Asian Journal of Chemistry; Vol. 38, No. 5 (2026), 1189-1195

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2026.35623

Anticancer Potential of Isolated Gymnemic Acid-III from *Gymnema sylvestre*: Insights from *In vitro* and *In silico* Analysis

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Received: 20 January 2026 *Accepted*: 13 March 2026 *Published online*: 4 May 2026 AJC-22343

Gymnemic acid-III is a naturally occurring triterpenoid saponin isolated from the leaves of *Gymnema sylvestre*, a medicinal plant widely recognized for its therapeutic potential. The current study attempts to isolate, characterize and assess its anticancer properties. Gymnemic acid-III was obtained by purifying the crude saponins from aqueous extraction using preparative HPLC. Using FT-IR, ^{13}C NMR and LC-MS investigations, the structural elucidation was accomplished. In comparison to the reference drug ursolic acid, cytotoxicity tests of gymnemic acid-III were employing the MCF-7 and A549 cell lines demonstrated concentration-dependent inhibitory effects. Molecular docking studies against the α- and β-tubulin (PDB ID: 1JFF) target protein demonstrated a significant binding affinity with a docking score of -10.08 kcal/mol. Gymnemic acid-III was classified as non-acutely toxic profile from computational toxicity prediction. The results highlight gymnemic acid-III is a promising natural molecule for further investigation as a lead compound for anticancer treatment.

Keywords: *Gymnema sylvestre*, Gymnemic acid, Cytotoxicity, Molecular docking, Apoptosis.

INTRODUCTION

Natural products have long been recognized as an important source of bioactive molecules for drug discovery and development [1]. Used in traditional medicine for centuries, plant-derived secondary metabolites possess structural diversity, biological selectivity and favourable safety profiles, making them valuable templates for modern therapeutics [2,3]. More than two-thirds of clinically approved anticancer drugs are natural products or their derivatives [4]. In addition, their ability to regulate multiple cellular pathways involved in tumor progression highlights their therapeutic significance [5,6]. Therefore, phytoconstituents from medicinal plants continue to represent a promising resource for the development of novel anticancer agents.

Cancer is a complex multifactorial disease characterized by uncontrolled cell proliferation, resistance to apoptosis, sustained angiogenesis, and the ability to invade surrounding tissues [7-9]. Although substantial progress has been made in chemotherapy and targeted therapies, treatment is still challenged by drug resistance, severe adverse effects and non-specific toxicity toward normal cells [10,11]. These limitations have created a continued need for safer and more effective anticancer agents.

Herbs hold significance in the therapeutic field since they offer alternative and complementary methods to traditional medicine. *Gymnema sylvestre* belongs to the Apocynaceae family and is a woody climber. Due to its pharmacological properties, which include hepatoprotective, antidiabetic anti-inflammatory and antibacterial properties, it has been regarded in Ayurvedic medicine for centuries [12-15]. *G. sylvestre* contains bioactive phytochemicals, including gymnemic acids, gymnema-saponins and the polypeptide gurmarin [16]. The plant contains a complex mixture of triterpenoid saponins referred to as gymnemic acids, which provide a majority of the bioactive properties [17]. Additionally, gymnemic acids have increased interest due to their structural characteristics and potential biological properties [18]. Recent studies have shown that gymnemic acid analogues possess various biological activities and mechanisms such as glucose regulation and lowering of lipid accumulation and antiulcer, antistress and antiallergic [19-21]. However, their potential anticancer properties have yet to be studied. Interestingly and specifically, gymnemic acid-III has shown significant interest due to its structure [22]. However, their potential anticancer properties have not been studied. Therefore, examining gymnemic acid-III for its chemical composition and biological efficacy may provide important information for understanding pharmacological relevance and developing next generation natural product-based therapeutics.

The current work focuses on the isolation of gymnemic acid-III due to significance of natural products as a source of stimulus for drug discovery. To the best of our knowledge, gymnemic acid-III's anticancer properties have not yet been reported. Thus, the aim of this study was to isolate gymnemic acid-III from *G. sylvestre* leaves, characterize its structure and examine its anticancer properties. The MTT assay and morphological analysis were used to evaluate the cytotoxic activity against human lung (A549) and breast (MCF-7) cancer cell lines. Furthermore, the computational toxicity predictions were used to evaluate safety and molecular docking studies were conducted to investigate its binding interactions with α- and β-tubulin protein (PDB ID: 1JFF).

EXPERIMENTAL

All solvents and reagents were provided from Sigma-Aldrich, USA and used without further purification. A Hicon melting point apparatus was employed to measure melting points using open capillary tubes. ^{13}C NMR spectra (100 MHz) were acquired on a Bruker AM 400 spectrometer using DMSO-d_6 as the solvent. Mass spectra were acquired on a Perkin-Elmer PE Sciex API/65 LC-MS instrument. The elemental analysis (CHN) was performed using the Perkin-Elmer model 240C analyzer.

Plant material: *Gymnema sylvestre* leaves were collected from the garden of the college campus, cleaned with water and allowed to air dry. In an electric mill, the dried leaves were ground into a powder and then kept at room temperature in a covered container.

