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Full Communication

Effects of Glucan on Immunosuppressive Actions of Mercury

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ABSTRACT Global cycling of mercury results in the presence of mercury salts in the environment. The well-established negative effects of mercury on the immune system led us to the study whether natural immunomodulator glucan can overcome the immunosuppressive effects of mercury. Two types of mercury, thimerosal and mercury acetate, were administered in a dose of 2–8 mg/L of drinking water to mice. After 2 weeks, all mice exhibited profound suppression of both cellular (phagocytosis, natural killer cell activity, mitogen-induced proliferation, and expression of CD markers) and humoral (antibody formation and secretion of interleukin-6, interleukin-12, and interferon-γ) responses. The mice were then fed with a diet containing a standard dose of glucan. Our results showed that simultaneous treatment with mercury and glucan resulted in significantly lower immunotoxic effects of mercury, which suggests that glucans can be successfully used as a natural remedy of low-level exposure to mercury.

KEY WORDS: • *glucan* • *immune system* • *immunosuppression* • *mercury* • *phagocytosis*

INTRODUCTION

FOR A LONG TIME, THIMEROSAL has been used as a wound disinfectant and a preservative in medical preparation, including human vaccines. Recently, concerns regarding the immunosuppressive effects of low-level exposure to mercury raised the question of thimerosal safety.[1,2] Thimerosal contains an organic ethylmercury with similar biological properties as the well-known immunotoxic methylmercury.[3,4] However, recent studies have shown that the effects on the immune system might be different.[5]

Additional studies showed that exposure to most mercury compounds, including mercuric chloride, resulted in cell toxicity[6] and immunosuppression[7] regardless of exposure duration.[8]

β1,3-Glucans are structurally complex homopolymers of glucose, usually isolated from yeast, fungi, wheat, and seaweed. β1,3-Glucan's role as a biologically active immunomodulator has been well documented for over 40 years. Interest in the immunomodulatory properties of polysaccharides was initially raised after experiments indicated that a crude yeast cell preparation stimulated macrophages via activation of the complement system.[9] Further work identified the immunomodulatory active component as β1,3-glucan.[10] Numerous studies (currently more than 4,000 publications) have subsequently shown that β1,3-glucans, either particulate or soluble, exhibit immunostimulating properties that include antibacterial and antitumor activities.[11,12] Studies showing the strong potential of glucans to help overcome immunosuppressive effects of factors, such as irradiation or chemotherapy,[13,14] led us to the hypothesis evaluated in this article. The aims of the present study are to compare immunosuppression caused by either organic (thimerosal) or inorganic (mercury acetate) mercury and to show if this suppression can be reversed by glucan.

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MATERIALS AND METHODS

Materials

RPMI 1640 medium, Iscoves's modified Dulbecco's medium, sodium citrate, antibiotics, sodium azide, thimerosal, mercury acetate, bovine serum albumin, Wright stain, *Limulus* lysate test E-TOXATE, Freund's adjuvant, ovalbumin, lipopolysaccharide, and concanavalin A were obtained from Sigma Chemical Co. (St. Louis, MO, USA). Fetal calf serum (FCS) was from Hyclone Laboratories (Logan, UT, USA). β-1,3-Glucan (#300) was purchased from Transfer Point (Columbia, SC, USA), NOW BETA glucan from NOW FOODS (Bloomingdale, IL, USA), Glucagel T from GraceLinc (Christchurch, New Zealand), and Epicor from Embria Health Sciences (Ankeny, IA, USA).

Animals

Female, 6–10-week-old BALB/c mice were purchased from Jackson Laboratory (Bar Harbor, ME, USA). All animal work was done according to the University of Louisville Institutional Animal Care and Use Committee protocol. Animals were sacrificed by CO_2 asphyxiation.