Original Research Article

Multiomics and Molecular Docking Approaches to Elucidate Desmostachya Bipinnata-Derived Multitargeting Agents for Oral Squamous Cell Carcinoma

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Nitya Krishnasamy[1], Ramya Ramadoss[1], Kochli Channapa Niranjan[2], Vikram S Amberkar[3], Haris Chandra Sahoo[4] and Poorna Devadoss[5]

Abstract

Background: Oral squamous cell carcinoma (OSCC) is a prevalent form of head and neck cancer characterized by aggressive behavior and a poor prognosis. Conventional therapies have demonstrated limited effectiveness, underscoring the need for innovative strategies that target the molecular mechanisms involved in OSCC progression. Multitargeting agents present a promising approach by simultaneously addressing several key pathways, potentially addressing issues of treatment resistance. Desmostachya bipinnata, a medicinal plant renowned for its anticancer properties, contains bioactive compounds that may serve as effective treatments for OSCC.

Objectives: This study aims to investigate the therapeutic potential of bioactive compounds from Desmostachya bipinnata in treating OSCC. It uses bioinformatics and molecular docking techniques to identify key molecular targets and pathways, evaluate compound binding affinities, and propose novel multitargeting agents for OSCC therapy.

Materials and Methods: This study aimed to explore the therapeutic potential of Desmostachya bipinnata compounds for OSCC using bioinformatics and molecular docking. Six of the 19 compounds screened were excluded due to toxicity, leaving 14 for further analysis. GeneCards, DisGeNet, and Gene Expression Omnibus (GEO) databases identified 3,278 OSCC-related genes, and SwissTargetPrediction predicted 221 targets. Protein–protein interaction and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis pinpointed significant hub genes. Molecular docking of four selected compounds (linoleic acid, kaempferol, daucosterol, stigmasterol-glucoside) with six key targets (MMP2, PTGS2, STAT3, MAPK1, MMP9, AKT1) revealed strong binding affinities, suggesting potential therapeutic efficacy.

Results: This study evaluated potential therapeutic compounds from Desmostachya bipinnata for OSCC through a comprehensive approach. After assessing the toxicity of 19 compounds, six were excluded due to predicted adverse effects, leaving 14 for further analysis. We identified 3,278 OSCC-related genes by integrating data from GeneCards, DisGeNet, and GEO databases. Using SwissTargetPrediction, we narrowed down 221 unique targets for these compounds and identified 95 common targets with OSCC genes. Protein–protein interaction analysis via STRING and Cytoscape, along with Molecular Complex Detection (MCODE), highlighted a significant gene cluster. Expression analysis with Gene Expression Profiling Interactive Analysis (GEPIA) led to the exclusion of low-expressing genes (IL6, MAPK3, ESR1, BCL2), focusing on MMP2, PTGS2, STAT3, MAPK1, MMP9, and AKT1, which are involved in cancer-related pathways. Molecular docking studies showed that linoleic acid, kaempferol, daucosterol, and stigmasterol-glucoside exhibit strong binding affinities to these targets, suggesting their potential as effective therapeutic agents. Activity predictions confirmed their antineoplastic properties, underscoring their potential utility in OSCC treatment.

Conclusion: The findings indicate that *Desmostachya bipinnata* compounds exhibit promising multitargeting activity against OSCC. The strong binding affinities and interaction profiles of these compounds with key OSCC-related targets support

[1]Department of Oral Biology, Saveetha Dental College & Hospitals, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India

[2]Department of Oral and Maxillofacial Pathology, SDM College of Dental Sciences, Shri Dharmasthala Manjunatheshwara University, Dharwad, Karnataka, India

[3]Department of Oral and Maxillofacial Pathology, College of Dental Sciences, Davangere, Karnataka, India

[4]Naturopathic Practitioner, Badarpur, New Delhi, India

[5]Thai Moogambigai Dental College and Hospital, Dr. MGR Educational and Research Institute, Chennai, Tamil Nadu

Corresponding author:
Ramya Ramadoss, Department of Oral Biology, Saveetha Dental College & Hospitals, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu 600077, India.
E-mail: ramyar.sdc@saveetha.com

their potential as effective therapeutic agents. Further experimental validation is needed to confirm these results and explore the clinical applicability of these compounds in OSCC treatment.

Keywords

Desmostachya bipinnata, oral squamous cell carcinoma (OSCC), gene targets, therapeutic agents, anticancer, multitarget, molecular docking, compounds

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Introduction

Oral squamous cell carcinoma (OSCC) is a major type of head and neck cancer, characterized by its aggressive nature and poor prognosis.[1] Despite advances in surgical techniques, radiotherapy, and chemotherapy, the survival rate for OSCC remains low, primarily due to late diagnosis and the development of resistance to conventional therapies.[2,3] This underscores the urgent need for novel therapeutic strategies that effectively target the molecular mechanisms driving OSCC progression.[4]

One promising approach is using multitargeting agents that can simultaneously modulate several critical pathways involved in cancer development and metastasis.[5] Such agents can potentially overcome the limitations of single-target therapies, which often lead to resistance and limited efficacy.[6] In this context, natural compounds have gained attention for their multitargeting capabilities and lower toxicity profiles than synthetic drugs.[7]

Desmostachya bipinnata, a medicinal plant known for its wide range of pharmacological properties, has shown potential as a source of bioactive compounds with anticancer activities.[8] Previous studies have highlighted various compounds from *Desmostachya bipinnata* that exhibit anti-inflammatory, antioxidant, and antiproliferative effects, making it a candidate for cancer therapy.[9]

To systematically explore the therapeutic potential of *Desmostachya bipinnata* in OSCC, this study employs bioinformatics and molecular docking approaches. Bioinformatics tools facilitate the identification of key molecular targets and pathways associated with OSCC, while molecular docking studies allow for the evaluation of binding affinities and interactions between bioactive compounds and these targets.[10,11] This integrated approach aims to uncover the multitarget potential of *Desmostachya bipinnata* compounds, providing insights into their mechanisms of action and paving the way for future experimental validation.

Materials and Methods

Compound Selection and Toxicity Analysis

Bioactive compounds from *Desmostachya bipinnata* were initially retrieved from existing literature, resulting in a list of 19 compounds. These compounds underwent rigorous toxicity analysis using ProTox II webserver[12] (https://tox.charite.de/protox3/) to evaluate their profiles for hepatotoxicity, carcinogenicity, mutagenicity, and cytotoxicity. The compounds exhibiting any of these toxic profiles or classified under Predicted Toxicity Class 1, 2, or 3 were excluded from further analysis.

