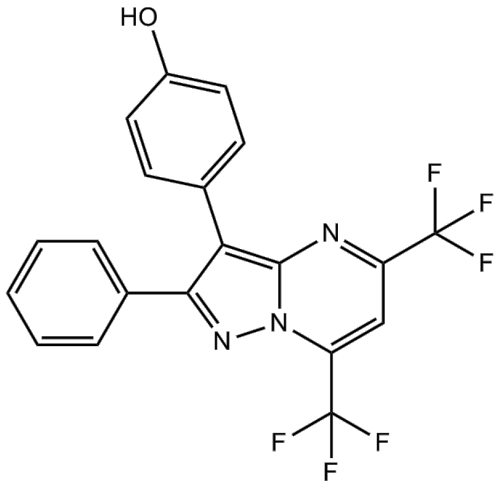
Product Data Sheet

Product Name: PHTPP
Cat. No.: GC11863

Chemical Properties

Cas. No.	805239-56-9		
Chemical Name	4-(2-phenyl-5,7-bis(trifluoromethyl)pyrazolo[1,5-a]pyrimidin-3-yl)phenol		
SMILES	FC(F)(C1=CC(C(F)(F)F)=NC2=C(C(C=C3)=CC=C3O)C(C4=CC=CC=C4)=NN21)F		
Formula	$C_{20}H_{11}F_6N_3O$	M.Wt	423.31
Solubility	≤30mg/ml in ethanol;50mg/ml in DMSO	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.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	MCF-7 cells
Preparation Method	MCF-7 cells were cultured in Minimum Essential Medium. All media were supplemented with 10% fetal bovine serum (FBS), penicillin (100U/mL) and streptomycin (100mg/mL). The cells were pre-treated with 5μM selective ERβ full antagonist (PHTPP) for 1h.
Reaction Conditions	5μM; 1h
Applications	PHTPP significantly weakened the inhibitory effect of silibinin on MCF-7 breast cancer cells by blocking the activity of Erβ.

Animal experiment [2]:

Animal models	Sprague-dawley rat model

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Preparation Method	Ninety female Sprague-Dawley rats, weighing 186±15g with an average age of approximately 8 weeks, were housed in a temperature and humidity-controlled environment with 12h light dark cycles and free access to food and water. The rats were randomly divided as follows into 9 groups of 10 rats each: Control, Carbon tetrachloride (CCl_4), CCl_4+E2, CCl_4+PPT, CCl_4+DPN, CCl_4+G1, CCl_4+E2+MPP, CCl_4+E2+PHTPP and CCl_4+E2+G15. The Control group underwent sham surgery, while the other 8 groups underwent bilateral ovariectomy. Two weeks after the surgeries, the 8 CCl_4 groups were subcutaneously injected with 40% CCl_4 in peanut oil at a dose of 0.2mL/100g body weight twice weekly. 5% alcohol was added to drinking water to induce P450 and intensify the development of hepatic fibrosis. Starting from the first CCl_4 injection day, the rats received subcutaneously injections of the corresponding drugs (E2, PPT, DPN, G1, MPP, PHTPP and G15; first dissolved in DMSO and then diluted with saline) at a dosage of 30nM/100g body weight/day for 12 weeks, according to the grouping classification. The Control and CCl_4 groups were treated subcutaneously with the same volume of placebos (peanut oil and/or DMSO diluted with saline).
Dosage form	0.091mg/kg; sc; 12 weeks
Applications	PHTPP could block the antifibrotic effects of E2.

Caution: Product has not been fully validated for medical applications. For research use only.
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Address: 10292 Central Ave. #205, Montclair, CA, USA

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References:
[1]. Zheng N, Liu L, Liu W, et al. ER? up-regulation was involved in silibinin-induced growth inhibition of human breast cancer MCF-7 cells. Archives of biochemistry and biophysics. 2016 Feb 1; 591: 141-149.
[2]. Zhang B, Zhang CG, Ji LH, et al. Estrogen receptor ? selective agonist ameliorates liver cirrhosis in rats by inhibiting the activation and proliferation of hepatic stellate cells. Journal of Gastroenterology and Hepatology. 2018 Mar; 33(3): 747-755.

Background

PHTPP is a selective ERβ full antagonist with 36-fold selectivity for ERβ over ERα. PHTPP can selectively antagonize the ligand binding and transcriptional functions of ERβ, blocking its inhibitory effect on tumor cells, thereby promoting cell proliferation. PHTPP was used to verify ERβ function [1-3].

In MCF-7 cells, PHTPP (5μM, 1h) significantly weakened the inhibitory effect of silibinin on MCF-7 breast cancer cells by blocking the activity of ERβ [4]. In Caco-2 cells, PHTPP (0.1μM, 24h) reversed the p-hydroxybenzoic acid-induced inhibition of the expression of proinflammatory factors (e.g., TNF-α and IL-6) and upregulated the expression of E-cadherin and occluding [5]. In SKOV3 cells, PHTPP (10μM, 24h) promotes the proliferation and migration of SKOV3 cells [6].

In colitis mouse model, PHTPP (1mg/kg, ip, 1d) reversed the improvement effect of p-hydroxybenzoic acid on the symptoms of colitis [5]. In sprague-dawley rat model, PHTPP (0.091mg/kg, sc, 12 weeks) could block the antifibrotic effects of E2 [7]. In sprague-dawley rat model, PHTPP (850μg/kg, ip, 12d) inhibited ERβ activation by E2 and naringenin by over 90% [8].

References:
[1]. Compton DR, Sheng S, Carlson KE, et al. Pyrazolo [1, 5-a] pyrimidines: estrogen receptor ligands possessing estrogen receptor β antagonist activity. Journal of medicinal chemistry. 2004 Nov 18; 47(24): 5872-5893.
[2]. Chan KK, Leung TH, Chan DW, et al. Targeting estrogen receptor subtypes (ERa and ERb) with selective ER modulators in ovarian cancer. J. Endocrinol. 2014; 221: 325-336.

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[3]. Boopathy GT, Hong W. Role of hippo pathway-YAP/TAZ signaling in angiogenesis. Frontiers in cell and developmental biology. 2019 Apr 10; 7: 49.
[4]. Zheng N, Liu L, Liu W, et al. ERβ up-regulation was involved in silibinin-induced growth inhibition of human breast cancer MCF-7 cells. Archives of biochemistry and biophysics. 2016 Feb 1; 591: 141-149.
[5]. Xu X, Luo A, Lu X, et al. p-Hydroxybenzoic acid alleviates inflammatory responses and intestinal mucosal damage in DSS-induced colitis by activating ERβ signaling. Journal of Functional Foods. 2021 Dec 1; 87: 104835.
[6]. Yan Y, Jiang X, Zhao Y, et al. Role of GPER on proliferation, migration and invasion in ligand-independent manner in human ovarian cancer cell line SKOV3. Cell biochemistry and function. 2015 Dec; 33(8): 552-559.
[7]. Zhang B, Zhang CG, Ji LH, et al. Estrogen receptor β selective agonist ameliorates liver cirrhosis in rats by inhibiting the activation and proliferation of hepatic stellate cells. Journal of Gastroenterology and Hepatology. 2018 Mar; 33(3): 747-755.
[8]. Lin P, Zhang X, Zhu B, et al. Naringenin protects pancreatic β cells in diabetic rat through activation of estrogen receptor β. European Journal of Pharmacology. 2023 Dec 5; 960: 176115.

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