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Nanocrystalline apatite: from fundamentals to bone substitute materials

Industrial and business point of view

Paulo Quadros, PhD
Head of Product &
Business Development

NEWGEN Workshop, Nantes, May 2014

About us

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Hydroxyapatite Nanoparticles

Fluidinova is a specialized manufacturer of synthetic nanocrystalline hydroxyapatite material, which is commercialized under the brand name **nanoXIM®**. Using an innovative proprietary technology – **NETmix®** – Fluidinova produces a highly pure, single phase nanoHydroxyapatite. **nanoXIM®** is supplied worldwide in different forms to manufacture Medical Devices, for Personal Care Product formulations, R&D activities and many other applications.

Follow us on **LinkedIn**

NEWS - Check out the new video of nanoXIM - The Enamel Repair Ingredient.

Download product brochure

Business areas

Medical Devices segment of the nanoXIM product

High-quality hydroxyapatite supplied to medical devices manufacturers.

Several clients using nanoXIM•HAp for manufacturing bone substitutes with CE mark in Europe and FDA approval in the USA.

Bone substitutes are the main nanoXIM Medical market, with special emphasis on the injectable bone substitutes devices.

nanoXIM possesses excellent properties of bone regeneration and biocompatibility.

Personal Care segment of the nanoXIM product

High-quality hydroxyapatite supplied for cosmetic manufacturers, with special focus on dentifrices (toothpastes, mouthwashes, whitening products…).

nanoXIM nanohydroxyapatite presents good enamel remineralization potential and high occlusion efficacy of dentine tubules, making it a solution for teeth hypersensitivity.

Tooth surface smoothness and additional whitening are a plus provided by nanoXIM.

R&D applications of the nanoXIM product in a broad applications fields

High-quality hydroxyapatite material for R&D projects like bio-separation, pharma, drug delivery and polymers functionalisation.

nanoHAP industrial manufacturing

nanoXIM Plant Facilities

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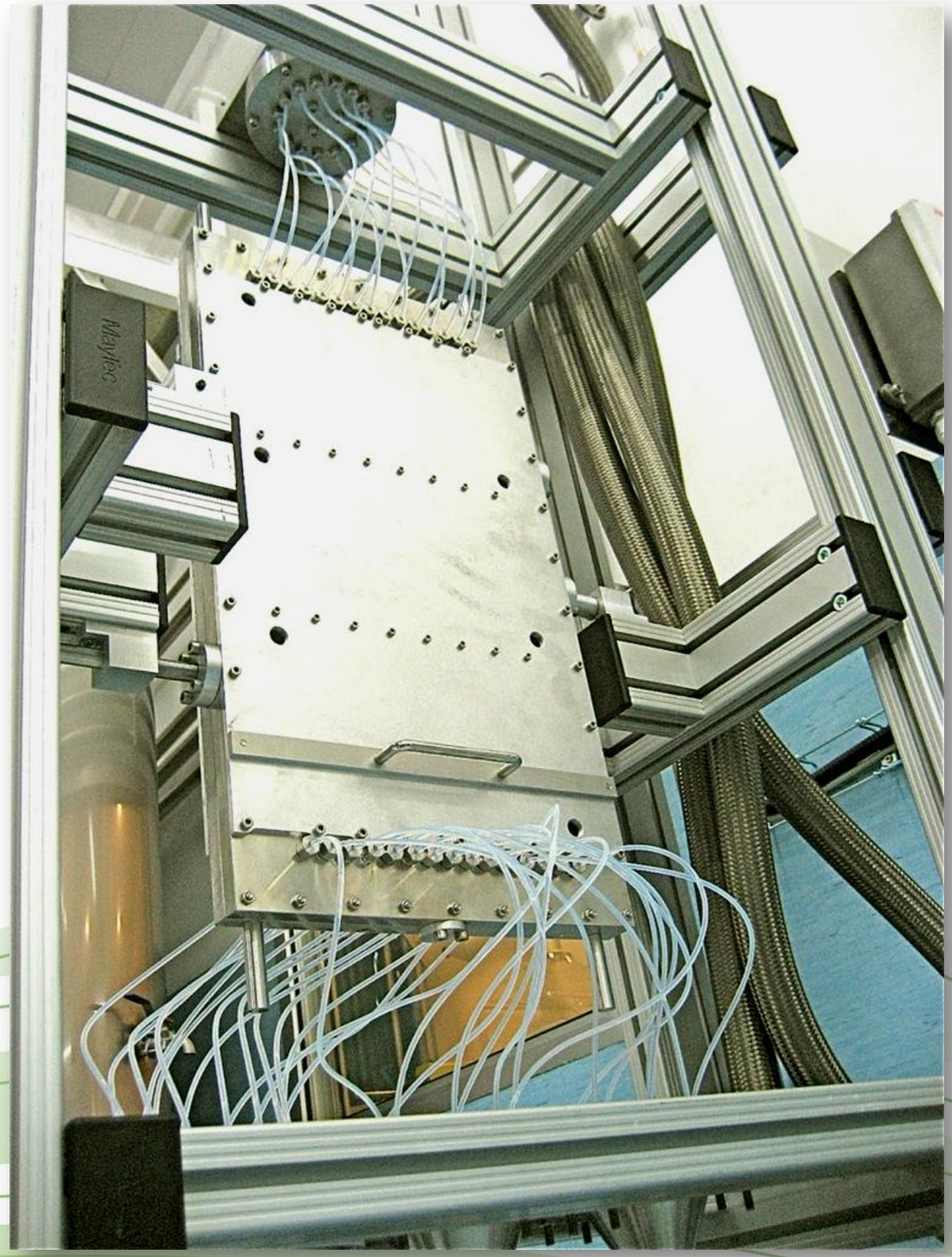