Extract preparation: Extraction (four times) of the dried leaves were prepared using 100 mL of distilled water at 60 ºC for 4 h each. The combined aqueous extracts' was adjusted at pH 3.0 with 2 N H_2SO_4 and the resulting precipitate was collected by contrifugation. The precipitate was dissolved in ethanol and centrifuged to remove the insoluble residues. The supernatant was concentrated under reduced pressure, followed by the addition of acetone. The resulting precipitate was collected by centrifugation and the remaining supernatant was evaporated under reduced pressure to yield 9.1 g of crude saponins.

Isolation of gymnemic acid-III: An ODS column (5 cm × 25 cm) was used for column chromatography of the crude saponin fraction (9.3 g) with a stepwise gradient of methanol-water (1:1→7:3→1:0, v/v) as eluent. Using methanol: 0.25% KH_2PO_4 buffer (pH 3) (60:40, v/v) as mobile phase, fraction six was further purified out of the eleven fractions using LC and preparative HPLC. Gymnemic acid-III was obtained using this purification method as a colourless powder (47 mg). Colourless powder. m.p.: 220-222 ºC, Anal. of $C_{41}H_{66}O_{13}$: calcd. (found) %: C, 64.21 (64.15); H, 8.67 (8.62); O, 27.12 (27.16); IR (KBr, ν_{max}, cm^{-1}): 3310, 2891, 1729; ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 11.2, 13.6, 16.1, 16.6, 17.3, 18.9, 23.8, 25.8, 26.1, 26.3, 26.6, 33.2, 35.6, 36.4, 38.2, 38.8, 40.3, 40.8, 41.5, 41.9, 43.8, 47.0, 47.6, 47.9, 48.7, 64.7, 65.8, 68.3, 72.1, 72.7, 73.8, 78.2, 79.2, 80.8, 86.3, 114.6, 123,2, 144.1, 173.2, 175.7; MS, *m/z*: 767.40 $[M+H]^+$.

Cytotoxic activity: The cell lines MCF-7 (human breast cancer) and A549 (human lung cancer) were procured from The National Centre for Cell Sciences (NCCS), Pune, India. In a humidified atmosphere with 5% CO_2, stock cells were cultivated in their respective media, namely MEM supplemented with 10% inactivated fetal bovine serum (FBS), penicillin (100 IU/mL), streptomycin (100 μg/mL) and amphotericin B (5 μg/mL), until viable. The cytotoxic impact of Gymnemic acid-III was assessed using the MTT test in a dose-dependent manner [23]. The cell viability test was run in six repetitions to ensure statistical significance and minimize experimental variability. GraphPad Prism 8.0 was used to compute the IC_{50} values from the MTT assay data.

Morphological analysis: Upon being plated at a density of 1 × 10^4 cells per well in six-well plates, MCF-7 and A549 cancer cells were incubated for 24 h. Gymnemic acid-III was then added to the cells at different concentration. An inverted phase-contrast microscope was used to analyze morphological changes after treatment in order to evaluate the structural alterations that gymnemic acid-III had caused in MCF-7 and A549 cells.

Molecular docking analysis: Employing AutoDock Vina integrated into UCSF Chimera, molecular docking studies were conducted to examine the binding mechanisms and interactions of gymnemic acid-III [24]. The protein data bank (PDB) provided the target α- and β-tubulin protein's crystal structure (PDB ID: 1JFF) for the docking study. The co-crystal ligand was removed from the protein's active site prior to protein preparation. The protein was given solvation parameters and hydrogen atoms and Kollman charges were added throughout the protein preparing process. Gasteiger charges were added and non-polar hydrogen atoms were combined throughout the ligand preparation process. For the preparation of proteins and ligands, the graphical user interface application AutoDock Tools may carry out intermediate steps such generating grid boxes and .pdbqt files. After the docking parameter file format was completed, the Autodock 4.2 application was started. Using the Lamarckian genetic algorithm technique, 100 runs of the docking analyses were conducted. The molecular docking interactions of Gymnemic acid-III were confirmed by re-docking the co-crystal ligand at the protein's active site. To obtain the best docking orientation, the grid box parameters were defined to achieve the RMSD values of less than 1.54 Å. The Discovery Studio software has been used to visualize the docking results. Furthermore, the ProTox 3.0 web server (https://tox.charite.de/protox3/) was used to forecast the toxicity profiles.

RESULTS AND DISCUSSION

In order to obtain gymnemic acid-III, a bioactive triterpenoid saponin, the aqueous extract of *Gymnema sylvestre* leaves underwent a series of purifying procedures. Crude saponins (9.1 g) were obtained through water extraction, acid precipitation, and solvent partitioning. Subsequent separation on an ODS column with a methanol-water gradient and purification by preparative HPLC afforded gymnemic acid-III as a colourless powder. Its melting point was recorded at 220-222 ºC, consistent with a pure crystalline compound.

The FT-IR spectrum displayed characteristic absorption bands of triterpenoid saponins. A broad band around 3310 cm^{-1} was attributed to O–H stretching vibrations of hydroxyl groups, while peaks near 2891 cm^{-1} corresponded to C–H stretching vibrations. A strong absorption band at 1729 cm^{-1} indicated the presence of ester carbonyl (C=O) groups and bands in the 1150-1050 cm^{-1} region were assigned to C–O stretching vibrations associated with glycosidic linkages. The mass spectrum exhibited a molecular ion peak at *m/z* 767.45, corresponding to the molecular weight of gymnemic acid-III and confirming its identity. The ^{13}C NMR spectrum further established the triterpenoid skeleton, showing signals for methyl, methylene, methine and quaternary carbons in the aglycone moiety. Signals at δ 114.6, 123.2 and 144.1 ppm were assigned to olefinic carbons, while peaks at δ 173.2 and 175.7 ppm corresponded to carboxylic acid and ester carbonyl carbons. These data were in-agreement with reported values for gymnemic acid-III [25]. The HPLC chromatogram showed a single sharp peak with a purity of 97.8%, indicating high purity and homogeneity (Fig. 1).

