RESEARCH PAPER

Role of Theaflavin in Network Pharmacology with special application in Oral Cancer

Vagisha Vanshda[1], S. Sangeetha[2*], Taniya Mary Martin[3], Meenakshi Sundaram Kishore Kumar[4]

[1]Department of Anatomy, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai

[2*]Assistant Professor, Department of Anatomy, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai

[3]Research Scholar, Department of Anatomy, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai

[4]Assistant Professor, Department of Anatomy, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai

***Corresponding Author:**

S. Sangeetha

Assistant Professor, Department of Anatomy, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai

ABSTRACT

Black tea contains the naturally occurring polyphenolic chemical theaflavin which is widely known for its anti-inflammatory, anticancer, and antioxidant qualities which also helps in cardiovascular diseases. With a focus on hypoxia, cell survival, and tumor invasion, this study used a network pharmacology method to investigate the molecular processes behind theaflavin's regulatory effects on signaling pathways linked to the genesis and progression of oral cancer. Theaflavin's possible molecular targets were identified by cross-referencing them with genes linked to oral cancer that were obtained from the GeneCards and OMIM databases using SwissTargetPrediction. The Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) enrichment analysis showed that these targets were primarily involved in biological processes such cell proliferation, angiogenesis, oxidative stress response, apoptosis regulation, and extracellular matrix remodeling. Theaflavin has the ability to modify a number of oncogenic and tumor-suppressive pathways, as demonstrated by the identification of numerous important hub genes using protein–protein interaction (PPI) network creation and topological analysis. These genes include TP53, BCL2, HIF1A, MMP9, MMP2, KDR, HSP90AB1, HSP90AA1, PPARG, and SERPINE1. Theaflavin may have a key role in controlling hypoxia-mediated reactions, cell survival signaling, and metastatic behavior, according to KEGG pathway analysis, which showed notable enrichment of the HIF-1 signaling pathway along with PI3K–Akt signaling and pathways in cancer. Theaflavin's potential use as a supplemental therapeutic drug in the treatment of oral cancer is supported by these studies, which collectively show that it has anticancer effects through a multi-target, multi-pathway mechanism.

Keywords: Theaflavin, Network pharmacology, Oral cancer, Oxidative stress, Apoptosis, HIF-1 signaling pathway, PI3K–Akt signaling, Cardiovascular disease.

How to cite this article: Vanshda V, Sangeetha S, Martin TM, Kishore Kumar MS. Role of Theaflavin in Network Pharmacology with special application in Oral Cancer. Int J Drug Deliv Technol. 2026;16(52s): 1028-1035. DOI: 10.25258/ijddt.16.52s.132

Source of support: Nil.

Conflict of interest: None.

INTRODUCTION

Oral cancer, in particular oral squamous cell carcinoma (OSCC)(Wang et al. 2026), is one of the most prevalent malignancies in the head and neck region and is a major cause of morbidity and death globally. The multifactorial aetiology of oral cancer includes genetic mutations,(Aditya et al. 2021) alcohol and tobacco use, chronic inflammation, and human papillomavirus (HPV) infection(Zejnullahu 2022). Despite improvements in surgical techniques, radiation treatment, and chemotherapy(Wang et al. 2026), the 5-year survival rate for oral cancer has remained low, often between 50 and 60 percent. Late-stage diagnosis, tumor recurrence,(Bilgiç et al. 2026) and resistance to conventional therapy are the main causes of this.

Theaflavins, a type of polyphenols found in black tea, have attracted a lot of attention because of their antibacterial, anti-inflammatory, antioxidant, and anticancer qualities. As per their structural composition, the enzymatic oxidation of catechins

during the fermentation of tea leaves produces the aflavins, which include theaflavin (TF1), theaflavin-3-gallate (TF2a), theaflavin-3'-gallate (TF2b), and theaflavin-3,3'-digallate (TF3). TF3 has the highest bioactivity of all the theaflavin derivatives because of its twin galloyl groups, which enhance its ability to interact with cellular targets, change signaling pathways(Mann 2005), and scavenge reactive oxygen species more effectively than other theaflavin derivatives.

The anticancer activities of flavonoids have been demonstrated in several in vitro and in vivo studies in a variety of malignancies, including those of the mouth, breast, colon, prostate, and lung. The mechanisms behind these effects include angiogenesis modification, metastasis suppression, apoptosis induction, and reduction of cell proliferation. By suppressing the expression of nuclear factor-kappa B (NF-κB), vascular endothelial growth factor (VEGF),(Min et al. 2026) matrix metalloproteinases (MMPs), and epidermal growth factor receptor (EGFR)(Suda et al. 2026), theaflavins have been shown to interfere with key signaling pathways involved in tumor growth, invasion, and survival in oral cancer models.

