RESEARCH ARTICLE

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Integrative Network Pharmacology and Experimental Validation of Sesbania grandiflora as a Multi-Targeted Therapeutic Agent Against Oral Squamous Cell Carcinoma (OSCC)

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Abstract

Background: Oral squamous cell carcinoma (OSCC) remains a significant health burden with limited therapeutic options and high mortality. Sesbania grandiflora, a medicinal plant rich in phytochemicals, has been traditionally used for its medicinal properties and is emerging as a potential anticancer agent. **Objective:** This study aimed to investigate the anticancer mechanisms of *S. grandiflora* against OSCC using an integrated approach, combining network pharmacology, molecular docking, ADME profiling, and *in vitro* validation. **Materials and Methods:** Network pharmacology was employed to identify hub genes and pathways associated with *S. grandiflora* bioactives. Molecular docking was performed to evaluate binding interactions of D-glucuronic acid, a major phytoconstituent, with key cancer-related targets. ADME profiling assessed drug-likeness and pharmacokinetic properties. *in vitro* assays, including MTT, flow cytometry, and Western blotting, were conducted on KB oral cancer cells to validate mechanistic insights. **Results:** Key hub genes identified included *AKT1, BCL2, PIK3CA, MTOR*, and *CASP8*, which were enriched in pathways such as the *PI3K–Akt, p53, HIF-1*, and *EGFR*-mediated apoptosis pathways. Molecular docking revealed strong and stable interactions of D-glucuronic acid with target proteins, supporting its multi-targeted activity. ADME analysis indicated favorable pharmacokinetic properties, including high GI absorption, BBB permeability, and minimal CYP450 inhibition. Experimental validation demonstrated significant cytotoxicity (IC_{50}: 250–300 µg/mL), dose-dependent G1-phase cell cycle arrest, downregulation of *BCL-2*, and upregulation of *BAX,* confirming the induction of apoptosis. **Conclusion:** *S. grandiflora* exerts anticancer effects through modulation of *PI3K-AKT-mTOR* and apoptotic pathways. D-glucuronic acid emerges as a promising bioactive compound, supporting further in vivo studies and clinical exploration for OSCC management.

Keywords: *S.grandiflora*, D-glucuronic acid, *PI3K-AKT-mTOR* pathway, Apoptosis, Molecular docking

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Introduction

Oral cancer is a major global health issue and is defined as uncontrolled growth of malignant cells in the oral cavity, including the lips, tongue, cheeks, gums, floor of the mouth, hard and soft palate, and oropharynx [1]. OSCC accounts for >90% of oral cancer cases and generally begins in the epithelial lining. The principal risk factors for oral cancer include tobacco use (both smoked and smokeless), heavy alcohol consumption, HPV infection (particularly HPV-16), and habitual chewing of betel quid and or areca nut, which is especially seen in South and Southeast Asia. Additional contributors include poor oral hygiene, prolonged exposure to ultraviolet radiation (lip cancers), dietary deficiencies, genetic predisposition, and occupational exposure to carcinogens [2]. Clinically, oral cancer often presents as a persistent ulcer, red or white patches (erythroplakia or leukoplakia), a lump, pain, bleeding, or difficulty in swallowing and speaking, often leading to late diagnosis. Globally, oral cancer ranks as the 13th most common cancer, with more than 377,700 new cases and 177,700 deaths annually, according to GLOBOCAN 2020 [3]. Early detection significantly improves prognosis, but most cases are diagnosed at advanced stages, resulting in a global 5-year survival rate of around 50–60%. Treatment involves surgery, radiation, chemotherapy, and in some cases, immunotherapy. With increasing awareness, preventive strategies, and HPV

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vaccination programs, efforts are being made worldwide to reduce incidence and improve patient outcomes [4].

Phytocompounds are bioactive chemical constituents derived from plants that have received considerable interest in recent years for their possible therapeutic effect against various cancers [5]. Agents like curcumin (from turmeric) [6], resveratrol (from grapes) [7], epigallocatechin gallate (from green tea) [8], quercetin [9], and berberine [10] have demonstrated anti-cancer effects through modulation of important molecular pathways that influence the progression of OSCC. Importantly, they tend to have low toxicity compared to conventional chemotherapeutics, making them attractive candidates for long-term use or as adjuvants to reduce side effects and resistance associated with standard treatments [11]. *in vitro* and *in vivo* studies have confirmed the efficacy of several phytocompounds in reducing OSCC cell viability, migration, and tumor volume. Given the growing resistance to traditional chemotherapy and the need for safer, more targeted therapies, phytocompounds represent a vital area of research for the development of novel, plant-based therapeutics against OSCC, highlighting their importance in both preventive and therapeutic oncology.

