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The venom of spider *Haplopelma hainanum* suppresses proliferation and induces apoptosis in hepatic cancer cells by caspase activation in vitro

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Abstract

Ethnopharmacological relevance

Spiders and spider venoms have been used in traditional Chinese medicine to treat various ailments for more than 1,000 years. For instance, several large spiders have been utilized by the Li People, who mainly live in Hainan Island of China, in their own unique traditional Chinese medicine therapy. Recent studies have indicated that spider venoms may be an important source of bioactive compounds for anti-tumor treatments. However, the specific mechanisms underlying these activities are not yet completely understood.

Aim of the study

The present study investigated how the venom of the spider *Haplopelma hainanum* regulate proliferation and apoptosis in HepG2 cells via the underlying molecular mechanisms.

Materials and methods

We treated HepG2 cells with various concentrations of the spider venom (0, 10, 50, 100 and 200 μg/mL) for 48 h, and then analyzed anti-proliferation activity, apoptosis-inducing effects, mitochondrial membrane potential ($\Delta\psi m$) and changes in the pro-apoptotic pathway. The anti-proliferation activity was detected by the MTT assay and Western blotting. Flow cytometry was used to analyze both apoptosis and mitochondrial membrane potential. The key pro-apoptotic molecules in the caspase-3 and -9 dependent mitochondrial pathway, including Bcl2 family, were assessed through realtime PCR, Western blotting and enzymatic test.

Results

Obvious morphological changes induced by the spider venom included decreased cell numbers, shorter cell length and reduced cell adhesion. MTT and Western blotting demonstrated that the spider venom potently suppressed cell proliferation in a dose- and time-dependent manner with IC_{50} of 126.00 μg/mL for 48 h. In addition, the spider venom caused a reduction in the mitochondrial membrane potential and cytochrome c release from mitochondria to cytoplasm under the participation of Bax. Finally, cytochrome c activated caspase-3 and caspase-9, and induced the apoptosis in the HepG2 cells.

Conclusion

The results indicated that the venom of *H. hainanum* exhibited potent inhibition effects in HepG2 cells through suppressing proliferation, reducing the mitochondrial membrane potential, activating caspase-3 and caspase-9, and inducing the apoptosis through a mitochondrial-dependent pathway.