Target Identification for OSCC

A comprehensive gene search was conducted across multiple databases to identify genes associated with OSCC. Three different databases were used: GeneCards, DisGeNet, and Gene Expression Omnibus (GEO).[13,14] Using GeneCards, a keyword search for "OSCC" yielded 2,304 genes. In the DisGeNET database, a search for "Oral cancer" identified 734 genes. Additionally, the GEO database (GSE37991) was analyzed to identify differentially expressed genes in OSCC samples. This analysis included 40 OSCC samples and 40 standard samples, resulting in identifying 999 upregulated genes with a log fold change (LogFC) greater than one and an adjusted p value of less than .05.

Compound–Target Prediction

The SwissTargetPrediction tool was utilized to predict potential targets for the selected 14 nontoxic compounds (http://www.swisstargetprediction.ch/).[15] Compounds with a probability score greater than 0.1 were considered significant, leading to the identification of 221 unique target genes.

Protein–Protein Interaction (PPI) and Expression Analysis

To understand the interactions and pathways involved, a PPI network was constructed using the STRING database (version 12.0) with a confidence score of 0.700 (https://string-db.org/).[16] The Molecular Complex Detection (MCODE) algorithm was applied to identify significant clusters within this network. Additionally, gene expression levels were analyzed for genes with top scores in MCODE using Gene Expression Profiling Interactive Analysis (GEPIA) (http://gepia.cancer-pku.cn/).[17] The genes with low expression in head and neck squamous cell carcinoma (HNSC) were excluded for further analysis. This analysis helped to narrow down the key targets for further investigation.

KEGG Pathway Enrichment

Significant hub genes with high expression profiles were analyzed to determine their involvement in various Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways. This analysis was conducted using the ShinyGo 0.76 web server, a tool designed for pathway enrichment analysis (http://bioinformatics.sdstate.edu/go/).[18] The resulting data highlighted genes that were significantly enriched in pathways related to cancer. These cancer-associated genes were selected for further in-depth analysis better to understand their roles and potential implications in cancer.

Molecular Docking Studies

The three-dimensional structure of the protein encoded by these genes was downloaded from Protein Data Bank (PDB) (https://www.rcsb.org/). Prior to docking, the identified genes were traced back to compound target analysis using the SwissTargetPrediction tool to identify potential compounds that could target these hub genes. Molecular docking studies were then performed to evaluate the binding affinities of the selected compounds with six key targets: MMP2, PTGS2, STAT3, MAPK1, MMP9, and AKT1. The four compounds tested were linoleic acid, kaempferol, daucosterol, and stigmasterol-glucoside. Carboplatin, a standard chemotherapeutic agent, was used as a control for comparison. All four compounds were docked with the hub genes to identify their multitargeting activity.

Docking studies were conducted using PyRx software. Initially, the proteins were prepared by removing water molecules and heteroatoms, and hydrogen atoms were added. The one with the best binding affinity was selected for each compound among the different conformations generated. The docking results were visualized using Discovery Studio Visualizer.

The docking interactions were assessed based on binding affinity (kcal/mol) and interacting amino acids. The results demonstrated the potential efficacy of the bioactive compounds from *Desmostachya bipinnata* in binding effectively with these key targets, indicating their promise as therapeutic agents against OSCC.

Activity Prediction

To predict the biological activities associated with the identified leads, the PASS (Prediction of Activity Spectra for Substances) webserver was utilized (https://www.way2drug.com/passonline/).[19] PASS is a computational tool that predicts a wide range of biological activities based on the chemical structure of compounds. By inputting the chemical structures of the identified leads into the PASS web server, we could obtain predictions about their potential pharmacological effects, mechanisms of action, and therapeutic targets. This information was crucial for understanding the possible biological relevance and efficacy of the leads in relation to the hub genes identified in our study.

Results

During the toxicity analysis, it was observed that out of 19 compounds, 6 compounds—quercetin, 2,6-dihydroxy-7-methoxy-3H-xanthen-3-one, eseroline, 5-hydroxymethyl-2-furfural, and oleic acid—were predicted to have adverse toxic effects. Consequently, these six compounds were excluded from further analysis to ensure the safety and efficacy of the potential leads. The remaining 14 compounds did not show significant toxicity and were selected for compound target prediction (Table 1). This step aimed to identify potential molecular targets and pathways associated with these compounds, facilitating the selection of promising candidates for further experimental validation and development.

OSCC Targets

Upon analysis, 2,304 genes were identified using GeneCards, and 734 genes were obtained from DisGeNet. Gene expression analysis was also performed on 40 OSCC samples and 40 normal samples from the GEO database. The criteria for upregulated genes were set with a LogFC (log fold change) > 1 and an adjusted p value < .05. This analysis resulted in the identification of 999 upregulated genes in GEO.

Combining the results from all three databases—GeneCards, DisGeNet, and GEO—and removing duplicate entries, a total of 3,278 genes related to OSCC were obtained. This comprehensive gene list serves as a valuable resource for further investigations into the molecular mechanisms and potential therapeutic targets for OSCC.

Compounds Target

The targets of the 14 compounds were predicted using the SwissTargetPrediction tool, with a probability score threshold set at >0.06 (Supplementary Figure S1). This analysis initially identified 383 potential targets. After consolidating the data and removing duplicates, 221 unique targets were obtained. These unique targets provide a focused list for further exploration of the compounds' potential interactions and therapeutic applications. A Venn diagram was constructed using the interactive Venn online web server (https://www.interactivenn.net/) to identify overlapping targets between the 221 unique targets of the 14 compounds and the genes associated with OSCC (Figure 1). This analysis revealed that 95 genes were common targets, indicating their potential relevance in OSCC (Figure 1). These 95 genes represent a crucial subset for further investigation, as they may play significant roles in the disease's pathology and could be potential therapeutic targets for the identified compounds.

Table 1. Toxicity Analysis for Phytochemicals Present in *Desmostachya bipinnata*.

