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JURNAL TEKNOSAINS

Computational screening of boswellic acid gor its antibacterial activity against acne-causing bacteria via molecular docking

Indonesian title: Skrining komputasional boswellic acid untuk aktivitas antibakterinya terhadap bakteri penyebab jerawat melalui pendekatan molecular docking

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ABSTRAK

Acne vulgaris (AV) adalah penyakit peradangan kulit yang umum terjadi dan berkaitan dengan infeksi bakteri seperti Cutibacterium acnes, Staphylococcus aureus, dan Staphylococcus epidermidis. Meningkatnya resistensi terhadap antibiotik konvensional mendorong eksplorasi senyawa alami seperti boswellic acid, yang dikenal memiliki potensi antibakteri. Penelitian ini bertujuan untuk mengevaluasi aktivitas antibakteri boswellic acid melalui pendekatan in silico menggunakan molecular docking terhadap sejumlah protein target penting dari bakteri penyebab jerawat. Ligan boswellic acid diperoleh dari basis data PubChem, sedangkan struktur protein target diunduh dari RCSB Protein Data Bank. Proses blind docking dilakukan menggunakan AutoDock Tools versi 1.5.7 dan AutoDock Vina, lalu dianalisis menggunakan Discovery Studio Visualizer dan Visual Molecular Dynamics (VMD). Sembilan protein target yang berperan penting dalam metabolisme, sintesis protein, pembentukan biofilm, dan replikasi DNA dipilih untuk dianalisis, termasuk transcriptional regulator TcaR, penicillin-binding proteins (PBP), tyrosyl-tRNA synthetase (TyrRS), 3-ketoacyl-ACP synthase III (KAS III), CRISPR-associated protein, DNA gyrase, transcriptional regulator MarR, methylmalonyl-CoA epimerase, dan accumulation-associated protein (Aap). Hasil docking menunjukkan bahwa semua protein target memiliki nilai energi pengikatan yang negatif (< 0), menandakan interaksi yang termodinamika stabil dan bersifat spontan. Protein TcaR menunjukkan afinitas tertinggi dengan energi pengikatan sebesar −10,2 kkal/mol dan membentuk sembilan ikatan hidrogen konvensional, menunjukkan interaksi spesifik yang sangat kuat. Interaksi ini melibatkan residu-residu penting seperti Gln:B61, HisA:42, AsnA:20, AsnB:17, dan Arg1:110. Sebaliknya, protein Aap hanya membentuk satu ikatan kovalen, menunjukkan afinitas terlemah. Hasil ini menunjukkan bahwa boswellic acid mampu menghambat aktivitas berbagai protein target kunci pada bakteri penyebab jerawat, terutama pada mekanisme regulasi transkripsi dan pembentukan biofilm. Dengan demikian, boswellic acid memiliki potensi tinggi

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sebagai kandidat agen antibakteri topikal yang efektif dan aman untuk dikembangkan lebih lanjut dalam formulasi berbasis rekayasa biomedis.

***Kata kunci**: boswellic acid; molecular docking; antiinflamasi; in silico; jerawat*

ABSTRACT

Acne vulgaris (AV) is a common inflammatory-skin disorder associated with bacterial infections, particularly Cutibacterium acnes, Staphylococcus aureus, and Staphylococcus epidermidis. The rising resistance to conventional antibiotics has prompted the exploration of natural compounds such as boswellic acid, which is known for its antibacterial potential. This study aimed to evaluate the antibacterial activity of boswellic acid using an in-silico approach through molecular docking against several essential bacterial target proteins implicated in acne pathogenesis. The boswellic acid ligand was obtained from the PubChem database, while the three-dimensional structures of the target proteins were retrieved from the RCSB Protein Data Bank. Blind docking was performed using AutoDock Tools version 1.5.7 and AutoDock Vina, followed by interaction analysis using Discovery Studio Visualizer and Visual Molecular Dynamics (VMD). Nine bacterial proteins involved in vital cellular processes such as metabolism, protein synthesis, biofilm formation, and DNA replication were selected, including transcriptional regulator TcaR, penicillin-binding proteins (PBPs), tyrosyl-tRNA synthetase (TyrRS), 3-ketoacyl-ACP synthase III (KAS III), CRISPR-associated protein, DNA gyrase, transcriptional regulator MarR, methylmalonyl-CoA epimerase, and accumulation-associated protein (Aap). The docking results demonstrated that all target proteins exhibited negative binding energy values (< 0), indicating thermodynamically stable and spontaneous interactions. Among these, TcaR displayed the highest binding affinity with a binding energy of −10.2 kcal/mol and formed nine conventional hydrogen bonds, reflecting a particular and stable interaction. Key interacting residues included Gln: B61, HisA:42, AsnA:20, AsnB:17, and Arg1:110. In contrast, the Aap protein formed only one covalent bond, indicating the weakest interaction. These findings suggest that boswellic acid effectively inhibits key bacterial proteins, particularly those involved in transcriptional regulation and biofilm development. Therefore, boswellic acid holds significant potential as a safe and effective topical antibacterial agent for further growth in biomedical engineering-based formulations.

