Investigation of Polyvinyl Alcohol (PVA)-Sakacin P Interaction by Molecular Docking Method

Nihan ÜNLÜ[*], Arzu ÖZGEN[**]

Abstract

Aim: Group IIA bacteriocins, which contain unmodified amino acids and have antimicrobial activity, are a very broad group. Sakacins in this group are bacteriocins produced by *Lactobacillus sakei*. The most well-known sakacins are Sakacin A, G, K, P, and Q. In particular, Sakacin A and P are well characterized. This study aims to examine the interaction between a single monomer of PVA polymer and Sakacin P bacteriocin.

Method: In t this study, the interaction of a single monomer of PVA polymer, which is among the water-soluble, biocompatible synthetic polymers, and Sakacin P bacteriocin, which has a protein structure, was investigated by molecular docking method.

Results: As a result of our molecular docking study, the presence of binding affinity between the C_2H_4O monomer of PVA selected as the ligand and the Sakacin P protein selected as the receptor was determined.

Conclusion: According to the results of the analysis, the presence of a strong inhibitor was detected between the ligand and the target. Therefore, this study can serve as a template for polymer-bacteriocin materials to be produced in the laboratory.

Keywords: Sakacin P, molecular docking, polyvinyl alcohol.

Moleküler Yerleştirme Yöntemi ile Polivinil Alkol (PVA)-Sakasin P Etkileşiminin İncelenmesi

Öz

Amaç: Modifiye edilmemiş amino asitler içeren ve antimikrobiyal aktiviteye sahip olan Grup IIA bakteriyosinler çok geniş bir gruptur. Bu gruptaki sakasinler, *Lactobacillus sakei* tarafından üretilen bakteriyosinlerdir. En iyi bilinen sakasinler Sakacin A, G, K, P ve Q'dur. Özellikle Sakacin A ve P, iyi karakterize edilmiştir. Bu çalışma, PVA polimerinin tek bir monomeri ile Sakacin P bakteriyosin arasındaki etkileşimi incelemeyi amaçlamaktadır.

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[*] Asst. Prof. Dr., Istanbul Gelisim University, Vocational School of Health Sciences, Department of Medical Services and Techniques, Istanbul, Türkiye, E-mail: nunlu@gelisim.edu.tr ORCID https://orcid.org/0000-0001-5772-2838
[**] Asst. Prof. Dr., Istanbul Gelisim University, Vocational School of Health Sciences, Department of Medical Services and Techniques, Istanbul, Türkiye. E-mail: aozgen@gelisim.edu.tr ORCID https://orcid.org/0000-0003-2104-6019

Yöntem: Bu çalışmada suda çözünebilen, biyouyumlu sentetik polimerlerden PVA polimerinin tek bir monomeri ile protein yapıya sahip Sakacin P bakteriyosinin etkileşimi moleküler yerleştirme yöntemi ile incelenmiştir.

Bulgular: Moleküler docking çalışması sonucunda ligand olarak seçilen PVA'nın C_2H_4O monomeri ile reseptör olarak seçilen Sakacin P proteini arasında bağlanma afinitesinin varlığı belirlenmiştir.

Sonuç: Analiz sonuçlarına göre ligand ile hedef arasında güçlü bir inhibitör varlığı tespit edilmiştir. Bu nedenle bu çalışma, laboratuvarda üretilecek polimer-bakteriosin materyalleri için bir şablon görevi görebilir.

Anahtar Sözcükler: Sakacin P, moleküler yerleştirme, polivinil alkol.

Introduction

Docking is a method that can predict the preferred orientation of one of the two molecules that bind together to form a stable complex in a computer environment. Both in the rational design of the materials to be produced, and plays an important role in understanding the chemical process. In docking studies, the binding energies of the ligand to the receptor in enzyme, nucleic acid, or protein structure can be determined and the position of the ligand in the binding region of the receptor can be animated. Thus, this method is useful for understanding the type of binding and for designing more compatible small molecule ligands that target proteins[1]. During binding, the ligand-protein structures are in motion as their orientation, conformation, and geometric poses of positions are determined. As a result of these movements, the structure becomes more stable in the lowest potential energy position. With this method, after finding the lowest free energy conformation of the protein-ligand system, it is possible to establish the targeted structure, visualize the structure, conformation analysis, estimation of inhibition activities, calculation of binding energy, and determination of molecular interactions[2].

