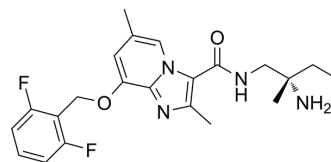


BAY-747

Cat. No.:	HY-153369
CAS No.:	1609342-18-8
Molecular Formula:	C ₂₂ H ₂₆ F ₂ N ₄ O ₂
Molecular Weight:	416.46
Target:	Guanylate Cyclase
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	BAY-747 is an orally active and brain-penetrant stimulator of soluble guanylate cyclase (sGC). BAY-747 reverses L-NAME induced memory impairments and enhances cognition of rats in the object location task (OLT). BAY-747 also decreases blood pressure in both conscious normotensive and spontaneously hypertensive rats (SHR). BAY-747 improves function of the skeletal muscle associated with Duchenne muscular dystrophy (DMD) in mdx/mTRG2 mice model ^{[1][2][3]} .									
IC₅₀ & Target	Soluble guanylate cyclase (sGC) ^[1]									
In Vitro	<p>BAY-747 (100 nM) enhances AMPA receptor dynamics in an ex vivo acquisition-like cLTP model, in combination with WS^[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Western Blot Analysis^[1]</p> <table border="1"> <tr> <td>Cell Line:</td> <td>ex vivo acquisition-like cLTP model</td> </tr> <tr> <td>Concentration:</td> <td>100 nM</td> </tr> <tr> <td>Incubation Time:</td> <td></td> </tr> <tr> <td>Result:</td> <td>Increased the phosphorylation levels of S845 on GluA1.</td> </tr> </table>		Cell Line:	ex vivo acquisition-like cLTP model	Concentration:	100 nM	Incubation Time:		Result:	Increased the phosphorylation levels of S845 on GluA1.
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Concentration:	100 nM									
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Result:	Increased the phosphorylation levels of S845 on GluA1.									
In Vivo	<p>BAY-747 shows a brain to plasma ratio of 0.6 ± 2.0 at the investigated time frame, reflecting a relatively high brain penetration of 60%^[1].</p> <p>BAY-747 (0.03-1.0 mg/kg, 2 mL/kg; po; 30 min before T1 in a 24 h interval OLT) enhance long-term memory acquisition processes in rat object location task (OLT) model, and also attenuates L-NAME induced short-term memory impairments. BAY-747 does not affect GluA1-containing AMPAR dynamics in the hippocampus^[1].</p> <p>BAY-747 (0.003-0.3 mg/kg; po; single dose) decreases blood pressure in rats, and also (3 mg/kg; po; once daily for 35 days) increases body weight of rats in L-NAME-Treated Renin Transgenic model^[2].</p> <p>BAY-747 (150 mg/kg of food; po; 16 weeks) improves grip strength and running speed in male mdx/mTRG2 mice, suggesting improved skeletal muscle function^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tr> <td>Animal Model:</td> <td>Rat object location task (OLT) model^[1]</td> </tr> </table>		Animal Model:	Rat object location task (OLT) model ^[1]						
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Dosage:	0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg
Administration:	PO; 30 min before T1 in a 24 h interval OLT
Result:	Resulted significantly higher long-term memory performance at 0.03, 0.1, 0.3 and 1.0 mg/kg dose, 30 min before T1. Attenuated L-NAME induced short-term memory impairments at 0.3 mg/kg and 1 mg/kg. Did not enhance GluA1 trafficking at 1 mg/kg 24 h after treatment.
Animal Model:	Anesthetized, conscious spontaneously hypertensive and conscious normotensive rats ^[2]
Dosage:	0 mg/kg, 0.003 mg/kg, 0.01 mg/kg, 0.03 mg/kg, 0.1 mg/kg, and 0.3 mg/kg
Administration:	IV; single dose
Result:	Produced a dose-dependent and long-lasting decrease in blood pressure in rats.
Animal Model:	L-NAME-Treated Renin Transgenic Rats ^[2]
Dosage:	0.3 mg/kg, 3 mg/kg
Administration:	PO; once daily for 35 days; L-NAME treatment: 30 mg/kg, po, for 6 days
Result:	Resulted a significant weight gain among rats. Led to a dose-dependent increase of plasma cGMP. Decreased blood pressure only at 3 mg/kg.

REFERENCES

- [1]. Nelissen E, et al. The sGC stimulator BAY-747 and activator runcaciguat can enhance memory in vivo via differential hippocampal plasticity mechanisms. *Sci Rep.* 2022 Mar 4;12(1):3589.
- [2]. Vakalopoulos A, et al. New Generation of sGC Stimulators: Discovery of Imidazo[1,2-a]pyridine Carboxamide BAY 1165747 (BAY-747), a Long-Acting Soluble Guanylate Cyclase Stimulator for the Treatment of Resistant Hypertension. *J Med Chem.* 2023 Apr 11.
- [3]. Krishnan SM, et al. Assessing the Use of the sGC Stimulator BAY-747, as a Potential Treatment for Duchenne Muscular Dystrophy. *Int J Mol Sci.* 2021 Jul 27;22(15):8016.

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

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