***Keywords**: boswellic acid; molecular docking; anti-inflammatory; in silico; acne vulgaris*

INTRODUCTION

Acne vulgaris is the most prevalent dermatological condition affecting the pilosebaceous unit. It is characterized by inflammatory and non-inflammatory lesions, which predominantly appear on the facial, cervical, and thoracic skin. These lesions arise primarily due to infection by the anaerobic, Gram-positive bacterium *Propionibacterium acnes* (*P. acnes*) (Liu *et al*., 2015), which has been recently reclassified as *Cutibacterium acnes* (*C. acnes*) based on updated taxonomic nomenclature (Dréno *et al*., 2018). The clinical manifestations of acne vulgaris include comedones, papules, nodules, and cysts (Liu *et al*., 2015).

The host immune response to *P. acnes*-induced inflammation plays a pivotal role in the pathogenesis of acne vulgaris (Agak *et al*., 2014). Various therapeutic approaches are currently employed to manage this condition, including topical formulations, systemic antibiotics, and oral hormonal treatments. However, due to the increasing prevalence of antibiotic resistance and potential adverse effects, there has been a growing interest in using natural products as alternative therapeutic agents for acne treatment (Azimi *et al*., 2012; Sinha *et al*., 2014).

P. acnes contribute to the inflammatory process by stimulating monocytes to release pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-8 (IL-8) (Vowels et al, 1995). Furthermore, *P. acnes* have been shown to activate Toll-like receptor 2 (TLR2), which in turn induces the production of IL-12 and IL-8 in primary human monocytes, as well as IL-6 in macrophages (Kim, 2005).

Although clindamycin, tetracycline, minocycline, tretinoin, benzoyl peroxide, and doxycycline commonly treat acne, their prolonged use gradually increases *C. acnes* resistance. It has significant adverse health effects (Purdy & De Berker, 2010). Therefore, targeted inhibition of *C. acnes* lipase activity would provide a safer alternative for managing acne. In the present study, docking, molecular dynamics (MD) simulations, and binding affinity analysis were conducted to identify

novel natural lead compounds capable of inhibiting lipase activity.

The crystal structure of *C. acnes* lipase protein (typically > 30 kDa) was determined at 1.75-Å resolution (PDB ID: 6KHM). The asymmetric unit consists of two subunits, the lid and core domains, which are specifically involved in ligand interactions. The core domains exhibit catalytic activity and share characteristics of the classic α/β hydrolase family, while the lid domain shields the active site through bulky hydrophobic residues. The active site comprises eight-stranded β-pleated sheets, flanked by helices on both sides, located between the N- and C-terminal regions (residues 38–192) (Kim *et al.*, 2020).

Molecular docking is a key in silico method in early structure-based drug discovery, enabling the computational screening and prioritization of potential ligands prior to *in vitro* or *in vivo* validation. It predicts bioactive compounds' binding conformation and interaction with target proteins, estimating binding affinity and biological activity. The process visualizes ligand placement within the receptor's active site, emphasizing interactions such as hydrogen bonding, hydrophobic effects, and electrostatic forces (Farmasi *et al.*, 2017). Binding free energy calculations offer insights into ligand-receptor complexes' thermodynamic stability and spontaneity (Feig *et al.*, 2004). By streamlining candidate identification, molecular docking reduces both time and cost in drug development.

Boswellia serrata Roxb., commonly called the Indian frankincense tree, belongs to the family Burseraceae and is widely distributed across India, Nigeria, Yemen, Somalia, Arabia, Oman, and Pakistan. Among approximately 43 recognized species within the Boswellia genus, *B. serrata* is the most extensively utilized by humans due to its therapeutic resin and essential oil (Ayub *et al.*, 2018). Traditionally, the resin has been used in folk medicine for its anti-inflammatory, analgesic, and antimicrobial properties.

The resin of B. serrata contains a group of pharmacologically active triterpenoids known as boswellic acids (BA), which include 11-keto-β-boswellic acid (KBA), α-boswellic acid, β-boswellic acid, acetyl-α-boswellic acid, acetyl-β-boswellic acid, and acetyl-11-keto-β-boswellic acid (AKBA). AKBA is the most abundant and pharmacologically potent among these compounds, constituting up to 11.6% of the resin content (Meins *et al.*, 2018). These BAs belong to the terpenoid class of secondary metabolites (Takada *et al.*, 2006) and have demonstrated a wide range of biological activities, including strong antibacterial effects. Pharma (2018) reported that BAs show effective antibacterial activity, particularly against pathogens associated with infections in the female reproductive tract.

