In Silico Structure Based Designing of Potent Peptide Inhibitors for Renin and Angiotensin Converting Enzymes

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The enzymes Renin and Angiotensin Converting Enzymes (ACE'S) are associated with hypertension, congestive heart failure and diabetic nephropathy. Renin is a protease and ACE's are carboxy peptidases. There are three kinds of ACE's in humans (evidence from databases). Renin is a prohormone acting on free floating angiotensinogen. All the three ACE's are membrane bound , one of the receptors of insulin participating in signal transduction and involved in the conversion of Angiotensin I to Angiotensin II, a potent vaso constrictor involved in raising blood pressure. These ACE's and renin are crucial key targets for development of drugs. The so- called anti hypertensive drugs used for treating hypertension are having their plasma half life less than that of their target enzymes. So this study was proposed with the aim to design peptide aptamers for all these enzymes. Computational tools such as Swiss model and Thematics server were used do design the 3D structure of all the enzymes and for identification of target sites. The small peptide aptamers were designed using the molecular builder tool of the Argus lab software and the target sequences were built into small peptide chains and then both the targets and aptamers were converted into PDB format. Docking results on this peptide using Hex software indicated that the peptide has potency to bind to the target sites on the enzymes. The proposed, small peptide has shown all the desirable features of a potent inhibitor and hence it may be a potential lead compound.