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Molecular Insights into the Therapeutic Potential of *Curcuma amada* Rhizome: A Network Pharmacology and Molecular Docking Approach

[Wawasan Molekuler terhadap Potensi Terapeutik Rimpang *Curcuma amada*: Pendekatan Farmakologi Jaringan dan Penambatan Molekuler]

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ABSTRACT

The rhizome of *Curcuma amada* (ginger mango) has traditionally been used for various medicinal purposes. However, its molecular targets and mechanisms of action are still poorly understood. This study aimed to predict the potential bioactive compounds and target proteins of *C. amada* using network pharmacology and molecular docking approaches. A total of 110 compounds were identified, and their predicted targets were analyzed through a protein-protein interaction (PPI) network, enrichment, and disease analysis. Key targets include phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha isoform (PIK3CA) and tyrosine-protein kinase JAK2 (JAK2), both of which are closely related to cancer-related pathways. Four compounds, β-eudesmol, (E,Z)-farnesol, spathulenol, and τ-muurolol, were selected for molecular docking studies. Validation of the docking protocol through re-docking showed low RMSD values (0.667 Å for PIK3CA and 0.474 Å for JAK2), confirming the reliability of the method. The docking results demonstrated that the native ligands and selected compounds formed multiple hydrogen bonds and extensive hydrophobic interactions with key residues in the active site. Notably, most of the interactions were hydrophobic, which is consistent with the volatile nature of the ligands. The binding affinity was below –5 kcal/mol for all tested compounds. These findings suggest that *C. amada* rhizomes contain bioactive compounds capable of modulating cancer-related targets, thus providing a molecular basis for their potential therapeutic effects.

Kata kunci:

Curcuma amada
Farmakologi jaringan
Molecular docking
Pengobatan herbal

ABSTRAK

Rimpang *Curcuma amada* (jahe mangga) secara tradisional telah digunakan untuk berbagai keperluan pengobatan, tetapi target molekuler dan mekanisme kerjanya masih terbatas dieksplorasi. Penelitian ini bertujuan untuk memprediksi senyawa bioaktif potensial dan protein target *C. amada* menggunakan pendekatan farmakologi jaringan dan *molecular docking*. Sebanyak 110 senyawa diidentifikasi, dan target prediksinya dianalisis melalui jaringan interaksi protein-protein (PPI), analisis pengayaan, dan penyakit. Target utama yaitu *phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha isoform* (PIK3CA) dan *tyrosine-protein kinase JAK2* (JAK2) yang terkait erat dengan jalur terkait kanker. Empat senyawa yaitu β-eudesmol, (E,Z)-farnesol, spathulenol, and τ-muurolol dipilih untuk studi *molecular docking*. Validasi protokol *docking* melalui *redocking* menunjukkan nilai RMSD rendah (0,667 Å untuk PIK3CA dan 0,474 Å untuk JAK2). Hasil *docking* menunjukkan ligan asli dan senyawa terpilih membentuk beberapa ikatan hidrogen dan interaksi hidrofobik yang luas dengan residu di situs aktif. Interaksi sebagian besar bersifat hidrofobik, konsisten dengan sifat volatil ligan. Afinitas pengikatan menunjukkan di bawah –5 kkal/mol pada semua senyawa yang diuji. Temuan ini menunjukkan rimpang *C. amada* mengandung senyawa bioaktif yang berpotensi memodulasi target terkait kanker dan menjadi dasar molekuler untuk efek terapeutik potensialnya.

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1. INTRODUCTION

Mango ginger (*Curcuma amada*) is a medicinal plant from the Zingiberaceae family that morphologically resembles ginger but possesses a distinctive aroma and flavor reminiscent of fresh mango. Traditionally, it has been widely used in herbal medicine, either as a decoction or applied externally in grated form (Choudhary et al., 2024; Meidatuzzahra & Swandayani, 2020). In several regions, such as Lampung, *C. amada* rhizome is also consumed as a fresh vegetable and is believed to promote overall health (Nurainy et al., 2019).

Phytochemical studies have revealed that *the C. amada* rhizome contains various bioactive compounds, including flavonoids, phenolics, terpenoids, curcuminoids, and essential oils. These compounds have been reported to exhibit diverse pharmacological activities, including antioxidant, anti-inflammatory, antibacterial, antiviral, anticancer, antituberculosis, antiallergic, anthelmintic, and antipyretic properties (Choudhary et al., 2024; Kumar et al., 2024; Mahadevi & Kavitha, 2020; Policegoudra et al., 2010; Sahoo et al., 2023). However, comprehensive in silico studies exploring the therapeutic potential of these compounds against biological targets are still limited.

Modern approaches, such as network pharmacology, offer opportunities to explore the effects of herbal compounds through multicomponent and multitarget interactions. This approach aligns with the complex nature of medicinal plants (Hopkins, 2008). This method enables the visualization and prediction of the interaction networks between active compounds and protein targets, providing a more holistic understanding of their therapeutic potential.

Functional characterization of proteins or genes and elucidation of their associations with various diseases are essential. Target enrichment analysis is a crucial tool that enables the identification of biological pathways related to target proteins (Reimand et al., 2019). Interpretation of the enrichment results can reveal the metabolic activities of the targets, helping to prioritize specific targets for subsequent molecular docking studies between active compounds and proteins.

