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Mangiferin Bioactive Roles in the Treatment of Lung Cancer

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ABSTRACT:

Mangiferin, a natural chemical present in many plants such as mango trees, is being studied for its potential in cancer therapy. Studies indicate that mangiferin, either by itself or in conjunction with other anticancer drugs, demonstrates potential in combating lung, brain, breast, cervical, prostate cancers, and leukemia. It has antioxidant and anti-inflammatory properties. Mangiferin, derived from several parts of the mango plant, possesses multiple health benefits such as antioxidant, antibacterial, antidiabetic, antiallergic, anticancer, hypocholesterolemic, and immunomodulatory effects. It inhibits peroxisome proliferator activated receptor isoforms, which helps guard against various cancers like lung, colon, breast, and brain tumors by reducing tumor necrosis factor α production, decreasing inducible nitric oxide synthase, and increasing apoptosis. In this review under covered all the therapeutic roles of mangiferin, their mechanism and other reported research work.

1. Introduction

The study examined the impact of mangiferin on lung cancer in mice at both the pre-initiation and post-initiation phases. Male Swiss albino mice were administered mangiferin (100 mg/kg body weight diluted in maize oil) for two weeks before and twelve weeks after being induced with lung cancer using B(a)P (50 mg/kg body weight). Animals exposed to carcinogens exhibited reduced body weight, higher lung weight, and increased levels of xenobiotic and liver marker enzymes. Mangiferin treatment reversed the effects, restoring the readings to nearly normal levels. Lysosomal enzyme activities were evaluated, showing elevated levels of acid phosphatase, β-glucuronidase, N-acetyl glucosaminidase, and β-galactosidase in rats with B(a)P-induced lung carcinogenesis. Supplementation of Mangiferin reduced these changes, demonstrating its anticancer properties. The research indicates that mangiferin is a strong chemopreventive drug against lung cancer, as it successfully reverses carcinogen-induced alterations in mice (Rajendran 2014).Mangiferin, a natural chemical present in many plants such as mango trees, is being studied for its potential in cancer therapy. Studies indicate that mangiferin, either by itself or in conjunction with other anticancer drugs, demonstrates potential in combating lung, brain, breast, cervical, prostate cancers, and leukemia. The methods of action involve targeting cancer cells and exhibiting antioxidant and anti-inflammatory characteristics. Nevertheless, there is a deficiency of pharmacological advancements and clinical experiments focused on cancer, as stated by Núñez Selles in 2016.

2. Mechanism Of Mangiferin Bioactive Roles In The Treatment Of Lung Cancer

2.1 Mangiferin inhibits lipopolysaccharide-induced epithelial-mesenchymal transition (EMT) and enhances the expression of tumor suppressor gene PER1 in non-small cell lung cancer cells.

Pulmonary infections in non-small cell lung cancer (NSCLC) might complicate treatment and affect prognosis. Bacterial lipopolysaccharide (LPS) triggers the generation of inflammatory cytokines and enhances tumor invasion. Mangiferin, a chemical obtained from plants, has antioxidant and anti-inflammatory properties. This study examined the anticancer properties of mangiferin on NSCLC cells generated by LPS. Mangiferin suppressed the proliferation of NSCLC cells stimulated by LPS and restored E-

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cadherin levels while reducing vimentin expression. It inhibited cell movement and caused an increase in CXCR4 expression induced by LPS. Mangiferin altered the levels of PER1 and NLRP3 proteins and decreased the release of IL-1β. The results indicate that mangiferin has promise as an anti-inflammatory and anticancer agent, with potential for use in future medication development.

(**Lin 2020)**.

2.2. Chemical and Biological Evidence of the Efficacy of Shengxian Decoction for Treating Human Lung Adenocarcinoma.

Shengxian Decoction (SXT), a traditional Chinese medicine including anti-cancer herbs, was investigated for its effectiveness in treating lung adenocarcinoma (LUAD). Mangiferin, a recognized anti-cancer agent, was detected in SXT by high-performance liquid chromatography analysis. In vitro, Serum SXT decreased the proliferation of A549 lung cancer cells and in vivo, it suppressed tumor growth in nude mice. Analysis of biochemical, histological, and imaging data revealed that SXT caused tumor necrosis and reduced the levels of hypoxia-inducible factor 1 alpha in the blood. In vivo biosafety testing showed minimal harm. The study indicates that SXT can successfully suppress the proliferation of cancer cells, demonstrating its promise as a safe anti-cancer treatment for LUAD (**Li 2022)**.

