

[PA1-43] [04/17/2003 (Thr) 14:00 – 17:00 / Hall P]

The Joins (SKI 306X) study : Effects on gastric mucosa and the diclofenac-induced gastric lesions

Kim JooHyon, Lee Haeln, Jung Inho, Jung Kiwon, Han ChangKyun, Kwak WieJong, Cho YongBaik, Joo HeeJae

Life Science Research Center SK Chemicals and Aju university Medical college

Joins (SKI 306X) is now clinically used for the treatment of osteoarthritis (OA). In previous reports, Joins, a natural herbal product extracted from three herbs Clematis Radix, Trichosanthes Radix and Prunella Flos, was shown to have good analgesic and anti-inflammatory effects and cartilage protective effects in several experimental models. In this study we characterized the effects of Joins on the gastric mucosa and compared to that of diclofenac. In addition, the gastro-protective effects of Joins were examined at diclofenac-induced ulcer models and attempted to determine the mechanism responsible for its apparent stomach-sparing properties. Acute gastric damaging properties of Joins and diclofenac were examined in the rat model. And the effects of Joins on diclofenac-induced gastric ulceration were investigated. After single or repeated administration, stomach was isolated and optically immuno-histochemically investigated. To study the protective effects of Joins, Joins was administered to rats which previously treated with diclofenac. To know the mode of action, arachidonic acid cascades were examined in gastric mucos and blood.

Joins demonstrated excellent gastrointestinal tolerability after single and repeated administration in animals. Joins did not cause significant gastric or duodenal irritations, erosions, or ulcerations at oral doses up to 4g/kg and at ip doses up to 125mg/kg. In contrast, diclofenac, conventional NSAID, caused mucosal erosion, ulcerations and bleeding in most of the studies when used at doses producing pharmacological effects. Joins inhibited diclofenac-induced erosion and ulceration of gastric mucosa. Joins significantly inhibited gastric and blood LTB₄ production of the tested doses. But, Joins showed no effects or preferably slight increase the level of PGE₂. These studies demonstrate that Joins did not produce any significant damage up to dose of 4 g/kg and was effective to protect or prevent significantly the damage associated to diclofenac-induced gastric ulcerations. Joins could spare the gastric mucosa through significantly suppressing gastric leukotriene synthesis.

[PA1-44] [04/17/2003 (Thr) 14:00 – 17:00 / Hall P]

SKLJI, a new herbal injectable agent with anti – inflammatory and analgesic effects

Rhee Hae In^o, Kim Joo Hyon, Cho Yong-Baik, Ryu KeunHo, Han Chang-Kyun, Yoo Hunseung, Kim TaekSoo, Jung InHo, Kwak Wie-Jong

SK 케미칼 (주)

Lonicera japonica is widely distributed in Southeast Asia and has been traditionally used as an anti – inflammatory, diuretic, abscessic, antipyretic, and antidotic agent. Lonicera japonica was investigated for its anti-inflammatory and analgesic effects using several in vivo models. SKLJI was purified for i.v. injection from Lonicera japonica as a potent anti-inflammatory and analgesic fraction, after activity-guided fractionation study.

In the croton oil-induced ear edema model, SKLJI showed significant anti-inflammatory effects in all tested doses (0.01, 0.1, and 1 mg/kg) at all administration routes (intravenous, intramuscular routes). Its effect was more potent than that of either diclofenac or mellilotus extracts. Intravenous administration was the most potent route among all administration routes. In the arachidonic acid-induced ear edema model, SKLJI also showed good effects at all administration routes.

SKLJI was tested for analgesic effects in the acetic acid-induced writhing test and the Randal-Sellitto model. At 0.1, and 1 mg/kg (i.v., i.m.), SKLJI significantly reduced the writhes number induced by acetic acid injection in mice. Higher dose of diclofenac (4.5, 45 mg/kg) was needed to elicit a similar effect. In the paw pressure test, SKLJI showed a significant effect at 10 mg/kg (i.v.), similar to potency of 100 mg/kg (p.o.) acetaminophen or 5 mg/kg (i.v.) diclofenac. To search for the mode of action, arachidonic acid cascades and other inflammatory mechanisms were investigated. SKLJI significantly inhibited LTB₄ production induced by calcium ionophore A23187 in human whole blood, and also significantly reduced TNF- α release in human whole blood. The major components of SKLJI were LO and SW, which also showed potent anti-inflammatory and analgesic effects.

These results suggest that SKLJI is a new herbal injectable agent with anti-inflammatory and analgesic effects and that its two active major ingredients are LO and SW.

[PA1-45] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Inhibitory effects of berberine on morphine-induced behavioral sensitization in mice

Yang Eunmi^o, Kim KyungIn, Yoo JiHoon, Lee SeokYong, Jang ChoonGon

Department of Pharmacology, College of Pharmacy, Sungkyunkwan University, Suwon 440-746

The present study was investigated the effect of berberine on the development of behavioral sensitization by morphine, methamphetamine, and cocaine. Repeated administration of morphine (10 mg/kg), methamphetamine (2 mg/kg), and cocaine (15 mg/kg) produced behavioral sensitization in mice. Pretreatment with berberine (2 mg/kg) did not inhibit methamphetamine- and cocaine-induced behavioral sensitization. However, Pretreatment with berberine significantly inhibited morphine-induced behavioral sensitization.

In this experiment, pretreatment with berberine did not decrease postsynaptic dopamine receptor supersensitivity induced by apomorphine 24h after morphine sensitization, suggesting that inhibition by berberine of morphine-sensitization is not related to the dopaminergic system. However, berberine was significantly reduced the morphine-induced NR2A and NR2B expression in the cortex and was tend to decrease morphine-induced NR1 expression, compared with morphine-treated group.

These results indicate that NMDA receptor subunit expression plays an important role in modulating of morphine-induced sensitization and suggests that inhibitory effect by berberine of morphine-induced behavioral sensitization are mediated by the inhibition of NMDA systems.

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[PA1-46] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Anti-angiogenic activity of mycelial extracts from *Cordyceps militaris*, *Cordyceps scarabaeicola* and *Paecilomyces tenuipes*

WON SO YOUNG^o, JUNG HYUN JOO, SOH JEE HYUN, PARK EUN HEE

College of Pharmacy, Sookmyung Women's University, Seoul, 140-742, Korea

Dongchunghacho is traditionally believed to be effective against various diseases. It includes many different genera such as *Cordyceps*, *Paecilomyces*, *Torrubiella* and *Podonectria*. The three fungus strains, *Cordyceps militaris*, *Cordyceps scarabaeicola* and *Paecilomyces tenuipes* were