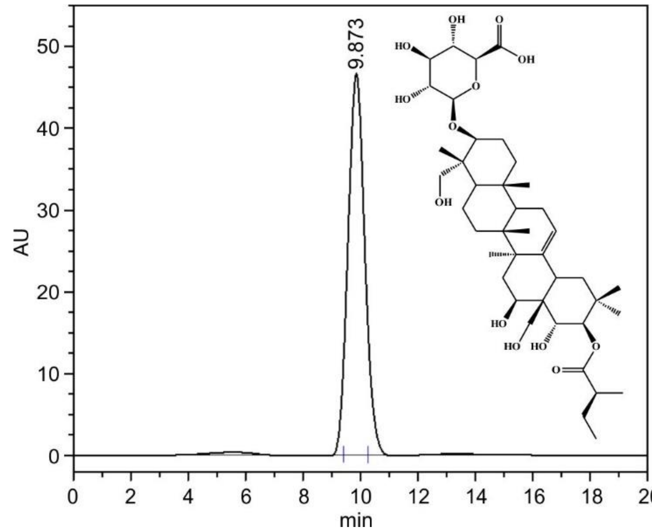

Fig. 1. HPLC chromatogram of gymnemic acid-III

Cytotoxic activity: Utilizing the MTT test, the cytotoxic capability of gymnemic acid-III against human breast (MCF-7) and lung (A549) cancer cell lines was assessed compared to the reference drug ursolic acid. In comparison to the untreated control, which was regarded as 100% vitality, the cell viability of the treated samples was computed and expressed as a percentage. Fig. 2 displays the results for cell viability. MCF-7 and A549 cell lines were chosen for this investigation due to their biological and clinical significance for common human malignancies. A model for researching estrogen-dependent breast cancer and assessing substances that impact hormone mediated pathways is MCF-7, a hormone receptor-positive breast adenocarcinoma cell line [26,27]. The A549 cell line, on the other hand, is frequently used to evaluate anticancer drugs that target epithelial lung cancer and represents non-small cell lung carcinoma [28,29]. By include these two different cell lines, it is important to evaluate the effectiveness of compounds against hormone-dependent and hormone-resistant cancer types, offering a more comprehensive view of their potential as therapeutics. The current findings showed that both gymnemic acid-III and the reference substance ursolic acid clearly decreased cell viability in a concentration-dependent manner. There was a noticeable decrease in cell viability as the concentration of the gymnemic acid-III increased among the tested concentrations, which suggesting dose-dependent cytotoxicity.

Compared to the reference drug ursolic acid, gymnemic acid-III demonstrated moderate cytotoxic potential. When tested on MCF-7 cells, the IC_{50} value for gymnemic acid-III was 173.58 μg/mL, but for ursolic acid is 91.58 μg/mL and on A549 cells gymnemic acid-III had an IC_{50} value of 105.26 μg/mL, while ursolic acid had an IC_{50} of 77.93 μg/mL. The results show that gymnemic acid-III might demonstrated moderate anticancer activity but not as significant as reference molecule ursolic acid. Both cancer cell lines showed a noticeable

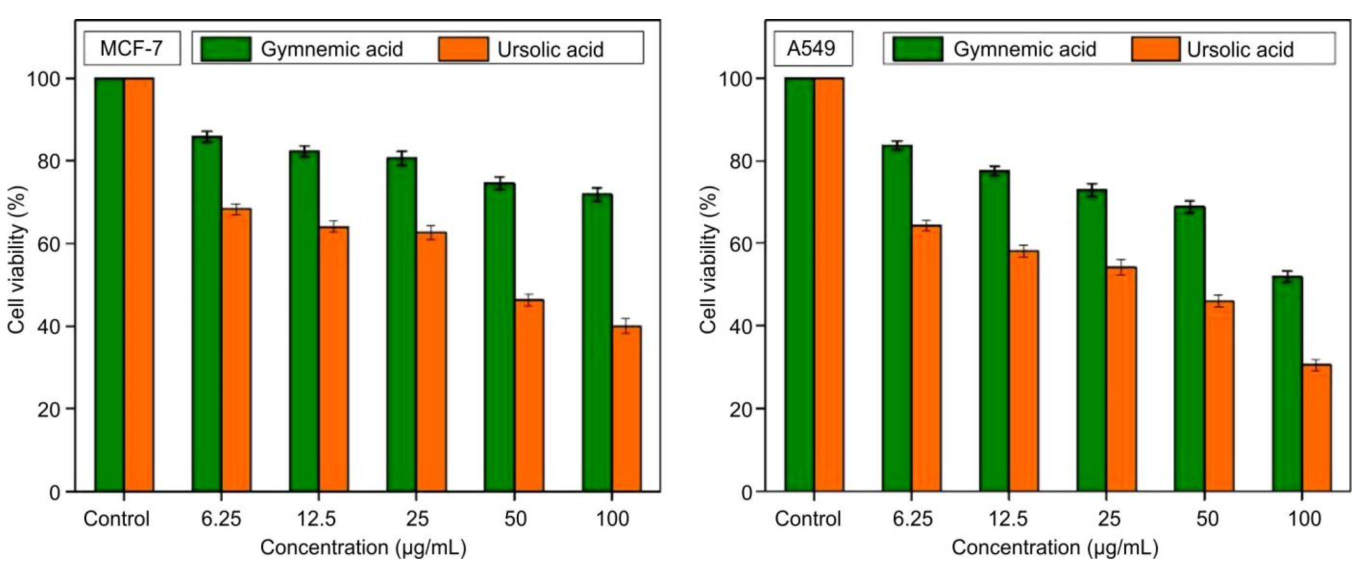

Fig. 2. Effect of gymnemic acid-III and ursolic acid on cell viability of MCF-7 and A549 cell lines

