

Product Data Sheet

Product Name: NF-56-EJ40

Cat. No.: GC38934

Chemical Properties

Cas. No. 2380230-73-7

SMILES O=C(NC1=C(CC(O)=O)C=CC=C1)C2=CC=CC(C3=CC=C(CN4CCN(C)CC4)C=C3)=C2

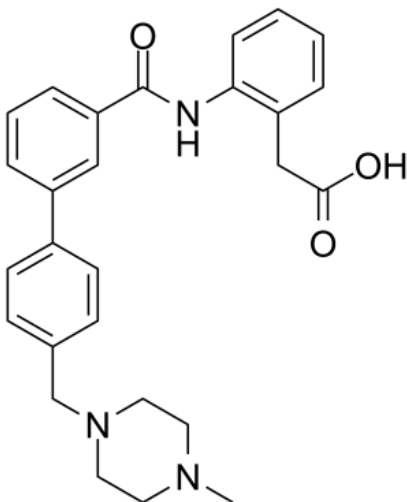
Formula C27H29N3O3 M.Wt 443.54

Solubility DMSO: 5 mg/mL (11.27 mM); Water: Storage Store at -20°C
4.55 mg/mL (10.26 mM; ultrasonic
and adjust pH to 9 with NaOH)

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

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell experiment [1]:

Cell lines intestinal epithelial cells (IECs)

IECs were plated in six-well plates and transferred to a 37°C incubator to let them attach to treatment with 5μM NF-56-EJ40 for 24 hours. Subsequently, Preparation Method IECs were stimulated with lipopolysaccharide (LPS) and then treated with the NF-56-EJ40 for 24 hours, followed by detection of the levels of inflammatory factors in IECs.

Reaction
Conditions 5μM; 24h

Applications The levels of IL-1β, IL-6, IL-10, and TNF-α were significantly increased in the LPS group. After the treatment of NF-56-EJ40, the expression of IL-1β, IL-6, IL-10, and TNF-α in IECs was decreased compared with the LPS group.

References:

[1] Huo L, Chen Q, Jia S, et al. Gut microbiome promotes succinate-induced ulcerative colitis by enhancing glycolysis through SUCNR1/NF-κB signaling pathway. *Am J Physiol Cell Physiol*. Published online June 23, 2025.

Background

NF-56-EJ40, a succinate receptor (SUCNR1) antagonist, blocks succinate's effect on promoting Treg numbers in CD4⁺ T cells isolated from healthy donor PBMCs with an IC₅₀ value of 0.025μM^[1-2]. NF-56-EJ40 enters SUCNR1 between TM-I and -II and does not unlock the extracellular loop (ECL)-2b^[3].

In vitro, after 24 hours of treatment with NF-56-EJ40 (5μM) in lipopolysaccharide (LPS)-stimulated intestinal epithelial cells (IECs), the expression of IL-1β, IL-6, IL-10, and TNF-α in IECs was decreased^[4]. The enteroids were pre-treated with 5μM NF-56-EJ40 for 30 minutes, and then cultured with 1mM succinate for 48 hours, resulting in a significant decrease in the promoting effects

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of succinate on the protein levels of leucine-rich repeat containing G protein-coupled receptor 5 (LGR5) and proliferating cell nuclear antigen protein (PCNA)^[5]. NF-56-EJ40 (4μM; 24h) treatment could significantly interrupt succinate/IL-1β signal in human umbilical vein endothelial cells (HUVECs) and macrophages^[6].

References:

- [1] Sinéad Kinsella, Colton W Smith, Kelly McKenna, et al. Elevated Metabolite Secretion Facilitates a Treg-Mediated Immunosuppressive Microenvironment in the Solid Tumor. *BLOOD*. 2023; 142 (Supplement 1): 3458.
- [2] Haffke M, Fehlmann D, Rummel G, et al. Structural basis of species-selective antagonist binding to the succinate receptor. *Nature*. 2019;574(7779):581-585.
- [3] Shenol A, Lückmann M, Trauelsen M, et al. Molecular dynamics-based identification of binding pathways and two distinct high-affinity sites for succinate in succinate receptor 1/GPR91. *Mol Cell*. 2024;84(5):955-966.e4.
- [4] Huo L, Chen Q, Jia S, et al. Gut microbiome promotes succinate-induced ulcerative colitis by enhancing glycolysis through SUCNR1/NF-κB signaling pathway. *Am J Physiol Cell Physiol*. Published online June 23, 2025.
- [5] Luo D, Zou M, Rao X, et al. Lactobacillus salivarius metabolite succinate enhances chicken intestinal stem cell activities via the SUCNR1-mitochondria axis. *Poult Sci*. 2025;104(2):104754.
- [6] Xu J, Zheng Y, Zhao Y, et al. Succinate/IL-1β Signaling Axis Promotes the Inflammatory Progression of Endothelial and Exacerbates Atherosclerosis. *Front Immunol*. 2022;13:817572.

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