This study aimed to elucidate the potential interactions of *C. amada* compounds with relevant biological targets using network pharmacology and molecular docking approaches. It is expected that this analysis will predict the biological pathways involved in the mechanisms of action of these compounds, particularly those related to their pharmacological activities.

2. METHODS

2.1. Retrieving Compounds of *Curcuma amada* Rhizome

Compound data related to the rhizome of *C. amada* were retrieved from KNApSAcK: A Comprehensive Species-Metabolite Relationship Database (https://www.knapsackfamily.com/KNApSAcK_Family/). Subsequently, the Simplified Molecular Input Line Entry System (SMILES) notations of the identified compounds were obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) (Kim et al., 2022). These SMILES data were then utilized for absorption, distribution, metabolism, and excretion (ADME) analysis, as well as target prediction.

2.2. ADME Predictions of the Compounds

Compounds obtained from the KNApSAcK database were predicted to have physicochemical and pharmacokinetic properties. SwissADME (http://www.swissadme.ch/) is an online tool that facilitates the evaluation of ADME parameters, pharmacokinetic profiles, and drug-likeness of small molecules to support drug discovery (Daina et al., 2017). The SMILES notations of the compounds were submitted to SwissADME to generate predictive target data.

2.3. Target Predictions of the Compounds

The SMILES notations of the compounds were submitted to the SwissTargetPrediction database (http://www.swisstargetprediction.ch/) to predict potential molecular targets associated with *Curcuma amada* rhizome compounds. SwissTargetPrediction is an online tool designed to identify the most probable protein targets of bioactive small molecules in humans and other vertebrates (Daina et al., 2019). In this study, target predictions were specifically conducted for *Homo sapiens*. Redundant targets were removed from the dataset, and the resulting non-duplicate targets were subsequently used to construct a protein–protein interaction (PPI) network.

2.4. Protein-Protein Interaction and Enrichment Analysis

Protein–protein interaction (PPI) data were obtained from the STRING 12.0 database (https://www.string-db.org/) (Szklarczyk et al., 2023) using the following parameters: required interaction score of 0.900 (highest confidence), full STRING network type, and a false discovery rate (FDR) stringency of 5%. The resulting network was visualized and analyzed using Cytoscape version 3.10.3 (Shannon et al., 2003). Network topological parameters, including degree, betweenness centrality, and closeness centrality, were calculated, and overall centrality scores were calculated using Principal Component Analysis (PCA) with Python as the programming language. This score was used as a filtering criterion to extract a high-confidence subnetwork comprising nodes with overall centrality values above the median threshold.

To identify potential key targets, clustering analysis was performed using the ClusterONE plugin from CytoCluster, while Maximal Clique Centrality (MCC) was calculated using the cytoHubba plugin. Potential targets for molecular docking were selected based on the combined results from both plugins and their associations with specific compounds and enrichment data. Functional enrichment analysis was performed for all targets, and relevant annotations, including Gene Ontology (GO), KEGG pathway, and DISEASES, were retrieved from the STRING database.

2.5. Construction of Network Pharmacology

Network pharmacology topology was constructed using Cytoscape. The integrated network included multiple interaction types, comprising target–target, compound–target, target–enrichment, compound–target–enrichment, and compound–target–DISEASES relationships. This comprehensive network facilitated the visualization and analysis of multilevel interactions between *C. amada* rhizome compounds, their predicted targets, and associated biological functions and diseases.

2.6. Molecular Docking

Molecular docking was conducted using AutoDock Vina (Trott and Olson, 2010). The three-dimensional (3D) structures of selected compounds identified from network pharmacology analysis, including espatulenol (spathulenol), (+)-beta-eudesmol (β-eudesmol), tau-muurolol (τ-muurolol), and (2E,6Z)-farnesol ((E,Z)-farnesol), were retrieved from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). The compound structures were optimized using the Avogadro2 software to obtain energy-minimized conformations (Hanwell et al., 2012).

The crystal structures of the key protein targets, tyrosine-protein kinase JAK2 (JAK2; PDB ID: 4IVA) and phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha isoform (PIK3CA; PDB ID: 5DXT), were obtained from the RCSB Protein Data Bank (https://www.rcsb.org/) (Berman et al., 2000). Protein and ligand preparation was carried out using AutoDockTools (Morris et al., 2009), including the addition of polar hydrogens, Gasteiger charges, and conversion to PDBQT format.

The docking grid box was defined around the active site using the coordinates of the native ligand with a grid size of 20 × 20 × 20 $Å^3$ to ensure proper coverage of the binding pocket. To validate the docking protocol, redocking of the native ligand into the binding site was performed, and the Root Mean Square Deviation (RMSD) between the native and redocked poses was calculated using PyMOL (The PyMOL Molecular Graphics System, n.d.). A low RMSD value indicated accurate binding of the ligand to the active site.

Subsequently, molecular docking simulations were performed for selected compounds and target proteins. The docking results were analyzed and visualized using BIOVIA Discovery Studio to examine the binding affinity and interaction profiles (BIOVIA Dassault Systèmes, 2021).