Sl. No.	Compounds	LD50 (mg/kg)	Predicted Toxicity class	Hepatotoxicity	Carcinogenicity	Mutagenicity	Cytotoxicity
1	Kaempferol	3919	5	Inactive	Inactive	Inactive	Inactive
2	Quercetin	159	3	Inactive	Active	Active	Inactive
3	Stigmasterol	890	4	Inactive	Inactive	Inactive	Inactive
4	Beta-sitosterol	890	4	Inactive	Inactive	Inactive	Inactive
5	Daucosterol	8000	6	Inactive	Inactive	Inactive	Inactive
6	2,6- dihydroxy-7-methoxy-3H-xanthen-3-one	4000	5	Inactive	Active	Active	Inactive
7	Beta-eudesmol	2000	4	Inactive	Inactive	Inactive	Inactive
8	Eseroline	2	1	Inactive	Inactive	Inactive	Inactive
9	Calarene	5000	5	Inactive	Inactive	Inactive	Inactive
10	Camphene	5000	5	Inactive	Inactive	Inactive	Inactive
11	Isobornyl acetate	3100	5	Inactive	Inactive	Inactive	Inactive
12	Tricyclene	15380	6	Inactive	Inactive	Inactive	Inactive
13	5-Hydroxymethyl 2-furfural	2500	5	Inactive	Active	Active	Inactive
14	Beta-amyrin	70000	6	Inactive	Inactive	Inactive	Inactive
15	Stigmasterol-glucoside	8000	6	Inactive	Inactive	Inactive	Inactive
16	Palmitic acid	900	4	Inactive	Inactive	Inactive	Inactive
17	Linoleic acid	10000	6	Inactive	Inactive	Inactive	Inactive
18	Oleic acid	48	2	Inactive	Inactive	Inactive	Inactive
19	2-methoxy-4-formylphenol	1000	4	Inactive	Inactive	Inactive	Inactive

The 95 common genes identified as potential OSCC targets were analyzed using the STRING web server to examine their PPI. The results of this PPI analysis were visualized using Cytoscape software (Figure 2a and b) (Supplementary Figure S2). To identify highly interconnected genes, MCODE analysis was performed. The highest MCODE score obtained was 10.727, indicating a highly significant cluster (Table 2). The genes within this high-scoring cluster included IL6, MMP2, PTGS2, MAPK3, SRC, STAT3, ESR1, MAPK1, MMP9, AKT1, BCL2, and MAPK14.

Expression Analysis

Expression profile analysis for the 12 identified genes was conducted using the GEPIA database. This analysis revealed that IL6, MAPK3, ESR1, and BCL2 had low expression levels in HNSC (Figure 3). Consequently, these four genes were excluded from further analysis due to their low expression in the relevant cancer type. This step ensured that the focus remained on genes with significant expression in HNSC.

KEGG Enrichment Analysis

KEGG enrichment analysis of the remaining eight genes was performed using the ShinyGO web server. The analysis indicated that these genes are enriched in various metabolic pathways. For the purposes of this study, genes involved in cancer-related pathways were specifically selected. The genes identified as being involved in pathways in cancer were MMP2, PTGS2, STAT3, MAPK1, MMP9, and AKT1 (Figure 4) (Supplementary Figure S3). These six genes were chosen for further investigation due to their potential roles in cancer biology and their relevance as therapeutic targets.

In their investigation, Zhang et al. scrutinized the KEGG enrichment for 27 target genes associated with stemazole, revealing their enrichment across 53 distinct KEGG pathways. This comprehensive analysis highlights the diverse roles these genes play in various biological contexts within their study. We derived inspiration from Zhang et al.'s study and conducted a parallel KEGG enrichment analysis for our three genes. The objective pursued by Zhang et al.

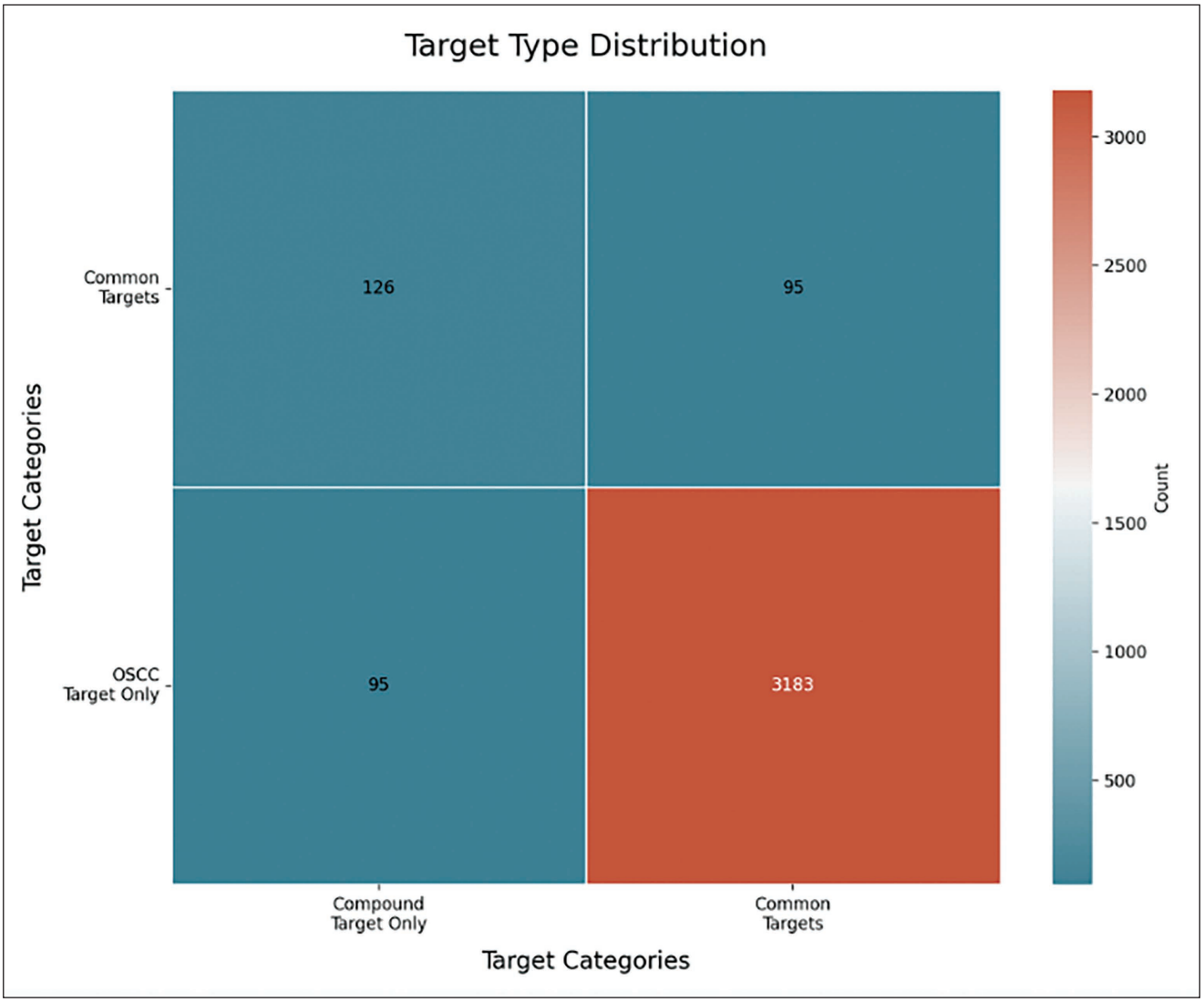

Figure 1. Heatmap Visualizing the Relationship Between Compound Targets and OSCC Targets.

resonates with our study, emphasizing the importance of understanding the significance of target genes within different pathways.[20]

Molecular Docking

From compound target analysis, the four compounds, namely, linoleic acid, kaempferol, daucosterol, and stigmasterol-glucoside, would target these six genes in OSCC (Table 3). Docking analysis revealed that all compounds exhibited good binding affinities towards all six target proteins. The binding affinities ranged from –4.4 to –10.6 kcal/mol, indicating strong interactions (Table 4, Figure 5). These affinities were comparable to those of the control drug, Carboplatin, suggesting that the compounds could potentially serve as effective therapeutic agents.

