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## [Mistletoe therapy from the pharmacologic perspective]

[Article in German]

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Because of their cytostatic/apoptotic and immunomodulatory effects mistletoe extracts are often applied in tumour patients. Recent experimental data suggest that the mistletoe lectins *Viscum album* agglutinin (VAA)-I and -II are play an important role in the efficacy of mistletoe therapy. VAA-I and -II are members of the type-II ribosome-inactivating proteins. VAA-I has been shown to induce cytostatic effects in cultures of various eukaryotic cells in vitro. In 24-hour cultures of human peripheral lymphocytes, flow-cytometric investigations with propidium iodide (PI) in hypotonic buffer and quantitative assessment of DNA breaks with terminal deoxynucleotidyl transferase (TdT)-mediated dUTP-digoxigenin nick end-labeling (TUNEL) assay were carried out; they revealed a dose-dependent VAA-I-induced apoptosis (lectin concentrations between 10 ng/ml and 1 microg/ml). In 24-hour cultures of peripheral blood mononuclear cells (PBMC), VAA-I in non-cytotoxic concentrations (1 +/- 10 ng/ml) induced mRNA expression and enhanced the secretion of proinflammatory cytokines. The stimulation of NK cells by VAA-I in vitro was enhanced in additive manner by the combination of VAA-I with IL-2 and IL-12. In culture of PBMC and bone marrow CD34+ cells coincubation of VAA-I with other haematopoietic growth factors induced a dose-dependent increase in clonogenic growth. In cancer patients the mechanisms of natural immunity, believed to be essential for their survival, are often significantly decreased. VAA-I and standardized mistletoe extracts are able to stimulate the cellular parameters of natural immunity with a bell-shaped curve of efficacy. Studies in animal models suggest that application of 0.5-3 ng/kg VAA-I twice a week is effective in sustaining the elevation of the number and activity of peripheral blood NK cells. These parameters often exhibit high intrinsic fluctuations, in healthy persons, however, blind crossover studies reveal an optimal lectin dose of about 0.5 and 1 ng/kg bw, suggesting a potential use of mistletoe preparations as a modulator of the natural immune system. Selective apoptotic effects of VAA-I may represent a novel approach for pharmacological manipulation of the balance between cell growth and programmed cell death. Appropriate combination of immunomodulatory and cytotoxic doses may open new clinical perspectives in the mistletoe therapy.

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