**Influence of chemical surface modification of AgNP on toxicity and biodistribution**

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**Abstract**

With the advance in material science, silver nanoparticles (AgNPs) are modified by different surface coating. However, how these surface modifications influence the effects of AgNPs to human health are still unknown. We have evaluated the uptake, toxicity, and pharmacokinetics of AgNPs coated with citrate, polyethylene glycol, polyvinylvpyrolidone or branched polyethyleneimine (Citrate AgNPs, PEG AgNPs, PVP AgNPs or BPEI AgNPs). Our results demonstrated that the toxicity of AgNPs depends on their intracellular localization that was highly dependent on the surface charge. BPEI AgNPs (ζ potential = +46.5 mV) induced the highest cytotoxicity (EC50=10.38 µg/ml) and DNA fragmentation in Hepa1c1c7 and also showed higher damage to the nucleus of liver cells in the exposed mice, which is associated with the highest cellular uptake and higher accumulation in liver tissues. The near neutral (ζ potential = -16.2 mV) PEG AgNPs showed the low toxicity (EC50 = 63.14 µg/ml) and the long blood circulation (t1/2 =1.04 h) as well as the high bioaccumulation in spleen (34.33 µg /g) which suggest better biocompatibility. Moreover, the adsorption ability with BSA revealed that the PEG surface of AgNPs with an optimal biological inertia can effectively resist opsonization or non-specific binding to protein in mice. Overall results indicated that the toxicity of AgNPs were surface chemistry dependent significantly: BPEI AgNPs > Citrate AgNPs = PVP AgNPs > PEG AgNPs. The toxicological data will be useful for making choices of AgNPs in safe design to the consumer products and drug delivery applications.

Keywords: Silver nanoparticles; Surface coating; Acute toxicity; Pharmacokinetics, Protein adsorption