Evaluation of galloflavin and genistein as a combination therapy to treat breast cancer in mice

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Abstract

Breast cancer is the major malice responsible for the highest cancer deaths rate among women. Many chemotherapeutic drugs have been developed either to be used as their own or to be co-administrated with other agent. Furthermore, several natural compounds proved their effectiveness against breast cancer, and hence were used in a combination treatment with chemotherapeutic agents. However, in respect of minimizing the side effects related to chemotherapy, numerous studies were allocated to investigate the efficacy of natural products combinations as an alternative therapy. Genistein, a natural isoflavone, isolated from soy food, has many health benefits beside having an anticancer activity. Many studies have been conducted on genistein described its anticancer mechanisms of actions. In this study, the antiangiogenic activity and apoptosis induction ability of genistein were detected. Galloflavin, a natural flavonoid that could be produced by gallic acid oxidation reaction. Galloflavin was recently recognized as LDH inhibitor which through this suppresses glycolysis and exerts anticancer activity. The LDH inhibitory effect and apoptosis stimulation capability of galloflavin were confirmed in this experiment. Each of genistein and galloflavin was experimentally tried in combination treatment with conventional chemotherapeutic drugs and other natural agents, however, this is the first study investigates

the effect of genistein and galloflavin combination against breast cancer. The anticancer activity of genistein and galloflavin as single and combination treatments was assessed against different breast cancer cell lines; EMT-6/P, MCF-7 and MDA-MB-231. The combination exerted synergistic anticancer effect on the three cell lines. The assessment of LDH, caspase 3 activities and VEGF concentration in treated EMT-6/P cells, revealed that each of genistein and galloflavin augments the activity of each other. The antitumor activity of genistein, galloflavin and their combination was tested on Balb/C mice, where the results reflected the efficacy against tumors of each agent alone, and the synergy of their combination. Also, measurement of ALT/AST serum levels reflected the absence of hepatotoxic impact of genistein when used in combination with galloflavin. Moreover, detection of creatinine serum levels disclosed that using of genistein and galloflavin as combination treatment reduced potential of nephrotoxicity occurrence. The cytotoxic effect of genistein and galloflavin combination was construed to angiogenesis inhibition, glycolysis suppression and apoptosis induction. This combination represents a considerable target to become an effective breast cancer treatment.