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Review

The role of wine and food polyphenols in oral health



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ABSTRACT

Background: There is a growing interest in understanding the human oral microbiome, due to its important role in promoting health, as reported in a number of studies. Several factors can affect the composition of the oral microbiota (e.g. hygienic habits, genetics, environment ...). Among them, diet is one of the most significant external factors that modulate oral microbiota, thereby affecting the balance between host health and disease. Although the composition of oral microbiota can be considered dynamic, there is an equilibrium between commensal bacteria and pathogens on which oral health status relies.

Scope and approach: This study emphasizes the alteration of the balance previously mentioned, when the pathogenic bacteria population increases to the detriment of beneficial commensal bacteria, which prompts microbial-derived oral diseases such as caries, gingivitis and periodontitis that may affect every human at some point in life. Dietary polyphenols and, in particular, wine polyphenols seem to modulate the composition of the oral microbiota suggesting plausible benefits in the prevention of caries and periodontal diseases. However, at this point, knowledge is still preliminary, and more research needs to be conducted at different levels.

Key findings and conclusions: This review focuses on the current research regarding polyphenols and their role in preventing microbial-derived oral diseases. It gives a holistic view that emphasizes the interactions of these bioactive compounds among oral pathogens as well as their potential metabolism by oral bacteria.

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1. Background

The term ‘microbiota’ is used as a reference to the microbial cells (symbiotic and pathogenic) colonizing the host surfaces and cavities, while the term ‘microbiome’ is commonly used to define the genes these cells harbor (Lloyd-Price, Abu-Ali, & Huttenhower, 2016). The microbiota colonizing the oral cavity is composed of diverse microbial species, each one possessing its specific nutritional and physico-chemical requirements. Although fungi, viruses, protozoa and archaea have been found, bacteria are the most common microorganisms present in the oral cavity. Oral microbiota is characterized by a high variability and abundance and comprises around 700 commonly occurring phylotypes, approximately half of which can be present at any time in any individual (Palmer, 2014).

Several stimuli and/or factors can contribute to the development of microbial-derived oral pathologies, such as dental caries, gingivitis and periodontitis, including host susceptibility, poor oral hygiene or food and drink habits, which can cause the overgrowth of oral pathogens in dental biofilms formed in the oral cavity. Preventive strategies against periodontal diseases are focused on controlling the formation of dental plaque, normally by mechanical and adjunctive antimicrobial treatments. However, the excessive use of synthetic/chemical antimicrobials, such as chlorhexidine or antibiotics, for the prevention of microbial-derived oral diseases triggers the generation of bacterial resistance, causing progressive loss of their effectiveness and highlighting the necessity for different approaches, in particular new natural preventive therapies against these recurrent complaints (Al-Haroni, Skaug, Bakken, & Cash, 2008).

Polyphenols are secondary plant metabolites that form a heterogeneous group characterized by the possession of a benzenic ring substituted by one or several hydroxyl groups (-OH) and a

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functional side chain. In terms of dietary polyphenols, grape fruits and red wines are good dietary sources of phenolic compounds, including hydroxybenzoic and hydroxycinnamic acids, phenolic alcohols, flavan-3-ol monomers, oligomeric and polymeric procyanidins, flavonols, stilbenes and anthocyanins (Cueva et al., 2017). Several health benefits have been associated to dietary polyphenols, including antioxidant properties (Biasi et al., 2014), anti-proliferative action (Tanaka et al., 1993), anti-inflammatory effects (Muñoz-González, Espinosa-Martos et al., 2014), anti-allergic, anti-hypertensive and antithrombotic activities (Rechner & Kroner, 2005), as well as positive effects on human microbiota composition and functionality (Cueva et al., 2010). In addition, the antibacterial, antiviral and antifungal activity of polyphenols has been previously established (Daglia, 2012). However, the knowledge of the effects of polyphenols in relation to the prevention of dental diseases is still at an early stage. Recent discoveries related the intake of specific polyphenol-rich beverages and foods to the maintenance of oral health and prevention of disease status (Hannig, Sorg, Spitzmüller, Hannig, & Al-Ahmad, 2009; Signoretto et al., 2010; Signoretto, Canepari, Pruzzo, & Gazzani, 2009; Witt-pahl et al., 2015). Wine polyphenols and oenological extracts, mainly derived from red wine and grape seed by-products, have previously demonstrated to be effective antimicrobials against certain bacterial species isolated from the oral cavity (Furiga, Lonvaud-Funel, & Badet, 2009; Muñoz-González, Thurnheer, Bartolomé, & Moreno-Arribas, 2014; Thimothe, Bonsi, Padilla-Zakour, & Koo, 2007). On the other hand, interactions between wine phenolics and oral microbiota can also include a possible bacterial catabolism of these compounds into less complex phenolic metabolic structures (Cueva et al., 2017; Mallery et al., 2011; Requena et al., 2010; Walle, Browning, Steed, Reed, & Walle, 2005).

In this article, a general view of the influence of wine polyphenols and polyphenol-rich foods on the prevention of microbial-derived oral diseases, as well as on the maintenance of oral health, is presented.

