Product Data Sheet

Product Name: Arhalofenate (MBX 102)
Cat. No.: GC31462

Chemical Properties

Cas. No.	24136-23-0		
SMILES	O=C(OCCNC(C)=O)[C@@H](C1=CC=C(Cl)C=C1)OC2=CC=CC(C(F)(F)F)=C2		
Formula	$C_{19}H_{17}ClF_3NO_4$	M.Wt	415.79
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	Arhalofenate (MBX 102)		

Protocol

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Animal experiment:

Male ZDF rats at 8 wk of age are used in the assay. ZDF rats are single housed and allowed access ad libitum to tap water and chow. ZDF rats are screened into three groups with similar mean plasma glucose levels. ZDF rats are cannulated in the jugular vein and the carotid artery and are allowed to recover at least for 2 d. Rats are dosed with either vehicle or Arhalofenate (MBX 102) (100 mg/kg) by oral gavage for 4-7 d. On the day of the clamp experiment, rats are dosed and food is withdrawn 1 h later. After rats are fasted for 4 h, blood samples are taken from the carotid catheter to measure basal glucose and insulin levels. Experiments are initiated with a priming injection (0.5 mL/rat of 5 μCi/mL of d-[3-3H] glucose) and initiation of a constant infusion of d-[3-3H] glucose tracer (8 μCi/mL) at a rate of 10 μL/min for 60 min. After the 1-h tracer-equilibration period, a post-tracer blood sample is collected for glucose, insulin and d-[3-3H] glucose specific activity (SA) measurements. Infusion of tracer glucose is then discontinued, and insulin infusion is initiated (10 μL/min equivalent to 40 mU/kg/min) along with glucose infusion. The glucose infusion rate is adjusted empirically to achieve plasma glucose level at 150 mg/dL ± 5% within the next 1.5-2 h. To facilitate this process, blood samples are collected at 10-min intervals for immediate plasma glucose measurements using a glucometer until the end of the study. Clamp is defined by three consecutive glucose measurements that are within the above defined range. Samples (300-400 μL) at the three time points (10-min interval) are collected for glucose, insulin, and d-[3-3H] glucose SA measurements.

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References:

[1]. Gregoire FM, et al. MBX-102/JNJ39659100, a novel peroxisome proliferator-activated receptor-ligand with weak transactivation activity retains antidiabetic properties in the absence of weight gain and edema. Mol Endocrinol. 2009 Jul;23(7):975-88.
[2]. Chandalia A, et al. MBX-102/JNJ39659100, a novel non-TZD selective partial PPAR-γ agonist lowers triglyceride independently of PPAR-α activation. PPAR Res. 2009;2009:706852.

Background

Arhalofenate is an orally bioavailable prodrug form of the free acid form of a peroxisome proliferator-activated receptor γ (PPARγ) partial agonist.[1] It is converted to the active

free acid form by nonspecific serum esterases. Arhalofenate has weak PPARγ transactivation activity in a reporter assay but strong transrepression activity, reducing LPS-induced chemokine (C-C motif) ligand 2 (CCL2) secretion in isolated mouse peritoneal macrophages. It reduces fasting plasma glucose levels in *ob/ob* mouse and Zucker diabetic fatty (ZDF) rat models of type 2 diabetes when administered at doses of 125 and 100 mg/kg, respectively. It also decreases fasting free fatty acid, triglyceride, and cholesterol levels in ZDF rats without increasing body weight when administered at a dose of 100 mg/kg.[2] Arhalofenate (250 mg/kg) prevents leukocyte and neutrophil infiltration and IL-1β, IL-6, and chemokine (C-X-C motif) ligand 1 (CXCL1) production in air pouch fluid in a mouse model of gout.[3]

1.Gregoire, F.M., Zhang, F., Clarke, H.J., et al.MBX-102/JNJ39659100, a novel peroxisome proliferator-activated receptor-ligand with weak transactivation activity retains antidiabetic properties in the absence of weight gain and edemaMol. Endocrinol.23(7)975-988(2009) 2.Chandalia, A., Clarke, H.J., Clemens, L.E., et al.MBX-102/JNJ39659100, a novel non-TZD selective partial PPAR-γ agonist lowers triglyceride independently of PPAR-α activationPPAR Res.706852(2009) 3.McWherter, C., Choi, Y.-J., Serrano, R.L., et al.Arhalofenate acid inhibits monosodium urate crystal-induced inflammatory responses through activation of AMP-activated protein kinase (AMPK) signalingArthritis Res. Ther.20(1)204(2018)

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