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INHIBITION OF CYCLOOXYGENASE-2 AND INDUCIBLE NITRIC OXIDE SYNTHASE BY SELECTED CHEMOPREVENTIVE PHYTOCHEMICALS VIA THE NF-κB SIGNALING PATHWAY

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A wide array of phenolic substances, particularly those present in dietary and medicinal plants, have been reported to possess substantial anticarcinogenic and antimutagenic activities. The majority of naturally occurring phenolics retain antioxidative and anti-inflammatory properties which appear to contribute to their chemopreventive or chemoprotective activity. Inducible cyclooxygenase (COX-2) and nitric oxide synthase (iNOS) are important enzymes that mediate inflammatory processes. Improper up-regulation of COX-2 and/or iNOS has been associated with pathophysiology of certain types of human cancers as well as inflammatory disorders. Since inflammation is closely linked to tumor promotion, substances with potent anti-inflammatory activities are anticipated to exert chemopreventive effects on carcinogenesis, particularly in the promotion stage. Examples are curcumin, a yellow pigment of turmeric (*Curcuma longa* L., Zingiberaceae), capsaicin, a major pungent principle of hot chili pepper (*Capsicum annuum* L., Solanaceae), [6]-gingerol from ginger (*Zingiber officinale* Roscoe, Zingiberaceae), some ginsenosides derived from Korean red ginseng (*Panax ginseng* C.A. Meyer), and resveratrol from grapes (*Vitis vinifera,* Vitaceae). Recent studies have demonstrated that the eukaryotic transcription factor nuclear factor kappa B (NF-κB) is involved in regulation of COX-2 and iNOS expression. Several chemopreventive phytochemicals have been shown to inhibit COX-2 and iNOS expression by blocking improper NF-κB activation. Multiple lines of compelling evidence indicate that extracellular-regulated protein kinase and p38 mitogen-activated protein kinase are key

elements of the intracellular signaling cascades responsible for NF-κB activation in response to a wide array of external stimuli. Some of the aforementioned edible phytochemicals have been shown to suppress activation of NF-κB through repression of degradation of the inhibitory unit IκBα, which hampers subsequent nuclear translocation of the functionally active subunit of NF-κB. This work was supported by the grant (2002-2-20800-003-5) from the Basic Research Program of the Korea Science and Engineering Foundation (KOSEF).

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