Despite these promising properties, the specific antibacterial mechanism of BAs against Propionibacterium acnes (P. acnes - recently reclassified as Cutibacterium acnes), a Gram-positive anaerobic bacterium implicated in the pathogenesis of acne vulgaris, remains insufficiently explored. Given the growing issue of antibiotic resistance and the need for safer, natural alternatives for acne treatment, this study aims to investigate the potential of boswellic acids to inhibit or eliminate P. acnes through molecular docking approaches. The research further seeks to elucidate the mechanism of action of BAs at the molecular level, thereby supporting their potential development as active compounds in topical anti-acne formulations.

Objectives

This study aims to evaluate the antibacterial potential of boswellic acid against acne-causing bacteria, particularly *Cutibacterium acnes, Staphylococcus aureus,* and *Staphylococcus epidermidis*. Considering growing antibiotic resistance and the side effects of prolonged use of conventional acne treatments, this research explores boswellic acid as a safer, natural alternative. Specifically, the study aims to investigate the molecular interactions between boswellic acid and several key bacterial proteins involved in critical

cellular functions such as transcription regulation, protein synthesis, cell wall formation, and DNA replication. By applying molecular docking methods, the study assesses the binding affinity and stability of boswellic acid against these targets to identify the most promising protein interactions. The ultimate goal is to provide insight into the mechanism of action of boswellic acid and its potential development as an active ingredient in topical antibacterial formulations for acne treatment.

Materials and Methods

The ligand data for boswellic acid (BA) compounds were obtained from the PubChem database (https://pubchem.ncbi. nlm. nih.gov/), while the protein structure data were retrieved from the RCSB Protein Data Bank (https://www.rcsb.org/). Blind docking was performed using AutoDock Tools version 1.5.7. Before docking, hydrogen atoms were added to the protein structure, nonpolar regions were merged, and the prepared structure was saved in pdbqt format. The same preprocessing steps were applied to the ligands and saved in PDBQT format.

Grid box configuration was subsequently conducted by considering the center of mass coordinates of the target protein and ensuring that the binding site pocket encompassed the entire 3D structure. The blind docking simulation was executed using AutoDock Vina, and the resulting binding energy values were used to assess ligand–receptor interaction affinity. Docking outcomes were visualized using Discovery Studio Visualizer 2021 and Visual Molecular Dynamics (VMD) version 1.9.1.

RESULTS AND DISCUSSION

Biological Functions of Target Proteins

The nine proteins utilized in this study were meticulously selected based on their indispensable roles in the survival, growth, and pathogenicity of *P. acnes*, *S. aureus*, and *S. epidermidis*. These proteins participate in critical metabolic and biosynthetic pathways essential to bacterial physiology. One of the enzymes, methylmalonyl-CoA epimerase (MCE), plays a central role in the catabolism of branched-chain amino acids and odd-chain fatty acids, facilitating bacterial adaptation to diverse nutrient sources (Kuhnl et al, 2005). The MCE enzyme catalyzes the stereochemical conversion of (S)-methylmalonyl-CoA to (R)-methylmalonyl-CoA, a precursor in the biosynthesis of succinyl-CoA, which subsequently enters the tricarboxylic acid (TCA) cycle and contributes to energy metabolism (Han *et al.*, 2012).

Penicillin-binding proteins (PBPs), another protein group analyzed in this study, are membrane-bound enzymes that mediate the final stages of peptidoglycan synthesis, an essential process in forming and maintaining the bacterial cell wall. By catalyzing the cross-linking of the peptidoglycan matrix, PBPs contribute to cellular integrity and resistance to osmotic stress. Their functional importance also makes them primary targets for β-lactam antibiotics (Macheboeuf *et al.*, 2006).

Tyrrosyl-tRNA synthetase (TyrRS) is a member of the aminoacyl-tRNA synthetase (aaRS) family. It is responsible for the high-fidelity charging of tRNA with tyrosine, which is fundamental to the accurate translation of the genetic code during protein synthesis. The inhibition of aaRSs, including TyrRS, disrupts protein biosynthesis and thus presents a potential strategy for antibacterial intervention (Khan *et al.*, 2018).

3-ketoacyl-acyl carrier protein synthase III (KAS III) is a key enzyme in the initiation phase of fatty acid biosynthesis. It catalyzes the condensation of acetyl-CoA with malonyl-ACP to form 3-ketoacyl-ACP, a critical step in the elongation cycle of fatty acid production. This pathway is vital for generating phospholipids, major constituents of bacterial membranes (Chang et al., 2010). Given their essential roles in fundamental cellular processes, these proteins represent promising molecular targets for novel antimicrobial development.

