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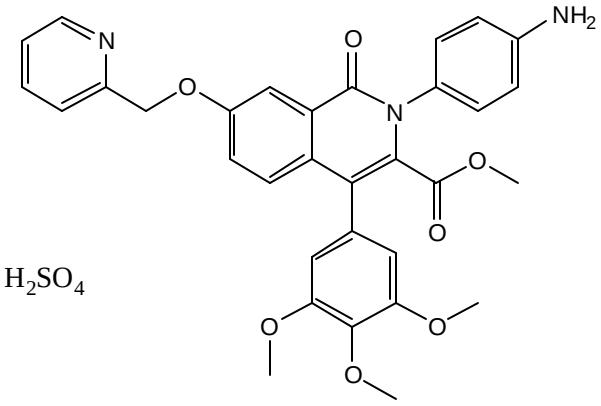
ProductInformation

T-1032

Product Number **T7692**
Storage Temperature 2-8 °C

Cas #: 212500-03-3
Synonyms: Methyl-(2-(4-aminophenyl)-1,2-dihydro-1-oxo-7-(2-pyridinylmethoxy)-4-(3,4,5-trimethoxyphenyl))-3-isoquinoline carboxylic acid, sulfate salt



Product Description
Molecular Formula: $C_{32}H_{29}N_3O_7 \bullet H_2SO_4$
Molecular Weight: 665.68 (anhydrous)
Supplied as white solid
Purity: 99% by HPLC
Melting Point: 176-182.5 °C

The isoquinolone derivative, T-1032, is a potent, selective inhibitor of cyclic GMP-specific phosphodiesterase (PDE5). In studies of PDE isoenzymes isolated from canine tissues, T-1032 was a competitive inhibitor of cyclic GMP hydrolysis by PDE5 at nanomolar concentrations (IC_{50} = 1.0 nM, K_i = 1.2 nM). In contrast, the IC_{50} values for inhibition of PDE1, PDE2, PDE3, and PDE4 were greater than 1 µM. T-1032 also inhibited PDE6 from canine retina with an IC_{50} = 28 nM. T-1032 increased the intracellular concentration of cyclic GMP in rat vascular smooth muscle cells in the presence or absence of C-type natriuretic factor, but had no effect on cyclic AMP levels.[1]

T-1032 in a concentration range of 10^{-10} to 10^{-7} M induced relaxation of both stimulated and unstimulated isolated rat aorta preparations that was accompanied by an increase in cyclic GMP but not of cAMP. The vasorelaxation was attenuated by N^{ω}-nitro-L-arginine methyl ester (L-NAME), an inhibitor of nitric oxide synthase. Thus, the vasorelaxant properties of T-1032 appeared to be due the activation of the cGMP/NO signaling pathway following the inhibition of PDE5.[2,3]

Preparation Instructions
T-1032 is soluble in DMSO at 23 mg/ml and methanol at 3.25 mg/ml, and is insoluble in water.

Storage/Stability
Store tightly sealed at 2-8 °C.

References
1. Kotera, J., et al., Characterization and effects of methyl-2- (4-aminophenyl)-1,2-dihydro-1-oxo-7- (2-pyridinylmethoxy)-4-(3,4,5-trimethoxyphenyl)-3-isoquinoline carboxylate sulfate (T-1032), a novel potent inhibitor of cGMP-binding cGMP-specific phosphodiesterase (PDE5)., Biochem. Pharmacol., **60**, 1333-1341 (2000).
2. Mochida, H., et al., Sildenafil and T-1032, phosphodiesterase type 5 inhibitors, showed a different vasorelaxant property in the isolated rat aorta. Eur. J. Pharmacol. **440**, 45-52 (2002).
3. Takagi, M., et al., Pharmacological profile of T-1032, a novel specific phosphodiesterase type 5 inhibitor, in isolated rat aorta and rabbit corpus cavernosum., Eur. J. Pharmacol., **411**,161-168 (2001).

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