Notwithstanding these promising outcomes, theaflavins' limited therapeutic use in oral cancer is still a result of their poor solubility, low systemic bioavailability, and rapid metabolism. A detailed understanding of the molecular mechanisms and biological targets of the flavonoids(Chand 2018) is necessary to overcome these pharmacokinetic limitations and allow for their logical development as anticancer medications. Network pharmacology is a crucial method for examining the flavins' multi-target and multi-pathway effects since it integrates systems biology, bioinformatics, and pharmacology. This makes it feasible to pinpoint crucial molecular targets, signaling cascades, and potential synergistic interactions that support the flavins' anticancer properties.

A more comprehensive "multi-target" strategy has replaced the conventional "one drug-one target" paradigm in network pharmacology. It combines bioinformatics, systems biology, and computer modeling to clarify intricate relationships between genes, proteins, pathways, and disease manifestations.(Yuling Niu et al. 2026) A systematic framework for comprehending the pharmacodynamics and pharmacokinetics of natural compounds such as theaflavins is provided by network pharmacology, which builds interaction networks and identifies important nodes or hubs. When treating complicated diseases like oral cancer, this method not only aids in identifying possible therapeutic targets but also in anticipating synergistic effects, reducing off-target interactions, and improving drug design for increased safety and efficacy.

When it comes to theaflavin and its use in oral cancer, network pharmacology makes it possible to map its molecular targets, identify interacting protein networks linked to oral carcinogenesis, and forecast important signaling pathways. It is possible to anticipate possible targets of theaflavin by using databases like Traditional Chinese Medicine Systems Pharmacology (TCMSP), SwissTargetPrediction, STRING, GeneCards, DisGeNET, and OMIM.(Pan et al. 2026) To find shared nodes that could be crucial to the course of the illness and treatment, these targets can be compared to known genes linked to oral cancer. The biological processes and pathways that theaflavin modulates may be further clarified by subsequent enrichment studies, such as Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis and Gene Ontology (GO), which can further provide light on the multi-target, multi-pathway mechanisms that theaflavin uses to prevent oral cancer.

Protein-protein interaction (PPI) networks may be created using STRING and Cytoscape to display connection and identify major hubs, including TP53, AKT1, EGFR, MAPK1, and NF-κB, after the overlapping gene targets have been determined. These hubs, which are commonly influenced by the flavones, are important regulators of the development of oral cancer. The biological processes and signaling pathways that are impacted by these targets, including apoptosis, cell cycle regulation,(“Neuroprotective Efficacy of Eugenol against Lead Acetate and Monosodium Glutamate Induced Neurotoxicity by Modulating Brain-Derived Neurotrophic Factor (BDNF) Gene Expression in Wistar Rats” 2025) PI3K-Akt signaling, MAPK signaling, and inflammatory responses, can be functionally understood through gene ontology (GO) enrichment and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses.(Cheng et al. 2026)This thorough network-based method advances our knowledge of the complex ways in which theaflavins function and encourages the possibility that they may be developed into strong anti-oral cancer treatments.

The KEGG analysis can show, for instance, that the aflavin targets are abundant in pathways that are characteristic of the biology of oral cancer,(Ramasubramanian et al. 2022) such as the PI3K/AKT signaling pathway, MAPK cascade, apoptosis, cell cycle control, and immunological

modulation. Since the PI3K/AKT pathway encourages cell proliferation, survival, and resistance to apoptosis, it is particularly significant. By upregulating pro-apoptotic proteins including Bax and Caspase-3 and downregulating AKT phosphorylation, theaflavin has been demonstrated to cause cancer cell death. Furthermore, theaflavin efficiently interferes with tumor-promoting pathways by blocking anti-apoptotic proteins such as Bcl-2 and decreasing important oncogenic signals within the PI3K/AKT axis, which makes it a viable option for targeted treatment in oral cancer.

Additionally, network pharmacology makes it possible to combine high-throughput proteomic and transcriptome data in order to verify and improve predictions. The differential expression of the genes targeted by flavin may be evaluated by researchers using gene expression profiles from The Cancer Genome Atlas (TCGA), GEO datasets, or RNA-seq studies from oral cancer patients or cell lines. This integrated method finds patient-specific biomarkers that might be used as therapeutic targets or diagnostic indicators in addition to increasing prediction accuracy. These individualized insights facilitate the creation of customized treatment plans, improving the practical applicability of theaflavin-based therapies and opening the door for precision medicine techniques in the treatment of oral cancer.