2.3. Cytoprotective Effects of Mangiferin and Z-Ligustilide in PAH-Exposed Human Airway Epithelium in Vitro.

The World Health Organization (WHO) has emphasized the health hazards linked to air pollution, such as cardiovascular and respiratory ailments, neurological disorders, and cancer. Certain plant molecules, referred to as phytochemicals, have demonstrated the ability to reduce these risks. Researchers studied how two phytochemicals, mangiferin (MNG) and Z-ligustilide (Z-LG), affected human lung bronchial epithelial cells (BEAS-2B) exposed to polycyclic aromatic hydrocarbons (PAHs), a prevalent air contaminant. The research used an organic extract of PAHs derived from urban fine particulate matter with a high benzo(a)pyrene concentration, gathered during the winter heating season in an Eastern European city. They analyzed cell growth and levels of oxidative stress within the cells. They studied the impact of MNG alone or in combination with PAH on wound healing in bronchial epithelium and examined the antioxidant capabilities of both phytochemicals in an acellular system.
MNG at a dosage of 0.5 µg/mL had a notable protective effect on cells exposed to PAH. In contrast, Z-LG had a detrimental effect on cell proliferation in both untreated and PAH-exposed cells. MNG had superior antioxidant activities in chemical tests compared to Z-LG and successfully decreased PAH-induced oxidative stress in cell cultures. MNG helped mend damages in the bronchial epithelium and increased proliferation rates in cells exposed to PAH. The results indicate that MNG has potential as a preventative agent against air pollution-induced damage to the airway epithelium, prompting additional investigation into its potential advantages (**Grauzdytė 2019)**.

2.4. Combination of Gentiana rhodantha and Gerbera anandria in the BL02 formula as therapeutics to non-small cell lung carcinoma acting via Rap1/cdc42 signaling

Non-small cell lung cancer (NSCLC) continues to be the most often diagnosed and deadly cancer globally, despite the presence of multiple treatment options. New treatment targets are urgently needed due to the heterogeneous and aggressive nature of the condition. The study aims to uncover possible targets of the herbal medicine BL02 through high throughput transcriptomics and network pharmacology. The study verified the quality and stability of BL02 using UHPLC analysis. BL02 has been shown to inhibit non-small cell lung cancer (NSCLC) in both living organisms and in a controlled environment, especially affecting EGFR-mutant HCC827 and wild type A549 cell lines. Transcriptomic study showed that EGFR and cellular adhesion-related signaling pathways are involved in BL02's mechanism of action. Subsequent bioinformatics investigation confirmed BL02's function via cdc42-regulated signaling. BL02 was discovered to break down the actin cytoskeleton by inhibiting cdc42 and deactivating its upstream protein Rap1. The effect was mainly caused by the direct attachment of certain chemicals from BL02 to the Rap1 protein. The paper suggests a comprehensive method that merges

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experimental, transcriptomic, and bioinformatics investigations to discover new treatment targets for NSCLC from BL02. Inhibiting Rap1/cdc42 signaling with active substances such as 5-methylcoumarin-4-cellobioside and mangiferin from BL02 may be a beneficial treatment for NSCLC (**Tan 2020)**.

2.5. Integrating Network Pharmacology and Experimental Validation to Explore the Effects and Mechanisms of Qinghao Biejia Decoction and Its Active Compound Artemisinin B Against Non-Small-Cell Lung Cancer.

