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1: [Biochem Pharmacol.](#) 2002 Apr 15;63(8):1415-21.

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**The alkaloid sanguinarine is effective against multidrug resistance in human cervical cells via bimodal cell death.**

[Ding Z](#), [Tang SC](#), [Weerasinghe P](#), [Yang X](#), [Pater A](#), [Liepins A](#).

Division of Basic Sciences, Faculty of Medicine, Memorial University of Newfoundland, 300 Prince Philip Drive, St. John's, NF, Canada A1B 3V6.

Sanguinarine, a benzophenanthrine alkaloid, is potentially antineoplastic through induction of cell death pathways. The development of multidrug resistance (MDR) is a major obstacle to the success of chemotherapeutic agents. The aim of this study was to investigate whether sanguinarine is effective against uterine cervical MDR and, if so, by which mechanism. The effects of treatment with sanguinarine on human papillomavirus (HPV) type 16-immortalized endocervical cells and their MDR counterpart cells were compared. Trypan blue exclusion assays and clonogenic survival assays demonstrated that MDR human cervical cells are as sensitive as their drug-sensitive parental cells to death induced by sanguinarine. Upon treatment of both types of cells with sanguinarine, two distinct concentration-dependent modes of cell death were observed. Treatment with 2.12 or 4.24 microM sanguinarine induced death in most cells that was characterized as apoptosis using the criteria of cell surface blebbing, as determined by light and scanning electron microscopy, and proteolytic activation of caspase-3 and cleavage of the caspase-3 substrate poly(ADP-ribose) polymerase (PARP), as detected by Western blot analysis. However, 8.48 and 16.96 microM sanguinarine caused a second mode of cell death, oncosis, distinguished by cell surface blistering, and neither caspase-3 activation nor PARP cleavage. This study provides the first evidence that sanguinarine is effective against MDR in cervical cells via bimodal cell death, which displays alternative mechanisms involving different morphologies and caspase-3 activation status.

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