The docking studies showed that the interacting amino acids of the compounds were located within the active sites of the target proteins, which support their potential efficacy. Detailed information, including the gene and its corresponding protein PDB ID, grid coordinates, and the amino acids involved in the active site interactions, is presented in Table 5. This comprehensive data provides valuable insights into the molecular interactions and supports the potential of these compounds for further development as cancer therapeutics.

These results also suggest that all four compounds can effectively interact with all six target proteins in OSCC, highlighting their potential multitargeting activity. This indicates that each compound has the capability to bind and potentially modulate multiple key proteins involved in OSCC pathways, which could enhance their therapeutic efficacy. The ability of these compounds to interact with multiple targets suggests a

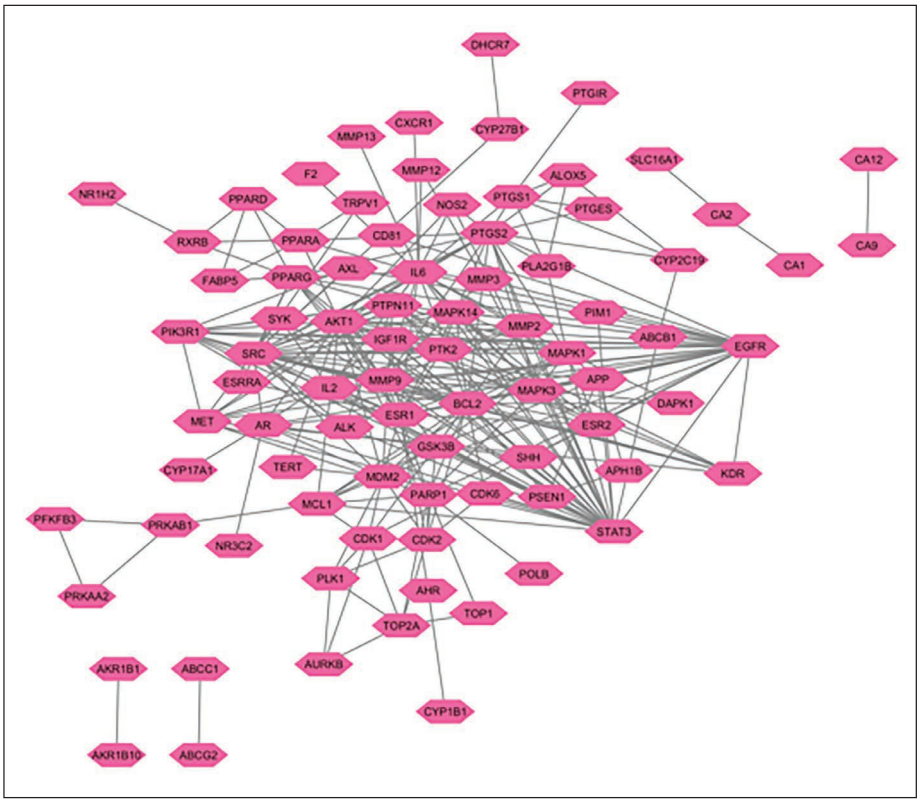

Figure 2. (a) PPI Visualized in Cytoscape.

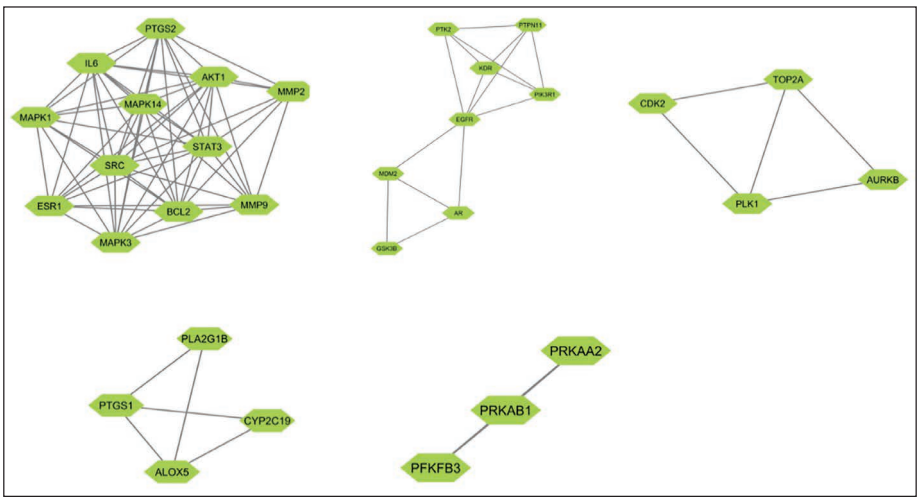

Figure 2. (b) MCODE Analysis with the Highest Score.

Table 2. MCODE Analysis of the Proteins with Scores.

Cluster	Score	Nodes	Edges	Proteins
1	10.727	12	59	IL6, MMP2, PTGS2, MAPK3, SRC, STAT3, ESR1, MAPK1, MMP9, AKT1, BCL2, MAPK14
2	4.286	8	15	KDR, AR, PTPN11, EGFR, GSK3B, PIK3R1, MDM2, PTK2
3	3.333	4	5	PLK1, CDK2, AURKB, TOP2A
4	3.333	4	5	PLA2G1B, ALOX5, CYP2C19, PTGS1
5	3	3	3	PRKAB1, PFKFB3, PRKAA2

