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A prooxidant mechanism of cancer chemopreventive properties of plant polyphenols

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Introduction: In the last couple of decades there has been some interest in alternative mechanisms of apoptosis induction which do not involve caspases. This is particularly of interest in relation to cancer cells. We have hypothesized that mobilization of endogenous copper ions by plant polyphenols such as EGCG and consequent oxidative degradation of cellular DNA could be an important mechanism of their anticancer properties.

Objectives: Over the years we have validated our hypothesis to a considerable degree. We further confirm the hypothesis by using analogues of EGCG to identify the structural features of tea catechins important for mobilizing endogenous copper and breakage of cellular DNA in cancer cells.

Methodology: Comet assay to study DNA breakage, MTT assay for cell proliferation and Histone/DNA Elisa for apoptosis induction was used to examine the catechin mediated oxidative breakage of cellular DNA in various cancer cell lines.

Results & Conclusion: Catechins have been shown to inhibit

cell proliferation and induce apoptosis in different cancer cell lines and that such cell death is prevented to a significant extent by copper chelator neocuproine. Further, normal breast epithelial cells (MCF-10A), cultured in a medium supplemented with copper (MCF-10A-Cu), become sensitized to EGCG induced growth inhibition. Copper transporters Ctr1 and ATP7A are found to have an increased expression in MCF-10A-Cu cells and EGCG inhibits the expression of both the copper transporters in such cells. Moreover, silencing of copper transporter Ctr1 by siRNA reduces the sensitivity of MCF-10A-Cu cells to EGCG. We conclude that the position and the number of hydroxyl groups in various catechins determine their capacity to mobilize endogenous copper and degrade cellular DNA.

Speaker Biography

Mohd Farhan is currently working as an assistant professor in King Faisal University, Saudi Arabia. He has many publications in the international journals.

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