Tolimidone

Cat. No.: HY-59047

CAS No.: 41964-07-2

Molecular Formula: $C_{11}H_{10}N_2O_2$

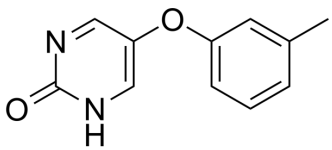
Molecular Weight: 202.21

Target: Src

Pathway: Protein Tyrosine Kinase/RTK

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 150 mg/mL (741.80 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.9454 mL	24.7268 mL	49.4535 mL
5 mM	0.9891 mL	4.9454 mL	9.8907 mL
10 mM	0.4945 mL	2.4727 mL	4.9454 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 (12.36 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (12.36 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (12.36 mM); Clear solution; Need warming

BIOLOGICAL ACTIVITY

Description

Tolimidone is a potent and selective allosteric activator of Lyn kinase with an EC_{50} of 63 nM.

IC_{50} & Target

EC50: 63 nM (Lyn kinase)[1]

In Vitro

Incubation of Tolimidone (MLR-1023) with Lyn kinase elicits a repeatable 50% increase in enzyme activity. Tolimidone elicits a concentration-dependent increase in Lyn kinase activation with a 2.3- and 2.1-fold increase achieved at concentrations of 3 and 10 μM, respectively. Inclusion of Tolimidone (100 μM) increases Lyn kinase activity by 3-fold at each ATP concentration

	tested (V_{max}=2601 U/mg). Tolimidone-mediated activation of Lyn kinase increases in proportion to the length of preincubation period in the absence of ATP[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Administration of Tolimidone (MLR-1023) (30 mg/kg i.p.) significantly ($p<0.05$) lowers blood glucose levels to 148 and 158 mg/dL, 30 and 90 min after administration, respectively. Tolimidone significantly increases adipocyte differentiation and adiponectin production by 3.7- and 19-fold, respectively[1]. Tolimidone elicits a dose-dependent potentiation of the insulin response, with a maximal effect observed with a dose level of 30 mg/kg[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	For each kinase assay, Tolimidone (MLR-1023) (10 μM) is preincubated with kinase and fluoroscein-labeled protein substrate. The reaction is initiated with the addition of ATP (at a concentration at or below the K_m for each kinase), and the level of fluoroscein phosphopeptide is measured. The assays are conducted in duplicate[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Adipocyte differentiation is assessed in mouse 3T3-L1 cells after 8 days of incubation with Tolimidone (MLR-1023) or rosiglitazone (10 μM). PPAR (α, σ and γ) transactivation studies are conducted in transiently transfected cells containing the appropriate DNA constructs (pGAL4/PPARα, σ or γ) cotransfected with a luciferase reporter vector. Tolimidone or an appropriate reference compound is incubated with transfected cells for 24 h. Luciferase activity is monitored as a measure of PPARα, σ and γ activation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Male mice, 8 to 10 weeks of age, are used in studies of baseline glucose, glucose tolerance, and insulin levels. Tolimidone (MLR-1023) is administered intraperitoneally at dose volumes of 5 to 10 mL/kg. Blood (5 μL) is acquired from a tail snip and directly applied to a glucose test strip. Blood levels of Tolimidone are measured by liquid chromatography/tandem mass spectrometry, and levels are determined by comparing them with a standard curve of Tolimidone prepared in blood[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Can J Cardiol. 2020 May 16;S0828-282X(20)30456-6.
- FASEB J. 2020 Oct;34(10):13586-13596.
- Food Chem Toxicol. 2020 Jan;135:110924.

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REFERENCES

[1]. Saporito MS, et al. MLR-1023 is a potent and selective allosteric activator of Lyn kinase in vitro that improves glucose tolerance in vivo. J Pharmacol Exp Ther. 2012 Jul;342(1):15-22.

[2]. Ochman AR, et al. The Lyn kinase activator MLR-1023 is a novel insulin receptor potentiator that elicits a rapid-onset and durable improvement in glucose homeostasis in animal models of type 2 diabetes. J Pharmacol Exp Ther. 2012 Jul;342(1):23-32.

Caution: Product has not been fully validated for medical applications. For research use only.

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