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产品名称：Tolimidone
产品别名： MLR-1023

生物活性：

Description	Tolimidone is a potent and selective allosteric activator of Lyn kinase with an EC50 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].
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].

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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (12.36 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (12.36 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

	Solubility: ≥ 2.5 mg/mL (12.36 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (12.36 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: 2.5 mg/mL (12.36 mM); Clear solution; Need warming 此方案可获得 2.5 mg/mL (12.36 mM)的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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].
Animal Administration	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].
Kinase Assay	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 Km for each kinase), and the level of fluoroscein phosphopeptide is measured. The assays are conducted in duplicate[1].
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.