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Short Communication

Predicting Binding Between Main Molecules of Iranian *Oliveria decumbens* and DPP-4 Enzyme Using Molecular DockingSalim Bouchentouf^{1,2*} and Ebrahim Talebi³¹Faculty of Technology, Doctor Tahar Moulay University of Saïda, Algeria.²Laboratory of Natural Products and Bioactives (LASNABIO), Algeria.³Darab Branch, Islamic Azad University, Darab, Fars, Iran.

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ABSTRACT

Type 2 Diabetes (T2D) is an endocrine disease affecting millions of humans around the world, causing many damages to human health. Many drugs are used for the treatment of T2D, but they have many secondary effects. Natural products, especially from plants, can be sources of important bioactive molecules which can serve as an alternative to T2D treatment. Constituent molecules of essential oil from Iranian *Oliveria decumbens* were investigated for their capacity to inhibit Dipeptidyl-Peptidase 4 (DPP-4) enzyme which has been implicated in type 2 diabetes. Formation of stable complexes between enzyme and ligands was carried out using molecular docking. The energy of the complexes formed was also calculated. The compounds with the lowest energy were predicted to have the best binding. The results obtained predicted myristicin to be the best binder of DPP-4 enzyme.

Keywords: Medicinal plant, *Oliveria decumbens*, DPP-4 enzyme, Molecular docking.

Introduction

Oliveria decumbens is a famous endemic plant of Flora Iranica used for therapeutic purposes.¹ Traditionally *Oliveria decumbens* is used for indigestion, diarrhea, abdominal pain and fever.² Major research about the therapeutic effect of *Oliveria decumbens* consists of antibacterial, antioxidant, antifungal and antimicrobial activities.³⁻⁵ No previously published studies have reported the effect of *Oliveria decumbens* on type 2 diabetes. A survey of literature indicates that 14 molecules were identified in essential oil from all parts of *Oliveria decumbens*.⁵ The aim of this work is to carry out the relationship between essential oil composition from all parts of *Oliveria decumbens* and type 2 diabetes by observation of complex formation with DPP-4 enzyme. The research-based pharmaceutical industry has increasingly employed modern medicinal chemistry methods, including molecular modeling, as powerful tools for the study of structure-activity relationships (SAR).⁶ Molecular docking is one of the most frequently used methods in computational chemistry because of its ability to predict, with a substantial degree of accuracy, the conformation of small-molecule ligands within the appropriate target binding site, molecular docking became an essential tool in drug discovery.^{7,8}

Molecular docking in this work permits a rapid means of identification of the best-predicted binder of 14 compounds from *Oliveria decumbens* against DPP-4 enzyme. The findings from this study may help researchers in the identification of new natural bioactive molecules which may be investigated further to develop new drugs for diabetes treatment.

Materials and Methods

The scientific procedure is based on computational methods (molecular dynamic and molecular mechanic). Scoring functions by molecular docking are the best way for observation of complex formation between DPP-4 enzyme and molecules from *Oliveria decumbens* and prediction of the strength of association or binding affinity. Molecular Operating Environment (MOE) software was used.⁹

Step 1

The first step was the downloading of DPP-4 three-dimensional structure from Protein Data Bank under 5T4B code and X-ray resolution equal to 1.76Å. Ligands were drawn using MOE builder and ChemDraw.

Step 2

The second step involved energy minimizing of the enzyme and geometry performed using Hamiltonian AM1 implanted in MOE software then isolation of the enzyme active site (target). The most stable conformer of each molecule (ligand) was also performed.

Step 3

The third step was positioning of the ligands into the active site of the enzyme using dock module implanted in MOE software. Binding energy between target and ligands was calculated by molecular mechanics.

Results and Discussion

According to the result obtained (Table 1), out of the 14 compounds studied, Myristicin (Figure 1) was predicted to be the strongest binder of DPP-4 enzyme forming the most stable complex (Figures 2 and 3), with H- π interaction with distance of 4.42 Å and energy about -0.9 kcal/mol. The second-best binder is β -Elemene, with H- π interaction with a distance of 4.07 Å and energy about -0.6 kcal/mol and the third-best binder was Torreyol, with H-donor interaction with a distance of 2.80 Å and energy about -0.6 kcal/mol.

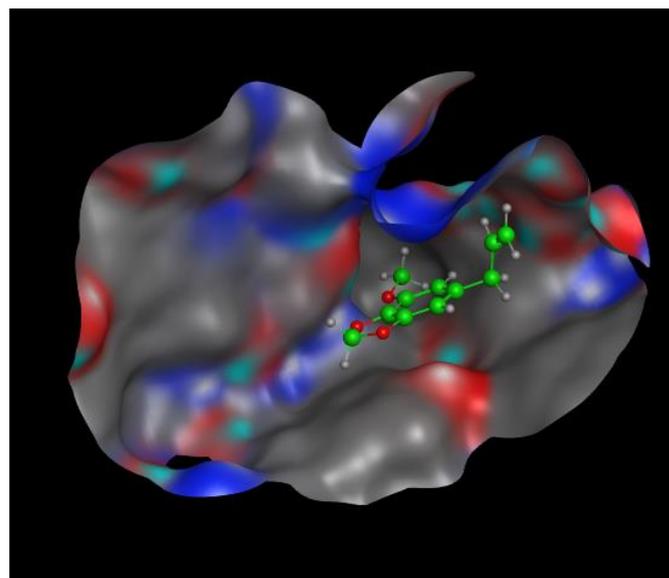
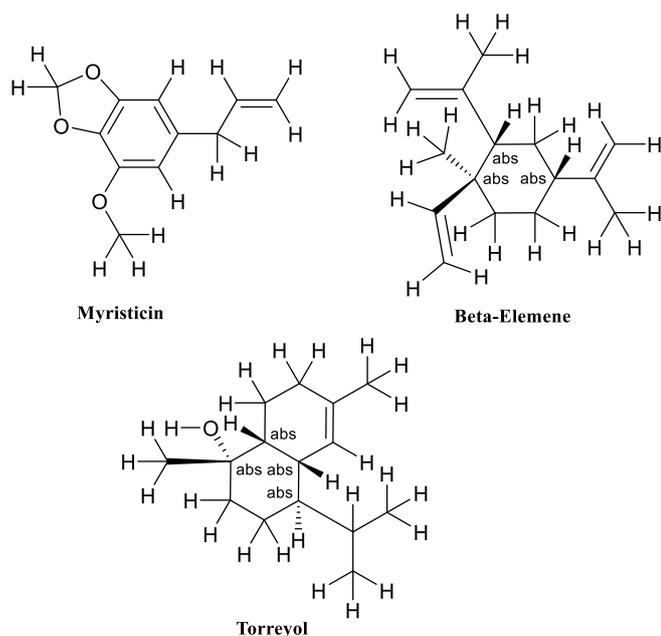
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Table 1: Energy balance of complexes (kcal/mol).

