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 1: [Cancer](#). 2007 Sep 1;110(5):1083-95.

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**Garlic compounds generate reactive oxygen species leading to activation of stress kinases and cysteine proteases for apoptosis in human glioblastoma T98G and U87MG cells.****Das A, Banik NL, Ray SK.**

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**BACKGROUND:** Garlic-derived organosulfur compounds such as diallyl sulfide (DAS), diallyl disulfide (DADS), and diallyl trisulfide (DATS) provide significant protection against carcinogenesis. **METHODS:** Dose-dependent cytotoxic effects of the garlic compounds (DAS, DADS, and DATS) were tested in human glioblastoma T98G and U87MG cells. Wright staining and ApopTag assay confirmed induction of apoptosis. Measurements showed that production of reactive oxygen species (ROS) and an increase in intracellular free  $[Ca^{2+}]$  promoted apoptosis. Western blot analysis indicated that increased expression and activities of the stress kinases and cysteine proteases caused apoptosis. Use of JC-1 showed changes in mitochondrial membrane potential ( $\Delta\psi(m)$ ) for mediation of apoptosis. Use of the specific inhibitors monitored the activation of different kinases and proteases in apoptosis. **RESULTS:** Treatment of glioblastoma cells with garlic compounds triggered production of ROS that induced apoptosis with the phosphorylation of p38 MAPK and activation of the redox-sensitive JNK1 pathway. Pretreatment of cells with ascorbic acid attenuated ROS production, p38 MAPK phosphorylation, and JNK1 activation. Pretreatment with JNK1 inhibitor I also significantly reduced cell death. Increases in intracellular free  $[Ca^{2+}]$ , expression of calreticulin, and activation of caspase-4 indicated involvement of endoplasmic reticulum (ER) stress in apoptosis. Other events in apoptosis included overexpression of Bax, down-regulation of Bcl-2 and some BIRC proteins, mitochondrial release of cytochrome c and Smac into the cytosol, and activation of calpain, caspase-9, and caspase-3. **CONCLUSIONS:** Garlic compounds induced apoptosis in glioblastoma cells due to production of ROS, increase in ER stress, decrease in  $\Delta\psi(m)$ , and activation of stress kinases and cysteine proteases.

PMID: 17647244 [PubMed - indexed for MEDLINE]

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