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated (Cas) proteins are integral components of the prokaryotic adaptive immune system, providing defense against invading genetic elements such as plasmids and bacteriophages. These proteins facilitate sequence-specific recognition and cleavage of foreign nucleic acids by interacting with CRISPR loci, where short sequences derived from previous infections are stored as genetic memory (Lintner *et al.*, 2011). In addition to their immune function, CRISPR-associated proteins are involved in transcriptional regulation and protein synthesis processes, making them potential targets for antimicrobial interventions.

DNA gyrases, another essential enzyme considered in this study, plays a pivotal role in bacterial DNA replication. It belongs to the type II topoisomerase family and functions by introducing negative supercoils into DNA, thereby relieving the torsional stress generated ahead of the replication fork. This activity is crucial for efficient DNA strand separation and replication (Tanitame *et al.*, 2004). Given its indispensable function, DNA gyrase has been a longstanding target for antibacterial agents, such as fluoroquinolones.

Transcriptional regulators from the MarR (Multiple antibiotic resistance Regulator) and TcaR (teicoplanin-associated locus regulator) families are key players in regulating bacterial gene expression, particularly those related to virulence and biofilm formation. These regulators contribute to polysaccharide intercellular adhesin (PIA) biosynthesis, a significant component of the extracellular matrix in bacterial biofilms. PIA consists primarily of β-1,6-linked N-acetylglucosamine (GlcNAc) residues and facilitates cell-to-cell adhesion, providing structural stability and resistance to environmental stresses and antimicrobial agents (Chang et al., 2010).

The accumulation-associated protein (Aap) is a surface-bound protein that plays a fundamental role in the formation and maturation of bacterial biofilms. Aap mediates intercellular aggregation and adherence to biotic and abiotic surfaces, promoting persistent colonization and biofilm stability. It has been identified as a crucial factor in the pathogenesis of *Staphylococcus epidermidis*, particularly in medical device-associated infections (Schaeffer *et al.*, 2015).

Molecular Docking and Binding Energy Analysis

Molecular docking simulations were conducted to evaluate the potential interaction between the BA (bioactive) compound and the selected protein targets. This computational approach aimed to predict the most favorable binding conformation of the test compound within the active site of each target receptor and to estimate the binding affinity through calculated free energy values. Binding energy serves as a fundamental parameter in ligand-receptor interactions, reflecting the strength and stability of the molecular complex. A more negative binding energy value indicates a stronger and more favorable interaction, as described by Pangastuti et al. (2016), where binding potentials are enhanced when the free energy values fall below zero (< 0). The outcomes of the docking analysis, including the binding energy values and specific amino acid residue interactions, are summarized in Table 1, providing insight into the molecular basis of the BA compound's affinity for each protein target.

Table 1.
Docking result of boswellic acid

Protein Code	Protein Name	Binding Energy
3kp5	Transcriptional regulator TcaR	-10,2 kkal/mol
5m18	Penicillin binding proteins	-9,1 kkal/mol
1hc7	Tyrosyl-tRNA synthetase	-8,3 kkal/mol
6a9n	3-Ketoacyl-ACP synthase-III	-8,8 kkal/mol
6nbu	CRISPR_associated protein	-8,7 kkal/mol
2xco	DNA-Gyrase	-8,6 kkal/mol
4hbl	Transcriptional regulator, MarR	-8,3 kkal/mol
1jc5	Methylmalonyl_CoA epimerase	-8,1 kkal/mol
4fum	Accumulation associated protein	-6,0 kkal/mol

Source: Binding energy analysis with AutoDock Tools version 1.5.7

The analysis of binding energy values was carried out to evaluate both the spontaneity of the molecular interactions and the thermodynamic stability of ligand–receptor complexes. These parameters are fundamentally reflected by the magnitude of the binding free energy values, where increasingly negative values indicate more stable and spontaneous interactions between the ligand and its target protein. Feig *et al.* (2004) reported that molecular interactions characterized by lower (negative) binding energy values indicate favorable thermodynamic profiles, suggesting that the ligand has a high propensity to associate with the receptor under physiological conditions.

In this study, all evaluated target proteins demonstrated binding energy values less than zero (< 0), signifying that the BA compound possesses affinity for the active sites of all receptor proteins tested. The transcriptional regulator TcaR exhibited the most negative binding energy value among the various protein targets, indicating the dataset's strongest and most stable interaction. Conversely, the accumulation-associated protein (Aap) displayed the least negative value, suggesting a relatively weaker, although still spontaneous, interaction. These results suggest that the TcaR protein forms the most energetically favorable complex with the BA compound.