Sesbania grandiflora, also referred to as agathi or vegetable hummingbird, is a rapidly growing tree that is indigenous to Southeast Asia and is commonly cultivated in tropical areas due to its edible leaves, edible flowers, and medicinal properties [12, 13]. Recently, studies have found anticancer activity in Sesbania grandiflora, which is often attributed to its powerful antioxidant and anti-inflammatory properties. *in vitro* studies have indicated that extract from the leaves and flowers induce cytotoxicity in a number of cancer cell lines, potentially including breast cancer and colon cancer models [14, 15]. For example, methanolic extracts of the leaves have shown cytotoxicity against human breast and colon cancer cell lines, suggesting that they may even prevent the growth of human tumors [16]. Moreover, the action of flavonoids, like quercetin and kaempferol present in *S.grandiflora*, which can quench free radicals and modulate genes that drive the cell cycle and apoptosis, contributes to that potentiality. While studies are in their infancy, this evidence is indicative of the potential of *Sesbania grandiflora* as a natural plant-based resource for initiating plant-derived drug development for cancer treatment [17]. But still, in order to establish its anticancer efficacy and therapeutic safety in humans, further molecular studies and clinical trials are necessary. Fifteen core genes, including *AKT1*, *BCL2*, *MTOR*, *PIK3CA*, and *CASP8*, were identified and linked to key cancer pathways like *PI3K-AKT*, *p53*, and apoptosis. Molecular docking confirmed strong binding of D-glucuronic acid, a primary compound, with these targets. ADME analysis revealed favorable drug-likeness, high GI absorption, and no interaction with major CYP450 enzymes. *in vitro*, the extract induced G1-phase arrest and significantly reduced KB cell viability in a dose-dependent manner, with an IC_{50} between 250–300 µg/mL. Western blotting showed decreased *BCL-2* and increased *BAX* expression, indicating apoptosis induction. These findings suggest that *S. grandiflora*, particularly D-glucuronic acid, holds promise as a natural therapeutic agent against OSCC, warranting further clinical validation.

Materials and Methods

Pharmacological network construction

The drug-protein interaction network is examined using CTD, as well as the STITCH database, an online tool for studying drug-protein interactions (http://stitch.embl.de/). In the established PPI network, the edges connecting the proteins are represented with a width proportional to the combined score, which describes the strength of interactions between the proteins, as achieved by the cytohubba-cytoscape plugins [18].

Gene Ontology and enriched pathway analysis

To conduct this analysis, we utilised the g:Profiler database, accessible at https://biit.cs.ut.ee/gprofiler/. In addition, KEGG pathway analyses were performed to detect those pathways that showed significant enrichment with the DEGs identified in oral cancer [19].

Molecular docking

Using the molecular docking software PyRx, we examined the binding interactions of a compound with target proteins of interest. Post-docking analysis was performed to identify and characterize significant poses of binding for the compound with the apoptosis regulating target proteins. Next, the binding affinities of ligand to receptors were evaluated to explore the binding mode. The ligand-protein complexes 3D structures from the docking simulations were viewed and analyzed with BIOVIA Discovery Studio to provide a better understanding of the molecular interactions and binding conformations. This approach lends itself to our understanding of how compounds may modulate apoptotic pathways with specific protein target interactions [20].

Cell culture and cell viability

The human oral cell line KB cells were sourced from NCCS, Pune, and were passaged and maintained in a CO_2 incubator in the presence of 10% FBS, 1% penicillin-streptomycin antibiotics, and DMEM media, Himedia. To evaluate the cytotoxic effects of compound on KB cell line, MTT assay was used as described previously [21]. Following the overnight incubation, the MTT reagent was added to the cell culture, and formazan crystals were dissolved in DMSO from which the absorbance was measured at 590nm.

Flow cytometry

Flow cytometry was utilized to study the distribution of cell cycle stages based on cellular DNA content as previously reported [22]. KB cells were seeded at a density of 1x106 cells per well onto six-well plates, and were allowed to adhere overnight. After the previously defined treatment times, cells were removed and fixed overnight in 70% ice-cold ethanol to preserve cellular DNA integrity prior to analysis. After RNase A treatment (10 mg/mL) fixed cells were exposed to propidium iodide (PI) dye to stain cellular nuclei. For optimal staining, cells were incubated for 30 min at room temperature (dark). . Using

a flow cytometer (BD FACS Calibur, Becton Dickinson, USA), the fluorescence that the PI-labeled nuclei produced was quantified

Protein expression by Western blot

The expression of *BAX* and *BCL2* proteins in KB cells was analyzed following the method of Jayaram et al. Briefly, KB cells (5×10^6) were cultured, harvested, and lysed using RIPA buffer. Protein concentration was measured by the Bradford assay, and equal amounts of protein were separated by SDS-PAGE and transferred to a PVDF membrane. After blocking with 2% blocking solution for 1 hour, membranes were incubated overnight with primary antibodies against *BAX* and *BCL2* (1:1000 dilution). Protein bands were visualized using enhanced chemiluminescence (ECL) and quantified using the Quantity One system (Bio-Rad, USA) [23].

