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(54) **Title**: PREPARATION FOR REGENERATION OF POSTOPERATIVE, POST-TRAUMATIC BONE DEFECTS AND METHOD FOR IMPLANTATION OF THIS PREPARATION

(57) **Abstract**: According to the invention preparation for regeneration of bone defects is employed in many branches of medicine, especially in orthopedics, dental surgery, reconstructive surgery, periodonthology and implantology. The preparation has been developed on the basis of inorganic chemical compound naturally occurring, i.e. deproteinized human bone, and on the basis of at least one of inorganic chemical compounds synthetically occurring, i.e. bioglass in the form of granulated highcalcium product (54% mol. CaO), obtained with the use of zol-gel method in the system $CaO\text{-}SiO_2\text{-}P_2O_5$, of density 2,9082 g/cm^3, with phase composition with a dominant glassy phase and beginnings of crystallization of apatite, heat treated at temperature of 800°C, having a specific surface BET 57,8166 m^2/g and/or tricalcium phosphate - TCP in the form of granulated product with chemical formula $Ca_3(PO_4)_2$. As a component deproteinized particlesof human bone are used, favourably with granulation 0,3-0,5 mm, bio-glass favourably with granulation 0,3-0,5 mm and/or TCP — tricalcium phosphate favourably with granulation 0,3-0,5 mm. The amount of bone material in the preparation amounts favourably to 70-80% of the preparation weight, the amount of bioglass in preparation amounts favourably to 10-15% of the preparation weight, the amount of TCP in the preparation amounts favourably to 10-15% of the preparation weight. During implantation binder in the form of blood from patient's operative wound is introduced into the preparation. Amount of the preparation in mixture favourably amounts to 75-80% of the mixture weight and the amount of own blood favourably amounts to 20-25% of the mixture weight.

PREPARATION FOR REGENERATION OF POSTOPERATIVE, POST-TRAUMATIC BONE DEFECTS AND METHOD FOR IMPLANTATION OF THIS PREPARATION

The subject of the invention is a preparation for regeneration of postoperative and post-traumatic bone defects and method for implantation of this preparation, employed in many branches of medicine especially in orthopedics, dental surgery, reconstructive surgery, periodenthology and implantology.

Nowadays popularly applied xenogeneic grafts or implants e.g. compositions of horse bone and cattle bone create a risk of transmission of animal diseases, e.g. BSE (Bovine Spongiform Encephalopathy). There is also a potential risk of transmission of pathogenic micro-organisms.

There are also autogenic bone implants of patient's own bone, most often taken from oral cavity area. Bone can also be collected from other patient's anatomic areas, but it cannot be done in a dentist's office. Most often such surgery is performed in a clinic.

The objective of this invention is creating a new therapeutically effective preparation for regeneration bone defects, which will show low biotoxicity and small systematic side effects at surgical application.

This invention helps to fulfill the above task. For purposes of clarity the preparation components have been marked with letters A, B, C, TCP. The essence of this preparation is application of a deproteinized human bone (A), deprived of the smallest molecules of protein, with granulation from 0,3 to 0,5mm, bioglass (B) with granulation from 0,3 to 0,5mm and binder (C) favourably in the form of a patient's own blood in the amount of 20-25% in relation to the quantitative sum of the above components. For making this preparation one could use human bone (A) available in tissue bank in the form of hydroxyapatite, with appropriate granulation, as well as in the form of trochlea. The second component of the preparation bioglass (B), in the form of powder with granulation 0,3-0,5mm, can be obtained with use of zol-gel method in the system $CaO-SiO_2-P_2O_5$. This component can also be used as a high silica component (80% mol. SiO_2) or/and as a high calcium component (54% mol. CaO). High silica component of a density 2,4037 g/cm^3, heat treated at temperature of 700 °C, amorphous, has a specific surface BET 297, 9663m^2/g. Whereas high calcium component of a density 2,9082 g/cm^3, with phase composition with a dominant glassy phase and beginnings of crystallization of apatite, heat treated at temperature of 800°C, has a

specific surface BET 57,8166 m^2/g. This kind of bioactive glass of preparation spontenaously forms union with maternity tissue and stimulates regeneration of bone tissue. Under "in vivo" conditions on the surface of biomaterial hydroxyapatite layer (HAp) crystallizes with chemical and mineralogical composition similar to bone HAp (natural). In this way an exceptionally durable chemical bond (bonding interface) is formed. In a living organism in the presence of bioglass numerous biochemical and biological processes take place, e.g. proteins adsorption, synchronized cells occurrences which result in a quick forming of administered bone tissue. The invention also anticipates that instead of bioglass (B), a tricalcium phosphate (TCP) could be applied – favourably with granulation 0,3-0,5mm, in the amount of 15-20% of the preparation weight.

