New Product Highlights

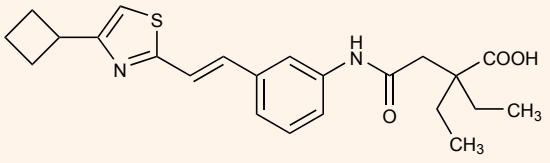
Cinalukast (Ro 24-5913): subtype selective, orally active, cysteinyl leukotriene ($CysLT_1$) receptor antagonist

First available from Sigma-RBI!

Cysteinyl leukotriene (CysLT) receptors mediate a range of pro-inflammatory effects, such as constriction of airways and vascular smooth muscle, increased permeability of endothelial membranes leading to plasma exudation and edema, and enhanced secretion of thick, viscous mucus. CysLT leukotriene receptors have therefore been implicated in a range of inflammatory diseases, notably asthma [1-3]. There are at least two subtypes of CysLT leukotriene receptors, referred to as $CysLT_1$ and $CysLT_2$, and although there is some evidence for further subdivision, this remains to be confirmed [4].

Sigma-RBI is pleased to be the first company to offer the subtype selective $CysLT_1$ receptor antagonist, **cinalukast** (Ro 24-5913; Prod. No. **C 6239**). Cinalukast has been shown to be highly potent, specific and orally active, as well as possessing a long duration of action. *In vitro*, cinalukast competes with [^{3}H]-LTD_4 binding to $CysLT_1$ leukotriene receptors present in guinea-pig lung membranes, displaying an IC_{50} value of 6.4 nM [4]. When administered intravenously (i.v.), orally or by aerosol to guinea-pigs, cinalukast produced a dose-dependent inhibition of both the non-subtype selective CysLT agonist **LTC_4**- (Prod. No. **L 4886**) and the $CysLT_1$ selective agonist **LTD_4**- (Prod. No. **L 5011**) induced bronchoconstriction, (ID_{50} values 0.06, 0.13 mg/kg (i.v); 0.06, 0.12 mg/kg (orally) and IC_{50} values 0.009, 0.008 % (aerosol), respectively) [4]. In addition, cinalukast induced 100% inhibition of both LTC_4- and LTD_4- induced bronchoconstriction at a dose of 1 mg/kg [4]. Moreover, a single oral dose of cinalukast (10 mg/kg) produced a long-lasting inhibition of bronchoconstriction, with pharmacological effects being observed within 1 hr and maintained for up to 36 hr [4].

In summary, cinalukast is a potent, orally active $CysLT_1$ receptor antagonist that should serve as a useful research tool to study the role of this receptor in asthma as well as other inflammatory diseases.



Cinalukast
(Prod. No. C 6239)

References

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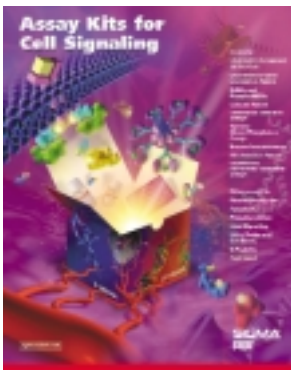

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