Pro-oxidant and cytotoxic activities of atractylenolide I in human promyeloleukemic HL-60 cells

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Abstract

The dried rhizome of Bai Zhu (Atractylodes ovata) is widely used as a Chinese herbal medicine. Two sesquiterpenolides of similar structures (atractylenolide I, AT-I; atractylenolide III, AT-III) were isolated from dried rhizome of Atractylodes ovata. Incubation of AT-I with recombinant human Cu,Zn-superoxide dismutase (rhCu,Zn-SOD) resulted in rhCu,Zn-SOD fragmentations and Zn releases. However, these were not observed in the AT-III reaction. The AT-1 showed dose-dependent cytotoxic activities (7.5, 15, and 30 microg/ml) on the human promyeloleukemic HL-60 cells while AT-III did not, and the IC50 of the former being 10.6 microg/ml (corresponding to 46 microM) on 12 h-treated cells. The results of DNA ladder and DNA contents in sub-G1 type revealed that AT-I induced apoptosis in human promyeloleukemic HL-60 cells. The cytotoxic and pharmacological mechanisms of AT-I against human promyeloleukemic HL-60 cells was investigated. The AT-I appeared to exhibit both pro-oxidant and antioxidant properties afteran ESR spectrometer was used to detect hydroxyl radical productions in vitro and flow cytometry to detect intracellular ROS productions in AT-I treated cells. The AT-1 also showed dose-dependent Cu,Zn-SOD inhibitory activity in HL-60 cells treated for 12 h, confirmed by activity and immune stainings. However, catalase, Mn-SOD, and glutathione peroxidase did not apparently change activities under the same treatments. The addition of commercial rhCu,Zn-SOD (25-100 U/mL) to the AT-I-treated HL-60 cells (15 microg/ml) resulted in significant differences ($p<0.01$) and could reduce the AT-I cytotoxicity from 78% to 28% on HL-60 cells. It was proposed that the AT-I might work via Cu,Zn-SOD inhibition in HL-60 cells to induce apoptosis and bring about cytotoxicity.