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MEETING ABSTRACT

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Oxyresveratrol as a promising drug candidate for metabolic diseases: a pharmacoinformatics study

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Background: Resveratrol is a polyphenol with demonstrated cardioprotective, chemopreventive, anti-inflammatory and antioxidant effects. Recently it was shown that resveratrol binds to the PPAR-γ receptor and that it can reduce insulin resistance associated with obesity. Low solubility in water is the major limiting factor for widespread pharmaceutical use of resveratrol. Therefore, the aim of our study was to identify analogues of resveratrol with improved pharmacokinetic properties and higher binding affinities towards the PPAR-γ receptor.

Methods: 3D structures of resveratrol and its analogues were retrieved from the ZINC database, while the PPAR-γ structure was obtained from the Protein Data Bank. Docking studies were performed using the Molegro Virtual Docker software. Molecular descriptors relevant to solubility and pharmacokinetics were calculated from ligand structures using the VolSurf+ software.

Results: Using a structural similarity search method in the ZINC database, 57 compounds were identified and subjected to docking analyses. Binding energies (MolDock scores) ranged from −136.69 to −90.89 kcal/mol. The MolDock score for resveratrol was −118.04 kcal/mol. Sixteen compounds exerted lower binding energies, *i.e.* higher affinities towards PPAR-γ. Calculated values of the SOLY descriptor, as logarithm of intrinsic solubility, ranged from −5.05 to −3.24, and 23 studied compounds were found to be more soluble in water than resveratrol. By combining these results it was revealed that only two tetrahydroxy stilbene derivatives, piceatannol and oxyresveratrol, had both better solubility and affinity towards PPAR-γ. Calculated pharmacokinetic parameters showed that both these compounds were more stable metabolically and more widely distributed in the body than resveratrol, but only oxyresveratrol had a higher value of the amphiphilic moment, which determines the ability to permeate membranes and absorption.

Discussion: The results of our study demonstrate that oxyresveratrol is a promising drug candidate that should be investigated more in-depth for a potential use in metabolic diseases.

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