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Original Article

Identification and *in silico* characterization of a novel peptide inhibitor of angiotensin converting enzyme from pigeon pea (*Cajanus cajan*)

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ABSTRACT

Background: Plants are important sources of bioactive peptides. Among these, angiotensin converting enzyme (ACE) inhibitory peptides have a major focus on their ability to prevent hypertension. Inhibition of ACE has been established as an effective approach for the treatment of ACE associated diseases.
Hypothesis/purpose: Some synthetic ACE inhibitory drugs cause side effects and hence there is a constant interest in natural compounds as alternatives.
Study design: The study was designed to identify and characterize a peptide molecule from pigeon pea which has the biological property to inhibit ACE and can be developed as a therapeutic approach towards hypertension.
Methods: Seeds of pigeon pea (*Cajanus cajan* (L.) Millsp.) was fermented with *Aspergillus niger*, a proteolytic fungus isolated from spoiled milk sweet. The extract was purified by size exclusion chromatography by FPLC system. The fractions that showed ACE inhibition was subjected to LC-MS/MS for sequence identification. The stability of the peptide was analyzed by molecular dynamic simulations and the interaction sites with ACE were identified by molecular docking.
Results: The study report a novel ACE inhibitory octapeptide Val-Val-Ser-Leu-Ser-Ile-Pro-Arg with a molecular mass of 869.53 Da. The Lineweaver–Burk plot indicated that the inhibition of ACE by this peptide is in competitive mode. Also, molecular docking and simulation studies showed a strong and stable interaction of the peptide with ACE.
Conclusion: The results clearly show the inhibitory property of the peptide against ACE and hence it can be explored as a therapeutic strategy towards hypertension and other ACE associated diseases.

Introduction

Hypertension is one of the primary risk factors for heart disease and stroke, the leading causes of death worldwide. Awareness, prevention, treatment and control of hypertension are a significant public health measure. Angiotensin-converting enzyme (ACE, EC 3.4.15.1) is one of the key enzymes in blood pressure regulation because it generates the vasoconstrictor angiotensin-II and inactivates the vasodilator bradykinin. Apart from its regular function, ACE is expressed in several malignancies and influences tumor cell proliferation, tumor cell migration, angiogenesis, and metastatic behavior (Yoshiji et al., 2002). Inhibition of ACE is considered to be a useful therapeutic approach in the treatment of pathophysiologies in which ACE is involved. Anti-ACE drugs act as vasodilators by reducing the levels of Angiotensin II in the renin angiotensin system or by inhibiting the degradation of bradykinin in the kallikrein-kinin system (Erdos, 2006). They have been prescribed as a first-line treatment for hypertension in patients with type 1 diabetes, proteinuria and left ventricular systolic dysfunction (Flint, 2004). Some synthetic ACE inhibitory drugs such as captopril, enalapril, fosinopril lisinopril etc., cause well-defined side effects such as allergic reactions, hypotension, increased potassium levels, reduced renal function, cough, angioedema, skin rashes, and foetal abnormalities

Abbreviations: ACE, Angiotensin Converting Enzyme; FPLC, Fast Protein Liquid Chromatography; HHL, Hippuryl-Histidine-Leucine; PBC, Periodic Boundary Conditions; RMSD, Root Mean Square Deviation

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