Statistical analysis

For analysis of the study's data, we used the R programming language, which is well-known for statistical computing. The student's t-test, was utilized. Additionally, the log-rank test and one-way ANOVA was used to compute p-values for the analysis of mRNA expressions. Statistical significance at *p<0.05, **p<0.001, and ***p<0.0001.

Results

Networking pharmacology

The figure presents a comprehensive network pharmacology and enrichment analysis of targets associated with *Sesbania grandiflora* (*S. grandiflora*) bioactivity. The Venn diagram (top left) reveals 15 overlapping genes common between the CTD and GeneCards databases, indicating potential core targets for the extract. The protein-protein interaction (PPI) network (top center) and its hub gene map (top right) show strong interconnectivity among key targets, suggesting functional collaboration, with major hub genes such as *AKT1*, *BCL2*, *PIK3CA*, *MTOR*, and *CASP8* highlighted for their central roles. These are well-known regulators of apoptosis, survival, and cancer signaling pathways. The functional enrichment analysis (bottom left) identifies significant GO terms, including regulation of apoptotic process, response to chemical stress, and EGFR signaling. Cellular components include mitochondrial intermembrane space and death-inducing signaling complex, suggesting involvement in intrinsic apoptosis. Molecular function terms highlight kinase and protease binding. The KEGG pathway enrichment analysis (bottom right) further validates these findings, with top-ranked pathways being *PI3K-AKT*, apoptosis, HIF-1, and *p53* signaling all critical in cancer progression and cell survival. Collectively, these data suggest that *S. grandiflora* may exert its anticancer effects by modulating apoptosis, cell signaling, and stress response through a network of interconnected pathways and core regulatory genes.

Molecular docking

The molecular docking analysis illustrates the binding interactions of a key bioactive compound from *Sesbania grandiflora* (D-Glucuronic acid) with five crucial target proteins involved in oral cancer signaling: *AKT1*, *BCL2*, *CASP8*, *MTOR*, and *PI3K*. The docked complexes reveal stable binding conformations (Figure 2). For *AKT1*, the ligand forms conventional hydrogen bonds with residues such as *SER204, ASN204*, and *THR292,* suggesting strong stabilization within the active site. In *BCL2*, significant hydrogen bonding with residues like GLU159 and LYS226 indicates disruption of anti-apoptotic function. *CASP8* interaction reveals critical bonding with THR317 and PHE319, potentially activating apoptotic signaling. The *MTOR*-ligand complex demonstrates hydrogen bonding with residues such as TYR334, LEU400, and THR467, implicating inhibition of cell growth and proliferation pathways. PI3K binding shows strong interactions with ARG886, ASP859, and VAL860, essential for blocking

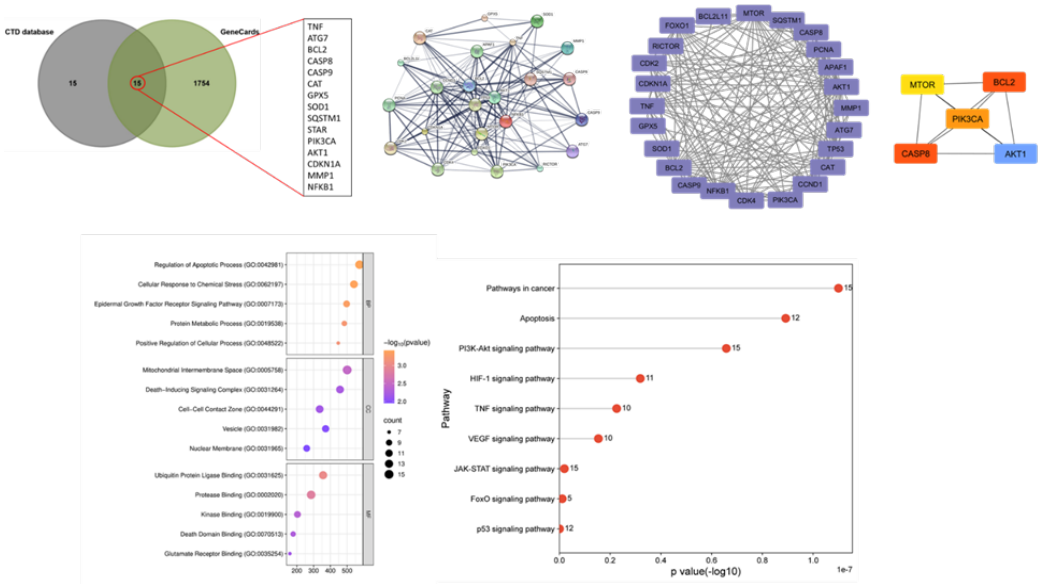

Figure 1.Comprehensive network pharmacology and enrichment analysis of targets associated with *S. grandiflora* bioactivity

