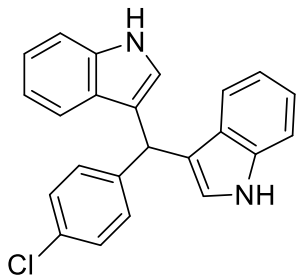
Product data sheet

MedKoo Cat#: 522683 Name: C-DIM12 CAS#: 178946-89-9 Chemical Formula: $C_{23}H_{17}ClN_2$ Exact Mass: 356.108 Molecular Weight: 356.853	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
C-DIM12 is a novel synthetic activator of Nurr1. C-DIM12 induces dopaminergic gene expression and protects against 6-hydroxydopamine neurotoxicity in vitro. C-DIM12 activates Nurr1 in cancer cells and prevents loss of dopaminergic neurons in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) model of PD in mice. C-DIM12 induced expression of Nurr1-regulated genes that was abolished by Nurr1 knockdown. C-DIM12 increased expression of transfected human Nurr1, induced Nurr1 protein expression in primary dopaminergic neurons and enhanced neuronal survival from exposure to 6-OHDA. C-DIM12 stimulates neuroprotective expression Nurr1-regulated genes in DA neurons.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	100	280.23

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.80 mL	14.01 mL	28.02 mL
5 mM	0.56 mL	2.80 mL	5.60 mL
10 mM	0.28 mL	1.40 mL	2.80 mL
50 mM	0.06 mL	0.28 mL	0.56 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Hammond SL, Safe S, Tjalkens RB. A novel synthetic activator of Nurr1 induces dopaminergic gene expression and protects against 6-hydroxydopamine neurotoxicity in vitro. Neurosci Lett. 2015 Oct 21;607:83-89. doi: 10.1016/j.neulet.2015.09.015. Epub 2015 Sep 14. PMID: 26383113; PMCID: PMC4631643.

2. De Miranda BR, Popichak KA, Hammond SL, Jorgensen BA, Phillips AT, Safe S, Tjalkens RB. The Nurr1 Activator 1,1-Bis(3'-Indolyl)-1-(p-Chlorophenyl)Methane Blocks Inflammatory Gene Expression in BV-2 Microglial Cells by Inhibiting Nuclear Factor κB. Mol Pharmacol. 2015 Jun;87(6):1021-34. doi: 10.1124/mol.114.095398. Epub 2015 Apr 9. PMID: 25858541; PMCID: PMC4429718.

In vivo study

1. Hammond SL, Popichak KA, Li X, Hunt LG, Richman EH, Damale PU, Chong EKP, Backos DS, Safe S, Tjalkens RB. The Nurr1 Ligand,1,1-bis(3'-Indolyl)-1-(p-Chlorophenyl)Methane, Modulates Glial Reactivity and Is Neuroprotective in MPTP-Induced

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Parkinsonism. J Pharmacol Exp Ther. 2018 Jun;365(3):636-651. doi: 10.1124/jpet.117.246389. Epub 2018 Apr 6. PMID: 29626009; PMCID: PMC5941193.

7. Bioactivity

Biological target:

C-DIM12 is Nurr1 activator that stimulates Nurr1 mediated apoptosis axis in bladder cancer cells and tumors and inhibits NF-κB–dependent gene expression in glial cells.

In vitro activity

The synthetic, phytochemical-based compound, 1,1-bis (3'-indolyl)-1-(p-chlorophenyl) methane (C-DIM12) activates Nurr1 in cancer cells and prevents loss of dopaminergic neurons in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) model of PD in mice. In the present study, we examined the capacity of C-DIM12 to induce expression of Nurr1-regulated genes in two dopaminergic neuronal cell lines (N2A, N27) and to protect against 6-hydroxydopamine (6-OHDA) neurotoxicity. C-DIM12 induced expression of Nurr1-regulated genes that was abolished by Nurr1 knockdown. C-DIM12 increased expression of transfected human Nurr1, induced Nurr1 protein expression in primary dopaminergic neurons and enhanced neuronal survival from exposure to 6-OHDA. These data indicate that C-DIM12 stimulates neuroprotective expression Nurr1-regulated genes in DA neurons.

Reference: Neurosci Lett. 2015 Oct 21;607:83-89. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26383113/

In vivo activity

Pharmacokinetic analysis of C-DIM12 in mice by liquid chromatography-mass spectrometry demonstrated that approximately three times more compound concentrated in the brain than in plasma. Mice treated with four doses of MPTP + probenecid over 14 days were monitored for neurobehavioral function, loss of dopaminergic neurons, and glial activation. C-DIM12 protected against the loss of DA neurons in the substantia nigra pars compacta and DA terminals in the striatum, maintained a ramified phenotype in microglia, and suppressed activation of astrocytes. In vitro reporter assays demonstrated that C-DIM12 was an effective activator of Nurr1 transcription in neuronal cell lines. Computational modeling of C-DIM12 binding to the three-dimensional structure of human Nurr1 identified a high-affinity binding interaction with Nurr1 at the coactivator domain. Taken together, these data suggest that C-DIM12 is an activator of Nurr1 that suppresses glial activation and neuronal loss in vivo after treatment with MPTP, and that this receptor could be an efficacious target for disease modification in individuals with Parkinson's disease and related disorders.

Reference: J Pharmacol Exp Ther. 2018 Jun;365(3):636-651. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/29626009/