The study aims to explore the pharmacological effects and mechanisms of Qinghao Biejia decoction (QBD) on non-small-cell lung cancer (NSCLC) utilizing network pharmacology. The study aimed to confirm the anticancer properties of artemisinin B (ART B), a primary component of QBD, on H1299 cells. The chemical composition of QBD was analyzed using ultra-performance liquid chromatography combined with quadrupole-time-of-flight mass spectrometry (UPLC-QTOF-MS/MS) methods. The antitumor effectiveness of QBD was evaluated using a zebrafish xenograft model. Cell counting kit-8 test, terminal deoxyribonucleotide transferase-mediated-dUTP nick-end labeling assay, immunofluorescence, and flow cytometry were used in vitro to assess the impact of QBD and ART B on H1299 cells. Network pharmacological studies were used to anticipate the associated targets and mechanisms of action of QBD and ART B. These predictions were confirmed by real-time PCR and Western blot assays. The analysis identified 69 chemicals in QBD, such as ART B, mangiferin, and artemisinic acid. QBD significantly inhibited the development of H1299 cells in in vivo experiments. QBD triggered apoptosis in H1299 cells and controlled the expression of different apoptosis-related proteins in in vitro tests. ART B had anti-proliferative and pro-apoptotic effects on H1299 cells by decreasing the levels of specific proteins and increasing the levels of others. ART B induced apoptosis by blocking the PI3K/Akt signaling pathway through its mechanism of action. Quinazolinone derivative (QBD) had effective results against non-small cell lung cancer (NSCLC), with artemisinin B (ART B) playing a vital role in its anti-cancer properties by regulating the PI3K-Akt pathway. The results indicate that QBD and ART B could be considered as potential options for treating NSCLC (**Ye 2023)**.

2.6. Protective role of mangiferin against Benzo(a)pyrene induced lung carcinogenesis in experimental animals.

Recently, there has been a notable emphasis on finding new chemopreventive drugs for human health. A study examined how mangiferin protects against lung cancer development by analyzing its effects on DNA damage and detoxifying enzymes. The study discovered a drop in levels of detoxifying enzymes such as glutathione transferase (GST), quinone reductase (QR), and uridin 5'-diphosphate-glucuronosyl transferase (UDP-GT) in mice with lung cancer, alongside an increase in lipid peroxidation. Supplementation of Mangiferin at a dosage of 100 mg/kg body weight increased the activity of detoxifying enzymes and decreased DNA damage, as evidenced by single cell electrophoresis. Mangiferin supplementation also controlled DNA-protein cross-links, which were increased in animals with lung cancer. The findings clarify the link between mangiferin's antioxidant characteristics and its ability to inhibit cancer (**Rajendran 2008)**.

2.7. Cytoprotective effect of mangiferin on benzo(a)pyrene-induced lung carcinogenesis in swiss albino mice.

The study examined how mangiferin affects antioxidant levels in lung cancer caused by benzo(a)pyrene in Swiss albino mice. Animals were categorized into five groups, and groups II, III, and IV were administered benzo(a)pyrene to stimulate carcinogenesis. Group III was administered mangiferin one week before to benzo(a)pyrene exposure and the treatment continued for 18 weeks. Antioxidant levels and enzyme activity were evaluated at the conclusion of the experiment. Animals in Group II exhibited reduced levels of antioxidants. Groups III and IV, when treated with mangiferin and benzo(a)pyrene, showed enhanced antioxidant levels in lung and liver tissues. Mangiferin decreased reactive oxygen species levels, indicating its potential in reducing benzo(a)pyrene-induced lung carcinogenesis (Rajendran 2008).

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2.8. Effect of mangiferin on benzo(a)pyrene induced lung cancer

The study aims to identify a possible cancer-preventing substance that focuses on oxidative stress. The study investigated the effect of mangiferin on benzo(a)pyrene-induced lung cancer in mice. Mice with lung cancer exhibited decreased activity in crucial enzymes associated with mitochondrial lipid peroxidation, TCA cycle, and electron transport chain. Mangiferin treatment at a dosage of 100 mg/kg for 18 weeks reversed the observed alterations, demonstrating its ability to prevent and treat cancer. The results back mangiferin's potential as a cancer-preventive agent **(Rajendran 2008).**

