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产品名称：Benoxaprofen
CAS 号：51234-28-7
产品货号：T35991

生物活性：

Description	Benoxaprofen (LRCL 3794) is a nonsteroidal anti-inflammatory agent that blocks the biosynthesis of inflammatory mediators such as leukotrienes and prostaglandins by inhibiting 5-LOX, PGH2 synthase and cytochrome P-450. Benoxaprofen exhibits significant toxicity: it not only alters cellular redox status, uncouples oxidative phosphorylation and disrupts calcium ion homeostasis, but also causes liver injury through the formation of covalent adducts between its active metabolites and hepatic proteins. Benoxaprofen shows strong phototoxicity under ultraviolet irradiation, and induces erythrocyte lysis, mast cell degranulation and histamine release. Benoxaprofen is widely used in studies of urticaria and related phototoxic mechanisms[1][2][3][4].
IC50 & Target	5-LOX
In Vitro	Benoxaprofen (0.25-2.5 mM; 10-15 min) 可与大鼠肝微粒体细胞色素 P-450 结合形成 I 型光谱复合物，并以竞争方式抑制氨基比林脱甲基作用，其 Ki 值为 0.38 mM[1]。 Benoxaprofen (0.75-1.25 mM; 2-4 h) 不会改变其在未诱导的分离大鼠肝细胞中引起的 L/P 比值升高或 ALT 释放[1]。 Benoxaprofen 可抑制 RBL-1 细胞中 A-23187 刺激的 iSRS、i12-HETE 和 PGE2 的生成，IC50 分别为 0.4 μM，0.45 μM，和 1.3 μM)[2]。 Benoxaprofen (50 μg/mL; 24 h) 在 pH 7.4、37 °C 条件下不会与人血清白蛋白形成可检测的不可逆加合物[3]。 Benoxaprofen (8 μM; 10 min, 经辐照) 可诱导人红细胞发生光溶血；与厌氧条件相比，有氧条件下溶血发生得更快、更早；在黑暗环境中则不会发生溶血[4]。 Cell Line: human erythrocytes Concentration: 8 μM Incubation Time: 10 min; irradiated Result: Induced photohemolysis of human erythrocytes in a concentration-dependent manner, with faster and earlier onset of lysis under oxygenated conditions compared to anaerobic conditions; no lysis occurs in the dark.
In Vivo	Benoxaprofen (20 mg/kg；静脉注射) 经静脉给予雄性 Sprague-Dawley 大鼠后，可在 8 h 内检测到血浆蛋白加合物，其全身 BNX-G 的 AUC0→8h 为 1.98 μg h/mL，经肝胆排泄的 BNX-G 占给药剂量的 10.8 %，而肝脏蛋白加合物仍未被检测到[3]。 Benoxaprofen (20-200 mg/kg；腹腔注射；单次) 经腹腔注射给予雄性 Sprague-Dawley 大鼠后，在给药后 8 h 会引发与剂量成比例的肝脏蛋白加合物形成，以及对分子量约 70 kDa 和约 110 kDa 的肝脏蛋白的剂量依赖性共价修饰[3]。 Benoxaprofen (100 mg/kg；腹腔注射；单次) 经腹腔注射给予雄性 Sprague-Dawley 大鼠后，会以时间依赖的方式共价修饰分子量约 70 kDa 和 110 kDa 的肝脏蛋白，该修饰在给药后 4 至 24 h 可被检测到[3]。 **Animal Model:** Sprague-Dawley rat (male, 200-300 g)[3] **Dosage:** 20 mg/kg **Administration:** i.v.; single bolus dose **Result:** Detectable plasma protein adducts at 1, 4, and 8 h post-administration. Had liver protein adducts below the detection limit (~1 pmol/mg protein).

		Achieved a systemic exposure ($AUC_{0\rightarrow 8h}$) of benoxaprofen glucuronide (BNX-G) of 1.98 ± 0.59 μg h/mL. Reached a hepatobiliary exposure ($A_{e,bile,0\rightarrow 8h}$) of BNX-G of 10.8 ± 1.4% of the dose.
	Animal Model:	Sprague-Dawley rat (male, 200-300 g)[3]
	Dosage:	20 mg/kg; 50 mg/kg; 100 mg/kg; 200 mg/kg
	Administration:	i.p.; single dose
	Result:	Exhibited dose-proportional liver protein adduct formation, with ~1.5 pmol/mg protein at 50 mg/kg, ~2.8 pmol/mg protein at 100 mg/kg, and ~6.5 pmol/mg protein at 200 mg/kg. Showed dose-dependent covalent modification of two major liver proteins with molecular masses of ~70 kDa and ~110 kDa, with signal intensity more prominent in benoxaprofen-treated livers compared to controls.
	Animal Model:	Sprague-Dawley rat (male, 200-300 g)[3]
	Dosage:	100 mg/kg
	Administration:	i.p.; single dose
	Result:	Showed time-dependent covalent modification of ~70 kDa and ~110 kDa hepatic proteins, with signal intensity more prominent in benoxaprofen-treated livers compared to controls, and signals persisting through 24 h post-administration.
参考文献		[1]. Knights KM, et al. Benoxaprofen induced toxicity in isolated rat hepatocytes. Toxicology. 1986;40(3):327-339. [2]. Levine L, et al. Inhibition of the A-23187-stimulated leukotriene and prostaglandin biosynthesis of rat basophil leukemia (RBL-1) cells by nonsteroidal anti-inflammatory drugs, antioxidants, and calcium channel blockers. Biochem Pharmacol. 1983;32(20):3023-3026. [3]. Dong JQ, et al. Role of benoxaprofen and flunoxaprofen acyl glucuronides in covalent binding to rat plasma and liver proteins in vivo. Biochem Pharmacol. 2005;70(6):937-948. [4]. Sik R H, et al. The phototoxic effect of benoxaprofen and its analogs on human erythrocytes and rat peritoneal mast cells[J]. Photochemistry and photobiology, 1983, 38(4): 411-415.