decrease in cell viability upon exposure to gymnemic acid-III. These inhibitory effects indicate its potential as a natural anticancer agent, although its activity was lower than that of the reference compound, ursolic acid. Further physiological and molecular studies are required to elucidate its mechanism of action and enhance its therapeutic potential.

Effect of gymnemic acid-III on morphology of MCF-7 and A549 cells: Phase-contrast microscopy was used to evaluate the morphological changes in MCF-7 and A549 cells after treatment with gymnemic acid-III. Untreated control cells (Figs. 3a and 4a) showed normal morphology with a high number of viable cells. Treatment with gymnemic acid-III (6.25-100 μg/mL) produced concentration-dependent morphological alterations in both cell lines. In MCF-7 cells (Fig. 3b-f), lower concentrations (6.25 and 12.5 μg/mL) caused cell shrinkage and reduced cell density, while higher concentrations

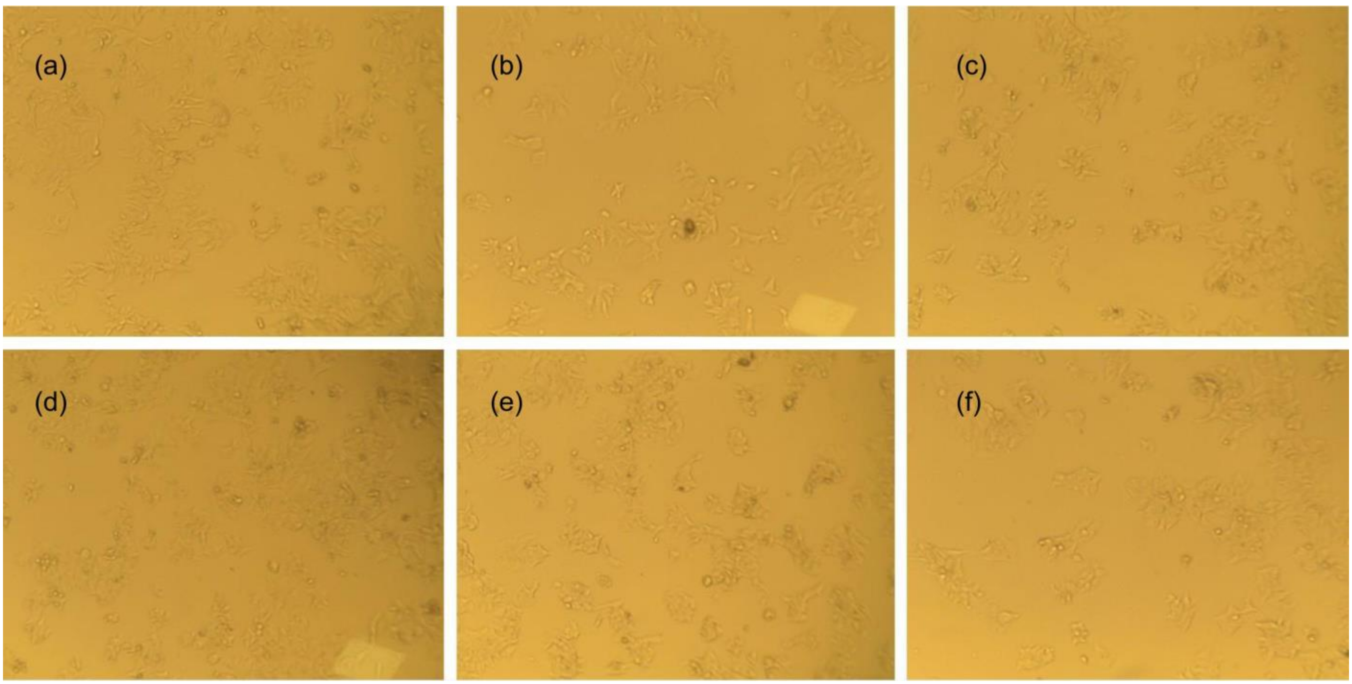

Fig. 3. Gymnemic acid-III induced morphological variation in MCF-7 cells using phase-contrast microscopy at magnification 40× (a) control; (b) 6.25 μg/mL; (c) 12.5 μg/mL; (d) 25 μg/mL; (e) 50 μg/mL; (e) 100 μg/mL

