

aporphine alkaloids.

[PB3-3] [ 04/19/2002 (Fri) 10:00 - 13:00 / Hall E ]

### $\beta$ -Hydrastine derivatives inhibit dopamine biosynthesis in PC12 cells

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The effects of (+)- $\beta$ -hydrastine hydrochloride and (-)- $\beta$ -hydrastine on dopamine biosynthesis in PC12 cells were investigated. (+)- $\beta$ -Hydrastine hydrochloride and (-)- $\beta$ -hydrastine significantly decreased the intracellular dopamine content in dose- and time-dependent manner, and the IC50 values were 9.3  $\mu$ M and 20.7  $\mu$ M, respectively. Dopamine content was lowered at 6 h and reached a minimal level at 18 h and 12 h after the exposure to 10  $\mu$ M (+)- $\beta$ -hydrastine hydrochloride and 20  $\mu$ M (-)- $\beta$ -hydrastine. The decreased dopamine content was maintained for up to 48 h, and then dopamine content completely recovered to the control level at about 72 h. Intracellular tyrosine hydroxylase (TH) activity was also inhibited by these compounds and reached the minimal level at about 6 h and 12 h, respectively. Intracellular cAMP and Ca<sup>++</sup> concentrations were also decreased by  $\beta$ -hydrastine derivatives. These results indicate that  $\beta$ -hydrastine derivatives contributes partially to the decrease in dopamine content by the inhibition of TH activity in PC12 cells.

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### EVALUATION OF ABUSE LIABILITY OF EPHEDRINE IN RATS.

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Ephedrine is a main component of ma huang, *Ephedra sinica*, which has been used as a medicinal agent to treat hay fever or asthma. Nowadays, this sympathomimetic drug is abused in many countries. In this study, we investigated the abuse liability of ephedrine by measuring locomotor activities (LA) and self-administration (SA) profiles in Sprague-Dawley rats. LA was determined in rats treated i.p. with 3, 10 and 30 mg/kg ephedrine once a day for 14 days. Intravenous SA by ephedrine (0.23, 1 and 2.3 mg/kg) was examined in food-trained rats, and the changes of ephedrine-induced SA by treating dopamine receptor antagonist, spiperone (30  $\mu$ g/kg, s.c. 1 hr before testing) were examined. We also tested the reinforcing effect of ephedrine in rats maintained to self-administer 0.1 mg/kg/inj. Methamphetamine (METH, i.v.). Body weight was not changed, but LA was dose-dependently increased in ephedrine-treated group. Saline substitution for ephedrine increased SA rates. The SA of ephedrine was decreased by spiperone. And SA rates of 1.15, 2.3 and 4.6 mg/kg/inj. ephedrine were similar to that of saline in rats trained SA by METH. These findings suggested that ephedrine may have abuse liability, partially related to dopaminergic system, but it may not substituted for METH self-administration.

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### Activation of p38 MAP kinase and AP-1 during the promotion of neurite extension of PC-12 cells by 15-deoxy- $\Delta$ 12,14-prostaglandin J2

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