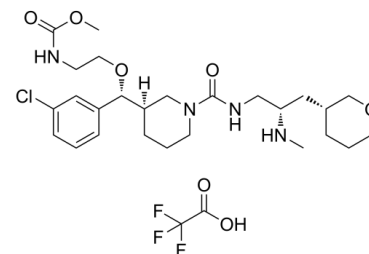


Data Sheet

Product Name:	VTP-27999 (TFA)
Cat. No.:	CS-0312
CAS No.:	1013937-63-7
Molecular Formula:	C ₂₈ H ₄₂ ClF ₃ N ₄ O ₇
Molecular Weight:	639.10
Target:	Renin
Pathway:	Metabolic Enzyme/Protease
Solubility:	H ₂ O : 10 mg/mL (ultrasonic); Ethanol : 2.4 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

VTP-27999 TFA is an alkyl amine Renin inhibitor; VTP-27999 TFA is useful for Hypertension and End-Organ Diseases.

PROTOCOL (Extracted from published papers and Only for reference)

Kinase assay [3] Renin was measured with the renin III IRMA (detection limit 1 pg/mL). This assay, which makes use of a monoclonal antibody (4G1) directed against renin's active site, also recognizes intact, open prorenin. This implies that intact prorenin can be measured with this assay after incubating it with acid or after exposing it, for 48 hours at 4°C, to 10 µM aliskiren because both procedures induce the conversion of all prorenin molecules into the open conformation. Additionally, we converted prorenin to renin by cleaving off the prosegment with immobilized trypsin (72 hours at 4°C). In plasma, this approach yields identical total renin (renin+prorenin) levels as aliskiren exposure and thus, subtracting the renin levels measured before trypsin treatment or aliskiren exposure from those after these procedures indirectly provides an indication of the prorenin levels. Intact, closed prorenin was measured with an ELISA (detection limit 10 pg/mL) that recognizes residues 32 to 39 of the prosegment. This prorenin assay was performed according to the instructions of the manufacturer, making use of the above-mentioned human recombinant prorenin to construct the standard curve. In a select set of samples, intact, open prorenin was measured on the basis of its prosegment, replacing the 125I-labeled active site-directed monoclonal antibody of the Cisbio kit by a prosegment-directed 125I-labeled monoclonal antibody (F258-37-B1) in the IRMA (F258 IRMA; detection limit 10 pg/mL). F258-37-B1 is directed against the C-terminal part (p20-p43) of the propeptide and does not react (<0.1%) with renin. F258-37-B1 also does not react (<0.1%) with intact, closed prorenin. However, it does react with prorenin after the above treatment of prorenin with aliskiren. Thus, the aliskiren-induced nonproteolytic conformational change, causing the propeptide to move to the surface of the molecule, allows the recognition of prorenin by both the active site-directed antibody of the Cisbio kit and the prosegment-directed antibody of the prorenin IRMA. Finally, because VTP-27999 seemed to affect the outcome of the Cisbio IRMA, renin measurements in the presence of VTP-27999 were also performed with an alternative renin IRMA. This IRMA makes use of the active site-directed monoclonal antibody R1-20-5,10 and has a detection limit of 0.9 pg/mL.

References:

- [1]. New renin inhibitor VTP-27999 alters renin immunoreactivity and does not unfold prorenin. Hypertension. 2013 May;61(5):1075-1082.
- [2]. Lanqi Jia? et al. Discovery of VTP-27999, an Alkyl Amine Renin Inhibitor with Potential for Clinical Utility ACS Med. Chem. Lett., 2011, 2 (10), pp 747-

[3]. Ishchenko A, et al. Structure-based design technology contour and its application to the design of Renin inhibitors. J Chem Inf Model. 2012 Aug 27;52(8):2089-97. Epub 2012 Jul 25.

CAIndexNames:

Carbamic acid, N-[2-[(R)-(3-chlorophenyl)][(3R)-1-[[[(2S)-2-(methylamino)-3-[(3R)-tetrahydro-2H-pyran-3-yl]propyl]amino]carbonyl]-3-piperidinyl]methoxy]ethyl]-, methyl ester, 2,2,2-trifluoroacetate (1:1)

SMILES:

O=C(O)C(F)(F)F.COC(NCCO[C@@H](C1=CC(Cl)=CC=C1)[C@@]2([H])CN(CCC2)C(NC[C@@H](NC)C[C@H]3CCCCOC3)=O)=O

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

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