

Product Data Sheet

Product Name: Febuxostat

Cat. No.: GC16319

Chemical Properties

Cas. No. 144060-53-7

Chemical Name 2-[3-cyano-4-(2-methylpropoxy)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid

SMILES CC1=C(SC(=N1)C2=CC(=C(C=C2)OCC(C)C)C#N)C(=O)O

Formula $C_{16}H_{16}N_2O_3S$ M.Wt 316.37

Solubility $\geq 15.55\text{mg/mL}$ in DMSO, ≥ 15.95 mg/mL in EtOH with ultrasonic 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.

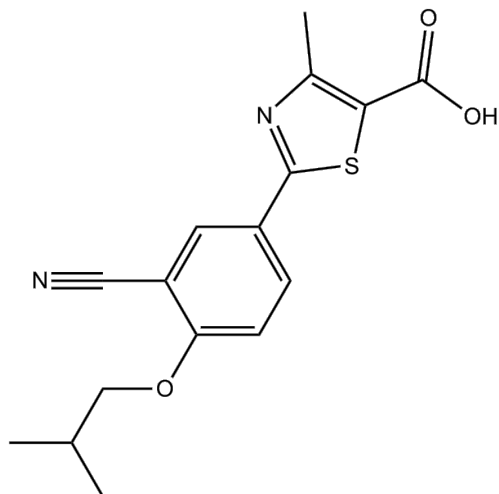
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

Cell experiment [1]:	
Cell lines	Murine bone-marrow-derived macrophages (BMDMs)
Preparation Method	Murine bone-marrow-derived macrophages were primed overnight with Pam3CSK4, exposed to Febuxostat, and stimulated with nigericin or monosodium urate crystals; interleukin-1 β , cell viability, intracellular adenosine triphosphate, and mitochondrial membrane potential were measured.

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Reaction Conditions	200μM ; 30min
Applications	Febuxostat reduced interleukin-1β secretion and cell death, preserved intracellular adenosine triphosphate and mitochondrial membrane potential, and improved mitochondrial bioenergetics in macrophages.
Animal experiment [2]:	
Animal models	Hyperuricemic 5/6-nephrectomized Sprague-Dawley rat model of cardiorenal injury
Preparation Method	Male Sprague-Dawley rats underwent 5/6 nephrectomy and received oxonic acid to establish hyperuricemic chronic kidney injury. Febuxostat was delivered in drinking water; serum uric acid, urinary protein, and cardiorenal tissue injury were assessed at the endpoint.
Dosage form	3mg/kg/day; oral intake in drinking water ; 8 weeks
Applications	Febuxostat reduced serum uric acid and proteinuria, attenuated glomerular, tubulointerstitial, and renal arteriolar injury, and reduced cardiac hypertrophy, cardiac fibrosis, and oxidative stress in renal and cardiac tissues.
References:[1] Nomura J, Kobayashi T, So A, Busso N. Febuxostat, a xanthine oxidoreductase inhibitor, decreases NLRP3-dependent inflammation in macrophages by activating the purine salvage pathway and restoring cellular bioenergetics. Sci Rep. 2019;9:17314. doi:10.1038/s41598-019-53965-x.[2] Omizo H, Tamura Y, Morimoto C, Ueno M, Hayama Y, Kuribayashi-Okuma E, et al. Cardio-renal protective effect of the xanthine oxidase inhibitor febuxostat in the 5/6 nephrectomy model with hyperuricemia. Sci Rep. 2020;10:9326. doi:10.1038/s41598-020-65706-6.	

Background

Febuxostat is a potent, selective, non-purine inhibitor of xanthine oxidase (XO) and xanthine

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dehydrogenase (XDH), with an inhibition constant (K_i) of 0.6nM against XO^[1]. Febuxostat binds the molybdenum-pterin center of oxidized and reduced xanthine oxidoreductase (XOR), suppressing hypoxanthine-to-xanthine and xanthine-to-uric-acid conversion and reducing endothelial-bound XOR-derived reactive oxygen species (ROS)^[1,4]. Febuxostat is used in research on purine and urate metabolism, macrophage inflammation, endothelial oxidative injury, atherosclerosis, and hyperuricemia-associated cardiorenal injury^[1-7].

