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# Dual antidiabetic and anticancer potential of *Melia dubia* seed extract: An integrated *in silico* and *in vitro* study

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**ABSTRACT**

**Introduction:** *Melia dubia* seeds are traditionally used against diabetes mellitus and cancer. Molecular docking studies were performed to evaluate the binding affinity of major compounds against α-glucosidase and the mechanistic target of rapamycin (mTOR), a key regulator of cell growth and proliferation.

**Methods:** Phytoconstituents of the alcoholic seed extract were analyzed using network pharmacology to identify key molecular targets along with signaling pathways involved in diabetes and cancer. Molecular docking studies were performed to identify the binding affinity for major compounds against α-glucosidase and mTOR, which regulates cell division and proliferation. In vitro antidiabetic activity was assessed using an α-glucosidase inhibition assay, while anticancer activity was evaluated through a cytotoxicity assay using the MTT method.

**Results:** Network pharmacology analysis revealed that the phytoconstituents modulate critical pathways, consisting of phosphoinositide 3-kinase–Akt, adenosine monophosphate-activated protein kinase, nuclear factor kappa-B, vascular endothelial growth factor, and insulin signaling pathways. Molecular docking demonstrated strong binding affinities of compounds such as 2-phenylanthraquinone, 2,2-dimethylpropyl, and quebrachamine with α-glucosidase and the mTOR. The extract exhibited significant α-glucosidase inhibition with an $IC_{50}$ value of 33.59 µg/mL, against 28.11 µg/mL for Acarbose. A cytotoxicity assay showed dose-dependent cancer cell inhibition with an $IC_{50}$ of 31.82 µg/mL, compared to 20.41 µg/mL for cisplatin.

**Conclusion:** The findings may support the dual antidiabetic and anticancer potential of the alcoholic extract of *M. dubia* seeds. The integrated *in silico* and *in vitro* results suggest a promising natural therapeutic candidate requiring further validation.

*Implication for health policy/practice/research/medical education:*
This study supports *Melia dubia* as a promising multitarget natural candidate for diabetes and cancer, encouraging further translational research and integration of evidence-based phytomedicine and computational–experimental approaches into healthcare practice and education.

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## Introduction

Cancer and diabetes mellitus are two of the biggest worldwide health issues of the twenty-first century, with rising rates and socioeconomic costs. According to estimates from the International Diabetes Federation (IDF), 537 million people (20–79 years old) globally had diabetes in 2021. This figure is predicted to climb to 643 million by 2030 and then to 783 million by the end of 2045 (1). Similarly, according to GLOBOCAN data, there were almost 19.3 million new cases and 10 million cancer-related deaths in 2020 alone, making cancer one of the leading causes of death worldwide (2). Both diseases share overlapping mechanisms involving chronic inflammation, oxidative stress, immune dysregulation, and activation of key signaling pathways such as PI3K-Akt, NF-κB, MAPK, and mechanistic target of rapamycin (mTOR) (3,4). mTOR

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is a major regulator of cell growth, proliferation, and metabolism, and its dysregulation is strongly implicated in cancer and metabolic disorders. Notably, mTOR is a validated therapeutic target, with inhibitors such as rapamycin widely used in anticancer research (4).

While conventional therapies such as insulin analogs, α-glucosidase inhibitors, and chemotherapeutic agents such as cisplatin have improved disease outcomes, they are often associated with side effects, limited bioavailability, and high costs (5). This has driven the search for plant-based therapeutics that are effective, affordable, and safer alternatives. Medicinal plants, particularly those used in traditional medicine, offer a prominent reservoir for bioactive compounds with multitarget actions against both metabolic and neoplastic disorders (6).

*Melia dubia* Cav. (family: Meliaceae) is a quickly growing deciduous tree that originates from tropical Asia and has been historically employed in traditional medicine to address a variety of health issues, including inflammation, infections, and metabolic disorders (7). Previous studies have reported that bark and leaf extracts of *M. dubia* exhibit antidiabetic, antioxidant, and cytotoxic properties, mainly due to their rich content of limonoids, alkaloids, and triterpenoids (8,9). However, the seeds of *M. dubia* remain largely unexplored, despite their potential to harbor pharmacologically active metabolites.

Recent advancements in network pharmacology and molecular docking allow the prediction of phytochemical–target interactions and biological pathway enrichment, offering a robust platform for drug discovery (10,11). When integrated with *in vitro* assays such as α-glucosidase inhibition and MTT cytotoxicity, computational approaches provide supportive evidence for assessing the antidiabetic and anticancer potential of plant extracts.