2.9. Molecular mechanisms underlying mangiferin-induced apoptosis and cell cycle arrest

Mangiferin, a chemical extracted from plants, is known for its wide range of biological effects. A recent study examined the apoptotic impact on A549 human lung cancer cells. Mangiferin was found to decrease cell proliferation and trigger apoptosis in these cells in in vitro tests. Studies conducted on A549 xenograft mice in vivo provided additional evidence of its anti-tumor effects. Mangiferin was discovered to halt the cell cycle at the G2/M phase by inhibiting the cyclin-dependent kinase 1-cyclin B1 pathway and trigger apoptosis by blocking the protein kinase C-nuclear factor-κB pathway. Furthermore, it improved the effectiveness of cisplatin, indicating promise for combined treatment. Mangiferin decreased tumor size and weight in animal studies, while also prolonging the lifetime of mice. The discoveries clarify the molecular pathways responsible for mangiferin's anticancer properties, suggesting its potential as a future antineoplastic medication.

(Shi 2016).

2.10. Probing Baicalin as potential inhibitor of Aurora kinase B: A step towards lung cancer therapy.

Cell cycle regulator dysregulation leads to aberrant cell proliferation and genetic instability in cancer. Aurora kinase B (AURKB) plays a role in cancer formation and is a target for therapy. Mangiferin and Baicalin exhibited considerable AURKB inhibition, with IC50 values of 20.0 μM and 31.1 μM, respectively, during the screening of polyphenols. Molecular docking and molecular dynamics simulations validated their attachment to the active site of AURKB. Baicalin showed cytotoxic and anti-proliferative effects on lung cancer cells in a laboratory setting, indicating its potential as a medication targeting AURKB in cancer therapy. Baicalin has potential as a lead compound in the development of anti-cancer drugs (**Noor 2024)**.

3. Others Therapeutic Activities

3.1. Mangiferin alleviates diabetic pulmonary fibrosis in mice via inhibiting endothelial-mesenchymal transition through AMPK/FoxO3/SIRT3 axis.

Diabetes mellitus results in multiple consequences, one of which being Diabetic Pulmonary Fibrosis (DPF), a less recognized condition. Mangiferin (MF), a natural chemical, has several pharmacological actions such as anti-inflammatory, anti-cancer, anti-diabetes, and anti-fibrosis activities. This study examined the influence of chronic diabetes on DPF and the potential shielding role of MF. Fibrosis surrounding pulmonary arteries with increased endothelial-mesenchymal transition (EndMT) was observed in lung tissues from 20 diabetes patients. A mouse model of diabetic pulmonary fibrosis (DPF) was created, demonstrating fibrotic lesions surrounding pulmonary arteries. These lesions were reduced by MF therapy without impacting blood glucose levels. MF dose-dependently suppressed EndMT in human endothelial cells exposed to high glucose levels. Moreover, MF enhanced SIRT3 expression through the AMPK/FoxO3 pathway, counteracting diabetes-induced EndMT. The results indicate that MF could be a promising preventive and therapeutic treatment for DPF (**Fu 2024)**.

3.2. Mangiferin induces apoptosis in human ovarian adenocarcinoma OVCAR3 cells via the regulation of Notch

Our study focused on ovarian cancer, which is the most lethal gynecological malignancy worldwide. We studied mangiferin, derived from plants, for its anti-cancer effects, namely its capacity to trigger apoptosis in human ovarian carcinoma OVCAR3 cells. Mangiferin dramatically decreased OVCAR3 cell survival in in vitro tests and enhanced their sensitivity to cisplatin, a conventional chemotherapy agent. The therapy induced

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caspase-dependent apoptosis in the ovarian cancer cells. Mangiferin notably decreased the expression of Notch, emphasizing its involvement in promoting apoptosis. Notch3 overexpression reversed the apoptotic effects of mangiferin, verifying the role of the Notch pathway. Mangiferin therapy in OVCAR3 cell xenograft models not only suppressed tumor development but also extended survival. The results indicate that mangiferin has the potential to be an effective treatment for ovarian cancer by affecting apoptotic pathways and improving the response to cisplatin, possibly by regulating Notch3 (**Zou 2017)**.

