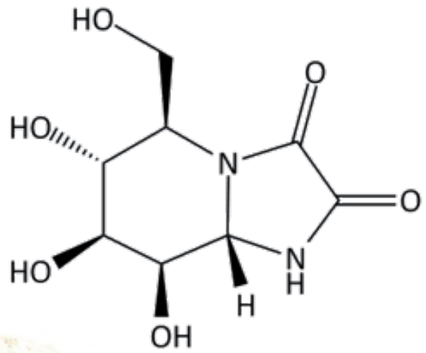


Kifunensine

Kifunensine is an alkaloid originally isolated from Kitasatosporia kifunenis, a soil-borne actinobacterium. [1,2,3]

Pricing

Quantity	Cost (USD)
10 mg	$190
25 mg	$400
100 mg	$1,100
500 mg	$3,300
2 g	$9,600

Enzyme inhibition

Kifunensine is a potent inhibitor of mannosidase I.[4,5] It is 50 to 100 times more potent than deoxymannojirimycin. Adding 5–20 µM of kifunensine to a mammalian cell culture medium can achieve complete mannosidase I inhibition.

Kifunensine inhibits human endoplasmic reticulum α-1, 2-mannosidase I and Golgi Class I mannosidases IA, IB and IC with K_i values of 130 and 23 nM, respectively.

Kifunensine does not inhibit mannosidase II or the endoplasmic reticulum α-mannosidase. It weakly inhibits aryl-mannosidase.

Because kifunensine is a neutral molecule, it can permeate inside cells. Once inside a cell, kifunensine blocks endoplasmic reticulum (ER) mannosidase I (ERM1). This blocks processing of glycoproteins in the ER, to leave them with glycoforms with mainly nine mannose residues attached to two N-acetylglucosamine residues ($Man_9GlcNAc_2$).

Kifunensine offers an excellent off-the-shelf solution for groups wishing to leverage already developed cell lines to control glycosylation levels.

Kifunensine

Appearance: Off-white solid
Molecular weight: 232.19
Formula: $C_8H_{12}N_2O_6$
CAS number: 109944-15-2
Storage: Store dry at ambient temperature or below

Applications

Therapeutic Antibodies and Biosimilar Manufacture

Antibody effector function: human IgG1 antibodies produced from cells treated with kifunensine resulted in increased Fc receptor binding, and increased antibody dependant cytotoxicity (ADCC).[6]

Enzyme Replacement Therapies

High mannose proteins can be used to target delivery by receptor mediated endocytosis to lysosomes to treat various lysosomal storage diseases.[7]

Recombinant Protein Vaccines

High mannose glycoprotein HIV-1 viral antigen: broadly neutralizing antibodies bound 82-fold tighter to envelope proteins of gp120Ba-L-expressing HEK293F cells when cell culture was treated with kifunensine.[8,9]

Gene Therapies

Lentiviral vector particles encoding an antigen will preferentially bind dendritic cells expressing DC-SIGN receptors when surface proteins display high mannose glycoform.[10]

Apoproteins for Structural Studies

Kifunensine (5 µM) can be used to prepare deglycosylatable glycoproteins, without compromising protein yield – use of kifunensine increased expression by 30%. These apoproteins are crystallizable and show lower structural heterogeneity which facilitates purification.[11]

Details

Manufacture

Kifunensine is made by GlycoSyn in an eight-step synthesis from *N*-acetylmannosamine in a process developed and patented by GlycoSyn.[12]

Quality

Each batch of kifunensine is analysed by HPLC, IR and NMR to ensure it meets our rigorous quality standards. A Certificate of Analysis accompanies each purchase, which details and confirms its purity according to our criteria.

GMP grade

If required, cGMP grade kifunensine is available from GlycoSyn (*www.glycosyn.com*).