nanoXIM Laboratory

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R&D projects:

- **NEWGEN:** New Generation Biomimetic and Customized Implants for Bone Engineering, COST EU RTD (2013-2017)
- **IMCOSS:** Injectable Medical Ceramics for Bone Repair and Augmentation, FP7 EU (2012-2014)
- **NanoForBone:** Development and scale-up of 3D structures and coatings for medical applications based on nanosized hydroxyapatite, AdI Portugal (2009-2012)

Applications, Products & Studies

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nanoXIM

Medical

APPLICATIONS >

nanoXIM•Medical materials are precursors of high quality medical devices biomaterials used in:

Trauma & Orthopedics

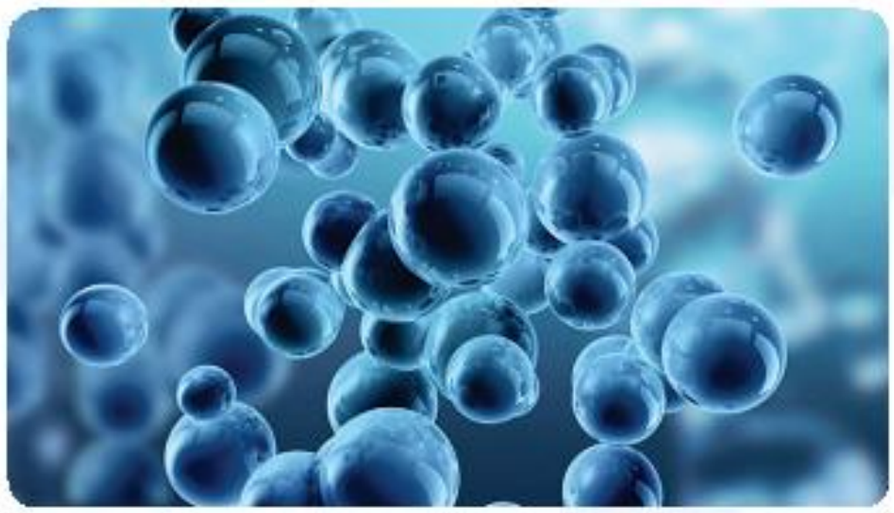
> Filling bone voids or gaps not intrinsic to the stability of the bony structure caused by trauma, disease or related surgical procedures reducing significantly the use of autologous grafts.
nanoXIM•Medical pastes are suitable to be injectable, moldable and easily adaptable to bone defect shape, allowing a high bone-implant interface.