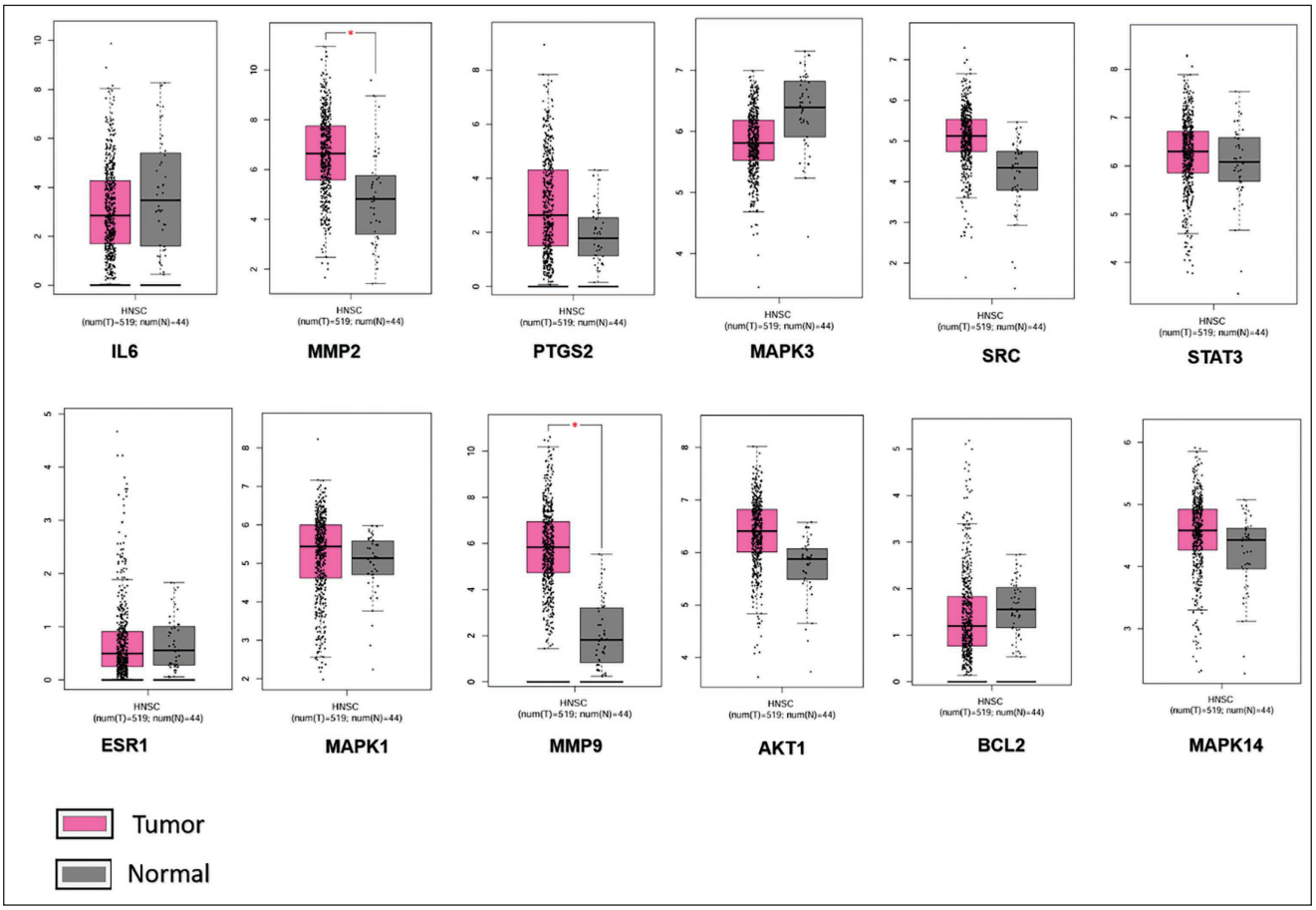

Figure 3. Expression Profile of Hub Genes.

promising strategy for developing multifaceted treatments for OSCC, potentially leading to better clinical outcomes by simultaneously influencing various molecular mechanisms of the disease.

Known for its antioxidant and anti-inflammatory properties, kaempferol demonstrated strong binding to STAT3 and AKT1. By inhibiting these proteins, kaempferol could potentially reduce tumor growth and metastasis. Linoleic acid showed significant interactions with MMP2 and PTGS2. Linoleic acid's anti-inflammatory properties might help in reducing OSCC-related inflammation. Daucosterol exhibited strong binding to MAPK1 and MMP9. Daucosterol could play a role in inhibiting cell proliferation and metastasis through these interactions. Stigmasterol-glucoside demonstrated a high affinity for MMP9 and PTGS2, suggesting its potential to modulate inflammation and prevent tumor invasion.

In a parallel study, Alamri investigated the interaction between five phytochemicals sourced from indigenous plants and targets associated with hepatocellular carcinoma (HCC). Their findings revealed binding affinities ranging from –8 to –9.5 kcal/mol.[21] Similarly, in our study, we conducted docking analyses between three fatty acids and three targets linked to oral cancer. Our results exhibited comparable variations in binding affinities. This congruence across studies validates the consistency of our findings and underscores the potential therapeutic relevance of these bioactive compounds in targeting specific disease pathways.

Activity Prediction

Activity prediction using the PASS web server revealed that all four compounds possess antineoplastic activity, meaning they have the potential to inhibit or prevent the growth of tumors. The probability scores for active antineoplastic properties were higher than the probability scores for inactive properties for each compound (Table 6). This finding underscores the potential of these compounds as effective agents in cancer treatment, particularly in targeting OSCC. The high probability scores further validate the compounds' potential utility in therapeutic applications and warrant further investigation into their efficacy and mechanisms of action.

In this study, we sought to identify and evaluate potential therapeutic compounds from *Desmostachya bipinnata* for OSCC through a multi-step approach. Initially, we identified

