Characterization of multilayered drug delivery systems for orthopedic implants by beam deflection spectrometry

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Advances in transplantation surgery lead to a significant increase in the use of implantable medical components to replace the hips, knees, some spinal joints etc. The most commonly used materials for orthopedic purposes are titanium alloys, different ceramics, and stainless steel. Such materials must be biocompatible with body tissues and fluids, be able to withstand wear and corrosion, exhibit similar mechanical properties as bone, etc. To fulfil all these requirements, they need a deposition of a coating loaded with special combination of drugs. Among the coatings of interest, the polysaccharide-based systems were found to be the most promising regarding the enhancement of implant compatibility and functionality [1, 2]. They are used to construct a sophisticated drug delivery system (DDS) that delivers drug to the target tissue in a controlled way [3]. This leads to enhancement of patient compliance, drug efficiency and reduces the side effects of drugs.

In this study the smart drug delivery device was constructed by the use of the layer-by-layer (LbL) technology that forms multilayered systems of tailored architecture and with a high level of control of drug usage [4]. The multilayered structures (Fig. 1) consist of hyaluronic acid (HA), amoxicillin (AX) and fucoidan (FU) layers that are deposited on a medical grade stainless AISI 316LVM type support (MSS).

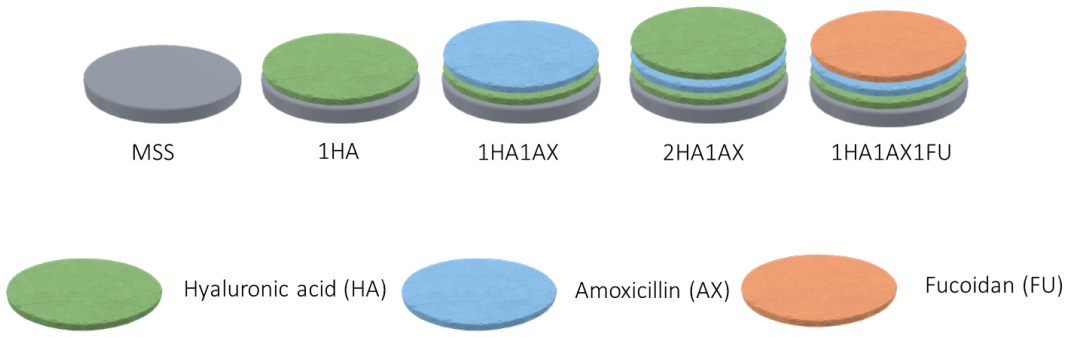

Fig. 1. Structure of examined multilayered drug delivery system.

Such systems require the development of new techniques for their characterization that provide high quality control, precision, sensitivity and reproducibility, as well as proper chemical and structural characterization of the examined materials, which includes the determination of their physical properties. The characterization of such polysaccharide multilayered structures was performed by the use of photothermal beam deflection spectrometry (BDS). It was based on monitoring the changes in

thermal parameters of different layers of the system to obtain information about the structure of sub-surface microlayers, as well as changes in concentration of pharmaceutical compounds in the layers.

In the BDS an intensity modulated excitation beam (EB) of light illuminates the surface of an absorbing sample [5]. As a result of nonradiative deexcitation processes the absorbed light is converted into heat that diffuses into the sample and into the adjacent medium generating periodic temperature disturbance, i.e., the thermal waves (thermal oscillations – TOs). TOs further cause changes in the refractive index of the medium in which they are induced. The resulting refractive index gradients in turn affect the propagation of the probe beam (PB) passing through the adjacent medium while grazing the sample surface. The BDS signal contains information about the thermal parameters (thermal diffusivity and conductivity) of the examined sample, which are governed by the chemical composition and structural characteristics (thickness, porosity, surface roughness) of the sample.

The results of this work show that substantial diffusion of AX into HA as well as FU occurs. It is demonstrated as the decrease of the thermal properties within the diffusion layer. This observation is possible because of the large difference in the thermal properties of AX ($D = 0.036$ mm^{2}s^{-1}) as compared to HA ($D = 0.078$ mm^{2}s^{-1}) and FU ($D = 0.106$ mm^{2}s^{-1}), which are the consequence of larger relative proportion of carboxylic groups in HA as compared to AX, while FU contains sulfonic acid groups. All these functional groups contribute to higher polarity of chemical compounds present in the coatings. Higher polarity is in turn related to higher values of thermal parameters, as it was also confirmed experimentally [6].

It can be concluded from the changes in thermal parameters that after doping AX diffuses into the HA, while a similar process occurs also after deposition of the second HA layer or the FU layer on top of the AX layer. Diffusion of AX extends 18-19 μm into the initial HA layer, while the diffusion into the second HA or FU layer is slightly shorter (16 μm). At the same time, as could be expected, the thickness of the layer dominated by the thermal properties of AX in 2HA1AX and 1HA1AX1FU samples is reduced as compared to 1HA1AX sample. The change in concentration of AX with distance is however not linear, but a gradient of AX concentration within HA and FU layers can be predicted, since the distance required for the same change in D values becomes longer and longer in direction of layers which contain no AX.

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