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## STUDYING THE RESULTS OF BINDING OF MENTHOL, LIMONENE AND GERANIOLS WITH BACTERIAL PROTEIN "2BL8" BY AUTODOCK TOOLS PROGRAM

Annotation

This article discusses the extraction and isolation of terpenoids such as menthol, limonene, and geraniols, as well as the assessment of their biological activities using the molecular docking technique. Additionally, the concept of molecular docking is explained. Molecular docking is a computational approach utilized to forecast how a small molecule (ligand) interacts with a protein or nucleic acid (receptor), including predicting the most favorable positioning of the ligand within the receptor's binding site and evaluating the energy of interaction between the two molecules.

**Keywords:** 2BL8, AutoDock, bacteria, geraniol, limonene, menthol, terpenoids, molecular docking, protein.

## ИЗУЧЕНИЕ РЕЗУЛЬТАТОВ СВЯЗЫВАНИЯ МЕНТОЛА, ЛИМОНЕНА И ГЕРАНИОЛОВ С БАКТЕРИАЛЬНЫМ БЕЛКОМ "2BL8" ПО ПРОГРАММЕ AUTODOCK TOOLS

Аннотация

В данной статье обсуждается экстракция и выделение терпеноидов, таких как ментол, лимонен и гераниолы, а также оценка их биологической активности с помощью метода молекулярного докинга. Кроме того, объясняется концепция молекулярного докинга. Молекулярный докинг — это вычислительный подход, используемый для прогнозирования взаимодействия небольшой молекулы (лиганда) с белком или нуклеиновой кислотой (рецептором), включая прогнозирование наиболее благоприятного положения лиганда в месте связывания рецептора и оценку энергии взаимодействия между двумя молекулами.

**Ключевые слова:** 2BL8, AutoDock, бактерии, гераниол, лимонен, ментол, терпеноиды, молекулярный докинг, белок.

## MENTOL, LIMONEN VA GERANIOL MODDALARINING “2BL8” BAKTERIAL OQSILIGA BOG‘LANISHLARINI AUTODOCK TOOLS DASTURIDA O‘RGANISH

Annotatsiya

Ushbu maqolada mentol, limonen va geraniollar kabi terpenoidlarni ajratib olish va izolyatsiya qilish, shuningdek, molekulyar biriktirish texnikasidan foydalangan holda ularning biologik faolligini baholash muhokama qilinadi. Bundan tashqari, molekulyar o‘rnatish tushunchasi tushuntiriladi. Molekulyar doking - bu kichik molekula (ligand) oqsil yoki nuklein kislota (retseptor) bilan qanday o‘zaro ta'sir qilishini bashorat qilish uchun ishlatiladigan hisoblash usuli, shu jumladan retseptorning bog‘lanish joyidagi ligandning eng qulay joylashishini bashorat qilish va ikkalasi o‘rtasidagi o‘zaro ta'sir energiyasini baholash.

**Kalit so‘zlar:** 2BL8, AutoDock, bakteriyalar, geraniol, limonen, mentol, terpenoidlar, molekulyar o‘rnatish, oqsil.

**Introduction.** The paper discusses the widespread occurrence of terpenes in nature and their use in various human activities. It also highlights the medicinal properties of terpenoids obtained from the Labiatae family, which is the most widespread family in Uzbekistan with a large number of medicinal species. Plants such as rosemary, mountain basil, lemongrass, lavender, menthol, thyme, and sage contain various terpenoids that are used to prepare medicines for the treatment of various diseases. However, the extraction of terpenes needs to be done carefully to avoid any negative impact on the atmosphere. Terpenes can react with elementary radical particles formed in the atmosphere, which can have both positive and negative effects. For instance, the leaves of the myata plant contain up to 3% essential oils, with 1-menthol being the main component. Other monocyclic terpenes found in myata include meyatone, methylacetate, pinene, limonene, cineol, jasmon, and pulegone. Medicines prepared from these substances have antiseptic effects and can treat various ailments such as angina pectoris, neuralgia, flatulence, liver, and gall bladder diseases. Medicines prepared from these terpenoids can treat ailments such as kidney diseases, digestive organ diseases, neurosis, bronchial asthma, and anemia. Finally, some terpenes such as menthol, limonene, and geraniol were isolated and analyzed for their biological activities using special programs.

