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Gold Nanoparticle Conjugated with Andrographolide Ameliorates Viper Venom-Induced Inflammatory Response and Organ Toxicity in Animal Model

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Abstract : Since 1894 anti-snake venom serum (ASVS) is the only available treatment against snake envenomation, although there are many side effects and limitations. The need for a supportive treatment was felt for a long time to overcome the side effects and limitations of ASVS. Andrographolide conjugated with gold nanoparticle (A-GNP) has been found to antagonize viper venom-induced local damages. The present study was aimed to study the protective efficacy of A-GNP against Viper venom-induced inflammatory response and organ toxicity in animal model. Ethical clearance was obtained from animal experiments. Physico-chemical characterization of A-GNP was done by DLS (diameter and zeta potential), FE-SEM and XRD. Swiss albino male mice were divided into 4 groups: Gr.1-Sham control, Gr.2- Russell's Viper venom (RVV) control, Gr.3-andrographolide treated and Gr.4- A-GNP treated. The 1/5th minimum lethal dose of RVV (500µg/kg, s.c.) was induced in animals of group 2, 3 & 4 animals, followed by treatment with andrographolide (100mg/kg, i.p.) and A-GNP (100mg/kg, i.v.) in group 3 & 4 animals, respectively. Blood was collected after 18 h, serum was prepared, and inflammatory markers (IL 1β, 6, 17a, 10, TNF α) and biochemical markers (AST, ACP, LDH, urea, creatinine) were assessed. Values were expressed as mean±SEM (n=4), one way ANOVA was done, $P<0.05$ was considered as statistically significant. DLS size showed the hydrodynamic diameter of A-GNP to be 230-260nm with polydispersity index of 0.103 and zeta potential was -18.32mV. XRD data confirmed the presence of crystalline gold in A-GNP, and FESEM indicated the presence of nearly spherical particle with size18-24nm.Treatment with A-GNP significantly decreased viper venom-induced proinflammatory markers (IL 1β, 6, 17, TNF α) increased anti-inflammatory markers (IL 10) and decreased organ toxicity markers (AST, ACP, LDH, urea, creatinine) in animal model. Venom neutralization efficacy of A-GNP was > andrographolide, which confirmed the increased efficacy of andrographolide after gold nanoparticle conjugation. Venom neutralization by A-GNP was due to anti-oxidant/anti-inflammatory activity of andrographolide, which showed increased efficacy after gold nanoparticle tagging. Thus, A-GNP may serve as a supportive therapy in snake-bite (against inflammatory response and organ toxicity) subject to further detail studies.

Keywords : andrographolide, gold nanoparticle, inflammatory response, organ toxicity, snake venom, snake venom neutralization, viper venom
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