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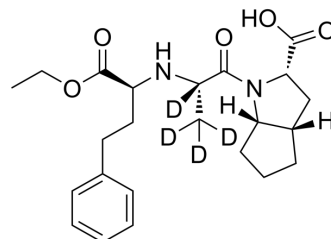
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Ramipril-d₄

Cat. No.:	HY-B0279S2
CAS No.:	1132661-83-6
Molecular Formula:	C ₂₃ H ₂₈ D ₄ N ₂ O ₅
Molecular Weight:	420.54
Target:	Apoptosis; Angiotensin-converting Enzyme (ACE); Isotope-Labeled Compounds
Pathway:	Apoptosis; Metabolic Enzyme/Protease; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Ramipril-d ₄ is deuterated labeled Ramipril (HY-B0279). Ramipril (HOE-498) is an angiotensin-converting enzyme (ACE) inhibitor with IC ₅₀ of 5 nM.
In Vitro	<p>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].</p> <p>Ramipril (HOE-498) is an angiotensin-converting enzyme (ACE) inhibitor with IC₅₀ of 5 nM^[2]. Ramipril (HOE-498) enhances the activity of ACE-associated CK2 and the phosphorylation of ACE Ser1270 in cultured endothelial cells, but is unable to activate JNK or stimulate the nuclear accumulation of c-Jun in endothelial cells expressing a S1270A ACE mutant or in ACE-deficient cells. Prolonged Ramipril treatment increases ACE expression in primary cultures of human endothelial cells and in vivo (mouse lung), which can be prevented by pretreatment with the JNK inhibitor SP600125^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>Chronic in vivo administration of Ramipril (HOE-498) to rats at a dosage that has similar hypotensive effects in vitro HUVECs significantly reduces the rate of LPS-induced apoptosis compared to the other ACE inhibitors, which contrasts with the apoptosis effect in vitro^[4]. Ramipril (HOE-498) inhibits systolic blood pressure (SBP) with IC₅₀ of 1.97 mg/kg in spontaneously hypertensive rats (SHR). When in combination with AT1-receptor blockade by candesartan-cilexetil increases SBP reduction synergistically rather than additively^[5].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

REFERENCES

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- [2]. Stevens, B.R., M.I. Phillips, and A. Fernandez, Ramipril inhibition of rabbit (*Oryctolagus cuniculus*) small intestinal brush border membrane angiotensin converting enzyme. *Comp Biochem Physiol C*, 1988. 91(2): p. 493-7.
- [3]. Kohlstedt, K., et al., Angiotensin-converting enzyme is involved in outside-in signaling in endothelial cells. *Circ Res*, 2004. 94(1): p. 60-7.
- [4]. Ceconi, C., et al., Differences in the effect of angiotensin-converting enzyme inhibitors on the rate of endothelial cell apoptosis: in vitro and in vivo studies. *Cardiovasc Drugs Ther*, 2007. 21(6): p. 423-9.
- [5]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. *Ann Pharmacother*. 2019 Feb;53(2):211-216.

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

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