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Oral administration of synthetic selenium nanoparticles induced robust Th1 cytokine pattern after HBs antigen vaccination in mouse model

Mehdi Mahdavi[a,b,c], Faranak Mavandadnejad[d], Mohammad H. Yazdi[a,e], Elnaz Faghfuri[d], Hura Hashemi[d], Somayeh Homayouni-Oreh[d], Ramin Farhoudi[f], Ahmad R. Shahverdi[a,d,*]

[a] *Biotechnology Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran*
[b] *Recombinant Vaccine Research Center, Tehran University of Medical Sciences, Tehran, Iran*
[c] *Department of Immunology, Pasteur Institute of Iran, Tehran, Iran*
[d] *Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran*
[e] *Department of Research and Development, Pasteur Institute of Iran, Karaj, Iran*
[f] *Department of Laboratory Animal Science, Pasteur Institute of Iran, Karaj, Iran*

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Summary Hepatitis B virus (HBV) infection is known as a life-threatening liver infection and leads to chronic liver disease if left untreated. Nevertheless, the prevalence of HBV infection has been reduced by an approved vaccination approach using recombinant Hepatitis B surface Antigen (HBsAg) and Alum, known as the HBV vaccine. Alum can be used as an adjuvant to increase HBsAg immunogenicity as a strong Th2 stimulator. There is a vital need to stimulate Th1 immunity by HBsAg

Abbreviations: HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; SeNPs, selenium nanoparticles; ELISA, enzyme-linked immunosorbent assay; PBS, phosphate buffered saline; CHB, chronic hepatitis B; LC, liver cirrhosis; HCC, hepatocellular carcinoma; HEPES, 4-2-hydroxyethylpiperazine-1-2-ethanesulfonic acid; FBS, fetal bovine serum; BrdU, 10X 5-bromo-2′-deoxyuridine; PBS-BSA, phosphate buffered saline with bovine serum albumin; PBMCs, peripheral blood mononuclear cells; PHA, phytohaemagglutinin; NK, natural killer; TMB, tetra-methyl benzidine; SI, stimulation index; HRP, horseradish peroxidase.

* Corresponding author at: Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Tehran University of Medical Sciences, P.O. Box 14155-6451 Tehran, Iran. Tel.: +98 2166461178; fax: +98 2166461178.
E-mail address: shahverd@sina.tums.ac.ir (A.R. Shahverdi).

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vaccination; however, the present vaccine does not induce a prophylactic immune response in some groups. The main aim of the present study was to induce a Th1 cytokine pattern and stimulate an immune response after HBsAg vaccination. Experimental mice were fed selenium nanoparticles (SeNPs) and were later immunized with 5 μg of Hepatitis B Vaccine. After a period of 30 days, the experimental animals were given two booster doses of SeNPs during their vaccination course. Group one, *i.e.*, the control vaccine group, was only administered the HBsAg vaccine. The two treated groups, Groups 2 and 3, were daily fed different doses of SeNPs (100 μg and 200 μg, respectively) *via* gavage. Group four was considered the control group and was only given phosphate buffered saline (PBS). Lymphocyte proliferation, IFN-γ and IL-4 levels, total antibody and the isotypes of IgG1, IgG2a, IgG2b, and IgM were measured by Enzyme Linked Immunosorbent Assay (ELISA). The administration of SeNPs and the HBs antigen vaccine affected the lymphocyte proliferation; moreover, the total antibody responses also increased the IFN-γ level and induced a Th1 response.
Conclusions: The present study proposed that the administration of SeNPs with a conventional HBs antigen vaccine induces a better immune response with a Th1 bias.

Background

Hepatitis B virus (HBV) infection is a hazardous liver infection. Globally, over 350 million people suffer from persistent HBV infection. At least 600,000 patients die of hepatitis B virus (HBV)-related diseases, including Chronic Hepatitis B (CHB), Liver Cirrhosis (LC), and Hepatocellular Carcinoma (HCC) annually [1]. A significant reduction in HBV infection prevalence has been achieved by an approved vaccination approach using recombinant Hepatitis B surface Antigen (HBsAg) [2]. However, some diabetic and hemodialysis patients and 12—21% of healthy vaccinated adults do not develop an adequate response following the HBsAg vaccine [3]. It has been demonstrated that a Th1 immune response is related to the successful development of humoral immune responses against HBs antigen [4]. One important immunologic finding in the non-responder patients is a defect in IFN-γ production due to the interference of the virus with cytokine production, which finally weakens the cellular immune response and results in disease progression [5], stimulation of cellular immune response and the Th1 cytokine platform that is critical for the disease control and treatment. This strategy, known as therapeutic vaccination, is effective in patients and viably controls the disease. Although alum is used as an ordinary adjuvant in the HBs vaccine formulation for its induction of a strong humoral immune response, it failed to induce cellular immune responses [6]. Herein, the utilization of an immunomodulator agent in parallel with HBs vaccination may be useful to induce both cellular as well as humoral immune responses. Selenium plays a dominant role in many processes such as immune system modulation, antioxidant and anticarcinogenic effects, cancer prevention, and antiviral activities [7].

Elemental selenium in the Se^0 state is an insoluble metalloid compound chemically or biologically produced at the nanoscale. Selenium nanoparticles (SeNPs) have gained attention in recent years due to their excellent biological properties, which are similar to selenium ions but in even lower doses and with less toxicity [8]. According to previous studies, the administration of SeNPs to mice increased Th1 immune responses and triggered cytokine production such as IFN-γ, TNF-α, IL-12 and IL-2 [9]. This immunologic profile clearly showed that selenium possesses the ability to polarize the immune system toward a Th1 pattern and thereby increase the efficacy of vaccines against many viral and bacterial pathogens specifically controlled by cellular immune responses. This in turn authenticated the relationship between IFN-γ release and successful antibody secretion [4].

Therefore, in the present study, we hypothesized that the oral feeding of SeNPs to mice immunized with HBsAg will result in IFN-γ secretion in addition to improving their humoral immune responses.

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