Biochempartner
瀚香生物科技

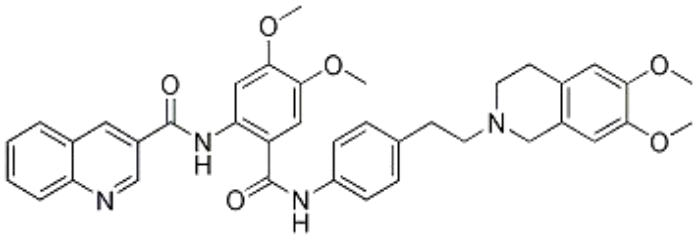
Product Introduction

Tariquidar

Tariquidar (XR9576) is a potent and selective noncompetitive inhibitor of P-glycoprotein with Kd of 5.1 nM, reverses drug resistance in MDR cell Lines. Phase 3.

Technical Data:

Molecular Weight (MW):	646.73
Formula:	$C_{38}H_{38}N_4O_6$
Purity:	>98 %
Storage:	at -20℃ 2 years
CAS No:	206873-63-4



Biological Activity

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] Tariquidar restored the cyto-toxicity of doxorubicin and vinblastine in the National Cancer Institute (NCI)/ADRRES multicellular tumor spheroid model derived from the MCF7WT breast cancer cell line. [4]

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. Br J Pharmacol, 1999, 128(2), 403-411.

[2] Robey RW, et al. Cancer Res, 2004, 64(4), 1242-1246.

[3] Mistry P, et al. Cancer Res, 2001, 61(2), 749-758.

[4] Walker J, et al. Eur J Cancer, 2004, 40(4), 594-605.