Although previous studies have reported biological activities of *M. dubia* seeds, including antifeedant, antibacterial, and quorum-sensing inhibitory effects (12,13), comprehensive evaluations combining computational and experimental methods for dual antidiabetic and anticancer potential remain limited. Therefore, using a comprehensive approach that encompassed network pharmacology, molecular docking, and *in vitro* tests, the goal of this study was to investigate the combined antidiabetic and anticancer properties of the alcoholic extract of *M. dubia* seeds.

## Materials and Methods

### Seed collection and authentication

The seed samples were authenticated by the Central Ayurveda Research Institute, Bengaluru (Ministry of AYUSH, Government of India). It was authenticated as *M. Dubia* Cav. (Family: Meliaceae) with herbarium number RRCB1-mus606, authentication number SMPU/CARI/BNG/2024-25. Seeds of *M. dubia* were collected from a farm located in Shivamogga district, Karnataka state. The collected seeds were properly cleaned, the pulp was manually removed, and the seeds were dried in the shade.

### Solvent extraction

The *M. dubia* seed powder was subjected to solvent extraction with 95% ethanol. The total quantity of the powder used was 250 grams, and it was placed in the Soxhlet extractor for approximately 20 hours. These extracts were further concentrated using a rotary evaporator. This yielded solvent-free extracts, which were subsequently weighed and stored at 5-6 °C (14).

### Network pharmacology

#### *Identification of active compounds*

The compounds selected in this study were obtained through literature review and database mining approaches, and were not confirmed by direct phytochemical characterization of the specific extract used in this study (15,16), and cross-referenced with TCMSP, PubChem, and SwissADME databases to assess drug-likeness and ADME (Absorption, Distribution, Metabolism, and Excretion) properties.

#### *Target prediction*

The potential targets of the obtained compounds were predicted by SwissTargetPrediction and SEA (Similarity Ensemble Approach). The targets were validated using STRING and GeneCards databases.

#### *Construction of protein-protein interaction (PPI) network*

The PPI network was constructed using STRING to show the interactions among the target proteins. Cytoscape v3.9.0 software was used for the visualization of the network. Hub genes were identified using network topology.

### Molecular docking

#### *Protein structure preparation*

The 4JT6 protein (α-glucosidase) and 2IUI protein (mTOR) structures were obtained from the Protein Data Bank (RCSB PDB) and imported into Maestro for processing using the Protein Preparation Wizard. The PDB structure contained missing information regarding connectivity, bond orders, and formal charges, which were corrected during preprocessing. The wizard's "display hydrogen polar only" option was enabled to visualize only polar hydrogen atoms, ensuring accurate representation of hydrogen bonding interactions.

#### *Pre-processing of the protein structure*

The pre-processing involved assigning bond orders, adding hydrogens, removing water molecules, and assigning missing loops in the protein structure.

#### *Ligand structure preparation*

Ligand structures were generated and optimized using LigPrep. The input ligands, provided in 2D (SDF format)

or 3D (Maestro format), were converted into high-quality, all-atom 3D structures. LigPrep was used to generate tautomer and ionization states while optimizing ligand geometry using the OPLS_2005 force field to ensure accurate molecular conformations (17).

### *In vitro* studies

#### *Inhibitory action of α-glucosidase*

A standardized *in vitro* assay approach was used to assess the *M. dubia* seed extract's α-glucosidase inhibitory activity (18). In short, 50 µL of α-glucosidase (1 U/mL) from yeast (SRL, Bangalore, India) was dissolved in phosphate buffer (50 mM, pH 6.9) and pre-treated with different sample concentrations (0-100 µg/mL) separately for 10 minutes at 37 °C. 50 µL of 5 mM p-nitrophenyl-α-D glucopyranoside was added to the phosphate buffer to start the reaction. For thirty minutes, the enzyme reaction was conducted at 37 °C. $Na_2CO_3$ (1 M) was added to stop the reaction, and absorbance was measured at 405 nm. The formula used to determine the percentage of inhibition was (OD of blank - OD of test/OD of Blank) × 100. All experiments were performed in triplicate (n = 3), and the results were expressed as mean ± standard deviation.

#### *Cytotoxicity activity by MTT assay*

The human breast cancer cell line MCF-7 was acquired from NCCS, Pune, and cultivated in DMEM media supplemented with 10% fetal bovine serum, 2 mM L-glutamine, antibiotics (penicillin-streptomycin), and incubated at 37 °C in a humidified environment with 5% $CO_2$.

