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Induction of Apoptosis and Inhibition of Cell Migration by Ethyl Alcohol Extract of *Hizikia fusiforme* in Human Breast cancer Cells

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Hizikia fusiforme is a kind of brown edible seaweed that mainly grows in the temperate seaside areas of the northwest Pacific including Korea, Japan and China. Recently, *H. fusiforme* has been known to exert antioxidant, antimutagenic and anticoagulant activity, however, the molecular mechanisms of *H. fusiforme* in malignant cells have been poorly studied until now. In this study, we investigated the effects of ethyl alcohol extract of *H. fusiforme* (EAHF) on the anti-proliferative effects of MDA-MB-231 and MCF-7 human breast cancer cells. EAHF treatment resulted in a concentration-dependent growth inhibition by including apoptosis in MDA-MB-231 cells and G1 phase arrest in MCF-7 cells. In MDA-MB-231 cells, the increase in apoptosis induced by EAHF was correlated with up-regulation of pro-apoptotic Bax and down-regulation of cIAP-2 expression. EAHF treatment induced the proteolytic activation of caspase-3 and caspase-9, and a concomitant inhibition of poly (ADP-ribose) polymerase (PARP), β -catenin, phospholipase (PLC)- γ 1 protein and DNA fragmentation factor 45/inhibitor of caspase-activated DNase (DFF45/ICAD). Furthermore, the EAHF inhibited cell migration in a concentration- and time-dependent manner of MDA-MB-231 and MCF-7 cells, as evidenced by the results of the wound healing assay. Taken together, these findings provide important new insights into the possible molecular mechanisms of the anti-cancer activity of *H. fusiforme*. [This work was supported by a grant from Marine Bioprocess Research Center of the Marine Bio 21 Center funded by the Ministry of Land, Transport and Maritime, Republic of Korea.]

Key words: *Hizikia fusiforme*, breast cancer, apoptosis, Bax, migration

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Anti-Invasive Activity of Anthocyanins Isolated From *Vitis coignetiae* in Human Hepatocarcinoma Cells

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Anthocyanins belong to a class of flavonoids, exhibiting antioxidant and anti-inflammatory actions as well as a variety of chemotherapeutic effects. However, little is known about the cellular and molecular mechanism of anti-cancer activity. In this study, we isolated anthocyanins (delphinidin-3,5-diglucoside : cyanidin-3,5-diglucoside : petunidin-3,5-diglucoside : delphinidin-3-glucoside : malvidin-3,5-diglucoside : peonidin-3,5-diglucoside : cyanidin-3-glucoside : petunidin-3-glucoside : peonidin-3-glucoside : malvidin-3-glucoside = 27 : 63 : 8.27 : 1 : 2.21 : 6.7 : 1.25 : 5.72 : 1.25) from fruits of *Vitis coignetiae* Pulliat (*Meoru* in Korea) (AIMs) and investigated if the exerted anti-invasive effects in human hepatoma Hep3B cells. The AIMs inhibited the invasion of Hep3B cells in a dose-dependent manner as determined through a Matrigel-coated chamber assay. In Hep3B cells, AIMs also inhibited expression and activity of matrix metalloproteinase (MMP)-2 and MMP-9, and activation of NF- κ B stimulated by tumor necrosis factor (TNF)- α . Taken together, the results of this study indicates that the anthocyanins isolated from meoru have anti-invasive effects on human hepatoma Hep3B cells, and inhibited MMP-2 and MMP-9 gene expression at least in part through the inhibition of NF- κ B activation. These phytochemicals therefore may be useful to inhibit invasion and metastasis of human hepatitis B associated hepatoma. [This study was supported by a grant from the National R&D Program for Cancer Control, Ministry of Health & Welfare, Republic of Korea. (0820050).]

Key words: Anthocyanins, MMPs, invasion, Hep3B, NF- κ B