3.3. Mangiferin induces radiosensitization in glioblastoma cells by inhibiting nonhomologous end joining

Studies show that traditional treatments for glioblastoma multiforme (GBM), such as surgery and high-dose radiotherapy, are palliative because of the high occurrence of local relapse. The study focused on investigating how mangiferin, which is recognized for its anti-neoplastic properties in several malignancies, can improve the sensitivity of GBM to radiotherapy. Mangiferin pretreatment before radiation inhibited growth and enhanced DNA damage in GBM cells in in vitro tests. Mangiferin was discovered to hinder the non-homologous end-joining (NHEJ) DNA repair process by particularly affecting crucial proteins such as ATM, TP53-binding protein 1, and γ-H2AX. Mangiferin specifically inhibited DNA repair in GBM cells while without impacting normal neural Schwann cells. Tumor-bearing mice treated with mangiferin after radiation in in vivo experiments had reduced tumor sizes, lower weights, and longer lifespans. The results indicate that mangiferin may improve the sensitivity of GBM to radiation, offering a promising approach for new therapeutic treatments (Mu 2018).

3.4. Mangiferin in a Syngeneic Immunocompetent Colorectal Cancer Mouse Model Involves Changes in Mitochondrial Energy Metabolism.

Colorectal cancer (CRC) continues to be a serious worldwide health issue because of medication resistance, adverse effects, and high rates of metastasis and recurrence, despite advancements in cancer treatment. A study explored the therapeutic potential of mangiferin (MGF), a chemical present in mango tree bark and leaves, for treating CRC. Researchers discovered that treating with MGF resulted in tumor shrinkage, decreased lung metastasis, and enhanced overall survival in animal models and laboratory studies. MGF displayed antiangiogenic and antimetastatic characteristics by affecting many signaling pathways such as mitochondrial metabolism, PPAR, SIRT, NFκB, Stat3, HIF, Wnt, and GP6. Moreover, MGF impacted fatty acid β-oxidation metabolism and CPT1 protein expression, confirming its effectiveness in treating CRC. MGF has potential as a therapeutic agent for CRC by focusing on mitochondrial energy metabolism in the tumor microenvironment. This could enhance treatment success and minimize unwanted effects (Rodriguez-Gonzalez 2021).

3.5. Mangiferin: a natural miracle bioactive compound against lifestyle related disorders

The therapeutic possibilities of mangiferin, a bioactive component present in mango, for lifestyle-related illnesses. Mangiferin, derived from several parts of the mango plant, possesses multiple health benefits such as antioxidant, antibacterial, antidiabetic, antiallergic, anticancer, hypocholesterolemic, and immunomodulatory effects. It inhibits peroxisome proliferator activated receptor isoforms, which helps guard against various cancers like lung, colon, breast, and brain tumors by reducing tumor necrosis factor α production, decreasing inducible nitric oxide synthase, and increasing apoptosis. It inhibits the growth of brain and breast malignancies by reducing the expression of matrix metalloproteinase (MMP)-9 and MMP-7, which limits metastasis and the activation of the β-catenin pathway. Mangiferin inhibits lipid peroxidation and boosts the monocyte-macrophage system, demonstrating antibacterial properties. The article examines research that provides evidence for the health advantages of mangiferin (Imran 2017).

Mangiferin, a powerful plant component with anticancer properties, encounters difficulties because of its limited solubility in water and low bioavailability. Solid lipid nanoparticles loaded with mangiferin and modified with transferrin (Tf-modified MGF-SLNs). Solid lipid nanoparticles (SLNs) containing Tf-modified MGF were prepared by the emulsification-solvent evaporation technique. The physical and chemical

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characteristics such as particle size, zeta potential, and drug release patterns in a laboratory setting were assessed. The effectiveness of Tf-MGF-SLNs was evaluated in lung cancer models. The Tf-MGF-SLNs had an average hydrodynamic diameter of 121.8±2.9 nm and a polydispersity index of 0.134±0.03. Transmission electron microscopy verified the spherical and consistent shape of the particles, with an encapsulation effectiveness of 72.5±2.4%. Release experiments conducted in a laboratory setting showed an immediate release of the drug followed by a continuous release, with drug levels reaching over 68% at pH 4.0 and 72% at pH 7.4 after 6 hours. Studies conducted in living organisms showed that Tf-MGF-SLNs improved cell internalization and drug transport efficiency, leading to a notable reduction in tumor development in xenograft models. Tf-MGF-SLNs showed strong effectiveness in slowing tumor growth due to continuous drug release and enhanced cell uptake through transferrin alteration. Tf-MGF-SLNs show potential as a focused therapy approach for treating lung cancer (Zhou 2022).