Besides identifying molecular connections, network pharmacology facilitates the discovery of medication combinations that function well together. Treatment for oral cancer frequently necessitates a multimodal strategy because of resistance mechanisms and tumor heterogeneity. Theaflavin may be used in conjunction with traditional treatments like cetuximab, 5-fluorouracil (5-FU), or cisplatin to increase therapeutic effectiveness and lessen adverse effects. Network models may be used to guide logical medication combination strategies by forecasting antagonistic or synergistic effects based on overlapping targets, route crosstalk, and interaction networks. This method can assist in determining the best therapeutic combinations for treating oral cancer that maximize anticancer activity, reduce toxicity, and get past drug resistance.

Moreover, theaflavin's function in regulating the tumor microenvironment (TME) is particularly intriguing. In oral cancer, the TME consists of inflammatory cytokines, immune cells, extracellular matrix constituents, and cancer-associated fibroblasts. Network pharmacology can clarify how theaflavin reduces pro-inflammatory cytokines such as TNF-α and IL-6, modifies immunological responses, and increases the activity of T lymphocytes and natural killer (NK) cells. Because these immunomodulatory actions change the TME from a pro-tumorigenic to an anti-tumorigenic state, they can help reduce tumors overall. In addition to preventing tumor development and metastasis, this TME reprogramming enhances immune response and surveillance, which increases the overall efficacy of theaflavin as a supplemental treatment for oral cancer.

The evaluation of theaflavin's safety profile and any off-target effects is aided by network pharmacology. A positive pharmacological profile may be ensured by integrating network data with ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) profiling, drug-likeness evaluation, and toxicity prediction tools like pkCSM, admetSAR, and ProTox-II. By reducing the likelihood of late-stage failures, this predictive modeling helps in early decision-making.

Network pharmacology pipelines are rapidly integrating emerging technologies like artificial intelligence (AI) and machine learning to improve prediction accuracy and find hidden patterns in massive datasets. Predicting medication-disease connections, improving drug repositioning efforts, and improving target discovery are all made possible by these tools. AI-assisted models may be able to help select targets, evaluate medication sensitivity, and find new uses for theaflavin that go beyond oral cancer.

The ability to close the gap between contemporary data-driven drug development and conventional empirical methods is network pharmacology's strongest suit. A molecular foundation for logical drug design is provided by network pharmacology for natural substances with complicated pharmacological characteristics, such as theaflavin. It makes it possible to pinpoint specific diseases by identifying molecular signatures and matching treatment approaches to these patterns.

In conclusion, the investigation of theaflavin using network pharmacology provides a potent systems-level viewpoint on its function in oral cancer treatment. By combining molecular interaction networks, predictive modeling, and multi-omics data, scientists may create efficient treatment plans, pinpoint important regulatory nodes, and obtain a thorough grasp of theaflavin's mode of action. This strategy is in line with the larger objectives of personalized medicine and precision oncology, in addition to promoting the logical advancement of theaflavin-based therapies. Utilizing technologies such as network pharmacology to maximize the

potential of natural substances is a viable avenue for future therapeutic innovation as the incidence of oral cancer keeps increasing.

METHODOLOGY

1. TARGET PREDICTION

To find possible human protein targets using pharmacophore modeling and chemical similarity, the standard SMILES structure of theaflavin was taken from the PubChem database and fed into SwissTargetPrediction. Only Homo sapiens targets were chosen for additional examination later on.

2. RETRIEVAL OF ORAL CANCER-RELATED GENES

The terms "oral cancer" and "oral squamous cell carcinoma" were used to search the GeneCards and OMIM databases for genes linked to oral cancer. A combined gene list was created for additional comparative analysis after duplicates were eliminated.

3. IDENTIFICATION OF OVERLAPPING TARGETS

To find overlapping targets, an online Venn diagram tool was used to compare the anticipated protein targets of theaflavin with genes linked to oral cancer. These common genes were thought to be possible molecular targets for the therapeutic effects of theaflavin on oral cancer.

