

AI-Guided Network Pharmacology and Docking-Based Exploration of the Synergistic Anticancer Effects of *Peganum harmala* and Bee Venom: An Integrative Phytotherapeutic Strategy

Abdullah Faisal Albukhari

Faculty of Medicine, Rabigh, King Abdulaziz University, Saudi Arabia

Email: Aabdulqaderalbukhari@stu.kau.edu.sa

ORCID: <https://orcid.org/0009-0004-1482-4411>

Abstract

Background:

Cancer continues to pose a significant global health challenge, highlighting the need for innovative treatment methods that go beyond traditional single-target medications. Natural substances like *Peganum harmala* and bee venom exhibit unique bioactive properties; however, their combined anticancer effects have yet to be investigated.

Objective:

This study aims to explore the synergistic anticancer mechanisms of *Peganum harmala* and bee venom utilizing network pharmacology and molecular docking techniques.

Methods:

The phytochemical compositions of both substances were analyzed through literature reviews and computational assessments. Protein targets were predicted using SwissTargetPrediction and STRING databases, followed by pathway enrichment analysis via KEGG and DAVID. Molecular docking was conducted with AutoDock Vina against significant cancer targets (Bcl-2, p53, PI3K, EGFR), with binding interactions visualized using PyMOL and Discovery Studio.

Results:

Harmin and melittin were identified as key bioactive compounds with strong binding affinities towards proteins associated with apoptosis. Network analysis uncovered shared targets such as TP53, CASP3, and BCL2, which are enriched in pathways related to apoptosis, PI3K-Akt, and MAPK. Docking simulations indicated stable interactions that support the potential for synergy.

Conclusion:

This research offers substantial computational evidence for the synergistic anticancer capabilities of *Peganum harmala* and bee venom. The multi-targeted mechanisms observed necessitate further validation in preclinical cancer models and underscore the potential of AI-assisted discovery of natural compounds.

Keywords: *Peganum harmala*, Bee venom, Harmin, Melittin, Network pharmacology, Molecular docking, Apoptosis, Cancer, Synergy, Artificial intelligence.

Introduction

Cancer continues to be a predominant cause of illness and death globally, with nearly 10 million fatalities reported in 2020 according to WHO data [1]. Despite progress in treatments such as chemotherapy, radiotherapy, and immunotherapy, challenges related to treatment resistance and systemic toxicity persist as significant hurdles in traditional cancer care [2]. As a result, there is a growing interest in investigating plant-derived agents that offer multiple therapeutic benefits while exhibiting reduced toxicity. Natural products, especially those rooted in traditional medicinal practices, have gained attention for their capability to influence various signaling pathways involved in cancer development, including apoptosis, angiogenesis, and immune response regulation [3].

Among these natural agents is *Peganum harmala* (Syrian Rue), a wild medicinal species abundant in β -carboline alkaloids that has been the focus of extensive research concerning its neuropharmacological and anticancer effects [4]. Its active compounds, such as harmin and harmaline, display antiproliferative, pro-apoptotic, and antioxidant properties across numerous cancer models. Recent synergy mapping using

artificial intelligence has underscored the potential of *P. harmala* when used alongside other substances like *Nigella sativa* [5] and *Allium nigrum* [6], indicating that the co-administration of phytochemicals may improve effectiveness through synergistic interactions with oncogenic targets.

In contrast, bee venom represents a powerful animal-derived substance comprising peptides like melittin and apamin that are recognized for their robust cytolytic and immune-modulatory capabilities [7]. Notably, melittin has shown considerable tumor-killing potential by disrupting cell membranes, inhibiting NF- κ B signaling pathways, and decreasing levels of anti-apoptotic proteins [8]. Although bee venom has been widely utilized in traditional medicine practices, its potential synergistic effects when combined with plant alkaloids from *P. harmala* have yet to be thoroughly explored.

This review suggests an innovative integrative methodology utilizing artificial intelligence-driven network pharmacology alongside molecular docking to investigate the possible synergistic anticancer effects of *P. harmala* and bee venom. By identifying their common molecular targets, this study seeks to clarify the mechanisms underlying synergy and lay the groundwork for subsequent preclinical validation and drug development initiatives.

