NCS-382

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Proteins

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Description	NCS-382 is a potent GABA r	receptor antagonist and also a GHBR receptor antagonist. NCS-382 has anticonvulsant and 382 is used in the related research of hereditary nervous system diseases ^{[1][4]} .
In Vitro	NCS-382 (0.5 nM, 24 h) shows no capacity for inhibition of microsomal CYPs (CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6 and 3A4) and minimal potential for activation of xenobiotic nuclear receptors in HepG2 cells ^[2] . NCS-382 (0.01-1000 μM, 24 h) shows low probability of cellular toxicity in HepG2 cells ^[2] . NCS-382 is a GHBR antagonist with IC ₅₀ s of 134.1 nM and 201.3 nM in isolated rat striatum and hippocampus membranes, respectively ^[4] . MCE has not independently confirmed the accuracy of these methods. They are for reference only. Cell Cytotoxicity Assay ^[2]	
	Cell Line: Concentration: Incubation Time:	HepG2 cells 0.01-1000 μM 24 h
	Result:	Reduced HepG2 cell viability at a concentration of 1 mM, and this same concentration did not induce apoptosis or cytotoxicity in HepG2 cells.
In Vivo	the brain and 10 times that in mouse model ^[1] . At a dose of 500 mg/kg, it m At a dose of 500 mg/kg, bra NCS-382 (0.83-2.08 mmol/k indicating anti-sedative act NCS-382 (2.3 mmol/kg; i.p.) a rat model of petit mal epi	of mouse serum and tissue at a dose of 100mg/kg ^[1]



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Product Data Sheet

-	Tissue	Dose (mg/kg)	AUC (µg•h/L)	C _{max} (μmol/L)	T _{1/2} (h)
5	Serum	100	119	241	0.243
	Brain	100	139	60	0.967
	Liver	100	1150	1695	/
ł	Kidney	100	24.5	23.6	0.308

Pharmacokinetic analysis of mouse serum and tissue at a dose of 300mg/kg $^{\left[1\right] }$

Tissue	Dose (mg/kg)	AUC (µg•h/L)	C _{max} (μmol/L)	T _{1/2} (h)
Serum	300	436	374	0.468
Brain	300	313	141	0.883
Liver	300	/	/	/
Kidney	300	/	/	/

Pharmacokinetic analysis of mouse serum and tissue at a dose of 500mg/kg $^{[1]}$

Tissue	Dose (mg/kg)	AUC (µg•h/L)	C _{max} (µmol/L)	T _{1/2} (h)
Serum	500	717	451	0.683
Brain	500	1280	530	0.761
Liver	500	/	/	/
Kidney	500	/	/	/

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

Animal Model:	GBL induced mouse model ^[1]
Dosage:	300 mg/kg(Combined with diclofenac (25 mg/kg))
Administration:	Intraperitoneal injection (i.p.), Thirty minutes later, mice were given an i.p. injection of GBL (100 mg/kg diluted in PBS)
Result:	In the presence of diclofenac, it was highly protective against GBL mediated responses.

Animal Model:	GBL induced mouse model ^[3]
Dosage:	0.83, 1.25, 1.66, 2.08mmol/kg
Administration:	Intraperitoneal injection (i.p.), 30 min before the test
Result:	At a dosage of 2.08 mmol/kg, completely blocked the effect of GHB when administered at 3.18 mmol/kg

REFERENCES

[1]. Ainslie GR, et al. A pharmacokinetic evaluation and metabolite identification of the GHB receptor antagonist NCS-382 in mouse informs novel therapeutic strategies for the treatment of GHB intoxication. Pharmacol Res Perspect. 2016 Oct 18;4(6):e00265.

[2]. Vogel KR, et al. In vitro toxicological evaluation of NCS-382, a high-affinity antagonist of γ-hydroxybutyrate (GHB) binding. Toxicol In Vitro. 2017 Apr;40:196-202

[3]. Schmidt C, et al. Anti-sedative and anti-cataleptic properties of NCS-382, a gamma-hydroxybutyrate receptor antagonist. Eur J Pharmacol. 1991 Oct 22;203(3):393-7.

[4]. Maitre M, Hechler V, Vayer P, Gobaille S, Cash CD, Schmitt M, Bourguignon JJ. A specific gamma-hydroxybutyrate receptor ligand possesses both antagonistic and anticonvulsant properties. J Pharmacol Exp Ther. 1990 Nov;255(2):657-63.

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

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