Hemolytic properties of synthetic nano- and porous silica particles: The effect of surface properties and the protection by the plasma corona

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1. Introduction

The unique physicochemical properties of nanostructured materials (arbitrarily defined as materials with structures between 1 and 100 nm, at least in one dimension) offer a promising future for myriad applications in the biomedical field, such as drug delivery, gene delivery and diagnostics [1]. Size in the nanometer range endows them with the ability to minimize recognition and clearance by the reticuloendothelial system and therefore to enhance blood circulation time. Optimal pharmacokinetics have generally been identified for nanoparticles with a mean diameter of ~100 nm and a neutral and hydrophilic polymer-extended surface (such as polyethylene glycol (PEG)), with a plasma elimination half-life of a few hours [2]. Interestingly, a toxicity study showed that 22-nm Fe2O3 particles were able to persist in the circulation following intratracheal instillation in rats [3]. The nano-size of materials is also particularly useful for tumor tissue targeting by exploiting their characteristic large vasculature and defective lymphatic drainage which possess enhanced permeation and retention effects for substances <200 nm in size [4]. Moreover, a class of porous materials with pore diameters between 2 and 50 nm, termed mesoporous materials, offer attractive advantages for loading and releasing large quantities of biomedical agents such as drugs, genes and proteins [5–7]. In recent years, the scientific community has witnessed growing interest in nanostructured silica materials for biomedical purposes, either per se [7] or as surface coatings over other functional materials [8], owing to their high biocompatibility and versatile surface engineering properties [9].

These materials are intended to be directly administered into the circulation following intravenous injection, or they may end up in the circulation following other routes of administration such as oral administration. They are also intended to prolong blood circulation half-time. Any material in contact with the blood encounters red blood cells (RBC). Moreover, the hemolysis assay is recommended as a reliable test for material biocompatibility [10]. Micro-size silica, in both crystalline and amorphous form, is well known to induce hemolysis of RBC [11–13]. It was further suggested that surface silanol groups (ionized or unionized) of silica