Quercetin, a Natural Dietary Flavonoid Inhibits, Reverses, Retards Tumorigenesis in Prostate and Breast Cancer

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Short Communication

Epidemiological and dietary intervention studies in animals and humans have suggested that bioflavonoids such as quercetin plays a beneficial role in inhibiting, reversing or retarding tumorigenesis in prostate and breast cancer. Quercetin 3,3',4',5,7 - pentahydroxyflavone a naturally occurring flavonoid, is a component of most edible fruits and vegetables with the highest concentrations being found in onions, apples and red wine [1]. Quercetin has a broad range of pharmacological properties that include antioxidant, anticancer and anti-inflammatory activities [2]. Quercetin has been shown to exert anticancer effects on prostate and breast cancer cell lines [3-6]. We have studied recently chemo preventive effect of quercetin in MNU and testosterone induced prostate cancer of Sprague – Dawley rats [7]. Epidermal growth factor (EGF) plays a key role in epithelial malignancies by enhancing cancer cell proliferation, survival, invasion and metastasis. Quercetin prevented EGF induced cell proliferation and survival by regulating EGFR/P13K/Akt/mTOR and EGFR/Raf/ERK. Epidermal growth factor receptor (EGFR) is a key factor in epithelial malignancies and its activity, enhances tumor growth, invasion and metastasis [8]. EGFR is a member of the ErbB family of tyrosine kinase receptors that transmit growth inducing signals to cells that have been stimulated by an EGFR ligand example TGFα and EGF [9]. The activation of the EGFR signaling pathway stimulates downstream signaling cascades involved in cell proliferation [Ras/mitogen-activated protein kinase (MAPK)] and anti-apoptosis (phosphatidylinositol 3 – kinase P13K/Akt) [Nicholson and Anderson, 2002]. Protein kinase B/Akt is activated by the P13K pathway. Generation of P1P3 and P1 [3,4] P2 is necessary for the localization of PKB to the membrane surface. Protein dependent kinase (PDKI) phosphorylates AKt at threonine 308. The fully active multi phosphorylated AKt then dissociates from the plasma membrane and targets substrates located in the cytoplasm and nucleus. It causes the activation of genes involved in diverse cellular processes [10-11]. Epidermal growth factor regulates cancer metastasis by regulating epithelial to mesenchymal transitions (EMT) [12]. EMT trans-differentiation process involve the conversion of adherent epithelial cells into individual migratory cells leading to changes in cell phenotype into more loose mesenchymal like cells and promoting local invasion and metastatic dissemination of tumor cells [13].

Proliferating cell nuclear antigen (PCNA) is a ubiquitously expressed protein that plays crucial roles in many vital cellular processes. It is synthesized in all stages of the cell cycle with a half of approximately 20h and is elevation in early S phase to support cell cycle progression [14]. Over expression of PCNA is also a reliable biomarker for other tumor types including breast cancer [15]. PCNA is involved in DNA replication, repair and epigenetic maintenance and is often used as a diagnostic and prognostic marker. PCNA has been used as an independent marker for various cancers [16].

Quercetin prevents prostate cancer growth via EGFR signaling and prostate cancer progression by regulating cell adhesion molecules like E – cadherin, N cadherin and vimentin vix snail, slug and twist gene. Interestingly quercetin was effective in preventing carcinogenesis in both ventral and dorsolateral prostate. Quercetin supplementation significantly decreased the PCNA expression in both the lobes of chemically induced cancer rats [17].

In in vitro model quercetin prevents EGF induced EMT via EGFR/P13K/Akt/ERK1/2 pathway and by suppressing transcriptional repressor snail, slug and twist in prostate cancer cell line (PC 3). Thus, quercetin prevents cancer metastasis by targeting EMT [18]. We synthesized gold nanoparticle conjugated quercetin (AuNPQ-5) using a simple efficient method that was thoroughly characterized by several physico – chemical methods. AUNPs – Q5 showed an effective cytotoxicity and induction of apoptosis in breast cancer cell lines (both estrogen dependent and independent). AUNPs – Q5
[19] inhibited the EGFR phosphorylation and downstream molecules of P13K / AKT pathway in breast cancer cells. AUNPs – QU5 inhibits epithelial – mesenchymal transition, angiogenesis and invasiveness via EGFR / VEGFR-2 mediated pathway in breast cancer [20]. Thus our studies proved that quercetin is effective in preventing prostate and breast cancer.

References


