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## **Modulation of thiol pools by vitamin K3 and its effect on survival of sensitive and resistant murine tumor cells.**

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### **Abstract**

Cytotoxic effects of vitamin K3 were evaluated utilizing the P388/S, L1210, EAT, S-180 and a multidrug-resistant variant of the P388 leukemia cells (P388/ADR). Antitumorigenic potential of vitamin K3 was assessed by MTT and DNA and RNA biosynthesis inhibition assay. A dose-dependent inhibition of P388/S and P388/ADR cell survival and [3H]thymidine and [3H]uridine incorporation (as a function of DNA and RNA biosynthesis) was observed in tumor cell types exposed to vitamin K3 concentrations ranging from 1 to 100 microM. One hundred mg/kg vitamin K3 caused a 32 and 52% increase in life span of the sensitive and resistant P388 leukemia tumor-bearing mice. Induction of DNA strand breaks at 100 microM vitamin K3 was greater in P388/S than in P388/ADR cells. In vitro treatment with vitamin K3 (100 microM) reduced the intracellular levels of GSH by 40, 47, 6, 15 and 14% in P388/S, P388/ADR, EAT, S-180 and L1210 tumor cells, respectively. In vivo treatment with 100 mg/kg vitamin K3 reduced the GSH content by 18 and 38% and increased the activity of the enzyme GSH-S-transferase and gamma-glutamyl transpeptidase. Effects of free radical scavengers and of compounds that modulate the GSH metabolism on the cytotoxicity of vitamin K3 were also investigated. Results indicate that vitamin K3 interacts with the tumor cell thiol pools while eliciting its antitumor effects and suggest the utility of vitamin K3 in dealing with the growing problem of multidrug resistance.

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