Innovative Realizations in the Research of Dental Implants

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Abstract – This article describes a method that can be used in experimental dentistry for investigations of osteointegration processes of dental implants. The procedure was patented (Patent BOPI AGEPI MD nr.12.2010). The researches accomplished below represent a component part of the subject area consecrated to the Evaluation of coordinative compounds of Zink and Vanadium at the stimulation of osteo-regenerative processes in periodontal tissues and at the application of dental implants. The experimental investigation included experiments carried out on 280 white rats. There were taken for the study 24 substances that contained Zink, Vanadium and Nickel. Testing of the influence of some new coordinative compounds of transitive metals (Zn, V, Ni) on osteo-regenerative processes in normal physiological conditions was determined in bone tissues of periodontium and femoral bones were extracted later on used for the determination of principal biochemical indices of bone tissue. There has been determined the most active biologic coordinative compound Zn(CF3CO2)2(γPic)2 (Patent Nr. 950188 AGEPI MD) in regenerative processes of periodontal tissues during the modeling of experimental periodontitis. The detailed study of the influence of the coordinative compounds of Zn and V that have a better biological activity was executed on the rats that had been inserted dental implants made out of Titan. Before the application of the treatment and at the end of the treatment with the above mentioned compounds, there were made blood tests of every rat on hemolymphogram of hematologic analyzer PCE-170 ERMA Japan. There was elaborated a new method of modeling experimental periodontitis at laboratory animals (Patent Nr. 5388 din 2008.01.14, RM). There were studied the following biochemical parameters: alkaline phosphatase, acid phosphatase, substances with medium and small molecular mass (SMSM), necrotic substances (NS), carnosine, nitric oxide, adenosine deaminase, adenylate deaminase. There were accomplished radiovisiographic densitograms.

Investigational methods of patients with periodontal diseases and dental implants. The examination was carried out in accordance with the algorithm of estimation of contraindications and indications suggested by us while inserting dental implants. The elaboration of the algorithm became possible on the base of the experience in insertion of implants Alpha Bio; MIS; Alpha Dent; CeraRoot Zirconium Oxide Dental Implants; and the procedures elaborated by us (patent Nr. 2379 from 2004.02.29; patent Nr.8,AGEPI MD from 2008-02-18).

57 patients with diverse periodontal diseases were subjected to the study. A profound investigation of biochemical indices of 27 patients was accomplished; out of them 15 patients were inserted dental implants. Zink picolinate was administrated per os 1 x 3 times a day before meals. The duration of the treatment was 30 days.

I. INTRODUCTION:

One of the most important problems of modern implantology is the bone integration of dental implants including the management of its process. The essential stage is the surgical one; the insertion of the implant in the alveolar socket and obtaining the adherence of the bone to the implant and achieve a direct bone implant surface without involving connective tissue layer. Branemark's concepts of bone integration of the implants are based on clinical and experimental studies, describing the complexity of the process of bone integration of the implants. His postulates confirm that until now the research assures clinical efficacy of implant use, but nevertheless require continued research [1, 2, 6]. Hystomorphological data of osteointegration process of dental implants are in continuous research [3, 4, 5, 7], in this way the studies of the microscopic structure of the implant-bone contact surfaces require a better examination.

II. MATERIAL AND METHODS.

In general, the procedures of insertion of implants in maxillary bones of known laboratory animals are related to a massive traumatism of periodontal tissues as a result of surgical interference, the major risk of inflammation of the wound, the development of inflammatory reactions, sepsis and other complications that influence negatively the results of the investigation. Successful attempts of dental extractions at rats are impossible, because anatomic maxillary dental peculiarities of theses animals, as well as those of rabbits or dogs will lead to maxillary fractions or other complications.

We have elaborated a new experimental model of bone regeneration at the use of which are removed all the above mentioned shortcomings (Invention BOPI MD, nr.12. 2010). The principal stages of the implementation are schematically represented in figure 1.

The advantages of the presented procedure in comparison with the known procedure consists in the removal of the major trauma in the area of the surgical operation where the implant is to be inserted, as well as in the prevention of the risk of the appearance of inflammatory processes, the preservation of the crown part of the central incisor, maximum possible preservation of bone and soft tissues due to the adaptation of the procedure to the real conditions and the optimum choice of the place of the insertion of the implant namely there, where the anatomic place of the tooth root can be found.

