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## In vitro and in vivo immunomodulating effects of traditionally-prepared extract and purified compounds from *Cetraria islandica*

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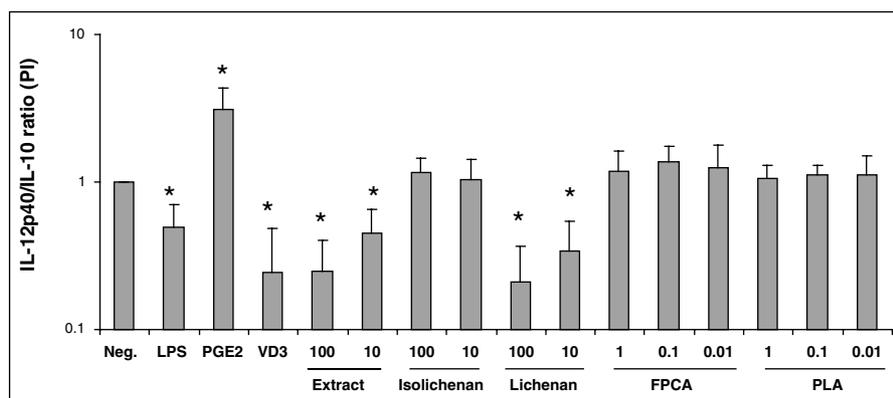
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*Cetraria islandica* has been used for centuries in folk medicine in many countries to treat a number of conditions, mainly as an aqueous extract<sup>(1,2)</sup>. *C. islandica* contains many compounds, some of which have shown biological activity<sup>(3–6)</sup>. However, very little is known about their effect on the immune system. Thus, the effect of traditionally-prepared aqueous extract and purified compounds isolated from *C. islandica* (polysaccharides lichenan and isolichenan and secondary metabolites protolichesterinic acid (PLA) and fumarprotocetraric acid (FPCA)) on the maturation of dendritic cells was assessed.

Human monocytes were isolated from healthy individuals and differentiated into immature dendritic cells by culturing them in the presence of IL-4 and granulocyte-macrophage colony-stimulating factor. They were subsequently cultured in the presence of maturation factors (IL-1 $\beta$  and TNF $\alpha$ ), either alone (Neg) or with positive controls lipopolysaccharides (LPS), PGE2, cholecalciferol (VD3) or the aqueous extract or purified compounds from *C. islandica*. Their effect on the maturation of the dendritic cells was assessed by measuring secretion of IL-10 and IL-12 by ELISA and expression of the surface molecules CD86 and CD209 by flow cytometry. In addition, the effect of the aqueous extract on antigen-induced arthritis in rats was investigated.

The aqueous extract up regulated secretion of both IL-10 and IL-12, with IL-10 secretion being more prominent (Figure). Lichenan had similar effects, but not isolichenan or the secondary metabolites, suggesting that the effect observed with the aqueous extract was mainly mediated by lichenan. Significantly less arthritis was observed for rats treated with the aqueous extract compared with rats treated with saline (9 g NaCl/l) alone (data not shown).

These results suggest that the aqueous extract of *C. islandica* has an anti-inflammatory effect, possibly by changing the cytokine secretion bias from IL-12 towards IL-10.



**Figure.** IL-12p40:IL-10 secretion by dendritic cells cultured with maturation factors alone (Neg); LPS; PGE2; VD3; extract, lichenan and isolichenan at 100 and 10 µg/ml; or FPCA and PLA at 1, 0.1 and 0.01 µg/ml. Values are means and standard deviation represented by vertical bars. Mean values were significantly different from that for the control (Neg): \* $P < 0.05$ .

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