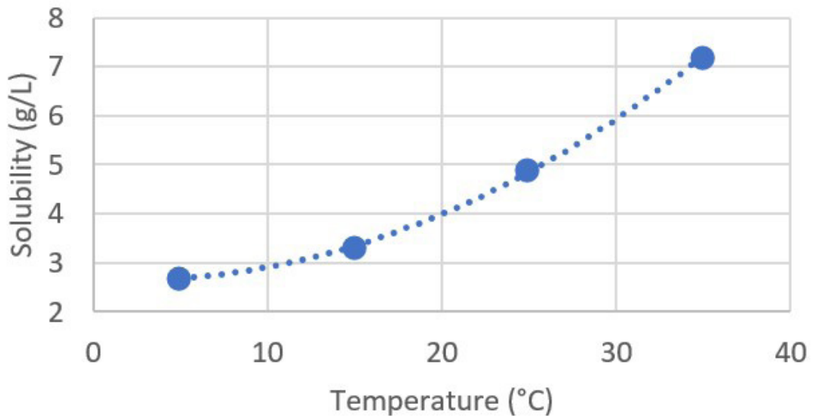
Stability

Kifunensine is a stable, crystalline compound. We recommend storing it in dry conditions at ambient temperature or below.

Our ongoing stability studies have shown kifunensine to be stable for at least four years at 25˚C in 60% relative humidity. (These are the formal ICH stability conditions).

Solubility

Kifunensine is soluble to 50 mM (11 g/L) in water with gentle warming as it is slow to dissolve.



About GlycoFineChem & GlycoSyn

Kifunensine is one of more than 50 products manufactured and sold by GlycoFineChem and/or GlycoSyn to scientists worldwide. We can provide milligram quantities for laboratory trials right through to the kilogram-scale quantities needed for preclinical and clinical drug development programmes. We specialise in the synthesis and process development of complex molecules.

Our chemistry staff are all PhD-qualified, and we have modern facilities that enable us to manufacture a wide range of products at various scales.
Please contact us if you would like to find out more about our contract manufacturing service.

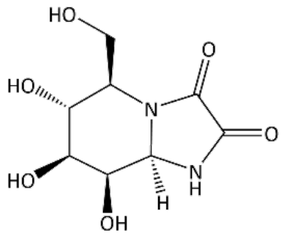
GlycoSyn

Discovery, development and GMP manufacturing arm of Callaghan Innovation www.glycosyn.com

Related Products

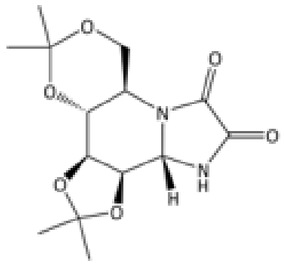
epi-Kifunensine

Rare isomer of kifunensine



Kifunensine diacetonide

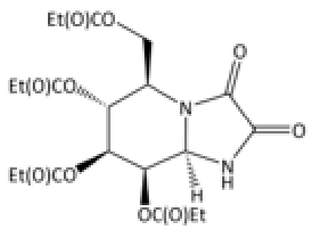
Synthetic building block



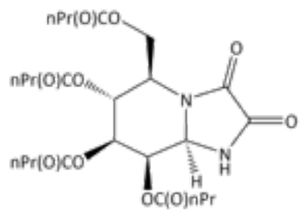
Ester derivatives

The most potent mannosidase I inhibitors in cellular assays described to date.[13,14,15] The propionate ester demonstrated a 50-fold higher potency and the butyrate ester a 75 fold higher potency compared to kifunensine due to their increased lipophilicity. This improved activity allows nM instead of µM concentrations to be used.

Perpropanoyl kifunensine



Perbutanoyl kifunensine



Kifunensine Reference Standards

Assay Standard

Used to determine Potency (%w/w) and confirm Identification by LC-UV retention time (minutes). GRM036

Chromatographic Marker

Used for determination of system suitability and retention time of named impurities
(i.e. epi-kifunensine). GRM128

References

1 https://en.wikipedia.org/wiki/Kifunensine

2 Iwami, M.; Nakayama, O.; Terano, H.; Kohsaka, M.; Aoki, H.; Imanaka, H., A new immunomodulator, FR-900494: taxonomy, fermentation, isolation, and physico-chemical and biological characteristics. J. Antibiot. (Tokyo) 1987, 40 (5), 612-22. https://doi.org/10.7164/antibiotics.40.612

3 Kayakiri, H.; Takase, S.; Shibata, T.; Okamoto, M.; Terano, H.; Hashimoto, M.; Tada, T.; Koda, S., Structure of kifunensine, a new immunomodulator isolated from an actinomycete. J. Org. Chem. 1989, 54 (17), 4015-4016. https://doi.org/10.1021/jo00278a003

