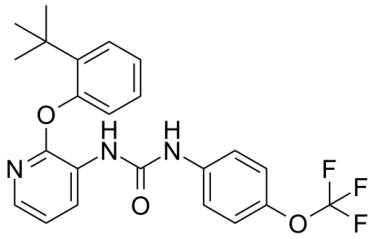
Data Sheet

Product Name:	BPTU
Cat. No.:	CS-8114
CAS No.:	870544-59-5
Molecular Formula:	C23H22F3N3O3
Molecular Weight:	445.43
Target:	P2Y Receptor
Pathway:	GPCR/G Protein
Solubility:	DMSO : ≥ 33.3 mg/mL (74.76 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

BPTU is a novel **P2Y1** allosteric antagonist. IC50 & Target: P2Y1[1] **In Vitro:** BPTU blocks the supramaximal fast inhibitory junction potentials (fIJP) in a concentration-dependent manner both in the rat and mouse colon ($P<0.0001$ for both). The EC_{50} of BPTU is approximately 0.3 μM and 0.06 μM for the rat and mouse colon, respectively. In the rat colon, addition of the P2Y agonist ADPβS at 10 μM significantly reduces spontaneous contractions to a 43.2±13.4% (N=5) ($P=0.0002$), and this reduction is blocked by 15 min incubation with BPTU at a concentration of 3 μM (93.3±5.1%). Similar results are obtained in the murine colon where ADPβS at 10 μM reduces the area under the curve (AUC) of contractions to a 15.8±5.1% (N=4) ($P<0.0001$) and its effect is reversed with BPTU at 3 μM (82.7±3.6%). Addition of MRS2365, a selective P2Y1 agonist, at a concentration of 5 μM significantly reduces spontaneous contractions to a 21.2±4.8% (N=5) ($P=0.0002$) in the murine colon, and this reduction is blocked by 15 min incubation with BPTU at a concentration of 3 μM (93.1±3.8%). The blockage of the MRS2365-induced response by BPTU at 3 μM also occurs in control conditions (N=5) (10.2±5.5% vs. 86.7±5.0%)[1]. **In Vivo:** Uptake of BPTU from the peritoneal cavity is relatively rapid. Blood boron levels are maximal within 1 h after administration. After only 1 h, a boron tumor-to-blood ratio above 1 is found for BPTU in pigmented tumors, which is indicative of drug retention. This is not seen in the non-pigmented tumor variant, in which tumor boron levels closely follow blood levels. Up to 24 h, Borocaptate sodium (BSH) exhibits no selective retention in either tumor, but achieves higher maximum tumor boron concentrations than BPTU as a result of the administration of higher amounts of boron. During the tissue distribution phase, liver-to-kidney boron concentration ratios range from 2 to 4 for BSH and from 0.5 to 1 for BPTU[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]Electrophysiological experiments are performed with colonic rat and mouse strips. Inhibitory junction potentials (IJP) are elicited by electrical field stimulation (EFS) using two silver chloride plates placed 1.5 cm apart perpendicular to the longitudinal axis of the preparation. The protocol consists of single pulse trains of EFS (0.4 ms pulse duration) at increasing voltages (8, 12, 16, 20, 24, 28, 32, 36, 40 V). The voltage responsible for the supramaximal response is used to elicit single pulses during incubation with BPTU at increasing concentrations (1×10^{-8} M, 1×10^{-7} M, 3×10^{-7} M, 1×10^{-6} M and 3×10^{-6} M). Another train of single pulses at increasing voltages is elicited after the highest dose of BPTU. The amplitude of the IJP (mV) is measured considering it as the difference between the maximal hyperpolarization and the resting membrane potential (RMP)[1]. **Animal Administration:** BPTU is suspended in 0.1 M sodium hydroxide at a concentration of 11.2 mg/mL and diluted with water to a final concentration of 6.75 mg/mL and a pH not exceeding 8. (Suspended solution)[2]Mice are given BPTU intraperitoneally at doses of 3.15 mg of boron per kg body weight. Injection volumes range from 0.25 to 0.5 mL for both intravenous and intraperitoneal administrations. Six mice are not given any drug to allow measurement of boron background levels. Animals are killed with carbon dioxide 0.2, 0.4, 1, 2, 4, 24 and 48 h after drug administration and samples are taken from tumor, blood, skin, muscle, brain, kidneys and liver. Tumor tissue from mice bearing B16.013 tumor is checked by eye for the absence of pigmentation. BPTU is also given in a multiple dose scheme. Every 2 h 0.4 to 0.5 mL of the above-mentioned BPTU solution is given intraperitoneally (4×3.15 mg/kg boron). Twenty-four hours after the last administration, the animals

are sacrificed and samples are taken[2].

References:

[1]. Ma?é N, et al. BPTU, an allosteric antagonist of P2Y1 receptor, blocks nerve mediated inhibitory neuromuscular responses in the gastrointestinal tract of rodents. Neuropharmacology. 2016 Nov;110(Pt A):376-385.

[2]. Verrijk R, et al. Pharmacokinetics in melanoma-bearing mice of 5-dihydroxyboryl-6-propyl-2-thiouracil (BPTU), a candidate compound for boron neutron capture therapy. Br J Cancer. 1994 Apr;69(4):641-7.

CAIndexNames:

Urea, N-[2-[2-(1,1-dimethylethyl)phenoxy]-3-pyridinyl]-N'-[4-(trifluoromethoxy)phenyl]-

SMILES:

O=C(NC1=CC=C(OC(F)(F)F)C=C1)NC2=CC=CN=C2OC3=CC=CC=C3C(C)(C)C

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