Ligand–Protein Interaction Profile and Mechanistic Implications

The stability of a ligand–receptor interaction is often directly correlated with the strength of the chemical bonds formed between the interacting molecules. Adelina et al. (2013) state that greater stability is associated with a compound's capacity to establish strong and specific chemical interactions, including hydrogen bonds, hydrophobic contacts, and van der Waals forces. In this context, the data supports that all selected bacterial proteins can form stable chemical interactions with the BA compound. However, the strongest interaction—based on binding energy and likely bonding characteristics—was observed in the TcaR-BA complex.

These findings collectively imply that the BA compound may exert antibacterial effects by interfering with the normal metabolic functions of these essential bacterial proteins. Similar observations of intense biological activity have also been reported for other plant-derived secondary metabolites, such as flavonoids from *Premna serratifolia* (Singkel), which exhibit high antioxidant potential and low IC50 values, depending on extraction conditions (Luliana & Zahid, 2025). The most pronounced inhibitory potential appears to be directed at the transcriptional regulator TcaR, which plays a key role in biofilm formation and gene regulation. Thus, targeting

TcaR with the BA compound may significantly disrupt the cellular processes of *P. acnes*, *S. aureus*, and *S. epidermidis*, highlighting its potential as a candidate for antimicrobial drug development.

Based on the results of molecular interaction visualization, the ligand–receptor interactions observed in this study can be broadly categorized into two major types: hydrogen bonding and hydrophobic. Hydrogen bonds, which are critical for specificity and stability in molecular recognition, include several subtypes such as water-mediated hydrogen bonds (WHB), conventional hydrogen bonds (CoHB), carbon hydrogen bonds (CaHB), and Pi-donor hydrogen bonds (PdHB). These interactions often contribute to the ligand's directional stability and orientation within the target protein's active site.

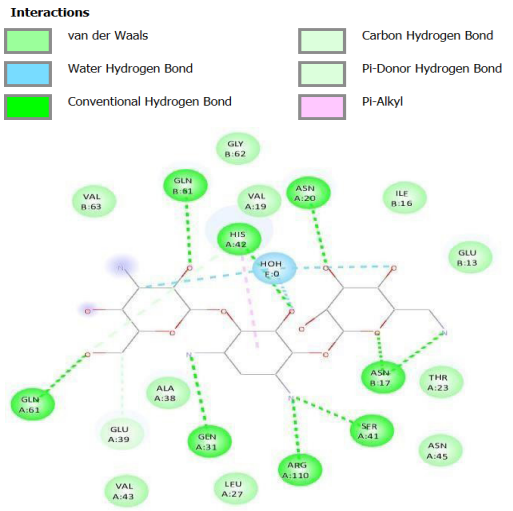
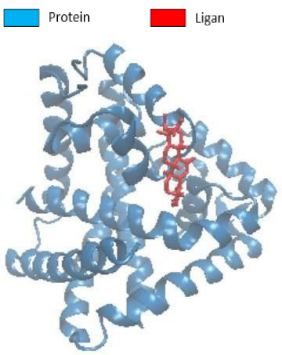
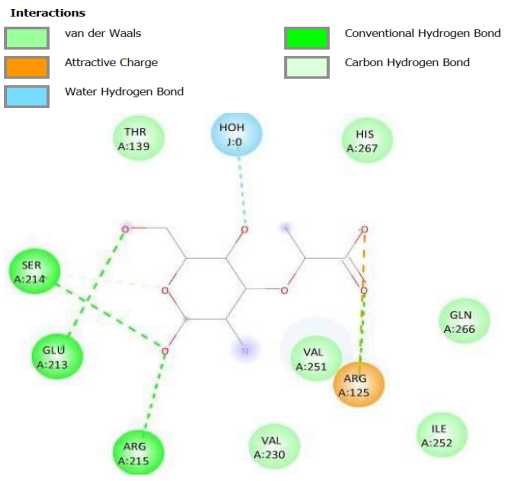
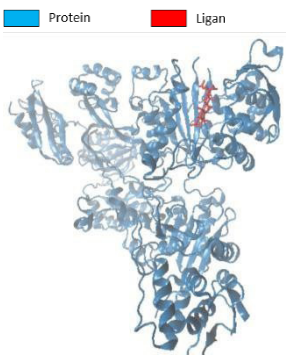
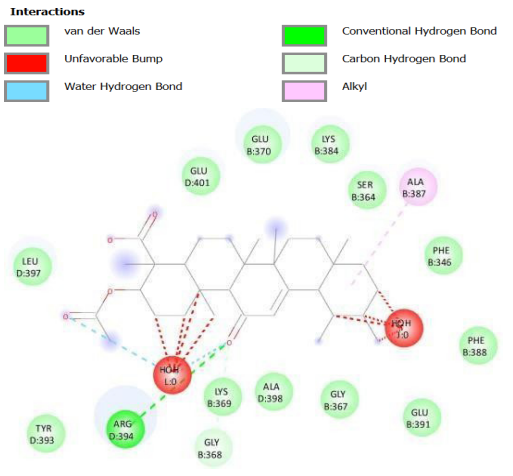
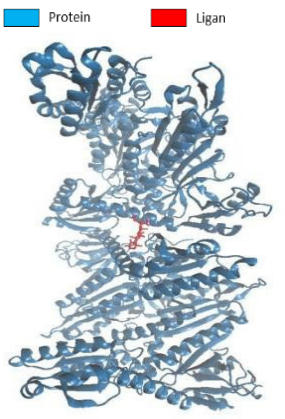
In contrast, hydrophobic interactions contribute primarily to the binding affinity and stabilization of the ligand–protein complex by promoting nonpolar contacts in the binding pocket. These interactions encompass various forms, including Pi-alkyl interactions (PAl), unfavorable bumps (UB), unfavorable donor–donor interactions (UDd), alkyl interactions (Al), attractive charge interactions (AC), and covalent bonds (CB). Although hydrophobic interactions are generally less specific than hydrogen bonds, they significantly contribute to the complex's overall binding energy and entropic gain.

