Product Data Sheet

Chemical Properties

Product Name: MK-0974
Cas No.: 781649-09-0
M.Wt: 566.54
Formula: C26H27F5N6O3
Synonyms: Telcagepant; MK0974; MK 0974

Chemical Name: N-([(3R,6S)-6-(2,3-difluorophenyl)-2-oxo-1-(2,2,2-trifluoroethyl)azepan-3-yl]-4-(2-oxo-3H-imidazo[4,5-b]pyridin-1-yl)piperidine-1-carboxamide

Canonical SMILES: C1CC(C(=O)N(CC1C2=C(C(=CC=C2)F)F)CC(F)(F)NC(=O)N3CCC(CC3)N4C5=C(NC4=O)N=CC=C5

Solubility: Soluble in DMSO
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.

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

Biological Activity

Targets: Neuroscience
Pathways: CGRP
Description:
MK-0974 (Telcagepant) is a highly potent, selective, and orally bioavailable antagonist of CGRP receptor with IC50 value of 0.77 nM [1].

Calcitonin gene-related peptide (CGRP) receptor is a heteromeric transmembrane receptor composed of a G protein-coupled receptor which is called calcitonin receptor-like receptor (CALCRL) and a receptor activity modifying protein 1 (RAMP1). CGRP receptor is functional for mediating the activity of CGRP, which is widely distributed in human peripheral and central neuron system. The CGRP/CGRP receptor signaling pathway modulate a variety of physiological functions of respiratory, immune and cardiovascular system, and play a key role in the pathophysiology of migraine headache.

When binding study was carried out, it was found MK-0974 had high affinity for CGRP receptor but had no affinity for related human adrenomedullin receptors, which suggested the high specificity of MK-0974 [1]. In human HEK293 cells expressing CGRP receptor, treatment of MK-0974 resulted in potent blockage of α-CGRP-stimulated cAMP production, which indicated a significant inhibition of CGRP receptor activity. However, addition of 50% human serum reduced the inhibition potency of MK-0974 by 5-fold [1]. MK-0974 displayed reversible and saturable binding to both SK-N-MC membranes and rhesus cerebellum with a Kd of 1.9 nM and 1.3 nM, respectively [2].

In rhesus model, capsaicin-induced release of endogenous CGRP resulted in dermal vasodilation. Following treatment of MK-0974 produced a dose-dependent inhibition of dermal vasodilation, with plasma concentrations of 127 and 994 nM required to block 50 and 90% of the blood flow increase, respectively. The suppression of CGRP function indicated the inhibition of CGRP receptor by MK-0974 [1]. In monkey model, MK-0974 showed moderate clearance (14-20 ml min⁻¹ kg⁻¹), while oral bioavailability was 6%. The pharmacokinetics of MK-0974 remained linear across 0.5-10 mg kg⁻¹ intravenous dose in monkeys, but the oral area under the plasma concentration-time curve (AUC) increase (5-30 mg kg⁻¹) was 15-fold over dose-proportional [3].

Reference:

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes
shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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