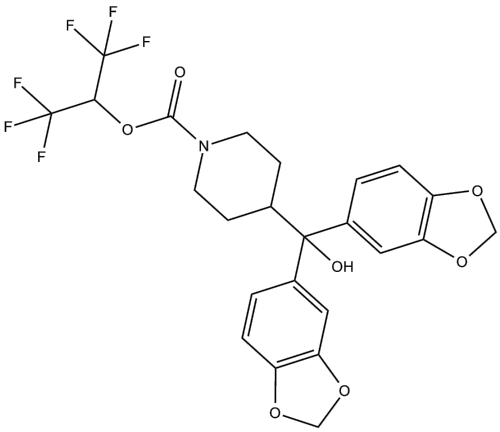
Product Data Sheet

Product Name: KML 29
Cat. No.: GC17385

Chemical Properties

Cas. No.	1380424-42-9		
Chemical Name	1,1,1,3,3,3-hexafluoropropan-2-yl 4-(bis(benzo[d][1,3]dioxol-5-yl)(hydroxy)methyl)piperidine-1-carboxylate		
SMILES	FC(F)(F)C(OC(N1CCC(C(C2=CC3=C(OCO3)C=C2)(O)C4=CC5=C(OCO5)C=C4)CC1)=O)C(F)(F)F		
Formula	$C_{24}H_{21}F_6NO_7$	M.Wt	549.42
Solubility	DMSO: 2 mg/ml	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines A431, H1975, B16-F10, OVCAR-3, HT-29, HCC827, Hela, A549

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Preparation Method	cells (~1,000 per well) in 100 µl of culture medium were plated in a 96-well plate for 24 h and 100 µl of medium with KML29 was added to each well for 48 h. Then 10 µl of CCK8 solution was added and incubated at 37°C for 2 h.
Reaction Conditions	20 µM KML29 for 48 h
Applications	The selective MAGL inhibitor KML29 showed antiproliferative activity against B16-F10 and HT-29 cells.

Animal experiment [2]:

Animal models	MCAO rats
Preparation Method	1 mg/kg KML 29, a potent covalent inhibitor of MAGL, was administered intravenously for three days.
Dosage form	intravenous injection, 1 mg/kg/d for 3 days
Applications	Treatment with KML 29 reduced the area showing lower radioactivity in the ipsilateral region. In the ipsilateral side of the ischemia rat with no medication, the AUC ratios in the cortex and striatum were 0.49 ± 0.04 and 0.73 ± 0.02, respectively. The corresponding ratios were improved 0.72 ± 0.07 in the cortex and 0.88 ± 0.04 in the striatum by KML 29 treatment, respectively.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

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References:
[1]: Deng H, Lei Q, Yang N, et al. Discover Monoacylglycerol Lipase Inhibitors by Combination of Fluorogenic Substrate Assay and Activity-Based Protein Profiling[J]. Frontiers in pharmacology, 2022: 3328.
[2]: Yamasaki T, Hatori A, Zhang Y, Mori W, Kurihara Y, Ogawa M et al Neuroprotective effects of minocycline and KML29, a potent inhibitor of monoacylglycerol lipase, in an experimental stroke model: a small-animal positron emission tomography study.Theranostics. 2021 Sep13;11(19):9492-9502.

Background

KML 29 is reported to display IC50 values of 43, 15, and 5.9 nM toward rat, mouse, and human monoacylglycerol lipase (MAGL), respectively [1]. KML29 potently and selectively inhibited MAGL in vitro and in vivo with minimal cross-reactivity toward other central and peripheral serine hydrolases, including no detectable activity against FAAH [1].

KML 29 acted as a selective MAGL inhibitor showed antiproliferative activity against B16-F10 and HT-29 cells, while showed no significant effect on A431, H1975, OVCAR-3, HCC827, Hela and A549 cell lines [2].

KML 29 delays onset, progression and survival in the low-copy SOD1G93A Amyotrophic lateral sclerosis (ALS) mouse. oral administration of KML 29 is therapeutic by delaying onset, improving symptoms and extending lifespan, which was associated with increasing tissue levels of neurotrophic factors and decreasing pro-inflammatory cytokines [3]. Acute administration of KML 29 mostly increased 2-AG levels in fat, brain and spinal cord without any effect on AEA levels. KML 29 also reduced arachidonic acid levels in the CNS and peripheral organs [4].

References:
[1]. J.W. Chang, M.J. Niphakis, K.M. Lum, A.B. Cognetta 3rd, C. Wang, M.L. Matthews, S. Niessen, M.W. Buczynski, L.H. Parsons, B.F. Cravatt. Highly selective inhibitors of monoacylglycerol lipase bearing a reactive group that is bioisosteric with endocannabinoid substrates. Chem. Biol., 19 (2012), pp. 579-588
[2]. Deng H, Lei Q, Yang N, et al. Discover Monoacylglycerol Lipase Inhibitors by Combination of

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Fluorogenic Substrate Assay and Activity-Based Protein Profiling[J]. Frontiers in pharmacology, 2022: 3328.
[3]. N. Pasquarelli, M. Engelskirchen, J. Hanselmann, S. Endres, C. Porazik, H. Bayer, E. Buck, M. Karsak, P. Weydt, B. Ferger, A. Witting. Evaluation of monoacylglycerol lipase as a therapeutic target in a transgenic mouse model of ALS. Neuropharmacology, 124 (2017), pp. 157-169
[4]. N Pasquarelli, et al., Comparative biochemical characterization of the monoacylglycerol lipase inhibitor KML29 in brain, spinal cord, liver, spleen, fat and muscle tissue. Neuropharmacology 91, 148-156 (2015).

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