

Nanocomplexes on the Base of Triterpene Saponins Isolated from Glycyrrhiza glabra and Saponaria officinalis Plants as an Efficient Adjuvants for Influenza Vaccine Use

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Abstract : Introduction: Triterpene saponins of plant origin are one of the most promising candidates for elaboration of novel adjuvants. Due to the combination of immunostimulating activity and the capacity interact with amphipathic molecules with formation of highly immunogenic nanocomplexes, triterpene saponins could serve as a good adjuvant/delivery system for vaccine use. In the research presented adjuvants on the base of nanocomplexes contained triterpene saponins isolated from Glycyrrhiza glabra and Saponaria officinalis plants indigenous to Kazakhstan were elaborated for influenza vaccine use. Methods: Purified triterpene saponins 'Glabilox' and 'SO1' with low toxicity and high immunostimulatory activity were isolated from plants Glycyrrhiza glabra L. and Saponaria officinalis L. by high-performance liquid chromatography (HPLC) and identified using electrospray ionization mass spectrometry (ESI-MS). Influenza virus A/St-Petersburg/5/09 (H1N1) propagated in 9-days old chicken embryos was concentrated and purified by centrifugation in sucrose gradient. Nanocomplexes contained lipids, and triterpene saponins Glabilox or SO1 were prepared by dialysis technique. Immunostimulating activity of experimental vaccine preparations was studied in vaccination/challenge experiments in mice. Results: Humoral and cellular immune responses and protection against influenza virus infection were examined after single subcutaneous and intranasal immunization. Mice were immunized subunit influenza vaccine (HA+NA) or whole virus inactivated influenza vaccine in doses 3.0/5.0/10.0 µg antigen/animal mixed with adjuvant in dose 15.0 µg/animal. Sera were taken 14-21 days following single immunization and mice challenged by A/St-Petersburg/5/09 influenza virus in dose 100 EID₅₀. Study of experimental influenza vaccine preparations in animal immunization experiments has shown that subcutaneous and intranasal immunization with subunit influenza vaccine mixed with nanocomplexes contained Glabilox or SO1 saponins stimulated high levels of humoral immune response (IgM, IgA, IgG1, IgG2a, and IgG2b antibody) and cellular immune response (IL-2, IL-4, IL-10, and IFN-γ cytokines) and resulted 80-90% protection against lethal influenza infection. Also, single intranasal and single subcutaneous immunization with whole virus inactivated influenza vaccine mixed with nanoparticulated adjuvants stimulated high levels of humoral and cellular immune responses and provided 100% protection against lethal influenza infection. Conclusion: The results of study have shown that nanocomplexes contained purified triterpene saponins Glabilox and SO1 isolated from plants indigenous to Kazakhstan can stimulate a broad spectrum of humoral and cellular immune responses and induce protection against lethal influenza infection. Both elaborated adjuvants are promising for incorporation to influenza vaccine intended for subcutaneous and intranasal routes of immunization.

Keywords : influenza vaccine, adjuvants, triterpene saponins, immunostimulating activity

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