Unexpectedly it has also turned out that it in possible to get very good therapeutic results in regeneration of bone defects, by compiling all the above mentioned components of the preparation. As components are simultaneously used deproteinized preparation of bone (A) with granulation 0,3-0,5mm in the amount favourably 70-80% of the preparation weight, bioglass (B) in the form of granulated product in the amount favourably 10-15% of the preparation weight, tricalcium phosphate TCP favourably 10-15% of the preparation weight, and binder (C) favourably in the amount of 20-25% of the preparation weight in relation to the quantitative sum of the amount of the above components.

Particular components are mixed in strictly defined proportions and strictly defined granulation. There are several reasons why it should be done this way. The main reason is atrophy of bone structure during spontaneous healing of wounds that reaches 20-30% of volume. Application of deproteinized human bone supplements natural hydroxyapatite in a wound, TCP slows down the process of atrophy and in this way reduces biodegradation, whereas bioglass due to its biologically active surface stimulates osteogenesis and functions as space filler when not being subjected to biodegradation.

This invention enables a faster regeneration of human bone tissue defects arising from intended activities, such as surgical activities, or unintended activities – injuries and disease process. Application of the above preparation results in a fast and complete regeneration of anatomic profile and physiological function. This invention helps to speed up the process of regeneration of damaged bone, and it contributes to compensation of biodegradation during the process of healing, due to active surfaces of the applied filler.

According to this invention an appropriate amount of the preparation is being mixed with binder i.e. the blood from operative wound (the mixture should be homogeneous). The obtained mixture which has consistency of Plasticine, is implanted into bone defects.

Application of a patient's own blood enriches the implanted preparation with organic components, e.g. collagen type 1, proteins, polysaccharides, lipids, necessary for osteogenesis and for preventing the preparation components from moving inside the operative wound. The components contained in a regenerating bone amount to 25% of the bone's weight. The components enumerated above, especially collagen, increase bone's resistance to mechanical destruction caused by tension that occurs during work, and reduce brittleness of bones. More over collagen and protein fibers accelerate crystallization of hydroxyapatite.

Patent claims

1. Preparation for regeneration of postoperative and post-traumatic bone defects based on inorganic chemical compound naturally occurring and synthetically occurring, is characterized by the fact that the said preparation contains as its component particles of deproteinized human bone (A) favourably with granulation from 0,3 to 0,5mm, bioglass (B) in the form of granulated product and binder (C), and the amount of bone material in the preparation amounts favourably to 80-85% of the preparation weight, bioglass favourably 15-20% of the preparation weight, and binder 20-25% of the preparation weight in relation to the sum of amounts of the above components.
2. According to the claim 1, the preparation is characterized by the fact, that bioglass (B) is obtained with use of zol-gel method in the system CaO-SiO_2-P_2O_5 as high silica material (80% mol SiO_2) or as a high calcium material (54% mol CaO).
3. According to the claim1, the preparation is characterized by the fact, that a patient's own blood is favourably used as binder (C).
4. According to the claim 1, the preparation is characterized by the fact that instead of bioglass (B) a tricalcium phosphate marked below as component TCP is applied, favourably with granulation 0,3-0,5mm, and the amount of bone material (A) in the preparation amounts favourably to 80-85% of the preparation weight, and TCP favourably 15-20% of the preparation weight.
5. According to claims 1-4 the preparation is characterized by the fact that the following materials are applied as components: bone material (A) with granulation 0,3-0,5mm favourably in the amount 70-80% of the preparation weight, bioglass (B) in the granulated product in the amount favourably 10-15% of the preparation weight, tricalcium phosphate TCP favourably in the amount 10-15% of the preparation weight and binder (C) favourably in the amount 20-25% of the preparation weight in relation to the sum of the amount of the bone components.
6. The manner of implantation of the preparation for regeneration of postoperative and post-traumatic bone defects is characterized by the fact that during operation an appropriate amount of the preparation is mixed with binder, i.e. the blood from operative wound (the mixture should be homogenous). The obtained mixture, which

has consistency of Plasticine, is implanted into bone defects, and the amount of the preparation in the mixture favourably amounts to 75-80% of the mixture weight, and the amount of blood in the mixture favourably amounts to 20-25% of the mixture weight.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	EP 2 080 528 A1 (CIESLIK TADEUSZ [PL]; NOCON JACEK [DE]; RAUCH JAN [PL]) 22 July 2009 (2009-07-22) the whole document	1-6
E	US 2009/186063 A1 (CIESLIK TADEUSZ [PL] ET AL) 23 July 2009 (2009-07-23) the whole document	1-6
A	HANKER J S ET AL: "SETTING OF COMPOSITE HYDROXYLAPATITE/PLASTER IMPLANTS WITH BLOOD FOR BONE RECONSTRUCTION" PROCEEDINGS OF THE ANNUAL MEETING OF THE ELECTRON MICROSCOPYSOCIETY OF AMERICA, XX, XX, vol. 22, 1 January 1986 (1986-01-01), page 328/329, XP009025391 the whole document	1-6

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Information on patent family members

International application No
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