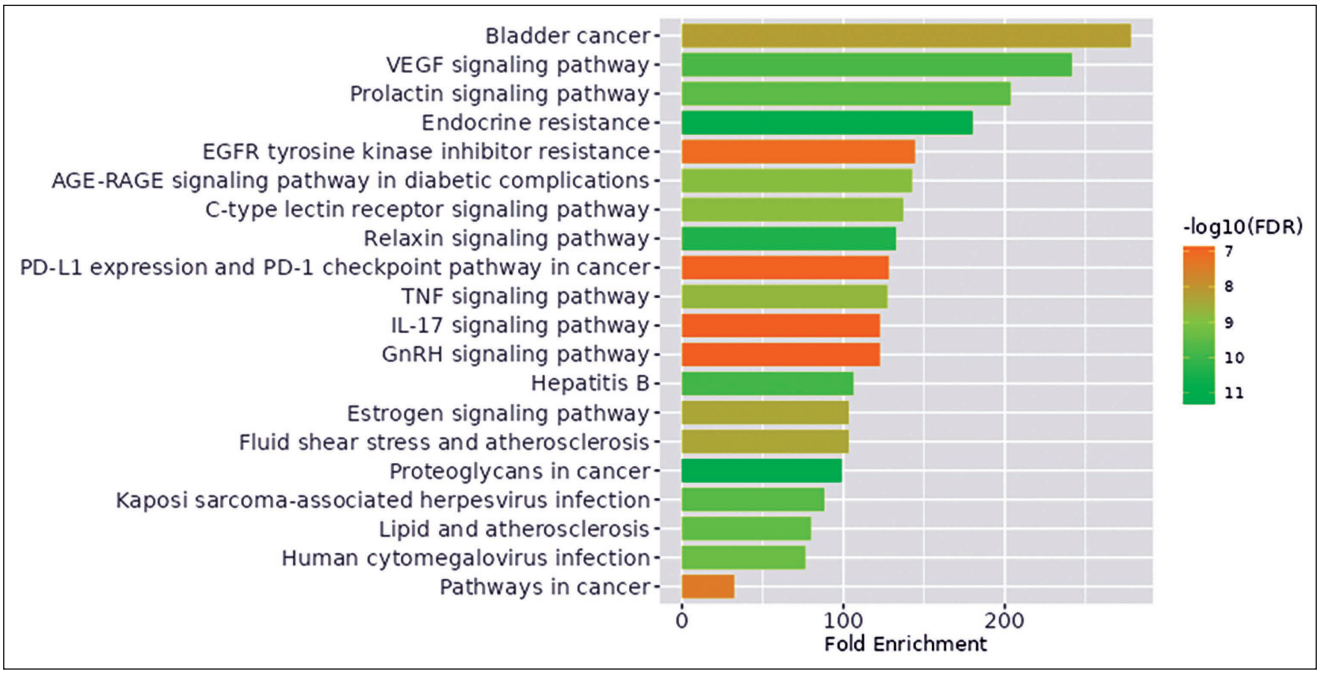

Figure 4. Hub Genes Enrichment in Pathways in Cancer.

Table 3. Gene Compound Targets.

Gene	Compounds
MMP2	Kaempferol
MMP2	Linoleic acid
PTGS2	Linoleic acid
PTGS2	Kaempferol
STAT3	Daucosterol
STAT3	Stigmasterol-glucoside
MAPK1	Linoleic acid
MMP9	Kaempferol
AKT1	Kaempferol

3,278 OSCC-related genes by integrating data from GeneCards, DisGeNet, and GEO databases. Using SwissTargetPrediction, we filtered 221 unique targets for 14 selected compounds and identified 95 common targets with OSCC-related genes. PPI analysis using STRING, Cytoscape, and MCODE highlighted a critical cluster of genes. Subsequent GEPIA analysis led to the exclusion of low-expressing genes (IL6, MAPK3, ESR1, and BCL2), focusing our study on MMP2, PTGS2, STAT3, MAPK1, MMP9, and AKT1, which are involved in cancer-related pathways according to KEGG enrichment analysis via ShinyGO.

Molecular docking studies revealed that the four compounds—linoleic acid, kaempferol, daucosterol, and stigmasterol-glucoside—exhibited strong binding affinities to the six key target proteins MMP2, PTGS2, STAT3, MAPK1, MMP9, and AKT1, with binding affinities comparable to Carboplatin suggesting their potential as effective multitarget agents against OSCC. The interacting amino acids were located in the active sites of the target proteins, indicating potential efficacy. PASS web server predictions confirmed the antineoplastic activity of these compounds. These findings suggest their promise as multitargeting agents for OSCC treatment.

Discussion

The study investigates the potential of compounds derived from *Desmostachya bipinnata* as novel therapeutic agents for OSCC. By employing a comprehensive approach encompassing compound screening, toxicity assessment, and in silico analysis, several key compounds have been identified, showing promising anticancer properties. Notably, linoleic acid, kaempferol, daucosterol, and stigmasterol-glucoside have emerged as significant candidates for further investigation. Utilizing the SwissTargetPrediction tool, these compounds have been mapped to their respective gene targets, elucidating their potential roles in OSCC treatment.

The findings are validated through PPI networks analyzed via the STRING database and visualized using Cytoscape. This network analysis highlights key interactions between the identified compounds and crucial proteins involved in the progression of OSCC. Subsequent gene expression profiles obtained from GEPIA corroborate these interactions, suggesting that these compounds might influence key pathways associated with OSCC.

Table 4. Binding Affinity of the Sample.