Cytotoxicity of the seed extract of *M. dubia* was evaluated by MTT assay. The cells were seeded at a density of $1 \times 10^5$ cells per well in 96-well plates and incubated for 48 hours after treatment with varying concentrations of the extract. After that, 100 µL of MTT reagent was added, dissolved in DMSO, and incubated for four hours. The absorbance was measured at 590 nm, and the dose-response curve was used to get the $IC_{50}$ value (19).

### Statistical analysis

The analysis of the data included one-way ANOVA, after which Tukey's post-hoc test was performed ($P < 0.05$ was taken as significant). In case of network analysis, enrichment scores were determined based on the hypergeometric test with Benjamini-Hochberg adjustment (false discovery rate [FDR] < 0.05). All experimental data are presented as means ± SD (n=3); statistical significance was indicated for $P < 0.05$.

## Results

The constructed network highlighted a dense interaction pattern between the identified phytoconstituents and multiple protein targets, reflecting a systems-level mode of action as depicted in Figure 1. Hub proteins such as AKT1, AKT2, PIK3R1, mTOR, MAPK1, and GSK3B exhibited higher degree values, indicating their central regulatory roles within the network. Pathway enrichment

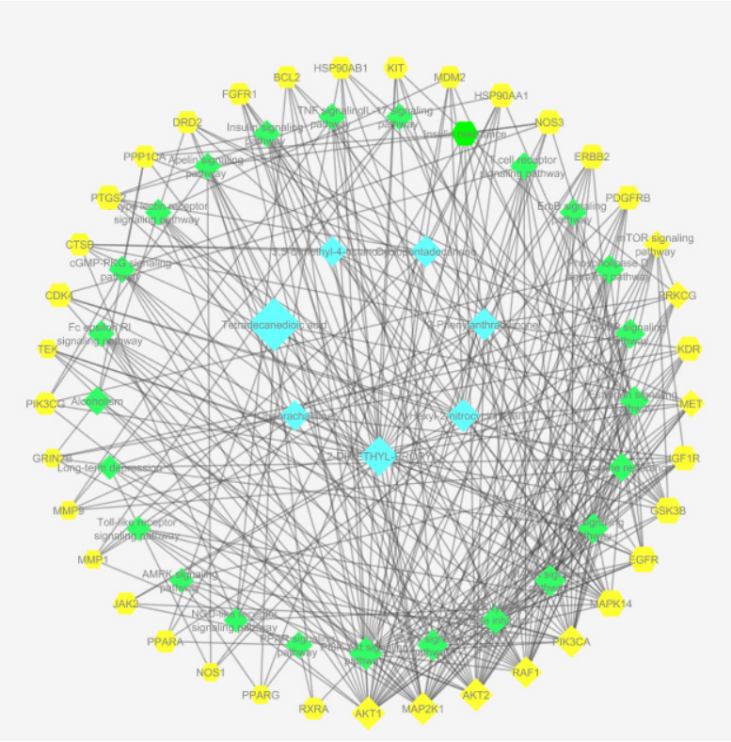


**Figure 1.** Network representation of molecular pathways and protein targets modulated by phytoconstituents of *Melia dubia* alcoholic seed extract. Blue nodes represent phytoconstituents, yellow nodes represent predicted protein targets, and green diamond-shaped nodes represent enriched signaling pathways. Key hubs include AKT1, mTOR (mechanistic target of rapamycin), and MAPK1, indicating involvement in metabolic and cell survival pathways.

analysis demonstrated the significant association of these targets with PI3K-Akt, AMPK, TNF, VEGF, NF-κB, and insulin signaling pathways, which are critically involved in cellular metabolism, inflammatory responses, and proliferation.

The distribution of nodes and edges suggested coordinated modulation rather than single-target interaction. In addition, certain phytocompounds, including 2-phenylanthraquinone, 2,2-dimethylpropyl, and quebrachamine, showed stronger connectivity with multiple targets, implying their potential as key contributors to the observed biological effects.

The overall network architecture supports a multi-component, multi-target interaction pattern, indicating that the extract may influence interconnected biological processes through simultaneous modulation of several signaling cascades.

The molecular interaction analysis of selected *M. dubia* compounds with α-glucosidase (PDB ID: 4JT6) demonstrated stable binding within the enzyme active site through a combination of hydrogen bonding and hydrophobic interactions (Figure 2). Compounds such as 2-phenylanthraquinone and quebrachamine exhibited prominent interactions with key amino acid residues, suggesting stronger binding affinity. Moderate interactions were observed for 2,2-dimethylpropyl and cyclopentadecanone, while weaker interactions were noted for tetradecanedioic acid. The presence of multiple contact points, including hydrogen bonds and hydrophobic contacts, indicates favorable ligand–enzyme stability. Overall, the interaction patterns support the potential of these phytoconstituents to bind effectively to α-glucosidase and contribute to its inhibition.

