Abstract

Injury of interstitial cells of Cajal (ICC) is associated with gut dysmotility in diabetic rats. We have shown an acceleration of the colonic contractility by electroacupuncture stimulation (EAS). However, little is known about potential roles of EAS on colonic transit and ICC. In this study, we evaluate the effect of EAS on colonic transit and investigate whether apoptosis/proliferation of ICC was involved in regulative effect of EAS on colonic transit. Rats were randomly assigned to normal, diabetic, diabetic-plus-sham stimulation, diabetic-plus-low-frequency stimulation, and diabetic-plus-high-frequency stimulation groups. Bead expulsion test was used for measuring the distal colonic transit. The Kit (ICC marker) was detected by western blot. Apoptotic ICC was detected by terminal dUTP nucleotide end labeling. Proliferating ICC was identified by Kit/Ki67 double immunofluorescent staining on whole mount preparations. Ultrastructure changes of ICC were studied using electron microscopy. Results showed that high-frequency stimulation significantly promoted colonic transit. Low- and high-frequency stimulation markedly rescued intramuscular ICC from apoptosis. Abundant proliferating intramuscular ICC was found in low- and high-frequency stimulation groups. Our results indicate that high-frequency EAS has stimulatory effect on the distal colonic transit, which may be mediated by downregulation of the apoptosis and upregulation of the proliferation of intramuscular ICC.

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Targeting TRPV1 for Body Weight Control using TRPV1$^{-/-}$ Mice and Electroacupuncture

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Abstract

Obesity is a global social medical problem resulting in morbidity as high as 20—30%. Here we investigated whether the manipulation of TRPV1 can control mice body weight through electroacupuncture (EA). The results demonstrated that body weight increased with time in the control group (108.19 $\pm$ 1.31%, n = 7). The increase of mice body weight was significantly less in the EA group (104.41 $\pm$ 0.76%, $p < 0.05$, compared with the control group, n = 7) but not in the sham EA group (109.1 $\pm$ 0.63%, $p < 0.05$, compared with EA group, n = 7). EA did not decrease the gain of body weight in TRPV1 knock mice (107.94 $\pm$ 0.41% and 107.79 $\pm$ 1.04% for TRPV1$^{-/-}$ and TRPV1$^{-/-}$ with EA, respectively, $p > 0.05$). The visceral white adipose tissue (WAT) weight was lower in the EA group at 4 weeks after manipulation. Moreover, the protein levels of TRPV1, pPKA, pPKC, and pERK were increased in the dorsal root ganglion (DRG) and spinal cord (SC) after EA treatment but not in the sham EA and TRPV1$^{-/-}$ mice. This study suggests that targeting TRPV1 is beneficial in controlling body weight and TRPV1-associated mechanisms in mice.

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Analgesic Effects of Toad Cake and Toad-cake-containing Herbal Drugs

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Abstract

Objectives: This study was conducted to clarify the analgesic effect of toad cake and toad-cake-containing herbal drugs.
Methods: We counted the writhing response of mice after the intraperitoneal administration of acetic acid as a nociceptive pain model and the withdrawal response after the plantar surface stimulation of the hind paw induced by partial sciatic nerve ligation of the mice as a neuropathic pain model to investigate the analgesic effect of toad cake and toad-cake-containing herbal drugs. A co-treatment study with serotonin biosynthesis inhibitory drug 4-chloro-*DL*-phenylalanine methyl ester hydrochloride (PCPA), the catecholamine biosynthesis inhibitory drug α-methyl-*DL*-tyrosine methyl ester hydrochloride (AMPT) or the opioid receptor antagonist naloxone hydrochloride was also conducted.
Results: Analgesic effects in a mouse model of nociceptive pain and neuropathic pain were shown by oral administration of toad cake and toad-cake-containing herbal drugs. The effects of toad cake and toad-cake-containing herbal drugs disappeared upon co-treatment with PCPA, but not with AMPT or naloxone in the nociceptive pain model; the analgesic effect of toad-cake-containing herbal drugs also disappeared upon co-treatment with PCPA in the neuropathic pain model.