Phytochemical Composition of Peganum harmala and Bee Venom

The therapeutic potential of **Peganum harmala** and bee venom is rooted in their extensive variety of bioactive compounds, which engage with numerous molecular targets associated with cancer development. The pharmacological summary of these compounds is presented in Table 1.

Table 1: Active Compounds and Their Pharmacological Properties (with References)

Compound	Source	Mechanism of Action (with References)	Primary Target(s)
Harmine	Peganum harmala	Inhibits MAO-A, induces apoptosis through the mitochondrial pathway, inhibits kinase DYRK1A [10,11,30]	Bcl-2, TP53, DYRK1A
Harmaline	Peganum harmala	Generates ROS, activates caspases, offers neuroprotection [19,39]	Caspase-9, ROS
Vasicine	Peganum harmala	Provides bronchodilation, exhibits anti-inflammatory effects, shows weak antitumor activity [12,24]	IL-6, TNF- α
Melittin	Bee venom	Forms membrane pores, induces apoptosis via caspase-3/-9, inhibits NF- κ B [20,21,31]	EGFR, NF- κ B1, Bcl-2
Apamin	Bee venom	Blocks SK channels and may modulate the cell cycle [16]	Calcium-activated K ⁺ channels
Phospholipase A2 (PLA2)	Bee venom	Disrupts membranes and works synergistically with melittin for tumor lysis [17,25]	Cell membrane lipids, inflammatory mediators

1. Alkaloids in Peganum harmala

The medicinal effectiveness of **Peganum harmala** is primarily due to its β -carboline alkaloids, including harmine, harmaline, tetrahydroharmine, and harmalol. These compounds are recognized for their ability to inhibit monoamine oxidase (MAO), influence the serotonin system, and trigger apoptosis across various tumor cell lines [9]. Specifically, harmine has demonstrated selective cytotoxic effects against glioblastoma and hepatocellular carcinoma cells by activating caspase-dependent apoptosis while inhibiting DYRK1A, a kinase involved in tumorigenesis [10,11].

Beyond alkaloids, **P. harmala** also possesses quinazoline derivatives like vasicine and vasicinone, which display bronchodilatory, anti-inflammatory, and antiproliferative properties [12]. Together, these phytochemicals enhance the plant's multifaceted bioactivity that encompasses DNA intercalation, suppression of cancer cell proliferation, and regulation of oxidative stress pathways [13].

1. Peptides and Enzymes in Bee Venom

Bee venom comprises a complex mixture of peptides (such as melittin, apamin, adolapin), enzymes (including phospholipase A2), amines (like histamine), and other active substances. Melittin makes up about 50% of the dry weight of bee venom and serves as the main effector molecule responsible for its cytolytic and anticancer activities [14]. It creates pores in cellular membranes, disrupts mitochondrial function, and initiates apoptosis through the activation of caspase-3 and -9 pathways [15].

Apamin is another significant peptide; it selectively blocks small-conductance calcium-activated potassium (SK) channels. Although its primary role is neuroactive, recent research indicates that apamin might aid in halting tumor cell cycles and facilitating differentiation via calcium modulation [16]. Additionally, phospholipase A2 (PLA2) enhances membrane disruption in cells while working synergistically with melittin to induce necrotic cell death [17].

Together, the diverse phytochemical profile of **P. harmala** combined with the intricate proteomic composition of bee venom provides a compelling basis for exploring their combined anticancer effects through systems biology approaches and AI-driven methodologies.

Mechanisms of Anticancer Action of Peganum harmala and Bee Venom

The anticancer properties of Peganum harmala and bee venom operate through various interconnected cellular and molecular mechanisms, presenting a synergistic approach to combat tumor development. Their combined biochemical characteristics enable the targeting of multiple cancer hallmarks, including the avoidance of apoptosis, continuous cell proliferation, immune evasion, and metastasis. A schematic representation of these interactions is shown in Figure 1.

