Ertiprotafib

Cat. No.: HY-19383

CAS No.: 251303-04-5

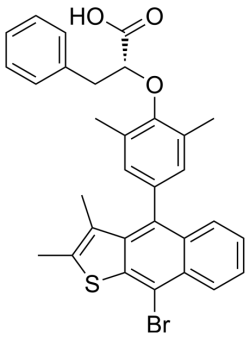
Molecular Formula: $C_{31}H_{27}BrO_3S$

Molecular Weight: 559.51

Target: Phosphatase; IKK; PPAR

Pathway: Metabolic Enzyme/Protease; NF-κB; Cell Cycle/DNA Damage

Storage: 4°C, sealed storage, away from moisture and light
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (178.73 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7873 mL	8.9364 mL	17.8728 mL
	5 mM	0.3575 mL	1.7873 mL	3.5746 mL
	10 mM	0.1787 mL	0.8936 mL	1.7873 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (4.47 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ertiprotafib is an inhibitor of PTP1B, IkB kinase β (IKK-β), and a dual PPARα and PPARβ agonist, with an IC_{50} of 1.6 μM for PTP1B, 400 nM for IKK-β, an EC_{50} of ~1 μM for PPARα/PPARβ.

IC_{50} & Target

PTP1B	IKK-β	PPARα	PPARβ
1.6 μM (IC_{50})	400 nM (IC_{50})	~1 μM (EC50)	~1 μM (EC50)

In Vitro

Ertiprotafib is a potent inhibitor of IKK-β, with an IC_{50} value of 400±40 nM, which is much lower than that required for the half-maximal inhibition of the p-nitrophenyl phosphatase activity of PTP1B. The reported IC_{50} value of Ertiprotafib against PTP1B ranges from 1.6 to 29 μM depending on the assay conditions[2]. Ertiprotafib is at least a dual PPARα and PPARβ agonist with EC_{50} values for transactivation of 1 μM. Such activities readily explain the observations with suprapharmacologic doses of these[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	As seen with treatment of ob/ob mice, both Ertiprotafib and compound 3 seem to significantly improve glucose metabolism in rats. At 25 mg/kg/day, these compounds decrease both fasting blood glucose and insulin levels compared with vehicle treated rats. Furthermore, both Ertiprotafib and compound 3 increase glucose disposal after an oral challenge. It is noteworthy that lipid levels are also reduced in treated animals. Both triglyceride and free fatty acid levels are substantially reduced in rats treated with 25 mg/kg/day of either compound. To summarize, both Ertiprotafib and compound 3 seem to be robust agents in improving glucose utilization in fa/fa rats while also decreasing lipid levels in these animals. Decreased lipid levels may be unexpected for a pure PTP1b inhibitor. It is more telling, as mentioned above, that rats treated with suprapharmacologic doses of Ertiprotafib show signs of PPAR family activation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice, Rats[2] Male Ob/ob mice and Zucker fa/fa rats are used. They are kept on a 12-h/12-h light/dark cycle and fed Rodent Diet 5001 (for mice and rats) from Purina Mills. Compounds are dosed orally by gavage in an aqueous suspension of 2% Tween 80 and 0.5% methylcellulose. Whole blood (5 μL) is used for glucose readings via tail nick for measurement using the Ascensia Elite XL glucometer and glucose strips by preloading a strip into the meter and touching the end to a small drop of blood on each tail. Insulin levels are quantified by enzyme-linked immunosorbent assay[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Shrestha S, et al. PTP1B inhibitor Ertiprotafib is also a potent inhibitor of IkappaB kinase beta (IKK-beta). Bioorg Med Chem Lett. 2007 May 15;17(10):2728-30. Epub 2007 Mar 3.

[2]. Erbe DV, et al. Ertiprotafib improves glycemic control and lowers lipids via multiple mechanisms. Mol Pharmacol. 2005 Jan;67(1):69-77.

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