PI3K/AKT pathway signaling. These docking results support the compound's multi-targeted binding potential, with strong molecular interactions across anti-apoptotic, pro-apoptotic, and proliferative regulatory proteins. Collectively, the findings provide mechanistic insights into how *S. grandiflora* may exert anticancer effects by simultaneously modulating multiple oncogenic pathways, especially through the *PI3K-AKT-MTOR* axis and apoptosis regulation.

Pharmacokinetic-ADME for

The ADME (Absorption, Distribution, Metabolism, and Excretion) profiling of the selected bioactive compound from *Sesbania grandiflora* reveals favorable pharmacokinetic properties supportive of drug-likeness. According to IMPAAT database, *Sesbania grandiflora* shows 3 pre-dominant potential bioactive compounds (D-glucuronic acid, Oleanolic acid, and Linoleic acid). Among them, D-glucuronic acid shows zero violations of lipinski's rule and shows good TPSA score. The compound shows high gastrointestinal (GI) absorption, indicating efficient oral bioavailability (Table 1). It is also blood-brain barrier (BBB) permeant, suggesting potential activity within the central nervous system (CNS), although this may raise considerations regarding off-target effects in CNS-related tissues The compound is not a substrate for P-glycoprotein (P-gp), indicating a reduced likelihood of being actively effluxed out of cells, which may enhance its intracellular retention and therapeutic efficacy. Additionally, the compound shows no inhibitory effects on major cytochrome P450 (CYP450) isoenzymes such as *CYP1A2, CYP2C19, CYP2C9, CYP2D6*, and *CYP3A4.* This suggests a low risk of drug-drug interactions and metabolic complications, which is desirable for safety and compatibility in polypharmacy settings. Collectively, these pharmacokinetic parameters suggest that the compound from *S. grandiflora* has promising drug-like characteristics, including high

Table 1. Pharmacokinetic-ADME

Molecule	D-Glucuronic acid	Oleanolic acid	Linoleic acid
Canonical SMILES	OC1O[C@H](C(=O)O)[C@H]([C@@H]([C@H]1O)O)O	O[C@H]1CC[C@]2([C@H](C1(C)C)CC[C@@]1([C@@H]2CC=C2[C@@]1(C)CC[C@@]1([C@H]2CC(C)(C)CC1)C(=O)O)C)C	CCCCC/C=C\C/C=C\CCCCCCCC(=O)O
Formula	C6H10O7	C30H48O3	C18H32O2
MW	194.14	456.7	280.45
#Heavy atoms	13	33	20
#Aromatic heavy atoms	0	0	0
Fraction Csp3	0.83	0.9	0.72
#Rotatable bonds	1	1	14
#H-bond acceptors	7	3	2
#H-bond donors	5	2	1
MR	36.35	136.65	89.46
TPSA	127.45	57.53	37.3
iLOGP	-1.17	3.94	
XLOGP3	-2.34	7.49	
Ali Log S	0.2	-8.53	
Ali Solubility (mg/ml)	3.08E+02	1.34E-06	
Ali Solubility (mol/l)	1.59E+00	2.94E-09	
Ali Class	Highly soluble	Poorly soluble	
Silicos-IT LogSw	3.07	-6.12	
CYP2C9 inhibitor	No	No	
CYP2D6 inhibitor	No	No	
CYP3A4 inhibitor	No	No	
log Kp (cm/s)	-9.15	-3.77	
Lipinski #violations	0	1	
Ghose #violations	2	3	
Veber #violations	0	0	
Egan #violations	0	1	
Muegge #violations	2	1	
Bioavailability Score	0.56	0.85	
PAINS #alerts	0	0	
Brenk #alerts	0	1	
Leadlikeness #violations	1	2	
Synthetic Accessibility	3.94	6.08	

