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Titel des Beitrags: Antimetastatic activity of honokiol in osteosarcoma.
Abstract:
Metastasizing osteosarcoma has a mean 5-year survival rate of only 20% to 30%. Therefore, novel chemotherapeutics for more effective treatment of this disease are required. The antineoplastic activity of honokiol, which was demonstrated previously in numerous malignancies, was studied in vivo in C3H mice subcutaneously injected with syngeneic β-galactosidase bacterial gene (lacZ)-expressing LM8 osteosarcoma (LM8-lacZ) cells. In vitro cytotoxic effects of honokiol were investigated in 8 human and 2 murine osteosarcoma cell lines with different in vivo metastatic potential. Seven days after subcutaneous flank injection of LM8-lacZ cells, daily intraperitoneal treatment of mice with 150 mg/kg honokiol reduced the number of micrometastases in the lung by 41% and reduced the number of macrometastases in the lung and liver by 69% and 80%, respectively, compared with control. Primary tumor growth was not inhibited. In osteosarcoma cell lines, honokiol inhibited the metabolic activity with a half-maximal concentration (IC(50)) between 8.0 ?g/mL and 16 ?g/mL. Cyclosporin A partially reversed the inhibition of metabolic activity in LM8-lacZ cells. Cell proliferation and wound healing migration of LM8-lacZ cells were inhibited by honokiol with an IC(50) between 5.0 ?g/mL and 10 ?g/mL. Higher concentrations caused rapid cell death, which was distinct from necrosis, apoptosis, or autophagy but was associated with
swelling of the endoplasmic reticulum, cytoplasmic vacuolation, and morphologically altered mitochondria. Honokiol exhibited prominent antimetastatic activity in experimental osteosarcoma and caused rapid cell death in vitro that was unrelated to necrosis, apoptosis, or autophagy. The authors concluded that honokiol has considerable potential for the treatment of metastasizing osteosarcoma.