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ProductInformation

REVERSIN 205

Product Number **R 1401**
Storage Temperature –20 °C

[Boc-Glu(Obzl)]$_2$-Lys-Ome

Product Description

Appearance: White powder
Molecular Formula: $C_{41}H_{58}N_4O_{12}$
Formula Weight: 798.9
Purity: >97 % by HPLC

- Peptide chemosensitizer
- Inhibitor of P-glycoprotein (MDR1).[1]

P-glycoproteins (P-gp) belong to a family of plasma membrane proteins encoded by the MDR (multidrug resistance) gene(s) that are well conserved in nature. P-gp acts as a transmembrane pump that removes drugs from the cytoplasm. ATP hydrolysis provides the energy for active drug transport, which can occur against steep concentration gradients.
Multidrug resistance can be reversed by the action of a group of compounds known as chemosensitizers. Two novel hydrophobic peptide chemosensitizers are reversin 121 and reversin 205. Reversin 121 is a simple dipeptide, containing standard protecting groups and reversin 205 is a similarly modified branched-chain tripeptide. The reversins bind to purified P-glycoprotein with high affinity. They modulate P-glycoprotein ATPase activity in membranes expressing recombinant MDR1, plasma membrane vesicles from multidrug resistant cells, and reconstituted proteoliposomes. Both peptides induce stimulation of ATPase activity of Pgp. But in higher concentrations (above 1 µM) reversin 205 leads to inhibition, while reversin 121 does not. Using both membrane vesicles and reconstituted proteoliposomes, 1 µM to 2 µM of the reversins were more effective than cyclosporin A at blocking colchicine transport.[1]
In MDR1-expressing intact cells, reversin 121 and reversin 205 had effects similar to those of known drug resistance reversing agents, e.g. verapamil or cyclosporin A and in several systems acted at significantly lower concentrations. Moreover, reversins had little effect on non-MDR1 expressing tumor or normal cells.

Preparation Instructions

Soluble in DMSO or ethanol.
Insoluble in water.

Storage/Stability

Store tightly sealed and desiccated at –20 °C. Allow powder to reach room temperature before opening vial. May be stored desiccated in solid form at room temperature for one year. Store DMSO/ethanol solutions at –20 °C for up to 6 months.

Sold under Patent EP770091 (WO 95/31474)

Reference

1. Sharom, F.J., et al., Interaction of the p-Glycoprotein Multidrug Transporter (MDR1) with High Affinity Peptide Chemosensitizers in Isolated Membranes, Reconstituted Systems, and Intact Cells. Biochem. Pharm., **58**, 571-586 (1999).

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Parameters for interaction of reversins 121, 205 and verapamil with Pgp[1]

Parameter	System	Reversin 121	Reversin 205	Verapamil
K_d (50% maximal fluorescence quenching	Purified Pgp	0.077 µM	0.154 µM	2.4 µM
IC_{50} (50% of inhibition of photolabeling	CH^RC5 plasma membrane	8.0 µM	12.0 µM	50 µM
K_a (50% of maximal stimulation of ATPase activity)	Sf9 insect cell membranes	0.080 µM	0.040 µM	2.5 µM
K_a	$CH^{RB}B30$ plasma membrane	0.30 µM	0.22 µM	10 µM
D_m (50% inhibition of colchine uptake)	$CH^{RB}B30$ plasma membrane	0.56 µM	0.44 µM	2.9 µM
D_m	Pgp proteoliposomes	0.24 µM	0.32 µM	3.2 µM
m	Pgp proteoliposomes	1.2	1.1	0.51