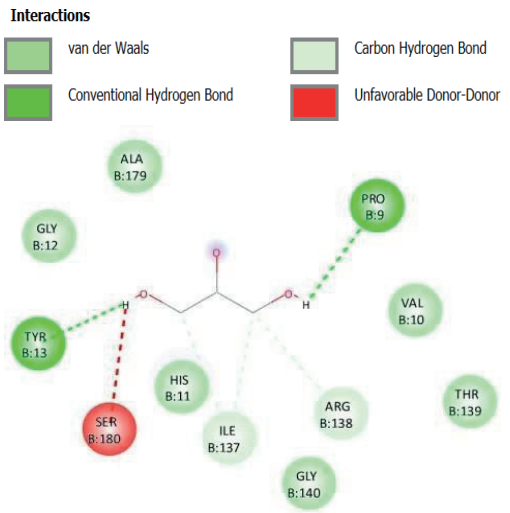
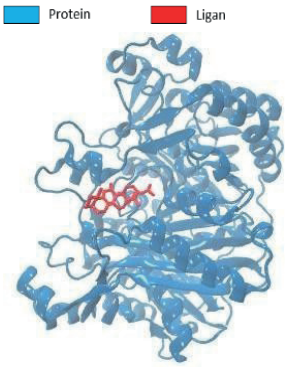
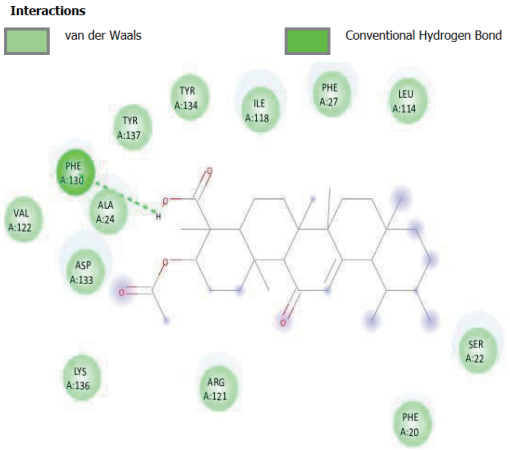
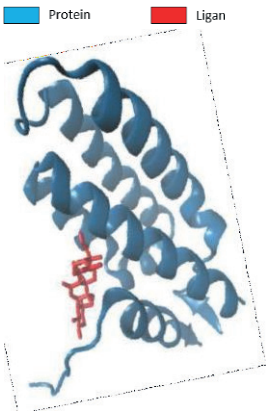
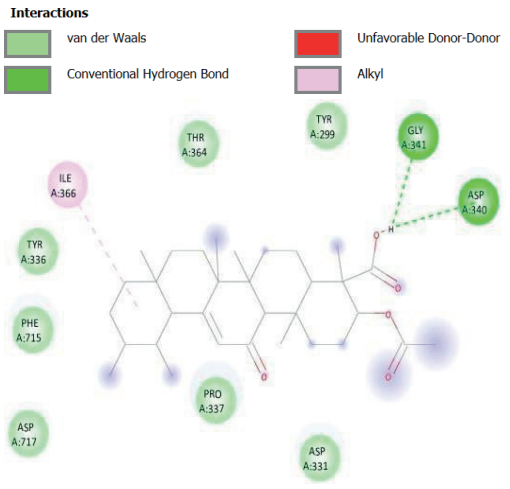
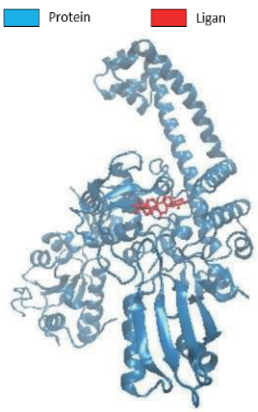
Among all tested protein targets, the transcriptional regulator TcaR demonstrated the most extensive interaction network with the BA compound, highlighting its potential as a high-affinity binding partner. Specifically, the TcaR–BA complex exhibited a total of nine conventional hydrogen bonds (CoHB) involving residues Gln: B61, HisA:42, AsnA:20, AsnB:17 (×2), SerA:41, Arg1:110, GlnA:31, and GlnA:61. In addition, one carbon hydrogen bond (CaHB) with GluA:39, two water hydrogen bonds (WHB) with HohE:0 (×2), one Pi-donor hydrogen bond (PdHB) with HisA:42, and one Pi-alkyl interaction (PAl) also with HisA:42 were identified. This extensive interaction profile indicates a highly stable and specific binding mode, reinforcing TcaR as the primary target with the strongest ligand affinity.

