

## **Girinimbine from *Murraya koenigii* - Currying therapy for cancer**

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Therapy that can potentially target apoptosis, inflammation and/or angiogenesis is now being strongly considered in treatment of cancer. *Murraya koenigii*, the curry leaf tree, is a tropical to sub-tropical shrub from the Rutacea family. Its leaves are an important ingredient in curries and other South and South-East Asian dishes and has also been used in Ayurvedic medicine for centuries. Here we report that girinimbine, a carbazole alkaloid isolated from *M. koenigii*, induced apoptosis and inhibited inflammation and angiogenesis in vitro as well as in vivo. In human colon cancer cells (HT-29), girinimbine induced apoptosis without any significant cytotoxicity in normal colon cells. In vitro anti-inflammatory action was evidenced by significant dose-dependent girinimbine inhibition of nitric oxide production in LPS/IFN- $\gamma$ -induced cells while anti-angiogenic activity was confirmed by girinimbine inhibition of HUVECs cell proliferation, and endothelial cell invasion, migration, tube formation, and wound healing. In vivo studies using girinimbine showed a significant number of apoptotic cells in zebrafish embryos after a 24-hour treatment period, while in carrageenan-induced peritonitis in mice, oral pre-treatment with girinimbine inhibited neutrophil migration and reduced pro-inflammatory IL-1 $\beta$  and TNF- $\alpha$  cytokine levels in peritoneal fluid. The antiangiogenic potential of girinimbine was evidenced by inhibition of blood vessel formation in zebrafish embryos. Taken together, these results showed that girinimbine could effectively induce apoptosis, as well as suppress inflammation and angiogenesis, which strongly suggest that girinimbine could be a potential chemopreventive and/or chemotherapeutic agent.

**Keywords:** targeted therapy, cancer, apoptosis, inflammation, angiogenesis, girinimbine, natural products