Group II bacteriocins are a very large group containing amino acids smaller than 10 kDa, generally heat stable and unmodified[3]. Group II bacteriocins with antimicrobial activity are divided into 3 subgroups[4]. Grup IIA bacteriocins are pediocin-like anti-listerial bacteriocins with activity against *Listeria* species. Sakacin P, one of the members of this group, also has high anti-listerial activity and a narrow inhibitory spectrum. For this reason, Sakacin P is one of the most promising bacteriocins for the preservation of foods that has problematic contamination with listeria[5]. The packaging industry is also one of the common areas used to protect foods from spoilage or contamination. In the

production of food packaging materials, biodegradable polymers are generally used due to the increase in environmental pollution and the limited petroleum resources[6]. PVA, one of the biodegradable polymers, is a non-toxic, water-soluble, and semi-crystalline synthetic polymer[7,8]. Since PVA and Sakacin P are suitable for use in similar fields such as biomedicine, and the packaging industry, it is tempting to examine the interaction between these two structures. Therefore, in this study, the interaction of a monomer of PVA polymer as ligand and Sakacin P bacteriocin as protein was investigated by the Molecular Docking method.

Material and Methods

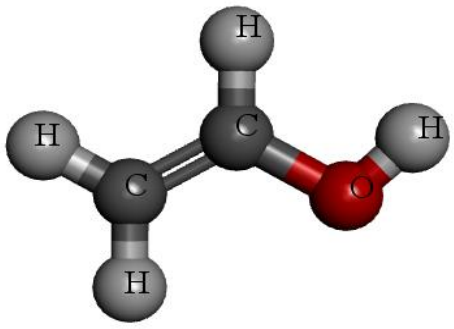
Sakacin P (PDB ID: 1OHM) structure was obtained from The Protein Data Bank (PDB, https://www.rcsb.org/). The pdb file of the 2DDE protein was prepared using chain A and transferred to AutoDockTools (ADT ver.1.5.6). Water molecules of the structures were removed and the pdbqt files of the proteins were saved. The chemical structure of the PVA (PubChem CID: 11199) ligand was obtained from the National Library of Medicine (https://www.ncbi.nlm.nih.gov/). Torsions of the ligand were examined and then the files of the ligand were saved as pdbqt format by Autodock Tools (ADT ver.1.5.6).

The molecular docking study was performed using Autodock 4.1[9]. Each docking was performed according to standard Autodock steps[10]. The most suitable possible binding modes obtained as a result of the Molecular Docking processes were determined with Autodock 4.1, and their analyzes and visuals were obtained with the Biovia Discovery Studio Visualizer 2021 program.

Results

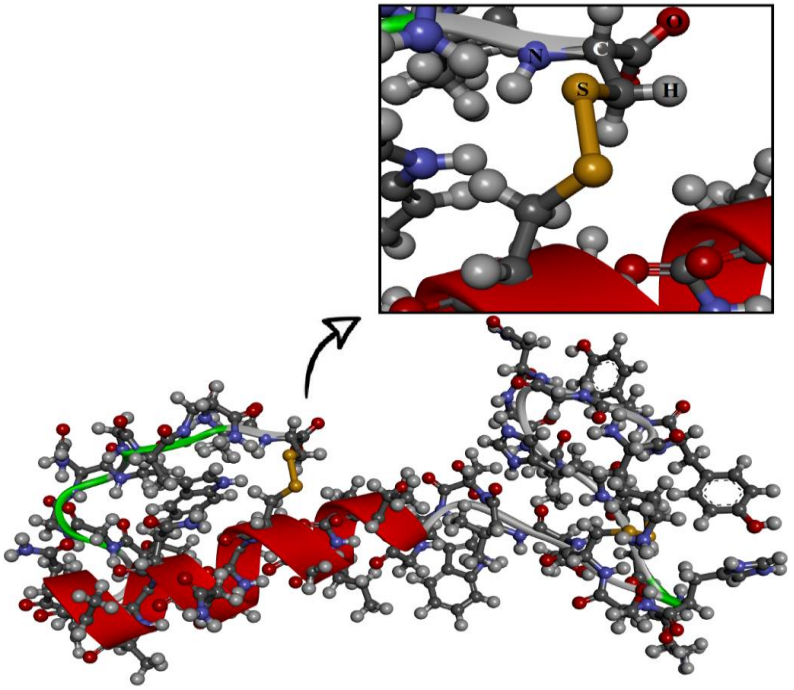
The interaction of the ligand and the protein, whose molecular structures are given in Fig.1 and Fig.2, was investigated with the Autodock4.1 program, which has proven itself in the discovery of stable structures that can be used in suitable areas. In Fig.1, a single monomer of PVA polymer that is used as a ligand is illustrated. As shown in the figure, the atom in red denotes oxygen, light gray represents hydrogen, and dark gray represents carbon.

