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Title: Flavonoids-Induced Redox Cycling of Copper Ions Leads to Generation of Reactive Oxygen Species: A Potential Role in Cancer Chemoprevention

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1 Flavonoids-Induced Redox Cycling of Copper Ions Leads to 2 Generation of Reactive Oxygen Species: A Potential Role in 3 Cancer Chemoprevention

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17 **Abstract:** Flavonoids, a class of polyphenols are known to be effective inducers of apoptosis and
18 cytotoxicity in cancer cells. It is believed that antioxidant activity of polyphenols cannot fully account
19 for induction of apoptosis and chemotherapeutic prevention in various cancers. In this article, by
20 employing single cell alkaline gel electrophoresis (comet assay), we established that antioxidants,
21 flavonoids such as (myricetin=MN), fisetin=FN, quercetin=QN, kaempferol=KL and galangin=GN) can
22 cause cellular DNA breakage, also act as pro-oxidant in presence of transition metal ion such as copper.
23 It was observed that the extent of cellular DNA breakage was found significantly higher in presence of
24 copper. Hydroxyl radicals are generated as a sign of flavonoids' pro-oxidant nature through redox
25 recycling of copper ions. Further, a dose-dependent inhibition of proliferation of breast cancer cells
26 MDA-MB-231 by MN was found leading to pro-oxidant cell death, as assessed by MTT assay. Since
27 levels of copper are considerably elevated in tissue, cell and serum during various malignancies,
28 suggesting that cancer cells would be more subject to copper induced oxidative DNA breakage. Such a
29 copper dependent pro-oxidant cytotoxic mechanism better explains the anticancer activity and
30 preferential cytotoxicity of dietary phytochemicals against cancer cells.
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34 **Keywords:** Flavonoids; comet assay; pro-oxidant: copper; myricetin; reactive oxygen species,
35 MTT assay
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37 1. Introduction

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