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The selective CYP1B1 inhibitor tetramethoxystilbene induces apoptosis of human acute promyelocytic leukemia (HL-60) cells.

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Previous studies demonstrated that 2,4,3',5'-tetramethoxystilbene (TMS), a synthetic trans-stilbene analogue, is one of the most potently selective inhibitor of human cytochrome P450 1B1 in vitro and in vivo. In this studies, the effects of TMS on proliferation of human acute promyelocytic leukemia cells (HL-60) were evaluated. In MTT assay, TMS inhibited the proliferation of HL-60 cells. Moreover, cotreatment with TMS and etoposide, a well-known topoisomerase II inhibitor, strongly enhanced the cytotoxicity. The apoptotic characteristics such as enhancing fluorescence of the cell membrane with Annexin V-FITC and the chromosomal DNA fragmentation were increased with TMS treatment for 24 h. We also have found that TMS induced cytochrome c release, caspase-3 activation and poly(ADP-ribose) polymerase (PARP) cleavage. A caspase inhibitor zVAD-fmk could block TMS-induced apoptosis. Taken together, those results showed that the apoptosis-inducing activity and inhibitory activity of cytochrome CYP1B1 by TMS make this compound be useful for anticancer strategies of hormone-mediated carcinogenesis.

Keyword : TMS, Apoptosis, HL-60, Anticancer stratergies