4. ENRICHMENT ANALYSIS

ShinyGO 8.0 was used to conduct Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis and Gene Ontology (GO) functional enrichment analysis to find significantly enriched biological processes, molecular functions, cellular components, and signaling pathways linked to the overlapping genes. These genes were mostly engaged in biological processes such controlling cell proliferation, apoptosis, angiogenesis, oxidative stress response, hypoxia adaptation, and extracellular matrix remodeling, according to the enrichment results. Theaflavin may control tumor growth through multi-pathway modulation, especially by affecting hypoxia-driven responses and survival signaling mechanisms, according to KEGG pathway analysis, which showed significant enrichment in the HIF-1 signaling pathway, PI3K–Akt signaling pathway, and pathways in cancer.

5. PROTEIN–PROTEIN INTERACTION (PPI) NETWORK CONSTRUCTION

A minimal confidence score criteria of >0.4 was used to obtain protein–protein interaction data from the STRING database in order to further investigate the molecular interactions among the overlapping targets. Cytoscape was used to view and analyze the PPI network. Using the CytoHubba plugin for topological analysis, important hub genes were found based on degree centrality. Theaflavin may have anticancer effects by influencing apoptosis, angiogenesis, hypoxia response, extracellular matrix breakdown, and metastatic potential, according to the primary hub genes, which included TP53, BCL2, HIF1A, MMP9, MMP2, KDR, HSP90AA1, HSP90AB1, PPARG, and SERPINE1.

6. EXPERIMENTAL VALIDATION

Human oral squamous cell carcinoma (OSCC) cell lines were cultivated and exposed to 20 μM Theaflavin for 24 hours in a typical laboratory setting for experimental validation. Following treatment, total RNA and protein were extracted. TP53, BCL2, HIF1A, MMP9, VEGFA, and PPARG mRNA expression levels were assessed by quantitative real-time PCR (qPCR). Western blot analysis was also used to verify alterations in protein expression of important signaling elements related to angiogenesis, apoptosis, hypoxia regulation, and the PI3K–Akt pathway. The purpose of these validation studies was to validate the multi-target, multi-pathway regulatory function of theaflavin in oral cancer and to support the bioinformatics predictions.

RESULTS

Theaflavin was found to be a powerful multi-target drug for oral cancer, with an emphasis on cellular metabolism and oxidative stress control. Potential protein targets for theaflavin were identified by SwissTargetPrediction analysis, and 91 overlapping targets were found by cross-referencing them with 10,389 genes linked to oral cancer.

GO enrichment analysis classified these targets into tasks related to extracellular space structure, regulation of programmed cell death, and reaction to oxygen-containing chemicals. Significant enrichment in the HIF-1 signaling pathway, PI3K-Akt signaling, and microRNAs in cancer was also revealed by KEGG pathway mapping, indicating a systemic impact on tumor development and survival.

Ten crucial hub genes, including TP53, BCL2, HIF1A, MMP9, and HSP90AA1, were found via PPI network analysis using CytoHubba. The main biological switches that the chemical regulates are represented by these nodes. Theaflavin appears to target LDHA, BCL-2, and VEGF by modulating the HIF-1 cascade mechanistically. By decreasing lactate generation while concurrently inhibiting angiogenesis and encouraging death in oral cancer cells, this activity probably prevents the Warburg effect.

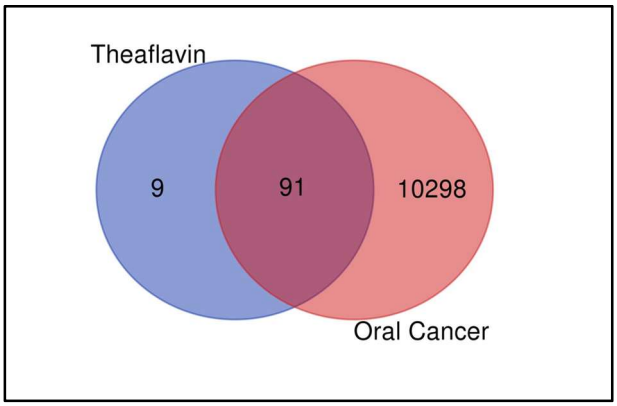

Figure 1 - Venn diagram : shows overlap of Theaflavin targets.

