Exploring ACE-167 and the Future of Oral Peptide Therapies

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History & Mechanism of Action

ACE-167, developed by Acesis BioMed US, Inc., is a VDAC1-derived small molecule peptide, which is based on a scientific publication from 2023 and a preceding patent.[1] VDAC1, the voltage-dependent anionic channel located in the outer mitochondrial membrane, is part of a larger protein complex capable of importing cholesterol into the mitochondrion. Cholesterol itself is the precursor for a large family of hormones, including all sex hormones in humans.

The transport of cholesterol to the inner mitochondrial membrane is the rate - limiting step in the biosynthesis of these hormones. In some studies, it was found that a 25-amino acid peptide that blocks the interaction of VDAC1 with another protein could increase testosterone levels in animals. Later, it was discovered that this effect could also be achieved by smaller peptide fragments, approximately 4-7 amino acids long, including ACE-167.

The advantage of these small fragments lies in their oral bioavailability, creating an opportunity to effectively increase testosterone levels through the ingestion of small peptide doses. RVTQ was first described as a small bioactive peptide sequence and later modified.

Identity of ACE-167

There are several possible candidates for the identity of ACE-167. In the publication, the peptide RdVTQ—where the natural L-valine in RVTQ is replaced by the unnatural D-valine—is prominently featured. The effects of oral administration were most thoroughly studied in the case of RdVTQ. It was shown that testosterone levels significantly increased when RdVTQ was administered orally to rats at doses ranging between 10 and 800 µg/kg.

In addition, the effect was strongest in younger animals and almost nonexistent in those aged over 12 months. The effects on other hormones were also assessed, including luteinizing hormone (increased) and corticosterone (lowered). Based on this specific focus and the positive data, there is a good chance that ACE-167 is indeed RdVTQ.

Furthermore, a few online sources claim that ACE-167 is RdVTQ; however, it cannot be said with certainty that these sources are entirely reliable.

Other likely candidates include KVSQ and Ac-RITQdS-NH_2 , both of

which produced higher testosterone spikes compared to RdVTQ. However, the increase in testosterone induced by Ac-RITQdS-NH_2 appeared to be relatively short-lived. KVSQ, on the other hand, seems to suffer from low plasma stability, whereas RdVTQ and Ac-RITQdS-NH_2 are both significantly more stable. The plasma half-life of RdVTQ is around 2 hours, Ac-RITQdS-NH_2 exceeds 5 hours, and that of KVSQ is only about 10 minutes.

A patent (WO 2020/093142 A1) extensively covers a variety of small peptide structures for use in hormone replacement therapy, specifically including the peptides mentioned above. The patent also describes sequences up to 11 amino acids long, although it is unlikely that longer peptides can be effectively used via oral administration due to their increased susceptibility to degradation in the stomach and intestine. The patent largely reiterates the experimental data from the paper, and no new information about efficacy, metabolism, or pharmacological properties is provided.

Conclusion

ACE-167 represents an interesting approach to potentially increase testosterone levels in human patients. The required human dosing would likely range between approximately 0.5 mg and 5 mg per day orally, making it cost-effective and easy to administer. However, in rats, significant increases in testosterone were observed only in young individuals, and it remains unclear how this will translate to humans. So far, no results from clinical trials in humans are available.

References

[1] Martinez-Arguelles DB, Nedow JW, Gukasyan HJ, Papadopoulos V. Oral administration of VDAC1-derived small molecule peptides increases circulating testosterone levels in male rats. *Front Endocrinol (Lausanne).* **2022**;13:1003017. doi: 10.3389/fendo.2022.1003017.

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