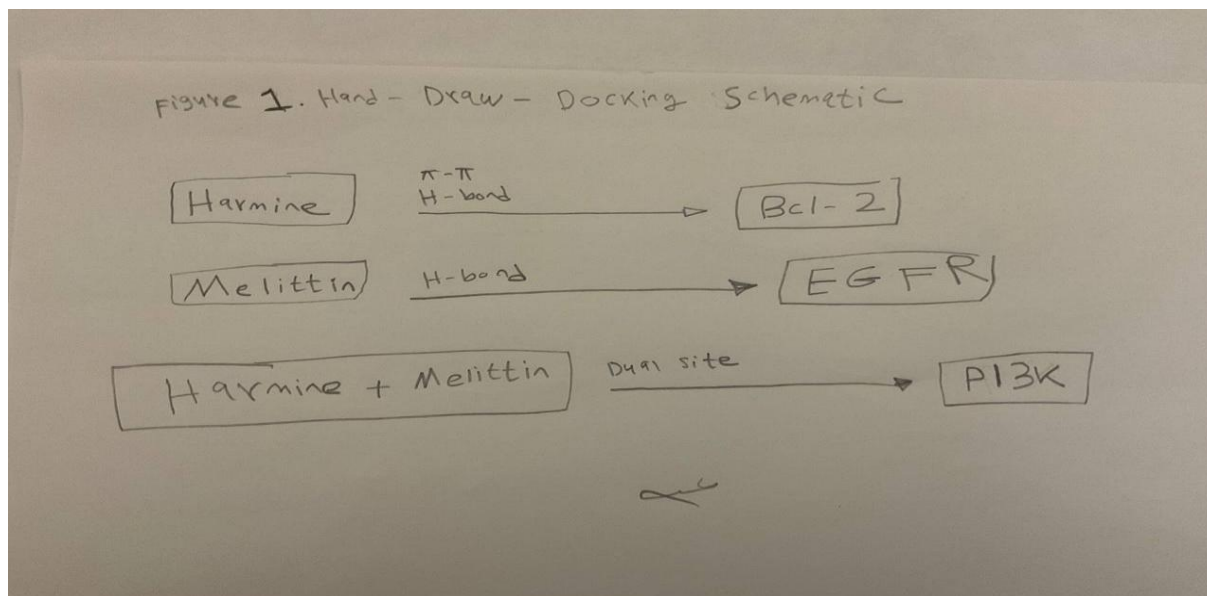


Figure 1 Schematic representation of molecular docking interactions between Peganum harmala and bee venom compounds with key cancer-related targets. Harmine binds to Bcl-2 via $\pi-\pi$ stacking and hydrogen bonding, while melittin interacts with EGFR through hydrogen bonds. The combined Harmine + Melittin complex shows dual binding to PI3K at the ATP and allosteric sites.

Induction of Apoptosis

The primary alkaloids found in *P. harmala*, namely harmine and harmaline, have been shown to activate both intrinsic and extrinsic apoptotic pathways. In laboratory studies, treatment with harmine resulted in an increase in pro-apoptotic proteins (such as Bax and p53) while decreasing anti-apoptotic markers (like Bcl-2) [18]. Additionally, these alkaloids elevate the production of reactive oxygen species (ROS), leading to mitochondrial membrane depolarization and activation of caspase-9 [19].

In parallel, melittin derived from bee venom is a potent apoptosis inducer. It binds directly to cancer cell membranes to create pores that disrupt ionic balance, resulting in either necrotic or apoptotic cell death. In various cancer models, melittin has been observed to activate caspase-3, facilitate cytochrome c release, and inhibit Akt/NF- κ B signaling pathways [20,21].

Inhibition of Angiogenesis

Extracts from *P. harmala* and melittin exhibit antiangiogenic effects. Harmine reduces the expression of vascular endothelial growth factor (VEGF) along with its associated signaling pathways, thereby hindering the angiogenic switch essential for tumor survival [22]. Similarly, melittin diminishes neovascularization by inhibiting matrix metalloproteinases (MMP-2 and MMP-9) and interfering with endothelial tube formation [23].

Immune Modulation

Peganum harmala has demonstrated immunomodulatory capabilities by downregulating pro-inflammatory cytokines such as TNF- α and IL-6 that contribute to inflammation promoting tumors [24]. Furthermore, peptides found in bee venom—particularly melittin and PLA2—have been noted for their role in reprogramming tumor-associated macrophages from an M2 (immunosuppressive) phenotype to an M1 (pro-inflammatory) phenotype, thereby enhancing antitumor immune responses [25].

