

[Jpn. J. Pharmacol., **68**, 47-55 (1995)]

[Lab. of Pharmacology]

**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.

[Biol. Pharm. Bull., **18**, 876-881 (1995)]

[Lab. of Pharmacology]

**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, TOSHIKI SUMITA, MICHIAKI HORIBA, 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.

[Prostaglandins Leukotrienes Essential Fatty Acids, **53**, 123-133(1995)]

[Lab. of Pharmacology]

**The effect of a TXA<sub>2</sub> receptor antagonist ON-579 on experimental allergic reactions.**

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

The effect of a thromboxane A<sub>2</sub> (TXA<sub>2</sub>) 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<sub>2</sub> antagonist, especially in the airways, and indicate the efficacy of ON-579 on antigen-induced increase in Rrs and airway hyperreactivity in guinea pigs.