



Barbara Rinehart

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My responsibilities were:

- Completed extensive and comprehensive literature search
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Loratadine

A Review of Recent Findings in Pharmacology, Pharmacokinetics, Efficacy, and Safety, with a Look at Its Use in Combination with Pseudoephedrine

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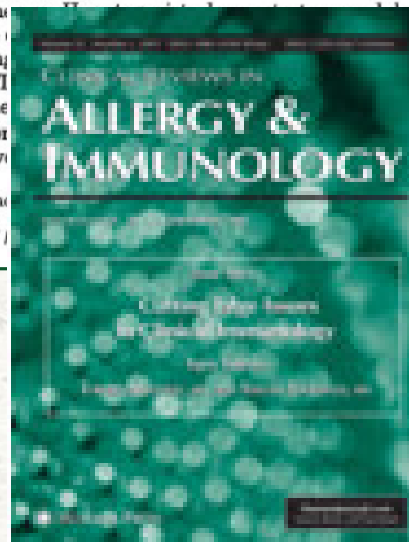
Introduction

Antihistamines have been used as therapeutic agents for over six decades. During this time, they have gained wide acceptance and have been used to treat a variety of conditions mediated by histamine. Until the discovery of the second-generation H₁-receptor antagonists, however, patients had to accept the often troublesome sedation and anticholinergic side effects common to older antihistamines.

The profile of loratadine is more efficacious in treating allergic rhinitis and urticaria (1-3). The role of loratadine in the treatment of allergic rhinitis and urticaria is well established (4).

Loratadine is a nonclassical antihistamine (Fig. 1), which does not cross the blood-brain barrier (5).

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CH₂CH₃

of loratadine C₂₂H₂₃ClN₂O₂.

It is active following oral administration. Loratadine is devoid of central nervous system effects, and as proven loratadine's safety and efficacy in the treatment of allergic symptoms.

In addition to our understanding of the pharmacology and safety of loratadine, we have provided a better understanding of its mechanism of action, particularly with respect to its safety profile. Recent efficacy and safety data for the acceptance of loratadine as an antihistamine are discussed.

Pharmacology

Loratadine blocks histamine (H₁) receptor sites and prevents histamine release. They have a nonselective effect on the central nervous system (CNS) and peripheral nervous system, sedation and other adverse effects, sedation and drug's ability to cross the blood-brain barrier, central histamine and cholinergic effects.

Second-generation antihistamines selectively work on H₁-receptor sites, probably because they preferentially bind to H₁-receptors, do not cross the blood-brain barrier, and their plasma levels are of such low concentration that block-

level, inhibition of leukotrienes averaged 100%. Inhibition was also demonstrated in a similar study using human lung mast cells (HLMC) and skin tissues (HSMC). Preincubation of HLMC and

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receptors does not occur. Possible mechanism of molecular size, electrostatic interactions, and binding (5). Loratadine's effect on central H₁-receptors using intracerebroventricularly administered bronchoconstrictions in man was found to be 10 times less potent than that of peripheral H₁-receptors. This effect was more potent against loratadine (ED₅₀ = 5 mg/kg) than terfenadine (ED₅₀ = 5 mg/kg) as measured by methospasm.

The role of loratadine is to block histamine release. However, it also has cell-regulating effects on the release of histamine in the treatment of the allergic rhinitis. Loratadine, unlike the first-generation antihistamine terfenadine, has a noninhibitory effect on the release of histamine induced with histamine-releasing agent, calcium ionophore A23187 showed that loratadine inhibited histamine release when incubated with mast cells (7). Histamine release was inhibited at concentrations of 31 μM for antiIgE, calcium ionophore A23187. Loratadine inhibited histamine release and leukotriene release in a concentration-dependent manner. In studies with mast cells, the effect of loratadine on mediator release was compared with antihistamine terfenadine, loratadine was more potent than terfenadine in inhibiting histamine release (8). Calcium ionophore A23187-stimulated histamine and leukotriene release and histamine release from MC9 cells were inhibited by loratadine (8). Both histamine release and leukotriene release were inhibited by loratadine in studies with mast cells stimulated with antiIgE antigen. In studies with mast cells, loratadine, histamine release was inhibited by 7%. At this same concentration, inhibition of leukotrienes averaged 100%.