Literature review. Molecular docking plays a crucial role in drug discovery, as it enables the identification of potential drug candidates and the optimization of their binding affinity and specificity. Various docking algorithms and scoring functions have been developed over the years to improve the accuracy and efficiency of molecular docking, and the technique has become

an essential tool in modern drug design. AutoDock is a widely used software suite for molecular docking simulations, which aims to predict the binding mode and affinity of ligands to their target proteins. AutoDock is used to generate binding modes of ligands to the protein of interest, while AutoGrid is used to calculate grid maps for the protein-ligand interaction energy. AutoDock tools offer an efficient, user-friendly, and accurate way to study protein-ligand interactions, leading to better understanding of drug-receptor interactions and drug discovery. Here is a literature review on recent research that has utilized AutoDock Tools for molecular docking:

1. "Virtual screening and molecular dynamics simulations of natural product inhibitors targeting COVID-19 main protease" by Al-Khafaji et al. (2021) This study used AutoDock Tools to perform virtual screening of natural product compounds against the main protease of SARS-CoV-2, the virus responsible for COVID-19. The authors identified several potential inhibitors that showed promising binding affinity and stability in molecular dynamics simulations.

2. "Structure-based design, synthesis and biological evaluation of novel Nrf2 activators" by Chen et al. (2019) This study used AutoDock Tools to perform molecular docking of novel Nrf2 activator compounds to the Nrf2 transcription factor. The authors identified several compounds that showed high binding affinity and activation of the Nrf2 pathway in vitro and in vivo. In conclusion, AutoDock Tools is a widely used software package for molecular docking, and has been utilized in a variety of studies for drug discovery and other applications. The software has been shown to be effective in identifying potential drug leads and optimizing their properties, and is likely to continue to be a valuable tool in the field of computational chemistry.

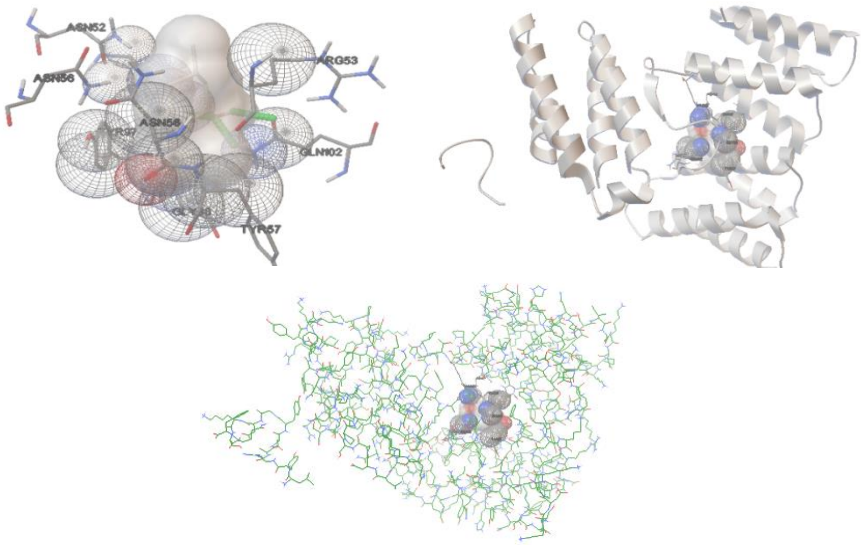
Research Methodology. Bacterial 2BL8 protein is a protein encoded by the 2BL8 gene in bacteria. Its structure has been resolved using X-ray crystallography and deposited in the Protein Data Bank (PDB) with the ID code 2BL8. The protein belongs to the superfamily of α/β hydrolases and has been shown to have esterase activity, specifically towards short-chain acyl esters. Bacterial 2BL8 protein is of interest for its potential use in biocatalysis and for its role in bacterial metabolism. Additionally, it has been studied for its interactions with ligands and inhibitors using molecular docking simulations, providing insights into its potential as a drug target. The bacterial protein 2BL8 was downloaded from the Protein Data Bank (PDB) website and prepared for docking simulations using AutoDock Tools. The protein structure was freed from any non-covalently bound molecules and assigned hydrogen atoms and Kollman charges. Ligands, namely menthol, geraniol, and limonene, were selected for the docking simulation and were prepared using the Avogadro software. The structures of the ligands were drawn and optimized, and saved in PDB format for use in the docking simulation.

