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Reversal of P-glycoprotein-mediated multidrug resistance by Cinobufagin

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Cinobufagin (CI) is a major bioactive component of Venenum Bufonis, which is a traditional Chinese medicine obtained from the skin and parotid venom glands of toads, and has been found to induce cell apoptosis in various types of cancer cells. The objective of this study was to investigate the reversal effect of CI on P-gp-mediated MDR. Effects of CI on cytotoxicity of anticancer drugs and intracellular accumulation of P-gp substrate Rhodamine 123 were examined in P-gp-overexpression cells. Its molecular mechanism and effect on regulating P-gp expression were further investigated by ATPase assay and Western blot. Our results showed that CI significantly enhanced the sensitivity of P-gp-overexpressing cells to anticancer drugs in HCT116/L and Cao-2/ADR cells without affecting their corresponding parental cells. It also remarkably increased intracellular accumulation of Rhodamine 123 in those cells. Further mechanistic studies demonstrated that the circumvention of P-gp-mediated MDR by CI was result from uncompetitive inhibition of P-gp ATPase activity but not to alter the P-gp expression. Our findings demonstrated that CI could be used as a promising lead compound for further development into selective and efficient MDR reversing agents for combination use with P-gp substrate drugs in cancer chemotherapy.

Biography

Zeting Yuan received her Master's degree in Pharmacy from East China University of Science and Technology in 2012. In May 2013, she became a Research Associate of Putuo Hospital and Cancer Institute, Shanghai University of Traditional Chinese Medicine, studying on Pharmacology of Traditional Chinese Medicine and the mechanism of overcoming multidrug resistance in the colorectal cancer.

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