Molecular docking and 3D-QSAR analysis of milk dipeptides with antihypertensive activity

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Hypertension is one of the major public cardiovascular diseases worldwide which usually occurs with other metabolic disorders such as atherosclerosis and obesity [1]. In recent years, much attention has been paid to the discovery and synthesis of novel bioactive peptides with ACE inhibitory activity. In silico methods such as 3-dimensional quantitative structure activity relationship (3D-QSAR) and molecular docking simulations have been effectively used in similar researches with the aim to predict compound activity and explain its mechanism [2,3]. Studies regarding the QSAR of milk bioactive peptides are insufficient, although some 3D-QSAR models of bioactive peptides have been reported. Therefore, we hypothesized that ACE inhibitory activities of milk dipeptides could be predicted using 3D-QSAR method and that these activities could be explained through evaluation of structural features (hydrogen bond donor/acceptor, hydrophobic, steric, and electrostatic) that are responsible for this bioactivity. The most potent inhibitory peptides contain hydrophobic amino acids (such as tryptophan) that enter deep within the hydrophobic pocket of the ACE active site and make constructive interactions with the surrounding residues. CoMFA results point toward favourable steric interactions and electronegativity at the C-terminus of the peptides. These results indicate high ACE inhibition of digestible milk proteins as well as peptides obtained by their digestion, point out the high nutritive value of milk proteins, and recommend them for human consumption. Furthermore, our results will aid screening and design of novel ACE inhibitors. Milk-derived peptides have emerged as a novel alternative strategy to current pharmaceutical therapeutics.

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References

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