Two polymethoxylated flavones exhibited an inhibitory effect on fibroblast-mediated breast tumorigenesis

Chien-Chun Wang (王建鈞)[1], Yo-An Lin (林宥安)[1], Bo-Kai Yang (楊博凱)[1], Kuan-Han Lee (李冠漢)[2,3], Wen-Jong Vong (汪文忠)[4*], Shiaw-Wei Tyan (田孝威)[1,3*]

[1] Department of Biotechnology, Chia Nan University of Pharmacy and Science, Tainan, Taiwan, R.O.C. (嘉南藥理大學 生物科技系)

[2] Department of Pharmacy, Chia Nan University School of Pharmacy and Science, Tainan, Taiwan, R.O.C. (嘉南藥理大學 藥學系)

[3] Drug Discovery and Development Center, Chia Nan University of Pharmacy and Science, Tainan, Taiwan, R.O.C. (嘉南藥理大學 新藥創建研究中心)

[4] Department of Medicinal Chemistry, Chia Nan University School of Pharmacy and Science, Tainan, Taiwan, R.O.C. (嘉南藥理大學 醫藥化學系)

Some polymethoxylated flavones, such as sinensetin (5,6,7,3',4'-pentamethoxyflavone), isolated from citrus, have been shown to possess anti-cancer activity and lower toxicity. We synthesized two polymethoxylated flavones, which were sinensetin analogs, from 3,4,5-trimethoxyphenol in three steps. The inhibitory effects of the polymethoxylated flavones, 3,4,5-trimethoxyphenol and a synthesis intermediate product on breast tumorigenesis and pancreatic tumorigenesis were tested. By using a co-culture system of cancer cells and fibroblasts, fibroblast-mediated colony formation of breast cancer MDA-MB-468 cells and pancreatic cancer PANC-1 cells in soft agar was examined with treatment of these compounds. The results showed that the polymethoxylated flavones and the intermediate product exhibited an inhibitory activity on colony formation of breast cancer MDA-MB-468 cells rather than colony formation of pancreatic cancer PANC-1 cells. In addition, the MTT assay revealed that the polymethoxylated flavones had low toxicity to MDA-MB-468 cells and fibroblasts. These results showed that the polymethoxylated flavones we synthesized possessed anti-breast tumorigenesis activity and low toxicity, which might offer potential chemotherapy in treatment of breast cancer.