## NCS-382

| Cat. No.:HY-101207CAS No.:520505-01-5Molecular Formula: $C_{13}H_{14}O_3$ Molecular Weight:218.25Target:GABA ReceptorPathway:Membrane Transporter/Ion Channel; Neuronal SignalingStorage:Please store the product under the recommended conditions in the Certificate of Analysis. | HO OH |
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| Description      | NCS-382 is a potent GABA re<br>antisedative activity. NCS-3  | eceptor antagonist and also a GHBR receptor antagonist. NCS-382 has anticonvulsant and 82 is used in the related research of hereditary nervous system diseases <sup>[1][4]</sup> .  |
| 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 <sup>[2]</sup> .         NCS-382 (0.01-1000 μM, 24 h) shows low probability of cellular toxicity in HepG2 cells <sup>[2]</sup> .         NCS-382 is a GHBR antagonist with IC <sub>50</sub> s of 134.1 nM and 201.3 nM in isolated rat striatum and hippocampus membranes, respectively <sup>[4]</sup> .         MCE has not independently confirmed the accuracy of these methods. They are for reference only.         Cell Cytotoxicity Assay <sup>[2]</sup> Cell Line:       HepG2 cells         Concentration:       0.01-1000 μM         Incubation Time:       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          | NCS-382 (100, 300, 500 mg/l<br>the brain and 10 times that<br>in mouse model <sup>[1]</sup> .<br>At a dose of 500 mg/kg, it m<br>At a dose of 500 mg/kg, brai<br>NCS-382 (0.83-2.08 mmol/kg<br>indicating anti-sedative acti<br>NCS-382 (2.3 mmol/kg; i.p.)<br>a rat model of petit mal epil<br>Pharmacokinetic analysis o   | kg; i.p.) shows at a dose of 100 mg/kg has a maximum serum concentration that is 4 times that of<br>of the kidney, and a maximum liver concentration that is more than 700% higher than the serum<br>hay preferentially reside in the liver after intraperitoneal administration in mouse model <sup>[1]</sup> .<br>in permeability improves, as evidenced by an increase in brain serum ratio in mouse model <sup>[1]</sup> .<br>g; i.p.) reduces GHB-induced increases in the time mice spent immobile in the forced swim test,<br>ivity, when administered at doses of 1.66 and 2.08 mmol/kg in mice model <sup>[3]</sup> .<br>decreases spike and wave discharges in audiogenic seizure-susceptible Swiss Rb mice, as well as<br>lepsy <sup>[4]</sup> .<br>f mouse serum and tissue at a dose of 100mg/kg <sup>[1]</sup> |
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# Product Data Sheet

| Tissue | Dose (mg/kg) | AUC (µg•h/L) | C <sub>max</sub> (µmol/L) | T <sub>1/2</sub> (h) |
|--------|--------------|--------------|---------------------------|----------------------|
| Serum  | 100          | 119          | 241                       | 0.243                |
| Brain  | 100          | 139          | 60                        | 0.967                |
| Liver  | 100          | 1150         | 1695                      | /                    |
| Kidney | 100          | 24.5         | 23.6                      | 0.308                |

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

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| Tissue | Dose (mg/kg) | AUC (µg•h/L) | C <sub>max</sub> (μmol/L) | T <sub>1/2</sub> (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  $^{[1]}$ 

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| Tissue | Dose (mg/kg) | AUC (µg•h/L) | C <sub>max</sub> (μmol/L) | T <sub>1/2</sub> (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 <sup>[1]</sup>  |
|-----------------|---|
| 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 <sup>[3]</sup>   |
|-----------------|--|
| 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 a 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  $\gamma$ -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.

 Tel: 609-228-6898
 Fax: 609-228-5909
 E-mail: tech@MedChemExpress.com

 Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA