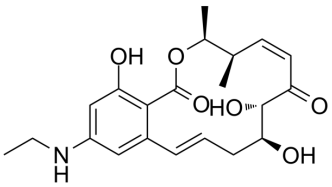
E6201

Cat. No.:	HY-15496
CAS No.:	603987-35-5
Molecular Formula:	$C_{21}H_{27}NO_6$
Molecular Weight:	389.44
Target:	MEK; FLT3
Pathway:	MAPK/ERK Pathway; Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

E6201 (ER-806201) is an ATP-competitive dual kinase inhibitor of MEK1 and FLT3. E6201 inhibits MEK1- induced ERK2 phosphorylation with an IC_{50} value of 5.2 nM, MKK4-induced JNK phosphorylation with an IC_{50} value of 91 nM, and MKK6-induced p38 MAPK phosphorylation with an IC_{50} value of 19 nM. Anti-tumor and anti-psoriasis efficacy[1][2].

IC_{50} & Target

MEK1
5.2 nM (IC_{50})

In Vitro

E6201 is an inhibitor of MEKK1 and MEK families but not the MAPK family. E6201 inhibits MEKK1- induced phosphorylation of MEK1, MKK4, and MKK6 with IC_{50} values of 31, 522, and 65 nM, respectively. E6201 has no effect on other MAPK family enzymes such as ERK2, JNKs, and p38 MAPK at 10 μM[1].

E6201 inhibits LPS-induced TNF transcription with an IC_{50} value of 50±14 nM, but does not suppress β-actin transcription at 3 μM and only slightly at 10 μM[1].

E6201 inhibits the receptor tyrosine kinases VEGFR2, PDGFR, hepatocyte growth factor receptor, and EGFR with IC_{50} values of 350, 860, 1100, and 5400 nM, respectively, as well as the nonreceptor tyrosine kinase Syk with an IC_{50} value of 460 nM. E6201 does not inhibit ZAP-70 or IKK at 10 μM or PKC activity at 100 μM[1].

E6201 inhibits IL-2 production 48 h after stimulation with the T-cell mitogen PHA-P, with an IC_{50} value of 18 nM[1].

E6201 inhibits the proliferation of EGF-stimulated human keratinocytes with an IC_{50} value of 160 nM[1].

E6201 suppresses IL-8 production in human keratinocytes 24 h after stimulation with IL-1α or TNFα, with IC_{50} values of 60 and 30 nM, respectively[1].

E6201 inhibits TNFα, IL-1, IL-6, and IL-8 production from human PBMCs with IC_{50} values of 20, 16, 52, and 53 nM, respectively[1].

E6201 (0.08-20.0 μM) significantly inhibited triple-negative breast cancer (TNBC) cell proliferation and anchorage-independent colony formation in a dose-dependent manner[2].

E6201 (1 μM) inhibits expression of phospho-ERK and induces G1 phase cell cycle arrest, and apoptosis in TNBC[2].

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

Cell Viability Assay[2]

Cell Line:	Human TNBC cell lines BT20, HCC70, MDA-MB-231, HCC1806, HCC1937, SUM149 and SUM159
Concentration:	0.00, 0.08, 0.16, 0.31, 0.63, 1.25, 2.50, 5.00, 10.0, 20.0 μM
Incubation Time:	5 days

Result:	Inhibited TNBC cell proliferation and anchorage-independent colony formation in a dose-dependent manner.

Western Blot Analysis[3]

Cell Line:	Human TNBC cell lines BT20, HCC70, MDA-MB-231, HCC1806, HCC1937, SUM149 and SUM159
Concentration:	1 μM
Incubation Time:	0, 1, 24 hours
Result:	pERK expression level showed a rapid (apparent by 1 hour) and sustained (still apparent at 24 hours) decrease in the tested TNBC cell lines following treatment.

In Vivo

E6201 (30 mg/kg; administered via tail vein injection three times per week) inhibits TNBC xenograft tumor growth. E6201 strongly inhibits pERK and Ki-67 expression in xenograft tumor tissues[2].

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

Animal Model:	Female Nod.Scid gamma mice (age 4 to 6 weeks old) bearing MDA-MB-231-LM2 xenograft tumors[2]
Dosage:	30 mg/kg
Administration:	Administered via tail vein injection three times per week for 17 days
Result:	Compared with mice treated with vehicle control, the E6201-treated mice showed 60% tumor growth suppression.

REFERENCES

[1]. Masaki Goto, et al. E6201 [(3S,4R,5Z,8S,9S,11E)-14-(ethylamino)-8, 9,16-trihydroxy-3,4-dimethyl-3,4,9,19-tetrahydro-1H-2-benzoxacyclotetradecine-1,7(8H)-dione], a novel kinase inhibitor of mitogen-activated protein kinase/extracellular signal-regulated kinase kinase (MEK)-1 and MEK kinase-1: in vitro characterization of its anti-inflammatory and antihyperproliferative activities. J Pharmacol Exp Ther. 2009 Nov;331(2):485-95.

[2]. Jangsoon Lee, et al. Anti-tumor and anti-metastasis efficacy of E6201, a MEK1 inhibitor, in preclinical models of triple-negative breast cancer. Breast Cancer Res Treat. 2019 Jun;175(2):339-351.

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