Natural products to inhibit dental plaque formation

An insight into the importance of glucans

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INTRODUCTION

Dental plaque is a biofilm established on the tooth surface that can cause oral diseases. It consists on a dynamic multi-species community in which microorganisms are forming complex and differentiate colonies. Its composition is governed by bacterial adherence, co-aggregation, growth and survival in the environment. It is coated with a matrix of exopolysaccharides, which promotes adhesion of bacteria and stability of the tridimensional structure. *Streptococcus mutans* constitutes 30% of cariogenic dental plaque, and its adhesion is mainly governed by glucans. There are several ways to inhibit dental plaque formation, and here we will explain the main targets, focusing on glucans.

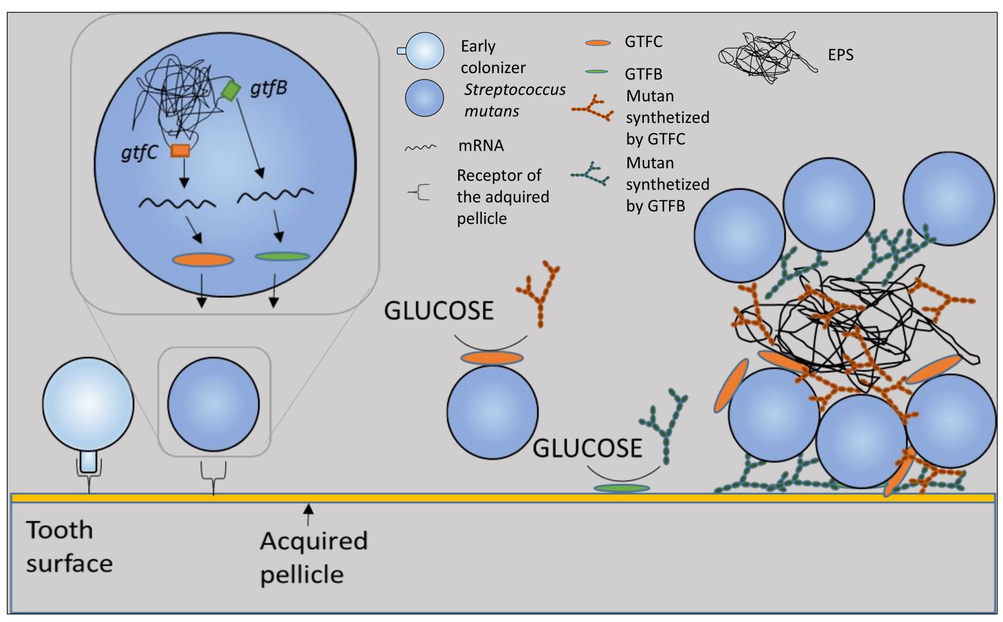

Figure 1. Process of *S. mutans* colonization of dental plaque: it expresses diferent glucosyltransferases, that bind to diferent surfaces and synthesize glucans from glucose. Glucans bind to cells and extracellular polysaccharide (EPS), increasing adhesion and stabilizing the plaque structure.

Bactericidal and bacteriostatic effect

Antibiotic treatment is the most studied strategy to inhibit plaque formation, but it has some drawbacks, like the increasing of antibiotic resistances and that within a biofilm, tolerance to antimicrobial is 1000 times greater than in plankotic cells. Moreover, antibacterial treatments can affect oral and digestive microbiota.

Quorum sensing

It's the main communication pathway within a biofilm. Therefore its suppression disrupt the biofilm structure.

ADHESION

3 main pathways of dental plaque adhesion

Proteins

Many microorganisms adhere by interaction with pellicle receptors. Inhibite these proteins would prevent colonization.

Surface hydrophobicity

Some microorganisms bind the surface by hydrophobic interactions. Therefore, decreasing surface hydrophobicity would prevent adherence.

GLUCANS

Extracellular polysaccharides synthesized from glucose by Glucosyltransferases (GTF) enzymes from *S. mutans*. They can be water-soluble or water-insoluble (mutans). The mutans contribute to the adhesion of *S. mutans* and the matrix cohesivesness. Therefore, decrease of mutan synthesis by GTF decreases cellular adhesion and plaque structure.

GTF activity

Inhibition of glucosyltransferase activity (figure 3) is one of the most studied targets to decrease the adherence of plaque. In the table, there are some examples of natural products that do this action. The most studied products are:

XANTHONE DERIVATIVE alpha-mangostin *(Garcinia mangostana)*: binds the catalytic or mutan binding regions of GTF.