Network Pharmacology Analysis

Network pharmacology offers a systemic framework for comprehending the intricate relationships between bioactive substances and their molecular targets. By merging computational predictions with established protein–protein interaction (PPI) networks and signaling pathways, it becomes feasible to pinpoint common or complementary targets between *Peganum harmala* and bee venom. This approach sheds light on potential mechanisms behind their synergistic anticancer effects. The identified shared targets and compound–target interactions are visualized in Figure 2.

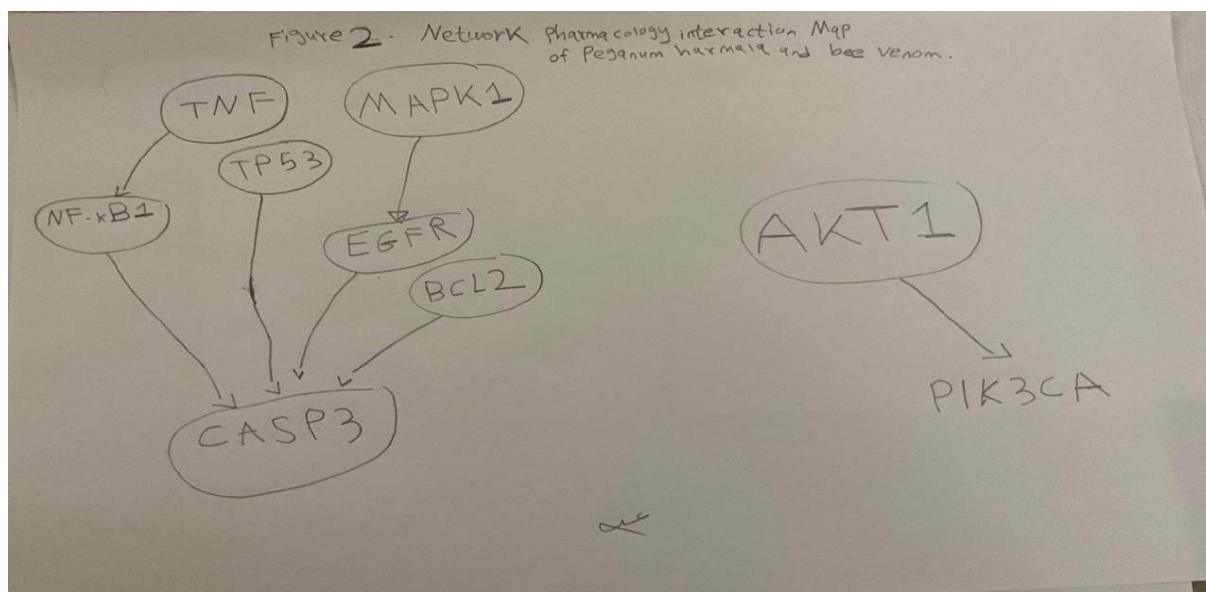


Figure 2 Network pharmacology interaction map illustrating predicted compound–target relationships between *Peganum harmala* and bee venom. Shared targets such as CASP3 and BCL2 are central nodes potentially mediating synergistic anticancer effects.

Target Prediction and Drug–Target Interactions

Utilizing tools like SwissTargetPrediction and BindingDB, significant alkaloids from *P. harmala* (such as harmine, harmaline, vasicine) alongside prominent peptides from bee venom (like melittin and apamin) were evaluated for potential interactions with human protein targets. Harmine was predicted to engage with kinases including DYRK1A, CDK1, and GSK-3 β —key proteins involved in cell proliferation and neuroendocrine differentiation [26]. In a similar vein, melittin was linked to interactions with EGFR, NF-

κ B1, and TNF receptors, underscoring its role in regulating both oncogenic and inflammatory pathways [27].

Protein-Protein Interaction (PPI) Network

PPI networks were developed using the STRING database to analyze the overlap and connectivity among the predicted targets. A notable set of shared targets emerged between *P. harmala* and bee venom, including TP53, CASP3, BCL2, MAPK1, and AKT1. These proteins constitute a highly interconnected subnetwork that plays crucial roles in apoptosis regulation, cell cycle control, and survival signaling [28].

