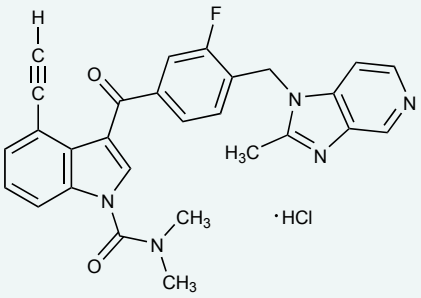
New Product Highlights

ABT-491: A potent and selective PAF receptor antagonist
First available from Sigma-RBI!

Intense interest exists in the biology of **platelet-activating factor** (PAF; Prod. No. P 7568), a diacylphosphatidylcholine [1]. PAF is released directly from cell membranes and mediates a wide range of potent and specific biological effects on target cells. These include the aggregation of platelets, which gives rise to the term platelet-activating factor. Injection of PAF into mammals produces pathophysiological events characteristic of shock [1]. In both animals and man, inhalation of PAF causes immediate bronchoconstriction followed by long-term inflammation of the airways. This response is very similar to a severe asthma attack, and as such, PAF is thought to play a role in the pathogenesis of this disease [2]. In support of this proposal, elevated levels of PAF have been found in lung lavages from asthmatics, and PAF antagonists have been shown to be active in animal models of asthma [3,4]. In addition, PAF has been characterized as an important mediator of inflammation in other conditions such as pancreatitis, ischemia-reperfusion syndrome and oral inflammation [1,5]. Recently, PAF has also been implicated as a mediator of tumor-associated angiogenesis and a contributor to neuronal death in HIV infection [6].

ABT-491 (Prod. No. A 9227) is a potent and selective PAF receptor antagonist that inhibits binding of PAF to human platelets displaying a K_i value of 0.6 nM [3]. Unlike the first generation PAF receptor antagonist **CV-3988** (Prod. No. C 7238), which has to be administered intravenously, ABT-491 is orally active. In a rat model of allergic rhinitis, in which PAF was perfused through the nasal passages of Brown Norway rats, nasal vascular permeability was significantly inhibited when ABT-491 was orally administered 1 hr prior to PAF administration (ED_{50} = 0.3 mg/kg) [4]. In a separate study, intranasal perfusion of **ovalbumin** (OA; Prod. No. A 5503) in rats sensitized to this antigen also increased vascular permeability. Pre-treatment with ABT-491 inhibited this effect by 75% (3 mg/kg p.o.; ED_{50} = 0.5 mg/kg). In addition, the antihistamine **mepyramine** (Prod. No. P 5514), the serotonin receptor antagonist **methysergide** (Prod. No. M-137), and the 5-lipoxygenase inhibitor A-79175 also inhibited the permeability response (56%, 87% and 77%, respectively), suggesting that inflammatory mediators other than PAF are involved [4]. Almost complete inhibition was achieved with a combination of ABT-491 and the serotonin receptor antagonist mepyramine [4]. This suggests that combination therapy may be efficacious in the treatment of allergic rhinitis.

In summary, ABT-491 is a potent, orally active PAF receptor antagonist that should serve as a useful research tool in the study of PAF's role in allergic rhinitis as well as other PAF-related biological effects.



ABT-491
Prod. No. A 9227

References

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2. Curtin, M.L., *Patents*, **8**, 703-711 (1998).
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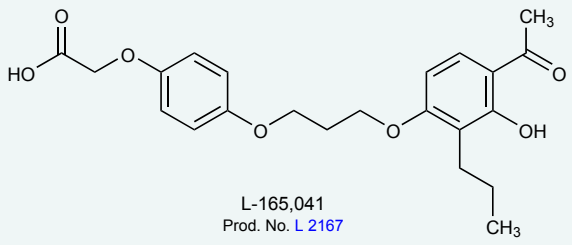
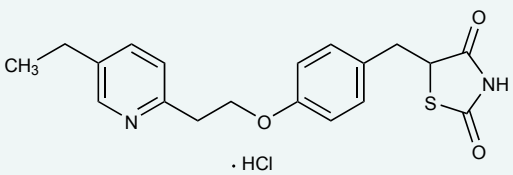
New PPAR Products Available from Sigma-RBI



L-165,041
Prod. No. L 2167



Pioglitazone
Prod. No. P 4120

L-165,041
Selective PPARβ (also known as PPARδ) agonist.
J. Biol. Chem., **274**, 6718-6725 (1999).

Pioglitazone HCl
Selective PPARγ agonist.
Nature, **405**, 421-424 (2000).