causing pathogens [43, 44].

3.1. Herbal medicines from plants

The use of natural remedies from medicinal plants could be an alternative for the side effects of antibiotics like supra-infections, hypersensitivity, and teeth staining. Due to this the search for new antibiotics continues persistently. In fact the failure of different chemotherapeutics and increasing resistant against antibiotics also led to screening of different medicinal plants and their potential use against these microbial pathogens [45]. The significant contribution of medicinal plants to the drug industry, all over the world, was due to the increasing number of phytochemical and biological studies. Medicinal plants are important sources of developing new therapeutic agents. Almost 100 new plant-based medicines were introduced in the United States during 1950–1970. These include vinblastine, deserpidine, etc. From 1991 to 1995, 2% of drugs were introduced in the world including irinotecan, paclitaxel, topotecan, and many

Plant name	Part of plant	Application	Reference
<i>Asteracantha longifolia</i>		Diabetic patients	[50]
<i>Mangifera indica</i>	Leaves	Antidiabetic activity	[51]
<i>Citrus lemon</i> L.	Peel	Antibacterial	[52]
<i>Soymida febrifuga</i> , <i>Tinospora cordifolia</i> (Willd.)	Whole plant	Antioxidant, anti-inflammatory	[53]
<i>Terminalia chebula</i> , <i>Ocimum sanctum</i>	Whole plant	Urinary tract infections	[54]
<i>Syzygium cumini</i>	Leaves	Dental caries	[55]
<i>Diospyros blancoi</i> , <i>Phoenix dactylifera</i> , and <i>Morus nigra</i>	Leaves	Antibacterial, caries	[56]
<i>Capsicum annum</i>	Fruit	Antibacterial, antimicrobial	[57, 58]
<i>Psidium guajava</i> L.	Leaves	Antimicrobial, antioxidant	[59, 60]
<i>Aloe vera</i> L.	Leaves/gel	Antimicrobial, skin infections	[61–63]
<i>Azadirachta indica</i>	Whole plant, leaves	Antimicrobial, antioxidant	[64, 65]

Table 1. Medicinal plants used in traditional medicines.

others [46]. Drugs derived from plants are used to treat cancer, tuberculosis, different skin diseases, diabetes, hypertension, and many more [47]. The National Cancer Institute collected around 35,000 plants from 20 different countries and evaluated almost 114,000 extracts for potential anticancer activity [48]. Among the approved anticancer drugs worldwide, between 1983 and 1994, 60% are of natural origin [49]. Some medicinal plants that are used to treat different diseases are given in **Table 1**.

Today, oral care products combined with medicinal plant extracts are gaining high interest due to their low toxicity [66, 67]. Cetylpyridinium chloride, amine fluorides, triclosan, and chlorhexidine are not only toxic, but they cause staining of teeth.

4. Secondary metabolites of plants

Different secondary metabolites produced by plants like terpenoids, flavonoids, alkaloids, and tannins are new sources of antimicrobial substances which help in combating resistant pathogens. Plants synthesize different useful substances, majority of which are secondary metabolites and almost 12,000 of them have been isolated [68]. Owing to their diverse structures, synthesizable analogues [69] and frequent usage [70] natural products have become an important source of medicine. Plants have evolved multiple defense systems for their survival because of plethora of rivals in order to fight the environmental stresses [71]. Plants are in fact the complex storehouse of undiscovered bioactive compounds with great potential to be used in medicines [72].

Basically the chemicals produced by plants are divided into two categories, the primary and the secondary metabolites [73]. The *primary metabolites* are involved in the synthesis of the basic building blocks of the plant, while the *secondary metabolites* are involved in the defense mechanism of the plant against different microbial infections [74]. The important secondary metabolites in medicine include flavonoids, alkaloids, terpenes, tannins, and phenolic compounds [75–78]. Unlimited opportunities for drug discovery have been provided by plant extracts, whether pure compounds or standardized extracts, because of their chemical diversity [79]. All the plants that are used in traditional medicine contain diverse substances that can be used to treat different infectious and chronic diseases [80, 81].

The significant contribution of medicinal plants to the drug industry is due to the increasing number of phytochemical and biological studies. In developing countries the herbal medicines are important sources of products in order to treat different infectious diseases and also to overcome the problems related with the available antimicrobial agents. Herbal remedies are getting popularity as they provide safe alternatives for treating various types of cancers [82–85]. These remedies are gaining interest because of their multidimensional health benefits like they are even used in different alternative treatments like acupuncture and massage therapy and by various traditional practitioners. The medicinal uses of the plants range from administration of leaves, stem, barks, seeds, and roots to using of the decoction from different plants [86]. There has been an increase in the demand of different herbal products in the last few decades and even in countries like United States, herbal remedies are in use in the form of different dietary supplements [84, 87, 88].