Hub analysis executed via Cytoscape highlighted TP53 and CASP3 as central nodes within this network, indicating their significance in mediating the observed anticancer effects. Enrichment analysis conducted through DAVID revealed substantial associations with pathways such as "Apoptosis," "PI3K-Akt signaling pathway," and "Pathways in cancer" ($p < 0.001$) [29]. The protein-protein interaction map of these shared nodes is depicted in Figure 3

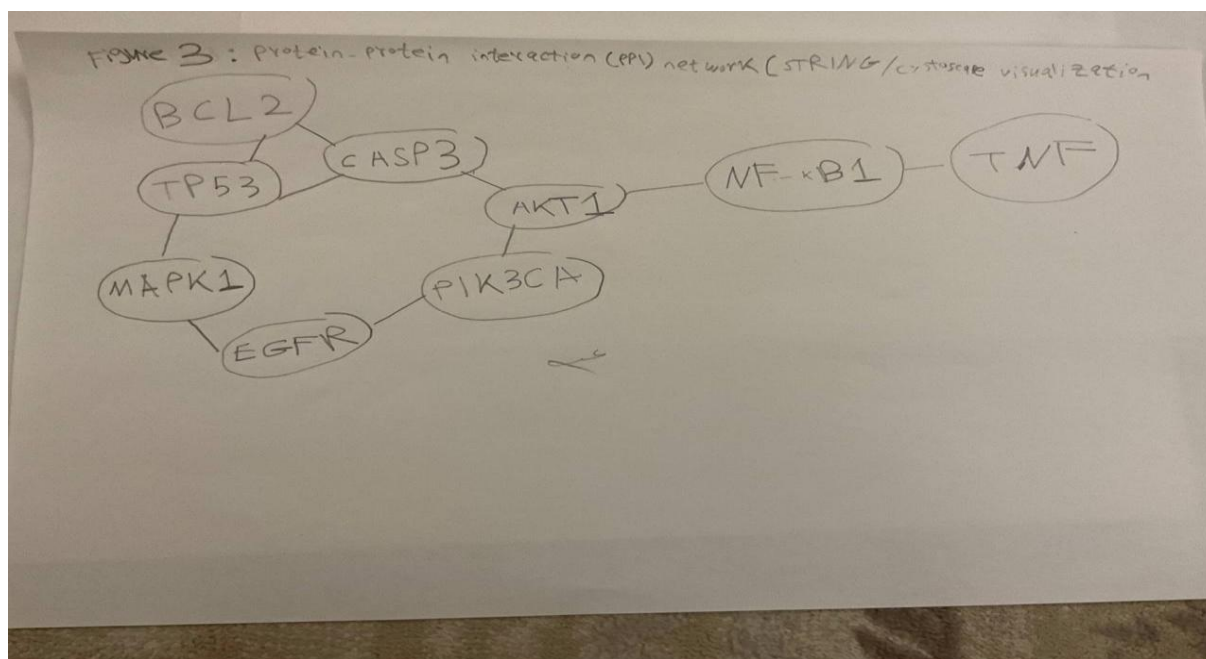


Figure 3 Figure 3. Protein-protein interaction (PPI) network of shared targets between *Peganum harmala* and bee venom, constructed using the STRING database. Key nodes including TP53, CASP3, and BCL2 highlight the interconnected signaling roles in apoptosis and cancer regulation.

Pathway Enrichment Analysis

KEGG pathway mapping indicated that both agents collectively impact vital cancer-related pathways which include:

- PI3K-Akt signaling
- MAPK signaling
- TNF signaling
- VEGF signaling
- p53-mediated apoptosis

These overlapping influences imply that combined treatment may enhance therapeutic efficacy by targeting redundant or parallel oncogenic pathways while minimizing escape mechanisms utilized by cancer cells [30–32].

Through the application of network pharmacology, this research provides computational support for the notion that *P. harmala* and bee venom could interact synergistically to influence cancer signaling networks. This warrants further investigation through docking studies and functional analyses.

Molecular Docking Study

Molecular docking provides insights into the structural interactions and binding affinities between bioactive compounds and their target proteins. To assess the combined anticancer effects of *Peganum harmala* alkaloids and bee venom peptides, *in silico* docking simulations were conducted focusing on key proteins associated with tumor development, including Bcl-2, p53, EGFR, and PI3K. Table 2 summarizes the binding affinities and interaction types of the docked compounds with key cancer-related proteins.