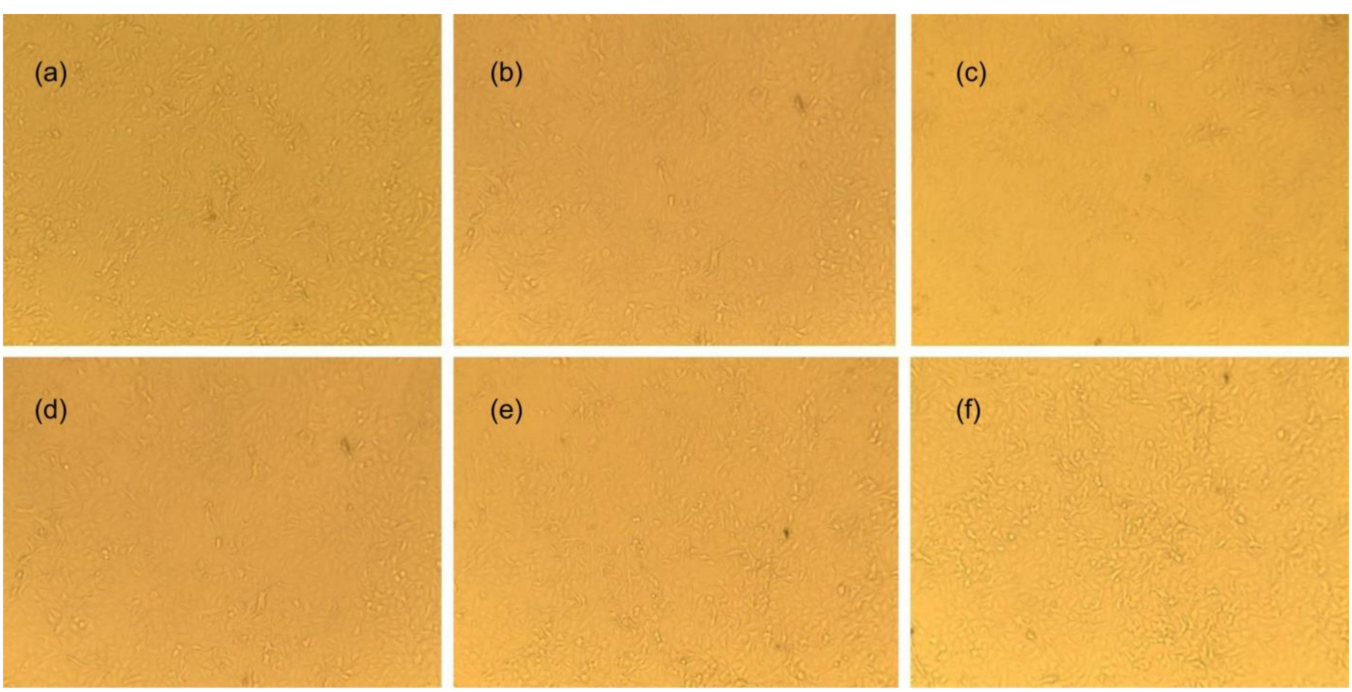

Fig. 4. Gymnemic acid-III induced morphological variation in A549 cells using phase-contrast microscopy at magnification 40× (a) control; (b) 6.25 μg/mL; (c) 12.5 μg/mL; (d) 25 μg/mL; (e) 50 μg/mL; (e) 100 μg/mL

(25-100 μg/mL) resulted in marked cell rounding, loss of adherence and detachment, indicating cytotoxic effects.

Similarly, A549 cells (Fig. 4b-f) showed a progressive reduction in cell number and changes in morphology with increasing concentrations. Treated cells became rounded and loosely attached, whereas control cells retained their elongated spindle-shaped appearance. At 100 μg/mL, extensive cell disintegration and membrane blebbing were observed, suggesting apoptotic-like cell death. These findings indicate that gymnemic acid-III exerts concentration-dependent cytotoxic effects against both MCF-7 and A549 cancer cells. The observed morphological alterations suggest possible apoptosis, which requires confirmation through specific mechanistic assays.

Molecular docking studies: Comprising α- and β-tubulin heterodimers, microtubules are essential for intracellular transport, cell shape preservation and mitosis [30]. Cell cycle arrest and apoptotic cell death result from a disruption of their dynamic equilibrium [31]. As a result, compounds that interfere with tubulin or alter microtubule dynamics can successfully prevent cell division and mitosis, which can have cytotoxic potential [32]. Consequently, microtubules are a well established and prospective target for the development of anticancer drugs. Through emphasizing on the α- and β-tubulin proteins, compounds that bind at the Taxol-binding site and impact microtubule dynamics can be found. Therefore, by evaluating the molecules' capacity to replicate Taxol's stabilizing interactions within the binding pocket, molecular docking with the target α- and β-tubulin protein (PDB ID: 1JFF) helps in determining the anticancer potential of compounds such as gymnemic acid-III. Using Autodock software, a molecular docking analysis was conducted to assess gymnemic acid-III's binding relationship with the target α- and β-tubulin protein (PDB ID: 1JFF). The native ligand Taxol was redocked into the active site of 1JFF protein in order to validate the docking processes. Fig. 5 displays the 3D and 2D interaction plot of gymnemic acid-III within the target protein's active region based on the molecular docking data. Table-1 provides a summary of the docked compound's binding parameters with the target 1JFF protein.

