Process for Instant Nanoporous BioArtificial Bone Tissue Composite Engineering

Description

This process for engineering instant nanoporous bio-artificial bone tissue composite is designed aiming the prevention of body immune reaction when integrated with host bone tissue and also reduces its period of integration. Its composition permits instant transplantation of any implantable devices into this biocomposite because of its instant hardening property and instant integration in any part of the skeleton. This nanoporous biocomposite is compounded as follow: With *first ingredient* as Hydroxylapatite (HA), or/and alpha- or beta-tricalcium phosphate (α- or β-TCP), or/and biphasic calcium phosphate (BCP) which results of combining HA and TCP, or/and Calcium sulfate ($CaSO_4$) whose particles do not exceed 99 nm. *Next ingredient*, polycaprolactone (PCL) or polylactic acid (PLA) also with particles do not exceeding 99 nm. *Other ingredients* are: gelofusine or any gelatinable solution or gel, then water is added in relevant quantity for producing gel or injectable solution of this biocomposite. Later on, any substance composed of any connective collagen tissue (f. ex. catgut etc.). after this, recombinant Human Vascular Endothelial Growth Factor A165 (rhVEGF-A165) with a dosage inferior to 1-3 ng/ml of the final compound measured by the dose-dependant stimulation of the proliferation of Human Vascular Endothelial Cell (HUVEC). *Afterwards*, any kind of acrylate (cyanoacrylate or sulfacrylate etc.) used as molecular ligand, when the hardening and final process of all this compound is acquired immediately by ultrasound

treatment at a frequency between 24 and 32 Khz applied for a very short period of time under 60 s. The proportions of the different components are very variable and may be adapted to the type and form of the treated bone individually. In any case the first ingredient of the compound (HA or α- or β-TCP and so on) proportion with PCL or/and PLA is between 58% and 66% of the resulting intermediate compound. The acrylate (cyanoacrylate or sulfacrylate etc.) is never less than 2 drops and not more than 6 drops for 0.6 ml of the composite. Using 3D CAD modelling and press forming, it is possible to build with this biocomposite any part of the skeleton (human or animal). β-TCP may be reinforced with biodegradable Fe-Mg metal phase or Fe-Ag nanocomposites. In any kind of jointure parts relevant coating (e.g. Titanium Nitrite also called Tinite (TiN) coating or Diamond Like Carbon (DLC) coating etc.) will be added. In the vertebral parts it is possible to add to this biocomposite biocompatible phospholipids.

Abstract

Process for engineering instant nanoporous bio-artificial bone tissue composite is designed aiming the prevention of body immune reaction when integrated with host bone tissue and also reduces its period of integration. This nanoporous biocomposite is compounded by a number of ingredients. Hydroxylapatite (HA), or/and alpha- or beta-tricalcium phosphate (α- or β-TCP). Polycaprolactone (PCL) or polylactic acid (PLA). Any gelatinable solution or gel, then water is added in relevant quantity for producing gel or injectable solution of this biocomposite. Any substance composed of any connective collagen tissue. Recombinant Human Vascular Endothelial Growth Factor. Any kind of acrylate when the hardening and final process of all this compound is acquired immediately by ultrasound treatment.

Claims

1. The size of the first ingredient (HA or/and α- or β-TCP or/and etc.) granules must be reduced by any enabling and approved process for this procedure with suitable cooling measures (f. ex. high energy milling attritor etc.).

2. Bone regeneration is made possible by the interaction between two kinds of cells: osteoblast and osteoclast. Osteoclast is a giant cell with a diameter of about 50 μm, and it independently absorbs (destroys) old bones. Osteoblast, on the other hand, is a small cell with a diameter of about 10 μm, and it forms new bones by working with many other cells. Bones are always regenerating through a perpetual cycle of bone resorption and bone formation.

3. Idem as §1 for the size of PCL or PLA granules which must be reduced by any enabling and approved process for this procedure with suitable cooling measures (e.g. high energy milling attritor etc.).

4. The association of the first ingredient (HA or/and α- or β-TCP or/and etc.) and PCL or/and PLA is possible with any laboratory mixer adequate for this process.

5. β-TCP-15Fe15Mg composite with human osteoblasts monocultures and human osteoblast-endothelial-cell co-cultures indicated that composition was biocompatible for the growth and survival of both cell types and cell exhibited tissue-specific markers for bone formation and angiogenesis respectively.

6. Bioresorbable β-TCP-polymer and Fe-Ag nanocomposites may be part of the compound.

7. Idem as §4 is the addition of Gelofusine or any gelatinable solution or gel with any laboratory mixer till the transformation of the whole compound into a gel with an ad hoc addition of water to obtain an usable gel.

8. Addition of water to the above till transformation into an injectable solution.

9. The grinding of any element containing connective collagen tissue (f. ex. catgut etc.) until obtaining tiniest particles as possible with the help of a laboratory grinder. Dosage of catgut or of any substance composed of any connective collagen tissue is variable and depending to form and type of the bone to be treated.

10. Any element containing connective collagen tissue and any crylate drops are attached to the compound close to the surgical procedure which is finalized with the ultrasound treatment.

11. From this composite, it is really easy to prepare artificial bones for plastic, traumatologic and orthopedic surgeries.

12. Transplants and grafts made from this instant biocomposite are free of any immune reaction, while others may have many reactions and influences on the recipient's body, specially those based on animal bones.

13. In vitro, with 3D CAD modelling and press forming to build bones, it is possible to get transplants made of this composite with natural bone aspect, white colored and smooth surfaced. The resulting transplant is equivalent mechanically to natural bones in hardness, torsion and flexion.

14. In articulations, TiN or DLC coating or any other carbon like coating onto the transplant grants it natural like friction.

15. Recombinant human Vascular Endothelial Growth Factor A165 (rhVEGF-A165) which is part of this biocomposite is provided and acts as a potent and effective factor for micro-vascular perfusion enhancement and for the development of new micro-vascular capillaries in an organized structural network in living tissues.

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Organizational chart of the process

Schema