Gene	Compounds	Binding Affinity (Kcal/mol)	Interacting Amino Acids
MMP2	Linoleic acid	–6.5	Val198, Pro221, Leu163, His166, Ala167, His205, His211, Ala165, Glu202, His201, Leu197, Tyr223, Leu218, Leu164, Thr227, Thr229, Phe232
	Kaempferol	–8.3	Gly162, Leu163, Ala165, Glu202, Tyr223, Val198, Leu197, Leu218, His201, Ala220, Pro221, Leu164, Ile 222
	Daucosterol	–8.2	Leu163, His166, Ala167, Phe168, Ala169, Gly175, Val174, Ile222, Tyr155, His211, Glu202, Ala165, His201, Tyr223, Leu164, Pro221, Leu164, Gly162
	Stigmasterol-glucoside	–8.4	Ala169, Phe168, Tyr155, His166, Leu163, Gly162, Leu164, Tyr223, Ile222, Pro221, His201, Ala165, Glu202, His211, Ala167, Gly175, Val174
	Carboplatin	–5.4	Leu163, Leu164, Ile222, Pro221, Tyr223, Val198, His201, Ala165, Glu202
PTGS2	Linoleic acid	–7	Lys532, Leu534, Phe529, Leu531, Phe209, Phe205, Val349, Val523, Ala527, Leu352, Phe518, Ser353, Met522, Trp387, Tyr385, Leu384, Tyr348, Phe381, Gly533, Val344
	Kaempferol	–9.5	Val344, Leu531, Phe381, Leu534, Phe209, Phe205, Val228, Gly533, Phe529, Tyr385, Val349, Gly526, Ala527, Trp387, Leu384, Met522, Val523
	Daucosterol	–8.7	Gln405, Tyr409, Tyr404, Ile408, Leu294, Ala443, Val295, Leu391, His388, Gln203, His207, Tyr385, His386, Leu390, Ala202, Ala199, Val447, Trp387, Val444
	Stigmasterol-glucoside	–8.5	Val444, Ile408, Ala413, Tyr404, val447, Leu294, Gln203, His207, Val291, Gln289, Lys211, Glu290, Ile274, Asn222, Lys215, Asp213, Thr212, His214
	Carboplatin	–5.8	Ala202, Ala199, Leu391, His388, Trp387, His386, His207, Tyr385, Leu390, Thr206, Gln203
STAT3	Linoleic acid	–4.4	Gln247, Ile258, Arg325, Pro333, Asp334, ala250, Gly254, Ile252, Gly253, Ser514, Cys251, Gln326, Pro336, Cys328
	Kaempferol	–7.2	Pro333, Arg325, Asn257, Cys259, Ile258, Glu324, Gln247, Gln326, Cys251, Pro336, Cys328
	Daucosterol	–7.5	Lys517, Ser513, Ser514, Pro256, Gly254, Gly253, Pro333, Pro336, Cys328, Arg325, Gln326, Cys251, Ile258, Gln247, Ala250, Asp334, Thr516
	Stigmasterol-glucoside	–8	Thr526, Trp510, Ie522, Asp502, Ala505, Leu525, Glu506, Ser509, Ser513, Gly254, Gly253, Ser514, Pro256, Pro255, Trp510, Ser54
	Carboplatin	–5.3	Ala651, Tyr686, Ser649, Tyr575, Phe650, Leu645, Ile576, Leu579, Leu577, Ala578
MAPK1	Linoleic acid	–5.2	Thr110, Asp111, Lys114, Leu107, Met108, Ile31, Leu156, Ala52, Gln105, Lys54, Cys166, Val39, Gly34, Gly32
	Kaempferol	–8.2	Lys114, Glu109, Met108, Leu107, Gln105, Asp106, Lys54, Cys166, Asp167, Tyr36, Ala35, Val39, Ala52, Leu156, Ile31, Gly32
	Daucosterol	–8.9	Tyr113, Lys114, Glu33, Gly32, Met108, Ile31, Leu107, Leu156, Asp106, Ala52, Ile84, Gln105, Lys54, Ile53, Val39, Gly34, Asp111, Pro152, Lys151, Ser153, Thr190, Tyr193, Trp192
	Stigmasterol-glucoside	–8.3	Thr190, Trp192, Gly34, Val39, Ala52, Leu156, Asp106, Leu107, Met108, Glu109, Thr110, Ile31, Lys114, Gly32, Asp111, Glu33, Tyr193, Ser152, Tyr113, Pro152, Lys151
	Carboplatin	–4.7	Lys151, Thr190, Tyr193, Trp192, Glu220, Pro152, Tyr113, Ser153
MMP9	Linoleic acid	–6.5	Tyr218, Gly186, Leu188, His226, Arg249, Met247, Leu243, Ala242, Leu222, Tyr248, Val223, Ala189, Glu227, Pro246
	Kaempferol	–9.3	Leu187, Gly186, Ala189, Glu227, Val223, His226, Arg249, Leu222, Leu243, Tyr245, Tyr248, Met247, Leu188, Pro246
	Daucosterol	–7.8	Tyr179, Leu187, Tyr248, Leu188, Tyr218, Asp185, Gly186, Met247, His226, Pro246, Glu227, His236, Ala189, His230, Ala191, His190, Phe192
	Stigmasterol-glucoside	–8.2	Pro193, Tyr179, Leu187, Leu188, Tyr248, Asp185, Tyr218, Gly186, Met247, His226, Pro246, His236, His230, Glu227, Ala189, His190, Ala191, Phe192
	Carboplatin	–5.2	Glu227, His236, His226, Pro246, Tyr248, Met247, Tyr245, Leu243, Leu188, Val223
AKT1	Linoleic acid	–6.7	Thr82, Val271, Val270, Tyr272, Thr211, Leu210, Ser205, Trp80, Leu264, Lys268, Asp292, Thr81
	Kaempferol	–9.4	Lys268, Ser205, Tyr263, Thr211, Ile290, Thr291, Leu210, Asp292, Trp80, Leu264, Tyr272, Val270, Val271, Gln79
	Daucosterol	–10.2	Asn53, Val271, Asn54, Gln79, hr82, Val83, Ile84, Cys296, Glu298, Gly294, Asp274, Asn279, Thr272, Val270, Trp80, Leu264, Ser205, Lys268, Val201, Asn204
	Stigmasterol-glucoside	–10.6	Gln59, Leu78, Ser56, Ala58, Gln79, Asn54, Val271, Arg273, Ile84, Thr82, Cys296, Gly294, Gly298, Asp274, Asn279, Asp292, Val270, Tyr272, Lys268, Trp80, Leu264, Asn53
	Carboplatin	–5.7	Leu213, Met227, Thr211, Asp292, Ile290, eu210, Trp80, Thr291, Tyr272, Leu264

