NuMat Medtech

NM_973 SURFACE

SURFACE TECHNOLOGIES ADDRESSED TO DENTAL AND ORTHOPEDIC MARKETS

A. Background

Flavonoids are a group of small polyphenolic molecules **derived from plants** with antioxidant, anti-inflammatory and antibacterial properties. They are present in the **daily human diet** and their intake has been related to the prevention of cancer, cardiovascular and neurological diseases. Furthermore, flavonoids have shown beneficial effects on the bone metabolism. **Quercitrin** (quercetin-3-O-rhamnoside) is a yellow coloured flavonoid obtained from Tartary buckwheat and from the bark of different species of oak trees.

We have developed and patented a method to covalently bind quercitrin to titanium surfaces with both promising bone and soft tissue stimulating properties, and antimicrobial and anti-inflammatory activities.

B. Aim

Our medium-term goals involve confirming our *in vitro* and *in vivo* results in further *in vivo* preclinical models and in clinical studies. Thus, we expect to see:

- Improvement in **bone and gingiva regeneration**, based on increased differentiation of osteoblasts and gingival fibroblasts cultured on surfaces modified with flavonoids.
- Increased tissue integration and **protection against bacterial infection**, based on the decrease of bacterial adhesion and the increase of mesenchymal stem cell adhesion to modified surfaces with flavonoids.
- **Decrease of inflammation** around the implant, based on the decrease of the production of inflammatory mediators and the re-establishment of the impaired collagen metabolism induced by inflammation in human gingival fibroblasts.

Our long-term goal is to generate third-generation implants that overcome the gaps of current technologies and that have better tissue integration based on osteopromotive, antimicrobial and anti-inflammatory properties.

C. How?

Quercitrin-modified titanium surfaces retain the osteoconductive properties of titanium while adding other bioactivities:

- ✓ Decrease of inflammation
- ✓ Antimicrobial
- ✓ Decrease of oxidative stress
- ✓ Increase of bone formation
- ✓ Decrease of bone resorption

The coating process based on wet chemistry is robust, reproducible and simple, and can be applied to any 2D and 3D implants. The coating is stable, and it maintains its properties after sterilisation.

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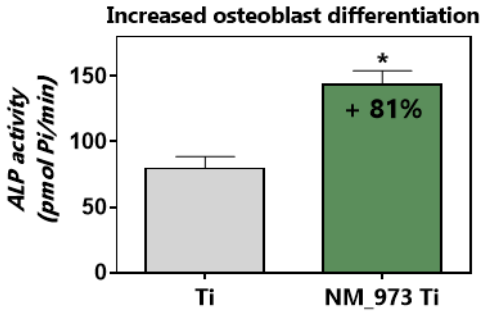
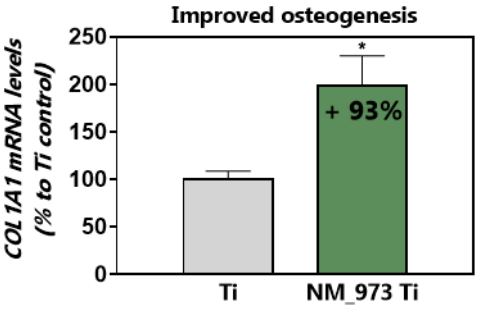
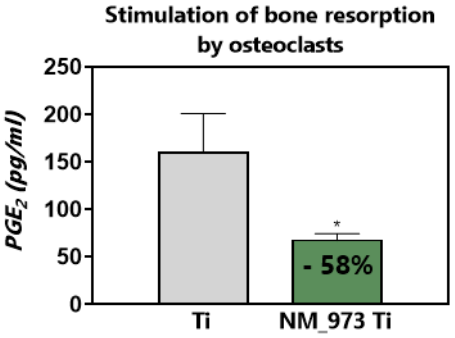
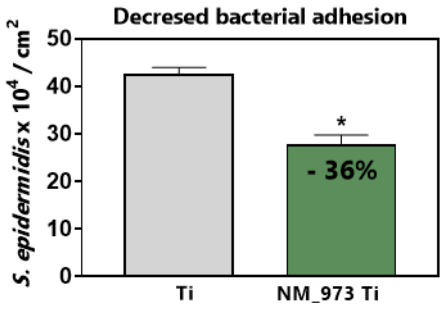
D. What do we know so far?