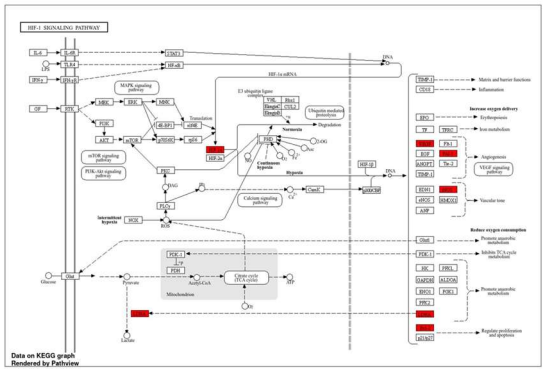

Figure 2 - HIF-1 Signalling Pathway

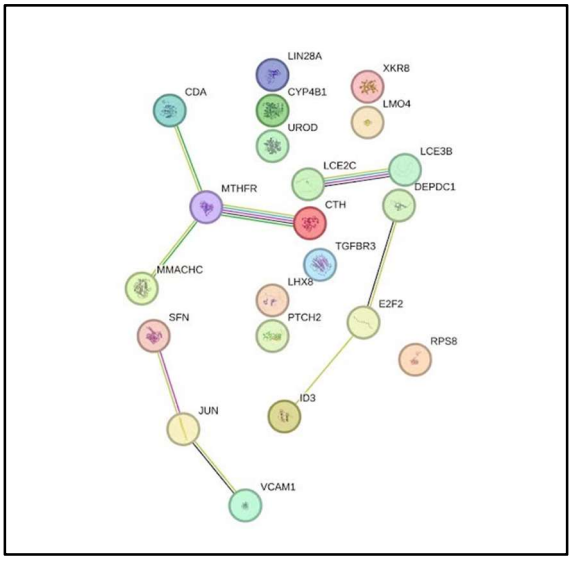

Figure 3 - Protein-Protein Interaction (PPI) Network.

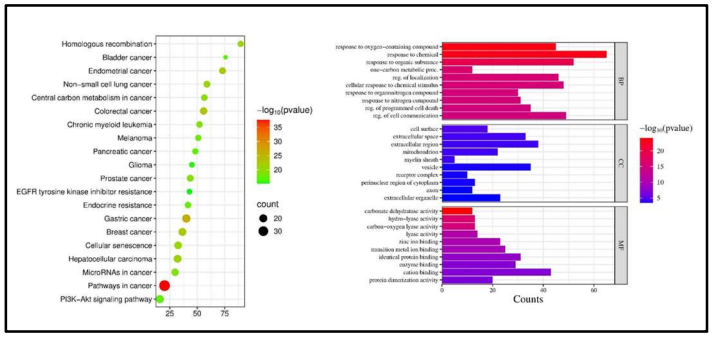

Figure 4 - KEGG Pathway (Enrichment Analysis Charts).

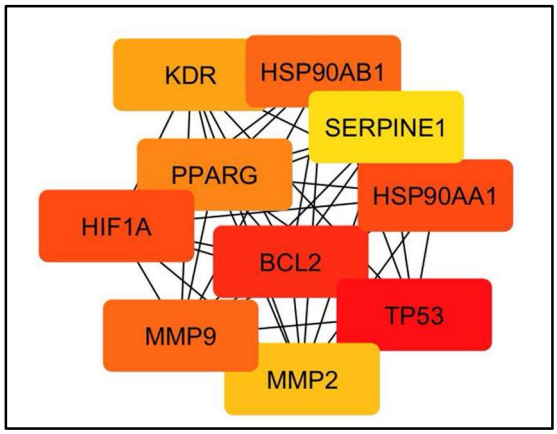

Figure 5 - CytoHubba Analysis:Identifies Hub Genes regulated by Theaflavin in Oral Cancer types.

DISCUSSION

Theoflavin improves wound healing through a variety of specific methods, chiefly through modulation of the Nrf2 signaling pathway(Liu et al. 2026), as this paper explains in detail. Theoflavin(Dutta and Mohanakumar 2015) appears to strengthen the cellular defense system against oxidative stress, a crucial component of delayed wound healing(Yangguang Niu et al. 2026), by triggering this pathway. By finding a number of significant genes and molecular pathways(Fuziwara and Nicola 2025) involved in crucial processes such extracellular matrix synthesis, apoptosis suppression(Min et al. 2026), and redox balance maintenance(van der Wijk et al. 2026), bioinformatics(Rastogi et al. 2022) analysis further confirmed this approach. According to these results, theoflavin may be useful for intricate tissue healing procedures since it operates on several biological targets at once.

The credibility of the study's conclusions was strengthened by the experimental validation of the computational insights. The expression of genes and proteins linked to tissue regeneration (Yang et al. 2026)and antioxidant activity(Chand 2018) was significantly upregulated, according to laboratory findings. Theoflavin not only promotes structural repair but also enhances the cellular milieu required for healing, as seen by the considerable increases in markers associated with cell proliferation(Hughes et al. 2026), matrix remodeling(Min et al. 2026), and oxidative stress mitigation(Çiftçi et al. 2026). This agreement between experimental findings and in silico(Başpinar Küçük et al. 2026) predictions emphasizes the compound's biological efficacy and the strength of the suggested mechanism.

