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Nanodrug delivery of a multimodal novel drug cerebrolysin reduces engineered nanoparticles induced aggravation of heat stroke induced ubiquitin expression and brain pathology

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Accumulation of ubiquitin within the brain after trauma leads to neurodegenerative changes or brain pathology. Our previous reports show that acute heat exposure leads to breakdown of the blood-brain barrier (BBB) resulting in edema formation and cellular injury. Thus, military personnel engaged in combat operations in summer heat and prone to silica dust (SiO₂ nanoparticles) exposure may result in exacerbation of their brain dysfunction. Since ubiquitin expression is increased following CNS injury we examined ubiquitin expression in brain following SiO₂ exposure in heat stress in rats. Furthermore, neuroprotective efficacy of cerebrolysin, a multimodal drug with pleotropic activity due to several neurotrophic factors and active peptide fragment on ubiquitin expression was also evaluated in these conditions. Our observations show that rats subjected to 4 h heat stress in a Biological Oxygen Demand incubator (BOD) resulted in over expression of ubiquitin in several brain areas (+40 to 120 %) from control group. Chronic SiO₂ intoxication (50-60 nm, 50 mg/kg, i.p. daily for 7 days) resulted in exacerbation of ubiquitin accumulation by further 150 to 260% in the identical brain areas following heat exposure. Cerebrolysin in low doses reduced the ubiquitin expression in heat stress but required high doses or TiO₂ nanowired delivery to have similar effects in SiO₂ intoxicated group. These observations are the first to suggest that (i) ubiquitin expression in the brain following heat stress is involved in neuronal damages, (ii) that is further exacerbated by SiO₂ intoxication, (iii) and cerebrolysin downregulates ubiquitin expression to induce neuroprotection, not reported earlier.

Biography

Hari S Sharma is the Director of Int. Experimental CNS Injury Research & Repair, University Hospital, Uppsala University, Sweden. He is actively engaged on research in brain injuries, blood-brain barrier and brain edema since last 30 years. He received the 1st US Neurosurgeon Anthony Marmarou Brain Edema award by the International Brain Edema Society, Tokyo, Japan in October 2011 and Top Innovation Award on "Nanowired cerebrolysin for neuropathic Pain" at National Innovation & Showcase Summit Washington DC, USA May 12-16, 2013. He published over 350 research papers in reputed Neuroscience journals.

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