



## Protein adsorption on colloidal alumina particles functionalized with amino, carboxyl, sulfonate and phosphate groups

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### ARTICLE INFO

#### Article history:

Received 6 July 2011

Received in revised form 11 September 2011

Accepted 14 September 2011

Available online 18 September 2011

#### Keywords:

Surface functionalization  
Protein–particle interaction  
Protein adsorption  
Alumina

### ABSTRACT

Colloidal oxide particles in biomedical or biotechnological applications immediately become coated with proteins of the biological medium, a process which is strongly influenced by the surface characteristics of the particles. Fundamental correlations between surface characteristics and the, so far mainly uncontrollable, protein adsorption are still not clear. In this study the surface of colloidal alumina particles ( $d_{50} = 179 \pm 8$  nm) was systematically adjusted with  $\text{NH}_2$ ,  $\text{COOH}$ ,  $\text{SO}_3\text{H}$  and  $\text{PO}_3\text{H}_2$  functional groups to investigate the influence on the adsorption of the three model proteins, bovine serum albumin (BSA), lysozyme (LSZ) and trypsin (TRY). The surface functionalization is characterized and discussed in detail with regard to the morphology, isoelectric point, zeta potential, hydrophilic/hydrophobic properties, functional group density and stability. Protein–particle interaction was then assessed by evaluating the amount of protein adsorbed and the zeta potentials of protein–particle conjugates. Protein adsorption was found to be influenced by the type of functional group as well as the expected electrostatic forces under the given experimental conditions. The level of protein adsorption might, hence, be specifically controlled by the type of surface functionalization. Possible adsorption modes of BSA, LSZ and TRY on the particles are suggested by considering the spatial surface potential distribution of the proteins calculated from the protein database file. The particles presented provide an excellent prerequisite for further investigation of fundamental particle–protein interactions and the design of functionally graded materials for biomedical and biotechnological applications, e.g. as drug carriers or for protein purification.

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### 1. Introduction

When colloidal particles for biomedical or biotechnological uses (e.g. drug carriers, imaging systems, protein purification or waste water treatment) are exposed to biological fluids, protein adsorption occurs on the particle surface leading to the formation of protein–particle conjugates [1,2]. A surface protein layer can potentially have an impact on a variety of subsequent interactions of the colloids in the biological surrounding, due to the different protein functions such as, for example, signalling (growth factors), catalysis (enzymes), targeting (antibodies, opsonins) and many others [3–5]. As a prominent example, cellular up-take and toxicity of nanoparticles are hypothesized to be influenced by the type and amount of surface adsorbed proteins [6–8].

Controlling or guiding the mainly non-specific reaction of protein adsorption allows for improved applications of colloids in biomedical and biotechnological fields, but is a technological

challenge [3]. A specific design of the colloidal particle itself by surface functionalization might be a tool to control driving forces of protein–particle interaction: effects of particle surface charge [9–13], hydrophobicity [14,15] and type of functional surface groups [2,16–18] on protein adsorption and protein activity are reported next to, for example, the effects of the curvature and morphology of the particles [5,19,20]. Variations of the physico-chemical surface properties influence in particular the electrostatic as well as the hydrophilic/hydrophobic protein–particle interactions, when the morphology of the particles is unchanged. In what way and to what extent the specific surface characteristics of the particles contribute to protein adsorption are still not fully understood [4].

Studies that demonstrate a correlation between surface functionalization and protein adsorption mainly focus on polymeric/silica particles or planar surfaces as substrate materials [2,16,17]. In this study we want to broaden this knowledge by investigating the effect of different acidic and basic surface groups on protein adsorption using colloidal  $\alpha$ -alumina ( $\text{Al}_2\text{O}_3$ ) particles as substrates.  $\text{Al}_2\text{O}_3$  is itself a widely used metal oxide material with many existent and potential applications in the biomedical and

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