With a docking score of -10.08 kcal/mol, gymnemic acid-III demonstrated a stronger binding affinity for the target protein than the native ligand, Taxol (-9.16 kcal/mol), according to the docking results. The docking interactions shows that gymnemic acid-III forms five hydrogen bonding interactions (Fig. 5) with important amino acid residues Val-172, Ile-204, Met-259, Gly-379 and Phe-388, with bond distances ranging from 1.75 Å to 3.71 Å. The stability of the ligand within the

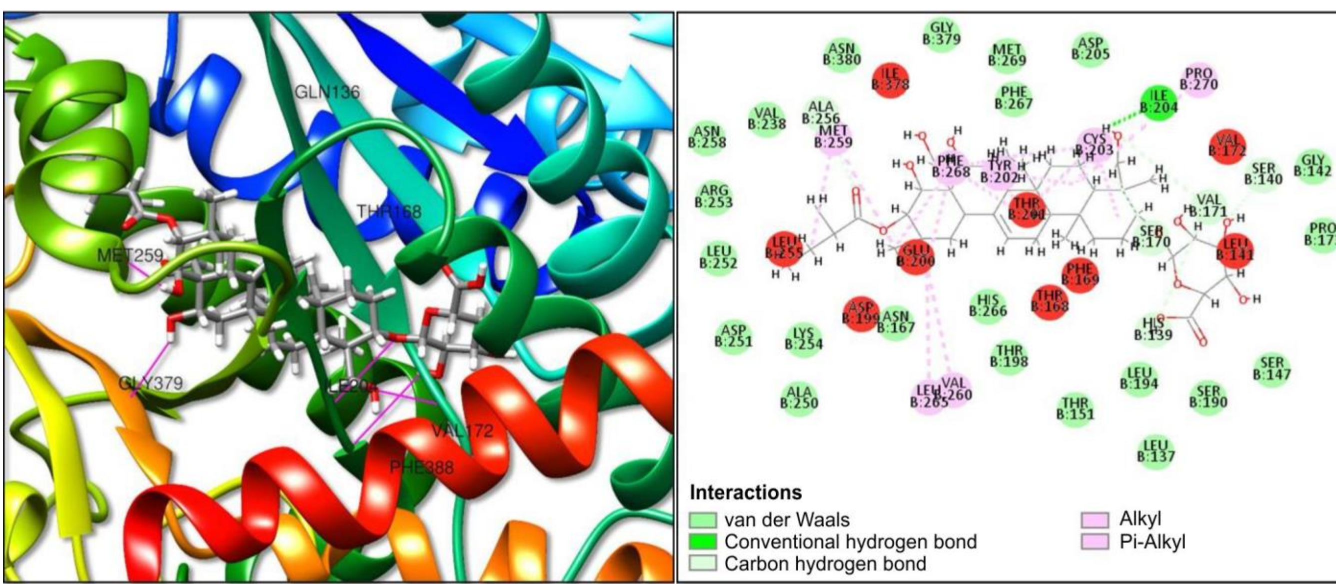

Fig. 5. 3D and 2D Docking interactions of the gymnemic acid-III with target 1JFF protein

TABLE-1
DOCKING BINDING INTERACTIONS VALUES OF GYMNEMIC ACID-III WITH TARGET 1JFF PROTEIN

Compound	Docking score (kcal/mol)	Interacting residues			
		H-bond	Bond length (Å)	Hydrophobic	π-Alkyl
Gymnemic acid-III	-10.08	Val-172	1.75	Leu-137, Gly-142, Ser-147, Thr-151, Asn-167, Pro-173, Ser-190, Leu-194, Thr-198, Asp-205, Val-238, Ala-250, Asp-251, Leu-252, Arg-253, Lys-254, Ala-256, Asn-258, His-266, Phe-267, Met-269, Gly-379, Asn-380	Cys-203, Tyr-202, Val-260, Leu-265, Phe-268, Pro-270
		Ile-204	3.14		
		Met-259	3.71		
		Gly-379	3.11		
		Phe-388	3.32		
Taxol	-9.16	Thr-168	2.97	Ile-16, Leu-137, Thr-138, Ser-140, Pro-173, Val-191, Leu-194, Thr-201, Val-238, Leu-252, Arg-253, Lys-254, Leu-255, Ala-256, Asn-258, His-266, Phe-267, Pro-270, Phe-377, Phe-388, Met-269, Gly-379, Asn-380, Ile-384	His-139, Cys-203
		Ser-170	2.72		
		Gly-379	3.06		

target α- and β-tubulin protein's active pocket depends on these interactions. Furthermore, the binding stability was further enhanced by a hydrophobic interaction with residues like Leu-137, Ser-147, Thr-151, Asn-167 and Val-194. The ligand binding within the hydrophobic split of the binding site was further facilitated by π-alkyl interactions with residues like Cys-203, Tyr-202, Val-260, Leu-265, Phe-268 and Pro-270. The native ligand Taxol, on the other hand, formed hydrogen bonds with residues Thr-168, Ser-170 and Gly-379, achieving a docking score of -9.16 kcal/mol. Although the crucial residue Gly-379 was bound by both ligands, gymnemic acid-III formed more hydrogen bonds and hydrophobic interactions, which results in a higher binding affinity. Based to these results, gymnemic acid-III forms strong interactions with the target α- and β-tubulin protein's Taxol-binding pocket, potentially disrupting microtubule dynamics and preventing cell proliferation. Gymnemic acid-III has a higher binding affinity than the native ligand Taxol, which indicates that it may be an effective natural compound for the creation of anticancer drugs that target the microtubule polymerisation in lung carcinoma cells.

