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Release of Angiotensin-Converting Enzyme (ACE) and Dipeptidyl Peptidase-IV (DPP-IV) inhibitory peptides from oilseed proteins – a bioinformatic prediction approach

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Defatted oilseeds, such as flaxseed, rapeseed, sunflower and sesame seed, are by-products from the food industry and currently used as animal feeds or waste. In the last two decades, these under-utilised food materials have gained growing interest due to their high protein content, which could be an abundant and low-cost source of bioactive peptides. Experimental approaches have been widely applied for exploring the biological activities of peptides. However, drawbacks of this approach are time-consuming, expensive and low yields of targeted peptides. Therefore, this study aimed to use a bioinformatic approach to assess the potential of different oilseed storage proteins as precursors of ACE and DPP-IV inhibitory peptides.

Four predominant oilseed storage proteins were selected to undergo *in silico* simulated pepsin (pH > 2) (EC 3·4·23·1) hydrolysis using 'Enzyme(s) action tool' available through BIOPEP[(1)]. The frequency of occurrence and the potency index of ACE and DPP-IV inhibitors released from precursor proteins were calculated based on peptide profiles. The peptide sequences obtained through *in silico* hydrolysis were aligned with scores using PeptideRanker based on the likelihood of bioactive peptide generation[(2)]. Finally, the peptides with a score > 0·80 (score ranges from 0-poorest to 1-most promising) were selected to predict binding sites in ACE and DPP-IV using Pepsite2, a molecular docking program[(3)]. Bovine beta-lactoglobulin was used as a comparison.

Frequency of occurrence and potency index of ACE and DPP-IV inhibitors were variable among the five proteins. In general, the peptides generated from these proteins had relatively more potent ACE inhibiting activities, despite the higher frequency of DPP-IV inhibitors (Table 1). 51 out of 1060 peptide sequences, aligned the score > 0·8, underwent the binding-site simulation using Pepsite2. These selected peptides were predicted to bind with several subsites in ACE (such as Q281, H353, H513 and Y523) and DPP-IV (such as Y547, Y666, W627 and S630) to lower the catalytic activities of both enzymes.

Table 1. Frequency and Potency Index of ACE and DPP-IV inhibitors obtained using pepsin hydrolysis.

		Frequency of occurrence		Potency Index [μM^{-1}]	
Storage proteins	Resources	ACE inhibitor	DPP-IV inhibitor	ACE inhibitor	DPP-IV inhibitor
Conlinin	Flaxseed	0·0311	0·0777	0·0016593	0·0000021
Curciferin	Rapeseed	0·0520	0·0806	0·0029150	0·0001787
11S Globulin	Sunflower	0·0424	0·0654	0·0011667	0·0000600
2S Seed Storage Protein	Sesame	0·0523	0·0640	0·0007415	0·0001051
Beta-lactoglobulin	Bovine	0·0488	0·0927	0·0014245	0·0002157

This study concludes that, based on the amino acid sequences, oilseed proteins can be considered as good precursors of ACE and DPP-IV inhibitors as compared to animal proteins, such as beta-lactoglobulin. A number of peptides have demonstrated to bind both active and none-active sites in ACE and DPP-IV, which indicates competitive and non-competitive inhibition, respectively. Further studies are required to detail the inhibition mechanisms involved and verify the predicted findings through *in vitro* and *in vivo* models.

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