



Biscoclaurine alkaloid cepharanthine protects DNA in TK6 lymphoblastoid cells from constitutive oxidative damage

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Abstract:

Cepharanthine (CEP), a biscoclaurine (bisbenzylisoquinoline) alkaloid isolated from *Stephania cepharantha Hayata*, is widely used in Japan to treat variety of diseases. Among a plethora of its biological activities CEP was reported to be able to scavenge radicals and prevent lipid peroxidation. We have recently described the phenomenon of constitutive ATM activation (CAA) and histone H2AX phosphorylation (CHP), the events that report DNA damage induced by endogenously generated radicals, the product of oxidative metabolism in otherwise healthy, untreated cells. The aim of the present study was to explore whether CEP can attenuate the level of CAA and CHP, which would indicate on its ability to protect DNA against endogenous oxidants. The data show that indeed the levels of CAA and CHP in human lymphoblastoid TK6 cells were distinctly lowered upon treatment with CEP. Thus, exposure of cells to 8.3 μM CEP for 4 h led to a reduction of the mean level of CAA and CHP by up to 60% and 50%, respectively. At 1.7 μM CEP the reduction of CAA and CHP after 4 h was 35% and 25%, respectively. Cells exposure to CEP led to a decrease in the level of endogenous oxidants as measured by the ability to oxidate the fluorescent probe 5-(and-6)-carboxy-2',7'-dichlorodihydro-fluorescein diacetate. No evidence of apoptosis was seen during the first 8 h of treatment with CEP but initiation of apoptosis (caspase-3 activation) was detected in relatively few (< 10%) cells after exposure to 8.3 μM CEP for 24 h. The data strongly suggest that the scavenging properties of CEP provide a protection of DNA from the radicals generated endogenously during oxidative metabolism.

Key words:

oxidative DNA damage, DNA repair, reactive oxygen species, ROS, oxygen radicals, radicals' scavenger, cell cycle, apoptosis, bisbenzylisoquinoline alkaloid
