

Cancer Therapy

Salvinal has antimitotic activity in drug-resistant human tumor cells

2004 MAR 8 - (NewsRx.com) -- Salvinal, a novel microtubule inhibitor isolated from *Salvia miltiorrhizae* Bunge (Danshen), possesses antimitotic activity in multidrug-sensitive and -resistant human tumor cells.

"Aqueous extracts of *Salvia miltiorrhizae* Bunge have been extensively used in the treatment of cardiovascular disorders and cancer in Asia. Recently, a compound, 5-(3-hydroxypropyl)-7-methoxy-2-(3'-methoxy-4'-hydroxyphenyl)-3-benzo[b]furancarbaldehyde (salvinal), isolated from this plant showed inhibitory activity against tumor cell growth and induced apoptosis in human cancer cells. In the present study, we investigated the cytotoxic effect and mechanisms of action of salvinal in human cancer cell lines," scientists in Taiwan report.

"Salvinal caused inhibition of cell growth (IC₅₀ range, 4-17 micromolar) in a variety of human cancer cell lines," stated Jang-Yang Chang and collaborators at National Taiwan University. "Flow cytometry analysis showed that salvinal treatment resulted in a concentration-dependent accumulation of cells in the G₂/M phase. We observed, using Hoechst 33258 dye staining, that salvinal blocked the cell cycle in mitosis. In vitro and in vivo examinations showed that salvinal inhibited tubulin polymerization in a concentration-dependent manner. Immunocytochemical studies demonstrated that salvinal treatment caused the changes of cellular microtubule network, similar to the effect of colchicine."

"In addition, salvinal treatment resulted in upregulation of cyclin B1 levels, activation of Cdc2 kinase, and Cdc25c phosphorylation," reported the researchers. "Furthermore, elevation of levels of MPM-2 phosphoepitopes in salvinal-treated cells in a concentration-dependent manner was also observed. Similar to the effect of other antitubulin agent, hyperphosphorylation of Bcl-2, induction of DNA fragmentation and activation of caspase-3 activity occurred in salvinal-treated cells. In particular, salvinal exhibited similar inhibitory activity against parental KB, P-glycoprotein-overexpressing KB vin10 and KB taxol-50 cells, and multidrug resistance-associated protein (MRP)-expressing etoposide-resistant KB 7D cells."

"Taken together, our data demonstrate that salvinal inhibits tubulin polymerization, arrests cell cycle at mitosis, and induces apoptosis," concluded the investigators. "Notably, Salvinal is a poor substrate for transport by P-glycoprotein and MRP. Salvinal may be useful in the treatment of human cancers, particularly in patients with drug resistance."

Chang and associates published their study in *Molecular Pharmacology* (Salvinal, a novel microtubule inhibitor isolated from *Salvia miltiorrhizae* Bunge (Danshen), with antimitotic activity in multidrug-sensitive and -resistant human tumor cells. *Mol Pharmacol*, 2004;65(1):77-84).

For more information, contact Jang-Yang Chang, National Taiwan University Hospital, Division of Cancer Research, National Health Research Institutes, Cancer Cooperative Ward, 7 Chung Shang South Road, Taipei, Taiwan. E-mail: jychang@nhri.org.tw.

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