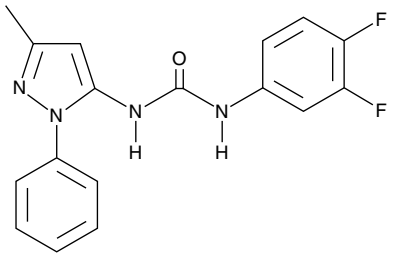
Product Information

ML-297

Item No. 14792

CAS Registry No.:	1443246-62-5
Formal Name:	N-(3,4-difluorophenyl)-N'-(3-methyl-1-phenyl-1H-pyrazol-5-yl)-urea
Synonyms:	CID-56642816, VU0456810
MF:	$C_{17}H_{14}F_2N_4O$
FW:	328.3
Purity:	≥98%
Stability:	≥2 years at -20°C
Supplied as:	A crystalline solid
UV/Vis.:	λ_{max}: 244 nm



Laboratory Procedures

For long term storage, we suggest that ML-297 be stored as supplied at -20°C. It should be stable for at least two years.

ML-297 is supplied as a crystalline solid. A stock solution may be made by dissolving the ML-297 in the solvent of choice. ML-297 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of ML-297 in ethanol is approximately 20 mg/ml and approximately 30 mg/ml in DMSO and DMF.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of ML-297 can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of ML-297 in PBS, pH 7.2, is approximately 10 mg/ml. We do not recommend storing the aqueous solution for more than one day.

G protein-regulated inwardly rectifying potassium ($GIRK_{1-4}$) channels are a family of $K_{ir}3.1$-$K_{ir}3.4$ ion channels that modulate cell excitability. The four different GIRK subunits are composed in different homo- and heterotetrameric combinations, which are expressed with regional specificity throughout the central nervous system and in the periphery.[1] ML-297 is a selective GIRK1/2 activator (EC_{50}s = 0.16 and 1.8 µM for GIRK1/2 and GIRK1/4, respectively, and is completely inactive at GIRK2/3).[1,2] In two different mouse models of epilepsy, ML-297 at 60 mg/kg was shown to delay seizure onset and to prevent convulsions.[1]

References

1. Kaufmann, K., Romaine, I.M., Days, E., *et al.* ML297 (VU0456810), the first potent and selective activator of the GIRK potassium channel, displays antiepileptic properties in mice. *ACS Chem. Neurosci.* **4(9)**, 1278-1286 (2013).
2. Wen, W., Wu, W., Romaine, I.M., *et al.* Discovery of 'molecular switches' within a GIRK activator scaffold that afford selective GIRK inhibitors. *Bioorg. Med. Chem. Lett.* **23(16)**, 4562-4566 (2013).

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