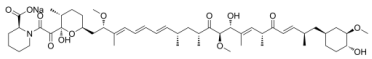
Data Sheet

Product Name:	Seco Rapamycin (sodium salt)
Cat. No.:	CS-5489
CAS No.:	148554-65-8
Molecular Formula:	$C_{51}H_{78}NNaO_{13}$
Molecular Weight:	936.15
Target:	Drug Metabolite
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : ≥ 46 mg/mL



BIOLOGICAL ACTIVITY:

Seco Rapamycin sodium salt is the ring-opened product of Rapamycin. Seco-rapamycin is reported not to affect the mTOR function. ***In Vitro:*** Disposition of Seco Rapamycin in Human Tissue Homogenates and Caco-2 Cell Monolayers. To determine whether Seco Rapamycin (D2) can be metabolized to dihydro Sirolimus (M2), 20 μM Seco Rapamycin is incubated with human liver, jejunal mucosal, and Caco-2 homogenates. All of these homogenates produced M2 in an NADPH-dependent manner. Ketoconazole, at a high concentration (100 μM), has no effect on the formation of M2 in any of the homogenates examined. To determine whether Seco Rapamycin can be metabolized to M2 in intact cells, 20 μM Seco Rapamycin is added to Caco-2 cell monolayers. When applied to the apical compartment, little Seco Rapamycin is detected in the basolateral compartment and in the cellular fraction after 4 h. In addition, little M2 is detected. LY335979 has little effect on the distribution of Seco Rapamycin after an apical dose, although M2 became detectable in the apical compartment. In contrast, when Seco Rapamycin is applied to the basolateral compartment, both Seco Rapamycin and M2 are readily detected in the apical compartment; LY335679 decreases the flux of Seco Rapamycin to the apical compartment and increases the amount of M2 in both apical and basolateral compartments[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]To determine whether the Sirolimus metabolite M2 is formed from the degradation product Seco Rapamycin, duplicate Caco-2 cell cultures are dosed apically or basolaterally with 20 μM Seco Rapamycin and incubated for 4 h. To determine whether Seco Rapamycin is a substrate for P-gp, duplicate cultures are incubated with 0.5 μM LY335979 in the same manner for Sirolimus. For comparison, a parallel set of cultures is incubated similarly with 20 μM Sirolimus, but dosed apically only. M2 formation is also examined in human jejunal mucosal and liver homogenates and Caco-2 homogenates by incubating each preparation, in duplicate, with 20 μM Seco Rapamycin in the same manner for Sirolimus. For comparison, a parallel set of incubations containing 20 μM Sirolimus is also performed. To determine whether a high dose of Ketoconazole (100 μM) inhibits the formation of M2, parallel experiments with Caco-2 cells and the various homogenates are performed in a similar manner, only Ketoconazole (dissolved as a 100-fold concentration solution in ethanol) is included in the incubation medium/mixtures[1].

References:

[1]. Paine MF, et al. Identification of a novel route of extraction of sirolimus in human small intestine: roles ofmetabolism and secretion. J Pharmacol Exp Ther. 2002 Apr;301(1):174-86.

CAIndexNames:

2-Piperidinecarboxylic acid, 1-[oxo[tetrahydro-2-hydroxy-6-[14-hydroxy-22-(4-hydroxy-3-methoxycyclohexyl)-2,13-dimethoxy-3,9,11,15,17,21-hexamethyl-12,18-dioxo-3,5,7,15,19-docosapentaenyl]-3-methyl-2H-pyran-2-yl]acetyl]-, monosodium salt, [2R-[2α,2(S*),3α,6β[2S*,3E,5E,7E,9S*,11R*,13R*,14R*,15E,17R*,19E,21R*,22(1S*,3R*,4R*)]]]-

SMILES:

O=C([C@H]1N(C(C([C@@]2(O)[C@H](C)CC[C@@H](C[C@H](OC)/C(C)=C/C=C/C=C/[C@@H](C)C[C@@H](C)C([C@H](OC)[C@H](O)/C(C)=C/[C@@H](C)C(/C=C/[C@H](C)C[C@H]3C[C@@H](OC)[C@H](O)CC3)=O)=O)O2)=O)=O)CCCC1)O[Na]

Caution: Product has not been fully validated for medical applications. For research use only.

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