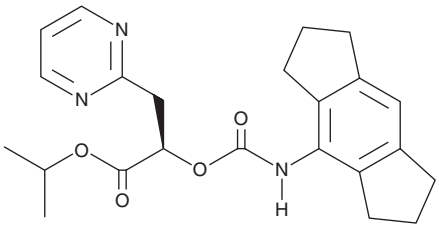
PRODUCT INFORMATION

NT-0796

Item No. 41237

CAS Registry No.:	2272917-13-0
Formal Name:	(αR)-α-[[[(1,2,3,5,6,7-hexahydro-s-indacen-4-yl)amino]carbonyl]oxy]-2-pyrimidinepropanoic acid, 1-methylethyl ester
MF:	$C_{23}H_{27}N_3O_4$
FW:	409.5
Purity:	≥98%
Supplied as:	A 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

NT-0796 is supplied as a solid. A stock solution may be made by dissolving the NT-0796 in the solvent of choice, which should be purged with an inert gas. NT-0796 is slightly soluble (0.1-1 mg/ml) in acetonitrile and sparingly soluble (1-10 mg/ml) in DMSO.

Description

NT-0796 is an inhibitor of the NOD-like receptor protein 3 (NLRP3) inflammasome and a prodrug form of NDT-19795.[1] It selectively inhibits NLRP3 over NLR family CARD domain-containing protein 4 (NLRC4) at 3 nM, as well as a panel of 121 other receptors at 10 µM, but does inhibit the serotonin (5-HT) receptor subtype 5-HT_{2B} by 90% at 10 µM. NT-0796 inhibits LPS- and ATP-induced IL-1β release in isolated human peripheral blood mononuclear cells (PBMCs) and whole blood (IC_{50}s = 0.32 and 6.8 nM, respectively), however, it does not affect LPS-induced TNF-α or IL-6 release in isolated human PBMCs (IC_{50}s = >2 µM for both), indicating NLRP3 selectivity. It decreases body weight, food intake, and plasma levels of total cholesterol, HDL, and proprotein convertase subtilisin kexin type 9 (PCSK9) in a model of high-fat diet-induced obesity using transgenic mice expressing human carboxylesterase-1 (CES1), the enzyme that converts NT-0796 to NDT-19795, when administered at a dose of 100 mg/kg three times per day.[2]

References

1. Harrison, D., Billinton, A., Bock, M.G., *et al.* Discovery of clinical candidate NT-0796, a brain-penetrant and highly potent NLRP3 inflammasome inhibitor for neuroinflammatory disorders. *J. Med. Chem.* **66(21)**, 14897-14911 (2023).
2. Thornton, P., Reader, V., Digby, Z., *et al.* Reversal of high fat diet-induced obesity, systemic inflammation, and astrogliosis by the NLRP3 inflammasome inhibitors NT-0249 and NT-0796. *J. Pharmacol. Exp. Ther.* **388(3)**, 813-826 (2024).

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