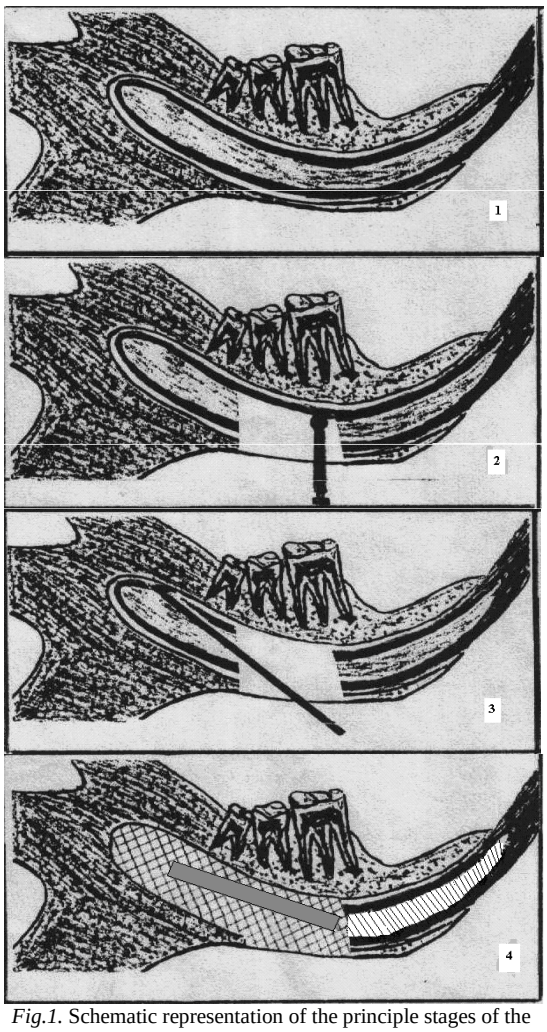


Fig.1. Schematic representation of the principle stages of the accomplishment of the experimental model of the investigation in the process of bone regeneration : 1) rat's mandibulae and teeth ; 2) the appearance of bone deffect in the apical portion of alveolus ; 3) the removal of the apical root portion of the incisive ; 4) the insertion of the implant and of the investigational remedy in the dental alveolus in the root part and the crown one which remained, there was realised devitalixation and obstruction.

The animals were put to sleep with the intervals of 2 weeks and 1 month with a light anesthesia overdose. During the surgical operation the mandibles were realized the preparations of the implants with the surrounding bone tissues. Hemi-mandibular samples were kept for 10 days in 10% formalin solution and then 2 days in 70% alcohol, ethyl alcohol 90% 2 days, 2 days 96% alcohol, absolute alcohol one week, 24 hours a mixture of ethanol + acetone (1:1) 100% acetone for a week with daily changes of acetone. After these procedures, the portion of jaw bone where the implant had been inserted and placed into a propylene resin solution. Solidification of the preparations lasted one week. The slice cuts of the preparations on the limit bone-implant were performed at different depths and parts of the implant and haematoxylin-eosin staining was performed.

III. PURPOSE OF THE RESEARCH:

a comparative histological examination of the potential of osteointegrated implants in different groups of rats which have been given coordinative compounds Zn $(LH)_2$, Zn (LH) etazol, [VO (L-H) etazol] $_2SO_4$ respectively with indices TS-1Z, 2Z-TS, TS-9V, in this way getting the opportunity to study the contact area between the surface of the substrate of the titanium implant with the surrounding tissue structures, including the dynamics of their formation.

Results: Groups of control. Mandibular bone plus implant film were made 15 days later after the experiment had been done (Fig. 2, b) from the moment of the insertion of the implant where existed a powerful intensification of the process of bone regeneration.

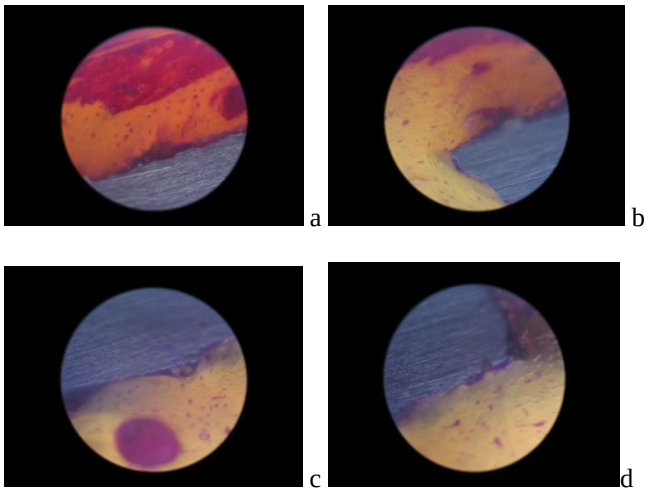
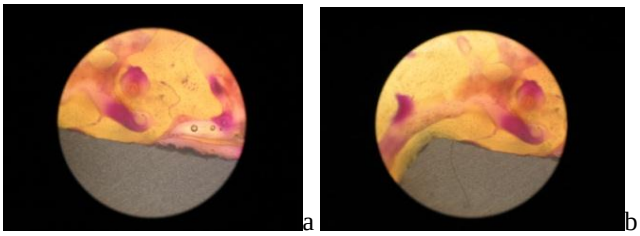


