

Novel ACE-I Inhibitory Peptides Derived From *Limnospira platensis*

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Microalgae are unicellular organisms that are found both in marine and freshwater ecosystems, ranging from tropical water habitats to subpolar areas. They have recently gained attention due to their numerous applications in medicine and nutrition. *Limnospira platensis*, known as spirulina, has a promising potential in pharmacology. However, further research is necessary to explore its antihypertensive applications. The study aims to discover novel human Angiotensin Converting Enzyme I (ACE-I) inhibitory peptides from *L. platensis* proteins. Simulated gastrointestinal digestion, ACE-I inhibitory activity prediction with pLM4ACE, ADMET screening and molecular docking using FlexPepDock were performed to identify best candidates for novel ACE-I inhibitory peptides in all available protein sequences of *L. platensis*. In total, 15 novel peptides with potential ACE-I inhibitory activity were identified, ten of which exhibited the most favorable interactions with ACE-I in molecular docking simulations. The computational approach was later verified by *in vitro* gastrointestinal digestion, followed by liquid chromatography with mass spectrometry (LC-MS), during which all of the peptides designated as inhibitors were identified in *L. platensis* biomass. Four peptides were synthesised, all of which were proven to exhibit ACE-I inhibitory activity during the *in vitro* assessments.

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