[PA1-35] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Ginsenoside saponin Rg3 relaxes canine corpus cavernosum not by activation endothelial nitric oxide synthase but by phosphodiesterase inhibition

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Exposure of UV light (366 nm) to vascular smooth muscle induces relaxation by the release of nitric oxide (NO), which was termed photorelaxation. This nonenzymatical release of NO is a useful tool to measure NO-mediated response in many tissues including corpus cavernosum. The recognition of the importance of NO in the mechanism of penile erection has led to consideration of NO as a possible mediator of ginsenoside's action. In the present study, exploiting this and other measures to release NO by ACh, we investigated the relaxation mechanism of ginsenoside Rg3 in isolated canine corpus cavernosal smooth muscle (CCSM). Ginsenoside Rg3 concentration-dependently relaxed the phenylephrine (PE)-contracted isolated endothelium-intact CCSM, in which IC_{50} was 1.68×10^{-5} g/ml. Endothelium-dependent relaxation by ACh (enzymatical release of NO) was significantly ($P < 0.05$) potentiated by the presence of Rg3. Methylene blue, but not L-NAME or 1H-[1,2,4]oxadiazolo[4,3-α] quinoxalin-1-one (ODQ), modified the dose-response curve of ginsenoside Rg3. On the other hand, UV light (366 nm)-induced relaxation was further potentiated by streptozotocin (STZ), photorsensitizer (nonenzymatical release of NO). Ginsenoside Rg3 significantly ($P < 0.05$) increased the STZ+UV-induced relaxation, an effect that was significantly ($P < 0.01$) antagonized by ODQ. Ginsenoside Rg3 concentration-dependently increased both cAMP and cGMP contents in the corporal smooth muscle. Finally, ginsenoside Rg3 inhibited phosphodiesterase enzyme activity concentration-dependently. These results indicate that the mechanism responsible for ginsenoside Rg3 relaxation of the canine isolated CCSM is not by stimulating endothelial nitric oxide synthase (eNOS) but by phohodiesterase inhibitory action.

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Anti-arthritis effect of aqueous extracts of bee venom (Apis melifera)

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Bee venom (BV) is used as a traditional medicine for treatment of arthritis. The anti-inflammatory and anti-nociceptive activities of the hexane, ethyl acetate, and aqueous extracts of bee venom (Apis melifera) have been studied using cyclooxygenase (COX) activity and proinflammatory cytokines (TNF-α and IL-1β) production, in vitro, and on adjuvant induced arthritis model, in vivo. COX-2 is involved in the production of prostaglandins that mediate pain and support the inflammatory process. Of these extracts, aqueous extracts (BVA) in particular showed strong dose-dependent inhibitory effects on COX-2 activity and COX-2 mRNA expression, but did not effect COX-1 activity. TNF-α and IL-1β are potent proinflammatory cytokines and are early indicators of the inflammatory process. Accordingly, TNF-α and IL-1β production were investigated by ELISA method and all extracts inhibited TNF-α and IL-1β production. On adjuvant-induced arthritis model, subcutaneous BVA treatment (0.9 mg/kg per day) was found to dramatically inhibit paw edema caused by Freund's adjuvant injection. Furthermore, BVA therapy significantly reduced arthritis-induced nociceptive behaviors (i.e. the nociceptive scores for mechanical hyperalgesia and thermal hyperalgesia). In addition, BVA treatment significantly suppressed adjuvant-induced Fos expression in the lumbar spinal cord at 3 weeks post-adjuvant injection. These results may help to explain the pharmacological activities of BVA and the possibility that BVA acupuncture may be a promising alternative medicine therapy for the long-term treatment of rheumatoid arthritis.