Conclusion: Toad cake and toad-cake-containing herbal drugs have potential for the treatments of nociceptive pain and of neuropathic pain, such as post-herpetic neuralgia, trigeminal neuralgia, diabetic neuralgia, and postoperative or post-traumatic pain, by activation of the central serotonin nervous system.
Keywords: neuropathic pain, nociceptive pain, serotonin, toad cake

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Ethanolic Extract of Marsdenia condurango Ameliorates Benzo[a]pyreneinduced Lung Cancer of Rats

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Abstract
Objectives: Condurango is widely used in various systems of complementary and alternative medicines (CAM) against oesophageal and stomach ailments including certain types of cancer. However, until now no systematic study has been conducted to verify its efficacy and dose with proper experimental support. Therefore, we examined if ethanolic extract of Condurango could ameliorate benzo[a]pyrene (BaP)-induced lung cancer in rats, in vivo to validate its use as traditional medicine.
Methods: Fifteen male and 15 female Sprague-Dawley (SD) rats were treated with 0.28 mg/kg of Sweet Bee Venom (SBV) (high-dosage group) and the same numbers of male and female SD rats were treated with 0.2 mL/kg of normal saline (control group) for 13 weeks. We selected five male and five female SD rats from the high-dosage group and the same numbers of male and female SD rats from the control group, and we observed these rats for four weeks. We conducted body-weight measurements, ophthalmic xaminations, urinalyses and hematology, biochemistry, histology tests.
Results: A histological study revealed gradual progress in lung tissue-repair activity in Condurango-fed cancer-bearing rats, showing gradual tissue recovery after three months of drug administration. Condurango has the capacity to generate reactive oxygen species (ROS), which may contribute to a reduction in anti-oxidative activity and to an induction of oxidative stress-mediated cancer cell-death. Condurango-activated pro-apoptotic genes (Bax, caspase-3, caspase-9, p53, cytochrome-c, apaf-1, ICAD and PARP) and down-regulated antiapoptotic-Bcl-2 expression were noted both at mRNA and protein levels. Studies on caspase-3 activation and PARP cleavage by western blot analysis revealed that Condurango induced apoptosis through a caspase-3-dependent pathway.
Conclusion: The anticancer efficacy of an ethanolic extract of Condurango for treating BaP-induced lung cancer in rats lends support for its use in various traditional systems of medicine.
Keywords: apoptosis, caspase-3, complementary and alternative medicine (CAM), Condurango, lung cancer, reactive oxygen species (ROS)

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Assessment of Factors Associated with the Safety Depth of GV15 Yamen

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Abstract
Objectives: This study was performed to check for reversibility in the changes induced by a 13-week, repeated, dose toxicity test of Sweet Bee Venom (SBV) in Sprague-Dawley (SD) rats.
Methods: Fifteen male and 15 female SD rats were treated with 0.28 mg/kg of SBV (high-dosage group) and the same numbers of male and female SD rats were treated with 0.2 mL/kg of normal saline (control group) for 13 weeks. We selected five male and five female SD rats from the high-dosage group and the same numbers of male and female SD rats from the control group, and we observed these rats for four weeks. We conducted body-weight measurements, ophthalmic examinations, urinalyses and hematology, biochemistry, histology tests.
Results: (1) Hyperemia and movement disorder were observed in the 13-week, repeated, dose toxicity test, but these symptoms were not observed during the recovery period. (2) The rats in the high-dose group showed no significant changes in weight compared to the control group. (3) No significant differences in the ophthalmic parameters, urine analyses, complete blood cell counts (CBCs), and biochemistry were observed among the recovery groups. (4) No changes in organ weights were observed during the recovery period. (5) Histological examination of the thigh muscle indicated cell

infiltration, inflammation, degeneration, necrosis of muscle fiber, and fibrosis during the treatment period, but these changes were not observed during the recovery period. The fatty liver change that was observed during the toxicity test was not observed during the recovery period. No other organ abnormalities were observed.
Conclusion: The changes that occurred during the 13-week, repeated, dose toxicity test are reversible, and SBV can be safely used as a treatment modality.
Keywords: acupuncture, melittin, pharmacopuncture, Sweet Bee Venom, 13-week repeated dose toxicity, 4-week recovery test

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