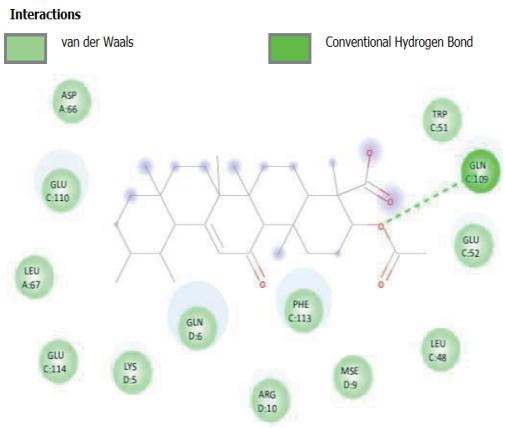
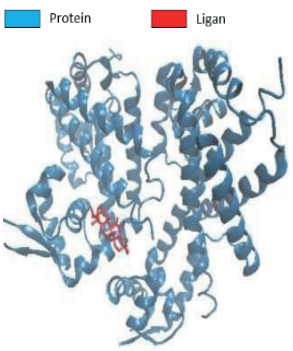
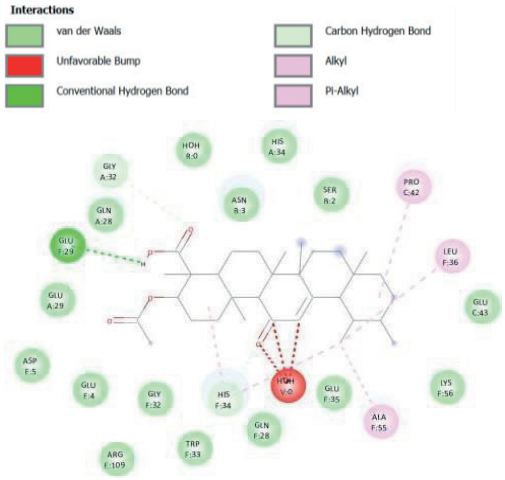
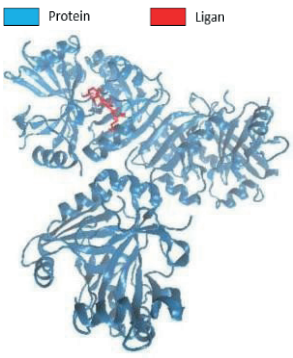
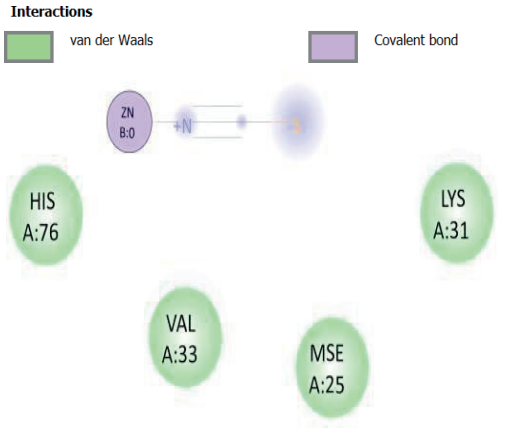
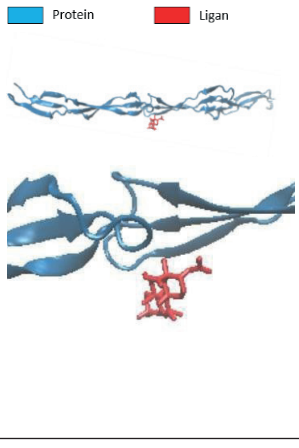
In stark contrast, the accumulation-associated protein (Aap) displayed the fewest ligand–protein interactions, forming only a single covalent bond (CB) with ZnB:0, suggesting a relatively weaker and less complex binding mode than the other protein targets. The complete list of interaction types and corresponding amino acid residues for each protein is detailed in Table 2, providing a comprehensive overview of the molecular interaction landscape between the BA compound and the selected bacterial protein targets.