Periodontal & Maxillofacial

> Periodontal defects filling, alveolar bone filling, sinus base augmentation and elevation, reconstruction of mandibular cyst defects and voids after tooth socket extractions.

Otology

> Components in otology implants and cements suitable for middle ear surgeries. Innovative otology products enable simpler surgical procedures, reducing recovery times, thus improving patient's quality of life.



Pharma

> The high surface area and biocompatibility of nanoXIM spray-dried powders makes them particularly suitable for the development of new drug delivery systems.

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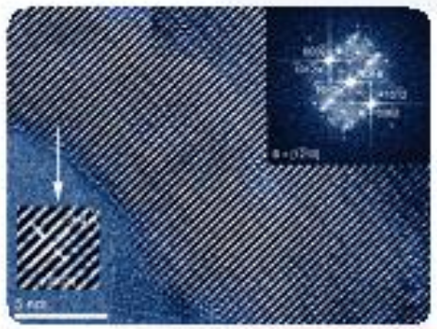
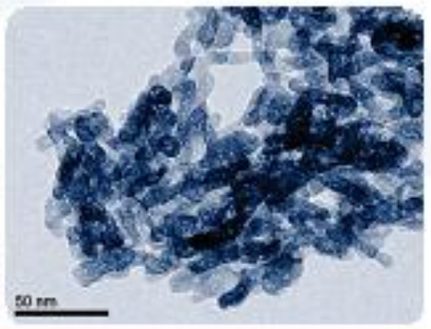
nanoXIM•Medical Pastes

> nanoXIM•HAp100 series are water based nano-hydroxyapatite pastes specially recommended for medical devices manufacturing such as bone injectable substitutes for bone repair and reconstruction.

ADVANTAGES

> Highly osteostimulative
> Highly resorbable material replaced by new bone during the healing process
> Optimal defect filling due to pasty consistency
> 100% synthetic and safe material
> High surface area





Product Reference	Description
nanoXIM•HAp102	15.0 ±1.0% wt. hydroxyapatite nanoparticles aqueous paste
nanoXIM•HAp103	30.0 ±3.0% wt. hydroxyapatite nanoparticles aqueous paste

nanoXIM•Medical Powders

> nanoXIM•HAp200 series are spray-dried hydroxyapatite powders used as precursors of porous granules and blocks scaffolds for bone repair and reconstruction.

