Docking and *in silico* pharmacokinetic studies for barbinervic acid, a triterpene isolated from *Eugenia punicifolia* (Myrtaceae)

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Introduction and Objective

Mammalian nitric oxide synthase (NOS) is a homoprotein of a flavo-hemoprotein. Molecular weight of the monomer ranges from 110 kDa to 160 kDa, depending on the isoform – neuronal, inducible or endothelial. NOS is particularly interesting and complicated because of the variety of redox cofactors in the catalytic assembly. We have successfully isolated and identified a triterpene, barbinervic acid, from dichloromethane extract of Eugenia punicifolia (Myrtaceae)[1]. Results showed that barbinervic acid reduced vascular tonus in rat renal circulation and also in rat thoracic aorta, likely by interactions on nitrergic pathway.Thus, to gain insights on chemical and pharmocokinetics characteristic of barbinervic acid and on putative interactions with nNOS enzyme, we applied molecular modeling methodologies and physicochemical and both ADME-Tox *in silico* analysis for barbinervic acid. The terpene was constructed in Spartan 14 (Wavefunction, Inc.). Conformational analysis was done from the starter structure by Metropolis Monte Carlo method to achieve more stable structures to be employed for calculating chemical properties[2]. Electronic and structural descriptors were calculated in Spartan 14 program using *ab initio* Hartree-Fock 6-31G* method. Barbinervic acid interactions on nNOS were investigated by docking methodology with Molegro using MolDock algorithm utilizing enzyme retrieved from protein data bank (PDB).

Results and Discussion

Barbinervic acid made interactions with HEME group and the aminoacids Tyr706, Gln478, Trp678, and Pro565. Results of Lipinski rule of five for barbinervic acid were also obtained: MW 489.09, logP 5.07, HBD 4, HBA 5.
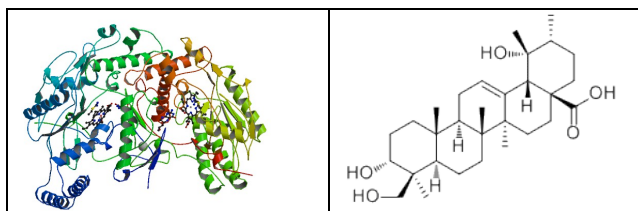

Figure 1. Secundary structure of nNOS and 2D chemical structure of barbinervic acid.

Conclusions

Computational studies were useful to knowing barbinervic acid 3D structure and chemical characteristics, and demonstrated its druglikeness properties as potential nNOS inhibitor. The docking results showed the possible interactions of the ligand on nNOS enzyme and will be of importance for structural optimizing of the compound.

ACKNOWLEDGEMENTS

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