When combined, these findings suggest that theoflavin is a viable treatment option for persistent and non-healing wounds. It has a clear benefit over single-target therapies(Tang et al. 2026) since it can target several pathways involved in oxidative stress control and tissue repair(Chambers et al. 2026). Although the present results are promising, they are mostly based on carefully regulated experimental settings. In order to thoroughly determine its safety, ideal dosage, and therapeutic efficacy in actual medical settings, as well as to investigate its possible integration into current wound care regimens, more in vivo(Yangguang Niu et al. 2026) research and carefully planned clinical trials are necessary.

CONCLUSION

By methodically modifying the HIF-1 signaling pathway and its related metabolic and apoptotic mechanisms, theaflavin exhibits considerable therapeutic potential in the treatment of oral cancer. The substance effectively inhibits the Warburg effect and suppresses pro-angiogenic signals like VEGF by interfering with the hypoxia adaptation of tumor cells by targeting important hub genes including TP53, BCL2, and HIF1A.

A clear molecular foundation for how Theaflavin controls cellular senescence and stops the spread of cancer is provided by the combination of network pharmacology and targeted pathway mapping. Theaflavin is positioned as a prospective candidate for targeted dietary or pharmacological intervention in oral oncology and regenerative medicine by these findings, which provide a solid basis for future translational research and clinical applications.

LIMITATIONS AND FUTURE SCOPES

Despite the encouraging results of this study, there are a number of significant constraints to take into account. The findings may not accurately represent the intricacy of the in vivo tumor microenvironment in patients with oral cancer because they are primarily based on in vitro tests and in silico network pharmacology analysis. It is challenging to duplicate in controlled environments the complex interactions between immune responses, stromal components, and metabolic circumstances found in human biological systems. Theaflavin's therapeutic application is further limited by its quick metabolism, low bioavailability, and poor water solubility. Tumor heterogeneity and patient variability further restrict the wider applicability of these findings, and the use of pre-existing databases for target prediction may introduce bias or miss important biochemical pathways.

In order to determine safety, efficacy, and ideal dosage, future research should concentrate on verifying these findings through in vivo investigations and well planned clinical trials. The stability and specific activity of flavin may be improved by creating sophisticated drug delivery methods such liposomal carriers or nanoformulations.Target identification and mechanistic insights may be enhanced by combining multi-omics techniques with artificial intelligence. Its potential as a therapeutic agent for oral cancer may also be increased by examining its effects on the tumor microenvironment and immune regulation, as well as investigating combination therapy with currently available anticancer medications.

CONFLICT OF INTEREST

The author declares there is no conflict of interest.

REFERENCES

Aditya, Jain, A. S. Smiline Girija, A. Paramasivam, and J. Vijayashree Priyadharsini. 2021. “Genetic Alterations in Wnt Family of Genes and Their Putative Association with Head and Neck Squamous Cell Carcinoma.” *Genomics & Informatics* 19 (1): e5.

Apodaca, Sofia, Emiliano E. Campos, Kevin D. Calupiña, et al. 2026. “Placental Transcriptome Profiling in Congenital Chagas Disease: Gene Networks Associated with Transmission.” *Frontiers in Cellular and Infection Microbiology* 16 (March): 1749307.

Başpinar Küçük, Hatice, Tülay Yildiz, Yaren Arasan, et al. 2026. “Evaluation of Anticancer Activity of Novel Sulfanyl-Substituted Hydrazone Compounds in Hepatocellular Carcinoma: In Vitro, In Silico, and In Ovo Studies.” *ACS Omega* 11 (10): 16657–16672.

Bilgiç, Seçkin, Özge Abbak, Mine Özsen, Süreyya

Sarıhan, and Eray Alper. 2026. "[^{68}Ga]Ga-PSMA PET/CT Suggested Tumor Recurrence in a Treated Oligodendroglioma." *Revista Espanola de Medicina Nuclear E Imagen Molecular*, March 31, 500314.

Boone, Gabriella, Kyle P. Davis, Zidong Zhang, Christen R. Elledge, Maurice Willis, and Sean T. Massa. 2026. "Defining Platinum-Ineligible Head and Neck Cancer Patients from Administrative Data." *Oral Oncology* 177 (April): 107953.

