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SZABO-SCANDIC HandelsgmbH

Quellenstraße 110, A-1100 Wien

T. +43(0)1 489 3961-0

F. +43(0)1 489 3961-7

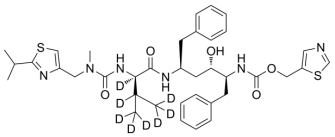
mail@szabo-scandic.com

www.szabo-scandic.com

linkedin.com/company/szaboscandic

Ritonavir-d_8

Cat. No.:	HY-90001S2
Molecular Formula:	$C_{37}H_{40}D_8N_6O_5S_2$
Molecular Weight:	728.99
Target:	Apoptosis; HIV Protease; SARS-CoV; HIV; Isotope-Labeled Compounds
Pathway:	Apoptosis; Anti-infection; Metabolic Enzyme/Protease; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Ritonavir-d_8 is deuterated labeled Ritonavir (HY-90001). Ritonavir (ABT 538) is an inhibitor of HIV protease used to treat HIV infection and AIDS. Ritonavir is also a SARS-CoV $3CL^{pro}$ inhibitor with an IC_{50} of 1.61 μM.
In Vitro	Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1]. Ritonavir (ABT 538) is an inhibitor of CYP3A4 mediated testosterone 6β-hydroxylation with mean K_i of 19 nM and also inhibits tolbutamide hydroxylation with IC_{50} of 4.2 μM[2]. Ritonavir (ABT 538) is found to be a potent inhibitor of CYP3A-mediated biotransformations (nifedipine oxidation with IC_{50} of 0.07 mM, 17alpha-ethynylestradiol 2-hydroxylation with IC_{50} of 2 mM; terfenadine hydroxylation with IC_{50} of 0.14 mM). Ritonavir is also an inhibitor of the reactions mediated by CYP2D6 (IC_{50}=2.5 mM) and CYP2C9/10 (IC_{50}=8.0 mM)[3]. Ritonavir results in an increase in cell viability in uninfected human PBMC cultures. Ritonavir markedly decreases the susceptibility of PBMCs to apoptosis correlated with lower levels of caspase-1 expression, decreases in annexin V staining, and reduces caspase-3 activity in uninfected human PBMC cultures. Ritonavir inhibits induction of tumor necrosis factor (TNF) production by PBMCs and monocytes in a time- and dose-dependent manner at nontoxic concentrations[4]. Ritonavir inhibits p-glycoprotein-mediated extrusion of saquinavir with an IC_{50} of 0.2 μM, indicating a high affinity of ritonavir for p-glycoprotein[5]. Ritonavir inhibits human liver microsomal metabolism of ABT-378 potently with K_i of 13 nM. Ritonavir combined with ABT-378 (at 3:1 and 29:1 ratios) inhibits CYP3A (IC_{50}=1.1 and 4.6 μM), albeit less potently than Ritonavir (IC_{50}=0.14 μM)[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

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Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA