IMMUNOTROPIC ACTIVITY OF VRATIZOLIN
(ITCL, DENOTIVIR)

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The aim of this study was to evaluate immunotropic properties of vratizolin, a known antiviral drug, in several in vitro and in vivo assays in mouse and human models. We demonstrated that vratizolin exerted strong immunosuppressive actions both in the humoral and cellular immune response to SRBC in mice. The compound affected not only the inductive phase of delayed type hypersensitivity (DTH) but also the effector phase of that response. Vratizolin was effective when given intraperitoneally and orally. The inhibitory action of vratizolin was comparable to that of cyclosporin A (CsA), the reference drug. Vratizolin exhibited also suppressory properties with regard to PHA-induced proliferation of human peripheral blood lymphocytes and that effect exceeded the inhibitory action of CsA. We also showed that vratizolin inhibited to some degree LPS-induced cytokine production in human peripheral blood cultures. The activities of TNF-α, IL-1 and IL-6 were inhibited on average by 37, 26 and 35%, respectively. This was in contrast to the effects of CsA which strongly inhibited only IL-1 production. Lastly, we demonstrated that vratizolin markedly inhibited growth of several tumor cell lines. In particular, the compound significantly inhibited growth of mouse leukemia L-1210 and human acute lymphoblastoid leukemia CCRF-CEM cell lines. The presented data suggest that the immunosuppressory action of vratizolin, although similar to that of CsA, is mediated by a different mechanism. The properties of vratizolin, described in this report, indicate that the drug should be further investigated for possible immunosuppressory and antitumor application.

Key words: vratizolin, ITCL, Denotivir, humoral immune response, delayed type hypersensitivity, mice, cytokines, proliferation, human blood lymphocytes, tumor cell lines