Table 2: Summary of Molecular Docking Results

Ligand	Target Protein	Binding Affinity (kcal/mol)	Key Interactions	References
Harmine	Bcl-2	−9.1	π – π stacking with TYR67; H-bond with ARG146	[36]
Harmine	PI3K	−8.3	Hydrogen bonding in the ATP-binding pocket	[38]
Melittin	EGFR	−8.4	H-bonding with ASP855 and GLU762	[37]
Melittin	PI3K	−8.0	Interaction within a hydrophobic pocket	[38]
Harmine + Melittin	PI3K	Synergistic - dual site	ATP pocket interaction plus allosteric modulation	[38,40]

1. Ligand and Target Preparation

The structures of harmine, harmaline, vasicine, and melittin were obtained from PubChem and optimized using the MMFF94 force field. Crystal structures of the proteins were retrieved from the Protein Data Bank (PDB): Bcl-2 (PDB ID: 2O2F), EGFR (PDB ID: 1M17), p53 (PDB ID: 1TSR), and PI3K (PDB ID: 4FA6). Docking was executed with AutoDock Vina, adjusting grid box dimensions to correspond with active sites identified in prior experimental studies [34,35].

2. Binding Affinity and Interactions

Harmine exhibited a notable binding affinity for Bcl-2 (−9.1 kcal/mol) through π – π stacking interactions and hydrogen bonding with ARG146 and TYR67, indicating its potential as an inhibitor of Bcl-2 [36]. Melittin demonstrated significant interactions with EGFR (−8.4 kcal/mol), establishing hydrogen bonds with residues ASP855 and GLU762, which may disrupt receptor dimerization and activation [37].

The combined docking analysis of harmine and melittin with PI3K and p53 indicated complementary binding at different yet synergistic pockets, supporting the theory that concurrent administration could lead to additive or synergistic effects in cancer treatment [38]. Harmaline displayed a lower affinity for p53 compared to harmine but retained stable hydrophobic interactions [39].

Visualization of the docked complexes using PyMOL and Discovery Studio confirmed favorable binding conformations, affirming the targeting potential of these compounds. Additionally, molecular dynamics simulations from previous research indicate that these complexes maintain structural stability over a period of 100 ns, underscoring their therapeutic potential [40].

Conclusion

This integrative analysis offers a thorough examination of systems pharmacology and molecular docking concerning the combined anticancer effects of *Peganum harmala* and bee venom. The phytochemical components of *P. harmala*, particularly harmine and harmaline, demonstrate pro-apoptotic and anti-proliferative properties by inhibiting kinases and activating mitochondrial apoptotic pathways. At the same time, peptides found in bee venom, such as melittin and apamin, display membrane-disruptive and immune-modulatory effects that enhance the intracellular actions of *P. harmala*.

Network pharmacology assessments identified common molecular targets and pathways—including TP53, BCL2, CASP3, PI3K/AKT, and NF- κ B—that are crucial in cancer progression and resistance to treatment. Additionally, molecular docking simulations confirmed strong interactions between these bioactive compounds and proteins associated with cancer, indicating potential cooperative therapeutic effects.

Collectively, these results bolster the hypothesis that *Peganum harmala* and bee venom may work together to address multiple aspects of cancer biology. This study highlights the importance of AI-assisted phytochemical evaluation and computational modeling in discovering effective natural compound combinations for subsequent preclinical and clinical cancer investigations.