Toxicity prediction: Gymnemic acid-III's probable toxicity profile was assessed using the ProTox 3.0 webtool [33] and Table-2 provides an overview of the findings. The computational prediction of toxicity of gymnemic acid-III suggested a chance of being hepatotoxic, neurotoxic, respiratory toxic and mutagen to be on the lower side; but these predictions are the initial *in silico* results and should be considered as the starting point for further experimental evaluations. Nonetheless, it was anticipated that there would be minimal nephrotoxicity (0.72), cardiotoxicity (0.89) and immunotoxicity (0.99), which could indicate dose-dependent adverse effects. Gymnemic acid-III was classed as toxicity class 4 due to its predicted LD_{50} value of 3220 mg/kg, indicating that it is not acutely toxic. The prediction accuracy (70.97%) and average similarity (83.68%) provide additional evidence of the dependability of these computational assessment. The *in silico* toxicity analysis indicates relatively low acute oral toxicity; however, these findings require confirmation through experimental studies. Based on these results, gymnemic acid-III may serve as a promising and comparatively safe lead molecule for future development of natural therapeutic agents.

TABLE-2
TOXICITY PREDICTION ANALYSIS FOR THE GYMNEMIC ACID-III, WITH INACTIVE/ACTIVE TOXICITY CLASSIFICATIONS ESTABLISHED BY PROBABILITY SCORES (0-1 scale)

Toxicity parameters	Prediction (probability)
Gymnemic acid-III	
Hepatotoxicity	Inactive (0.95)
Neurotoxicity	Inactive (0.83)
Nephrotoxicity	Active (0.72)
Respiratory toxicity	Inactive (0.51)
Cardiotoxicity	Active (0.89)
Carcinogenicity	Inactive (0.65)
Immunotoxicity	Active (0.99)
Mutagenicity	Inactive (0.93)
Oral toxicity prediction results	
Predicted LD_{50} (mg/kg)	3220 mg/kg
Predicted Toxicity class	4
Average similarity (%)	83.68
Prediction accuracy (%)	70.97

Conclusion

In conclusion, gymnemic acid-III was isolated from *Gymnema sylvestre* leaves and characterized by chromatographic and spectroscopic techniques. The compound showed moderate dose-dependent cytotoxicity against MCF-7 and A549 cell lines, with morphological changes suggestive of apoptosis. Molecular docking revealed strong binding interactions with the 1JFF target protein and higher affinity toward α- and β-tubulin than Taxol. Toxicity prediction indicated low acute oral toxicity. These findings suggest that gymnemic acid-III is a promising natural lead compound for further anticancer drug development targeting microtubule polymerization.

ACKNOWLEDGEMENTS

The authors are immensely express their gratitude to the Management of B.N.M. Institute of Technology, Bangalore for providing lab facilities to carry out this work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

DECLARATION OF AI-ASSISTED TECHNOLOGIES

During the preparation of this manuscript, the authors used an AI-assisted tool(s) to improve the language. The authors reviewed and edited the content and take full responsibility for the published work.

REFERENCES

1. Z. Luo, F. Yin, X. Wang and L. Kong, *Chin. J. Nat. Med.*, **22**, 195 (2024); https://doi.org/10.1016/S1875-5364(24)60582-0
2. J. Darmadi, R.R. Batubara, S. Himawan, N.N. Azizah, H.K. Audah, A. Arsianti, E. Kurniawaty, I.S. Ismail, I. Batubara and K.A. Audah, *Sci. Rep.*, **11**, 6080 (2021); https://doi.org/10.1038/s41598-021-85383-3
3. C.B. Aware, D.N. Patil, S.S. Suryawanshi, P.R. Mali, M.R. Rane, R.G. Gurav and J.P. Jadhav, *S. Afr. J. Bot.*, **151**, 512 (2022); https://doi.org/10.1016/j.sajb.2022.05.028
4. D.J. Newman and G.M. Cragg, *J. Nat. Prod.*, **83**, 770 (2020); https://doi.org/10.1021/acs.jnatprod.9b01285
5. P. Chunarkar-Patil, M. Kaleem, R. Mishra, S. Ray, A. Ahmad, D. Verma, S. Bhayye, R. Dubey, H.N. Singh and S. Kumar, *Biomedicines*, **12**, 201 (2024); https://doi.org/10.3390/biomedicines12010201
6. G.M. Cragg and J.M. Pezzuto, *Med. Princ. Pract.*, **25(Suppl. 2)**, 41 (2016); https://doi.org/10.1159/000443404
7. J.A. Brown, S.R. Amend, R.H. Austin, E.U. Hammarlund, R.A. Gatenby and K.J. Pienta, *Mol. Cancer Res.*, **21**, 1142 (2023); https://doi.org/10.1158/1541-7786.MCR-23-0411
8. E. Abdallah, R.R. Mabrouk, M.M.S. Al Ward, S.I. Eissa, E.B. Elkaeed, A.B. Mehany, M.A. Abo-Saif, O.A. El-Feky, M.S. Alesawy and M.A. El-Zahabi, *J. Enzyme Inhib. Med. Chem.*, **37**, 573 (2022); https://doi.org/10.1080/14756366.2021.2017911
9. D. Hanahan and R.A. Weinberg, *Cell*, **144**, 646 (2011); https://doi.org/10.1016/j.cell.2011.02.013