Analysis and result

Table 1. Interactions between ligand molecules and protein amino acid residues in the molecular docking complexes.

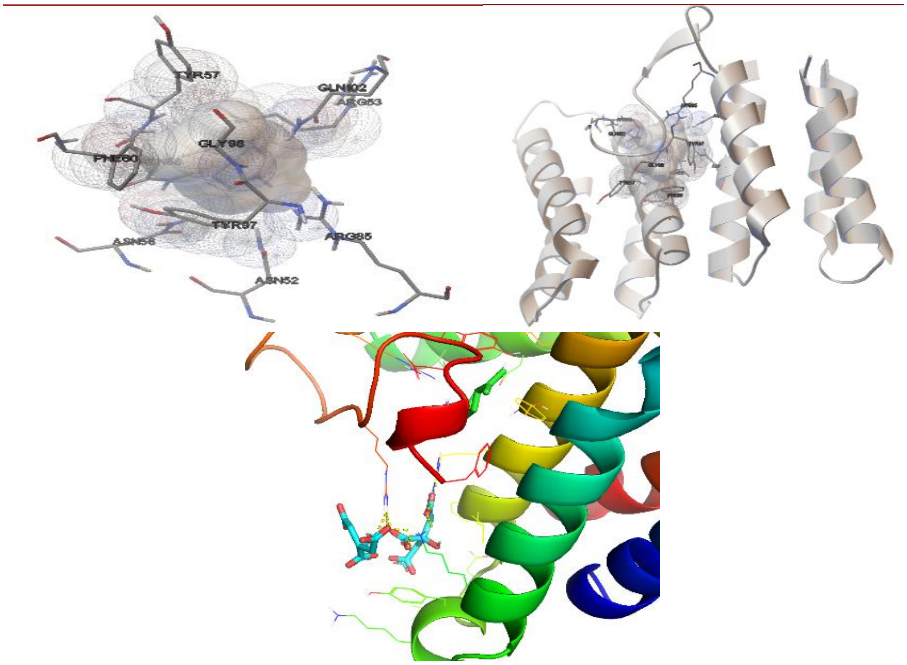
| Ligands | Groups involved in hydrogen bonding with the ligand. | Active amino acid residues involved in the interaction with the ligand. |
|---|---|---|
| Menthol | GLN102, ARG85 | ARG53, ASN52, ASN56, GLN102, ARG85, ASN58, TYR57, GLY98, |
| Limonene | ASN56 | TYR97, GLY98, TYR57, ASN56, ASN52, ASP99, PHE60, ARG85, PHE103, GLN102 |
| Geraniol | ILE67, ARG68 | THR64, TYR63, LYS66, ARG68, ILE67,GLU74 |