3. RESULTS AND DISCUSSION

3.1. Screening of the Compounds and Targets

C. amada is a medicinal plant widely utilized in traditional medicine, with the rhizome being one of its most commonly used parts. Based on the data retrieved from the KNApSAcK database, 110 compounds were identified in the rhizome of *C. amada* (**Supplementary File 1**). These compounds are predominantly volatile constituents, such as essential oils, which contribute to the characteristic aroma of the rhizome (Padalia et al., 2013; Rao et al., 1989; Srivastava et al., 2001).

Physicochemical screening of the 110 compounds using Lipinski's Rule of Five showed no violations, indicating favorable drug-likeness properties (**Supplementary File 2**). Lipinski's rule assesses the likelihood of oral bioavailability based on molecular weight, lipophilicity (logP), hydrogen bond donors and acceptors, and molecular polarity (Lipinski, 2004, 2016). Based on these results, all 110 compounds were subjected to target prediction using the SwissTargetPrediction platform for further network pharmacology analysis.

3.2. Protein-Protein Interaction Network

Target prediction of the 110 compounds yielded 498 protein targets, resulting in 1,757 predicted interactions (**Supplementary File 3**). To enhance the biological relevance of the network, a filtering step was performed based on the overall centrality scores, retaining nodes with values above the median (**Figure 1**). This analysis resulted in a subnetwork comprising 249 proteins and 1,242 interactions (**Figure 2**a). The overall centrality score was computed by integrating three key metrics: degree, betweenness, and closeness centralities (**Supplementary File 4**). These measures were selected because of their capacity to identify hub proteins, highly connected nodes, and those located centrally within the network. Such proteins often play critical roles in maintaining the structure and function of biological systems and are, therefore, promising targets for disease diagnosis, prognosis, and therapeutic intervention (Rout et al., 2024).

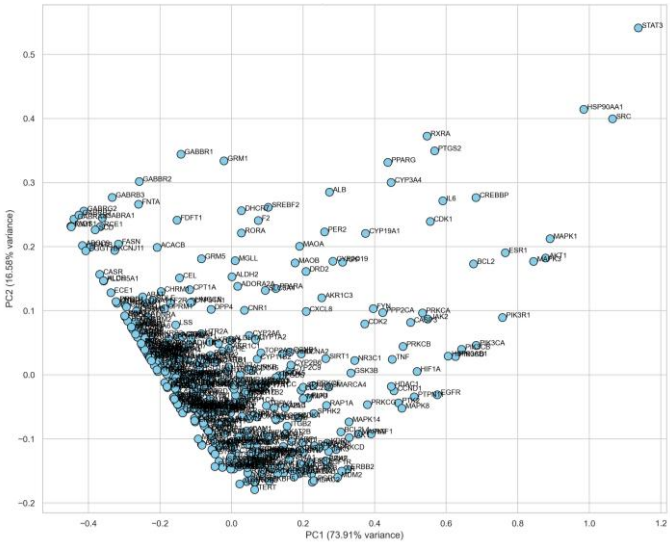

Figure 1. Principal Component Analysis (PCA) of node centrality measures in the protein–protein interaction (PPI) network.

As no single centrality measure fully encapsulates a protein's role within the network, we applied Principal Component Analysis (PCA) to calculate these three centrality metrics into a composite score we term overall centrality. Before applying PCA, all centrality measures were normalized using Min-Max scaling to ensure that differences in scale did not disproportionately influence the results and analyzed using Principal Component Analysis (PCA), with the first principal component (PC1) used to

represent the overall centrality score, as it explains the largest variance among the centrality features. The PCA implementation and associated codes are provided in **Supplementary File 5**.

After obtaining a subnetwork of proteins with overall centrality scores above the median, we clustered the subnetwork using the ClusterONE plugin in Cytoscape. This analysis identified 32 proteins and 221 interactions, with a statistically significant p-value of 2.30×10^{-6} (**Figure 2**b, **Supplementary File 6**). ClusterONE (Clustering with Overlapping Neighborhood Expansion) is designed to detect overlapping protein complexes in PPI networks, providing insight into functionally related protein groups (Nepusz et al., 2012).

Furthermore, key targets of the 249-protein subnetwork derived from overall centrality filtering were prioritized using the Maximal Clique Centrality (MCC) method implemented in the cytoHubba plugin. MCC identifies hub nodes by quantifying the number of maximal cliques to which a node belongs (Chin et al., 2014). This analysis highlighted 10 key targets with 45 interactions (**Figure 2**c, **Supplementary File 7**). The combined results from ClusterONE and MCC were used to determine the most influential targets within the PPI network that were selected for molecular docking studies.

