Title: Study of an inhibitory effect of plant polyphenolic compounds against digestive enzymes using bench-working experimental evidence predicted by molecular docking and dynamics.

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Abstract: The substantial nutritional content and diversified biological activity of plant-based nutraceuticals are due to polyphenolic chemicals. These chemicals are important and well-studied plant secondary metabolites. Their protein interactions are extensively studied. This relationship is crucial for the logical development of functional food and for enhancing the availability and usefulness of polyphenols. This study highlights the influence of protein types and polyphenols on the interaction, where the chemical bindings predominantly consist of hydrophobic interactions and hydrogen bonds. The interaction between polyphenolic compounds (PCs) and digestive enzymes concerning their inhibitory activity has not been fully studied. Therefore, we have examined the interaction of four digestive enzymes (α-amylase, pepsin, trypsin, and α-chymotrypsin) with four PCs (curcumin, diosmin, morin, and 2′,3′,4′-trihydroxychalcone) through in silico and in vitro approaches. In vitro plate assays, enzyme kinetics, spectroscopic assays, molecular docking, and simulations were performed. We observed all these PCs have significant docking scores and preferable interaction with the active site of the digestive enzymes, resulting in the reduction of enzyme activity. The enzyme-substrate binding mechanism was determined using the Lineweaver Burk plot, indicating that the inhibition occurred competitively. Among four PCs diosmin and morin has the highest interaction energy over digestive enzymes with IC50 value of 1.13 ± 0.0047 and 1.086 ± 0.0131 μM. Kinetic studies show that selected PCs inhibited pepsin, trypsin, and chymotrypsin competitively and inhibited amylase in a non-competitive manner, especially by 2′,3′,4′-trihydroxychalcone. This study offers insights into the mechanisms by which the selected PCs inhibit the enzymes and has the potential to enhance the application of curcumin, diosmin, morin, and 2′,3′,4′-trihydroxychalcone as natural inhibitors of digestive enzymes.

Keyword: α-Amylase, Trypsin, Molecular Docking, Molecular Dynamics, Enzyme Kinetics, Polyphenolic Compounds.

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