2. Current understanding of oral microbiota

Humans have developed a necessary and dependent relationship with the microorganisms that usually inhabit the human body and which play an important role in host physiology and local and systemic immunity (Lloyd-Price et al., 2016). The majority of these microbes reside in the gut, however they can be located in other mucosal parts of the organism, including vagina, nose, oral cavity and skin (McGuire et al., 2008). These microbial communities are extremely varied and their distribution is conditioned by environmental conditions (e.g. temperature, pH, nutrient accessibility, oxygen presence, etc.) (Structure, function and diversity of the healthy human microbiome, 2012). Despite commensal and pathogenic microbes are normally co-inhabiting in the human body, differences in the microbiota composition and microbiome between health and disease status have been demonstrated (Lloyd-Price et al., 2016). In absence of disease, commensal microorganisms dominate the microbial ecology of host body, preventing an overgrowth of pathogenic population (colonization resistance) (Camelo-Castillo, Benitez-Paez, Belda-Ferre, Cabrera-Rubio, & Mira, 2014; Wescombe, Heng, Burton, Chilcott, & Tagg, 2009). However, microbial community rapidly changes in response to environmental stimuli, leading to dysbiosis, understood as a misbalance on the composition and functionality of the established microbiota (Lloyd-Price et al., 2016).

Oral cavity host the second most complex microbial community in the human body, after the gut (Dewhirst et al., 2010; Structure, function and diversity of the healthy human microbiome, 2012;

Wade, 2013). The most prevalent oral bacteria (>1%) belong to thirteen genera (*Streptococcus*, *Corynebacterium*, *Neisseria*, *Haemophilus*, *Actinomyces*, *Rothia*, *Veillonellaceae*, *Granulicatella*, *Prevotella*, *Porphyromonas*, *Capnocytophaga*, *Firmicutes* and *Actinobaculum*), although there is still an elevated number of unidentified microbial sequences suggesting an even more complex ecology that the actual technologies do not let to identify for the moment (Palmer, 2014). Additionally, as the oral cavity is a dynamic open system, defining in general terms its precise composition is difficult (Wade, 2013). Inside oral cavity several heterogenic locations for microbial communities can be found, including supragingival plaque (dental plaque), the subgingival crevice (subgingival plaque), the tongue, cheeks (epithelial cells), tonsils, hard and soft palates and teeth (Aas, Paster, Stokes, Olsen, & Dewhirst, 2005; Dewhirst et al., 2010).

The most part of the studies related to oral microbial communities are focused on the bacterial component, however it is important to note that fungal species can also be part of biofilms in the oral cavity (especially *Candida albicans*), as well as viruses (Bahrani-Mougeot et al., 2008; Slots, 2007; Wade, 2013) such as herpes, human papilloma virus (HPV), hepatitis and human immunodeficiency virus (HIV). Protozoa such as *Entamoeba gingivalis* and *Trichomonas tenax* (Wantland, Wantland, Remo, & Winquist, 1958), and archaea, such as *Methanobrevibacter oralis*, can also be found (Wade, 2013).

The organization of the oral bacteria is based on multilayered structures called 'biofilms' or "dental plaque", where commensal and pathogenic microorganisms are embedded in a matrix of extracellular polymeric substances secreted by themselves (Flemming et al., 2016) (Fig. 1). Inside these structures several events take place, including phenomena of cooperation, competition and communication between microorganisms, as well as it provides microbes with some survival advantages, such as nutritional, oxygen and pH gradients, tolerance and resistance to antibiotics and environmental changes, and molecules recapture (Flemming et al., 2016). The formation of biofilm occurs in two differentiated moments: the first stage consists in the attachment of primary colonizers (usually streptococci) to the oral surface, originating a microbial monolayer; then, migration of these colonizers, secretion of bacterial exopolysaccharides (EPS), and the sequential attachment of secondary and late colonizers lead to the maturation of biofilm (Lemon, Earl, Vlamakis, Aguilar, & Kolter, 2008). During bacterial adherence to the oral surface, three different steps are defined (Signoretto et al., 2009). The initial adhesion is mediated by bivalent cations and bacterial surface recognition molecules, called 'adhesins', which are produced by several bacteria, such as streptococci, *P. gingivalis*, *F. nucleatum*, *A. naeslundii* and *Treponema medium* (Avila, Ojcius, & Yilmaz, 2009). Then, the merge is reinforced by the secretion of the EPS mutans, a sucrose-dependent exopolysaccharide originated by action of glucosyltransferase enzymes (GTFs) (Koo, Xiao, Klein, & Jeon, 2010).

As explained before, inside biofilms bacteria can develop a synergistic or antagonistic relationship between different species. The communication between microorganisms occurs via secretion and reception of certain signaling molecules, the so-called 'quorum sensing', which induce changes in microbial functionality (Fuqua, Winans, & Greenberg, 1994; Teles et al., 2007). For example, lactobacilli are related to the production of lactic acid associated to caries progression but recent evidences also associate the presence of certain probiotic strains of *Lactobacillus* spp. and bifidobacteria with the inhibition of the adherence and formation of oral pathogenic biofilm (Ciandrini et al., 2016; Jasberg, Soderling, Endo, Beighton, & Haukioja, 2016; Jiang, Stamatova, Kainulainen, Korpela, & Meurman, 2016).

Streptococcus mutans, a Gram-positive coccus, is considered as the main primary colonizer in the process of biofilm formation.

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