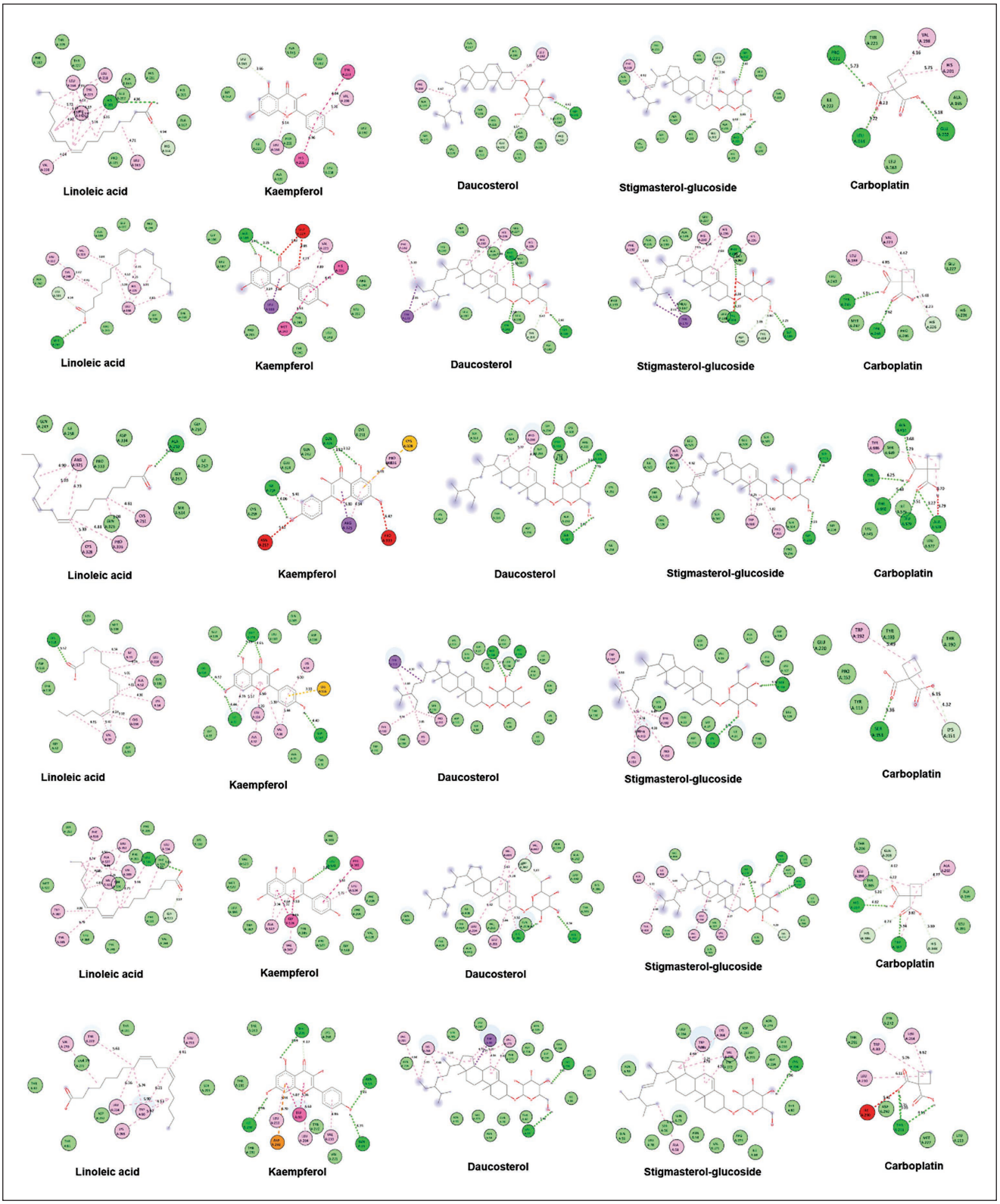

Figure 5. Docked Structure of Compounds and Targets.

Table 5. Details of Target Proteins.

Gene	PDB ID	Protein Name	Grid Box Dimension (XYZ)	Binding Site Amino Acids
MMP2	1QIB	Matrix metalloproteinase-2 (MMP-2)	66.250459 32.972962 20.512490	Asp107, Asp141, His151, Asp153, Asp158, Gly159, Asp161, Leu163, His166, Gly173, Gy175, Asp177, His179, Asp181, Asp182, Glu184, His201, His205, His211,
PTGS2	5f19	Prostaglandin-Endoperoxide Synthase 2	26.712972 34.489706 61.481312	Phe200, Ala202, Gln203, His207, Phe210, Thr212, Asn382, His386, Trp387, His388, Leu390, Leu391, Ile408, Val295
STAT3	6NJS	Signal transducer and activator of transcription 3	1.846983 32.106943 16.638040	Asp173, Tyr176, Lys290, Ser292, Tyr293, Arg609, Ser611, Glu612, Ser613, Thr620, Ser636, Val637, Glu638, Pro639, Tyr640, Gln644, Tyr657, Lys658, Ile659
MAPK1	6G54	MAP kinase ERK2	60.318596 10.363221 5.409584	Arg15, Ser29, Tyr30, Ile31, Glu33, Val39, Ala52, His61, Gln62, Arg67, Arg70, Arg91, Ala92, Gln97, Met98, Lys99, Asp100, Gln105, Asp106, Met108, Glu109, Lys114, Ser122, Asn123, Tyr139, Ser142, Lys151, Ser153, Asn158, Cys166, Asp167, Arg172, Thr190, Arg191, Arg194, His232, Tyr233, Leu234, Asn271, Arg277, Lys285, Asp288, Lys292, Ile302, His310, Pro311, Ala325, Glu326, Lys340
MMP9	4WZV	Matrix metalloproteinase 9	6.390190 10.987731 20.873503	Asp131, Ala146, Ser149, Asp165, Val172, His175, Asp177, Asp182, Gly183, Asp185, Leu187, Leu188, Ala189, His190, Ala191, Gly197, Gln199, Asp201, His203, Asp205, Asp206, Asp207, Glu208, His226, Glu227, His230, Asp235, His236, Leu243, Tyr245, Pro246, Met247, Tyr248, Arg249, Thr251,
AKT1	3O96	RAC-alpha serine/threonine-protein kinase AKT	7.929379 -3.061316 12.748674	Trp80, Ile84, Ser205, Leu210, Thr211, Leu264, Lys268, Tyr272, Ile290, Asp292, Cys296

Table 6. The Activity of the Leads.

Sl. No.	Compounds	Pa	Pi	Activity
1	Linoleic acid	0.225	0.015	Antineoplastic, alkylator
2	Kaempferol	0.791	0.013	Antineoplastic
4	Daucosterol	0.63	0.039	Antineoplastic
5	Stigmasterol-glucoside	0.695	0.027	Antineoplastic

Insights from molecular docking studies provide valuable information on the binding affinities and mechanisms through which these compounds exert their effects. The interaction of linoleic acid, kaempferol, daucosterol, and stigmasterol-glucoside with targeted proteins suggests that these compounds could disrupt critical signaling pathways implicated in OSCC.

Finally, the integration of compound screening, toxicological evaluations, and bioinformatics analyses underscores the potential of *Desmostachya bipinnata* compounds as multitargeting agents for OSCC. These findings lay a promising foundation for further preclinical and clinical investigations, offering the potential to enhance therapeutic strategies for OSCC and improve patient outcomes.

Conclusion

This study underscores the potential of *Desmostachya bipinnata* compounds as multifaceted therapeutic agents in OSCC treatment. The use of advanced in silico methodologies has provided a robust framework for identifying and validating the efficacy of these bioactive compounds. The significant interactions observed in molecular docking studies highlight their potential as multitarget agents, comparable to established chemotherapeutic drugs like carboplatin. The findings of this study suggest that linoleic acid, kaempferol, daucosterol, and stigmasterol-glucoside have significant potential as multitargeting agents against OSCC. Their strong binding affinities to key cancer-related proteins and predicted antineoplastic activities highlight their promise as therapeutic candidates. These findings pave the way for further experimental validation and clinical exploration, offering hope for more effective and less toxic treatments for OSCC.

Abbreviations

OSCC: Oral squamous cell carcinoma; **HNSC:** Head and neck squamous cell carcinoma; **PPI:** Protein–protein interaction; **KEGG:**

Kyoto Encyclopedia of Genes and Genomes; **MCODE:** Molecular Complex Detection; **GEPIA:** Gene Expression Profiling Interactive Analysis; **GEO:** Gene Expression Omnibus; **PASS:** Prediction of Activity Spectra for Substances; **PDB:** Protein Data Bank; **RMSD:** Root mean square deviation; **RCSB:** Research Collaboratory for Structural Bioinformatics; **MMP2:** Matrix metalloproteinase 2; **PTGS2:** Prostaglandin-endoperoxide synthase 2 (also known as cyclooxygenase-2 or COX-2); **STAT3:** Signal transducer and activator of transcription 3; **MAPK1:** Mitogen-activated protein kinase 1 (also known as ERK2 or extracellular signal-regulated kinase 2); **MMP9:** Matrix metalloproteinase 9; **AKT1:** AKT serine/threonine kinase 1; **IL-6:** Interleukin-6.

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Ethical Approval and Informed Consent

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ORCID iD

Nitya Krishnasamy https://orcid.org/0000-0001-6094-1206

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