In stark contrast, the accumulation-associated protein (Aap) exhibited the least number of ligands–protein interactions among all the analyzed targets, establishing only a single covalent bond (CB) with the ZnB:0 atom. This minimal interaction profile implies a weaker and less intricate binding mode, indicating that Aap may not serve as a primary target for the boswellic acid compound under the tested conditions. Such limited interaction may reflect a lack of structural complementarity or reduced binding affinity, potentially diminishing its therapeutic relevance in anti-acne activity. A comprehensive summary of all interaction types, including hydrogen bonds, hydrophobic contacts, electrostatic interactions, and covalent bonds, along with their associated amino acid residues for each protein, is presented in Table 2, offering a detailed molecular interaction landscape between boswellic acid and the selected bacterial protein targets.

Table 2.
2D and 3D structures of boswellic acid with test protein

No	Code-Name of Protein	2D Structure	3D Structure
1	3kp5- Transcriptional regulator TcaR		
2	5m18-PBD2a		
3	1hc7- Tyrosyl_tRNA Synthetase		

No	Code-Name of Protein	2D Structure	3D Structure
4	6a9n-KAS III		
5	6nbu- CRISPR_associated protein		
6	2xco-DNA Gyrase		

No	Code-Name of Protein	2D Structure	3D Structure
7	4hbl- Transcriptional regulator, MarR family		
8	1jc5- Methylmalonyl CoA epimerase		
9	4fum- Accumulation associated protein		

Source: Binding interaction with discovery studio visualizer and visual molecular dynamics version 1.9.1.

Ligand-protein interactions are generally considered more stable when more hydrogen bonds, particularly conventional ones (CoHBs), are formed compared to hydrophobic ones. Hydrogen bonds are directional and specific, making them a critical determinant of molecular recognition and binding specificity in biological systems. According to Rachmania (2019), although hydrophobic interactions contribute to decreasing the system's free energy—which indirectly supports the stability of the ligand–receptor complex—

hydrogen bonds, especially CoHBs, provide a more significant and direct contribution to the overall binding stability.

Furthermore, Syahputra, Ambarsari and Sumaryada (2014) emphasize that conventional hydrogen bonds are substantially stronger than other subtypes of hydrogen bonding, such as carbon-hydrogen or water-mediated hydrogen bonds. As such, more CoHBs within a ligand–protein complex strongly correlates with increased binding stability and affinity. The strength and stability conferred by these interactions enhance the capacity of the ligand to remain tightly bound within the protein's active site, even in dynamic physiological environments.

The findings of this study demonstrate a precise alignment between the visualization of ligand–protein interactions and the computational binding energy values obtained through molecular docking simulations. Specifically, more negative binding energy values indicate stronger and more stable ligand–protein interactions, and these were consistently associated with a higher prevalence of CoHBs in the interaction profiles. This trend underscores conventional hydrogen bonds' thermodynamic and structural importance in stabilizing the ligand–protein complex.

Through molecular docking simulations and interaction profiling, boswellic acid (BA) was shown to bind effectively to a range of key bacterial proteins, including transcriptional regulator TcaR, penicillin-binding proteins, tyrosyl-tRNA synthetase, 3-ketoacyl-ACP synthase-III, CRISPR-associated protein, DNA gyrase, transcriptional regulators of the MarR family, and the accumulation-associated protein. Among these, the TcaR protein exhibited the most stable and energetically favorable interaction with BA, as evidenced by the most significant number of CoHBs formed in the complex. This dominance of conventional hydrogen bonding reinforces the strength of the BA–TcaR interaction. It highlights TcaR as a primary molecular target with potential therapeutic significance in inhibiting bacterial growth and biofilm formation.

CONCLUSION

Boswellic acid exhibited strong and specific binding to several bacterial target proteins, with the most stable interaction observed on the transcriptional regulator TcaR, indicating its potential to inhibit the growth of P. acnes, S. aureus, and S. epidermidis by disrupting key metabolic processes. These molecular insights reinforce boswellic acid's role as a promising antibacterial agent and open opportunities for its application in biomedical engineering. Its interaction profile suggests suitability for integration into engineered drug delivery platforms such as nanofibers, liposomes, or hydrogel matrices, enabling controlled and targeted topical administration with minimal systemic exposure.

Further research should validate its antibacterial efficacy through in vitro and in vivo studies to enhance therapeutic outcomes, investigate its synergistic potential with conventional treatments, and optimize formulation characteristics such as skin permeability and stability. Leveraging molecular docking as a preclinical screening tool can streamline development, supporting the translation of boswellic acid into effective, nature-based therapeutics within modern biomedical frameworks for acne management.

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