### **Process for Building Artificial Multifunctional Injectable Filler**

### Description

This process for engineering nanoporous biodegradable artificial multifunctional injectable bio-composite filler is designed aiming the prevention of body immune reaction when integrated with host tissue. This nanoporous biodegradable artificial multifunctional filler is compounded as follow: First ingredient is a bio-composite of alpha- or beta-tricalcium phosphate ( $\alpha$ - or  $\beta$ -TCP) mixed with polycaprolactone (PCL) composite powder followed by high pressure consolidation of the blend at room temperature and in proportion not less than 7% and never more than 10% of the final compound product. Second ingredient, phospholipid – phosphatidilcholine (PC) which is worldwide known as the leader of lysolecithin produced under various names by different factories around the world, its proportion being not less than 20% and never more than 25% of the final compound product. *Third ingredient,* any product of microbiological synthesis of exopolysaccharides (EPS) using bacteria Xanthomonas Campestris and Bacillus Amyloliquefacience such as Xanthan, Levan, Pullulan, Kurdlan etc. In proportion not less than 8% and never more than 10% of the final compound product. Fourth Ingredient, any connective collagen tissue (f. ex. catgut etc.) in proportion not less than 11% and never more than 13% of the final compound product. Fifth Ingredient, gelatine powder in proportion of 1g for 5ml of distilled water, this solution being in proportion not less than 42% and never more than 54% of the final compound product. Sixth ingredient, 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). After injection, the final processing of all this bio-composite is acquired immediately by ultrasound treatment at a frequency between 24 and 32 Khz applied for a very short period of time under 60s.

#### Abstract

This process for engineering nanoporous biodegradable artificial multifunctional injectable bio-composite filler is designed aiming the prevention of body immune reaction when integrated with host tissue. This nanoporous biodegradable artificial multifunctional filler is compounded as follow: *First ingredient* is a bio-composite of alpha- or beta-tricalcium phosphate ( $\alpha$ - or  $\beta$ -TCP) mixed with polycaprolactone (PCL) composite powder. *Second ingredient*, phospholipid – phosphatidilcholine (PC) which is worldwide known as the leader of lysolecithin produced under various names by different factories around the world. *Third ingredient*, any product of microbiological synthesis of exopolysaccharides (EPS) using bacteria Xanthomonas Campestris and Bacillus Amyloliquefacience such as Xanthan, Levan, Pullulan, Kurdlan etc. *Fourth Ingredient*, recombinant Human Vascular Endothelial Growth Factor A165. After injection, the final processing of all this bio-composite is acquired immediately by ultrasound treatment at a frequency between 24 and 32 Khz applied for a very short period of time under 60s.

#### Claims

1. The powders size of the components of the first ingredient  $\alpha$ - or  $\beta$ -TCP and PCL must be reduced by any enabling and approved process for this procedure with suitable cooling measures (f. ex. high energy milling attritor etc.).

2. Tissue integration is made possible between numerous kinds of cells: myocites, fibrocites, dermocites etc.

3. Mixed with above §1 compound of any Lysolecithin produced Phospholipid.

4. Mixed with above §3 any product of microbiological synthesis of exopolysaccharides (EPS).

5. Mixed with above §4, grinding of any element containing connective collagen tissue (f. ex. catgut etc.) until obtaining the tiniest particles as possible with the help of a laboratory grinder. Dosage of catgut or any substance composed of any connective collagen tissue is variable and depending to the type of the tissue to be treated.

6. Idem as §5 is the addition of Gelatine powder mixed in distilled water 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 product.

7. Recombinant human Vascular Endothelial Growth Factor A165 (rhVEGF-A165) which is part of this bio-composite 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.

8. This artificial multifunctional bio-composite is activator of neovasculogenesis process in the treated tissue.

9. This artificial multifunctional bio-composite filler can be used in plastic, traumatologic and orthopedic surgery.

10. This artificial multifunctional bio-composite is free of any immune reaction, while others may have many reactions and influences on the recipient's body, especially those based on animal tissues or cancerogenic components.

11. This artificial multifunctional bio-composite may be liquid or gel.

12. Process of building of this artificial bio-composite filler is finalized with the ultrasound treatment.

13. It is important to notice that the ultrasound treatment is applied at a frequency between 24 and 32Khz during a very short period of time – under 60s.

14. The ultrasound treatment has to be performed in vivo.

# This artificial multifunctional bio-composite can be used to heal various damaged human or animal tissues!

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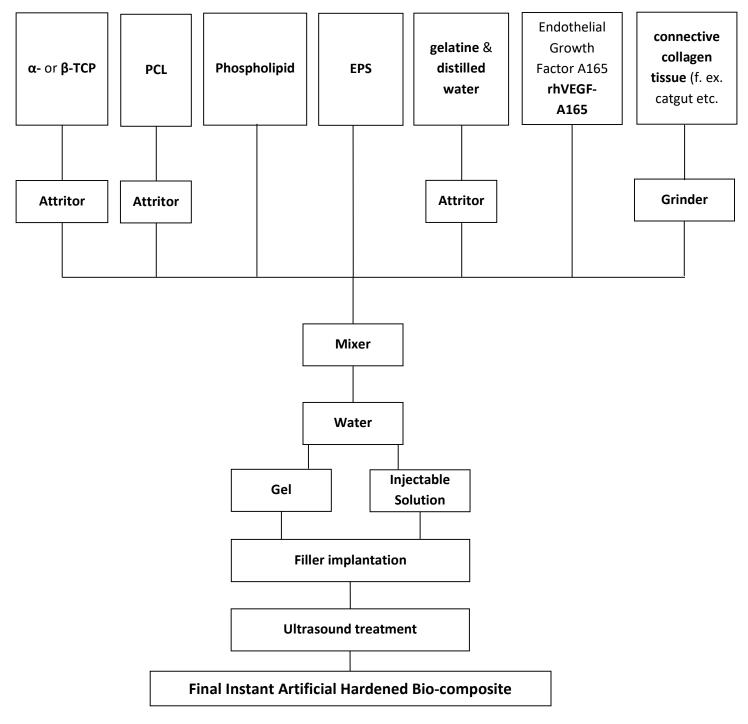
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12. Israeli Patent Application Number 250881 – PCT Application Number IL2018050096-IB304.

## Organizational chart of the process

Schema



Bio-composite tissue engineering