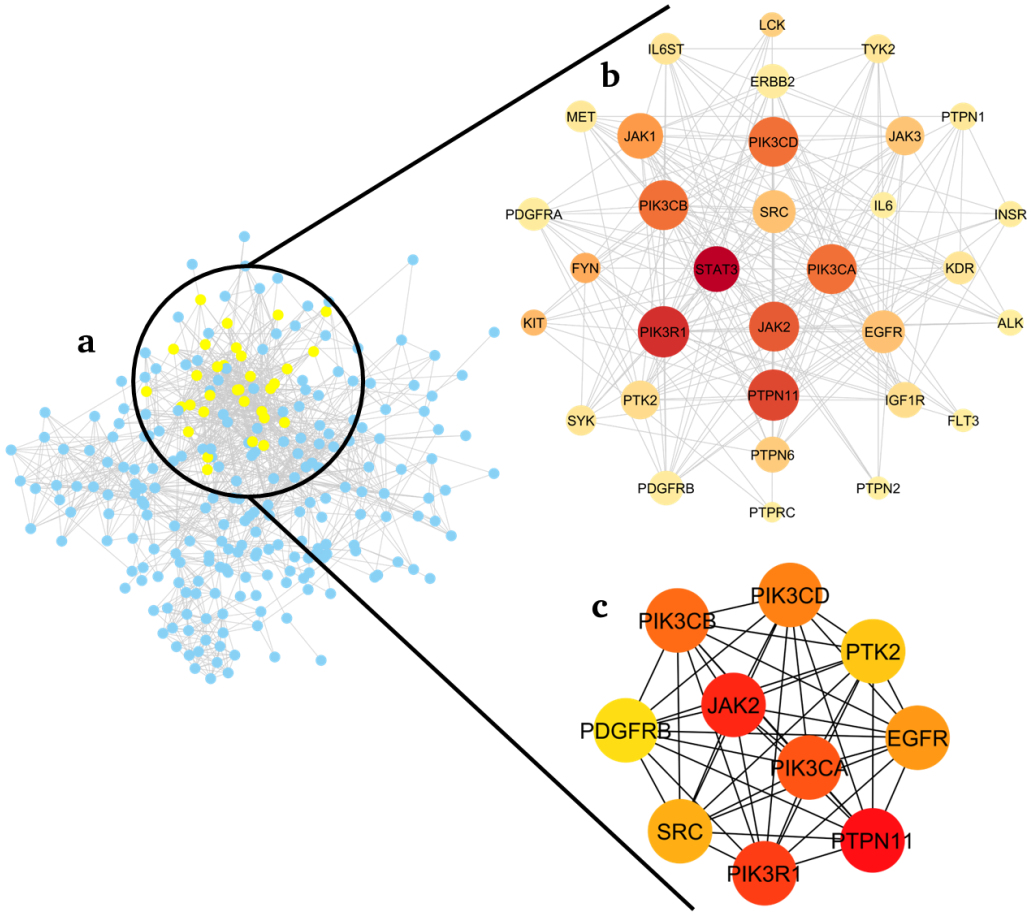

Figure 2. Topology of the protein–protein interaction (PPI) network: (a) high-confidence subnetwork filtered by overall centrality scores above the median, (b) network clusters identified using ClusterONE, and (c) key target ranking based on Maximal Clique Centrality (MCC) analysis.

3.3. Network Pharmacology

The network topology in **Figure 3a** illustrates the complex interactions between the predicted protein targets of *C. amada* rhizome compounds and their functional annotations, including Gene Ontology (GO) terms and KEGG pathways. This integrative visualization enhances our understanding of the potential mechanisms by which *C. amada* has therapeutic effects.

Enriched biological processes (pink nodes in the network), such as receptor protein signaling pathways, regulation of phosphorylation, and intracellular signal transduction, play essential roles in maintaining cellular homeostasis, cell proliferation, especially in tumors, and adaptive responses to external stimuli (Ardito et al., 2017; Valls & Esposito, 2022; Zambuzzi et al., 2011). From a molecular function perspective (purple), the network revealed significant enrichment in kinase activity, ATP binding, and protein tyrosine kinase activity. Kinases are important enzymes in signal transduction pathways, and their dysregulation is often involved in diseases such as cancer and inflammatory disorders (Sever & Brugge, 2015). In the cellular components category (cyan), enrichment in the plasma membrane, membrane protein complexes, and receptor complexes indicates that many target proteins are membrane-bound or interact at the cell surface.

