Trivial Molecules May Prevent or Hamper Tooth Decay: A Potential Voyaged?

In University of Alabama at Birmingham, the researchers have created a small molecule that prevents or obstructs dental caries (tooth cavities) in a preclinical archetypal. The inhibitor blocks the function of a key virulence enzyme in an oral bacterium; a molecular interruption that is similar to flinging a primate tug into apparatus to jam the mechanisms. In the presence of the molecule, *Streptococcus mutans* is unable to make the sticky biofilm that allows it to glue to the tooth surface, where it noshes away tooth enamel by creating lactic acid. This discriminating inhibition of the sticky biofilm appears to act specifically against *S. mutans* and the inhibitor drastically reduces dental caries, the researchers confirmed in experimental rats who were fed with a caries-promoting diet (sugar). The researchers explained"The compound is drug-like substance, which is non-bactericidal and also easy to synthesize, and it exhibits very potent effectiveness *in vivo*,". In an article, they claimed that the tested substance is "an excellent contender which can be developed into therapeutic drugs which can prevent dental caries."

About 2.3 billion people worldwide have dental caries in their permanent teeth, according to a 2015 Global Burden of Disease study. Current practices to prevent cavities, such as mouthwash and tooth brushing, indiscriminately remove oral bacteria through chemical and physical means and have limited success. If we develop a mechanism which can selectively take away the bacteria's ability to form biofilms, then it would be a tremendous development; "This is particularly exciting as it targets mainly the microorganisms by using chemical probes specifically tailored to the specific pathogen within a complex microbial community," stated the researcher.

Successful development of this selective lead inhibitor in the dental setting offers a proof of concept that selective targeting of underpinning bacteria is promising for the design of new treatments, claims the investigator. This is relevant for many insubstantial human diseases as the microorganisms are linked to diseases; the glucan biofilm is made by *S. mutans* glucosyltransferase, or Gtf, enzymes. The crystal structure of the GtfC glucosyltransferase is known, and the researchers used that structure to screen – through computer simulations – 500,000 drug-like compounds for binding at the enzyme's active site. Ninety compounds with diverse scaffolds showing promise in the computer screening were tested for their ability to block biofilm formation by *S. mutans* in culture. Seven showed potent, low-micromolar inhibition, and

one, #G43, was tested more extensively. #G43 inhibited the activity of enzymes GtfB and GtfC, with micromolar affinity for GtfB and nanomolar affinity for GtfC. #G43 did not inhibit the expression of the gtfC gene, and it did not affect growth or viability of *S. mutans* and several other oral bacteria tested. Furthermore, #G43 did not inhibit biofilm production by several other oral streptococcal species. In the rat-model of dental caries, animals on a low-sucrose diet were infected with *S. mutans* and their teeth were treated topically with #G43 twice a day for 4 weeks. The #G43 treatment caused very significant reductions in enamel and dentinal caries. Using structure-based design, researcher claims that they have developed a unique low-micromolar biofilm inhibitor that targets *S. mutans* Gtfs through binding to key virulence factors, Gtfs. "Successful development of this selective lead inhibitor in the dental setting offers a proof of concept that selective targeting of keystone bacteria is promising for the design of new treatments," "This is relevant for many elusive human diseases as the microbiome is being linked to overall health and disease."

Let us hope the plethora of research will be a boon to mankind.

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