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Mechanisms of Cardioprotective Effect of Aged Garlic Extract Against Doxorubicin-Induced Cardiotoxicity.

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Abstract

Aged garlic has been extensively studied and has been shown to have a number of medicinal properties, including immunomodulatory, hepatoprotective, antimutagenic, anticarcinogenic, and antioxidant effects. The objective of this study was to investigate the mechanisms of the cardioprotective effect of aged garlic extract (AGE), a widely used herbal medicine with potent antioxidant activity, against doxorubicin-induced cardiotoxicity. Moreover, the study investigated if the cardioprotective effect of AGE might be at the expense of the antitumor effect of the anticancer drug doxorubicin (DOX). Primary cultured neonatal rat cardiac myocytes were treated with DOX, AGE, and their combination for 24 hours. DOX increased p53 and caspase 3 activity-induced apoptotic cell death, whereas AGE pretreatment suppressed the action of DOX. AGE pretreatment did not interfere with the cytotoxic activity of DOX, but it increased the DOX uptake into tumor cells and increased the long term survivors of tumor-bearing mice from 30% to 70%. In conclusion, DOX impairs viability of cardiac myocytes, at least partially by activating the p53-mediated apoptotic signaling. AGE can effectively and extensively counteract this action of DOX and may potentially protect the heart from severe toxicity of DOX. At the same time, AGE did not interfere with antitumor activity of DOX.