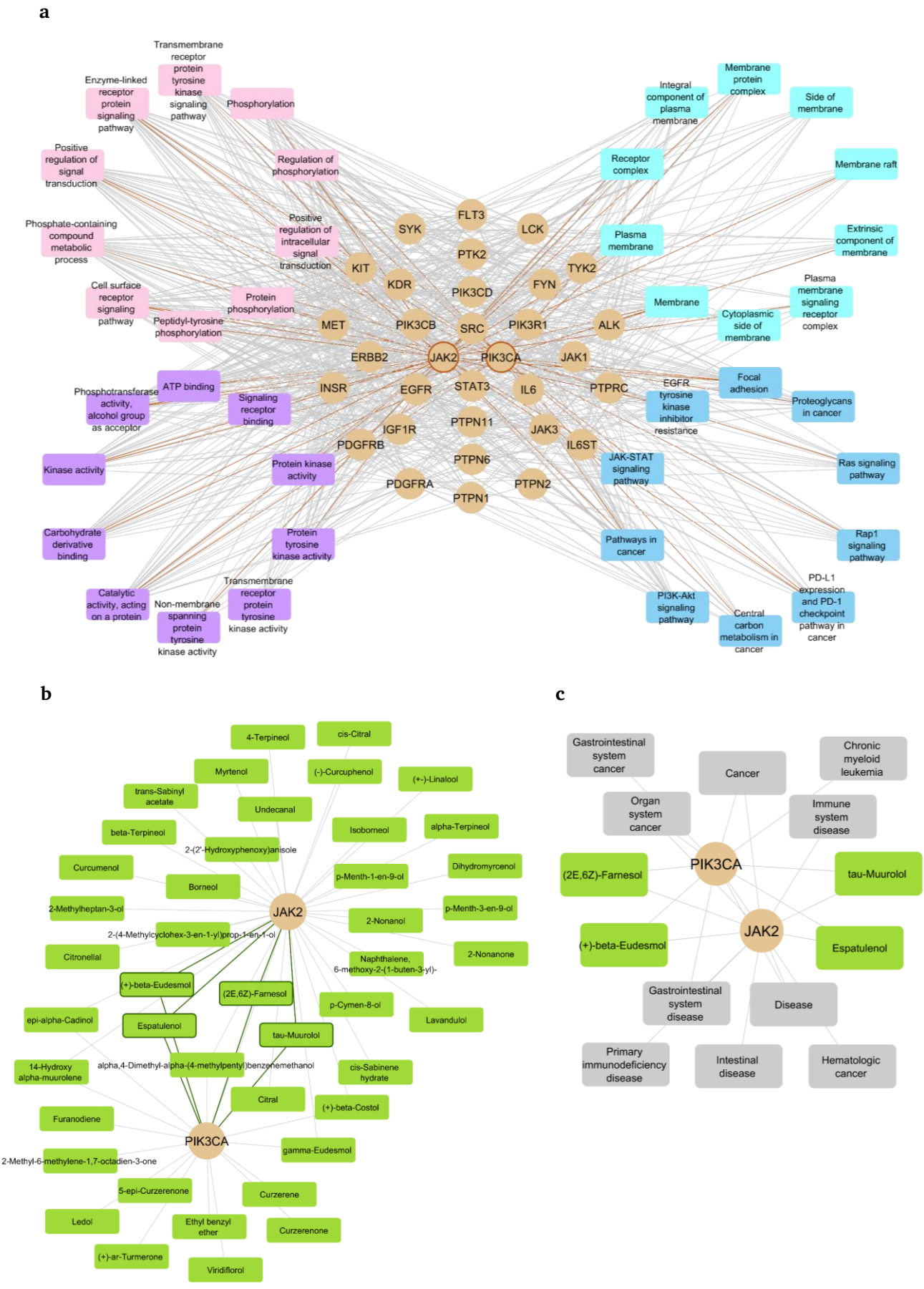

Figure 3. Topology of network pharmacology analysis: (**a**) integrated network of protein targets and top 10 enrichment terms, including Gene Ontology (GO) and KEGG Pathways; nodes are colored according to category, pink (GO biological process), purple (GO molecular function), cyan (GO cellular component), blue (KEGG Pathway), and brown (protein targets); (**b**) network of selected protein targets for molecular docking and their associated compounds; and (**c**) network of docking targets and related compounds integrated with DISEASES enrichment data.

KEGG pathway enrichment (blue) highlights the PI3K-Akt, Ras, and JAK-STAT signaling pathways, which are critical cascades involved in cell growth, survival, and immune responses. The PI3K-Akt pathway, particularly involving PIK3CA, plays a crucial role in oncogenesis and is frequently mutated in cancers (He et al., 2021). The JAK-STAT pathway, in which JAK2 is a major component, mediates cytokine signaling and has been implicated in various cancers and autoimmune diseases (Hu et al., 2021). Targeting these pathways with natural compounds is a promising strategy for multi-target therapy.

Based on the results of the network pharmacology analysis, PIK3CA and JAK2 emerged as key targets with high biological centrality and relevance. These proteins were identified through topology assessment methods, such as ClusterONE and MCC, highlighting their roles as hub nodes in protein-protein interaction (PPI) networks. Importantly, both PIK3CA and JAK2 are well-known oncogenes involved in various cancer-related pathways.

Further supporting these findings, DISEASES enrichment analysis (**Figure 3c**) revealed a strong association between the predicted *C. amada* rhizome compound targets and cancer-related pathways. This suggests that bioactive compounds may exert pharmacological effects through the modulation of these oncogenic targets. As shown in **Figure 3b**, 44 bioactive compounds were identified to be associated with PIK3CA and JAK2. From this subset, four compounds were selected for molecular docking studies. These selected compounds will be further evaluated to determine their binding affinities and interaction profiles, thereby validating their therapeutic potential against identified protein targets.

3.4. Molecular Docking

Root Mean Square Deviation (RMSD) values between the co-crystallized ligands and the re-docked conformations were calculated to validate the molecular docking protocol. The RMSD for ligand 5H5 (bound to PIK3CA) was 0.667 Å, and for ligand 1J5 (bound to JAK2), it was 0.474 Å. These low RMSD values indicate a high degree of overlap between the native and predicted binding conformations. Superimposition of the co-crystal ligand and the re-docked ligand can be seen in **Figure 4**.

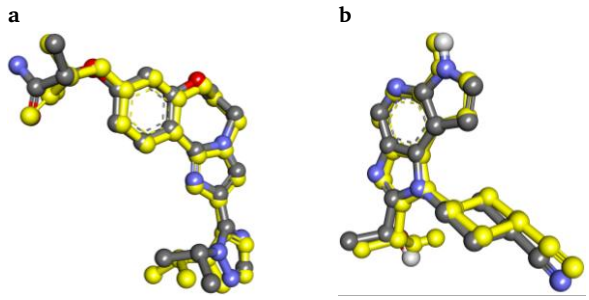

Figure 4. Superimposition of the co-crystal ligand (yellow) and the re-docked ligand (grey) to validate docking accuracy: (a) ligand 5H5 in complex with PIK3CA (PDB ID: 5DXT); (b) ligand 1J5 in complex with JAK2 (PDB ID: 4IVA).