Molecular docking studies showed that the selected compounds exhibit distinct binding interactions with the mTOR protein at its active site (Figure 3). 2,2-Dimethylpropyl showed stronger interactions with multiple contact points, indicating higher binding affinity, whereas quebrachamine demonstrated moderate interactions. Tetradecanedioic acid exhibited comparatively weaker binding with fewer interactions. The presence of hydrogen bonds and hydrophobic

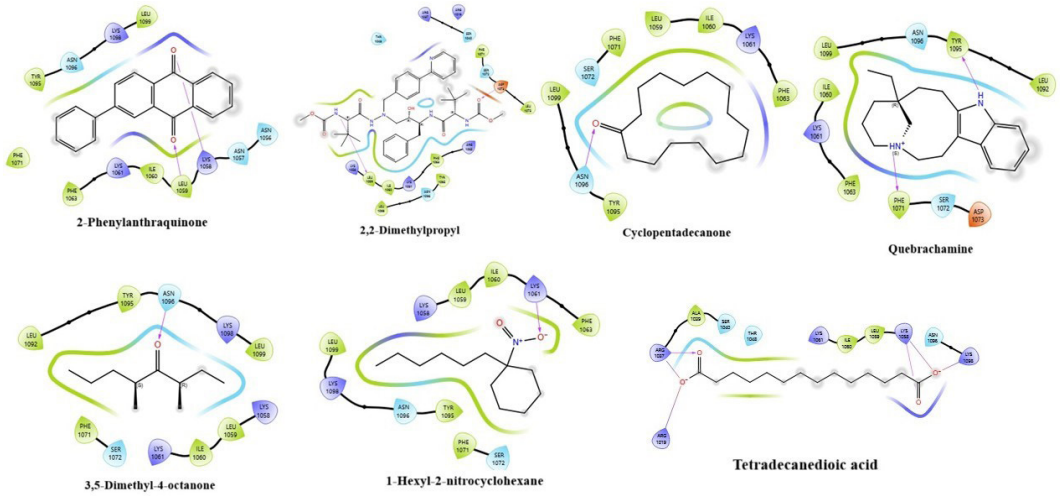


**Figure 2**. Two-dimensional molecular interaction diagrams of selected *Melia dubia* compounds with α-glucosidase (Protein Data Bank ID: 4JT6). Hydrogen bonds and hydrophobic interactions between the molecules and amino acid residues in the active site are shown in the diagrams. The purple and blue lines denote hydrogen bonds, whereas green lines denote hydrophobic interactions. These interactions indicate the possibility of an inhibitory affinity towards α-glucosidase.

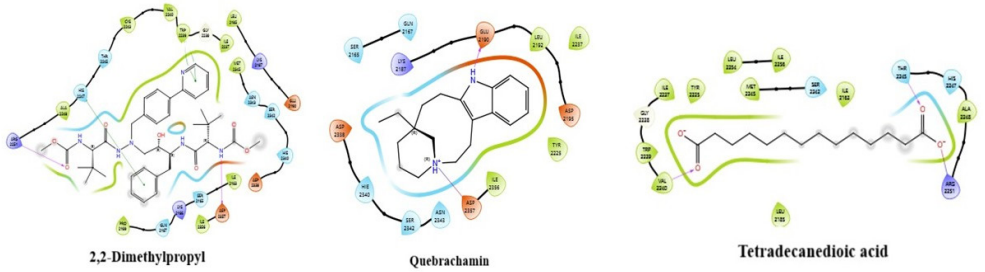


**Figure 3**. Two-dimensional molecular interaction diagrams of selected *Melia dubia* compounds with mTOR (Protein Data Bank ID: 2IUI). The diagrams illustrate hydrogen bonding (blue and purple arcs) and hydrophobic interactions (green arcs) with main amino acid residues at the binding site, indicating differences in binding affinity and interaction stability among the compounds.

contacts contributed to ligand stability within the binding pocket. These findings suggest that the phytoconstituents may interact with mTOR and potentially influence its regulatory function.

