Molecular modeling studies for barbinervic acid, a triterpene isolated from *Eugenia punicifolia* (myrtaceae)

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Introduction

We successful isolated and identified barbinervic acid (Fig.1) from dichloromethane extract[1]. Results showed that barbinervic acid reduced vascular tonus in rat renal circulation and also in rat thoracic aorta possible by interactions on nitrergic pathway. To get insights on chemical and pharmocokinetics characteristics of barbinervic acid and to gain knowledge on interactions on nNOS enzyme, we applied molecular modeling methodologies and physic-chemical and ADME-Tox *in silico* for barbinervic acid. The terpene was constructed in Spartan 14 program (Wavefunction, Inc.) and geometric was optimized with MMFF force field[2]. Conformational analysis was done from the starter structure by Metropolis Monte Carlo method to achieve more stable structures to be employed as a base for calculating chemical properties. Electronic and structural descriptors were calculated in Spartan 14 program using *ab initio* Hartree-Fock method. Barbinervic acid interactions on nNOS were investigated by docking methodology utilizing an enzyme from protein data bank (PDB) as a model (Fig. 2). The study was done in the MolDock program.

Figure 1. Barbinervic acid

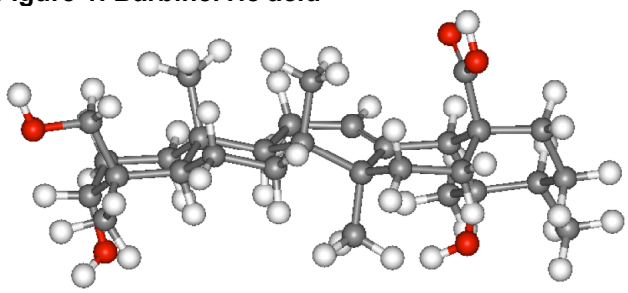
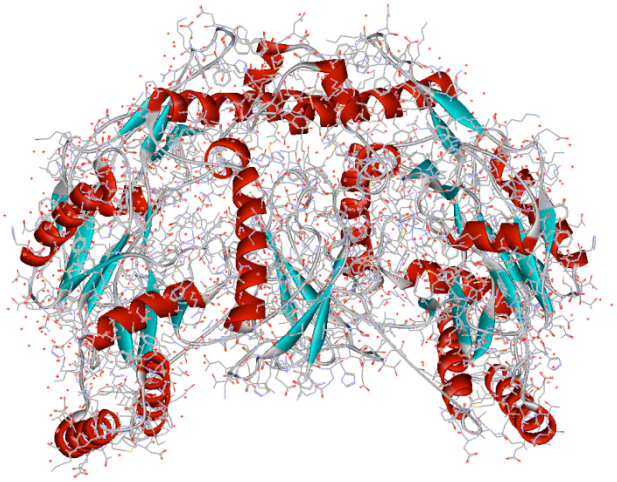


Figure 2. 3D structure for nNOS enzyme



Results and Discussion

It was found ten conformers with energy variation of nearby 2Kcal/mol. The conformer that presented less energy was isolated and submitted to geometric improvement by *ab initio* method; however, due to acid barbinervic rigid ring structure, any significant change in molecular skeleton was observed. The terpene holds a volume of 519.25Å3, polar surface area (PSA) of 85.539 Å^2 and 5.07l og P. It also holds 4 acceptors and 4 donors groups of hydrogen bonds; these might be of importance for *in vivo* nNOS interactions. The docking studies demonstrated the main 5 *poses* for possible interactions with nNOS. The main found interactions were of Van der Waals, which is done with apolar groups. This can be provided observing the hydrocarbon structure of the terpene, which possesses a MW of 488 a.m.u. One hydrogen bond was also observed. The aminoacids Pro565 and Val567 were found to be involved in the interactions.

Conclusions

Preliminary molecular modeling studies were useful for understanding barbinervic acid 3D structure 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 future strucutural optimizing for the compound.

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