4. Conclusion

Mangiferin, a bioactive compound commonly present in mango trees. Many researchers have been found that mangiferin in conjunction with other anticancer drugs, demonstrates potential in combating lung, brain, breast, cervical, prostate cancers, and leukemia. It has antioxidant and anti-inflammatory properties. It inhibits peroxisome proliferator activated receptor isoforms, which helps guard against various cancers like lung, colon, breast, and brain tumors by reducing tumor necrosis factor α production, decreasing inducible nitric oxide synthase, and increasing apoptosis but still required to do more research work for the identification of exact the reason of multipurpose action. This clue may give an idea to discover of novel drug.

References

1. Núñez Selles AJ, Daglia M, Rastrelli L. The potential role of mangiferin in cancer treatment through its immunomodulatory, anti-angiogenic, apoptopic, and gene regulatory effects. Biofactors. 2016 Sep 10;42(5):475-491. doi: 10.1002/biof.1299. Epub 2016 May 24. PMID: 27220275.
2. Lin YS, Tsai KL, Chen JN, Wu CS. Mangiferin inhibits lipopolysaccharide-induced epithelial-mesenchymal transition (EMT) and enhances the expression of tumor suppressor gene PER1 in non-small cell lung cancer cells. Environ Toxicol. 2020 Oct;35(10):1070-1081. doi: 10.1002/tox.22943. Epub 2020 May 18. PMID: 32307826.
3. Zhou Q, Hou K, Fu Z. Transferrin-Modified Mangiferin-Loaded SLNs: Preparation, Characterization, and Application in A549 Lung Cancer Cell. Drug Des Devel Ther. 2022 Jun 8;16:1767-1778. doi: 10.2147/DDDT.S366531. eCollection 2022. PMID: 34168448.
4. Zou B, Wang H, Liu Y, Qi P, Lei T, Sun M, Wang Y. Mangiferin induces apoptosis in human ovarian adenocarcinoma OVCAR3 cells via the regulation of Notch3. Oncol Rep. 2017 Sep;38(3):1431-1441. doi: 10.3892/or.2017.5814. Epub 2017 Jul 13. PMID: 28713970.
5. Li K, You F, Zhang Q, Yuan R, Yuan Q, Fu X, Ren Y, Wang Q, Li X, Zhang Z, Shichiri M, Yu Y. Chemical and Biological Evidence of the Efficacy of Shengxian Decoction for Treating Human Lung Adenocarcinoma. Front Oncol. 2022 Mar 18;12:849579. doi: 10.3389/fonc.2022.849579. eCollection 2022. PMID: 35372246.
6. Grauzdytė D, Raudoniūtė J, Kulvinskienė I, Bagdonas E, Stasiulaitienė I, Martuzevičius D, Bironaitė D, Aldonytė R, Venskutonis PR. Cytoprotective Effects of Mangiferin and Z-Ligustilide in PAH-Exposed Human Airway Epithelium in Vitro. Nutrients. 2019 Jan 22;11(2):218. doi: 10.3390/nu11020218. PMID: 30678356.
7. Tan HY, Ho VW, Chan YT, Zhang C, Wang N, Xia W, Feng Y. Combination of Gentiana rhodantha and Gerbera anandria in the BL02 formula as therapeutics to non-small cell lung carcinoma acting via Rap1/cdc42 signaling: A transcriptomics/ bio-informatics biological validation approach. Pharmacol Res. 2020 May;155:104415. doi: 10.1016/j.phrs.2019.104415. Epub 2019 Aug 26. PMID: 31465779.
8. Ye Y, Yang Y, Yan L, Zhou L, Yu S, Du Q, Dong X, Yuan Q, Shan L, Guo L. Integrating Network Pharmacology and Experimental Validation to Explore the Effects and Mechanisms of Qinghao

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 781-787 | ISSN:2251-6727

Biejia Decoction and Its Active Compound Artemisinin B Against Non-Small-Cell Lung Cancer. Drug Des Devel Ther. 2023 Aug 22;17:2461-2479. doi: 10.2147/DDDT.S414098. PMID: 35307102.