Fig. 2 (a, b, c, d). Microphotograms. Haematoxylin eosin stain. Images of the implants with surrounding tissue in the control group 2 weeks (a, b) from the surgery of insertion of the implant. The new young bone tissue covered the area directly bordering the implant. The tissue maturation is a continuous process, fibrous tissue is noticed on the bordering of the implant (a), bone only rarely adhere to the implant surface (a, b). Histology images (c, d)-images had been taken 1 month later after the surgery.

The structure of newly regenerated trabecular bone surrounds the whole surface of the implant. The tissue is partially separated from the implant surface by a few elongated cells like fibroblasts (fig. 2b). The preparations and photos made in 30 days do not show any big changes in comparison with those, taken after 15 days, the process of tissue maturation has not progressed further. The development and maturation of essential components of fibroblast cells is observed at the edge of the implant surface and new bone formation, but rarely the last more compact adhere to the implant surface (Fig. 2c, d). There are incomplete spaces between the implant and the bone is more limited, highlights rich blood vascularity.

Groups of vertebrates with implants inserted into the bone which were given *TS-1Z.* Histological examination 2 weeks after surgery (3 a, b) the defect is observed, the periphery of which is occupied by granulation tissue rich in cells and blood vessels. Mandibular bone is traumatized by trepanation of bone creating a cavity for insertion of the implant (Fig 3a), but no inflammatory phenomenon had been observed. Also, the microscope image (Fig. 3b) highlights the implant-bone postsurgical area with bone trabeculae since implant insertion and that image show precursors of tissue cells transformed into cells recruited osseoblastic bone formation process - osteoinduction.

After 1 month of surgical intervention (Fig. 3c, d) on mandible bone defect caused by insertion of the implant in cavity is regenerated with bone structure, which replaced fibrous tissue. The junction between implant and adjacent bone is completely renewed and implant is completely anchored into the bone.



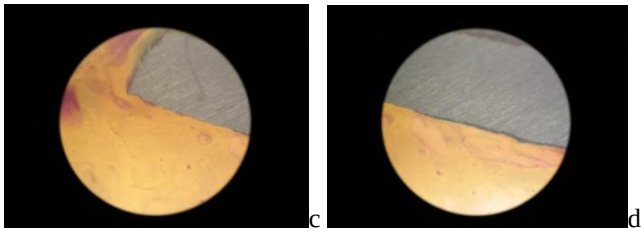
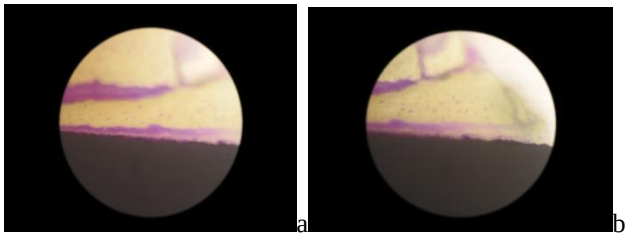
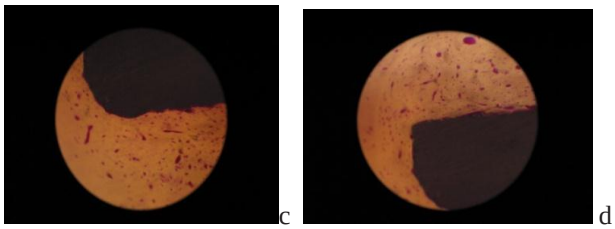


Fig.3 (a, b, c, d). Microphotograms (hematoxilin eosin staining) The group which were given TS-1Z. The results obtained in 2 weeks (a, b) after surgery.Bone implant is surrounded by fibrous tissue which may be substituted by bone tissue (c, d) - histology results in 1 month after the surgery.

We can notice the thin structure of bone trabeculae and newly formed bone, with a network which is mostly fibrous tissue.





