

Garlic Induces a Shift in Cytokine Pattern in *Leishmania major*-Infected BALB/c Mice

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The regulation of T helper (Th)1- and Th2-type cytokine patterns is important in the final outcome of leishmaniasis in human and murine models. We examined the efficacy of garlic therapy or a combination of garlic and an antimonial drug (glucantime) in promoting healing and regulation of Th1/Th2 cytokine patterns in highly susceptible BALB/c mice infected with *Leishmania major*. Separate groups of infected mice received 20 mg/kg/day garlic, 60 mg/kg/day glucantime or a combination of the two, from day 30 after infection for 2 weeks. An enzyme-linked immunosorbent assay (ELISA) was performed on spleen cell culture supernatants for interferon(IFN)- γ , interleukin(IL)-2, IL-4 and IL-10. The results indicate that garlic therapy is more effective than the usual antileishmanial drug in curing the infection. Garlic-treated mice developed Th1-type cytokine responses. In contrast, glucantime therapy led to a Th2-type response in the control group with a lower level of IL-2. However, a combination of garlic and glucantime treatment was more effective than either treatment alone, and resulted in a Th1-type response similar to that which developed with garlic treatment. These results suggest that garlic extract in combination with an antimonial drug, may provide effective therapy against *L. major*. The immunomodulatory properties of garlic were elucidated in terms of shifting the cytokine response to a Th1-type pattern and therefore causing the protective response.

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INTRODUCTION

An important advance in understanding the regulation of the specific immune response to pathogens was the identification of two functionally distinct types of T-helper cells, Th1 and Th2, on the basis of their cytokine profiles [1]. While the Th1 pattern is characteristic of a cellular immune response [interleukin(IL)-2, interferon(IFN)- γ , tumour necrosis factor(TNF)- β], the Th2 pattern (IL-4, IL-5, IL-10), provides efficient help for the generation of humoral responses [2, 3].

The critical role of Th1 and Th2 cytokine patterns is well characterized in the murine model of leishmaniasis [4, 5]. To a large extent, the murine leishmaniasis model mimics human disease states [6]. Most inbred strains of mice resist *Leishmania major* infection owing to a strong Th1 response. The Th1 response ensures production of IFN- γ , which is required for the healing process to start. BALB/c mice are highly susceptible to *L. major* infection and develop a Th2-type response that is incapable of mediating parasite clearance and interferes with the action of Th1-derived cytokines [6–11].

Various research has indicated that garlic (*Allium sativum* L.) modulates immune responses [12–15]. Our previous studies demonstrated that garlic enhances the delayed-type hypersensitivity(DTH) response [16], T-lymphocyte proliferation [17] and natural killer(NK) cell activity [18].

Recently we found that garlic induces DTH enhancement and augments the engulfment and destruction of parasite by resident peritoneal macrophages in *L. major*-infected BALB/c mice (unpublished results).

Here, we studied the effect of garlic extract on the status of established *L. major* infection in BALB/c mice, and the outcome of the immune response with regard to Th1 (IFN- γ , IL-2) and Th2 (IL-4, IL-10) cytokine patterns. We also considered the course of infection and cytokine profile (Th1/Th2) in *L. major*-infected BALB/c mice treated with glucantime (meglumine antimonate), an antimony compound commonly used in the treatment of human leishmaniasis. A combined garlic and glucantime therapy was also used in this study.

Our findings indicate that garlic extract is an effective agent for the treatment of chronic, nonhealing murine leishmaniasis.