Virtual Screening of *A. unedo* Phytochemicals as Potential Inhibitors of α-Amylase and α-Glucosidase Activities Using Computer Aided Drug Design

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Introduction & Objectives: In view that the oxidative stress is related to diabetes and its complications, some phenolic compounds obtained from *A.* unedo species act as antioxidants while limiting starch digestion, and protecting against hyperglycemia-induced chronic diseases. It is worthy to note that several studies have reported that the anti-diabetic properties of plant extracts are strongly correlated with their phenolic content, as well as the fact that phenolic compounds inhibit the α-amylase and α-glucosidase activities. Our research work aimed to determine the various chemical components contained in the methanolic extract, and then the impact of these polyphenols on *α*-amylase and *α*-glucosidase using *in vitro* and *in silico* methods.

Methodology:

The components contained in methanolic extract were tested for their antidiabetic activity via on one hand in vitro test using α-amylase and α-glucosidase inhibition method through starch iodine color assay, and acarbose was used as a positive control, on the other hand via *in silico* study in which carbohydrate-hydrolyzing enzymes such as *α*-amylase and *α*-glucosidase are targets mainly related to diabetes mellitus.

The AutoDock vina software was used for docking the isolated molecules and standards. **2ZE0 (***α*-glucosidase) and **1HNY (***α*-amylase) playing a critical role during enzymatic activities are suggested to be the main targets for the inhibition of *α*-glucosidase and *α*-amylase respectively.

Results and Discussion: The catechin isolated from ***A.unedo*** extract showed higher binding affinity than the standards toward **2ZE0** and **1HNY** and expressed good pharmacokinetic properties. Furthermore, the docking results showed that the complex catechin /**2ZE0** produces one hydrogen bond with TYR (63), six cycle-bonds with the amino acids ARG (197); HIS (325); ASP (326); GLU (256) PHE (163) and TYR(63), and eleven Vander Waals bonds with ARG(197);HIS(325);ASP(326); GLU(256) ;PHE(163);TYR(63). The binding energy was found -9 kcal/mol, while the complex catechin / **1HNY** produces five hydrogen bonds with the following residues : ASP (197) ; ASP (300) ; ARG (195); HIS(299);GLU(233), two cycle-bonds with the amino acids TYR (62); TRP(59),seven Vander Waals bonds with ALA(198);LEU(162);GLN(63);THR(163);LEU(165);HIS(101); TRP(58). The binding energy was found -8.6 kcal/mol.

Conclusion:

The *in-silico* results in terms of docking and molecular dynamics corroborated that catechin obtained from methanolic extract using different chromatographic methods could be exploited in diabetic therapy. Moreover, ***A.unedo*** extract could be recommended for the production of antioxidant-rich therapeutic diets and additional foods with enzyme inhibitory capacity as a significant technique for treating hyperglycemia ,and this will be extremely beneficial to the food field and pharmaceutical industries.

Keywords: Diabetes, *A.unedo*, Hyperglycemia, Antidiabetic activity, Docking, Molecular dynamics, Pharmaceutical industries.

References

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