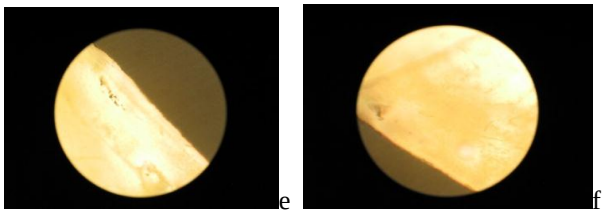


Fig. 4 (a, b, c, d, e, f) Microphotograms. Hematoxylin- eosin stain. Histological implant-bone preparations of rats that received the TS-2Z for 2 weeks (a, b) since implant insertion. On the implant surface we can notice roughness which is due to sandblasting. Rich in blood vascularity. The implant is surrounded by a capsule mostly fibrocellular (a, b) in image (b) the right to see the regeneration of new bone. Image (c, d) of preparation implant + bone after 1 month since implant insertion. (e, f) - another preparation from the same group - image after 1 month-final stage of osteointegration.

Groups of preparate animal implant + bone which were given TS-2Z. The administration of coordinative compounds TS-2Z showed that the defect is replaced by spongy bone, newly formed bone trabeculae and presence of osteoblasts (Fig. 4, b). In none of the histological preparations were observed inflammatory processes, changes in the prevalence of destructive or fibrous tissue.

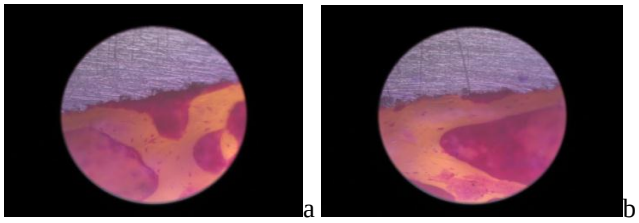
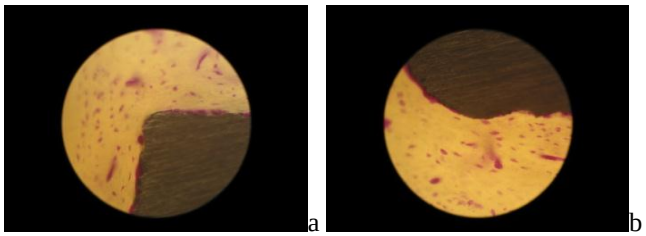


Fig.5 (a, b). Microphotograms 2 weeks since the implant insertion. Group that was administered TS-9V. At the implant-bone boundary is revealed reduced bone tissue regeneration (a) on the implant surface there are bone trabeculae with irregular outline (b).



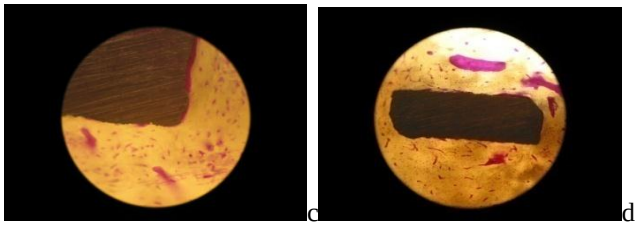


Fig.6 (a, b, c, d). Microphotograms. Implant-bone group preparations on mandible, which has been administered TS-9V. Hematoxylin eosin stain. Osteogenesis in 1 month after the implantion. Regeneration of the bone is anchoring on the implant surface flowing uniformly throughout the perimeter area of the implant. Osteoconduction of osteoblastic cells prevail.

Analysis of junction surface bone to implant after 1 month of implant insertion time (Fig. 4c, d) and (Fig. 4d, e) showed that there are areas where the trabeculae grow in size and regenerate bone in a lamellar structure in comparison to osteointegration processes after 15 days (Fig. 3, b). Formation of direct contact between bone and implant with connective tissue layer is considered low as a morphological manifestation process of osteointegration. Directly on the implant surface was formed bone, presence of fibrous tissue. *Groups of prepares implant + bone of animals which were administered TS-9V.* Histological analysis of preparations of this studied group demonstrated that TS-9V preparation stimulates the regeneration of bone tissue comparing to experiment with compounds administered in previous groups, but the process starts a little later. The images (Fig. 5 a, b) - in 15 days on implant surface there is newly formed bone present, continuing maturation, portions of connective tissue, the consequences of posttraumatic cavity formation in the stage insertion of the implant. After 1 month implant insertion (Fig. 6, b, c, d) - osteogenesis in evolution. The area around postsurgical implant bone defects are restored by a new bone structure, the osteointegrated implant is formed. The process has a satisfactory result.

