The evaluation of antipruritic effects of paracetamol and its metabolite AM404 in an acute allergenic mice model.

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Recent studies have been identified the role of endocannabinoid and endovanilloid system in the mechanism of pruritus, representing CB1 and TRPV1 receptors as a potential target in the treatment of itch. Although pain and itch appear to be different sensation, there is close interaction between two sensory systems. Paracetamol undergoes metabolic transformation in the brain to form N-arachydonylphenolamine (AM404), which is a potent activator of TRPV1, a ligand at CB1 receptors and an inhibitor of anandamide uptake. In this study, we investigated antipruritic effects of paracetamol and its metabolite AM404 in comparable with their effects on nociception.

Antipruritic effect was evaluated by using mast cell degralunator compound 48/80 induced scratching behavior models in male Balb-C (28-32) mice. Compounds 48-80 (100 µg) injected intradermally in a volume of 50 µl into the rostral part of skin on the back of mice and the frequency of scratching around injected site by the hind paw were counted throughout the 30-min observation period. Antinociception was evaluated by hot plate tests. Paracetamol and AM404 were given intraperitoneally (i.p.) 30 min prior to compound 48-80 administration and hot plate tests. The results were given mean ± S.E.M. Compounds 48-80 elicit a strong straching responses which were found to be 131.4 ± 7.3. A significant inhibition of straching responses was observed at the dose of 200 and 300 mg/kg of paracetamol (79.4 ± 10.2 and 6.8 ± 1.2, respectively), while 100 mg/kg was ineffective (126.7 ± 9.2). AM404 (1, 5 and 10 mg/kg, i.p.) did not alter straching responses (138.5 ± 11.2, 129.3 ± 7.3 and 143 ± 6.5, respectively). Paracetamol produced antinociceptive effect at 200 and 300 mg/kg), while 100 mg/kg was ineffective in hot plate test. AM404 (1, 5 and 10 mg/kg, i.p.) did not elicit antinociceptive effect. The present finding suggest that paracetamol induced antipruritic effect appears to be independent cannabinoid and TRPV1 and AM404 does not mediate antipruritic effect. Nevertheless, antipruritic effect of paracetamol is corresponding to its antinociceptive doses and thus, false positive results of compound 48-80 induced pruritus model remain to be clarified.

Our study indicate that paracetamol induces antipruritic effect in acute allergenic pruritus model independent of its metabolite AM404.