

Product Data Sheet

Product Name: A-867744

Cat. No.: GC15014

Chemical Properties

Cas. No. 1000279-69-5

Chemical Name 4-[5-(4-chlorophenyl)-2-methyl-3-propanoylpyrrol-1-yl]benzenesulfonamide

SMILES CCC(=O)C1=C(N(C(=C1)C2=CC=C(C(=C2)Cl)C3=CC=C(C(=C3)S(=O)(=O)N)C

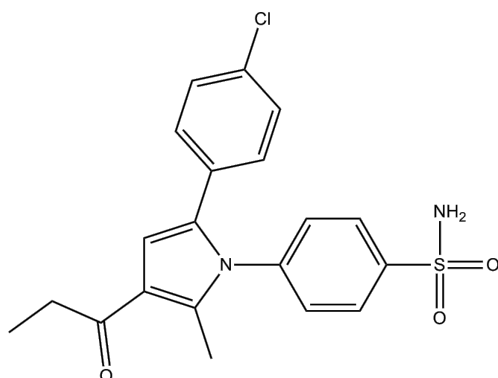
Formula $C_{20}H_{19}ClN_2O_3S$ M.Wt 402.89

Solubility DMF: 30 mg/ml, DMF:PBS (pH 7.2) (1:4): 0.20 mg/ml, DMSO: 10 mg/ml Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

Targeting $\alpha 7$ neuronal acetylcholine receptors (nAChRs) with selective agonists and positive allosteric modulators (PAMs) is considered a therapeutic approach for managing cognitive deficits in schizophrenia and Alzheimer's disease. A-867744 is a novel type II PAM with good potency and selectivity.

In vitro: In oocytes expressing $\alpha 7$ nAChRs, A-867744 potentiated acetylcholine (ACh)-evoked currents, with an EC₅₀ value of about 1 μ M. At highest concentrations of A-867744 tested, ACh-

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evoked currents were essentially nondecaying. At lower concentrations, no evidence of a distinct secondary component was evident in contrast to 4-naphthalen-1-yl-3a,4,5,9b-tetrahydro-3H-cyclopent-a[c]quinoline-8-sulfonic acid amide (TQS), another type II $\alpha 7$ PAM [1].

In vivo: A-867744 was assessed for its PK properties in rat, dog, and monkey. The animal pharmacokinetic profile of A-867744 was characterized by relatively low plasma clearance values (1.1-2.5 L/h/kg) and volumes of distribution (1.7-4.6 L/kg) across species, with terminal elimination half-lives in the 1.0-1.7 h. The bioavailability is 83% in rat and somewhat lower in dog (55%) and monkey (68%). These findings indicated that A-867744 showed acceptable pharmacokinetic profile across species and brain levels sufficient to modulate $\alpha 7$ nAChRs [2].

Clinical trial: A-867744 is currently in the preclinical development stage and no clinical data are available.

Reference:

[1] Malysz J, Grønlien JH, Anderson DJ, Håkerud M, Thorin-Hagene K, Ween H, Wetterstrand C, Briggs CA, Faghih R, Bunnelle WH, Gopalakrishnan M.

In vitro pharmacological characterization of a novel allosteric modulator of alpha 7 neuronal acetylcholine receptor, 4-(5-(4-chlorophenyl)-2-methyl-3-propionyl-1H-pyrrol-1-yl) (A-867744), exhibiting unique pharmacological profile. *J Pharmacol Exp Ther.* 2009;330(1):257-67.

[2] Faghih R, Gopalakrishnan SM, Gronlien JH, Malysz J, Briggs CA, Wetterstrand C, Ween H, Curtis MP, Sarris KA, Gfesser GA, El-Kouhen R, Robb HM, Radek RJ, Marsh KC, Bunnelle WH, Gopalakrishnan M. Discovery of 4-(5-(4-chlorophenyl)-2-methyl-3-propionyl-1H-pyrrol-1-yl) benzenesulfonamide (A-867744) as a novel positive allosteric modulator of the alpha7 nicotinic acetylcholine receptor. *J Med Chem.* 2009;52(10):3377-84.

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