9. Rajendran P, Rengarajan T, Nishigaki I, Ekambaram G, Sakthisekaran D. Potent chemopreventive effect of mangiferin on lung carcinogenesis in experimental Swiss albino mice. J Cancer Res Ther. 2014 Oct-Dec;10(4):1033-9. doi: 10.4103/0973-1482.137966.
10. Rajendran P, Ekambaram G, Sakthisekaran D. Protective role of mangiferin against Benzo(a)pyrene induced lung carcinogenesis in experimental animals. Biol Pharm Bull. 2008 Jun;31(6):1053-8. doi: 10.1248/bpb.31.1053.
11. Rajendran P, Ekambaram G, Sakthisekaran D. Cytoprotective effect of mangiferin on benzo(a)pyrene-induced lung carcinogenesis in Swiss albino mice. Basic Clin Pharmacol Toxicol. 2008 Aug;103(2):137-42. doi: 10.1111/j.1742-7843.2008.00254.x.
12. Imran M, Arshad MS, Butt MS, Kwon JH, Arshad MU, Sultan MT. Mangiferin: a natural miracle bioactive compound against lifestyle related disorders. Lipids Health Dis. 2017 May 2;16(1):84. doi: 10.1186/s12944-017-0449-y.
13. Rajendran P, Ekambaram G, Sakthisekaran D. Effect of mangiferin on benzo(a)pyrene induced lung carcinogenesis in experimental Swiss albino mice. Nat Prod Res. 2008 May 20;22(8):672-80. doi: 10.1080/14786410701824973.
14. Rodriguez-Gonzalez JC, Hernández-Balmaseda I, Declerck K, Pérez-Novo C, Logie E, Theys C, Jakubek P, Quiñones-Maza OL, Dantas-Cassali G, Carlos Dos Reis D, Van Camp G, Lopes Paz MT, Rodeiro-Guerra I, Delgado-Hernández R, Vanden Berghe W. Antiproliferative, Antiangiogenic, and Antimetastatic Therapy Response by Mangiferin in a Syngeneic Immunocompetent Colorectal Cancer Mouse Model Involves Changes in Mitochondrial Energy Metabolism. Front Pharmacol. 2021 Dec 3;12:670167. doi: 10.3389/fphar.2021.670167. eCollection 2021.
15. Mu F, Liu T, Zheng H, Xie X, Lei T, He X, Du S, Tong R, Wang Y. Mangiferin induces radiosensitization in glioblastoma cells by inhibiting nonhomologous end joining. Oncol Rep. 2018 Dec;40(6):3663-3673. doi: 10.3892/or.2018.6756. Epub 2018 Oct 1.
16. Shi W, Deng J, Tong R, Yang Y, He X, Lv J, Wang H, Deng S, Qi P, Zhang D, Wang Y. Molecular mechanisms underlying mangiferin-induced apoptosis and cell cycle arrest in A549 human lung carcinoma cells. Mol Med Rep. 2016 Apr;13(4):3423-32. doi: 10.3892/mmr.2016.4947. Epub 2016 Feb 29.
17. Noor S, Choudhury A, Raza A, Ashraf A, Islam KU, Hussain A, Imtiyaz K, Islam A, Hassan MI. Probing Baicalin as potential inhibitor of Aurora kinase B: A step towards lung cancer therapy. Int J Biol Macromol. 2024 Feb;258(Pt 1):128813. doi: 10.1016/j.ijbiomac.2023.128813. Epub 2023 Dec 18.
18. Fu TL(#), Li GR(#), Li DH(#), He RY, Liu BH, Xiong R, Xu CZ, Lu ZL, Song CK, Qiu HL, Wang WJ, Zou SS, Yi K, Li N, Geng Q. Mangiferin alleviates diabetic pulmonary fibrosis in mice via inhibiting endothelial-mesenchymal transition through AMPK/FoxO3/SIRT3 axis. Acta Pharmacol Sin. 2024 Jan 15. doi: 10.1038/s41401-023-01202-7. Online ahead of print