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## Therapeutic and immunostimulatory potential of *Azadirachta indica* bioactive fractions in murine visceral leishmaniasis

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Exploration of immunomodulatory antileishmanials of plant origin is strongly recommended to overcome the immune suppression evident during visceral leishmaniasis (VL) and high cost and toxicity associated with conventional chemotherapeutics. In accordance, we assessed the *in vitro* and *in vivo* antileishmanial and immunomodulatory potential of ethanolic fractions of *Azadirachta indica* leaves (ALE) and seeds (ASE). *A. indica* fractions were prepared by sequential extraction of the powdered plant parts in hexane, ethanol and water. ALE and ASE (500 µg ml<sup>-1</sup>) exhibited leishmanicidal activity in a time- and dose-dependent manner (IC<sub>50</sub> of 34 and 77.66 µg ml<sup>-1</sup>, respectively) with alterations in promastigote morphology and induction of apoptosis. ALE and ASE exerted appreciable anti-amastigote potency (IC<sub>50</sub> of 17.66 and 24.66 µg ml<sup>-1</sup>, respectively) in *Leishmania* parasitized RAW 264.7 macrophages that was coupled with profound *in vivo* therapeutic efficacy (87.76% and 85.54% protection in liver and 85.55% and 83.62% in spleen, respectively) in *L. donovani* infected BALB/c mice. ALE exhibited minimal toxicity to RAW macrophages as studied by MTT assay *ex vivo* with selectivity index of 26.10, whereas, ASE was observed to be non-toxic. The bioactive fractions revealed no hepato- and nephro-toxicity *in vivo*. ALE and ASE potentiated Th1-biased cell-mediated immunity along with upregulation of INF-γ, TNF-α and IL-2 and decline in IL-4 and IL-10 levels. Gas chromatography–mass spectrometry analysis revealed several secondary metabolites that may have contributed to the observed antileishmanial effect. Dual antileishmanial and immunostimulatory efficacy exhibited by the bioactive fraction merits their use alone or as adjunct therapy for VL.

### Biography

Hassan Hemeg has completed his Master's in Pathological Science from Sheffield University, UK and PhD from King Abdulaziz University, Jeddah, Saudi Arabia. He has earned several honors such as Fellow of Institute of Biomedical Science, UK and Certified Canadian Accreditation Specialist for Health Care Facilities. He acquired training in Microbiology from Sheffield and Bristol Universities, UK and US Department of Labor, Occupational Safety and Health Administration. He is a member, secretary and chairman of several committees. His research interest is in the field of Antimicrobial Resistance. He has published several papers in journals of international repute.

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