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## Biological effects of natural and recombinant mistletoe lectin and an aqueous mistletoe extract on human monocytes and lymphocytes in vitro.

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Mistletoe lectin is thought to constitute the active principle in extract preparations from mistletoe, which are widely used as immunomodulators in adjuvant tumor therapy. However, no study exists which compares the immunological potency of different well-defined mistletoe lectin preparations on human immune cells. Therefore, in the present study the biological effects of an aqueous mistletoe extract, standardized for mistletoe lectin I (eML), the isolated natural mistletoe lectin (nML), and the recombinant form of this lectin (rML) on human peripheral blood monocytes and lymphocytes were compared with respect to cell viability and cytokine induction. After 48-hr incubation of peripheral blood mononuclear cells (PBMC) with rML, nML, and eML, a continuous concentration-dependent decrease in cell viability was found with an IC<sub>50</sub> of about 3 ng/ml for rML and nML and 10 ng/ml for eML, respectively. This effect also was seen when isolated lymphocytes and monocytes were separately incubated with the lectin preparations. After incubation of PBMC and isolated monocytes of 5/10 blood donors with eML, an increase in cell viability was found at lectin concentrations between 10 and 1,000 pg/ml. This effect was not seen with the pure lectin preparations nML and rML. After 48-hr incubation of PBMC with rML, nML, and eML, induction of IL-1-beta, TNF-alpha, IL-2, IL-6, and IL-10 but not IFN-gamma was measured. For IL-1-beta it could be shown that cytokine induction took place at a broad lectin concentration range (0.1-100 ng/ml). Cytokine levels varied greatly in the PBMC cultures of the different blood donors. When monocytes were separately incubated with eML, nML, and rML for 48 hr, high levels of IL-1-beta were found. In contrast, in cultures of separated lymphocytes from the same donors only a minimal production of IL-1-beta and no production of IFN-gamma was found after incubation with rML, nML, and eML. It is concluded that there are quantitative differences in the immunomodulatory effects of the mistletoe lectin preparations on human monocytes and lymphocytes. Therefore, measurement of cell viability and cytokine induction may be a diagnostic laboratory tool to determine the immunological potency of various mistletoe preparations and may help to clarify the clinical benefit of therapies with these substances.

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