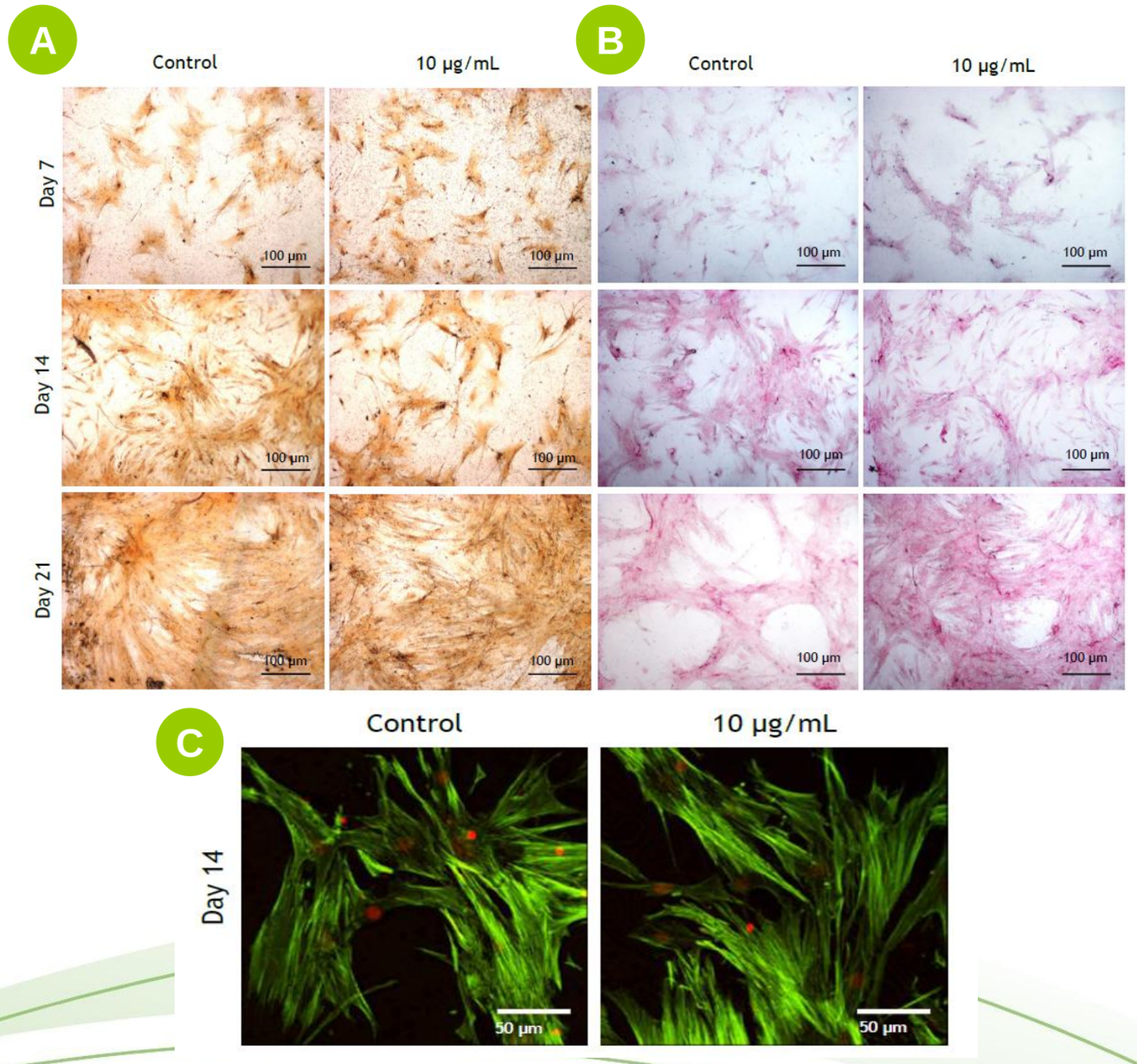
ADVANTAGES

> 100% synthetic and safe material
> High surface area and porosity
> Nanostructured micron sized material
> High biocompatibility
> Narrow particle size distribution

Product Reference	Description
nanoXIM•HAp202	5.0 ± 1.0 µm d_{50} hydroxyapatite spray-dried powder
nanoXIM•HAp203	10.0 ± 2.0 µm d_{50} hydroxyapatite spray-dried powder

Studies

In vitro study with nanoXIM paste



HMSCs cultured in the absence (control) and in the presence of 10 µg/mL of nanoXIM•HAp102 at days 7, 14 and 21. (A) Histochemical staining for ALP and (B) collagen. The synthesis of ALP is observed by the presence of a brown to black stain and collagen by a pink to red stain.
(C) Confocal laser scanning microscopy of HMSCs cultured for 14 days in the absence (control) and in the presence of 10 µg/mL of nanoXIM•HAp102. F-actin cytoskeleton organization is stained in green and nuclei in red.

