产品名称：**Rotigotine**
产品别名：罗替戈汀 ； **N-0437; N-0923**

## 生物活性：

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| **Description** | Rotigotine (N-0437; N-0923) is a full agonist of dopamine receptor, a partial agonist of the 5-HT1A receptor, and an antagonist of the α2B-adrenergic receptor, with $K_i$s of 0.71 nM, 4-15 nM, and 83 nM for the dopamine D3 receptor and D2, D5, D4 receptors, and dopamine D1 receptor. |
| **$IC_{50}$ & Target** | Ki: 0.71 nM (dopamine D3 receptor), 4-15 nM (D2, D5, D4 receptors), 83 nM (dopamine D1 receptor)[1][2], 176 nM (α1A), 273 nM (α1B), 338 nM (α2A), 27 nM (α2B), 30 nM (5-HT1A), 86 nM (5-HT7)[2] |
| **In Vitro** | Rotigotine (N-0437; N-0923) has a 10-fold selectivity for D3 (pKi 9.2) receptors compared with D2, D4 and D5 (pKi 8.5-8.0) and a 100-fold selectivity compared with D1 receptors (pKi 7.2). In functional studies, Rotigotine behaves as full agonist at all dopamine receptors but notably the potency for stimulation of D1 receptors is similar to that for D2 and D3 receptors (pEC50 respectively: 9.0, 9.4-8.6, 9.7)[1].<br>Rotigotine (10 μM) decreases the number of THir neurons by 40% in primary mesencephalic cell culture. Rotigotine (0.01 μM) slightly protects dopaminergic neurons against MPP+ toxicity, significantly protects dopaminergic neurons against rotenone-induced cell death, and significantly inhibits ROS production by rotenone[4]. |
| **In Vivo** | In primed rats, Rotigotine (N-0437; N-0923; 0.035, 0.1 and 0.35 mg/kg) induces contralateral turning behavior in a dose dependent manner. In drug naive rats, the turning behavior induced by Rotigotine, either alone or in combination with SCH 39166, is reduced compared to primed rats[3]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO : ≥ 50 mg/mL (158.49 mM)**<br>* "≥" means soluble, but saturation unknown. |

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
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| 1 mM | 3.1699 mL | 15.8494 mL | 31.6987 mL |
| 5 mM | 0.6340 mL | 3.1699 mL | 6.3397 mL |
| 10 mM | 0.3170 mL | 1.5849 mL | 3.1699 mL |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: 3.5 mg/mL (11.09 mM); Clear solution

此方案可获得 ≥ 3.5 mg/mL (11.09 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 35.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

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| | 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)<br>Solubility: ≥ 3.5 mg/mL (11.09 mM); Clear solution<br>此方案可获得 ≥ 3.5 mg/mL (11.09 mM，饱和度未知) 的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 35.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀<br><br>3.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: 3.5 mg/mL (11.09 mM); Clear solution<br>此方案可获得 ≥ 3.5 mg/mL (11.09 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 35.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **References** | [1]. Wood M, et al. Rotigotine is a potent agonist at dopamine D1 receptors as well as at dopamine D2 and D3 receptors. Br J Pharmacol. 2015 Feb;172(4):1124-35.<br>[2]. Scheller D, et al. The in vitro receptor profile of rotigotine: a new agent for the treatment of Parkinson's disease. Naunyn Schmiedebergs Arch Pharmacol. 2009 Jan;379(1):73-86.<br>[3]. Fenu S, et al. In vivo dopamine agonist properties of rotigotine: Role of D1 and D2 receptors. Eur J Pharmacol. 2016 Oct 5;788:183-91.<br>[4]. Radad K, et al. Neuroprotective effect of rotigotine against complex I inhibitors, MPP+ and rotenone, in primary mesencephalic cell culture. Folia Neuropathol. 2014;52(2):179-86. |

**实验参考：**

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| **Animal Administration** | Primed rats: Two weeks after the 6-OHDA lesions, rats are primed with apomorphine (0.5 mg/kg s.c.). Rats showing less than 150 contralateral rotations during the 1 h testing period are excluded from the study. Three days after priming, rats are divided into different experimental groups and treated with different doses of the dopamine receptor agonists (Rotigotine or pramipexole) alone or in combination with dopamine $D_1$ (SCH 39166) or $D_2$(eticlopride) receptor antagonists as reported: saline+Rotigotine (0.035 mg/kg s.c., n=9; 0.1 mg/kg s.c., n=9; 0.35 mg/kg s.c., n=8); SCH 39166 (0.1 mg/kg s.c.)+Rotigotine (0.035 mg/kg s.c., n=5; 0.1 mg/kg s.c., n=7; 0.35 mg/kg s.c., n=5); eticlopride (0.1 mg/kg s.c.) + Rotigotine (0.1 mg/kg s.c., n=5; 0.35 mg/kg s.c., n=5); Saline+pramipexole (0.035 mg/kg s.c., n=5; 0.1 mg/kg s.c., n=12; 0.35 mg/kg s.c., n=7); SCH 39166 (0.1 mg/kg s.c.)+pramipexole (0.035 mg/kg s.c., n=5; 0.1 mg/kg s.c., n=6; 0.35 mg/kg s.c., n=6); eticlopride (0.1 mg/kg s.c.)+pramipexole (0.1 mg/kg s.c., n=7; 0.35 mg/kg s.c., n=5). [3] |
| **Kinase Assay** | Binding assays are performed in 96-well polypropylene tubes in a final volume of 2 mL for D1 and D4 membranes and 1 mL for D2, D3 and D5 membranes containing: 50 μL radioligand, 10 μL drug/buffer/non-specific binding, buffer (final concentration 50 mM Tris-HCl pH 7.4, $MgCl_2$ 2 mM) and membranes (5 μg protein for D2 and D3 and 25 μg protein for D1 and D5). Following 120 min of incubation at 25°C, bound radioligand is determined by rapid vacuum filtration through A/C glass fibre filters presoaked in 0.1% polyethylenimine. The filters are washed four times with 2 mL ice-cold ishing buffer (Tris-HCl 50 mM, pH 7.4 at 4°C) and retained radioactivity is determined by liquid scintillation counting. [1] |
| | [1]. Wood M, et al. Rotigotine is a potent agonist at dopamine D1 receptors as well as at dopamine D2 and D3 receptors. Br J Pharmacol. 2015 Feb;172(4):1124-35. |

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| **References** | [2]. Scheller D, et al. The in vitro receptor profile of rotigotine: a new agent for the treatment of Parkinson's disease. Naunyn Schmiedebergs Arch Pharmacol. 2009 Jan;379(1):73-86.<br>[3]. Fenu S, et al. In vivo dopamine agonist properties of rotigotine: Role of D1 and D2 receptors. Eur J Pharmacol. 2016 Oct 5;788:183-91.<br>[4]. Radad K, et al. Neuroprotective effect of rotigotine against complex I inhibitors, MPP+ and rotenone, in primary mesencephalic cell culture. Folia Neuropathol. 2014;52(2):179-86. |