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## Effect of polyunsaturated fatty acids on drug-sensitive and resistant tumor cells in vitro.

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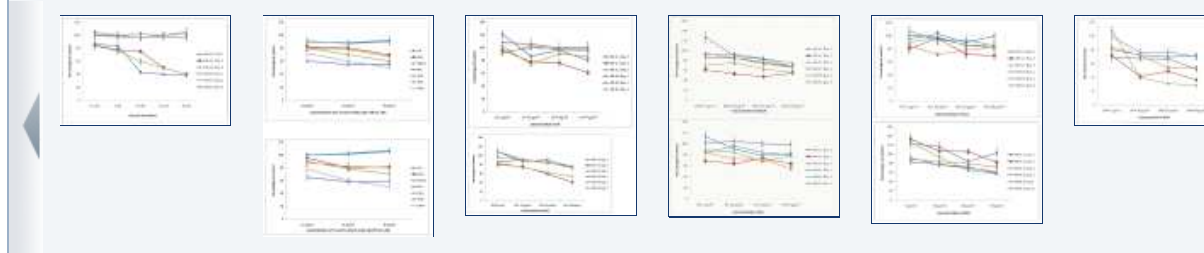
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### Abstract

ABSTRACT: Previous studies showed that  $\gamma$ -linolenic acid (GLA, 18:3  $\omega$ -6), arachidonic acid (AA, 20:4  $\omega$ -6), eicosapentaenoic acid (EPA, 20:5  $\omega$ -3) and docosahexaenoic acid (DHA, 22:6  $\omega$ -3) have selective tumoricidal action. In the present study, it was observed that dihomo- $\gamma$ -linolenic acid (DGLA) and AA, EPA and DHA have cytotoxic action on both vincristine-sensitive (KB-3-1) and resistant (KB-ChR-8-5) cancer cells in vitro that appeared to be a free-radical dependent process but not due to the formation of prostaglandins, leukotrienes and thromboxanes. Uptake of vincristine and fatty acids was higher while their efflux was lower in KB-3-1 cells compared with KB-ChR-8-5 cells, suggesting that drug resistant cells have an effective efflux pump. GLA, DGLA, AA, EPA and DHA enhanced the uptake and decreased efflux in both drug-sensitive and drug-resistant cells and augmented the susceptibility of tumor cells especially, of drug-resistant cells to the cytotoxic action of vincristine. These results suggest that certain polyunsaturated fatty acids have tumoricidal action and are capable of enhancing the cytotoxic action of anti-cancer drugs specifically, on drug-resistant cells by enhancing drug uptake and reducing its efflux. Thus, polyunsaturated fatty acids either by themselves or in combination with chemotherapeutic drugs have the potential as anti-cancer molecules.

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