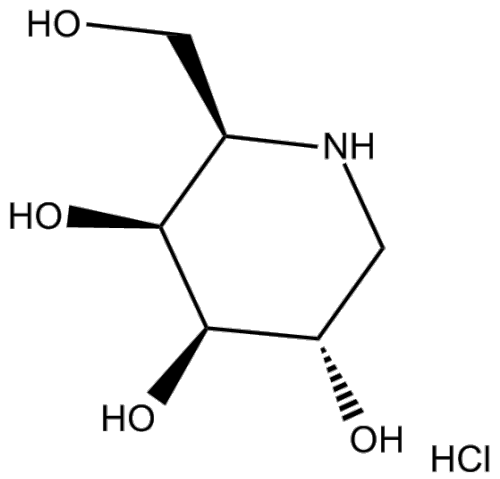
Product Data Sheet

Product Name: Migalastat (GR181413A) hydrochloride
Cat. No.: GC10430

Chemical Properties

Cas. No.	75172-81-5		
Chemical Name	(2R,3S,4R,5S)-2-(hydroxymethyl)-3,4,5-piperidinetriol, monohydrochloride		
SMILES	O[C@@H]1[C@@H](O)[C@@H](O)[C@@H](CO)NC1.Cl		
Formula	$C_6H_{13}NO_4$ • HCl	M.Wt	199.6
Solubility	≤10mg/ml in DMSO	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 Fabry patient-derived fibroblasts

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Preparation Method	Fabry patient-derived fibroblasts were seeded at a density of 1×10^6 cells per T-75 culture flask in the growth medium (Dulbecco modified Eagle medium+15% fetal bovine serum) and cultured overnight at 37°C and 8% CO_2. The cells were then seeded at a density of 10,000 cells per well in a sterile, transparent-bottom 96-well black culture plate and cultured for 1-2 hours at 37°C and 8% CO_2. Subsequently, the cells were incubated separately with rhα-galactosidase A (0.5nM) or together with rhα-galactosidase A (0.5nM) and Migalastat hydrochloride (0.1, 1, 10, 100, and 1000μM) for 5 hours. The cells were washed three times with the culture medium and then cultured in the medium for 2 days. Afterwards, the cells were washed twice with phosphate buffer and lysed for 5 minutes in 35μl of 0.2% Triton X-100, 27mM citric acid monohydrate, and 46mM phosphate buffer (pH 4.6) to detect the activity of α-galactosidase A.
Reaction Conditions	0.1, 1, 10, 100, and 1000μM; 5h
Applications	Migalastat hydrochloride/rhα-galactosidase A coincubation enhanced the α-galactosidase A levels and activity in Fabry fibroblasts in a dose-dependent manner.

Animal experiment [2]:

Animal models	hR301Q α-Gal A Tg/KO mice
Preparation Method	The hR301Q α-Gal A Tg/KO mice were raised in a standard sterile environment and were allowed to freely consume Migalastat hydrochloride (100mg/kg) in the drinking water once daily for 28 days. The mice were then euthanized by carbon dioxide inhalation. Whole blood was collected from the inferior vena cava into lithium heparin anticoagulant tubes and centrifuged at 2700g for 10 minutes at 4°C to separate the plasma. The heart, kidneys, brain and skin (after shaving and removal from the ventral side below the neck) were quickly extracted, rinsed with cold phosphate-buffered saline (PBS), dried, and analyzed.

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Dosage form	100mg/kg/day for 28 days; p.o.
Applications	Migalastat hydrochloride administration resulted in significant reductions in Lyso-Gb_3 levels in kidney, heart, and skin of mice.

References:
[1] Benjamin E R, Khanna R, Schilling A, et al. Co-administration with the pharmacological chaperone AT1001 increases recombinant human α-galactosidase A tissue uptake and improves substrate reduction in Fabry mice[J]. Molecular Therapy, 2012, 20(4): 717-726.
[2] Young-Gqamana B, Brignol N, Chang H H, et al. Migalastat HCl reduces globotriaosylsphingosine (lyso-Gb3) in Fabry transgenic mice and in the plasma of Fabry patients[J]. PLoS One, 2013, 8(3): e57631.

Background

Migalastat (GR181413A) hydrochloride an orally competitive inhibitor of α-galactosidase A, with an IC_{50} value of 0.04μM[1]. Migalastat hydrochloride targets the mutated form of α-galactosidase A via competitively binding to the enzyme, promoting the transport of the abnormal α-galactosidase A mutant to the lysosome and enhances the activity of enzyme processing globotriaosylceramide (GL-3)[2]. Migalastat hydrochloride has been widely used to increase the level of active α-galactosidase A, and has been employed in the development of new combined therapies[3].

In vitro, Migalastat hydrochloride (1000μM) combined with rhα-galactosidase A (0.5nM) and Fabry patient-derived fibroblasts incubated for 5 hours can increase the intracellular level and activity of α-galactosidase A, and reduce the GL-3 level[4].

In vivo, Migalastat hydrochloride treatment via oral administration at a dose of 100mg/kg/day for 28 days resulted in significant reductions in globotriaosylsphingosine (Lyso-Gb_3) levels in kidney, heart, and skin of hR301Q α-Gal A Tg/KO mice[5]. Daily oral administration of 300 mg/kg Migalastat hydrochloride (for 4 weeks) significantly increased the α-galactosidase A activity in hR301Q α-Gal A Tg/KO mice and decreased the GL-3 level[6].

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References:

[1] Lenders M, Menke E R, Brand E. Biochemical Amenability in Fabry Patients Under Chaperone Therapy—How and When to Test? M. Lenders et al[J]. BioDrugs, 2024, 38(6): 845-854.
[2] Giugliani R, Waldek S, Germain D P, et al. A Phase 2 study of migalastat hydrochloride in females with Fabry disease: selection of population, safety and pharmacodynamic effects[J]. Molecular genetics and metabolism, 2013, 109(1): 86-92.
[3] Warnock D G, Bichet D G, Holida M, et al. Oral migalastat HCl leads to greater systemic exposure and tissue levels of active α-galactosidase A in Fabry patients when co-administered with infused agalsidase[J]. PLoS One, 2015, 10(8): e0134341.
[4] Benjamin E R, Khanna R, Schilling A, et al. Co-administration with the pharmacological chaperone AT1001 increases recombinant human α-galactosidase A tissue uptake and improves substrate reduction in Fabry mice[J]. Molecular Therapy, 2012, 20(4): 717-726.
[5] Young-Gqamana B, Brignol N, Chang H H, et al. Migalastat HCl reduces globotriaosylsphingosine (lyso-Gb3) in Fabry transgenic mice and in the plasma of Fabry patients[J]. PLoS One, 2013, 8(3): e57631.
[6] Khanna R, Soska R, Lun Y, et al. The pharmacological chaperone 1-deoxygalactonojirimycin reduces tissue globotriaosylceramide levels in a mouse model of Fabry disease[J]. Molecular Therapy, 2010, 18(1): 23-33.

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