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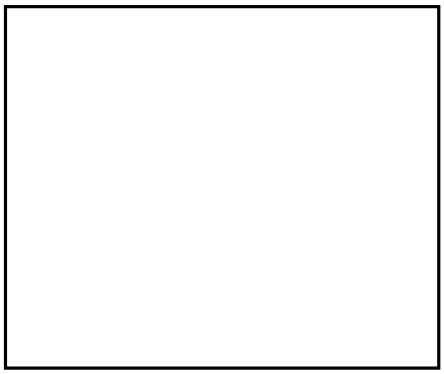
Tariquidar methanesulfonate, hydrate Data Sheet

Product Name:	Tariquidar methanesulfonate, hydrate
CAS No.:	625375-83-9
Cat. No.:	HY-10550A
MWt:	892.99
Formula:	C40H52N4O15S2
Purity :	>98%
Solubility:	Water > 5.35 mg/ml
Mechanisms:	Pathways: Membrane Transporter/Ion Channel; Target: P-glycoprotein



Biological Activity:

Tariquidar methanesulfonate hydrate(XR9576) is a potent and selective noncompetitive inhibitor of P-glycoprotein with Kd of 5.1 nM, reverses drug resistance in MDR cell Lines.
IC50 value: 5.1 nM (Kd) [1]
Target: P-glycoprotein
in vitro: Tariquidar displays high-affinity binding to P-gp with Bmax of 275 pmol/mg. Tariquidar shows non-competitive interaction with the P-gp substrates vinblastine and paclitaxel. Tariquidar increases the steady-state accumulation of these cytotoxics in CHr<>/supB30 cells to levels observed in non-P-gp-expressing AuxB1 cells with EC50 of 487 nM. Tariquidar is able to inhibit the vanadate-sensitive ATPase activity of P-gp by 60-70%, with potent IC50 values of 43 nM [1]. Tariquidar may inhibit other resistance mechanisms at higher concentrations. 1 μM Tariquidar abrogates ABCG2 (BCRP)-mediated resistance to camptothecins in vitro [2]. Tariquidar potentiates the cyto-toxicity of several drugs including doxorubicin, paclitaxel, etoposide, and vincristine; complete reversal of resistance is achieved in the presence of 25- 80 nM Tariquidar. In MC26, a murine colon carcinoma cell line with intrinsic chemoresistance, the doxorubicin IC50 is fivefold lower in the presence of 0.1 μM Tariquidar (36 vs 7 nM). In murine mammary carcinoma, human small-cell lung carcinoma and human ovarian carcinoma cell lines with acquired chemotherapeutic resistance (EMT6/AR1.0, H69/LX4 and 2780 AD), the in vitro doxorubicin IC50 is 22-150-fold lower in the presence of 0.1 μM Tariquidar. P-gp inhibition persists for 23 h after removal of Tariquidar from the culture system [3].
in vivo: Tariquidar (2- 8 mg/kg p.o.) is found to significantly potentiate the antitumor activity of doxorubicin (5 mg/kg, i.v.) against MC26 murine colon carcinoma in vivo. In human carcinoma xenografts, coadministration of XR9576 (6 -12 mg/kg p.o.) fully restored the antitumor activity of paclitaxel, etoposide, and vincristine against two highly resistant MDR human tumor xenografts (2780AD, H69/LX4) in nude mice [3].

References:

[1]. Martin C, et al. The molecular interaction of the high affinity reversal agent XR9576 with P-glycoprotein. Br J Pharmacol, 1999, 128(2), 403-411.
[2]. Robey RW, et al. Pheophorbide a is a specific probe for ABCG2 function and inhibition. Cancer Res, 2004, 64(4), 1242-1246.
[3]. Mistry P, et al. In vitro and in vivo reversal of P-glycoprotein-mediated multidrug resistance by a novel potent modulator, XR9576. Cancer Res, 2001, 61(2), 749-758.

18 Wilkinson Way, Princeton, NJ 08540, USA
Tel: 609-228-6898 Fax: 609-228-5909 Email: info@medchemexpress.com Web:www.medchemexpress.com