[S6-4] [10/18/2002(Fri) 10:50-11:10/Hall B]

Chemopreventive and Chemoprotective Potential of Naturally Occurring and Synthetic Anti-inflammatory Agents

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Chemoprevention, one of the most innovative and promising areas of cancer research, refers to the prevention of cancer through pharmacologic or nutritional intervention. Recently, considerable attention has been focused on the role of cyclooxygenase-2 (COX-2) in the carcinogenesis as well as inflammation. Inappropriate up-regulation of COX-2 is implicated in the pathophysiology of certain types of human cancers. Numerous experimental, epidemiologic and clinical investigations have demonstrated that nonsteroidal anti-inflammatory drugs (NSAIDS), particularly those with high selectivity towards COX-2, have promise as chemopreventive or anticancer agents. In this context, it is interesting to note that celecoxib, the first US FDA approved selective COX-2 inhibitor, has been found to suppress the formation/growth of polyps in patients with familial adenomatous polyposis. The drug has also been shown to be protective against experimentally induced carcinogenesis in rodents and also to induce apoptosis of various cancerous cells.

A wide array of anti-inflammatory phytochemicals present in dietary or medicinal plants have been reported to possess chemopreventive activities in experimental animals and cultured cells. Our previous studies have revealed that [6]-gingerol, a pungent principle present in ginger (*Zingiber officinale* Roscoe, Zingiberaceae) and yakuchinones derived from *Alpinia oxyphylla* Miquel (Zingiberaceae) inhibit 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced edema, production of tumor necrosis-□ and interleukin-1□, ornithine decarboxylase activity, and tumor promotion in mouse skin. Recent work from this laboratory has revealed that curcumin inhibits TPA-induced expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase through inactivation of nuclear transcription factor kappa B (NF-□B). Curcumin also blocked catalytic activity and/or activation via phosphorylation of mitogen-activated protein

kinases (MAPKs) as p38 and ERK1/2. Capsaicin, a principal pungent ingredient of hot chilli pepper (*Capsicum annuum* L., Solanaceae) with potential anti-inflammatory, analgesic and anti-tumor promoting activities, also repressed TPA-induced activation of NF-□B and another ubiquitous eukaryotic transcription factor, activator protein 1 (AP-1). The soy isoflavone, genistein, inhibited TNF-. □ or TPA-induced COX-2 expression and PGE_2 production through down-regulation of ERK1/2 and subsequent inactivation of NF-□B in cultured human breast epithelial cells. Supported by the grant (2000-2-20800-003-5) from the Basic Research Program of the Korea Science and Engineering Foundation.