RESEARCH ARTICLE

Molecular Docking Prediction of Carvone Towards GABA-ATase and Sodium Channel

Snigdha Srivastava*, Reema Sinha, Pallavi M. Lavhale, Rajan K. Kurmi

Abstract

Aim: Modern tool designs frequently employ molecular docking to anticipate small molecules' binding orientation and better comprehend drug-receptor interactions. Carvone's molecular docking analysis against sodium channels and GABA-AT is part of this research investigation.

Introduction: Carvone's molecular docking analysis against sodium channels and GABA-AT is part of this research investigation. The biological significance of carvone has been demonstrated to include anti-epileptic, anti-fungal, anti-inflammatory, anti-cancer, and antioxidant effects. In modern drug design, molecular docking is commonly used to get an understanding of drug-receptor interaction carried out an in-silico evaluation of derivatives of carvone.

Methodology: ChemDraw 2D (15.1) software is used to draw the ligands, ChemDraw-3D is utilized to decrease energy consumption, chimera is used to produce the protein, and Auto Dock 4.0 was used to examine the binding score. To determine whether it would cross to BBB+/BBB- or not, cheminformatics and fingerprint analysis were done using Molinspiration and Adaboost with SVM.

Result: Comparable metrics for newly created carvone derivatives included potential energy, docking score, glide score, and highest docking score. Compounds with docking scores of (-8.39, -5.06, -4.00 kcal/mol). The conformers at the active site are shown and predicted using Discovery Studio Visualizer.

Conclusion: The results of the molecular docking study showed that compound1 has a high affinity for the active pocket and a low binding energy, which made them potentially useful as an anti-convulsant.

Keywords: Terpenoid, Monoterpenoid, Stereochemistry, Anti-convulsant.

Journal of Applied Pharmaceutical Sciences and Research, (2023); DOI: 10.31069/japsr.v6i2.03

Introduction

The enantiomers of carvone R&S, from historical data to current potential therapeutic effects like anti-cancer activity, anti-epileptic activity, antimycotic activity, anti-fungal activity, antidiabetic activity, antimanic activity, anti-radial activity, etc., have drawn a lot of interest in the creation of cutting-edge prophylactic and therapeutic agents dating back to an ancient era.[1] *Carum carvi* (caraway), *Anethum graveolens* (dill), *Mentha spicata* (spearmint), and *Calamintha officinalis* are the main sources of carvone (calamint). More organic compounds, in particular, were discovered that may have disease-preventing properties.[2] The GABA-AT protein, Na+ channel, and on some sites as antioxidants are examples of powerful moieties with the highest binding energy and biological activity, and in-silico docking experiments demonstrate a straightforward and practical method to identify these molecules.[3] The online web-server molinspiration of R (+) Carvone derivative was used to calculate the molecular property and bioactivity score. Molecular docking provides useful data regarding drug candidates' drug receptor molecules when predicting a small molecule's affinity and activity. EC was effective in preventing the tonic convulsions induced by maximal electroshock (MES) in doses of 200, 300, or 400 mg/kg, resulting in 25, 25, and 100% of protection, respectively, and promoted protection of 75 and 87.5% against convulsions induced chemically by pentylenetetrazole (PTZ).[4]

Ram-Eesh Institute of Vocational & Technical Education, GreaterNoida, Uttar Pradesh, India.

Corresponding Author: Snigdha Srivastava, Ram-Eesh Institute of Vocational & Technical Education, GreaterNoida, Uttar Pradesh, India. Email: snigdhasrivastava2247@gmail.com

How to cite this article: Srivastava S, Sinha R, Lavhale PM, Kurmi RK. Molecular Docking Prediction of Carvone Towards GABA-ATase and Sodium Channel. Journal of Applied Pharmaceutical Sciences and Research. 2023; 6(2):16-18

Source of support: Nil

Conflict of interest: None

Received: 27/06/2023; **Accepted:** 08/09/2023; **Published:** 05/10/2023

Material and Method

In Chem Draw 15.1 (Chem Office program), the ligands were given the proper 2D orientation, and the structures of each compound were checked for connection and bond order problems. Adaboost and SVM with fingerprint were utilized in Molinspiration and BBB prediction. Carvone derivatives were docked into the receptors PDB ID 1OHV and 2KAV binding sites using the Auto Dock 4.0 tool. The protein grid, which was made after the ligand and protein were synthesized, determined the size of the grid box in which the ligand was anticipated to bind in order to reduce the energy of the molecules, Chem Draw 3-D was utilized. Following that, molecules with reduced energy were read as input into Auto Dock 4.2, which carried out the docking