The binding affinities in **Table 1** show that the native ligands of PIK3CA and JAK2 exhibited strong binding affinities of -9.1 kcal/mol (5H5) and -9.5 kcal/mol (JAK2), respectively, and serve as benchmarks for assessing the binding potential of the test compounds. Among the *C. amada* compounds, espatulenol (spathulenol) showed the highest affinity for JAK2 (-8.4 kcal/mol), approaching the native ligand's binding strength, suggesting promising inhibitory potential. Similarly, (E,Z)-farnesol showed the strongest binding affinity toward PIK3CA among the compounds (-7.2 kcal/mol).

Table 1. The docking affinity values of selected *C. amada* rhizome-derived compounds against the target proteins PIK3CA and JAK2

Ligand \ Protein	Affinity (kcal/mol)	
	PIK3CA	JAK2
Native ligand	-9.1	-9.5
β-eudesmol	-6.8	-7.3
(E,Z)-farnesol	-7.2	-5.9
Spathulenol	-6.1	-8.4
τ-muurolol	-6.5	-7.5

Figures 5 and **6** demonstrate that the native ligand exhibits a stable and specific interaction profile, forming multiple hydrogen bonds and hydrophobic contacts with key residues in the PIK3CA and JAK2 binding pockets. Hydrogen bonds were observed between the ligand and PIK3CA, at GLN859, VAL851, and ASP933, with distances of 1.86, 2.01, and 2,77 Å, respectively. Hydrogen bonds were observed between the ligand and JAK2, at GLU930, LEU932, and SER 936, with distances of 2.07, 2.09, and 2,49 Å, respectively.

Molecular docking analysis revealed that, in addition to hydrogen bonds, hydrophobic interactions play a crucial role in stabilizing the native ligand within the binding pocket. As shown in **Figures 5** and **6**, several surrounding residues formed extensive hydrophobic contacts that enhanced both the binding affinity and ligand orientation. These hydrophobic interactions include pi–sigma, pi–sulfur, pi–pi t-shaped, alkyl, and pi–alkyl interactions, all of which contribute to the stabilityligand of–receptor complexes.

Key hydrophobic interactions were observed between the native ligand and PIK3CA, involving residues ILE848, MET922, ILE932, TRP780, VAL851, and TYR836. These residues contribute to a nonpolar microenvironment within the binding pocket, enhancing ligand stabilization. Similarly, in the JAK2 binding site, critical hydrophobic contacts were identified with LEU855, LEU983, MET929, VAL863, ALA880, and VAL911, which also form a hydrophobic environment that supports ligand binding and orientation.

The interaction between protein and ligand residues from *C. amada* rhizome is predominantly hydrophobic, primarily due to the volatile nature of the ligands, which enables them to interact effectively with the hydrophobic regions of protein-binding sites. This observation aligns with the findings of Ren et al. (2024), who reported that most volatile compounds tend to engage in hydrophobic interactions.