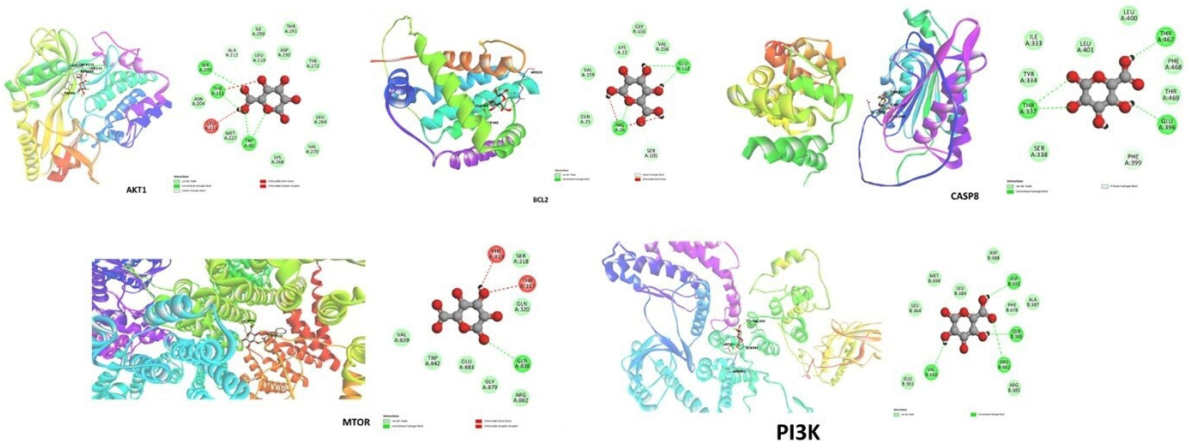

Figure 2. Molecular Docking Analysis of *S. grandiflora* with *AKT1, BCL2, CASP8, MTOR,* and *PI3K*

absorption, BBB permeability, metabolic stability, and minimal interaction with key metabolic enzymes or efflux transporters. D-glucuronic acid was selected for further studies and experiments. These attributes strengthen its candidacy for further development as a therapeutic

Plant extract inhibits cell growth in KB cells

MTT assay was conducted to assess extract's effect on KB cells in relation to oral cancer. The results of this were shown in Figure 3, which showed a statistically significant dose dependent decrease of cell viability in KB cells with exposure to plant extract over time. The IC_{50} concentration

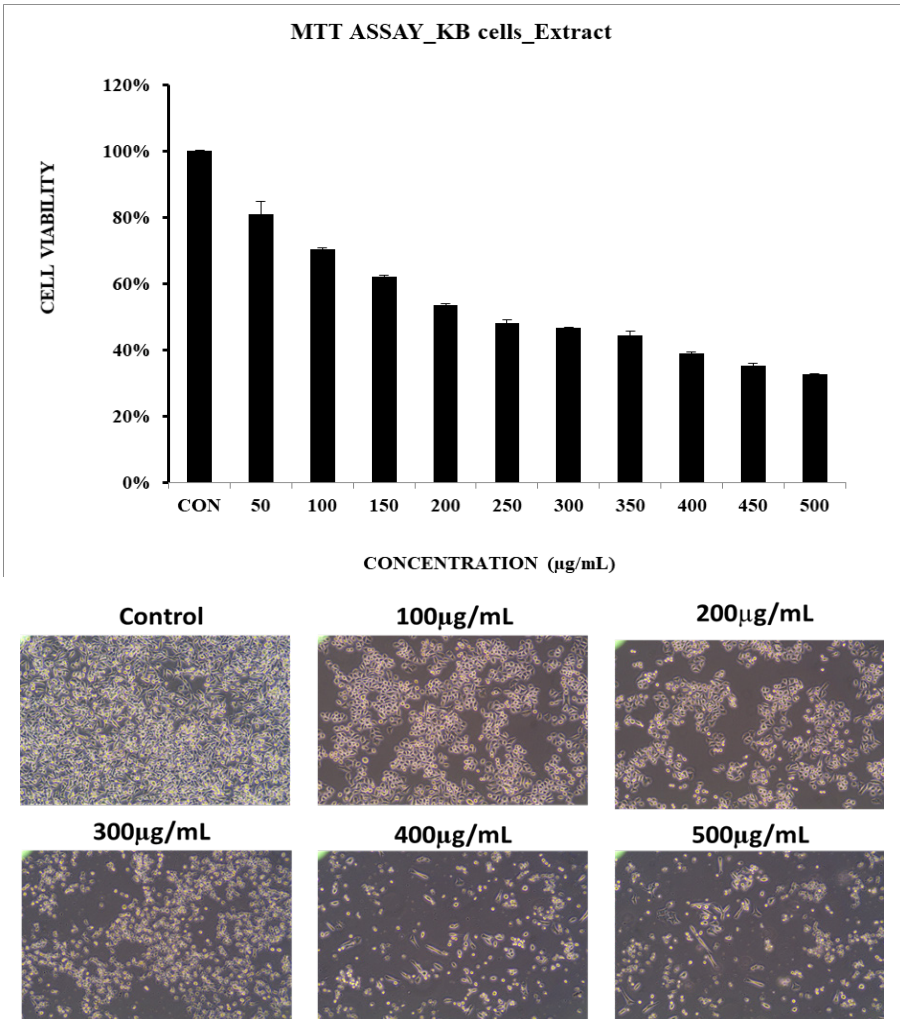

Figure 3. Inhibition of Cell Growth by Plant Extract in KB Cells. A. MTT assay for cell viability shows the increasing concentration of plant extract (50-500 µg/mL) for 48 hr intervals in KB cells. B. KB cells were exposed plant extract for increasing concentration (0, 100, 200, 300, 400, and 500µg/mL) for 48h. Morphology of KB cells were visualized (20X).

