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ORIGINAL ARTICLE

In vitro induction of apoptotic cell death in chronic lymphocytic leukemia by two natural products: preliminary study

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Summary

Purpose: *B cell chronic lymphocytic leukemia (B-CLL) is an neoplastic disorder characterized by alterations in the pathways of programmed cell death (apoptosis). Deregulation of apoptosis pathways also contributes to chemoresistance of B-CLL cells. Therefore, it is not surprising that induction and acceleration of apoptosis represent key point in novel B-CLL therapeutic protocols. The present study was designed to investigate the effects of two natural products, Immunarc forte and Korbazol on the in vitro survival of leukemic cells.*

Methods: *Peripheral blood mononuclear cells (PBMC) from 20 B-CLL patients and 20 healthy donors were used for cytotoxicity studies. Cytotoxic activity of the tested products were assessed by the MTT colorimetric assay and the type of cell death was determined by flow cytometry.*

Results: *We found that Korbazol was selectively cytotoxic against B-CLL cells, but the cytotoxic activity of Immunarc forte was much weaker. Of note, synergy was shown between these two drugs, and this effect was also selective, without affecting the normal mononuclear cells. According to Annexin-V binding, Korbazol and Immunarc forte induced apoptotic type of cell death in B-CLL cells. Moreover, treatment with Korbazol, but not with Immunarc forte, decreased spontaneous apoptosis in cultured normal polymorphonuclear cells.*

Conclusion: *Our findings imply that Korbazol is as potential therapeutic agent that induces apoptosis of B-CLL cells. The resistance of normal mononuclear cells and anti-apoptotic effects on normal polymorphonuclear cells, as well as its ability to synergize with Immunarc forte, warrants further investigation and supports their therapeutic application in the treatment of B-CLL.*

Key words: apoptosis, chronic lymphocytic leukemia, immunarc forte, korbazol, natural products

Introduction

Apoptosis, also called programmed cell death, has been introduced on the basis of observations that cells which die during development also have a characteristic set of structural changes notably different from necrosis. However, these characteristics may be observed on cells that die in different conditions: Natural killer (NK) cells, dendritic cells or T cells cytotoxicity [1-3]; negative selection of immune cells in the thymus [4]; normal cellular turnover in tissues [5,6]; in tumors and normal tissues when they are exposed to low doses of ionizing radiation [7,8]; chemotherapeutics [9,10] and even hypoxia [11,12]. Apoptosis essentially represents controlled breakdown of cells. Today, we know that apoptosis is involved in many physiological processes and that there is hardly any disease whose pathogenesis can be explained without apoptosis. Generally, there are diseases with too little apoptosis and diseases with too much apoptosis. For example, autoimmune diseases are characterized by impaired apoptosis of T lymphocytes, whereas cancer could be looked upon as a disease where the net increase in tumor burden is the sum of an increased growth rate and a decreased apoptotic rate.

Programmed cell death plays a central role in the selection and differentiation of lymphoid cells [4,6], as well as in regulating the size of the mature lymphocyt-

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