The 5th International Conference on Quality and Evidence Based in Prophetic Medicine

DOI 10.14293/ICQEBPM.2022.600
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The Antiproliferative Effect of Nutrients Against HTLV-1 Infections

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Abstract

Adult T-cell Leukemia (ATL) is a disease with no known cure. The disease manifests itself as an aggressive proliferation of CD4+ cells with the human T-cell Lymphotropic virus type 1 (HTLV-1). The leukemogenesis of the virus is mainly attributed to the viral oncoprotein Tax. Tax activates the Nuclear Factor kappa B (NF-κB) which stimulates the activity and expression of the matrix metalloproteinase-9 (MMP-9). The objective of this presentation is to explore the underlying mechanisms of antioxidants involved in the treatment of leukemia. To achieve the objectives, efficacy of non-cytotoxic concentrations of certain antioxidants were investigated on proliferation, apoptosis induction, Tax expression, NF-κB levels as well as on MMP activity and expression both at the transcriptional and translational levels against both Human T-cell Lymphotrophic Virus Type-1 (HTLV-1)-infected and non-infected T lymphocytes. Four leukemia cell lines were used. C91-PL and HuT-102 are HTLV-1 positive cell lines whereas CEM and Jurkat are HTLV-1 negative. The antioxidants used included: Ascorbic acid, Epigallocatechin-3-gallate (EGCG) and a formulation containing a combination of those with other antioxidants and minerals. Cytotoxicity of the tested compounds was assayed using CytoTox 96 Non-radioactive and proliferation was measured using Cell Titer96TM Nonradioactive Cell Proliferation kit (MTT- based assay). Enzyme linked immunosorbant assay (ELISA) and electrophoretic mobility shift assay (EMSA) was used to assess the effect of test compounds on NF-κB mobility. Zymography was used to determine the effects of test compounds on the activity and secretion of MMP-9. The expression of MMP-9 was done using RT-PCR at the translational level and Immunoblotting at the transcriptional level. Results: A significant inhibition of proliferation was seen in all the cell lines in a dose dependent manner. The test compounds induced a dose dependent decrease in Tax expression, which was paralleled by a down-regulation of the nuclearization of NF-κB. This culminated in the inhibition of the activity of MMP-9 and their expression both at the transcriptional and translational levels. Conclusions: The results indicated that the tested compounds targeted multiple levels pertinent to the progression of ATL at various capacities. Their activities were mediated through the NF-κB pathway, and hence has the potential to be integrated in the treatment of this disease as a natural potent anticancer agent.

Keywords

Acute T-cell leukemia, Specific Nutrient Synergy, HumanT-cell Lymphotropic Virus type I (HTLV-1), Tax, NF-κB pathway, MMP-9.