As presented in Table 1, the molecular docking analysis revealed differential binding affinities of *M. dubia* seed-derived compounds toward α-glucosidase (4JT6) and mTOR (2IUI), as indicated by their docking scores and glide energies. 2-phenylanthraquinone exhibited the strongest interaction with both targets, while 2,2-dimethylpropyl and quebrachamine showed moderate binding affinities. In contrast, cyclopentadecanone and 3,5-dimethyl-4-octanone demonstrated moderate interactions, whereas 1-hexyl-2-nitrocyclohexane and tetradecanedioic acid displayed comparatively weaker binding. The *P* values listed in Table 1 have been adjusted for multiple testing in pathway enrichment analysis by means of the Benjamini-Hochberg FDR correction procedure.

Pathway enrichment analysis showed that there is a statistically significant association between predicted targets and a number of signaling pathways like PI3K-Akt, AMPK, NF-κB, VEGF, TNF, and insulin signaling. These pathways are involved in glucose metabolism, inflammation, angiogenesis, and cell survival, therefore suggesting a possibility of multi-target mechanism of action of phytoconstituents.

As shown in Table 2, *M. dubia* extract demonstrated an increase in α-glucosidase inhibitory effect with increasing concentration, varying from 10.52 ± 1.0% at 10 μg/mL to 78.60 ± 2.0% at 50 μg/mL. Statistical analysis using one-way ANOVA and Tukey's post hoc test showed that all the treated groups had a notable increase in inhibitory activity compared to the control group (enzyme without inhibitor) ($P < 0.05$), and higher concentrations showed significant differences compared to lower concentrations, confirming a concentration-dependent effect. The $IC_{50}$ value of the extract was 33.59 ± 1.8 μg/mL, compared to 28.11 ± 1.3 μg/mL for the standard drug acarbose, indicating moderate inhibitory activity relative to the standard.

As shown in Table 3, *M. dubia* extract exhibited an increase in cytotoxic activity against MCF-7 cells with increasing concentration, ranging from 15.42 ± 1.1% at 10 μg/mL to 91.85 ± 1.3% at 160 μg/mL. All treated groups showed a significant increase in cytotoxic activity when compared to the control group ($P < 0.05$), according to a one-way ANOVA and Tukey's post hoc test. Higher concentrations showed significant differences when compared to lower concentrations, indicating a concentration-dependent effect. The extract's $IC_{50}$ value was 31.82 ± 2.1 μg/mL, while cisplatin's was 20.41 ± 1.5 μg/mL. This suggests that the extract has significant but comparatively less cytotoxic action than the usual medication.

**Table 1.** Molecular docking results of selected *Melia dubia* seed-derived compounds against α-glucosidase and mechanistic target of rapamycin (mTOR), along with enriched signaling pathways and false discovery rate (FDR) values

| Compound | Docking score (4JT6) | Glide energy kcal/mol (4JT6) | Docking score (2IUI) | Glide energy kcal/mol (2IUI) | Enriched pathway | FDR | In vitro evidence | Potential implications |
|---|---|---|---|---|---|---|---|---|
| 2-Phenylanthraquinone | -8.377 | -36.701 | -4.002 | -25.074 | PI3K-Akt signaling pathway | 1.77E-07 | Inhibited glucose uptake & cytokines in diabetic cell lines | Strongest binder; dual anti-diabetic & anti-inflammatory |
| 2,2-Dimethylpropyl | -6.604 | -56.017 | -4.617 | -42.068 | AMPK signaling pathway | 1.10E-04 | Improved lipid uptake; enhanced AMPK phosphorylation | Strong metabolic modulator |
| Cyclopentadecanone | -5.766 | -22.755 | -4.298 | -19.025 | VEGF signaling pathway | 1.45E-07 | Reduced VEGF and HIF-1α in angiogenesis assays | Moderate antiangiogenic and anticancer potential |
| Quebrachamine | -5.206 | -31.921 | -4.632 | -22.864 | NF-κB signaling pathway | 7.35E-05 | Suppressed IL-1β & IL-6 in inflammation models | Enzyme inhibition & immune modulation |
| 3,5-Dimethyl-4-octanone | -4.879 | -19.693 | -4.063 | -18.796 | Insulin signaling pathway | 1.77E-07 | Minor glucose uptake effect in adipocyte models | Mild insulin-sensitizing role |
| 1-Hexyl-2-nitrocyclohexane | -4.470 | -21.357 | -3.065 | -19.410 | TNF signaling pathway | 7.35E-05 | Slight TNF-α reduction; low cytotoxicity | Low therapeutic potential |
| Tetradecanedioic acid | -0.307 | -23.754 | -0.532 | -32.39 | β-cell dysfunction & insulin secretion | 2.38E-07 | Mild insulin marker modulation in β-cells | Weak binder; limited metabolic therapeutic use |

FDR, false discovery rate.