10. G. Sivaiah, R. Raveesha, S.B.B. Prasad, K.Y. Kumar, M.S. Raghu, F. Alharethy, M. Prashanth and B.-H. Jeon, *J. Mol. Struct.*, **1289**, 135877 (2023); https://doi.org/10.1016/j.molstruc.2023.135877
11. U. Anand, A. Dey, A.K.S. Chandel, R. Sanyal, A. Mishra, D.K. Pandey, V. De Falco, A. Upadhyay, R. Kandimalla, A. Chaudhary, J.K. Dhanjal, S. Dewanjee, J. Vallamkondu and J.M. Pérez de la Lastra, *Genes Dis.*, **10**, 1367 (2023); https://doi.org/10.1016/j.gendis.2022.02.007
12. P. Tiwari, B.N. Mishra and N.S. Sangwan, *BioMed Res. Int.*, **2014**, 830285 (2014); https://doi.org/10.1155/2014/830285
13. F. Khan, M.M.R. Sarker, L.C. Ming, I.N. Mohamed, C. Zhao, B.Y. Sheikh, H.F. Tsong and M.A. Rashid, *Front. Pharmacol.*, **10**, 1223 (2019); https://doi.org/10.3389/fphar.2019.01223
14. U.M. Muddapur, S. Manjunath, Y.S. Alqahtani, I.A. Shaikh, A.A. Khan, B.A. Mannasaheb, D. Yaraguppi and S.S. More, *Separations*, **11**, 50 (2024); https://doi.org/10.3390/separations11020050
15. M. Swetha, N. Saritha and N. Devanna, *Int. J. Sci. Eng. Res.*, **9**, 168 (2018).
16. V.A. Khramov, A.A. Spasov and M.P. Samokhina, *Pharm. Chem. J.*, **42**, 29 (2008); https://doi.org/10.1007/s11094-008-0051-8
17. V.R. Netala, T. Hou, R. Devarapogu, M.S. Bethu, Z. Zhang and T. Vijaya, *Heliyon*, **10**, e40850 (2024); https://doi.org/10.1016/j.heliyon.2024.e40850
18. S. Neel, A. Mandal, S. Saha, A. Das, A. Kundu and A. Singh, *Front. Plant Sci.*, **16**, 1508454 (2025); https://doi.org/10.3389/fpls.2025.1508454
19. G. Abbas, A. Al Harrasi, H. Hussain, A. Hamaed and C.T. Supuran, *Bioorg. Chem.*, **86**, 305 (2019); https://doi.org/10.1016/j.bioorg.2019.02.009
20. D. Kumar, M. Binwal, D.U. Bawankule, N.P. Yadav and P.K. Rout, *J. Drug Deliv. Sci. Technol.*, **83**, 104410 (2023); https://doi.org/10.1016/j.jddst.2023.104410
21. L.B. Arun, A.M. Arunachalam, K.D. Arunachalam, S.K. Annamalai and K.A. Kumar, *BMC Complement. Altern. Med.*, **14**, 70 (2014); https://doi.org/10.1186/1472-6882-14-70
22. G.D. Fabio, V. Romanucci, A. De Marco and A. Zarrelli, *Molecules*, **19**, 10956 (2014); https://doi.org/10.3390/molecules190810956
23. Y. Guan, M. Nguyen, A. Robert, Y. Liu and B. Meunier, *RSC Med. Chem.*, **15**, 3048 (2024); https://doi.org/10.1039/D4MD00171K
24. E.F. Pettersen, T.D. Goddard, C.C. Huang, G.S. Couch, D.M. Greenblatt, E.C. Meng and T.E. Ferrin, *J. Comput. Chem.*, **25**, 1605 (2004); https://doi.org/10.1002/jcc.20084
25. H.M. Liu, F. Kiuchi and Y. Tsuda, *Chem. Pharm. Bull.*, **40**, 1366 (1992); https://doi.org/10.1248/cpb.40.1366
26. R. Duan, W. Porter and S. Safe, *Endocrinology*, **139**, 1981 (1998); https://doi.org/10.1210/endo.139.4.5870
27. N.T. Telang, *Int. J. Mol. Sci.*, **23**, 4800 (2022); https://doi.org/10.3390/ijms23094800
28. B.Y. Kim, J. Lee, S.J. Park, O.S. Bang and N.S. Kim, *Evid. Based Complement. Alternat. Med.*, **2013**, 584604 (2013); https://doi.org/10.1155/2013/584604
29. A. Hanif, A.H. Ibrahim, S. Ismail, S.S. Al-Rawi, J.N. Ahmad, M. Hameed, G. Mustufa and S. Tanwir, *Molecules*, **28**, 2812 (2023); https://doi.org/10.3390/molecules28062812
30. J. Howard and A.A. Hyman, *Nature*, **422**, 753 (2003); https://doi.org/10.1038/nature01600
31. Y.N. Cao, L.L. Zheng, D. Wang, X.X. Liang, F. Gao and X.L. Zhou, *Eur. J. Med. Chem.*, **143**, 806 (2018); https://doi.org/10.1016/j.ejmech.2017.11.062
32. A.D. Tangutur, D. Kumar, K.V. Krishna and S. Kantevari, *Curr. Top. Med. Chem.*, **17**, 2523 (2017); https://doi.org/10.2174/1568026617666170104145640
33. P. Banerjee, E. Kemmler, M. Dunkel and R. Preissner, *Nucleic Acids Res.*, **52(W1)**, W513 (2024); https://doi.org/10.1093/nar/gkae303