The similar neurotoxic effects of nanoparticulate and ionic silver in vivo and in vitro

We compared the neurotoxic effects of 14nm silver nanoparticles (AgNPs) and ionic silver, in the form of silver acetate (AgAc), in vivo and in vitro. In female rats, we found that AgNPs (4.5 and 9mg AgNP/kg bw/day) and ionic silver (9mg Ag/kg bw/day) increased the dopamine concentration in the brain following 28 days of oral administration. The concentration of 5-hydroxytryptamine (5-HT) in the brain was increased only by AgNP at a dose of 9mg Ag/kg bw/day. Only AgAc (9mg Ag/kg bw/day) was found to increase noradrenaline concentration in the brain. In contrast to the results obtained from a 28-day exposure, the dopamine concentration in the brain was decreased by AgNPs (2.25 and 4.5mg/kg bw/day) following a 14-day exposure. These data suggest that there are differential effects of silver on dopamine depending on the length of exposure. In vitro, AgNPs, AgAc and a 12kDa filtered sub-nano AgNP fraction were used to investigate cell death mechanisms in neuronal-like PC12 cells. AgNPs and the 12kDa filtered fraction decreased cell viability to a similar extent, whereas AgAc was relatively more potent. AgNPs did not induce necrosis. However, apoptosis was found to be equally increased in cells exposed to AgNPs and the 12kDa filtered fraction, with AgAc showing a greater potency. Both the mitochondrial and the death receptor pathways were found to be involved in AgNP- and AgAc-induced apoptosis. In conclusion, 14nm AgNPs and AgAc affected brain neurotransmitter concentrations. AgNP affected 5-HT, AgAc affected noradrenaline, whereas both silver formulations affected dopamine. Furthermore, apoptosis was observed in neuronal-like cells exposed to AgNPs, a 12kDa filtered fraction of AgNP, and AgAc. These findings suggest that ionic silver and a 14nm AgNP preparation have similar neurotoxic effects; a possible explanation for this could be the release and action of ionic silver from the surface of AgNPs.