The comparison of the radiovisiographic densitograms of the rats' mandibles, which were operated and inserted titanium implants, made two weeks and a month after the operation under the influence of the most active coordinative compounds Zn(L-H)-etazol, Zn(L-2H)-sulfadimizin, $Zn(NH_2\text{-}C_6H_4\text{-}CH_2\text{-}C_6H_4\text{-}NH_2)_2SO_4$ and

$Zn(CH_3COO)_2•4H_2O$) show a high intensity of osteointegration activity of the edges of the bone cavity surrounding the implant (photo 7, 8, 9, 10). The most relevant results were registered during the application of the compound $Zn(NH_2\text{-}C_6H_4\text{-}CH_2\text{-}C_6H_4\text{-}NH_2)_2SO_4$, this indicates the fact of a more pronounced osteoinductive action of this substance in the graphic image (figure 11).

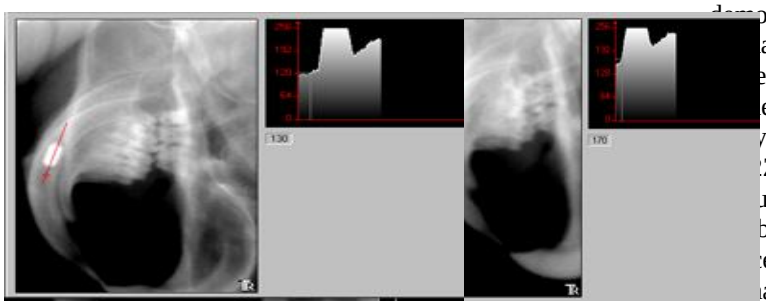


Foto 7. Control in two weeks.

Foto 8. Control in a month.

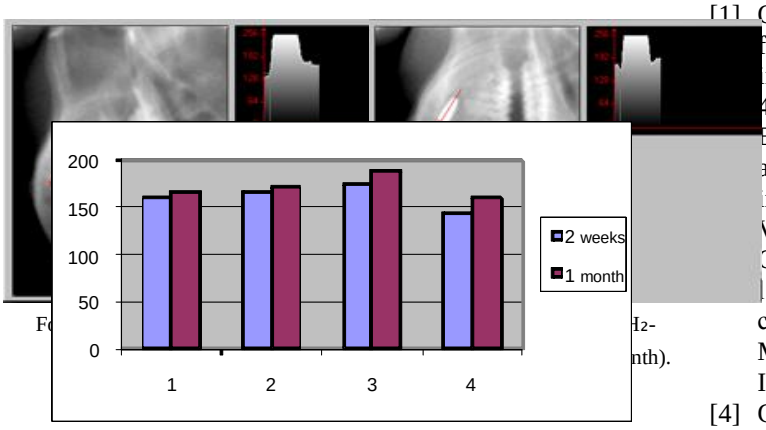


Fig.11. Statistic comparison of densitograms

two weeks and a month after the the insertion of the implants out of titan and the administration of the most active coordinative compounds : *1* – Zn(L-H)-etazol; *2* – Zn(L-2H)-sulphadimizyn; *3* – $Zn(NH_2\text{-}C_6H_4\text{-}CH_2\text{-}C_6H_4\text{-}NH_2)_2SO_4$; *4* – $Zn(CH_3COO)_2•4H_2O$.

IV. CONCLUSIONS:

Analyzing the histological examination with the results we conclude that the best indicators of osteointegration process are found in all groups which have been given coordinative compounds $Zn(LH)_2$, Zn(LH)etazol, $[VO(L\text{-}H)etazol]_2SO_4$.

The results of this study also come up with arguments of guidance on the use of dental implants with administering of coordinative compounds of Zn. There are coordinative compounds that can be used in implantology and there is a necessity to make direct studies of implant-bone interface involving molecular medicine studies. Histological analysis of the preparations which received the compounds mentioned above, in comparison with the control group, demonstrated success of the guided tissue and bone ation in intimate contact with implant surface but also enetration into the pores of the implant. Bone integration e implants were observed in most unique comparative ysis between group of study and the administration of Z compound, but TS-1Z compounds, TS-9V that ulated bone regeneration. Histological results confirm benefic results with biochemical and hematological es which improved after the implant application at the als that were administered coordinative compounds Zn $(LH)_2$, Zn (LH) etazol, $[VO (L\text{-}H) etazol]_2SO_4$.

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