Figure 1. Molecular structure of C_2H_4O.



Sakacin p, whose molecular structure is given in Fig. 2, was used as a receptor.

Figure 2. Molecular structure of Sakacin P.



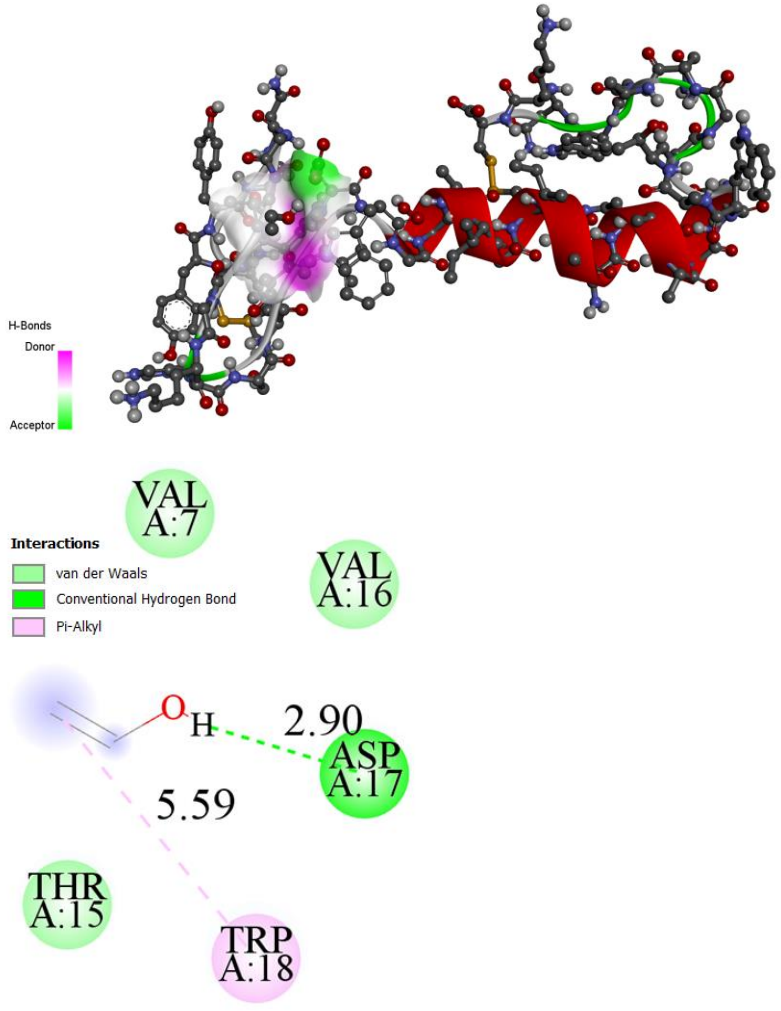
In this study, a molecular modeling study was carried out using ADT - 1.5.6 program to investigate the binding properties. Ligand-protein interaction was simulated based on free binding energy (ΔG)[11].

Table 1. Molecular docking analysis of Sakacin P and the monomer of PVA.

