Synergistic antileishmanial and immunomodulatory activity of nanoliposomal artemisinin

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Leishmaniasis encompasses an array of clinical syndromes ranging from self-resolving cutaneous to mucocutaneous and severe visceral manifestations, which result from infection of macrophages in the dermis, the naso-oropharyngeal mucosa, and the reticuloendothelial system, respectively. Cutaneous and mucosal leishmaniasis can cause substantial morbidity, whereas visceral leishmaniasis (VL) or kala-azar is systemic and can be life threatening. In the absence of effective vector control measures and vaccines, chemotherapy remains the mainstay in the control of VL, a neglected disease of poverty. There is a pressing need for alternate rescue therapy due to escalating drug refractoriness, coupled with adverse effects, emergence of HIV co-infection, and resurfacing in the form of post kala-azar dermal leishmaniasis after apparent cure. The *Leishmania* parasites evade host defensive machinery, encumbering antigen presentation to T cells, and eventually leading to subversion of cell-mediated immunity (CMI). Thus, a promising therapeutic approach would entail administration of antileishmanial compounds, which can concurrently rejuvenate an effective T-helper-1 response, for subsequent macrophage activation to eliminate intracellular *Leishmania* amastigotes.

Sesquiterpene lactones exhibit a wide spectrum of antimicrobial activities. Artemisinin belongs to a class of sesquiterpenes with potent antileishmanial activity but has limited access to infected cells, being a highly lipophilic molecule. Association of artemisinin with liposome is a desirable strategy to elude the problem of poor accessibility, thereby ameliorating its efficacy in a murine model of experimental VL. Nanoliposomal artemisinin (NLA) was prepared by thin film hydration method and optimized using Box-Behnkehn design. The NLA was free from concomitant signs of toxicity, both \textit{ex vivo} on murine macrophages as well as \textit{in vivo} in healthy BALB/c mice. NLA significantly denigrated the intracellular infection of *L. donovani* amastigotes \textit{ex-vivo} as well as \textit{in vivo}. Protection coincided with modulation of CMI as evidenced by the positive delayed type hypersensitivity response, lymphoproliferation after antigen recall \textit{in vitro}, induction of Th1 signature cytokines and protective antibody isotypes. This nanoliposomal drug delivery system for artemisinin with synergistic Th1 immunopotentiation may serve as a promising alternative intervention against VL.

Biography:

Dr. Farhat Afrin received her Ph.D. from Indian Institute of Chemical Biology, Kolkata, India where she worked on liposomal vaccines and drugs against visceral leishmaniasis. For 16 years, she was a Faculty member in the Department of Biotechnology, Hamdard University, New Delhi, India. She also worked at National Institutes of Health, Bethesda, MD, USA and Centre for Immunology and Infection, University of York, UK. She is a recipient of several honors including American Association of Immunologists Young Faculty Travel Grant, Commonwealth Academic Staff fellowship, Indian Council of Medical Research International fellowship for Young Indian Bio-medical Scientists and Department of Biotechnology Overseas Associateship. Her research interest is parasite immunology with emphasis on nanoparticles for vaccines and immunotherapeutics of *Leishmania* infection. She has published over 55 papers in Journals of International repute and is an Academic Editor and reviewer of several journals.