UNIVERSITY OF MEDICINE AND

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DOCTORAL SCHOOL

PhD THESIS

IMPROVING THE PROPERTIES OF SOME CERAMIC MATERIALS FOR DENTAL USE

-Summary -

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1. Introduction

Zirconia (ZrO_2) is a ceramic material with mechanical properties suitable for the manufacture of medical devices. The mechanical properties of fixed dental prosthesis made of zirconia based ceramics have been shown to be superior to other ceramic restorations. Y2O3-stabilized zirconia has proven to be the version with the best properties for these applications

The biocompatibility of zirconia was studied in vitro and in vivo, the results obtained certifying the good biological response offered by this group of biomaterials.

However, concerns have been raised about the degradation of Y2O3-stabilized zirconia at low temperature. Current data show a strong variability in the sensitivity of zirconia in vivo to a phenomenon called low temperature degradation (LTD) due to the strong influence of the microstructure and processing of zirconia.

The ability of zirconia to be doped with various elements allows to improve the chemical and physical properties of commercial products in this family of materials, so the original part of this thesis is the synthesis in the laboratory of experimental nanocrystalline powders of yttrium stabilized zirconium oxide and co-doped with aluminum or iron, the characterization of powders and sintered ceramics, their introduction into the biological environment for the evaluation of the tissue response, but also for the characterization of the sintered ceramics after the period spent in the aggressive biological environment.

2. Objectives

The main objectives that formed the basis of the experimental study carried out in the thesis and that were subsumed in the main objective were:

- Analysis and characterization of commercial ceramic materials currently used in the dental laboratory

- Synthesis and physico-chemical characterization of new nanocrystalline ceramic materials based on yttrium stabilized zirconium oxide and co-doped with Al or Fe;
- Evaluation of the sinterability of ceramic powders and structural and morphological investigation of sintered products;
- Investigating the biocompatibility of both commercial ceramic materials and the ceramic materials synthesized in the laboratory
- Evaluation of the structural stability of the new developed materials after in vivo testing.

3.Methods

The changes made on the materials composition aimed the evaluation of the various dopants effect on the morphostructural stability but also on the biocompatibility of yttrium stabilized zirconia ceramics, aiming to identify new materials with superior properties to those developed so far.

The Pechini method was used for the synthesis of oxide powders, and they were characterized using numerous techniques:

- X-ray diffraction (XRD) and Raman spectroscopy - to highlight the crystalline structure of the samples;

- scanning electron microscopy coupled with energy dispersive X-Ray spectroscopy (SEM / EDS) - to evaluate the morphology and chemical composition of the investigated samples;

- dilatometry - performed in order to identify the optimal conditions for the sintering of oxide powders.

To test the biocompatibility of these materials with potential use in dental prosthetics, skin but also oral mucosal irritation tests were used, by introducing subcutaneous and submucosal samples of materials to male Wistar rats. After 6 weeks, the biological samples harvested from the laboratory animals at the insertion site were evaluated clinically and then histologically to evaluate the local tissue response.

Finally, samples made from the experimental materials were recovered after exposure to the biological environment and they were again characterized using the same techniques, SEM / EDS and Raman spectroscopy, in order to analyze the morphological changes, the elemental identification in the surface layer, but also possible phase changes.

The topic covered in this thesis is generous and complex, opening new opportunities for interdisciplinary study and new collaborations.

4.Results

4.1. Characterization of commercial ceramic materials used in the dental laboratory

In all samples studied from precursor powders the detected phases were leucite and quartz. All sintered samples showed structural changes and also in the composition of the phases.

Although the EDXS analysis highlighted some differences in the composition of the conventional ceramic materials studied, it predominantly provided the chemical composition of the prismatic crystals corresponding to potassium feldspar. The examination made using scanning electron microscopy allowed the observation of crystals of different sizes grouped in bundles unevenly distributed within the matrix of the material with a branched appearance.