simulation. The protein was made using Chimera 1.15. The graphical user interface program "Auto Dock Tools" was used to prepare, run, and evaluate the docking simulations. The receptor for protein synthesis was given Kollman unified atom charges, solvation parameters, and polar hydrogen in a docking simulation. Auto Dock needs pre-calculated grid maps for each kind of atom present in the ligand being docked to preserve the potential energy arising from the interaction with the macromolecule. The grid center was set to 21.572, -5.701, and 30.404 for x, y, and z, respectively, which encompassed all seven amino acid residues in the presumed active pocket. The grid box sizes were set at 56, 64, and 74 for x, y, and z, respectively. The region of interest for the macromolecule must be surrounded by this grid (active site). The binding site in this study was selected based on the amino acid residues required for binding with Lys:329 amino acid. The grid was, therefore, concentrated on the area containing all seven amino acids for binding.[5,6]

Result and Discussion

The docking result shows that the protein and ligand are bonded to each other in the appropriate manner and within the specified limits. Comparable metrics for newly created carvone derivatives included potential energy, docking

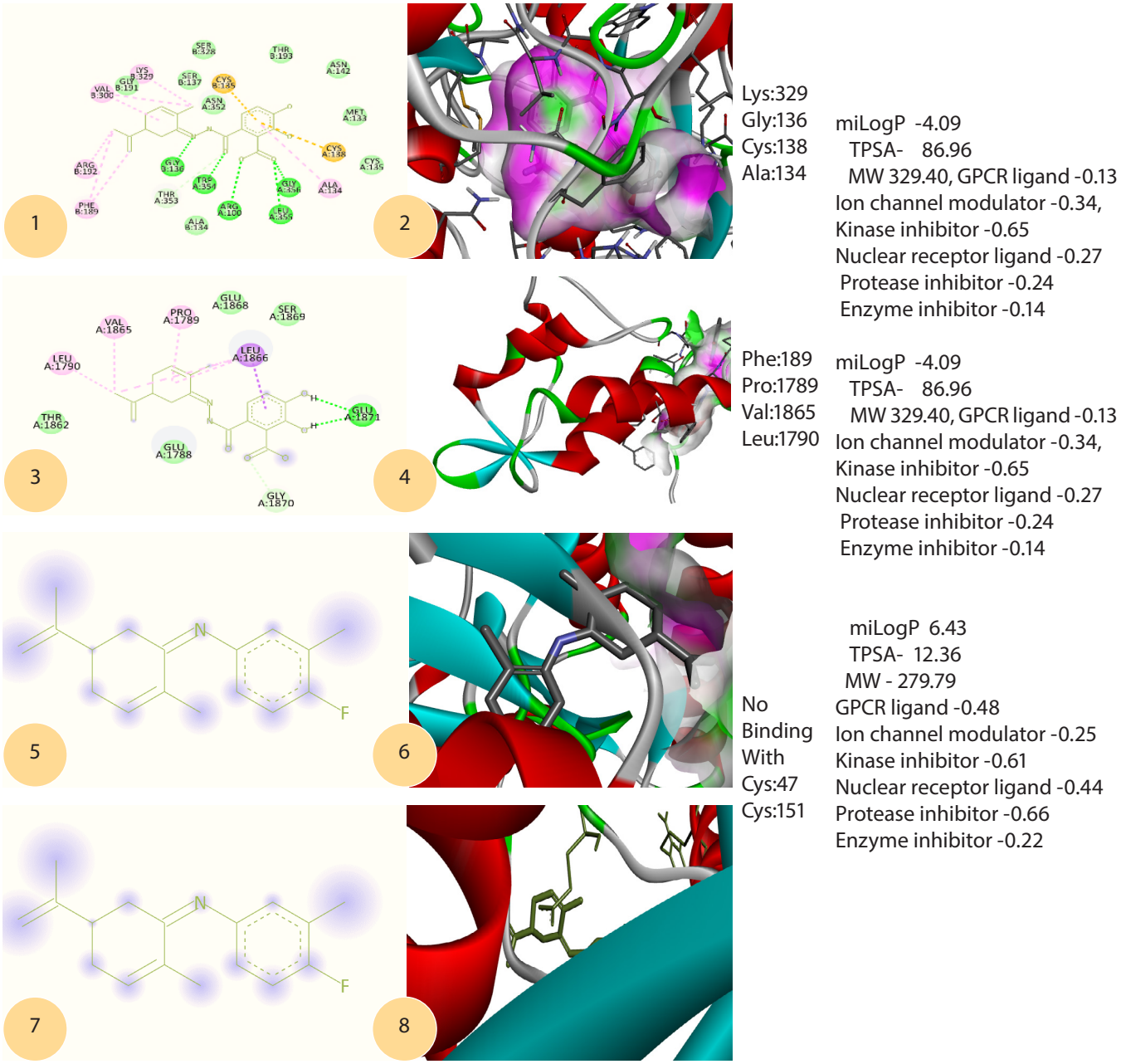

Figure 1: 1,3,5 and 7 explains the 2-D structure & and Figure 2,4, 6, and 8 explains the 3-D structure of the ligand-protein interaction of compound 1 and 2. Also its active binding amino acids (Lys:329, Gly:136, Cys:138, Ala:134Phe:189), (Pro:1789,Val:1865,Leu:1790) for compound 1 and No Binding with Cys:47Cys:151 for compound 3.