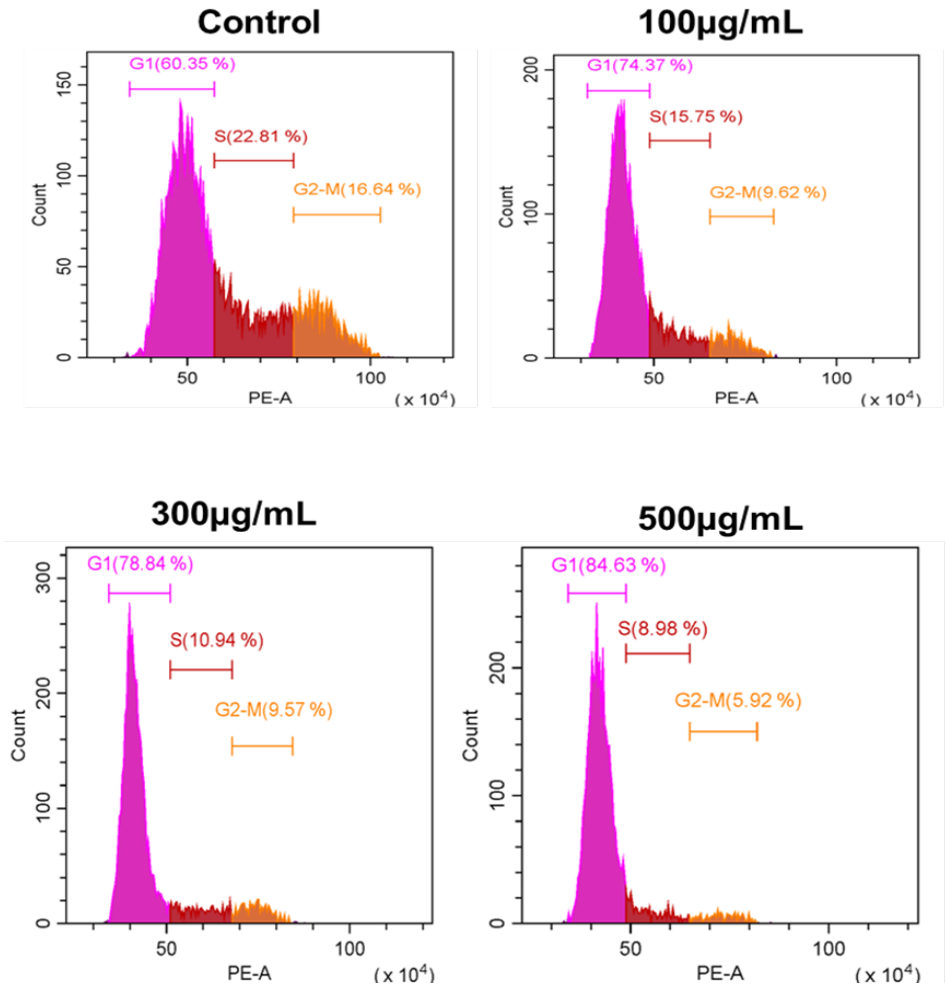

Figure 4. Cell Cycle Analysis by Treating *s. grandiflora* in KB Cells.

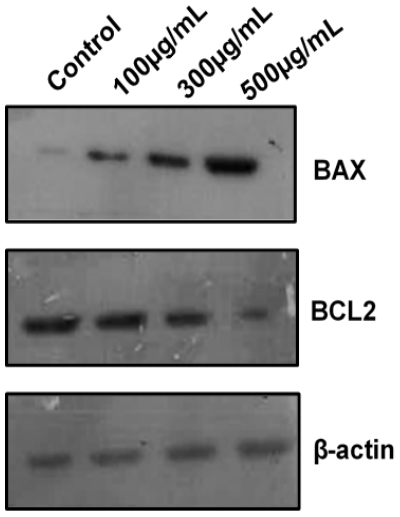

Figure 5. Western Blot Analysis by Treating *s. grandiflora* in KB cells.

of extract shows 221.58µg/mL. Furthermore, it was also assessed the effect of different concentrations of plant extract for 100, 200, 300, 400, and 500 µg/mL for 48 hours in KB cells which showed significant cellular damage and cell blebbing in KB cells, as shown in Figure 1B. Overall, this data, highlights the potent cytotoxic effects of plant extract on KB cells and its potential in oral cancer therapy.