1. Molecular docking results of menthol



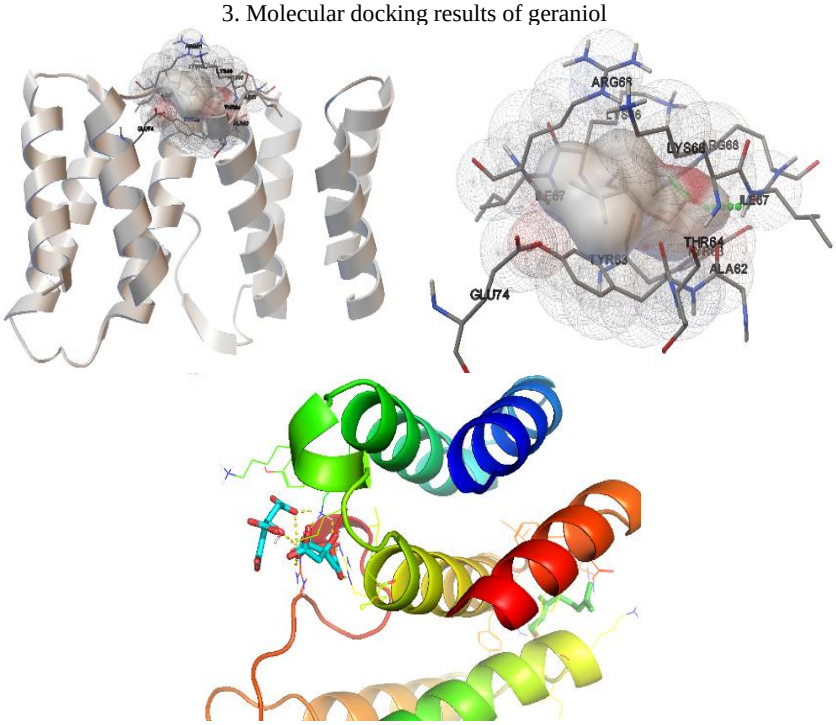

Picture-1. Interaction between menthol and specific amino acid residues of a protein in the complex formed by the binding of menthol and the protein.

2. Molecular docking results of limonene




Picture-2. Interaction between limonene and specific amino acid residues of a protein in the complex formed by the binding of menthol and the protein.

3. Molecular docking results of geraniol




Picture-3. Interaction between geraniol and specific amino acid residues of a protein in the complex formed by the binding of menthol and the protein.

Table 2. Binding energies between ligands and protein (ΔG-binding, kkal/mol)

| № | Menthol | Limonene | Geraniol |
|---|---|---|---|
| 1. | -6,50 | -5.61 | -5.55 |
| 2. | -6,44 | -5.56 | -5.48 |
| 3. | -5,55 | -5.33 | -4.99 |
| 4. | -5,45 | -5.35 | -4.59 |
| 5. | -5,43 | -5.30 | -4.57 |
| 6. | -5,41 | -5.04 | -4.54 |
| 7. | -5,35 | -5.02 | -4.52 |
| 8. | -5,09 | -5.02 | -4.23 |
| 9. | -5,09 | -5.02 | -4.24 |
| 10. | -5,04 | -5.02 | -3.92 |

Among the three ligands, it can be seen that menthol has the weakest binding energy with the bacterial protein, as represented by the ΔG-binding value of -6.50 (Table-2). This suggests that the interaction between menthol and the 2BL8 protein is relatively weak compared to the other two ligands. Conversely, the ligand with the highest ΔG-binding value (the most negative value)

indicates the strongest binding interaction with the protein. Autodock tools can calculate the binding energy (ΔG binding) between a protein and ligand complex using various computational methods, such as molecular docking and scoring functions. ΔG binding represents the free energy change that occurs when a ligand binds to a protein and is an important factor in determining the strength of the binding interaction. Lower values of ΔG binding indicate a stronger binding affinity between the protein and ligand, while higher values indicate weaker binding. Autodock tools can be useful for predicting and analyzing protein-ligand interactions, which has important applications in drug discovery and other areas of molecular biology.

Conclusion. In conclusion, the interaction between the bacterial protein 2BL8 and the ligands menthol, limonene, and geraniol was studied using Autodock software. The analysis revealed that the binding energy between menthol and the bacterial protein was the smallest among the three ligands. These findings could have important implications for the development of new drugs or other molecules that target the bacterial protein 2BL8.

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