Effects of NIP-502 on antigen-induced bronchial responses and allergic reactions in animal models.

AKIKO YAMAMOTO, TAKEHISA IWAMA, HIROSHI TAKEDA, HIROICHI NAGAI*

We examined the effect of a newly synthesized pyridazinone derivative, NIP-502 (4-chloro-5-(3-ethoxy)-4-phenoxybenzamine)-3(2H)-pyridazinone, on antigen-induced bronchial responses and allergic reactions in animal models. NIP-502 inhibited the antigen-induced immediate asthmatic response in passively sensitized guinea pigs. NIP-502 improved antigen-induced airway hyperresponsiveness to acetylcholine and inhibited the antigen-induced increase in the number of inflammatory leukocytes in bronchoalveolar lavage fluid in mice. The inhibitory effects of NIP-502 on bronchial responses are similar to those of prednisolone, but this compound seemed to act more selectively on the respiratory tract than prednisolone.

Effects of roxithromycin on proliferation of peripheral blood mononuclear cells and production of lipopolysaccharide-induced cytokines.

TOMOAKI YOSHIMURA, CHIKAKO KURITA, FUTOSHI YAMAZAKI, JOE SHINDO, ITSURO MORISHIMA, KAZUYA MACHIDA, TOSHIAKI SUMITA, MICHIAKI HOBIBA, HIROICHI NAGAI*

Roxithromycin (RXM), a new macrolide, has a 14-member macrocyclic ring structure. We investigated the effects of RXM on the proliferation of peripheral blood mononuclear cells (PBMCs) and the production of interleukin-1 \( \beta \) (IL-1 \( \beta \)) and tumor necrosis factor \( \alpha \) (TNF- \( \alpha \)) by PBMCs stimulated with lipopolysaccharide. RXM suppressed the production of IL-1 \( \beta \) and TNF- \( \alpha \) slightly during the entire course of the incubation. Suppression of the production of IL-1 \( \beta \) and TNF- \( \alpha \) by RXM suggested that this drug might have anti-inflammatory and immunosuppressive effects.

The effect of a TXA\(_2\) receptor antagonist ON-579 on experimental allergic reactions.

HIROICHI NAGAI*, HIROKAZU KAWASAKI, HIROSHI TAKEDA, YUKO TAKAOKA, NAOKI INAGAKI

The effect of a thromboxane A\(_2\) (TXA\(_2\)) receptor antagonist, ON-579, on experimental allergic skin and airway reactions was studied in vivo. ON-579 clearly inhibited U-46619-induced increase in respiratory resistance (Rrs), the aerosolized antigen-induced biphasic increase in Rrs and repeated aeroantigen-induced airway hyperreactivity in guinea pigs. ON-579, however, did not have any significant effects on allergic cutaneous reactions in rats. These results suggest that ON-579 is a relatively selective TXA\(_2\) antagonist, especially in the airways, and indicate the efficacy of ON-579 on antigen-induced increase in Rrs and airway hyperreactivity in guinea pigs.