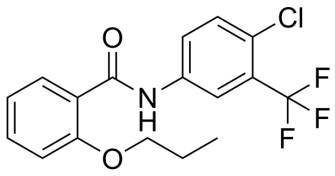
TTK21

Cat. No.:	HY-116673
CAS No.:	709676-56-2
Molecular Formula:	$C_{17}H_{15}ClF_3NO_2$
Molecular Weight:	357.75
Target:	Histone Acetyltransferase
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (279.52 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7952 mL	13.9762 mL	27.9525 mL
	5 mM	0.5590 mL	2.7952 mL	5.5905 mL
	10 mM	0.2795 mL	1.3976 mL	2.7952 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TTK21 is an activator of the histone acetyltransferases CBP/p300. TTK21 passes the blood–brain barrier, induces no toxicity, and reaches different parts of the brain when conjugated to glucose-based carbon nanosphere (CSP). TTK21 has beneficial implications for the brain functions of neurogenesis and long-term memory[1].CSP-TTK21 can ameliorate Aβ-impaired long-term potentiation (LTP). CSP-TTK21 may enhance the transcription of genes that promote synaptic health and cognitive function[2]. CSP-TTK21 is orally effective and leads to improvements in motor functions, histone acetylation dynamics in a spinal injury rat model[3].

IC_{50} & Target

CBP/p300

In Vitro

TTK21 (50-275 μM) is able to concentration-dependently activate CBP and p300 acetyltransferases and increase histone acetylation. Effectively activates CBP/p300 activity and increases the acetylation of histone H3 and H4. 100 μM TTK21 can promote the self-acetylation of p300[1].

TTK21 (50-275 μM; 6-24 h) in Hela cells, can't effectively penetrate the cell membrane to enter the cell by itself. However, when combined with carbon nanosphere CSP, it is able to enter SH-SY5Y neuronal cells and significantly increase the acetylation level of histone H3, indicating that the CSP-TTK21 complex has the ability to penetrate the cell membrane[1].
CSP-TTK21 (0.36 μg/ml; 1 h) can restor protein synthesis-dependent long-term potentiation (LTP) damage caused by Aβ (1-42) multimerst[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[2]

Cell Line:	Rat hippocampal CA1 area slices
Concentration:	CSP-TTK21 0.36 μg/ml
Incubation Time:	1 h
Result:	CSP-TTK21 upregulated certain genes whose expression was decreased under Aβ(1–42) treatment, such as genes involved in the Wnt signaling pathway. CSP-TTK21 also potentially downregulated genes associated with inflammation, helping to reduce the neuroinflammatory response caused by Aβ(1–42).

In Vivo

CSP-TTK21 (20 mg/kg; i.p.; single dose) can extend the memory duration[1].
CSP-TTK21 (20 mg/kg; p.o; single dose) enhances long-term potentiation comparably to intraperitoneal injection, suggesting effective memory enhancement in Wild-type mice[3].
CSP-TTK21 (10 mg/kg; p.o; weekly) promotes motor recovery after spinal cord injury in rats, and enhances the expression of regeneration-associated genes in the prefrontal cortex and cerebellum following spinal cord injury[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	B57BL/6J male [1]
Dosage:	CSP-TTK21; 20 mg/kg; single dose
Administration:	i.p.
Result:	Increased histone acetylation significantly in the hippocampus and frontal cortex. CSP-TTK21 crossed the blood-brain barrier and was primarily detected in the brain, liver, and spleen. It promoted differentiation of newly generated neurons in the dentate gyrus. Mice with CSP-TTK21 displayed a persistent memory of the platform location in a Morris water maze task for a longer period compared to controls, demonstrating enhanced long-term memory.

Animal Model:	Wild-type mice [3]
Dosage:	CSP-TTK21; 20 mg/kg; single dose
Administration:	p.o.
Result:	The administered compound crossed the blood-brain barrier, induced histone acetylation specifically H4K12ac and H3K14ac marks in the hippocampus, and did not alter basal synaptic transmission. It was found to enhance long-term potentiation comparably to intraperitoneal injection, suggesting effective memory enhancement through oral delivery.

Animal Model:	rats with spinal cord injury[3]

Dosage:	CSP-TTK21; 10 mg/kg; weekly
Administration:	p.o.
Result:	Rats with CSP-TTK21 showed significant improvement in locomotion and rearing activity compared to controls. Histone acetylation was notably increased in the spinal cord, suggesting enhanced gene expression linked to regeneration and functional recovery. Enhanced histone acetylation levels (H4K12ac, H3K27ac, H3K9ac) were observed in the prefrontal cortex and cerebellum of rats with CSP-TTK21, indicating active epigenetic modifications that support neuronal regeneration and functional recovery.

REFERENCES

[1]. Singh A et al. Glucose derived carbon nanosphere (CSP) conjugated TTK21, an activator of the histone acetyltransferases CBP/p300, ameliorates amyloid-beta 1-42 induced deficits in plasticity and associativity in hippocampal CA1 pyramidal neurons. Aging Cell. 2022 Sep;21(9):e13675.

[2]. Singh A, et al. Oral administration of a specific p300/CBP Lysine acetyltransferase activator induces synaptic plasticity and repairing spinal cord injury[J]. bioRxiv, 2023: 2023.10. 04.560982.

[3]. Chatterjee S, et al. A novel activator of CBP/p300 acetyltransferases promotes neurogenesis and extends memory duration in adult mice. J Neurosci. 2013;33(26):10698-10712.

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