

Apoptosis effect of girinimbine isolated from *Murraya koenigii* on lung cancer cells in vitro

ABSTRACT

Murraya koenigii Spreng has been traditionally claimed as a remedy for cancer. The current study investigated the anticancer effects of girinimbine, a carbazole alkaloid isolated from *Murraya koenigii* Spreng, on A549 lung cancer cells in relation to apoptotic mechanistic pathway. Girinimbine was isolated from *Murraya koenigii* Spreng. The antiproliferative activity was assayed using MTT and the apoptosis detection was done by annexin V and lysosomal stability assays. Multiparameter cytotoxicity assays were performed to investigate the change in mitochondrial membrane potential and cytochrome c translocation. ROS, caspase, and human apoptosis proteome profiler assays were done to investigate the apoptotic mechanism of cell death. The MTT assay revealed that the girinimbine induces cell death with an IC₅₀ of 19.01 μ M. A significant induction of early phase of apoptosis was shown by annexin V and lysosomal stability assays. After 24 h treatment with 19.01 μ M of girinimbine, decrease in the nuclear area and increase in mitochondrial membrane potential and plasma membrane permeability were readily visible. Moreover the translocation of cytochrome c also was observed. Girinimbine mediates its antiproliferative and apoptotic effects through up- and downregulation of apoptotic and antiapoptotic proteins. There was a significant involvement of both intrinsic and extrinsic pathways. Moreover, the upregulation of p53 as well as the cell proliferation repressor proteins, p27 and p21, and the significant role of insulin/IGF-1 signaling were also identified. Moreover the caspases 3 and 8 were found to be significantly activated. Our results taken together indicated that girinimbine may be a potential agent for anticancer drug development.

Keyword: Apoptosis effect; Girinimbine; *Murraya koenigii*; Lung cancer cells.