Soy isoflavone genistein induces cell death in breast cancer cells through mobilization of endogenous copper ions and generation of reactive oxygen species.


Source
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Abstract
SCOPE:
Worldwide geographical variation in cancer incidence indicates a correlation between dietary habits and cancer risk. Epidemiological studies have suggested that populations with high isoflavone intake through soy consumption have lower rates of breast, prostate, and colon cancer. Isoflavone genistein in soybean is considered a potent chemopreventive agent against cancer. Although several mechanisms have been proposed, a clear anticancer action mechanism of genistein is still not known.

METHODS AND RESULTS:
Here, we show that the cytotoxic action of genistein against breast cancer cells involves mobilization of endogenous copper. Further, whereas the copper specific chelator neocuproine is able to inhibit the apoptotic potential of genistein, the molecules which specifically bind iron (desferroxamine mesylate) and zinc (histidine) are relatively ineffective in causing such inhibition. Also, genistein-induced apoptosis in these cells is inhibited by scavengers of reactive oxygen species (ROS) implicating ROS as effector elements leading to cell death.

CONCLUSIONS:
As copper levels are known to be considerably elevated in almost all types of cancers, in this proof-of-concept study we show that genistein is able to target endogenous copper leading to prooxidant signaling and consequent cell death. We believe that such a
mechanism explains the anticancer effect of genistein as also its preferential cytotoxicity towards cancer cells.

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