**Table 2.** In vitro α-glucosidase inhibitory activity of *Melia dubia* seed extract

| Sample | Concentration (µg/mL) | Optical density (Mean ± SD) | % Inhibition (Mean ± SD) | $IC_{50}$ (µg/mL) (Mean ± SD) |
|---|---|---|---|---|
| Acarbose (Standard) | 10 | 0.737 ± 0.006 | 15.67 ± 0.9 | 28.11 ± 1.3 |
| | 20 | 0.583 ± 0.006 | 33.07 ± 1.2* | |
| | 30 | 0.406 ± 0.006 | 53.55 ± 1.5* | |
| | 40 | 0.213 ± 0.006 | 75.63 ± 1.8* | |
| | 50 | 0.087 ± 0.006 | 90.16 ± 1.2* | |
| *Melia dubia* | 10 | 0.783 ± 0.006 | 10.52 ± 1.0 | 33.59 ± 1.8 |
| | 20 | 0.626 ± 0.006 | 28.49 ± 1.3* | |
| | 30 | 0.496 ± 0.006 | 43.13 ± 1.5* | |
| | 40 | 0.356 ± 0.006 | 59.26 ± 1.9* | |
| | 50 | 0.187 ± 0.006 | 78.60 ± 2.0* | |

The values are displayed as mean ± SD (n = 3). Tukey's post hoc test and one-way ANOVA were used for statistical analysis. *$P < 0.05$ in comparison to the prior lower concentration within the same treatment group.

**Table 3.** Cytotoxic activity of *Melia dubia* seed extract on MCF-7 breast cancer cells by MTT (3-[4,5-Dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assay

| Sample | Concentration (µg/mL) | Optical density (Mean ± SD) | % Inhibition (Mean ± SD) | $IC_{50}$ (µg/mL) (Mean ± SD) |
|---|---|---|---|---|
| Cisplatin (Standard) | 10 | 1.373 ± 0.006 | 7.41 ± 0.8 | 20.341 ± 1.5 |
| | 20 | 1.146 ± 0.006 | 22.90 ± 1.2* | |
| | 30 | 0.733 ± 0.006 | 50.57 ± 1.7* | |
| | 40 | 0.327 ± 0.006 | 77.85 ± 2.1* | |
| | 50 | 0.027 ± 0.006 | 98.18 ± 1.0* | |
| *Melia dubia* | 10 | 1.256 ± 0.006 | 15.42 ± 1.1 | 31.82 ± 2.1 |
| | 20 | 0.906 ± 0.006 | 38.98 ± 1.4* | |
| | 30 | 0.643 ± 0.006 | 56.76 ± 1.8* | |
| | 40 | 0.426 ± 0.006 | 71.38 ± 2.0* | |
| | 50 | 0.116 ± 0.006 | 91.85 ± 1.3* | |

The values are displayed as mean ± SD (n = 3). Data were analyzed using one-way ANOVA, followed by Tukey's post hoc test. *$P < 0.05$ compared with the previous lower concentration within the same treatment group.

## Discussion

The important phytochemicals in *M. dubia*, such as 2-phenylanthraquinone, 2,2-dimethylpropyl, and quebrachamine, showed good binding affinity towards α-glucosidase and mTOR from their docking score, suggesting their involvement in both metabolic and proliferative regulatory mechanisms. Notably, 2-phenylanthraquinone demonstrated the strongest binding affinity among the selected compounds, supporting its potential role as a major contributor to the observed biological activity.

These results were further supported by the *in vitro* α-glucosidase inhibition experiment, which showed a concentration-dependent inhibitory effect with an $IC_{50}$ value of 33.59 µg/mL for the extract and 28.11 µg/mL for acarbose, showing moderate activity in comparison to the standard. Its potential anticancer action was also supported by cytotoxic examination using the MTT test, which showed dose-dependent inhibition of MCF-7 cells with an $IC_{50}$ value of 31.82 µg/mL compared to 20.41 µg/mL for cisplatin.

Inhibition of α-glucosidase may attenuate postprandial hyperglycemia by delaying carbohydrate hydrolysis and reducing glucose absorption (24,25). In addition to this, binding with mTOR, which is a crucial controller of cell growth, protein synthesis, and autophagy, suggests modulation of cancer cell viability and growth (26).

The enrichment of targets within PI3K-Akt, AMPK, and NF-κB signaling pathways provides further mechanistic insight into the observed activities. The PI3K-Akt pathway plays a significant role in insulin signaling, glucose uptake, and cell survival, while AMPK regulates cellular energy balance and metabolic homeostasis (20). Modulation of NF-κB signaling suggests a potential reduction in pro-inflammatory cytokine production, which is closely associated with insulin resistance and tumor progression (21,27). Additionally, involvement of VEGF signaling pathways may indicate possible regulation of angiogenesis, a key process in tumor growth and metastasis (26,28).