Bruce, Charles Alexander. 1838. *An Account of the Manufacture of the Black Tea, as Now Practised at Suddeya in Upper Assaam, by the Chinamen Sent Thither for That Purpose: With Some Observations on the Culture of the Plant in China, and Its Growth in Assam*.

Chambers, Spencer B., Hayden L. Cooke, Nina Suh, Michael B. Gottschalk, and Eric R. Wagner. 2026. "Volar-Dorsal Arthroscopic Repair for Scapholunate Ligament Injuries: A Case Series and Treatment Algorithm." *Journal of Wrist Surgery* 15 (2): 168–178.

Chand, Mukesh Babu. 2018. *Antioxidant Activity of Selected Wild Orchids of Nepal*. GRIN Verlag.

Cheng, Mengtao, Hongyu Pan, Xin Zhao, and Chunchao Han. 2026. "Integrative Network Pharmacology and Molecular Docking Elucidate the Multi-Target Mechanisms of the Artist's Conk Medicinal Mushroom Ganoderma Applanatum (Agaricomycetes) Triterpenoids against Hepatocellular Carcinoma." *International Journal of Medicinal Mushrooms* 28 (4): 71–86.

Çiftçi, Osman, Münevver Nazlıcan Kaplan, Neşe Başak Türkmen, Aslı Çetin, Bedriye Çiftçi, and İdris Ayhan. 2026. "Beneficial Effects of Taurine on 2,3,7,8-Tetrachlorodibenzo-P-Dioxin-Induced Oxidative and Histopathological Damage in the Heart Tissue of Rats." *Toxicology and Industrial Health*, March 23, 7482337261436345.

Dutta, Debashis, and Kochupurackal P. Mohanakumar. 2015. "Tea and Parkinson's Disease: Constituents of Tea Synergize with Antiparkinsonian Drugs to Provide Better Therapeutic Benefits." *Neurochemistry International* 89 (October): 181–190.

Fahrmann, Johannes, and Satyendra Chandra Tripathi. 2024. *Unmasking Metabolic Dependencies for Anti-Cancer Treatment in Cancer*. Frontiers Media SA.

Fuziwara, Cesar Seigi, and Juan Pablo Nicola. 2025. *New Molecular Pathways in Thyroid Biology: Role of Coding and Noncoding Genes in Thyroid Pathophysiology, Volume II*. Frontiers Media SA.

Hughes, Sean M., Fernanda L. Calienes, Claire N. Levy, et al. 2026. "Mucosal Tenofovir 1% Gel Stimulates Cell Proliferation and Type I/III Interferon Pathways." *Microbiology Spectrum*, March 23, e0168025.

Liu, Tan 'e, Fenqiao Chen, Lijuan Wu, He Zhang, and Pengying Yin. 2026. "Curculigoside Attenuates Influenza Virus-Induced Acute Lung Injury by Modulating the Keap1/Nrf2 Signaling Pathway." *Naunyn-Schmiedeberg's Archives of Pharmacology*, ahead of print, March 21. https://doi.org/10.1007/s00210-026-05124-z.

Li, Wen, Mingchun Wen, Lu Li, et al. 2026. "Interaction of Milk Protein and Black Tea Aroma Compounds: Selectivity, Binding Mechanism, and Theaflavin Effect." *Food & Function*, ahead of print, February 25. https://doi.org/10.1039/d5fo04942c.

Min, Yaqing, Chunlei Wang, Ping Zhao, and Bin Shi. 2026. "Spinal Manipulative Therapy Promotes Nucleus Pulposus Resorption and Alleviates Pain in a Rat Model of Lumbar Disc Herniation via JNK-Dependent Regulation of Inflammation and Tissue Remodeling." *American Journal of Translational Research* 18 (2): 1249–1263.

"Neuroprotective Efficacy of Eugenol against Lead Acetate and Monosodium Glutamate Induced Neurotoxicity by Modulating Brain-Derived Neurotrophic Factor (BDNF) Gene Expression in Wistar Rats." 2025. *TEXILA INTERNATIONAL JOURNAL OF PUBLIC HEALTH* 13 (01). https://doi.org/10.21522/tijph.2013.13.01.art048.

Niu, Yangguang, Jingyuan Ren, Kangxun Zhao, et al. 2026. "Tiger Tongue-Inspired Bionic Microneedle Patch With Dual Mechanical-Pharmacological Functions for Enhanced Wound Healing." *Journal of Biomedical Materials Research. Part A* 114 (4): e70062.

Niu, Yuling, Zhengyang Qiu, Yibang Zhou, et al. 2026. "Dynamic Changes in Genes and Metabolites during Embryonic Development of Jiangshan Black-Bone Chickens." *Poultry Science* 105 (6): 106783.