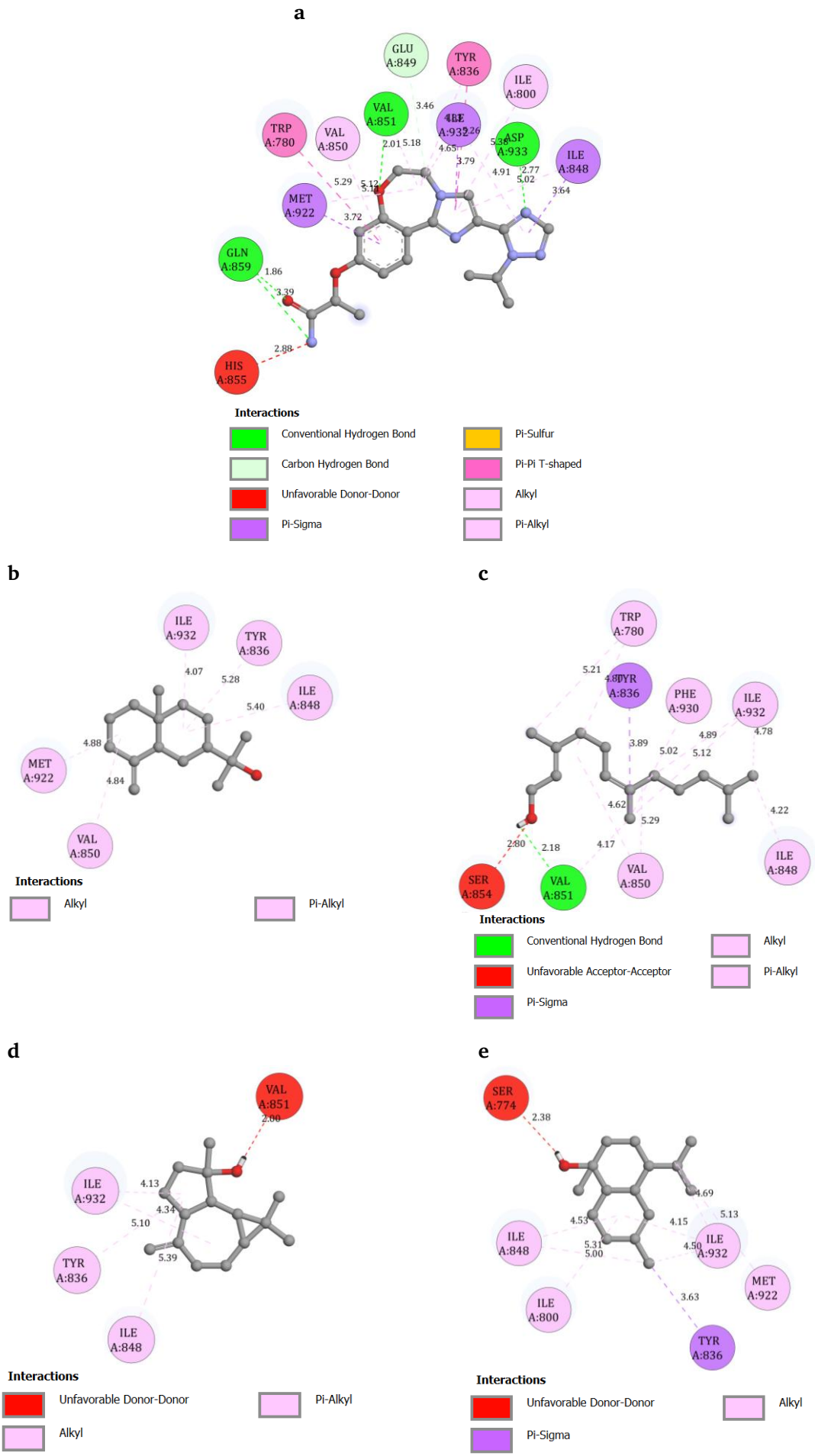

Figure 5. Binding poses of docking results between PIK3CA (PDB ID: 5DXT) and various ligands: (**a**) native ligand 5H5, (**b**) β-eudesmol, (**c**) (E,Z)-farnesol, (**d**) spathulenol, (**e**) τ-muurolol

