

Research and Development of Olopatadine hydrochloride, an Antiallergic Drug

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In terms of chemical structure, olopatadine would be distinguished from the other antiallergic drugs marketed so far. The compound possesses a dimethylamine moiety at the terminal of the side chain and a directly substituted acetic acid moiety on its tricyclic core structure. The introduction of a polar functional group to the tricyclic core was first attempted to reduce lipophilicity of an in-house lead compound in order to eliminate its CNS-related effects. Fortunately, the structural modifications provided a series of orally active compounds that showed retained antiallergic and reduced CNS-related effects in animal models. Further modifications were performed based both on the physicochemical properties and on the pharmacological activities. We finally selected olopatadine hydrochloride as a new drug candidate. Olopatadine has a potent and selective histamine H₁ receptor antagonizing effect. Its physicochemical properties, including the water solubility of 2.0 mg/mL at pH6.8, eventually turned out to be suitable for ophthalmologic application as well.

Two types of formulations containing olopatadine hydrochloride as the active ingredient, tablet and ophthalmic solution, were launched in 2001 (Japan) and in 1997 (USA), respectively. These prescriptions have contributed to the treatment of allergic disease conditions in 84 countries in the world up to now. The total annual sales of the tablet (Allelock®) and the ophthalmic solution (Patanol®) reached US\$500 million in 2006 fiscal year.

In this lecture, results of medicinal chemistry to provide olopatadine hydrochloride, properties of the compound, and some additional findings obtained from the research and development will be presented.