Flow cytometry

The flow cytometry histograms (Figure 4) depict the distribution of cell cycle phases (G1, S, G2-M) in response to treatment with *S. grandiflora* extract. Following *S. grandiflora* extract treatment at increasing concentrations (top right, bottom left, and bottom right), there is a progressive accumulation of cells in the G1 phase and a marked decrease in both S and G2-M phase populations. Specifically, at the highest concentration of *S. grandiflora* extract (bottom right), 84.63% of cells are arrested in the G1 phase, while the S and G2-M phases drop to 8.98% and 5.92%, respectively. This dose-dependent G1-phase arrest demonstrates that *S. grandiflora* extract effectively halts cell cycle progression, likely through the inhibition of glycolysis, thereby impeding DNA synthesis and mitotic entry. The observed reduction in S and G2-M populations supports the conclusion that *S. grandiflora* extract suppresses cellular proliferation, contributing to its anticancer potential by inducing cytostatic effects.

Protein expression by Western blot

The results of Western blot analysis demonstrate that *Sesbania grandiflora* extract has a dose-dependent effect

on the expression of *BCL-2* and *BAX* proteins in the treated cells (Figure 5). The *BCL-2* protein level decreased with increasing extract doses, suggesting that *S. grandiflora* downregulates anti apoptotic signalling . By contrast, *BAX* expression showed consistent increase. This shift in the BCL-2/*BAX* ratio suggests the induction of apoptosis. β-actin, used as a loading control, shows consistent expression across all samples, confirming equal protein loading and validating the observed expression changes. This study indicates that *S. grandiflora* extract shows proven potential as an anti-cancer treatment by inducing apoptotic pathways.

Discussion

The current study provides a detailed analysis of the anticancer efficacy of Sesbania grandiflora, focusing on Oral Squamous Cell Carcinoma (OSCC), through a combined approach that includes network pharmacology, molecular docking studies, ADME profiling, and experimental validation using KB oral cancer cells. For example, [24] reported that the ethanolic leaf extract of *S. grandiflora* exhibited potent antioxidant and hepatoprotective activities, achieved through the reduction of oxidative stress and DNA damage. The occurrence of flavonoids, saponins, and tannins that contribute to the anti-inflammatory and cytotoxic efficacy of the plant has also been substantiated [25]. Despite these contributions toward potential utilization of *S. grandiflora* as a treatment, the specific mechanisms at the molecular level, within an OSCC framework, has not been explored thoroughly which is aimed to be done here.

The network pharmacology analysis revealed 15 common genes shared between the CTD and GeneCards databases, indicating that the phytochemicals of *S. grandiflora* may exert targeted effects on cancer-associated molecular pathways. Several of the identified hub genes, including *AKT1*, *BCL2*, *CASP8*, *PIK3CA*, and *MTOR*, are well-known regulators of key cellular processes such as survival, proliferation, and apoptosis. These results are consistent with earlier reports [26] highlighting the pivotal role of the *PI3K–AKT* signaling pathway in oncogenic transformation, particularly in epithelial malignancies such as oral squamous cell carcinoma (OSCC).

Further support for this mechanistic association was provided by functional enrichment analysis, which identified Gene Ontology terms related to apoptosis, cellular responses to chemical stress, and EGFR signaling, along with KEGG pathways encompassing *PI3K–AKT*, *HIF-1, p53,* and apoptosis signaling cascades. Collectively, these pathways are critically implicated in OSCC initiation and progression. In agreement with these findings, previous studies [27] have documented frequent dysregulation of *p53* and *AKT* signaling in oral and head and neck cancers, contributing to uncontrolled cell proliferation and enhanced resistance to apoptosis.

Molecular docking analysis involving the D-glucuronic acid, one of the significant bioactive components identified from the IMPPAT database, indicated strong and stable interactions with all five targets of interest. The interactions with *AKT1* involved residues such as SER204 and THR292, which imply an inhibition of kinase activity and downstream signaling. Binding to *BCL2* and *CASP8* suggests modulation of the intrinsic apoptotic pathway, confirming that D-glucuronic acid has potential direct action on key components involved in apoptosis [28]. Moreover, ADME profiling of D-glucuronic acid revealed high gastrointestinal absorption, BBB permeability, and no inhibition of major cytochrome P450 enzymes, indicating favorable pharmacokinetics and minimal risk for drug-drug interactions. These characteristics are crucial for the development of effective oral therapeutics, especially for chronic diseases like cancer where combination therapy is often employed. In contrast, many synthetic chemotherapeutics suffer from poor ADME properties, leading to systemic toxicity and off-target effects [29].