POLYPHENOLS:

-Proanthocyanidins of *Vaccinium marcocarpon* by binding the catalytic or glucan-binding domain. Its action depends of the presence of A-type linkage and degree of polymerization.

-Catechins of *Camellia sinensis* are the more studied compound to interfere with GTF activity (*in vivo* studies).

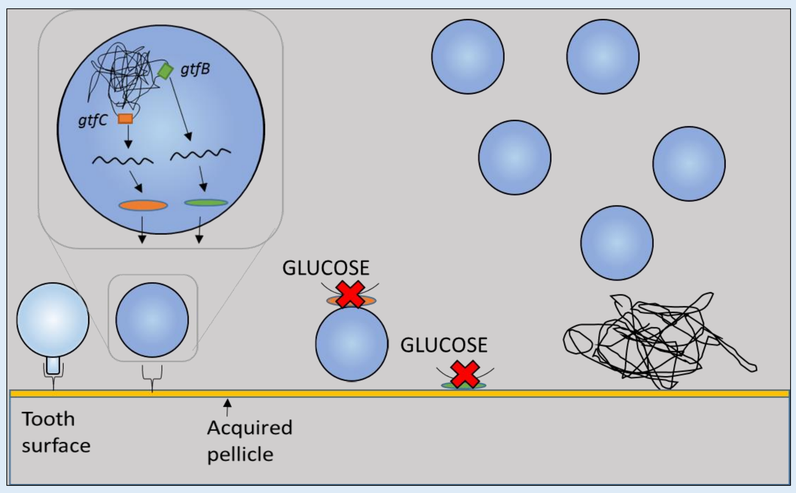

Figure 2. Inhibition of GTF activity. The product interacts with GTF, inhibiting its action.

Gene expression

GTF enzymes contribute to the structure of dental plaque. Disruption of GTF expression causes decrease of GTF synthesis, compromising the plaque cohesiveness.

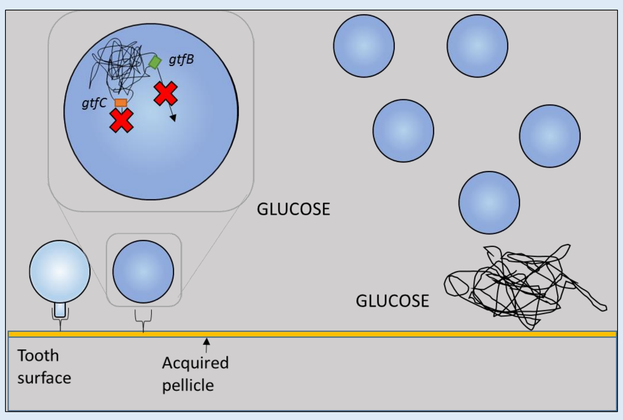

Figure 3. Inhibition of *gtf* expression. The product interacts with *gtf*, inhibiting its expression.

Table 1. Examples of natural products with GTF-inhibiting activity with the compound responsable of this activity.

	Plant	Compound
INHIBIT GTF ACTIVITY	*Areca catechu*	Procyanidins
	Camellia sinensis	Limonoid
	Citrus limonum	Essential oil
	Harrisonia spp.	Limonoid
	Ilex paraguariensis	Shikimic acid derivatives
	Morus alba	Alcoholic extract
	Pistacia atlantica	Flavonoids
	Polygenum cuspidatum	Ethil acetate fraction
INHIBIT SURFACE-ADHERED GTFs	*Cacao cacao*	Phenolic substances
	Garcinia mangostana	α-mangostin
	Malus domestica	Phenolic extract
	Propolis	Flavonoids and terpenoids
	Rosemarinus officianalis	Propanone extract
	Salvia officianalis	Propanone extract
	Vitis vinifera	Phenolic extract
	Zingiber officinale	Crude and methanolic extract

CONCLUSION

Glucans are a promising target for inhibiting plaque formation, and the natural products with more potential to decrease their content on dental plaque are polyphenols. The research of natural products to inhibit glucan in the plaque biofilm is in an initial point, and it's necessary to study more deeply the mechanisms of dental plaque development to know the direction of the research. It's necessary to establish protocols for these studies in order to obtain comparable results. It's a field with a hopeful future, but there is a long way to run before those substances can be applied at the oral health industry.

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