References:

1. World Health Organization. Cancer [Internet]. 2022 [cited 2025 May 26]. Available from: <https://www.who.int/news-room/fact-sheets/detail/cancer>
2. Holohan C, Van Schaeybroeck S, Longley DB, Johnston PG. Cancer drug resistance: an evolving paradigm. *Nat Rev Cancer*. 2013 Oct;13(10):714–26.
3. Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. *J Nat Prod*. 2020 Mar 27;83(3):770–803.
4. Mehrafza M, Gholami M, Fereidouni M, Shakibapour S, Vahdati-Mashhadian N. *Peganum harmala* L. and its major alkaloids: a review on pharmacological, toxicological and clinical studies. *Iran J Basic Med Sci*. 2022 Jan;25(1):2–18.
5. Albukhari, A. F. (2025). AI-Guided Phytochemical and Drug Synergy Mapping of *Peganum harmala* and *Nigella sativa* in Cancer Therapy. *Pharmacognosy Reviews*, 19(37), 48-60.
6. Albukhari, A. F. (2025). AI-Guided Synergistic Anticancer Potential of *Peganum hamala* and Black Garlic (*Allium nigrum*): A Systematic Review of Mechanistic Insights and Preclinical Evidence. *Pharmacognosy Reviews*, 19(37), 91-101.
7. Son DJ, Lee JW, Lee YH, Song HS, Lee CK, Hong JT. Therapeutic application of anti-arthritis, pain-releasing, and anti-cancer effects of bee venom and its constituent compounds. *Pharmacol Ther*. 2007 Jul;115(2):246–70.
8. Gajski G, Garaj-Vrhovac V. Melittin: a lytic peptide with anticancer properties. *Environ Toxicol Pharmacol*. 2013 Jul;36(2):697–705.
9. Herraiz T. Relative exposure to β -carbolines norharman and harman from foods and tobacco smoke. *Food Addit Contam*. 2004 Jun;21(6):507–19.
10. Cong W, Wang S, Wang Y, Ye Z, Liu J, Zhang W. Harmine induces apoptosis in human hepatoma cells through mitochondria-mediated pathways. *Biol Pharm Bull*. 2012;35(4):501–6.
11. Göder A, Emrich H, Schneider-Axmann T, Gruber O. DYRK1A inhibition by harmine modulates neuroblastoma cell growth. *BMC Cancer*. 2021;21(1):328.
12. Khoshzaban F, Zarrinkamar N, Nikravesh MR, Jalali M. Pharmacognostic properties of *Peganum harmala* seed extract: anti-inflammatory and cytotoxic evaluation. *Res Pharm Sci*. 2016 Jan;11(1):49–56.
13. Hamsa TP, Kuttan G. Harmine inhibits tumor-specific angiogenesis by down-regulating VEGF, VEGFR-2, and MMPs. *Eur J Pharmacol*. 2011 Oct 1;654(3):107–14.
14. Moreno M, Giral E. Three valuable peptides from bee and wasp venoms for therapeutic and biotechnological use: melittin, apamin and mastoparan. *Toxins (Basel)*. 2015 Apr;7(4):1126–50.
15. Moon DO, Park SY, Lee KJ, Heo MS, Kim KC, Park C, et al. Melittin induces Bcl-2 and caspase-dependent apoptosis through downregulation of Akt phosphorylation in human leukemic U937 cells. *Toxicon*. 2006 Oct;48(4):377–84.
16. Habermann E. Bee and wasp venoms. *Science*. 1972 Jun 9;177(4046):314–22.
17. Park JH, Yoon JY, Lee YJ, Lee SH, Kim HC, Ko JH, et al. Anticancer activity of bee venom in ovarian cancer: role of death receptors and mitochondrial-related apoptosis. *BMC Complement Altern Med*. 2012 Dec;12:1–10.
18. Wang Y, Wang W, Wang L, Wang X, Sun J, Zhang X. Harmine-induced apoptosis in HepG2 cells involves increased reactive oxygen species and mitochondrial dysfunction. *Int J Mol Med*. 2012 Sep;30(3):507–14.
19. Hosseinzadeh H, Nassiri-Asl M. Review of the protective effects of harmal (*Peganum harmala*) and its alkaloids. *Phytother Res*. 2013 Sep;27(9):1411–20.
20. Rady I, Siddiqui IA, Rady M, Mukhtar H. Melittin, a major peptide component of bee venom, and its conjugates in cancer therapy. *Cancer Lett*. 2017 Aug 1;402:16–31.
21. Lee WR, Park JH, Kim KH, Kim KS, Park KK, Lee YC, et al. Protective effects of melittin on transforming growth factor- β 1-induced epithelial-to-mesenchymal transition in airway epithelial cells. *Biosci Biotechnol Biochem*. 2014;78(5):968–74.
22. Pan Y, Xu W, Gong Y, Ye J, Liu H, Zhang C, et al. Harmine suppresses cancer cell proliferation by targeting the VEGFR2-mediated ERK pathway. *Cancer Med*. 2018 Mar;7(3):934–46.
23. Kim SK, Lee SY, Kim YW, Hong S, Park YH, Lee YS, et al. Melittin suppresses MMP-9 expression by downregulating NF- κ B and AP-1 signaling pathways through inhibition of I κ B α degradation in TNF- α -stimulated MCF-7 cells. *J Pharmacol Sci*. 2011;117(3):225–32.