4 Elbein, A. D.; Tropea, J. E.; Mitchell, M.; Kaushal, G. P., Kifunensine, a potent inhibitor of the glycoprotein processing mannosidase I. J. Biol. Chem. 1990, 265 (26), 15599-15605. https://doi.org/10.1016/S0021-9258(18)55439-9

5 Elbein, A. D.; Kerbacher, J. K.; Schwartz, C. J.; Sprague, E. A., Kifunensine inhibits glycoprotein processing and the function of the modified LDL receptor in endothelial cells. Archiv. Biochem. Biophys. 1991, 288 (1), 177-184. https://doi.org/10.1016/0003-9861(91)90181-H

6 McPherson, J. M.; Edmunds, T.; Zhou, Q. Antibody-based therapeutics with enhanced ADCC activity. U.S. Patent 8,071,336, issued 6 December 2011.

7 Daniel, P. F. High mannose proteins and methods of making high mannose proteins. U.S. Patent 7,138,262, issued 21 November 2006.

8 Dwek, R.; Rudd, P.; Ritchie, G.; Scanlan, C.; Crispin, M. Mannose immunogens for HIV-1. U.S. Patent Application 11/376,549, filed 9 November 2006.

9 Kong, L.; Sheppard, N. C.; Stewart-Jones, G. B. E.; Robson, C. L.; Chen, H.; Xu, X.; Krashias, G.; Bonomelli, C.; Scanlan, C. N.; Kwong, P. D.; Jeffs, S. A.; Jones, I. M.; Sattentau, Q. J., Expression-System-Dependent Modulation of HIV-1 Envelope Glycoprotein Antigenicity and Immunogenicity. J. Mol. Biol. 2010, 403 (1), 131-147. https://doi.org/10.1016/j.jmb.2010.08.033

10 Tareen, S. U.; Kelley-Clarke, B.; Nicolai, C. J.; Cassiano, L. A.; Nelson, L. T.; Slough, M. M.; Vin, C. D.; Odegard, J. M.; Sloan, D. D.; Van Hoeven, N.; Allen, J. M.; Dubensky, T. W., Jr.; Robbins, S. H., Design of a Novel Integration-deficient Lentivector Technology That Incorporates Genetic and Posttranslational Elements to Target Human Dendritic Cells. Mol. Ther. 2014, 22 (3), 575-587. https://doi.org/10.1038/mt.2013.278

11 Chang, V. T.; Crispin, M.; Aricescu, A. R.; Harvey, D. J.; Nettleship, J. E.; Fennelly, J. A.; Yu, C.; Boles, K. S.; Evans, E. J.; Stuart, D. I.; Dwek, R. A.; Jones, E. Y.; Owens, R. J.; Davis, S. J., Glycoprotein Structural Genomics: Solving the Glycosylation Problem. Structure 2007, 15 (3), 267-273. https://doi.org/10.1016/j.str.2007.01.011

12 Benjes, P. A.; Jarvis, A. N.; Evans, G. B.; Painter, G. F.; Dickison, J. A.; Mitchell, A.; Clinch, K. Process for preparing kifunensine intermediate and kifunensine therefrom. U.S. Patent 7,129,355, issued 31 October 2006. Assigned to Callaghan Innovation (GlycoSyn).

13 Kurhade, S. E.; Weiner, J. D.; Gao, F. P.; Farrell, M. P., Functionalized High Mannose-Specific Lectins for the Discovery of Type I Mannosidase Inhibitors. Angew. Chem. Int. Ed. 2021, 60 (22), 12313-12318. https://doi.org/10.1002/anie.202101249

14 Huang, A.; Kurhade, S. E.; Ross, P.; Apley, K. D.; Griffin, J. D.; Berkland, C. J.; Farrell, M. P., Disrupting N-Glycosylation Using Type I Mannosidase Inhibitors Alters B-Cell Receptor Signaling. ACS Pharmacology & Translational Science 2022, 5 (11), 1062-1069. https://doi.org/10.1021/acsptsci.2c00153

15 Farrell, M.P.; Kurhade, S.E.; Ross, P.A.; Weiner, J.D.; Gao, F.P. Kifunensine derivatives. Patent WO2022159781 A1, licensed by GlycoSyn.

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