Binding Energy/ΔG (kcal/mol)	**Inhibition Constant/Ki (mM)**	**Hydrogen Bond**	**Hydrophobic Bond**
-1.66	61.12	ASP-17–H	TRP-18–C

As seen in Figure 3, where ligand-protein interactions are shown, hydrogen and hydrophobic bonds were observed between the two molecules. A conventional hydrogen bond was detected between the amino acid aspartic acid (ASP-12) and the element oxygen at a distance of 2.90 nm. Pi-alkyl interaction, a type of hydrophobic bond, occurred at a distance of 5.59 nm between the element carbon and the amino acid tryptophan (TRP-18). In addition, the van der Waals bond, which is a weak interaction between the valine (VAL-7, VAL-16) and threonine (THR-15) amino acids of the Sakacin P protein and the ligand, formed.

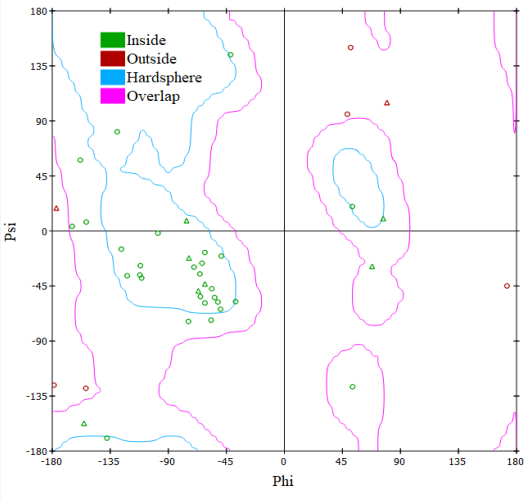
Figure 3. Ligand-protein interactions.



With molecular docking, it is possible to view the amino acid sequences and obtain the three-dimensional structure of the protein shape by estimating the three-dimensional protein folding from these sequences. In the Ramachadran chart developed by

Ramachandran and his team in 1963, it is possible to understand the distribution of dihedral angles within the protein structure and display the results by combining them. As a result of the rotations made by the protein chain, angles in two planes are formed at the point where the bonds between the α-carbon and nitrogen atoms of the amino acids forming the chain and the α-carbon and carbon (located in the carboxyl group) atoms are located. The phi (φ) angle, one of these angles called dihedral angles, occurs between the nitrogen atom and α-carbon atom, and the psi (ψ) angle occurs between carbon and α-carbon[12]. In the Ramachandran graph obtained for this purpose, the twisting angles of the amino acids in the Sakacin P peptide are shown in Fig.4. The ϕ and ψ distributions of the dihedral angles in this graph reveal changes in amino acid side chain conformations for this model.

Figure 4. Ramachandran plot showing the distribution of the phi (ϕ) and psi (ψ) dihedral angles (in degrees) of the model.



Discussion

In Fig.1 giving a single monomer of the PVA polymer used as a ligand, the red-colored atom represents oxygen, light gray hydrogen, and dark gray carbon. As seen in Fig.2, which gives the chemical structure of Sakacin P used as a receptor, the red atom indicates oxygen, light gray hydrogen, dark gray carbon, yellow sulfur, and blue nitrogen. According to the simulation result, we made using the molecular docking method, the binding energy of the ligand-protein interaction is -1.66 kcal/mol as given in Table 1. Considering this result, it can be said that the ligand has a good binding affinity to Sakacin P.

Conclusion

Sakacin P, which is one of the IIA group bacteriocins produced by Lactobacillus sakei bacteria, has increased potential for use in many areas such as food, packaging, and biomedical. The compatibility of the usage areas of PVA and Sakacin P with each other and the absence of a study examining the interaction between these two as a result of our research led us to this study. As a result of our molecular docking study, the existence of binding energy of -1.66 kcal/mol was determined between the C_2H_4O monomer of PVA selected as the ligand and the Sakacin P protein selected as the receptor. In addition, the inhibition constant value obtained according to the results of the analysis was determined as 61.12 mM. This result can be expressed as an indicator of how strong the inhibitor is. Considering the hydrogen bond and hydrophobic bond formed between the amino acids ASP-17 and TRP-18 of Sakacin P and the PVA monomer, it can be said that there is an interaction between them. As a result, this study can serve as a template for materials to be produced for use in appropriate fields, especially in the food industry.

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