- Human mesenchymal stem cells (HMSCs) are considered an excellent candidate for cell-based therapies since they are able to differentiate in a wide variety of cell types, including the osteogenic lineage;

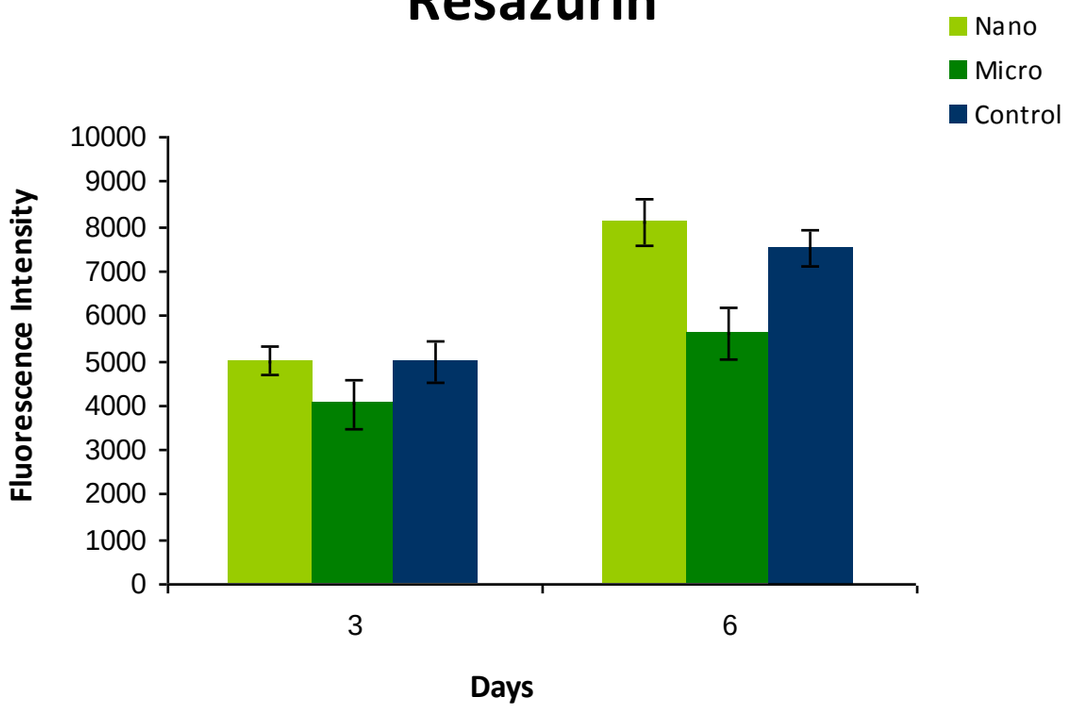
- HMSCs exposed to 10 µg/mL of nanoXIM·HAp102 showed **increased alkaline phosphatase (ALP)** (A) **and collagen synthesis** (B) and a **typical cytoskeleton organization** (C);

- These results demonstrate that nanoXIM·HAp102 formulation is able to modulate the HMSCs osteoblastic differentiation, being a promising product to be used in bone regeneration applications.

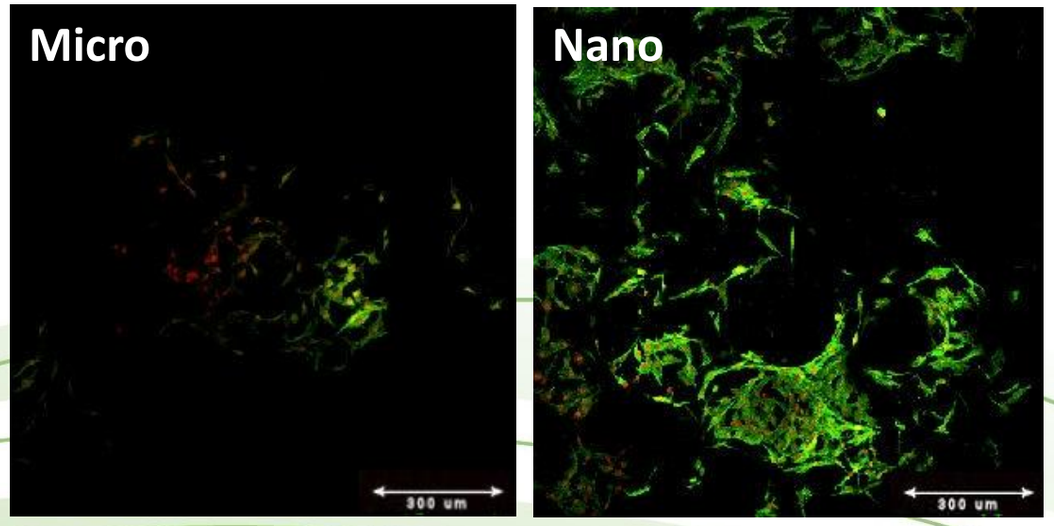
Source: E. Pires, "Effect of the nanohydroxyapatite Formulation NanoXIM.HAp102 on the Proliferation and Osteogenic Differentiation of Human Bone Mesenchymal Stem Cells", Integrated MSc Thesis in Bioengineering, Faculty of Engineering, University of Porto (2013).