The simultaneous interaction of these phytoconstituents with multiple targets and pathways, as supported by network pharmacology analysis, suggests a coordinated multi-target mechanism of action. This supports the concept of polypharmacology, in which bioactive

compounds exert therapeutic effects through modulation of interconnected biological networks rather than a single molecular target (22,23,29). However, as the selected compounds were identified through database mining and literature sources rather than direct phytochemical characterization of the extract, further analytical validation and isolation studies are required to confirm their presence and biological relevance.

### Limitations

Docking validation (redocking/RMSD) was not performed, and the results should be considered predictive. In vitro assessment involved only one cancer cell line (MCF-7). In addition, the extract was neither chemically analyzed nor standardized. Further experiments with more cancer cell lines, as well as in vivo assessments, are needed.

## Conclusion

The results from this study show that the alcoholic seed extract of *M. dubia* is biologically active on multiple targets, potentially facilitated through the modulation of key metabolic and proliferative signaling pathways. The combined *in silico* and *in vitro* evidence suggests that the extract may influence glucose metabolism, inflammatory responses, and cancer cell viability through coordinated pathway interactions. Although the observed activity was moderate compared to standard drugs, results suggest the possibility of using the seeds of *M. dubia* as a source of biologically active compounds targeting multiple targets. Further studies focusing on phytochemical characterization, mechanistic validation, and in vivo evaluation are necessary to establish its clinical relevance

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### Authors' contribution

**Conceptualization:** Santhosh Gangaraj and Manasa Gopal.
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**Formal analysis:** Santhosh Gangaraj and Manasa Gopal.
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**Investigation:** Santhosh Gangaraj and Megavath Subhash.
**Methodology:** Manasa Gopal and Bhagya Venkanna Rao.
**Project administration:** Santhosh Gangaraj and Bhagya Venkanna Rao.
**Resources:** Santhosh Gangaraj and Manasa Gopal.
**Software:** Manasa Gopal, Megavath Subhash and Santhosh Gangaraj.
**Supervision:** Malthesh Keppalingannanavar and Santhosh Gangaraj.
**Validation:** Manasa Gopal and Bhagya Venkanna Rao.
**Visualization:** Bhagya Venkanna Rao, Manasa Gopal and Praveen Bembalge.
**Writing–original draft:** Santhosh Gangaraj and Manasa Gopal.
**Writing–review & editing:** Santhosh Gangaraj and Manasa Gopal.

### Conflict of interests

The authors declared no competing interests.

### Ethical considerations

All authors observed ethical issues (including plagiarism, violations, falsification of data, falsification of double publication or submission, and redundancy).

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### References

1. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021. https://diabetesatlas.org/.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide. CA Cancer J Clin. 2021;71(3):209–249. doi:10.3322/caac.21660
3. Hanahan D. Hallmarks of cancer: new dimensions. Cancer Discov. 2022;12(1):31–46. doi:10.1158/2159-8290.CD-21-1059
4. Taniguchi CM, Emanuelli B, Kahn CR. Critical nodes in signalling pathways: insights into insulin action. Nat Rev Mol Cell Biol. 2006;7(2):85–96. doi:10.1038/nrm1837
5. Zengin G, Aktumsek. Plant-derived inhibitors of α-glucosidase: recent developments. Phytomedicine. 2022; 96:153888. doi:10.1016/j.phymed.2021.153888
6. Kim YM, Jeong YK, Wang MH, Lee WY, Rhee HI. Inhibitory effect of pine extract on α-glucosidase activity. J Agric Food Chem.2005;53(22):8890–8896.doi:10.1021/jf051379g
7. Sharma V, Janmeda P, Singh L, Bhardwaj R. Phytochemistry and bioactivity of *Melia dubia*. J Ethnopharmacol. 2015; 164:255–263. doi:10.1016/j.jep.2015.02.009
8. Rao KS, Sinsinwar S, Mahapatra DK. Antidiabetic activity of *Melia dubia* leaf triterpenoids. Phytomedicine. 2016; 23(5):518–523. doi:10.1016/j.phymed.2016.02.002
9. Singh G, Kumar R, Kapoor S, Arora A. Cytotoxic potential of *Melia dubia* bark extract. Asian Pac J Cancer Prev. 2014;15(6):2455–2460. doi:10.7314/APJCP.2014.15.6.2455
10. Hopkins AL. Network pharmacology: the next paradigm in drug discovery. Nat Chem Biol. 2008;4(11):682–690. doi:10.1038/nchembio.118
11. Zhou W, Wang Y, Lu A, Zhang G. Systems pharmacology in drug discovery. Acta Pharm Sin B. 2020;10(1):83–93. doi:10.1016/j.apsb.2019.10.001
12. Kitchen DB, Decornez H, Furr JR, Bajorath J. Docking and scoring in virtual screening for drug discovery. Nat Rev Drug Discov. 2004;3(11):935–949. doi:10.1038/nrd1549
13. Ravichandiran V, Lakshmi PT, Geetha A, Rameshkumar KB, Mohan S, Ravikumar S, et al. Screening of SdiA inhibitors from *Melia dubia* seeds extracts. Med Chem. 2013; 9(6):819–827. doi:10.2174/1573406411309060008
14. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. Sci World J. 2013;2013:162750.

