

Antitumor effect of Japanese apricot extract (MK615) on human cancer cells *in vitro* and *in vivo* through a reactive oxygen species-dependent mechanism

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ABSTRACT

Aims and background. MK615 is produced from Japanese apricot and contains several cyclic triterpenes, such as oleanolic and ursolic acids. MK615 was shown to strongly suppress cutaneous in-transit metastasis in a patient with malignant melanoma. The present investigation was undertaken to clarify the antitumor effects of MK615 *in vitro* and *in vivo*.

Methods. Several human cancer cell lines were exposed to MK615 for 7 days to examine its antiproliferative effects. The effect of MK615 on *in vivo* growth of human pancreatic cancer MIAPaCa-2 cells was also examined.

Results. MK615 inhibited the growth of several human cancer cell lines in a concentration-dependent way. Pancreatic cancer MIAPaCa-2 cells were highly sensitive to the growth-inhibiting effects of MK615. Treatment with MK615 preferentially induced cell death in human cancer cells while sparing normal cells such as human umbilical vein endothelial cells (HUVEC) and mouse bone marrow cells. When MIAPaCa-2 cells were incubated with MK615 in the presence of antioxidant, growth-inhibition was significantly reduced, and MK615 induced the accumulation of reactive oxygen species in cancer cells but not in HUVEC. MK615, in both the presence and absence of gemcitabine, significantly inhibited the growth of human pancreatic cancer cells as xenografts without apparent adverse effects.

Conclusions. MK615, a supplement produced from Japanese apricot, may have therapeutic value in treating human cancers through a reactive oxygen species-dependent mechanism.

Key words: Japanese apricot extract, triterpene, reactive oxygen species, combination therapy, gemcitabine, pancreatic cancer, xenograft.

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