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Dietary polyphenols influence antimetabolite agents: Methotrexate, 6-mercaptopurine and 5-fluorouracil in leukemia cell lines

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Polyphenols have been previously shown to sensitize leukemia cell lines to topoisomerase inhibitors; synergistically inducing cell-cycle arrest and apoptosis. Here, we assess the effects of polyphenols (quercetin, apigenin, emodin, rhein and cis-stilbene) when used alone and in combination with antimetabolites: methotrexate, 6-mercaptopurine and 5-fluorouracil; in lymphoid (JURKAT and CCRF-CEM), and myeloid (THP-1 and KG-1a) leukemia cells lines, and non-tumour control cells (CD133⁺HSC and CD34⁺HSC). The effects of combined treatments were investigated on ATP and glutathione levels, cell-cycle progression, DNA damage and apoptosis. Polyphenols antagonized methotrexate and 6-mercaptopurine induced cell-cycle arrest and apoptosis in all leukemia cells. This was associated with reduced DNA damage and increased glutathione levels, greater than that seen following individual treatments alone. In contrast, 5-fluorouracil when combined with quercetin, apigenin or emodin caused synergistic or additive decreases in ATP levels, increased cell-cycle arrest and apoptosis in all leukemia cells. However, antagonistic effects were observed when 5-fluorouracil was combined with rhein in myeloid cells; and cis-stilbene in all leukemia cells. The effects were dependant on polyphenol type and chemotherapy agent investigated, and cell type treated. Interestingly treatment of non-tumour control cells with polyphenols protected cells from antimetabolite treatments. This suggests that polyphenols modulate the action of antimetabolite agents; more importantly they antagonised methotrexate and 6-mercaptopurine actions, thus suggesting the requirement of polyphenol-exclusion during their use.

Biography

Mahbub Amani A completed MSc in Biomedical Basis of Disease in 2010 and PhD in Anti-Cancer Potential of Polyphenols in Treatment of Leukemia in 2015 at the Sheffield Hallam University of Biomedical Research Centre, UK. He is interested in investigating the biological effects of several nutraceutical compounds such as polyphenols alone and in combination with chemotherapies on the induction of apoptosis, reduced cell proliferation and signaling pathways that involved in the pathogenesis of leukemia. He has four published papers in the *Journal of Pathology* (2012), the *Journal of Anti-Cancer Agents in Medicinal Chemistry* (2013) and recently two in *Nature* (2015). In addition, he was awarded three prizes: The Alastair Currie prize for the best poster presentation at the Pathological Society of Great Britain & Ireland Conference in 2012, Sheffield, UK; best poster prize for research entitled: Polyphenols Act Synergistically with Doxorubicin and Etoposide in leukemia cell lines at the 4th International Conference on Blood Malignancies and Treatment: 18th-19th April (2016), Dubai; best poster award for research entitled: Polyphenols Act Synergistically with Doxorubicin and Etoposide in Leukemia cell lines at the 14th World Cancer and Anti-Cancer Therapy Convention and that held in Nov 21-23, 2016 in Dubai, UAE. Currently, he is working as Assistant Professor in the Department of Laboratory Medicine and Pathology at Umm Al-Qura University, Makkah, KSA.

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