Evaluation of Sage Phenolics for Their Antileishmanial Activity and Modulatory Effects on Interleukin-6, Interferon and Tumour Necrosis Factor-α-Release in RAW 264.7 Cells

Oliver A. Radtke[a], Lai Yeap Foo[b], Yinrong Lu[b], Albrecht F. Kiderlen[c], and Herbert Kolodziej[a,*]

[a] Institut für Pharmazie, Pharmazeutische Biologie, Freie Universität Berlin, Königin-Luise-Straße 2+4, D-14195 Berlin, Germany. Fax: +49-30-838-53729. E-mail: kolpharm@zedat.fu-berlin.de

[b] New Zealand Institute for Industrial Research, Gracefield Road, Lower Hutt, New Zealand

[c] Robert Koch-Institut, Department of Infectious Diseases, Nordufer 20, D-13353 Berlin, Germany

* Author for correspondence and reprint requests

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A series of sage phenolics was tested for activity against a panel of *Leishmania* parasites and for immunomodulatory effects on macrophage functions including release of tumour necrosis factor (TNF), interleukin-6 (IL-6), and interferon (IFN)-like activities. For this, functional bioassays were employed including an *in vitro* model for leishmaniasis in which macrophage-like RAW 264.7 cells were infected with *Leishmania* parasites, an extracellular *Leishmania* growth-inhibition assay, a fibroblast-lysis assay for TNF-activity, a cell proliferation assay using IL-6 sensitive murine B9 hybridoma cells, and a virus protection assay for IFN-like activity. Whereas none of the test samples exhibited marked activities against extracellular *Leishmania* promastigotes (IC_{50} > 700 to > 2800 nM; > 500 μg/ml), caffeic acid, salvianolic acids K and L as well as the methyl ester of salvianolic acid I showed pronounced antileishmanial activities against intracellular amastigote stages within RAW cells (IC_{50} 3–23 nM vs. 10–11 nM for the reference Pentostam®). Noteworthy, the phenolic samples showed no cytotoxicity against the host cells (IC_{50} > 600 to > 2200 nM; > 400 μg/ml). Tested sage phenolics activated Leishmania-infected RAW 264.7 for release of TNF ranging 22–117 U/ml and IL-6 ranging 3–42 U/ml. In contrast, their TNF- or IL-6-inducing potential in experiments with non-infected host cells was negligible. Furthermore, caffeic acid and salvianolic acid K induced a modest release of IFN-like activity (5–9 and 2–4 U/ml, respectively) as reflected by inhibition of the cytopathic effect of encephalomyocarditis virus on L929 cells. The results support the emerging picture that plant polyphenols may be credited for the profound health-beneficial properties of various herbal medicines and agricultural products.

Key words: Salvia officinalis, *Leishmania*, Immunomodulation