Ritonavir

Cat. No.: HY-90001

CAS No.: 155213-67-5

Molecular Formula: $C_{37}H_{48}N_6O_5S_2$

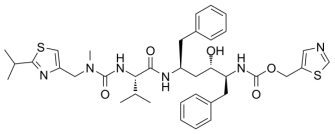
Molecular Weight: 720.94

Target: HIV Protease; HIV; SARS-CoV; Apoptosis

Pathway: Anti-infection; Metabolic Enzyme/Protease; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (34.68 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.3871 mL	6.9354 mL	13.8708 mL
	5 mM	0.2774 mL	1.3871 mL	2.7742 mL
	10 mM	0.1387 mL	0.6935 mL	1.3871 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.47 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (3.47 mM); Clear solution; Need warming
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (3.47 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (3.47 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: 0.5 mg/mL (0.69 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

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	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[1]. 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)[2]. 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[3]. 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[4]. 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)[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2021 May 29;6(1):212.
- Nat Commun. 2020 Sep 4;11(1):4417.
- Antimicrob Agents Chemother. 2020 Aug 20;64(9):e00872-20.
- Int J Antimicrob Agents. 2019 Dec;54(6):814-819.
- Biomed Pharmacother. 2020 Sep;129:110506.

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REFERENCES

[1]. Eagling VA, et al. Differential inhibition of cytochrome P450 isoforms by the protease inhibitors, ritonavir, saquinavir and indinavir. Br J Clin Pharmacol. 1997 Aug;44(2):190-4.

[2]. Kumar GN, et al. Cytochrome P450-mediated metabolism of the HIV-1 protease inhibitor ritonavir (ABT-538) in human liver microsomes. J Pharmacol Exp Ther. 1996 Apr;277(1):423-31.

[3]. Weichold FF, et al. HIV-1 protease inhibitor ritonavir modulates susceptibility to apoptosis of uninfected T cells. J Hum Virol. 1999 Sep-Oct;2(5):261-9.

[4]. Drewe J, et al. HIV protease inhibitor ritonavir: a more potent inhibitor of P-glycoprotein than the cyclosporine analog SDZ PSC 833. Biochem Pharmacol. 1999 May 15;57(10):1147-52.

[5]. Kumar GN, et al. Potent inhibition of the cytochrome P-450 3A-mediated human liver microsomal metabolism of a novel HIV protease inhibitor by ritonavir: A positive drug-drug interaction. Drug Metab Dispos. 1999 Aug;27(8):902-8.

[6]. Qi Sun, et al. Bardoxolone and bardoxolone methyl, two Nrf2 activators in clinical trials, inhibit SARS-CoV-2 replication and its 3C-like protease. Signal Transduct Target Ther. 2021 May 29;6(1):212.

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