

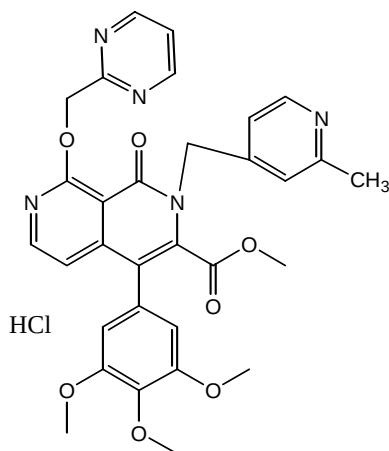
Product Information

T-0156

Product Number **T 8067**

Storage Temperature 2-8 °C

Synonym: 2-(2-Methylpyridin-4-yl)methyl-4-(3,4,5-trimethoxyphenyl)-8-(pyrimidin-2-yl)methoxy-1,2-dihydro-1-oxo-2,7-naphthyridine-3-carboxylic acid methyl ester hydrochloride



Product Description

Molecular Formula: $C_{31}H_{29}N_5O_7 \cdot HCl$

Molecular Weight: 620.07

Supplied as white solid.

Purity: 99% by HPLC.

Melting Point: 155-156.4 °C

T-0156, like the related compound T-1032, is a potent, inhibitor of cyclic GMP-specific phosphodiesterases PDE5 and PDE6. T-0156 specifically inhibited the hydrolysis of cyclic guanosine monophosphate (cGMP) by phosphodiesterase type 5, at low concentration ($IC_{50}=0.23$ nM), in a competitive manner. T-0156 also inhibited phosphodiesterase type 6 with IC_{50} value of 56 nM, which was 240-fold higher than that for inhibition of phosphodiesterase type 5. T-0156 had low potencies against phosphodiesterase types 1, 2, 3, and 4 ($IC_{50}>10$ μ M). In the isolated rabbit corpus cavernosum, T-0156 at 10 and 100 nM increased cGMP levels (100 nM T-0156-treated: 6.0 ± 1.5

pmol/mg protein, vehicle-treated: 1.1 ± 0.4 pmol/mg protein, $P<0.05$), causing relaxation of the tissue. T-0156 at 1 to 100 nM potentiates the electrical field stimulation-induced relaxation in the isolated rabbit corpus cavernosum in a concentration-dependent manner (100 nM T-0156). The effects of intravenous T-0156 or sildenafil on the pelvic nerve stimulation-induced penile tumescence and light-adapted flicker stimulation-induced electroretinogram, parameters of which are reported to be indicators for inhibition of phosphodiesterase type 5 and type 6, respectively. Both compounds potentiate the penile tumescence in a dose-dependent manner. T-0156 at 10 μ kg and sildenafil at 100 μ kg showed almost the same potentiation percentage ($181.5 \pm 31.1\%$ and $190.0 \pm 37.9\%$) in spite of the plasma concentration of T-0156 being about five times lower than that of sildenafil (16.7 ± 1.6 and 78.8 ± 5.3 ng/ml), indicating that the effect of T-0156 on tumescence is more potent than that of sildenafil.

Preparation Instructions

T-0156 is soluble in DMSO at 17.3 mg/ml and insoluble in water.

Storage/Stability

Store at 2-8 °C.

References

1. Mochida, H., et al., T-0156, a novel phosphodiesterase type 5 inhibitor, and sildenafil have different pharmacological effects on penile tumescence and electroretinogram in dogs. *Eur J Pharmacol.* **485**, 283-288 (2004).
2. Mochida, H., et al., Enzymological and pharmacological profile of T-0156, a potent and selective phosphodiesterase type 5 inhibitor *Eur J Pharmacol.* 2002 Dec 5;456(1-3):91-8.

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