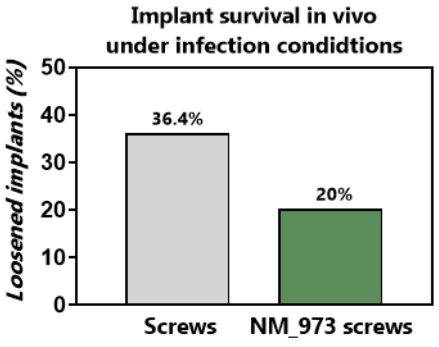
- Flavonoid modified surfaces **stimulate bone formation** *in vitro.*
- Quercitrin modified surfaces **increase initial cell adhesion** of human mesenchymal stem cells, human gingival cells and mouse osteoblast precursors, while significantly **decrease bacterial adhesion** of the tested strains: *S. mutans, S. aureus and S. epidermidis*.
- Quercitrin modified surfaces **decrease the expression of inflammation and profibrotic markers** *in vitro* on human gingival cells and on mouse osteoblast precursors.
- Quercitrin modified surfaces **inhibit bone resorption** *in vitro* and *in vivo* on a hard tissue tibial model in rabbit.
- Quercitrin modified surfaces under an inflammatory stimulus (mimicking the inflammatory status found in periodontal disease) help to effectively **inhibit COX2 expression** (an inflammatory mediator) **and decrease** its functional product **PGE2** under basal and inflammatory conditions.
- The **destruction of extracellular matrix is reduced** on quercitrin modified surfaces, even in inflammatory conditions.
- **Increased implant survival under infection conditions** in a dental mouse model *in vivo*.
- **Increased osseointegration** in a dental mouse model *in vivo*.











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E. Publications

• Córdoba, A.; et al. (2018). Quercitrin Nanocoated Implant Surfaces Reduce Osteoclast Activity In Vitro and In Vivo. *Int J Mol Sci 19(11): pii: E3319.*

• Gomez-Florit, M.; et al. (2016). Quercitrin-nanocoated titanium surfaces favour gingival cells against oral bacteria. *Scientific Reports 6: 22444*.

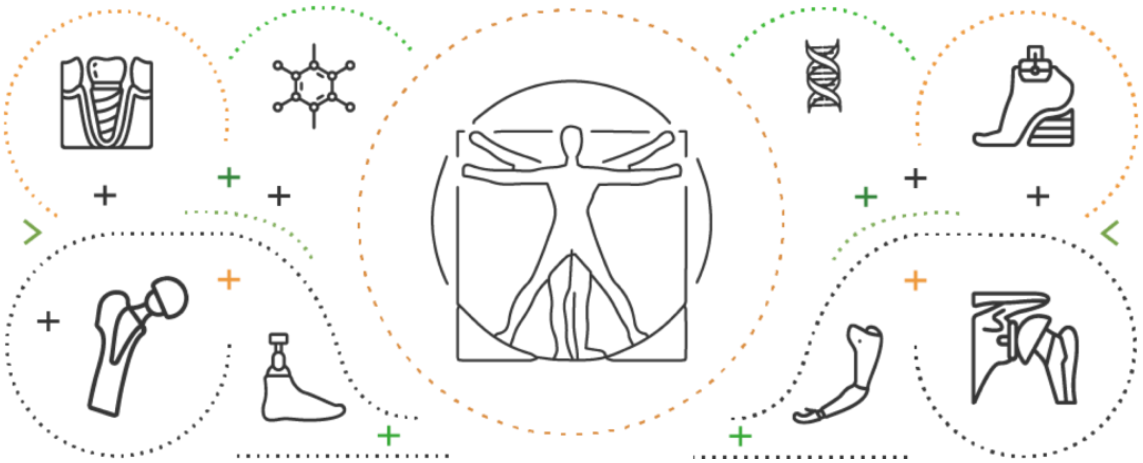
• Córdoba, A.; et al. (2015). Bioinspired quercitrin nanocoatings: A fluorescence-based method for its surface quantification, and its effect on stem cell adhesion and differentiation to the osteoblastic lineage. *ACS Applied Materials & Interfaces 7(30):16857–16864*.

• Córdoba, A.; et al. (2015). Flavonoid-Modified Surfaces: Multifunctional Bioactive Biomaterials with Osteopromotive, Anti-Inflammatory, and Anti-Fibrotic Potential. *Advanced Healthcare Materials 4(4): 540-549*.

• Gómez-Florit, M.; et al. (2015). Quercitrin for periodontal regeneration: effects on human gingival fibroblasts and mesenchymal stem cells. *Scientific Reports 5:16593*.

• Gómez-Florit, M.; et al. (2014). Identification of quercitrin as potential therapeutic agent for periodontal applications. *Journal of Periodontology 85(7):966-74*.

• Satúe, M.; et al. (2013). Quercitrin and Taxifolin stimulate osteoblast differentiation in MC3T3-E1 cells and inhibit osteoclastogenesis in RAW 264.7 cells. *Journal of Periodontology 85(7):966-74*.



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