Biochemical Pharmacology 69 (2005) 811–818

Molecular modes of action of cantharidin in tumor cells

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Received 30 August 2004; accepted 3 December 2004

Abstract

Cancer chemotherapy is often limited by patient's toxicity and tumor drug resistance indicating that new drug development and modification of existing drugs is critical for improving the therapeutic response. Traditional Chinese medicine is a rich source of potential anticancer agents. In particular, cantharidin (CAN), the active principle ingredient from the blister beetle, Mylabris, has anti-tumor activity, but the cytotoxic mechanism is unknown. In leukemia cells, cantharidin induces apoptosis by a p53-dependent mechanism. Cantharidin causes both DNA single- and double-strand breaks. Colony-forming assays with knockout and transfectant cells lines showed that DNA polymerase b, but not ERCC1, conferred increased cell survival after cantharidin treatment, indicating that base excision repair (BER), rather than nucleotide excision repair (NER), is important for CAN-induced DNA lesions. Oxidative stress-resistant thymic lymphoma-derived WEHI7.2 variants are also more resistant to cantharidin. These data suggest that cantharidin treatment causes oxidative stress that provokes DNA damage and p53-dependent apoptosis.