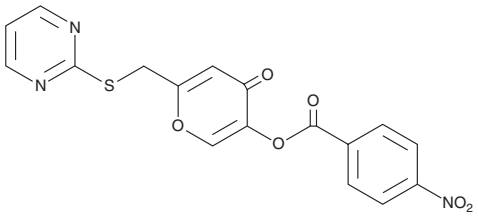
PRODUCT INFORMATION

ML-221

Item No. 27313

CAS Registry No.: 877636-42-5
Formal Name: 5-[(4-nitrobenzoyl)oxy]-2-[(2-pyrimidinylthio)methyl]-4H-pyran-4-one
MF: $C_{17}H_{11}N_3O_6S$
FW: 385.4
Purity: ≥98%
UV/Vis.: λ_{max}: 249 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

ML-221 is supplied as a crystalline solid. A stock solution may be made by dissolving the ML-221 in the solvent of choice, which should be purged with an inert gas. ML-221 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF). The solubility of ML-221 in these solvents is approximately 1 and 10 mg/ml, respectively.

ML-221 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, ML-221 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. ML-221 has a solubility of approximately 0.03 mg/ml in a 1:30 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

ML-221 is an antagonist of the G protein-coupled receptor (GPCR) APJ (IC_{50} = 4.8 µM).[1] It is selective for APJ over the angiotensin II type 1 (AT_1) receptor (IC_{50} = >78 µM). ML-221 antagonizes apelin 13-induced activation of APJ in cAMP and β-arrestin recruitment assays (IC_{50}s = 0.7 and 1.75 µM, respectively). It inhibits proliferation and angiogenesis in Mz-ChA-1 cholangiocarcinoma cells when used at concentrations ranging from 5 to 15 µM.[2] *In vivo*, ML-221 (150 µg/kg) reduces tumor growth in a Mz-ChA-1 mouse xenograft model. Intrathecal injection of ML-221 (10 µg per animal) reduces mechanical allodynia and heat hyperalgesia induced by chronic constriction injury (CCI) of the sciatic nerve in rats.[3] ML-221 also inhibits pathological angiogenesis and enhances normal vessel recovery in retinal ischemic regions in a mouse model of oxygen-induced retinopathy.[4]

References

1. Maloney, P.R., Khan, P., Hedrick, M., *et al.* Discovery of 4-oxo-6-((pyrimidin-2-ylthio)methyl)-4*H*-pyran-3-yl 4-nitrobenzoate (ML221) as a functional antagonist of the apelin (APJ) receptor. *Bioorg. Med. Chem. Lett.* **22(21)**, 6656-6660 (2012).
2. Hall, C., Ehrlich, L., Venter, J., *et al.* Inhibition of the apelin/apelin receptor axis decreases cholangiocarcinoma growth. *Cancer Lett.* **386**, 179-188 (2017).
3. Xiong, Q., He, W., Wang, H., *et al.* Effect of the spinal apelin APJ system on the pathogenesis of chronic constriction injury induced neuropathic pain in rats. *Mol. Med. Rep.* **16(2)**, 1223-1231 (2017).
4. Ishimaru, Y., Shibagaki, F., Yamamuro, A., *et al.* An apelin receptor antagonist prevents pathological retinal angiogenesis with ischemic retinopathy in mice. *Sci. Rep.* **7(1)**, 15062 (2017).

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