Pan, Minjuan, Xianghua Shuai, Hongya Sun, and Juan He. 2026. "Network Pharmacology and Experimental Validation Reveal That Polydatin Attenuates Glucocorticoid-Induced Growth Retardation via the AMPK/mTOR Axis and Autophagy." *Tissue & Cell* 101 (March): 103491.

Ramasubramanian, Abilasha, Paramasivam Arumugam, Pratibha Ramani, Bala Chander Kannan, and M. Senthil Murugan. 2022.

"Identification of Novel Cytochrome C1 (CYC1) Gene Expression in Oral Squamous Cell Carcinoma- An Evaluative Study." *Annals of Maxillofacial Surgery* 12 (2): 144–150.

Rastogi, S. C., Parag Rastogi, and Namita Mendiratta. 2022. *BIOINFORMATICS, FIFTH EDITION: METHODS AND APPLICATIONS - GENOMICS, PROTEOMICS AND DRUG DISCOVERY*. PHI Learning Pvt. Ltd.

Shafique, Muhammad, Muhammad Umer Ghori, Mubashir Hassan, Usman Ali Ashfaq, and Muhammad Shareef Masoud. 2026. "Network Pharmacology and Machine Learning Reveal Multi-Target Mechanisms of Poly Herbal Formulation against Atherosclerosis." *Pakistan Journal of Pharmaceutical Sciences* 39 (5): 1578–1589.

Suda, Kenichi, Kazuko Sakai, Masaoki Ito, et al. 2026. "Frequent RBM10 Comutation and a Mutually Exclusive Relationship With Other TP53 Pathway Aberrations in Early-Stage Non-Small-Cell Lung Cancer with EGFR Mutation." *Clinical Lung Cancer*, ahead of print, March 10. https://doi.org/10.1016/j.cllc.2026.03.002.

Tang, Patrick Ming-Kuen, Eric W-F Lam, Francis Jay Mussai, Dongmei Zhang, and Chunjie Li. n.d. *New Insights into Fibrotic Signaling in Cancer*. Frontiers Media SA.

Tang, Yuling, Menghong Long, Yuhang Gao, et al. 2026. "Remimazolam and Postoperative Delirium in Patients with Hyperlipidemia: A Retrospective Cohort Study with Target Trial Emulation Analysis." *Drug Design, Development and Therapy* 20 (January): 568452.

Vo-Quang, Erwan, Claudia Campani, Manon Allaire, et al. 2026. "Clinical Impact of Extrahepatic Metastatic Patterns in Patients with Unresectable Hepatocellular Carcinoma Treated with Atezolizumab and Bevacizumab." *European Journal of Cancer (Oxford, England : 1990)* 239 (March): 116704.

Wang, He, Yang Yu, Wenbin Zhou, et al. 2026. "Dual-Loaded Homotypic Exosomes with Endogenous IR808 and pH-Responsive DOX Drive Sequenced Chemo-PDT and Convert 'Cold' OSCC Tumors 'Hot.'" *Journal of Nanobiotechnology*, ahead of print, April 4. https://doi.org/10.1186/s12951-026-04359-5.

Wijk, Elmar van der, Jian Xu, and Rashmi Sasidharan. 2026. "Phytoglobin 1 in Plant Hypoxia Acclimation and Development: Integrating Oxygen Sensing, NO Homeostasis and Redox Balance." *Journal of Experimental Botany*, ahead of print, March 19. https://doi.org/10.1093/jxb/erag147.

Yang, Sichen, Kejia Li, Ning Wang, et al. 2026. "Engineering Approaches to Modify Immunomodulatory Functions of Mesenchymal Stromal Cells (MSCs): Tissue Regeneration and Clinical Application." *Advanced Science (Weinheim, Baden-Wurttemberg, Germany)*, March 23, e22601.

Yu, Xiao-Lan, Xizhe Zhu, Xinxin Lv, Jingming Ning, and Haibo Yuan. 2026. "Antagonistic Polyphenol Interactions Underlie the α-Glucosidase Inhibitory Activity of Keemun Black Tea." *Foods (Basel, Switzerland)* 15 (6). https://doi.org/10.3390/foods15061061.

Zejnullahu, Vjosa. 2022. *HPV Infection and TERT Gene Expression Levels. Association of the Telomerase Gene Expression with Cervical Cancer and Its Precursor Lesions and Human Papillomavirus Infection*. GRIN Verlag.