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Chemosensitization of Tumors by Natural Compounds

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Editorial

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Editorial

Many of cytotoxic anticancer natural drugs are used as an adjuvant therapy in cancer treatment and can potentially increase sensitivity of drug-resistant cancer cells to chemotherapeutical agents [1]. The treatment of cancer with chemotherapeutic agents faces two major problems: chemoresistance and nonspecific toxicity toward normal cells. Many natural polyphenols as genistein, curcumin, resveratrol, silymarin, caffeic acid phenethyl ester, emodin, green tea polyphenols, piperine, oleandrin, ursolic acid, and betulinic acid might be used to sensitize tumor cells to chemotherapeutic agents and radiation therapy by inhibiting pathways that lead to treatment resistance [2]. Saikosaponin B2, isolated from dried root of Bupleurumas, is an effective inhibitor for etoposide-induced NF-kB activation in B16F10NFkB cells. Saikosaponin B2 sensitized etoposide-induced cell death in B16F10 melanoma cells through the induction of apoptosis. In addition, an induction of g-H2AX expression observed, which is a molecular signature for DNA damage, upon the combination treatment of etoposide and saikosaponin B2 [3]. Spongistatin 1 is a macrocyclic lactone that has been isolated from the marine sponges *Spirastrella spinispirulifera* and *Hyrtioserecta.* Spongistatin degrades XIAP protein in leukemic cells, which might be the reason for its potentizing effect when combined with other caspase-activating anticancer drugs [4].

Cryptotanshinone, a natural compound isolated from the roots of *Salvia miltiorrhiza* Bge. (Danshen). Cryptotanshinone significantly induced ovarian cancer A2780 cells apoptosis by activating caspase cascade. It could sensitize A2780 cells to cisplatin treatment in a dose-dependent manner [5]. Celastrol, derived from the 'Thunder God Vine' and Pro-EGCG, a pre-drug version of green tea polyphenol. They have the ability to increase levels of leukemia cell killing, caspase 3 activation, and poly (ADP-ribose) polymerase cleavage. Furthermore, the higher levels of apoptotic indices were associated with decreased levels of Bcr-Abloncoprotein in K-562 cells [6].

Cucurbitacin B, an oxygenated tetracyclic triterpenoid compound extracted from the Thai medicinal plant *trichosanthes cucumerina*L. It showed cytotoxicity against the ovarian cancer cell lines, and pretreatment of A2780CP cells leads to a significant increase in the cytotoxicity of cisplatin. The mechanism behind the sensitization effect was dependent in part on the depletion of the total glutathione, an increase in ROS through a decrease in the level of dual-specificity tyrosine-regulated kinase (Dyrk1B), decrease in pERK1/2 and pSTAT3 level [7].

Conclusion

It is important to study the role of natural compounds in chemosensitization, since this may create novel drug in cancer treatment. Most natural compounds activity on cancer is mainly from cell-based experiments and partly from *in vivo* experiments. Clinical application of some of these combined drugs has not been obviously presented. As a result, additional research using *in vivo* systems and better clinical trials is needed to determine the safety and clinical usefulness of these drugs.

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