4.2 Characterization of experimental ceramic powders

The network parameters of the investigated samples were determined by pattern matching, calculating the tetragonality of each sample. Based on the ratio of the network parameters, two tetragonal crystalline phases can be distinguished: transformable t-phase, and metastable t-phase. Refining of X-ray diffraction data revealed only the presence of the t ’phase in the calcined powders obtained in this study.

The three calcined powders are nanocrystalline, the size of the crystallites being of the order of 4-5 nm. From a morphological point of view, all three powders have the characteristic appearance of oxide materials obtained by the sol-gel method, following a heat treatment. The powders are composed of nanometric granules, agglomerated in structures with dimensions of a few micrometers.

4.3 Characterization of sintered experimental ceramic materials

Refining the X-ray diffraction data revealed the co-existence of three crystalline phases in the sintered pellets: two tetragonal phases (t and t ’) and one cubic phase (c). The addition of aluminum and iron has led to a decrease in the content of phase t and an increase in the content of phases c and t ', as well of the tetragonal character of phases t and t'. Following the heat treatment, a decrease in the width of the peeks was observed, which indicates an increase in the size of the crystallites. Moreover, the addition of iron caused the practical density of the sintered pellet to increase, while the addition of aluminum led to a decrease in the practical density of the sintered materials.

The three sintered samples show the characteristic peeks of tetragonal zirconium oxide, located at about 145, 268, 314, 463, 604 and 639 cm-1, while the band characteristic of the cubic shape of zirconia is centered at about 616 cm-1. The band characteristic of the cubic form of zirconium oxide overlaps the two adjacent wide bands of the tetragonal phase for all three investigated samples.

EDXS maps revealed a uniform distribution of cations in the host matrix while the distribution of dopants (Y, Al, Fe) in the zirconium oxide host matrix was evaluated by the sum spectrum. It can be observed that by co-doping the yttrium-stabilized zirconium oxide with aluminum or iron its microstructure is significantly affected. Thus, the addition of aluminum leads to a decrease in the average size of the granules, while the use of iron as a co-dopant causes an increase in the size of the granules.

4.4 Evaluation of the biocompatibility of some commercial ceramic materials

Clinical, macroscopic evaluation of oral tissues located around the introduced samples, evaluation performed after euthanasia of the laboratory animal during sampling for histological study, revealed a good biological response, with no clinical inflammatory manifestations in samples collected from all study groups with ceramic commercial materials.

The histological examination showed the presence of minimal signs of inflammation, a foreign body reaction, in almost all the analyzed samples. The differences observed in the amplitude and pattern of the response mode of the local tissue were less related to the study group they were part of and implicitly from the commercial material from which the sample was made, but depended more on the depth of sample insertion, the presence of muscle structures or of nearby adipose tissue.

4.5 Evaluation of the biocompatibility of the experimental ceramic materials

The histological investigation of the tissue samples obtained six weeks after the introduction into the biological environment of the disks from the experimental ceramic materials showed similar results to those observed after the introduction of the ceramic materials already existing on the market. In short, the experimental zirconia-based samples tested proved to be biocompatible, even though the compositional changes may influence the pattern of soft tissue reactions.

Thus, on samples from the Ytrium Zirconia study group, we usually observed a mild or moderate inflammatory reaction with microhemorrhages and congested blood vessels, with a significant presence of well-structured collagen fibers at the periphery of the section, but partially disorganized in center.

On the sections obtained from the samples collected from the Iron

Ytrium Zirconia study group, we generally observed slightly more intense inflammatory reactions than in the previous group but with a more frequent presence of collagen fibers, although usually with a smaller diameter and an inhomogeneous arrangement. On the sections obtained from samples collected in the vicinity of the discs inserted in the oral mucosa, a more intense inflammatory reaction could be observed, consisting mainly of lymphocytes and plasma cells, with intense vascularization and vascular congestion, but also a dense layer of lamina propria with scattered fibers. Despite this more intense microscopic inflammatory picture in the oral mucosal samples from the Iron Ytrium Zirconia group, the preliminary clinical examination did not detect the existence of clinically visible manifestations in this group either.

