Autonomic blocking properties of Wy 21901

B. J. ALPS, MADELINE HILL*, E. S. JOHNSON and A. B. WILSON, *Department of Pharmacology, Wyeth Institute of Medical Research, Taplow*

3-[2-(4-Benzamidopiperid-1-yl)ethyl] indole hydrochloride (Wy 21901) is a member of a series of potent hypotensive compounds (Archibald, 1968). Agonist-antagonist studies, made on a number of isolated preparations, have identified several receptor sites of action and can account for its observed cardiovascular actions in intact animals (Alps, Johnson & Wilson, 1970).

On the longitudinal muscle of the guinea-pig isolated ileum, Wy 21901 was found to be a potent, reversible histamine antagonist (pA_2 8·2) fulfilling all the criteria for competitive antagonism (Arunlakshana & Schild, 1959), but was devoid of atropine-like activity even in concentrations as high as 10^{-5}M.

On the guinea-pig vas deferens and aortic strip Wy 21901 was an α-adrenoceptor antagonist (pA_2 7·4), an action reversed on washing continuously for 3 h. β-Adrenoceptor blocking activity was excluded by the failure of Wy 21901 (10^{-4}M) to inhibit relaxation induced by isoprenaline or noradrenaline in the guinea-pig tracheal spiral preparation. Studies with the rat isolated fundus and ileum demonstrated weak anti-5-hydroxytryptamine activity (pA_2 5·9) readily reversible on washing.

Like propranolol, Wy 21901 (10^{-6}–2×10^{-5}M) caused a dose-related reduction of the force and rate of contraction of the rabbit isolated heart. The inotropic and chronotropic actions of isoprenaline were reduced by higher concentrations of Wy 21901, but this effect was nonspecific since the cardiac stimulant actions of aminophylline were also reduced. In view of the known local anaesthetic activity of propranolol (Davis, 1970) the possibility was investigated that the cardio-inhibitory activity of Wy 21901 was caused by a local anaesthetic action. Experiments utilizing the guinea-pig weal test (Bülbring & Wajda, 1945) showed that the compound possessed local anaesthetic potency three times that of procaine.

It is concluded that Wy 21901 has α-adrenoceptor blocking, local anaesthetic and antihistamine properties, the first two of which may be responsible for its hypotensive and anti-arrhythmic actions.

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Changes in the amounts of high-energy phosphate compounds associated with the actions of phenylephrine and isoprenaline on smooth and cardiac muscle

A. H. WESTON, *Department of Pharmacology, University of Manchester*

Changes were measured in the amounts of adenosine triphosphate (ATP) and creatine phosphate (CP) associated with the actions of phenylephrine and isoprenaline on the rabbit aortic strip, the longitudinal muscle strip of rabbit duodenum,