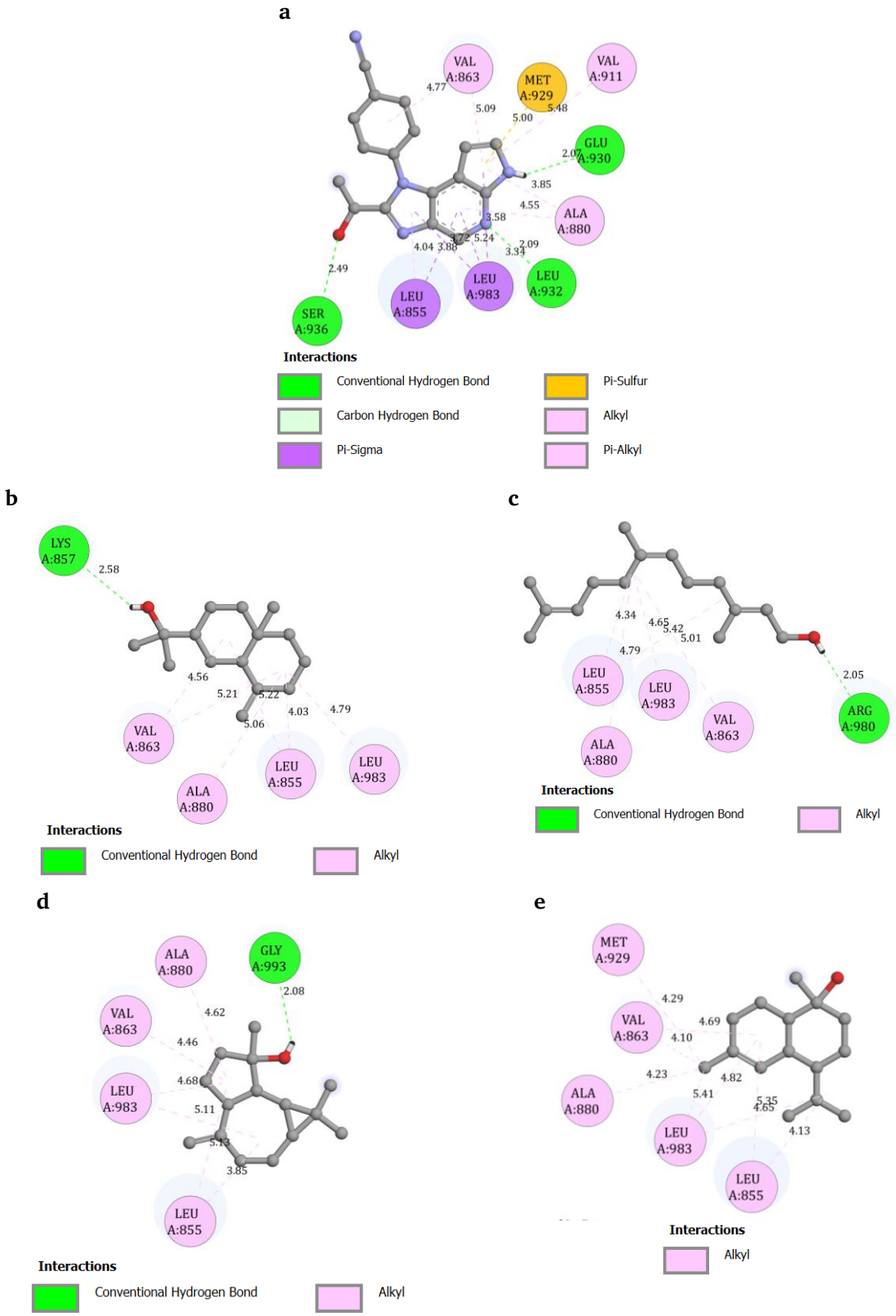

Figure 6. Binding poses of docking results between JAK2 (PDB ID: 4IVA) and various ligands: (a) native ligand 1J5, (b) β-eudesmol, (c) (E,Z)-farnesol, (d) spathulenol, (e) τ-muurolol

The interaction between protein and ligand residues from *C. amada* rhizome is predominantly hydrophobic, primarily due to the volatile nature of the ligands, which enables them to interact effectively with the hydrophobic regions of protein-binding sites. This observation aligns with the findings of Ren et al. (2024), who reported that most volatile compounds tend to engage in hydrophobic interactions.

The in silico analysis revealed that among the selected compounds, (E,Z)-farnesol exhibited the strongest binding affinity toward PIK3CA, followed sequentially by (+)-β-eudesmol, spathulenol, and τ-muurolol. Both farnesol and β-eudesmol have been previously reported to possess notable anticancer properties, particularly through modulation of the PI3K signaling pathway. These effects are primarily attributed to their ability to inhibit

PI3K/AKT pathway activation via transcriptional regulation rather than direct enzymatic inhibition. Farnesol treatment reduces PI3K/AKT phosphorylation levels, thereby suppressing pathway activation and promoting apoptosis in various cancer cell lines, including DU145 (prostate cancer) (Park et al., 2014), HEL299 (lung cancer) (Lee et al., 2019), and HeLa (cervical cancer) cells (Wang et al., 2018). β-Eudesmol exhibits antiproliferative effects and inhibits the migration and invasion of cholangiocarcinoma (CCA) cells, primarily by suppressing epithelial-mesenchymal transition (EMT) through modulation of the PI3K/AKT and p38 MAPK signaling pathways (Ziaei et al., 2011).

The Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling pathway is a conserved mechanism essential for transmitting extracellular signals to the nucleus and regulating cellular functions such as proliferation, metabolism, immune responses, and malignancy (Xue et al., 2023). Dysregulation of this pathway and associated genetic mutations are strongly linked to immune-related diseases and cancer progression (Owen et al., 2019). Furthermore, chronic activation of JAK-STAT signaling contributes to carcinogenesis, therapy resistance, and communication between tumor cells and the immune system, particularly in inflammation-driven cancers (Sabaawy et al., 2021). Various therapeutic strategies targeting the JAK-STAT pathway have been developed, including cytokine/receptor antibodies, JAK inhibitors, and STAT inhibitors. Molecular docking analysis revealed that spathulenol exhibited the strongest binding affinity for JAK2, followed by τ-muurolol, (+)-β-eudesmol, and (E,Z)-farnesol, suggesting that compounds from *C. amada* may selectively modulate distinct oncogenic targets, highlighting their therapeutic potential.

Spathulenol has been reported to exhibit potential anticancer effects by mitigating oxidative stress and preserving mitochondrial membrane integrity. It has also been shown to promote neuroregeneration in neuroblastoma cells (Manjima et al., 2021). Consistent with these findings, pharmacokinetic analysis (**Supplementary File 2**) indicated that spathulenol can cross the blood-brain barrier (BBB), supporting its potential role as a neuroprotective agent. Additionally, spathulenol has been shown to induce apoptosis in human melanoma cells (SK-MEL-28) (Beserra Santos et al., 2020) and suppress lymphocyte proliferation through a caspase-3-independent apoptotic pathway (Ziaei et al., 2011). Similarly, τ-muurolol demonstrated cytotoxic activity against A-549 lung carcinoma and MCF-7 breast adenocarcinoma cell lines (Ziaei et al., 2011). These findings align with the docking results, supporting the potential role of the compounds from *C. amada* as modulators of cancer-related targets, particularly PIK3CA and JAK2.

CONCLUSION

This study provides a comprehensive molecular insight into the therapeutic potential of *C. amada* rhizome, highlighting its bioactive compounds as promising modulators of cancer-related targets. Using network pharmacology and molecular docking approaches, we identified the key proteins, PIK3CA and JAK2, as significant targets within the protein-protein interaction network. The selected compounds, including β-eudesmol, (E,Z)-farnesol, spathulenol, and τ-muurolol, demonstrated strong binding affinities and favorable interaction profiles with these targets. Redocking validation with low RMSD values further confirmed the reliability of the docking protocol. The predominantly hydrophobic interactions observed, which are consistent with the volatile nature of the compounds, suggest a stable binding mechanism. These findings support the potential of *C. amada* rhizome as a source of anticancer agents and lay the groundwork for future experimental studies exploring its therapeutic efficacy.

SUPPORTING INFORMATION

Supplementary Files can be accessed via the following links: https://bit.ly/supplementary-files-jji-397

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