The *in vitro* findings provide a crucial layer of experimental validation for the computational analyses. Consistent with these predictions, the MTT assay demonstrated that the extract exerts pronounced cytotoxic effects in a concentration-dependent manner. The estimated IC_{50} value, ranging between 221.58 µg/mL, indicates moderate to strong cytotoxic potency, aligning well with earlier reports [30] that documented comparable IC_{50} values for plant-derived flavonoids in hepatocellular carcinoma models. Moreover, the minimal variability in absorbance measurements underscores the reliability and reproducibility of the experimental outcomes. Collectively, these results contribute to a clearer understanding of the extract's potential as an anti–oral cancer agent.

Flow cytometric analysis further revealed a marked induction of G1-phase cell cycle arrest, with the highest extract concentration resulting in 84.63% of cells accumulating in the G1 phase, accompanied by a substantial reduction in the S and G2/M populations. This pattern reflects effective inhibition of cell cycle progression prior to DNA synthesis, a well-recognized anticancer mechanism. Comparable G1-phase arrest has been previously reported in OSCC cells treated with natural flavonoids [31], thereby reinforcing the biological significance and consistency of the present findings.

Western blot analysis showed dose-dependent decreased *BCL2* expression and increased *BAX* expression, demonstrating a shift in the *BCL2*/*BAX* ratio towards apoptosis. This is similar to the studies [32] which indicated that natural extracts that induced this shift in protein expression led to mitochondrial-mediated apoptosis in oral cancer cells. The findings of the current study provide verification of the extract's apoptotic effects in the experimental setting and complement the earlier docking and pathway enrichment analysis.

The current study not only confirms earlier reports of *S. grandiflora*'s medicinal properties but also expands on them by systematically dissecting the molecular underpinnings of its anticancer activity. Identifying and validating D-glucuronic acid as a multi-targeted compound that also has beneficial ADME properties further support the therapeutic value of this plant.

Future *in vivo* investigations are essential to validate the therapeutic efficacy and safety of *Sesbania grandiflora* extract and D-glucuronic acid in physiologically relevant to OSCC models. Well-established animal models, such as

4-NQO–induced oral carcinogenesis or OSCC xenograft mouse models, should be employed to assess tumor growth inhibition, biodistribution, pharmacokinetics, and systemic toxicity. These studies will help confirm whether the molecular effects observed *in vitro* such as G1-phase arrest and apoptosis induction are reproducible within a complex tumor microenvironment. Additionally, evaluating immunomodulatory effects and angiogenesis-related changes will further clarify therapeutic mechanisms.

Moreover, Standard OSCC management currently relies on surgery, radiotherapy, and chemotherapy, often using agents like cisplatin or 5-fluorouracil, which are associated with significant toxicity and treatment resistance. In this context, *S. grandiflora*–derived compounds could be explored as adjuvant or combination therapies to enhance treatment efficacy while reducing adverse effects. Ultimately, successful *in vivo* validation would pave the way for translational and clinical studies.

In conclusion, this study presents a comprehensive investigation of *Sesbania grandiflora* and its key bioactive compound, D-glucuronic acid, highlighting their promising therapeutic potential against oral squamous cell carcinoma. Using an integrative and coordinated approach that included network pharmacology, molecular docking and scoring, ADME profiling, and experimental assays, the extract was predicted to target cancer relevant proteins including for example products encoded by *AKT1*, *BCL2*, *PIK3CA*, *MTOR*, and *CASP8*, which are all implicated in the regulation of apoptosis and cell survival. Docking simulations demonstrated strong binding interactions of D-glucuronic acid with these targets, while pharmacokinetic profiling confirmed favorable drug-like properties. *in vitro* experiments corroborated these findings, with flow cytometry showing G1-phase arrest, MTT assays indicating dose-dependent cytotoxicity (IC_{50}: 250–300 µg/mL), and Western blotting revealing pro-apoptotic protein modulation. Collectively, these results provide strong evidence for the multi-targeted anticancer activity of *S. grandiflora*,the key molecule being D- gucuronic acid supporting its advancement as a plant-based therapeutic for OSCC. Further *in vivo* studies and clinical evaluations are warranted to translate these preclinical findings into clinical applications.

Author Contribution Statement

Reyana Begum: Study Design and Concept, Data collection, Data Analysis, Manuscript Drafting, Formatting and Proofreading. Gheena S: Study Design and Concept, Data collection, Data Analysis, Formatting, Critical Review and Surveillance.

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Data Availability Statement

The datasets generated and/or analyzed during the current study are available in the manuscript.

Ethics Approval Statement

Ethical approval for this study was obtained from the Institutional Ethics Committee

Conflict of Interest Disclosure

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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