In vitro study with nanoXIM powder

A



B



MG63 osteoblast-like cells cultured on micro and nanoscale HA substrates. (A) Cell proliferation for 3 and 6 days estimated by resazurin assay; (B) Confocal microscopy images of cells cultured for 6 days on the two different materials. Data kindly provided by Marta Laranjeira.

- The substrates produced using nanoXIM·HAp202 showed **improved cell viability and proliferation** when compared with microscale hydroxyapatite substrates (A);

- Both substrates present well spread cells with typical morphology. However, nanoscale substrates possess a **higher number of cells** adhered on the material (B);

- Nanostructured hydroxyapatite substrates produced with nanoXIM·HAp202 provided a more adequate environment for bone regeneration.

Source: Laranjeira MS, Fernandes MH, Monteiro FJ. Innovative macroporous granules of nanostructured-hydroxyapatite agglomerates: Bioactivity and osteoblast-like cell behaviour. Journal of Biomedical Materials Research Part A. 2010;95A(3):891-900.

Next Generation Products

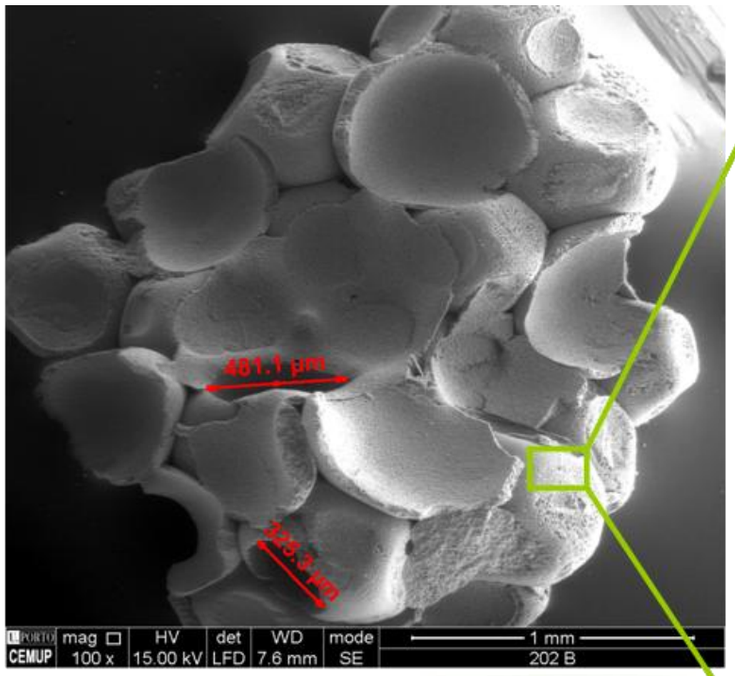
nanoXIM blocks and granules

Blocks

Granules 1-2 mm

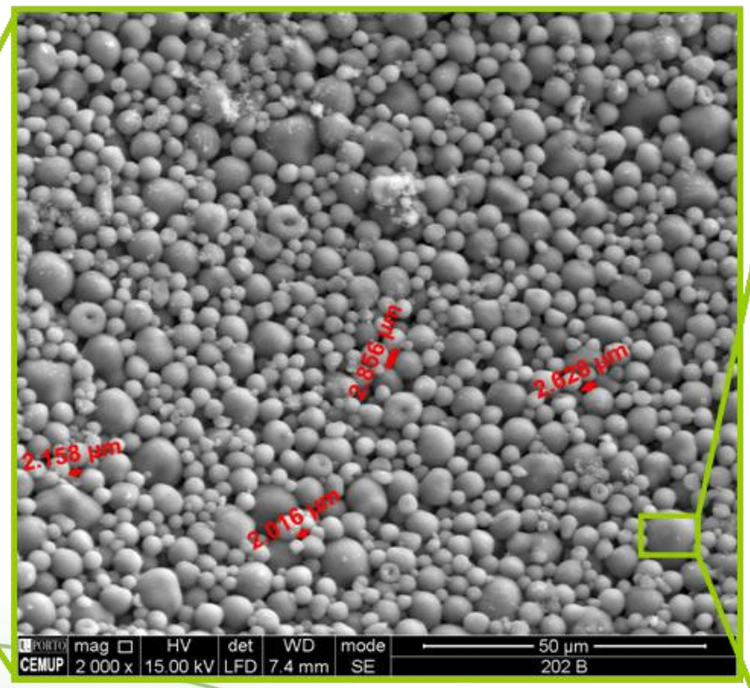
nanoXIM blocks and granules

Granules 1-2 mm



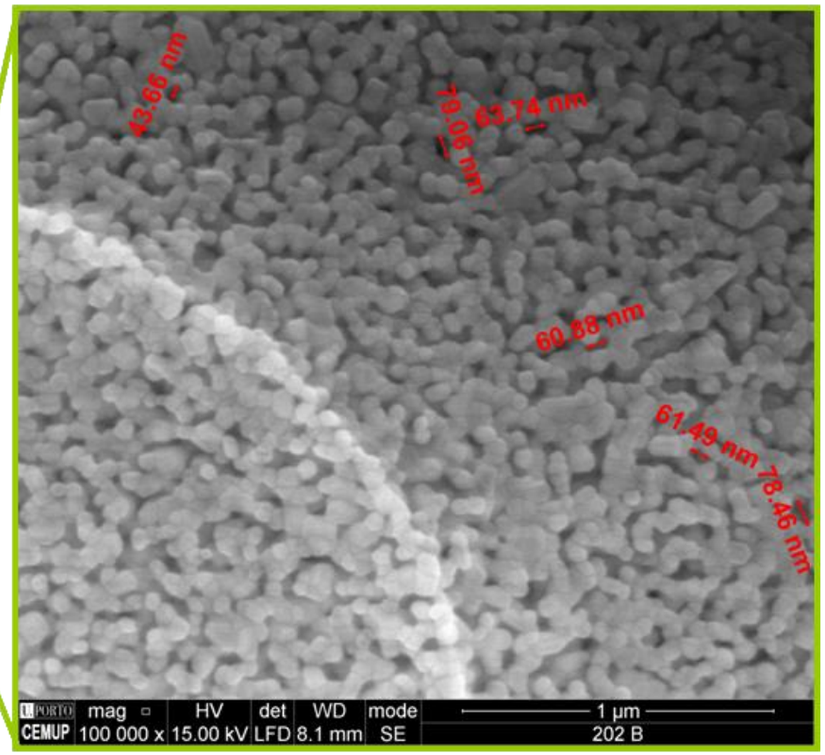
Macroporosity

(200-500 µm approx.)



Microporosity

(2-3 µm approx.)



Nanoporosity

(40-80 nm approx.)

FLUIDINOVA, SA

Tecmaia - Rua Engº Frederico Ulrich, nº 2650
4470-605 Moreira da Maia
PORTUGAL
☎ : +351 220 119 746

www.fluidinova.com

nanoxim@fluidinova.com