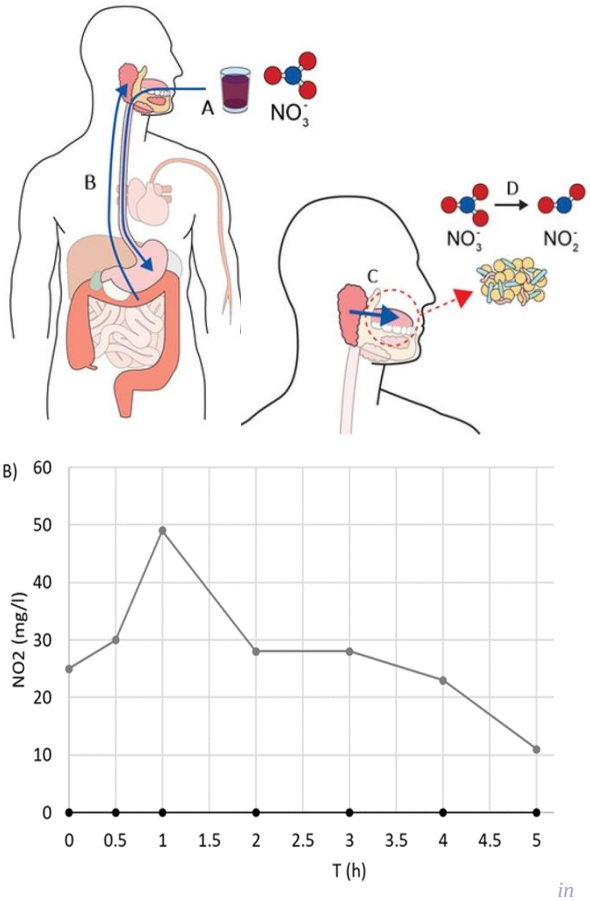
PREBIOTIC AND PROBIOTIC TREATMENT TO REDUCE ORAL DYSBIOSIS AND PREVENT OR TREAT PERIODONTITIS, HALITOSIS AND DENTAL CARIES

Description

In the Spanish population, >25% of adults have periodontitis and/or halitosis, ~50% of children have caries, and cardiovascular diseases are the 2nd leading cause of death. Research shows that these diseases have a possible common treatment centred on the oral microbiota.

Certain oral bacteria convert nitrate to nitrite and nitric oxide (a vasodilator), which lowers blood pressure, as well as having anti-diabetic effects. The research group has found that this bacterial function also prevents the 3 main oral diseases (caries, periodontitis and halitosis). A diagnostic test has been developed to determine whether a person has these bacteria. It has been shown that this nitrate transformation process can be enhanced with a new prebiotic and probiotics developed by our group. A prebiotic is a substance that, when administered in the diet, promotes the growth of beneficial bacteria present in the body; a probiotic is a micro-organism that, when administered in adequate doses, directly performs this beneficial function. This is the first time that a beneficial treatment for all these diseases has been described simultaneously.



in gestion of the prebiotic. When we consume foods with nitrate, s uch as beet juice, the compound reaches our intestine (A),passe s into the blood, and returns to the salivary glands(B). These glands concentrate nitrate in saliva u p to 10 times more than the concentration in blood plasma (C). Thus, our salivary glands supply dietary nitrate to oral bacteria to reduce it to nitrite (D), a function that cannot be performed by the human body. The graph on the right shows the salivary nitrite levels in one individual with and one without the reducing bacteria aft er ingestion of our supplement.

