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NMR solution structure of viscotoxin C1 from *Viscum album* species *Coloratum ohwi*: toward a structure-function analysis of viscotoxins.

Romagnoli S, Fogolari F, Catalano M, Zetta L, Schaller G, Urech K, Giannattasio M, Ragona L, Molinari H.

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The high resolution three-dimensional structure of the newly discovered plant viscotoxin C1, from the Asiatic *Viscum album* ssp. *Coloratum ohwi*, has been determined in solution by (^1H) NMR spectroscopy at pH 3.6 and 285 K. The viscotoxin C1-fold, consisting of a helix-turn-helix motif and a short stretch of an antiparallel beta-sheet is very similar to that found for the highly similar viscotoxins A2 and A3 and for other related thionins. Different functional properties of members of the thionin family are discussed here in light of the structural and electrostatic properties. Among the very homologous family of alpha- and beta-thionins, known for their antimicrobial activity, the viscotoxin subfamily differs from the other members because of its high toxicity against tumoral cells. Key residues for the modulation of viscotoxin cytotoxicity have been identified on the basis of sequence and structural alignment.

Acta Crystallogr D Biol Crystallogr. 2003 Dec; 59(Pt 12): 2125-32.

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Structure of viscotoxin A3: disulfide location from weak SAD data.

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The crystal structure of viscotoxin A3 (VT A3) extracted from European mistletoe (*Viscum album* L.) has been solved using the anomalous diffraction of the native S atoms measured in-house with Cu K α radiation to a resolution of 2.2 Å and truncated to 2.5 Å. A 1.75 Å resolution synchrotron data set was used for phase expansion and refinement. An innovation in the dual-space substructure-solution program SHELXD enabled the individual S atoms of the disulfide bonds to be located using the Cu K α data; this resulted in a marked improvement in the phasing compared with the use of super-S atoms. The VT A3 monomer consists of 46 amino acids with three disulfide bridges and has an overall fold resembling the canonical architecture of the alpha- and beta-thionins, a capital letter L. The asymmetric unit consists of two monomers related by a local twofold axis and held together by hydrophobic interactions between the monomer units. One phosphate anion (confirmed by ³¹P-NMR and MS) is associated with each monomer.

MAJOR NEW CANCER STUDY IS PUBLISHED AS MISTLETOE THERAPY IS IN THE NEWS

Alternative Therapies in Health and Medicine May 2001

PRESS RELEASE April 30, 2001

Mistletoe extract (Iscador) has been in the news since actress Suzanne Somers announced that she is using it as an adjunctive therapy to fight breast cancer following lumpectomy and radiation. Some medical experts have claimed that there is no scientific evidence to support taking this natural approach.

However, a major groundbreaking study being published in the May issue of the peer-reviewed journal *Alternative Therapies in Health and Medicine* found that individuals who took mistletoe extract in addition to their conventional medical treatment lived 40% longer.

"There is mounting basic science and clinical evidence for the efficacy of mistletoe as an adjunctive cancer therapy for solid tumors," says David Riley, MD, Editor in Chief of *Alternative Therapies*, and a Clinical Associate Professor at the University of New Mexico Medical School. "Mistletoe," Dr. Riley adds, "is the most commonly used cancer drug in Germany today."

The study* followed 35,000 residents of Heidelberg, Germany over 30 years, identifying 5,000 who had cancer. Six hundred of these cancer patients were sorted into pairs. One member of each pair took mistletoe extract in addition to conventional treatment; the other, who had a

similar type and stage of disease, received only conventional treatment. After comparing the length of survival, the study concluded that participants who added mistletoe extract to their treatment lived 40% longer than those who did not.

Research indicates that mistletoe extract is most effective when used in conjunction with conventional medical care for the treatment of solid tumors such as breast cancer, according to Dr. Riley. It does not appear to be useful as an adjunctive treatment for other cancers like lymphoma or leukemia.

*Grossarth-Maticek R, Kiene H, Baumgartner SM, Ziegler R: Use of Iscador, an Extract of European Mistletoe (*Viscum Album*), in Cancer Treatment. *Alternative Therapies in Health and Medicine* May 2001