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## **ACCEPTED MANUSCRIPT**

New procedure of quantitative mapping of Ti and Al released from dental implant and Mg, Ca, Fe, Zn, Cu, Mn as physiological elements in oral mucosa by LA-ICP-MS

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#### **Abstract**

A new procedure of simultaneous determination of elements derived from titanium implants and physiological elements in soft tissues by laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) is presented. The analytical procedure was developed which involved preparation of in-house matrix matched solid standards with analyte addition based on certified reference material (CRM) MODAS-4 Cormorant Tissue. Addition of gelatin, serving as a binding agent, essentially improved physical properties of standards. Performance of the analytical method was assayed and validated by calculating parameters like precision, detection limits, trueness and recovery of analyte addition using additional CRM - ERM-BB184 Bovine Muscle. Analyte addition was additionally confirmed by microwave digestion of solid standards and analysis by solution nebulization ICP-MS. The detection limits are in range 1.8  $\mu g$  g<sup>-1</sup> to 450  $\mu g$ g<sup>-1</sup> for Mn and Ca respectively. The precision values range from 7.3% to 42% for Al and Zn respectively. The estimated recoveries of analyte addition line within scope of 83% - 153% for Mn and Cu respectively. Oral mucosa samples taken from patients treated with titanium dental implants were examined using developed analytical method. Standards and tissue samples were cryocut into 30 µm thin sections. LA-ICP-MS allowed to obtain two-dimensional maps of distribution of elements in tested samples which revealed high content of Ti and Al derived from implants. Photographs from optical microscope displayed numerous particles with µm size in oral mucosa samples which suggests that they are residues from implantation procedure.

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