A composition comprising nitrate (from fruits or vegetables) is provided for use in the reduction or prevention of oral dysbiosis and/or the increase of oral eubiosis, i.e ., a change in the bacterial composition and functions of oral biofilms in humans an d domestic animals, by decreasing the amount of disease-associated bacteria and increasing the amount of health-associated bacteria. This provides an acute treatment or prevention with immediate effects that last several hours after ingestion or application, against the three main o ral diseases mediated by biofilms (caries, periodontal diseases – gingivitis, periodontitis or peri-implantitis – and halitosis). The prebiotic can be administered topically (e.g., toothpaste or dental varnish), in the f orm of a food supplement (e.g., ingested preparations), or in pill form, among others. Our prediction is that this patent will be the origin of a whole range of new oral health products and will pave the way for the developme nt of prebiotics as natural active ingredients complementary to fluoride and alternative s to oral antiseptics. Other protected productsare the anti halitosis pill, which stops the production of gases that cause bad breath for 6 hours;

The composition may also comprise a beneficial bacterial strain, which the research gr oup has developed as probiotics. This may be useful in individuals with an absence of these nitrate-reducing organisms for whom the supply of the prebiotic is not sufficient. For this reason, the personalized application of our inventions can be accompanied by a diagnostic test that uses a sal iva sample to determine if the person has a high, medium or low nitrate reduction capacity, in the latter case it is advisable to administer the prebiotic t ogether with the probiotic, to increase the nitrate reduction capacity. This test therefore allows a personalized treatment according to the individual ne eds of the patients.

Technical advantages

There are oral health products on the market that use arginine as a prebiotic, favoring bacteria that use arginine to neutralize acids. It is therefore a prebiotic suitable for preventing caries, but not halitosis or periodontitis. Therefore, our nitrate-based products have multiple aplications. In addition, the use of plant extract rich in nitrate that protects our invention will increase social acceptance (products of natural origin) and facilitate regulatory aspects.

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Some of the protected products also represent a revolution in the field of oral health, as would be the case of the anti-cavity pill. It would be a disruptive strategy consisting of a tablet or chewing gum that maintains the acid-neutralizing capacity of saliva for at least 6 hours, due to the natural recycling of nitrate by the salivary glands (Figure 1), to be used in those cases where there is no possibility of brushing teeth.

Another advantage of the product is that in addition to improving oral health, it would have a direct effect on improving cardiovascular health, through the production of nitrite, which can serve as a reservoir for the availability of vasodilator agents. Finally, the presence of nitrate-reducing organisms and the salivary recycling mechanism of nitrate make it possible to develop supplements and oral health products for oral health animals are incorporated into feed, and the contact time with the active ingredient is minimal, due to the speed with which pets usually consume them. In the case of nitrate, once the active ingredient (nitrate) has been swallowed, it is recycled, returned to the oral cavity, and mantains its effect for hours.

State of development and intellectual property rights

The dose required for the prebiotic to perform its function has been determined. Validation tests have been carried out in an in vitro oral biofilm model, showing benefits against caries, periodontitis and halitosis (published in Rosier et al. Sci. Reports 2020). Taking the nitrate (prebiotic) supplement has been shown to be effective in humans in preventing tooth decay in several clinical studies, by neutralizing salivary acids and by lowering the volatile compounds responsible for intraoral halitosis. The best probiotics have been isolated and selected, which have been characterized and tested in vitro in an oral biofilm model (published in Rosier et al. Frontiers Microbiol 2020). The absence of mobile elements, antibiotic resistance, and virulence genes in the genomes of patented probiotics has been established, as well as their gastric resistance, the absence of unwanted metabolite production, and various industrial scale up tests have been experimentally proven. Toxicity testing of probiotics in animals is currently underway. In addition, oral biofilm tests have been carried out in vitro to test the efficacy of the prebiotic and probiotic against periodontitis,and the efficacy of a nitrate diet to considerably improve the clinical parameters of periodontitis has been tested. Two types of diagnostic tests have been developed to measure the abilty to reduce salivary nitrate. Clinical trials are underway to test the efficacy of the prebiotic against periodontitis and halitosis in vivo.

The technology is protected under patent (PREBIOTIC AND PROBIOTIC TREATMENT TO REDUCE ORAL DYSBIOSIS AND PROMOTE EUBIOSIS, priority date December 17, 2019) and it has been extended internationally in Europe, Canada, Mexico, USA, China and Australia.

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