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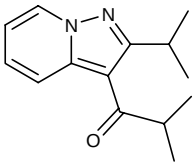
ProductInformation

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: $C_{14}H_{18}N_2O$
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).[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 (HUVECs) 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.[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.[3]

In rat glial cells 100 μM ibudilast inhibited PDE3 and suppressed TNFα production.[4] Ibudilast (10 -100 μM) demonstrated an anti-apoptotic effect in cultured astrocytes exposed to H_2O_2 via a cGMP-activated signaling pathway. In these cells, ibudilast inhibited the H_2O_2-induced cytochrome C release, caspase-3 activation, DNA ladder formation and nuclear condensation.[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
1. Obernolte, R., et al. The cDNA of a human lymphocyte cyclic-AMP phosphodiesterase (PDE IV) reveals a multigene family. Gene, **129**, 239-247 (1993).
2. Rile, G., et al., Potentiation of ibudilast inhibition of platelet aggregation in the presence of endothelial cells. Thromb. Res., **102**, 239-246 (2001).
3. Souness, J. E., et al., Possible role of cyclic AMP phosphodiesterases in the actions of ibudilast on eosinophil tromboxane generation and airways smooth muscle tone. Br. J. Pharmacol., **111**, 1081-1088 (1994).
4. Suzumura, A., et al., Ibudilast suppresses TNFα production by glial cells functioning mainly as type III phosphodiesteraze inhibitor in CNS. Brain Res., **837**, 203-212 (1999).
5. Takuma, K., et al., Ibudilast attenuates astrocyte apoptosis via cyclic GMP signaling pathway in an *in vitro* reperfusion model. Br. J. Pharmacol., **133**, 841-848 (2001)

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