

not reported yet. Therefore, in the present study we investigated anti-inflammatory effect of whole BV extract in the arthritis animal model, and further investigated the mechanism of BV-induced anti-inflammatory effect in a murine macrophage cell line Raw 264.7 cells. The present data showed that whole BV extract has a preventive effect on the mycobacterium butyricum-induced arthritis, and blocks lipopolysaccharide (LPS)-induced induction of COX-2, PLA2 and iNOS expression, and the production of NO and PGD2 through inactivation of NF- κ B.

[PA1-55] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of glycine on the development of tolerance to and physical dependence on morphine in mice

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This study was performed to investigate the effects of glycine on the development of tolerance to and physical dependence on morphine. Repeated administration of morphine developed tolerance and physical dependence. Glycine (100, 200 and 400 mg kg⁻¹ i.p.) was administered intraperitoneally to mice for 7 days once a day 30 minutes prior to the morphine (10 mg kg⁻¹ s.c.). Analgesic responses were estimated at 0, 30, 60, 90, 120 minutes by the tail flick methods 24 hours after the final injection of morphine. The inhibitory degree of morphine tolerance development of the test morphine (10 mg kg⁻¹ s.c.) by i.p. administration of glycine was evidenced by the increase in analgesic response to morphine (5 mg kg⁻¹ s.c.). Glycine inhibited the development of tolerance to morphine.

In addition, we separately measured the naloxone (5 mg kg⁻¹ i.p.)-precipitated withdrawal sign (jump) in mice that had received the same morphine (10 mg kg⁻¹ s.c.) for 7 days. Glycine (100, 200 and 400 mg kg⁻¹ i.p.) inhibited naloxone-precipitated withdrawal in morphine dependent mice.

These results suggest that glycine might be useful the prevention or treatment of morphine tolerance and physical dependence.

[PA1-56] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Inhibition of glycine on morphine-induced hyperactivity, reverse tolerance and postsynaptic dopamine receptor supersensitivity in mice

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We examined the effects of glycine on the morphine-induced hyperactivity, reverse tolerance and postsynaptic dopamine receptor supersensitivity in mice. A single administration of morphine (10 mg kg⁻¹ s.c.) induced hyperactivity as measured in mice. The morphine-induced hyperactivity was inhibited dose-dependently by the pretreatment with glycine (100, 200 and 400 mg kg⁻¹ i.p.). In addition, repeated administration of morphine (10 mg kg⁻¹ s.c.) to mice once a day for 7 days causes an increase in motor stimulation induced by a subsequent morphine dose, an effect known as reverse tolerance or sensitization. Glycine (100, 200 and 400 mg kg⁻¹ i.p.) also inhibited morphine-induced reverse tolerance, in a dose dependent manner. Mice that had received 7 days-repeated administration of morphine also developed postsynaptic dopamine

receptor supersensitivity, as shown by the enhanced ambulatory activity after administration of apomorphine (2 mg kg⁻¹ s.c.). Glycine inhibited the development of postsynaptic dopamine receptor supersensitivity induced by repeated administration of morphine. Opiate sensitization models demonstrate enhanced activating and rewarding effects of subsequent treatments which highlights the potential role of this phenomena in drug addiction. Accordingly, the inhibition of glycine on the morphine-induced hyperactivity, reverse tolerance and dopamine receptor supersensitivity suggests that glycine might be useful for the treatment of morphine addiction.

[PA1-57] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Effects of adenosine on the development of tolerance to and physical dependence on morphine in mice

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This study was performed to investigate the effects of adenosine on the development of tolerance to and physical dependence on morphine. Repeated administration of morphine developed tolerance and physical dependence. Adenosine (1, 2 and 4 mg kg⁻¹ i.p.) was administered intraperitoneally to mice for 7 days once a day 30 minutes prior to the morphine (10 mg kg⁻¹ s.c.). Analgesic responses were estimated at 0, 30, 60, 90, 120 minutes by the tail flick methods 24 hours after the final injection of morphine. The inhibitory degree of morphine tolerance development of the test morphine (10 mg kg⁻¹ s.c.) by i.p. administration of adenosine was evidenced by the increase in analgesic response to morphine (5 mg kg⁻¹ s.c.). Adenosine inhibited the development of tolerance to morphine. In addition, we separately measured the naloxone (5 mg kg⁻¹ i.p.)-precipitated withdrawal sign (jump) in mice that had received the same morphine (10 mg kg⁻¹ s.c.) for 7 days. Adenosine (1, 2 and 4 mg kg⁻¹ i.p.) inhibited naloxone-precipitated withdrawal in morphine dependent mice. These results suggest that adenosine might be useful for the prevention or treatment of morphine tolerance and physical dependence.

[PA1-58] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Alteration and significance of calcium signalings through ryanodine receptor in neuronal cell death

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Pathophysiological elevation of intracellular calcium concentration ($[Ca^{2+}]_i$) in the neuron has been considered as an important responsible factor in the neuronal cell damages. However, the mechanism of increase of $[Ca^{2+}]_i$ through ryanodine receptor (RyR), the relationship between $[Ca^{2+}]_i$ level and cell damages have not been fully demonstrated. We now report that PC12 cells and primary hippocampal neuron cells exhibit greatly increased levels of RyR and enhanced