IBUDILAST

Product Number I 0157

Storage Temperature 2-8 °C

Cas #: 50847-11-5
Synonyms: 3-Isobutyryl-2-isopropylpyrazolo(1,5-a)-pyridine; KC-404; 1-Propanone, 2-methyl-1-[2-(1-methylethyl)pyrazolo[1,5-a]pyridin-3-yl]

Product Description

Molecular Formula: C_{14}H_{18}N_{2}O
Molecular Weight: 230.32
Appearance: white solid
Purity: >99% by HPLC

The cyclic nucleotide phosphodiesterases (PDEs) catalyze the hydrolysis of the phosphoester bond on the 3'-carbon to yield the corresponding 5'-nucleotide monophosphate. Thus, they regulate the cellular concentrations of cyclic nucleotides. Since extracellular receptors for many hormones and neurotransmitters and light-sensitive receptors in the retina utilize cyclic nucleotides as second messengers, the PDEs also regulate cellular responses to these extracellular signals. There are at least eight classes of PDEs: Ca^{2+}/calmodulin-dependent PDEs (PDE1); cGMP-stimulated PDEs (PDE2); cGMP-inhibited PDEs (PDE3); cAMP-specific PDEs (PDE4); cGMP-binding PDEs (PDE5); photoreceptor PDEs (PDE6); high affinity, cAMP-specific PDEs (PDE7), and high affinity cGMP-specific PDEs (PDE9).\textsuperscript{1}

Ibudilast is a non-selective PDE antagonist that inhibits platelet aggregation and induces bronchodilation and vasodilation. The anti-platelet action appears to be due to the inhibition of cAMP phosphodiesterase activity (PDE4) and to the potentiation of the anti-aggregatory activity of PGI_{2}. Addition of human umbilical vein endothelial cells (HUCECs) to platelet rich plasma in vitro models the in vivo conditions of thrombus formation. Ibudilast produced a potent, dose-dependent inhibition of platelet aggregation in the presence of HUVEC cells.\textsuperscript{2} Ibudilast also inhibited membrane-bound PDE4 from guinea pig eosinophils with an IC_{50} of approximately 1 μM. In intact eosinophils ibudilast potentiated isoprenaline-induced cAMP accumulation. The cAMP-dependent protein kinase activity was also significantly increased following incubation with 20 μM ibudilast.\textsuperscript{3}

In rat glial cells 100 μM ibudilast inhibited PDE3 and suppressed TNFα production.\textsuperscript{4} Ibudilast (10 -100 μM) demonstrated an anti-apoptotic effect in cultured astrocytes exposed to H_{2}O_{2} via a cGMP-activated signaling pathway. In these cells, ibudilast inhibited the H_{2}O_{2}-induced cytochrome C release, caspase-3 activation, DNA ladder formation and nuclear condensation.\textsuperscript{5}

By increasing cellular levels of cyclic nucleotides, ibudilast can help identify physiological pathways that utilize cyclic nucleotide second messengers.

Preparation Instructions

Ibudilast is soluble in water at 4.5 mg/ml and in DMSO at 28 mg/ml.

Storage/Stability

Store ibudilast at 2-8 °C

References
