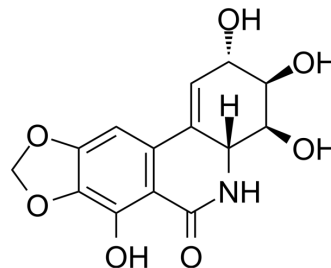


## Narciclasine

<b>Cat. No.:</b>	HY-16563		
<b>CAS No.:</b>	29477-83-6		
<b>Molecular Formula:</b>	C <sub>14</sub> H <sub>13</sub> NO <sub>7</sub>		
<b>Molecular Weight:</b>	307.26		
<b>Target:</b>	ROCK		
<b>Pathway:</b>	Cell Cycle/DNA Damage; Cytoskeleton; Stem Cell/Wnt; TGF-beta/Smad		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 26 mg/mL (84.62 mM)  
 \* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	3.2546 mL	16.2729 mL	32.5457 mL
	5 mM	0.6509 mL	3.2546 mL	6.5091 mL
	10 mM	0.3255 mL	1.6273 mL	3.2546 mL

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: ≥ 1.67 mg/mL (5.44 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
 Solubility: ≥ 1.67 mg/mL (5.44 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
 Solubility: ≥ 1.67 mg/mL (5.44 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Narciclasine is a plant growth modulator. Narciclasine modulates the Rho/Rho kinase/LIM kinase/cofilin signaling pathway, greatly increasing GTPase RhoA activity as well as inducing actin stress fiber formation in a RhoA-dependent manner.

#### IC<sub>50</sub> & Target

ROCK

#### In Vitro

Narciclasine activates Rho and stress fibers in glioblastoma multiforme cells. The mean IC<sub>50</sub> of ~50 nM calculated on the 6

human glioblastoma multiforme (U373, Hs683, GL19, GL5, GL16, GL17), The mean IC<sub>50</sub> value of 47 nM for Narciclasine across a panel of 60 cancer cell lines<sup>[1]</sup>. Bioassay-guided fractionation of the A. belladonna extract resulted in the identification of lycorine as the bio-active compound. The IC<sub>50</sub> measured for radicle growth inhibition is 0.1 μM for Narciclasine<sup>[2]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

The i.v. regimen of Narciclasine at 1 mg/kg significantly (P=0.02) increases the survival of GL19 glioblastoma multiforme-bearing mice. Narciclasine when given orally at the same dose five times a week for 5 consecutive weeks also significantly increases animal survival in this model (P=0.008). Oral treatment with Narciclasine at 1 mg/kg significantly increases the survival (P=0.004) of Hs683 glioblastoma multiforme-bearing mice. Increasing the number of doses administered per week does not increase the survival of these Hs683 glioblastoma multiforme-bearing mice. Narciclasine appears to show similar increased survival in these models to temozolomide but at appreciable lower doses and following both oral and i.v. administration<sup>[1]</sup>.

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## PROTOCOL

#### Kinase Assay <sup>[1]</sup>

The RhoA G-LISA assay is used. The assay uses a 96-well plate coated with the Rho binding domain of Rho family effector proteins. The active GTP-bound form of the Rho family protein but not the inactive GDP-bound form from biological samples will bind to the plate. Bound active Rho family protein is then detected by incubation with a specific primary antibody followed by a secondary antibody conjugated to horseradish peroxidase. The signal is then developed using OPD. U373 and GL19 glioblastoma multiforme cells are serum starved for 24 h and left untreated or treated with Narciclasine (100 nM) for 3 min, 5 min, 30 min, 1 h, and 2 h or treated with 2.0 μg/mL of the cell-permeable Rho inhibitor for 4 h in serum-free medium at 37°C with and without subsequent Narciclasine treatment. This product consists of highly purified C3 transferase covalently linked to a proprietary cell-penetrating moiety via a disulfide bond. The cell-penetrating moiety allows rapid and efficient transport through the plasma membrane. Once in the cytosol, the cell-penetrating moiety is released, thereby allowing C3 transferase to freely diffuse intracellularly and inactive RhoA, RhoB, and RhoC but not related GTPases such as Cdc42 or Rac1. C3 transferase inhibits Rho proteins by ADP ribosylation on Asn<sup>41</sup> in the effector binding domain of the GTPase. Cells are then lysed and RhoA activity is measured by the RhoA G-LISA Activation Assay or alternatively cells are stained for F-actin<sup>[1]</sup>.

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#### Cell Assay

Cell<sup>[1]</sup>The Narciclasine IC<sub>50</sub> concentration, the Narciclasine concentration that decreased by 50% the global growth rate of a given cell population, is assessed with the MTT assay. The cells are incubated for 72 h in the presence and absence of the Narciclasine (with concentrations ranging between 10<sup>-9</sup> and 10<sup>-5</sup> M concentrate) for the determination of Narciclasine IC<sub>50</sub> values<sup>[1]</sup>.

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#### Animal Administration <sup>[1]</sup>

Mice<sup>[1]</sup>

The Hs683 cell line and GL19 primoculture grafted into the brains of nude immunodeficient mice both produced invasive brain tumors. Xenograft-bearing mice receive vehicle alone, oral temozolomide at 40 mg/kg (5 administrations per week for 5 consecutive weeks), or Narciclasine at 1 mg/kg either oral (once per week for 5 weeks) or i.v. (twice per week for 5 weeks). Drug administration is initiated respectively on days 5 and 7 post-tumor grafting for the Hs683 and GL19 models. The temozolomide dose and treatment schedule are selected based on previous optimized regimens. Narciclasine dose and treatment schedule are selected based on Narciclasine toxicity study in rats after oral administration and pharmacokinetic study that we have recently published. In toxicity study, Narciclasine (25, 10, or 1 mg/kg) is administered five times a week for 3 weeks and the no adverse effect level dose is defined to be 1 mg/kg/d p.o., with minimal acanthosis reactive changes and minor variations in some biochemistry parameters observed at this dose level considered to be nonadverse.

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## CUSTOMER VALIDATION

- Research (Wash D C). 2023 Aug 24.
- Clin Transl Med. 2022 Jun;12(6):e850.
- Acta Biomater. 2021 Sep 4;S1742-7061(21)00586-9.
- Bioeng Transl Med. 2023 Mar 17.
- Life Sci. 2019 Apr 15;223:54-61.

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## REFERENCES

- [1]. Lefranc F, et al. Narciclasine, a plant growth modulator, activates Rho and stress fibers in glioblastoma cells. Mol Cancer Ther. 2009 Jul;8(7):1739-50.
- [2]. Wahyuni DS, et al. The use of bio-guided fractionation to explore the use of leftover biomass in Dutch flower bulb production as allelochemicals against weeds. Molecules. 2013 Apr 17;18(4):4510-25.
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**Caution: Product has not been fully validated for medical applications. For research use only.**

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