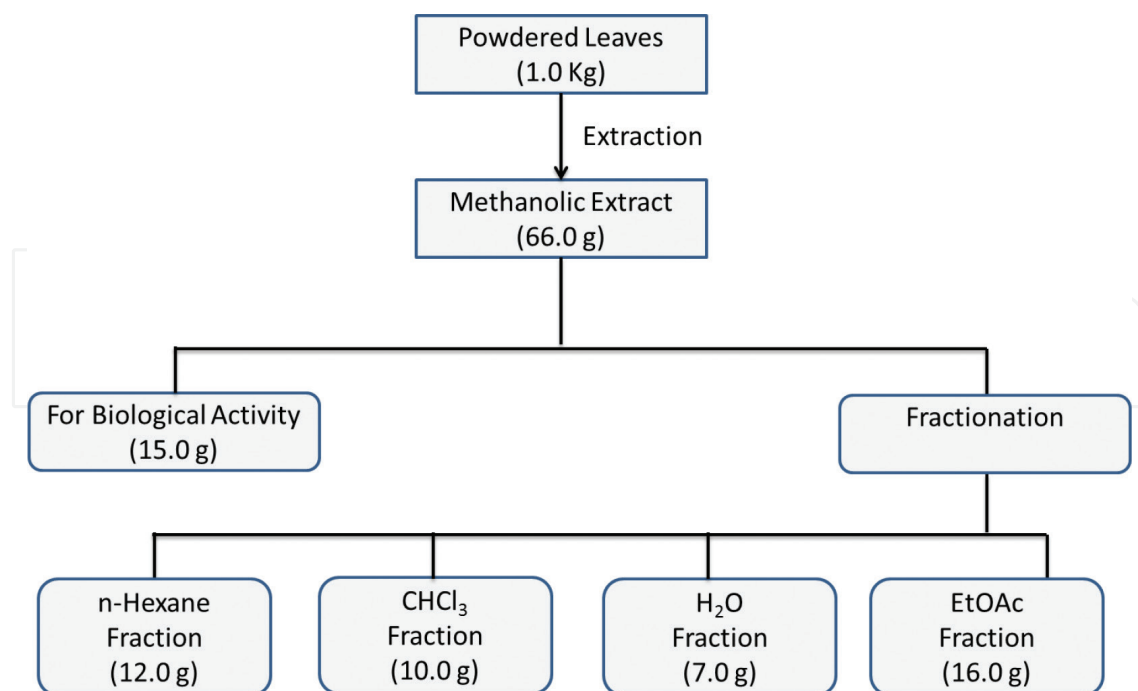


Figure 3. Extraction and fractionation from the leaves of *Syzygium cumunii*.

Figure 3 represents the general layout of extraction of useful secondary metabolites from plants taking *Syzygium cumini* as an example using different solvents.

5. Why to go for natural resources

The commercially available chemicals, if not all, to most of the antibiotics commonly available to treat oral infections, can alter the oral microbiota along with certain undesirable side effects [41, 89] and bacterial resistance [90]. An alteration in the microenvironment like wounds, malnutrition, abrasions, and different pathological conditions enhances disease development [91]. Also, the presence of ethanol that is commonly found in mouth washes has been linked to oral cancer [66, 67, 92, 93]. As a result of this, the indiscreet use of allopathic drugs and improper diagnosis of microbial infections not only lead to untar-geted therapy, but it also gives way to resistant pathogens [94, 95]. Therefore, the search for alternative methods and products continues, and for that the phytochemicals isolated from plants that are used in traditional medicines are proving to be the good alternative to synthetic chemicals [96].

In developing countries the herbal medicines are proving to be an important source of products in order to treat different infectious diseases and also to overcome the problems related with the available antimicrobial agents. Herbal remedies are also getting popularity for treating various types of cancers as they provide safe alternative [82–85].

6. Conclusion

Prevention of dental caries is challenging, as the incidence of the disease is very high in general population and it occurs in economically deprived people who cannot afford the commercially available oral hygiene products [97]. Even though caries is known to be an infectious disease for decades, very little effort has been done to use this information clinically [98]. Different from other commercially available chemicals, they not only alter the oral microbial environment but also play a role in developing the resistant strain. Hence, in order to prevent dental caries, it is time to focus our attention toward natural resources which have vast abilities to inhibit the growth of microbes that are responsible for caries. For this, we need to isolate the bioactive compounds from plants with little or no harmful effects.

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