Although on some of the sections obtained from the samples collected from the Aluminium Ytrium Zirconia study group, we noticed a more intense inflammation reaction, the characteristic of the group was rather the inconsistency of the histological pictures between the different samples of the group, on a significant number of sections being observed only normal histological aspects, all under the same conditions, the lack of clinically visible inflammatory manifestations. Thus, a massive subcutaneous inflammatory reaction, with the presence of lymphocytes, plasma cells, but also macrophages, could be found more frequently in oral mucosal samples.

4.6 Characterization of sintered experimental ceramic materials after in vivo testing

The morphology of the samples tested in the oral mucosa of laboratory rats was investigated by SEM / EDXS analysis. To determine the thickness of the tissue that adhered to the samples, they were cross-sectioned. SEM did not show significant changes in the morphology of the sample volume after insertion into the oral mucosa.

EDXS spectra resulting from scanning the line perpendicular to the free surface of the samples showed the presence of carbon species at a distance of several tens of micrometers from the free surface of the disks; Along with these, species such as Ca, Mg, P were also highlighted, species captured from the tissues around the inserted sample.

Six weeks after insertion into the oral mucosa, Raman spectroscopy revealed the presence of the monoclinic phase indicated by the appearance of peeks located at approximately 180 cm-1 and 190 cm-1 only in the spectra of co-doped samples. While for the yttrium stabilized zirconium oxide sample the monoclinic phase was not highlighted after testing, the monoclinic phase fractions in the co-doped samples were calculated to be 0.09 for the iron co-doped sample and 0.16 for the sample co-doped with aluminum.

Raman spectroscopy investigation of the tested samples showed that by using a 6% mol yttrium oxide stabilizer concentration the sample is stable to the LTD process after exposure to the aggressive environment of the oral mucosa for six weeks. Co-doping of yttrium-stabilized zirconium oxide with iron or aluminum causes an increase in Y-TZP susceptibility to low temperature degradation (LTD). In addition, the co-doped sample with aluminum proved to be the most susceptible to the LTD process among the samples investigated.

5.Conclusions

- The characterization of the commercial dental ceramics helps practitioners better understand the interaction of these biomaterials with the tissues, but also helps researchers to modify the composition and properties of the synthesized ceramics for a better integration into the oral cavity.
- The addition of aluminum in experimental ceramics caused a slight increase in the tetragonal character of yttrium-stabilized zirconia powder, while the addition of iron led to a decrease in the tetragonality of the system.
- After sintering the proposed ceramics, X-ray diffraction revealed the co-existence of three crystalline phases: two tetragonal phases (t and t ’) and a

cubic phase (c).

- The results of the study made on commercial ceramics showed a good clinical response of the intraoral soft tissues that surrounded the inserted samples, with only histological evidence of some signs of inflammation of foreign body reaction.
- The clinical and histological investigation of the tissue samples obtained six weeks after the introduction into the biological environment of the disks from the experimental ceramic materials showed results similar to those observed after testing the ceramic materials already existing on the market.
- Tissue samples collected around experimental zirconium oxide-based ceramics doped with Y and Fe generally showed slightly more intense inflammatory reactions than in the group of ceramics doped with Y alone, especially in the case of samples collected from the oral mucosa. Although some tissue samples collected around experimental ceramics based on zirconium oxide doped with Y and Al showed a more intense inflammatory reaction, the characteristic of the group was rather the inconsistency of the histological pictures between the different samples of the group.
- Raman spectroscopy revealed changes in the structure of co-doped samples after testing in the biological environment. While the yttrium stabilized zirconia sample proved to be stable to the low temperature degradation (LTD) process under the conditions of the test, co-doping with aluminum or iron led to an increase in the susceptibility of the stabilized zirconium oxide against LTD.
- Zirconia ceramics are an important option for making prosthetic structures in current dentistry. The ability of zirconia to be doped with various elements allows the improvment of the chemical and physical properties of the commercial products in this family. Although the tissue response appears to be generally good, even compositional changes may influence the pattern of reactions, a special attention should be paid to structural changes in these materials after theexposure in the biologically aggressive environment, especially in the oral environment.