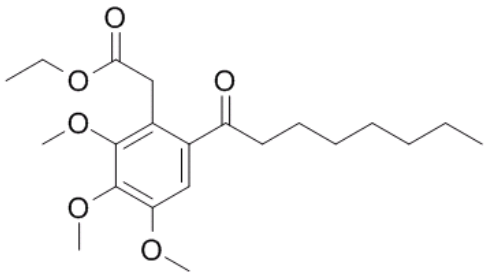
Product Data Sheet

Product Name: TMPA
Cat. No.: GC30015

Chemical Properties

Cas. No.	1258275-73-8		
SMILES	COC1=C(CC(OCC)=O)C(C(CCCCCCC)=O)=CC(OC)=C1OC		
Formula	$C_{21}H_{32}O_6$	M.Wt	380.48
Solubility	DMSO : ≥ 100 mg/mL (262.83 mM);Water : < 0.1 mg/mL (insoluble)	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.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			



Protocol

Cell experiment [1]:

Cell lines L02 cells

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Preparation Method	The human liver cell line (L02) was cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS), 100 units of penicillin, and 100μg/ml streptomycin. Cells were treated with 10μM TMPA for 1h, and the amount of AMPKα phosphorylation was determined by western blot.
Reaction Conditions	10μM; 1h
Applications	TMPA increased the phosphorylation of AMPK in hepatic L02 cells.

Animal experiment [2]:

Animal models	Male C57BL/KsJ-Lepr^{db}/Lepr^{db} (*db/db*) mice
Preparation Method	Male C57BL/KsJ-Lepr^{db}/Lepr^{db} (*db/db*) mice were randomly divided into three groups. One group of mice was injected intraperitoneally with TMPA once daily at a dose of 50mg/kg for 19 days. The remaining groups were injected with metformin (250mg/kg) or vehicle (DMSO) as positive and negative controls. Mice were fasted for 18h prior to measurement of blood glucose. Mouse blood glucose was measured every 4 days. After 19 days of treatment, mice were intraperitoneally injected with D-glucose (1g/kg) for a glucose tolerance test.
Dosage form	50mg/kg/day for 19 days; tail vein injection
Applications	TMPA treatment reduced blood glucose and improved glucose tolerance in diabetic mice.

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References:
[1] Li L, Liu Y, Chen H, et al. Impeding the interaction between Nur77 and p38 reduces LPS-induced inflammation[J]. Nature chemical biology, 2015, 11(5): 339-346.
[2] Zhan Y, Chen Y, Zhang Q, et al. The orphan nuclear receptor Nur77 regulates LKB1 localization and activates AMPK[J]. Nature chemical biology, 2012, 8(11): 897-904.

Background

TMPA, a Nur77 antagonist, prevents the binding of Nur77 and LKB1 as well as stimulates LKB1 transport to the cytosol and phosphorylation [1]. The binding of TMPA to Nur77 decreases the stability of Nur77-LKB1 complex by inducing an open-close motion of Nur77 and thereby facilitates the solvation of the interface region[2]. TMPA has been widely used in diabetic mouse models to regulate blood glucose levels[3].

In vitro, TMPA treatment at 10μM for 1 hour increased the phosphorylation of AMPK in hepatic L02 cells [4]. Treatment of mouse bone marrow-derived mast cells (BMMCs) with 10μM TMPA for 6 hours increased phosphorylation of LKB1 and AMPK and concomitantly reduced IgE/Ag-induced degranulation and eicosanoid production, which inhibited FcεRI-mediated mast cell signaling[5]. Treatment with 10μM TMPA for 18h significantly increased TNFα-induced IL-6 production in HeLa cells[6]. Pretreatment of HepG2 cells with 10μM TMPA for 6 hours reduced lipid accumulation after free fatty acid (FFA) stimulation[7].

In vivo, Intraperitoneal injection of TMPA (50mg/kg/day) once daily for 19 days significantly reduced insulin levels, lowered blood glucose, and improved glucose tolerance in diabetic mice[8].

References:
[1] Wu L, Chen L. Characteristics of Nur77 and its ligands as potential anticancer compounds[J]. Molecular medicine reports, 2018, 18(6): 4793-4801.
[2] Rungsung I, Rajagopalan M, Ramaswamy A. Molecular dynamics study of TMPA mediated dissociation of Nur77-LKB1 complex[J]. Computational Biology and Chemistry, 2018, 76: 67-78.
[3] Safe S. Natural products and synthetic analogs as selective orphan nuclear receptor 4A (NR4A) modulators[J]. Histology and histopathology, 2023, 39(5): 543.

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[4] Li L, Liu Y, Chen H, et al. Impeding the interaction between Nur77 and p38 reduces LPS-induced inflammation[J]. Nature chemical biology, 2015, 11(5): 339-346.
[5] Jin F, Li X, Deng Y, et al. The orphan nuclear receptor NR4A1 promotes FcεRI-stimulated mast cell activation and anaphylaxis by counteracting the inhibitory LKB1/AMPK axis[J]. Allergy, 2019, 74(6): 1145-1156.
[6] Huang B, Pei H Z, Chang H W, et al. The E3 ubiquitin ligase Trim13 regulates Nur77 stability via casein kinase 2α[J]. Scientific reports, 2018, 8(1): 13895.
[7] Wang X, Li G, Guo C, et al. Ethyl 2-[2, 3, 4-Trimethoxy-6-(1-Octanoyl) Phenyl] acetate (Tmpa) ameliorates lipid accumulation by disturbing the combination of Lkb1 with Nur77 and activating the ampk pathway in Hepg2 cells and mice primary hepatocytes[J]. Diabetes, Metabolic Syndrome and Obesity, 2021: 4165-4177.
[8] Zhan Y, Chen Y, Zhang Q, et al. The orphan nuclear receptor Nur77 regulates LKB1 localization and activates AMPK[J]. Nature chemical biology, 2012, 8(11): 897-904.

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