Product Data Sheet

Product Name: Setipafant (BN-50727)
Cat. No.: GC32559

Chemical Properties

Cas. No.	132418-35-0		
SMILES	O=C(N(C1)CCC2=C1SC3=C2C(C4=CC=CC=C4Cl)=NCC5=NN=C(C)N53)NC6=CC=C(OC)C=C6		
Formula	$C_{26}H_{23}ClN_6O_2S$	M.Wt	519.02
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	Setipafant (BN-50727)		

Protocol

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal experiment:

Piglets[1] Male and female newborn piglets weighing 1550±31 g are used in all experiments. Six groups are studied. Group U4 is the nonsurgical control group (n=15). No anesthesia is given. Animals are entrusted to their mother and killed at D4. Group S is the sham control group (n=15). At D2 animals undergo laparotomy, intestinal exteriorization, and manipulation for 10 minutes before reintroduction to the abdominal cavity. They are killed at D4. Group I4 consist of animals (n=15) in which ischemia surgery is performed at D2, and animals are killed at D4. Group IT4 consist of animals (n=15) treated as in I4 together with treatment with Setipafant (BN 50727), a PAF receptor antagonist, orally (50 mg/kg of body weight) the day before and daily after surgery until death, and intraperitoneally (50 mg/kg) during surgery. Group I9 consisted of animals (n=15) in which ischemia surgery is performed at D2, and animals are killed at D9. Group IT9 consist of animals (n=15) undergoing the same procedure as in Is together with treatment with Setipafant as in IT4. Another group, U9, is made up of control animals (n=15) that are used only for weight and blood sample studies at D9. Rats[2] Male, Wistar rats weighing 160-205 g are used. Between 09 h 00 min and 10 h 00 min each day the animals are given an intraperitoneal injection of the PAF receptor antagonists, BN 52021 (10 mg/kg) or BN 50727(1 mg/kg), or their vehicle, and 30 min later they receive a subcutaneous injection of Dexamethasone sodium phosphate or vehicle. The effectiveness of BN 52021 and BN 50727 treatments is tested in preliminary experiments in anaesthetized (Inactin, 100 mg/kg, i.p.) male rats by injecting 25 and 50 ng/kg PAF into the right femoral vein 30 min before and 30 min after administration of either BN 52021, 10 mg/kg, i.p., or BN 50727, 1 mg/kg, i.p. Mean arterial blood pressure is monitored through a catheter inserted into the right femoral artery by an electromanometer using a Statham P23 dB pressure transducer.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

References:

[1]. de Boissieu D, et al. Effect of BN 50727 on pathological findings and tissue platelet activating factor levels during ileal ischemia in newborn piglets. J Pediatr Surg. 1996 Dec;31(12):1675-9.
[2]. Filep JG, et al. Dexamethasone-induced gastric mucosal damage in the rat: possible role of platelet-activating factor. Br J Pharmacol. 1992 Apr;105(4):912-8.

Background

Setipafant is a platelet-activating factor (PAF) antagonist.

Animals are separated into six groups: U4, controls; S, sham operated animals undergoing laparotomy; I4 and I9, ligation of the mesenteric vessels in the last ileal loop; IT4 and IT9, same procedure together with treatment with Setipafant (50 mg/kg) orally before and after surgery and intraperitoneally during surgery. Animals are killed at day 4 in groups U4, S, I4 and IT4 and at day 9 in groups I9 and IT9, with histological studies and mediator measurements taken. Macroscopic and histological lesions of intestinal wall in groups I4, I9, IT4 and IT9 are similar to those of human neonatal necrotizing enterocolitis and do not vary according to the absence or the presence of Setipafant (BN 50727) treatment. Peritoneal bands

are significantly reduced in treated groups IT4 and IT9 as compared with untreated ones I4 and I9. Mucosal PAF levels in the terminal ileum are higher in group I4 than in groups U4 or I9. In the upper loop, mucosal PAF levels are comparable in all groups. An increase in stool PAF levels is observed only in group I9, whereas values comparable to those observed in controls are detected in other groups[1]. Pretreatment of the animals with one or other of the structurally unrelated PAF receptor antagonists, BN 52021 (10 mg/kg, i.p.) or BN 50727 (1 mg/kg, i.p.) significantly reduces Dexamethasone-induced gastric damage. In these animals neither petechiae nor erosions are observed[2].

[1]. de Boissieu D, et al. Effect of BN 50727 on pathological findings and tissue platelet activating factor levels during ileal ischemia in newborn piglets. J Pediatr Surg. 1996 Dec;31(12):1675-9. [2]. Filep JG, et al. Dexamethasone-induced gastric mucosal damage in the rat: possible role of platelet-activating factor. Br J Pharmacol. 1992 Apr;105(4):912-8.