Ligand	Docking Score
Carvacrol	-4.13835287
Caryophyllene oxide	-4.55230522
Hydroxyl-p-cymen	-4.40429163
Moslene	-4.13940716
Myristicin	-4.90596437
<i>p</i> -Cymene	-4.21636581
Spathulenol	-4.4098959
Thymol	-4.48379087
Torreyol	-4.71321297
Verbenone	-4.34800482
Zizanal	-4.35573578
β -Elemene	-4.72603416
α -Eudesmol	-4.67303276
γ -Cadinene	-4.54492235

**Figure 2:** Positioning of Myristicin in DPP-4 active site.**Figure 1:** Molecular structures of major binders of DPP-4 enzyme from *Oliveria decumbens*.

Conclusion

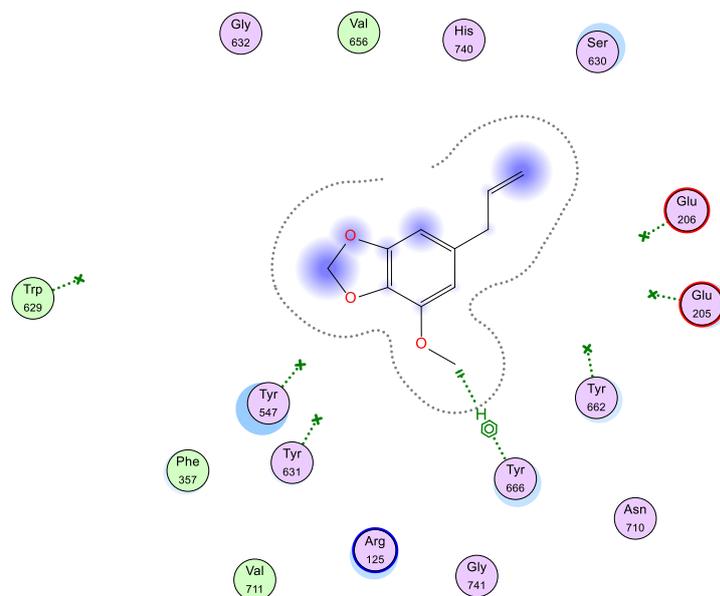
Molecules from *Oliveria decumbens* showed good inhibition of DPP-4 enzyme, especially Myristicin which gave the best score. This finding will encourage further investigation of the hypoglycemic effect of Iranian *Oliveria decumbens*.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

**Figure 3:** 2D Diagram of the interaction between Myristicin and DPP-4.

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References

- Mozaffarian V. A dictionary of Iranian plant names. Farhang Mo'aser: Tehran; 1996. 371-372 p.
- Amin GH, Salehi Sourmaghi MH, Zahedi M, Khanavi M, Samadi N. Essential oil composition and antimicrobial activity of *Oliveria decumbens* Vent. Fitoterapia. 2005; 76:704-712.
- Motamedi E, Darabpour M, Gholipour SM, Sayyed Nejad S. Antibacterial effect of Ethanolic and Methanolic extracts of *Plantago* and *Oliveria decumbens* Endemic in Iran Against some pathogenic bacteria. Int J Pharmacol. 2010; 6(02):117-122.

4. Hajimehdipoor H, Samadi N, Mozaffarian V, Rahimifard N, Shoeibi S, Pirali HM. Chemical Composition and Antimicrobial Activity of *Oliveria decumbens* Volatile Oil from West of Iran. J Med Plants 2010; 33(06):39-44.
5. Khosravinezhad M, Talebi E, Shivakumar, Nemati Z, Nasrollahi I. Essential oil composition and antimicrobial, antioxidant activities of *Oliveria decumbens* Vent. Int J Herbal Med. 2017; 5(2):102-106.
6. Hughes JP, Rees S, Kalindjian SB, Philpott KL. Principles of early drug discovery. Br J Pharmacol. 2011; 162:1239-1249.
7. Meng XY, Zhang HX, Mezei M, Cui M. Molecular docking: A powerful approach for structure-based drug discovery. Curr Comput Aided Drug Des. 2011; 7:146-157.
8. López-Vallejo F, Caulfield T, Martínez-Mayorga K, Giulianotti MA, Houghten RA, Nefzi A, Medina-Franco JL. Integrating virtual screening and combinatorial chemistry for accelerated drug discovery. Comb Chem High Throughput Screen. 2011; 14:475-487.
9. Molecular Operating Environment (MOE), 2013.08; Chemical Computing Group Inc., 1010 Sherbooke St. West, Suite #910, Montreal, QC, Canada.