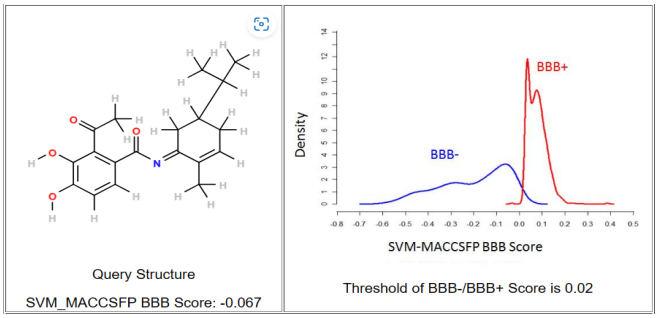

Figure 2: Support vector machine (SVM) BBB score of -0.067 and the threshold score of BBB is 0.02

score, glide score, and highest docking score. blood brain barrier prediction carvone derivatives were docked into the receptors PDB ID 1OHV and 2KAV binding sites using the Auto Dock 4.0 tool. The protein grid, which was made after the ligand and protein were synthesized, determined the grid box size in which the ligand was anticipated to bind. The docking result shows that the protein and ligand are bonded to each other in the appropriate manner and within the specified limits. Comparable metrics for newly created carvone derivatives included potential energy, docking score, glide score, and highest docking score. In (Figure 1), Compound 1 was identified as the most active with docking scores of (-8.39, -5.06, -4.00). (Figure 1). The conformers at the active site are shown and predicted using the Discovery Studio Visualizer. Brain-blood barrier forecast. In (Figure 2) explains the support vector machine (SVM) BBB score of -0.067 and the threshold score of BBB is 0.02, which explains the good penetration of compound 1.

Conclusion

Using the web-server Pro Tox-ii, where carvone has demonstrated its toxicity to the Class-IV organisms. So, carvone can easily penetrate the blood-brain barrier (BBB) with less toxic effects based on the analysis of prior studies on the carvone moiety. *In-silico* docking studies revealed the highest binding affinity for compound-1 is -8.39 kcal/mol and according to the molecular characteristics of the docking studies supported by molinspiration, SVM -0.067, and threshold score of 0.02. This may conclude that compound-1 is a potent anti-epileptic drug against 1OHV.

References

1. Morcia C, Tumino G, Ghizzoni R, Terzi V. Carvone (Mentha spicata L.) Oils. Essential Oils in Food Preservation, Flavor and Safety. 2016 Jan 1;309–16.
2. Bouyahya A, Mechchate H, Benali T, Ghchime R, Charfi S, Balahbib A, et al. Health Benefits and Pharmacological Properties of Carvone. Biomolecules 2021, Vol 11, Page 1803 [Internet]. 2021 Dec 1 [cited 2023 Jun 17];11(12):1803. Available from: https://www.mdpi.com/2218-273X/11/12/1803/htm
3. Aliye M, Dekebo A, Tesso H, Abdo T, Eswaramoorthy R, Melaku Y. Molecular docking analysis and evaluation of the antibacterial and antioxidant activities of the constituents of Ocimum cufodontii. Scientific Reports 2021 11:1 [Internet]. 2021 May 12 [cited 2023 Jun 17];11(1):1–12. Available from: https://www.nature.com/articles/s41598-021-89557-x
4. de Almeida RN, de Sousa DP, Nóbrega FF de F, Claudino F de S, Araújo DAM, Leite JR, et al. Anti-convulsant effect of a natural compound α,β-epoxy-carvone and its action on the nerve excitability. Neurosci Lett. 2008 Sep 26;443(1):51–5.
5. Yoshida E, Kojima M, Suzuki M, Matsuda F, Shimbo K, Onuki A, et al. Increased carvone production in Escherichia coli by balancing limonene conversion enzyme expression via targeted quantification concatamer proteome analysis. Scientific Reports 2021 11:1 [Internet]. 2021 Nov 11 [cited 2023 Jun 17];11(1):1–13. Available from: https://www.nature.com/articles/s41598-021-01469-y
6. Vijesh AM, Isloor AM, Telkar S, Arulmoli T, Fun HK. Molecular docking studies of some new imidazole derivatives for antimicrobial properties. Arabian Journal of Chemistry. 2013 Apr 1;6(2):197–204.