doi:10.1155/2013/162750
15. Sasidharan S, Chen Y, Saravanan D, Sundram KM, Latha LY. Extraction and characterization of bioactive compounds. Afr J Tradit Complement Altern Med. 2011;8(1):1–10. doi:10.4314/ajtcam.v8i1.60483
16. Sukhadiya ML, Thakur NS, Patel VR, Gunaga RP, Kharadi VB, Tyagi KK, et al. Phytochemical variation in *Melia dubia*. J For Res. 2021;32(1):119–131. doi:10.1007/s11676-020-01112-3
17. Ervina M, Sukardiman. Melia azedarach as a potential anticancer drug. Pharmacogn Rev. 2018;12(23):94–102. doi:10.4103/phrev.phrev_47_17
18. Prabhu S, Vijayakumar S, Manogar P, Maniam GP, Govindan N. Docking studies on diabetes-related receptors. Biomed Pharmacother. 2017;92:528–535. doi:10.1016/j.biopha.2017.05.101
19. Patil S, Alegaon SG, Gharge S, Ranade SD, Khatib NA. α-Glucosidase inhibition studies. Bioorg Chem. 2024;153:107783. doi:10.1016/j.bioorg.2023.107783
20. Tolosa L, Donato MT, Gómez-Lechón MJ. General cytotoxicity assessment by MTT assay. In: Vinken M, Rogiers V, eds. Protocols in In Vitro Hepatocyte Research. New York: Humana Press; 2015. p. 333–348.
21. Hardie DG. AMPK: a key regulator of energy balance. Nat Rev Mol Cell Biol. 2015;16(8):495–507. doi:10.1038/nrm4002
22. Liu T, Zhang L, Joo D, Sun SC. NF-κB signaling in inflammation. Signal Transduct Target Ther. 2017;2:17023. doi:10.1038/sigtrans.2017.23
23. Narayanaswamy R, Duraisamy R, Rajasekar P. Antidiabetic effect of medicinal plants. Biomed Res Int. 2019;2019:6267032. doi:10.1155/2019/6267032
24. Patel V, Patel B, Shukla V, Bhatt N. Anticancer activity of *Melia dubia*. J Appl Pharm Sci. 2020;10(3):114–119. doi:10.7324/JAPS.2020.103014
25. Saxton RA, Sabatini DM. mTOR signaling in growth and metabolism. Cell. 2017;168(6):960–976. doi:10.1016/j.cell.2017.02.004
26. Zhang Y, Wang Y, Yang L, Li X, Wang X, et al. Targeting mTOR signaling pathway in cancer therapy. Cell Mol Life Sci. 2020;77(11):2289–2307. doi:10.1007/s00018-019-03360-9
27. Aggarwal BB, Sung B. NF-κB in cancer: a matter of life and death. Cancer Discov. 2011;1(6):469–471. doi:10.1158/2159-8290.CD-11-0130
28. Chavan RS, Gangaraj S, Gopal M, Karthik SP, Anand S. Unveiling the anticancer potential of *Ziziphus mauritiana* seeds: A multi-targeted approach integrating network pharmacology, molecular docking, and *in vitro* validation. J Herbmed Pharmacol. 2026;15(2):207–216. doi:10.34172/jhp.2026.53282
29. Gopal M, Gangaraj S, Shivakumar AG, Lokesh P, Rangaswamy N, Devaraju SG, et al. Phytochemical, pharmacognostic, and *in silico* investigation of the anti-diabetic potential of *Elaeocarpus angustifolius* seeds. J Herbmed Pharmacol. 2025;14(4):435–446. doi:10.34172/jhp.2025.52961