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The apoptotic effect of brucine from the seed of Strychnos nux-vomica on human hepatoma cells is mediated via Bcl-2 and Ca\(^{2+}\) involved mitochondrial pathway

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In an attempt to dissect the mechanism of Strychnos nux-vomica, a commonly used Chinese folk medicine in the therapy of liver cancer, the cytotoxic effects of four alkaloids in Strychnos nux-vomica, brucine, brucine N-oxide, strychnine, and isostrychnine, on HepG2 cells were screened by MTT assay. Brucine, among the four alkaloids, exhibited the strongest toxic effect, the mechanism of which was found to cause HepG2 cell apoptosis, since brucine caused HepG2 cell shrinkage, the formation of apoptotic bodies, DNA fragmentation, cell cycle arrest, as well as phosphatidylserine externalization, all of which are typical characteristics of apoptotic programmed cell death. Brucine-induced HepG2 cell apoptosis was caspase-dependent, with caspase-3 activated by caspase-9. Brucine also caused the proteolytic processing of caspase-9. In addition, brucine caused depolarization of the mitochondrial membrane of HepG2 cells, the inhibition of which by cyclosporine A completely abrogated the activation of caspses and release of cytochrome c in brucine-treated HepG2 cells. These findings suggested a pivotal role of mitochondrial membrane depolarization in HepG2 cell apoptosis elicited by brucine. Furthermore, brucine induced a rapid and sustained elevation of intracellular [Ca\(^{2+}\)], which compromised the mitochondrial membrane potential and triggered the process of HepG2 cell apoptosis. Finally, Bcl-2 was found to predominantly control the whole event of cell apoptosis induced by brucine. The elevation of [Ca\(^{2+}\)]\(_i\) caused by brucine was also suppressed by overexpression of Bcl-2 protein in HepG2 cells. From the facts given above, Ca\(^{2+}\) and Bcl-2 mediated mitochondrial pathway were found to be involved in brucine-induced HepG2 cell apoptosis.

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Biological effects (anti-acne and wound healing) of honeybee (Apis melifera. L) venom

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Acne vulgaris is a chronic inflammatory disorder of the sebaceous follicles. Propionibacterium acnes plays a critical role in the development of these inflammatory lesions. The present study was conducted to evaluate the antimicrobial property of honeybee (Apis melifera L.) venom (BV) against the etiologic agents of acne vulgaris and the pharmacological activities of honeybee (Apis melifera L.) venom (BV) have been used in wound healing for centuries. Incubation of the skin bacteria P. acnes, clindamycin-resistant P. acnes, Staphylococcus epidermidis or Streptococcus pyrogenes with BV yielded the minimal inhibitory concentration (MIC). Production of inflammatory cytokines (interleukin-8 (IL-8) and tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)) were examined in THP-1 cells. To study wound healing, full thickness skin defects were produced on the dorsal area of mice. The wound sizes were small in the BV group compared to the Control and Vaseline groups. The BV group demonstrated decreased TGF-\(\beta\)1, fibronectin and VEGF mRNA levels and increased collagen-I mRNA levels. The expressions of TGF-\(\beta\)1, fibronectin and VEGF proteins was significantly lower in the BV group compared to the Control group, while the expression of collagen-I was increased in the BV group as indicated by immunohistochemical staining. These data suggested that BV has effective antimicrobial and anti-inflammatory activity against P. acnes, and we suggest that BV is an alternative treatment for antibiotic therapy of acne vulgaris and significant wound healing activity.