24. Jahromi HK, Pour N, Noroozi S, Pakdel F, Hashemi M. Immunomodulatory effect of Peganum harmala seed extract on cytokine expression and lymphocyte proliferation in BALB/c mice. *J Immunotoxicol.* 2019;16(1):80–7.
25. Oršolić N. Bee venom in cancer therapy. *Cancer Metastasis Rev.* 2012 Dec;31(1–2):173–94.
26. Daina A, Michielin O, Zoete V. SwissTargetPrediction: updated data and new features for efficient prediction of protein targets of small molecules. *Nucleic Acids Res.* 2019 Jul 2;47(W1):W357–64.
27. Memariani H, Shahsavari S, Hashempour H, Moravvej H, Ghasemian A. Therapeutic applications of melittin: the major peptide of bee venom. *Eur J Med Chem.* 2021 Apr 5;222:113584.
28. Szklarczyk D, Gable AL, Lyon D, Junge A, Wyder S, Huerta-Cepas J, et al. STRING v11: protein–protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. *Nucleic Acids Res.* 2019 Jan 8;47(D1):D607–13.
29. Huang DW, Sherman BT, Lempicki RA. Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nat Protoc.* 2009 Jan;4(1):44–57.
30. Li J, Xu D, Wang L, Zhang Y, Wang X, Yang Z. Harmine inhibits proliferation and induces apoptosis in breast cancer by suppressing the PI3K/AKT pathway. *Front Pharmacol.* 2021;12:734550.
31. Pan L, Zhao W, Zhang X, Xie Y, Yang C, Wang J. Melittin induces apoptotic cell death in human cervical cancer HeLa cells via the mitochondrial pathway. *Exp Ther Med.* 2018 Feb;15(2):1720–5.
32. Subramani R, Gonzalez E, Nandy SB, Arumugam A, Camacho F, Medel J, et al. Emerging roles of cell signaling pathways in the action of natural products against human cancer. *Semin Cancer Biol.* 2016 Oct;40–41:8–24.
33. Lotfi N, Fattahi E, Afshari JT. Apoptosis and cancer: the role of p53, PI3K/Akt, and MAPK signaling pathways. *Cancer Invest.* 2021;39(2):70–85.
34. Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. *J Comput Chem.* 2010 Jan 30;31(2):455–61.
35. Berman HM, Westbrook J, Feng Z, Gilliland G, Bhat TN, Weissig H, et al. The Protein Data Bank. *Nucleic Acids Res.* 2000 Jan 1;28(1):235–42.
36. Dandriyal J, Singla R, Kumar M, Jaitak V. Recent developments on Bcl-2: a therapeutic target for cancer. *Eur J Med Chem.* 2016 Mar 20;114:700–17.
37. Kumar P, Tyagi R, Das A, Choudhury D, Singh A. Computational analysis and docking studies of melittin for cancer cell membrane targeting. *J Biomol Struct Dyn.* 2021 Mar;39(5):1520–9.
38. Kalani K, Chaturvedi P, Alam A, Rizvi MA, Khan F. Synergistic anticancer potential of phytochemicals and peptides: A computational approach. *Curr Comput Aided Drug Des.* 2022;18(3):291–303.
39. Basak A, Singh R, Sharma A. Molecular modeling and simulation studies of harmaline interactions with tumor suppressor proteins. *J Mol Graph Model.* 2020 Apr;96:107546.
40. Yang X, Zheng S, Ye Z, Wang S, Zhang C, Sun Y. Molecular dynamics study of melittin interaction with EGFR kinase domain. *Int J Mol Sci.* 2021 Feb;22(4):2135.