In vitro, Febuxostat (30 μ M; 10min pretreatment followed by 100ng/mL lipopolysaccharide for 20h) reduced monocyte chemoattractant protein-1 (MCP-1) production in phorbol 12-myristate 13-acetate-differentiated THP-1 macrophages, increased mitogen-activated protein kinase phosphatase-1 (MKP-1) activity, and reduced c-Jun N-terminal kinase (JNK) phosphorylation^[2]. Febuxostat (200 μ M; 30min pretreatment followed by 2.5 μ M nigericin or 0.25mg/mL monosodium urate crystals for 2h) reduced interleukin-1 β (IL-1 β) secretion and cell death in murine bone-marrow-derived macrophages and preserved intracellular adenosine triphosphate (ATP) and mitochondrial membrane potential^[5]. Febuxostat (5 μ M and 10 μ M; 6h) reduced oxidized low-density lipoprotein-induced mitochondrial ROS production, cellular injury, and monocyte attachment in human aortic valve endothelial cells^[6].

In vivo, Febuxostat (2.5mg/kg/day; oral intake in drinking water once daily for 12 weeks) reduced aortic plaque area and arterial ROS, decreased aortic MCP-1 expression, and improved endothelial-dependent relaxation in apolipoprotein E-deficient (ApoE^{-/-}) mice fed a high-cholesterol diet^[3]. Febuxostat (approximately 3mg/kg/day; oral intake in drinking water once daily for 8 weeks) reduced serum uric acid and proteinuria, attenuated glomerular, tubulointerstitial, and renal arteriolar injury, and reduced cardiac hypertrophy and fibrosis in hyperuricemic 5/6-nephrectomized Sprague-Dawley rats^[7].

References:

- [1] Takano Y, Hase-Aoki K, Horiuchi H, Zhao L, Kasahara Y, Kondo S, et al. Selectivity of febuxostat, a novel non-purine inhibitor of xanthine oxidase/xanthine dehydrogenase. *Life Sci.* 2005;76(16):1835-1847. doi:10.1016/j.lfs.2004.10.031.
- [2] Nomura J, Busso N, Ives A, Tsujimoto S, Tamura M, So A, et al. Febuxostat, an inhibitor of xanthine oxidase, suppresses lipopolysaccharide-induced MCP-1 production via MAPK phosphatase-1-mediated inactivation of JNK. *PLoS One.* 2013;8(9):e75527. doi:10.1371/journal.pone.0075527.

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- [3] Nomura J, Busso N, Ives A, Matsui C, Tsujimoto S, Shirakura T, et al. Xanthine oxidase inhibition by febuxostat attenuates experimental atherosclerosis in mice. *Sci Rep.* 2014;4:4554. doi:10.1038/srep04554.
- [4] Malik UZ, Hundley NJ, Romero G, Radi R, Freeman BA, Tarpey MM, et al. Febuxostat inhibition of endothelial-bound XO: implications for targeting vascular ROS production. *Free Radic Biol Med.* 2011;51(1):179-184. doi:10.1016/j.freeradbiomed.2011.04.004.
- [5] Nomura J, Kobayashi T, So A, Busso N. Febuxostat, a xanthine oxidoreductase inhibitor, decreases NLRP3-dependent inflammation in macrophages by activating the purine salvage pathway and restoring cellular bioenergetics. *Sci Rep.* 2019;9:17314. doi:10.1038/s41598-019-53965-x.
- [6] Liang X, Li P, Xie W, Lin Z, Wang Z, Zeng S, et al. Febuxostat protects human aortic valve endothelial cells from oxidized low-density lipoprotein-induced injury and monocyte attachment. *J Cardiovasc Pharmacol.* 2022;80(6):861-868. doi:10.1097/FJC.0000000000001326.
- [7] Omizo H, Tamura Y, Morimoto C, Ueno M, Hayama Y, Kuribayashi-Okuma E, et al. Cardio-renal protective effect of the xanthine oxidase inhibitor febuxostat in the 5/6 nephrectomy model with hyperuricemia. *Sci Rep.* 2020;10:9326. doi:10.1038/s41598-020-65706-6.

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