SR 12813: PXR agonist and HMG-CoA reductase inhibitor

Prod. Code S 4194

The pregnane X receptor (PXR), a member of the nuclear receptor family of ligand-activated transcription factors, is a transcriptional regulator of multiple cytochrome P450 and multidrug resistance-associated proteins. SR12813 activates both human and rabbit PXR [1,2]. SR12813 inhibits cholesterol synthesis by reducing cellular HMG-CoA reductase activity, displaying an IC_{50} value of 0.85 µM [3].

References

DAPT (LY-374973): γ-secretase inhibitor

Prod. Code D 5942

Alzheimer’s disease (AD) accounts for the majority of the dementia diagnosed over the age of 60 and represents the largest unmet medical need in neurology with over 12 million sufferers worldwide. The pathogenesis of AD is believed to result from the progressive accumulation in the brain of β-amyloid (Aβ), a 4 kDa protein. Aβ originates from the proteolytic cleavage of amyloid precursor protein (APP) by γ-secretase followed by β-secretase cleavage [1]. Because inhibition of γ-secretase blocks the production of Aβ, the identification of compounds that block the activity of this enzyme has become a major focus of AD research.

Sigma-RBI is pleased to offer DAPT, a γ-secretase inhibitor. DAPT inhibits γ-secretase in cultured cells, thus reducing Aβ levels. In transgenic mice, which develop amyloid plaques due to the overexpression of mutant βAPP, DAPT dose-dependently (10, 30, 100 mg/kg, sc) reduces the Aβ burden within 3 hr post administration and maintains reduced levels 18 hr after treatment [2]. In addition, DAPT causes Notch phenotyping in zebrafish embryos and Drosophila due to the inhibition of Notch intracellular domain generation, which is involved in gene transcription regulation, processing, translocation and signaling [3,4].

References

Related Product

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<td>L-685,458</td>
<td>Potent, selective, structurally novel γ-secretase inhibitor; equipotent in inhibition of both Aβ1-42 and Aβ1-40 Peptide fragment production</td>
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Exo 1: Reversible inhibitor of exocytosis

Prod. Code E 8280

Exo 1 [2-(4-fluorobenzyloxy)benzoic acid methyl ester] is a cell-permeable methylenetrinitol analog that reversibly inhibits vesicular traffic from the ER (endoplasmic reticulum) to Golgi in mammalian cells. It is a selective and potent modifier of Golgi ADP-ribosylation factor (ARF) 1 GTPase activity and has no effect on other endocytic organelles such as endosomes and trans-Golgi network (TGN). Exo 1 inhibits exocytosis displaying an IC_{50} value of 20 µM [1].

Reference

YM-53601: Squalene synthase inhibitor

Prod. Code Y 0128

Squalene synthase is an enzyme vital for cholesterol biosynthesis. YM-53601, a squalene synthase inhibitor, lowered not only plasma cholesterol, but also plasma triglyceride levels. YM-53601 equally inhibited squalene synthase function in hepatic microsomes prepared from several animal species and suppressed cholesterol biosynthesis in rats (ED_{50} 32 mg/kg). In rhesus monkeys, when dosed at 50 mg/kg twice daily for 21 days, YM-53601 decreased plasma non-HDL-C (high density lipoprotein cholesterol) by 37%, whereas the HM-G-CoA reductase inhibitor, pravastatin, when dosed at 25 mg/kg twice daily for 28 days, failed to do so.

Reference

sPLA2 inhibitor

Available First from Sigma-RBI

Prod. Code S 3319

Orally active, potent secretory Phospholipase A_2 (sPLA2; Group IIA) inhibitor - IC_{50} = 29 nM against human recombinant nonpancreatic sPLA2.

References