NANOPARTICLES FOR THE TREATMENT OF INFECTIONS CAUSED BY BIOFILMS

DESCRIPTION OF THE TECHNOLOGY

According to the World Health Organisation (WHO), infectious diseases are a leading cause of death, second only to cardiovascular diseases. Today, although most acute infectious diseases have been virtually eradicated thanks to the development of vaccines and antibiotic treatment, this is not the case for chronic infectious diseases in which the infectious agent is recalcitrant and does not respond effectively to antimicrobial treatment. In most of these cases, antibiotics do not work effectively because these micro-organisms are attached to surfaces forming biofilms. Biofilms facilitate the evasion of the immune system and increase the antibiotic resistance of the microorganism up to 1000 times.

Researchers from the Polytechnic University of Valencia, Network Biomedical Research Center and the Foundation for the Promotion of Health and Biomedical Research of the Valencian Community (Fisabio) have developed a nanodevice with movement that contains the antimicrobial agent inside, as well as a "molecular drill" attached to the surface, capable of penetrating and disintegrating bacterial and fungal biofilms.

The molecular drill in combination with the self-propulsion system allows to break the biofilm matrix and release the antimicrobial substance inside through a pH-sensitive molecular gate.

The device can be used for any infection caused by biofilms, both single-species and multi-species as in the case of endodontic infection treatment, where our *in vitro* tests have shown that the self-propulsion system can reach and disintegrate the biofilm. Other applications include disinfection of medical devices and surgical material, treatment of oral and vaginal candidiasis and onychomycosis or nail infections.

MARKET APPLICATION SECTORS

Pharmaceutical companies. Companies in the oral health sector.

TECHNICAL ADVANTAGES AND BUSINESS BENEFITS

Allows the penetration and release of a greater quantity of therapeutic agent inside the biofilm, and therefore greater therapeutic efficacy.

Disintegration and drastic reduction of the extracellular matrix of the biofilm formed by the infectious agent, superior to that observed with other known systems.

Drastic reduction of cell viability (around 90%) at low concentrations of therapeutic agent.
Versatility of the nanodevice to be functionalised with different antimicrobials or biomolecules in a simple way, and therefore to treat different types of infections caused by biofilms generated by a wide range of infectious agents. Efficacy has already been tested to prevent and eradicate biofilms of *Staphylococcus aureus* bacteria and human dental plaque, as well as to prevent the formation of *Candida* biofilms by antifungals.

In the case of endodontic use, tests in an artificial mouth system show that the use of the developed device, with endogenous movement generated from H_2O_2 and with a particle size smaller than the diameter of the endodontic canals, allows disintegrating the biofilm and releasing the antimicrobial agent along the root canals.

CURRENT STATE OF DEVELOPMENT

Nanodevice movement and cargo release tests have been performed for different antimicrobials (the antibiotics vacomycin and metronidazole, the antifungal micafungin and the antiseptic chlorhexidine).

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In vitro tests have been performed on two biofilm models for Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Pseudomonas aeruginosa*) bacteria, as well as for yeasts (*Candida albicans*).
Ex vivo tests have been performed in an oral biofilm model with human samples and in a real tooth (relevant environment).

Safety/toxicity tests in animal models are scheduled for 2023.

INTELLECTUAL PROPERTY RIGHTS

A patent has been applied for at the OEPM (Spanish Patent and trademark Office) with application number P202230450 and priority date 26 May 2022. International extension is foreseen.

COLLABORATION SOUGHT

A licensee company interested in the commercialisation of the product.

RELATED IMAGES

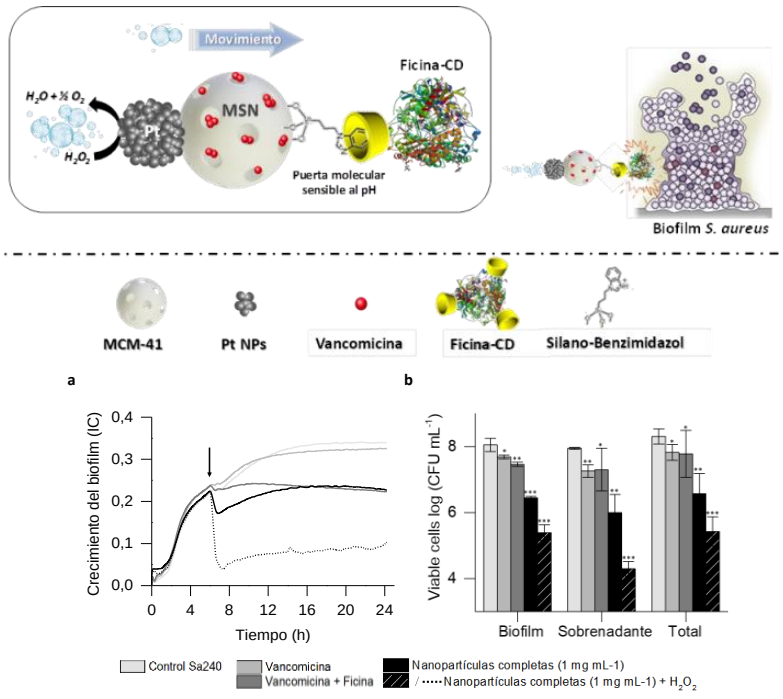

Figure 1: Schematic of the nanodevice against Staphylococcus aureus biofilms. In this case, the device is loaded with the antibiotic vancomycin, and contains a molecular drill based on the enzyme ficin, which degrades the biofilm matrix as it is propelled by hydrogen peroxide at low concentrations.

*Figure 2: Effect of the nanodevice on S. aureus biofilm in vitro: Figure a) shows the monitoring of S. aureus biofilm growth, expressed as cell index (CI) in the presence of the components (separately and together) of the nanodevice. The black arrow indicates the time at which the different elements were added. In ascending grey scale order, the composition containing a control (the untreated S. aureus strain) starts, followed by the composition comprising vancomycin only; the composition comprising vancomycin and ficin added separately; the composition of the complete nanodevice (nanoparticle with self-propulsion system, ficin, and vancomycin) (1mg) without fuel and the black dotted line the composition comprising the complete nanodevice (nanoparticle with self-propulsion system, ficin, and vancomycin) (1mg) plus 0. 2% H_2O_2. Figure b) shows cell viability expressed as logarithm of colony forming units per millilitre, log (CFU ml-1) in the biofilm formed in the presence of each component (*p<0.05, **p<0.01, ***p<0.001).*

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