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Quercetin and Cancer: Investigating Therapeutic Benefits of Neem-Derived Flavonoids

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Abstract

Quercetin, a flavonoid compound isolated from Azadirachta indica (neem), has gained significant attention in recent research for its potential as an anti-cancer agent. Neem, widely used in traditional medicine, contains a variety of bioactive compounds, with quercetin being one of the most studied for its therapeutic properties. Quercetin possesses promising anticancer effects, including the ability to inhibit cancer cell growth, induce apoptosis (programmed cell death), and regulate immune responses. Additionally, quercetin has been found to inhibit angiogenesis, the process by which tumors form new blood vessels to sustain their growth. These properties highlight quercetin's dual role as both a direct anti-cancer agent and an immune system modulator, positioning it as a potential natural therapeutic in cancer treatment.

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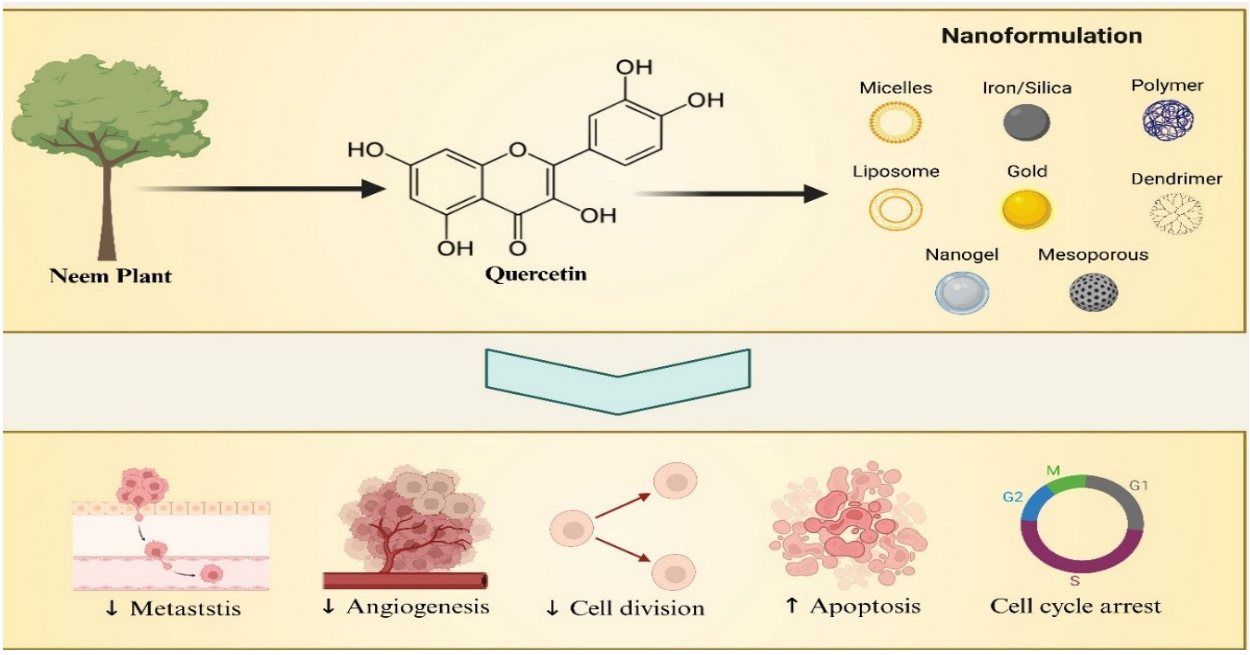
Quercetin's ability to target multiple stages of cancer progression, including cell proliferation, metastasis, and tumor growth, makes it an attractive candidate for further investigation. While preclinical studies have shown encouraging results, the translation of these findings to clinical applications remains a critical step. Further clinical trials are necessary to determine the efficacy, safety, and optimal dosage of quercetin in human cancer treatment. This review summarizes the current understanding of quercetin's anticancer properties, explores its mechanisms of action, and discusses its potential as a therapeutic agent in cancer therapy, highlighting the need for continued research in this promising area.

Graphical Abstract



Caption: Illustration showing quercetin from neem and its formulation into various nanomaterials for cancer treatment. The figure highlights quercetin's effects on inhibiting metastasis, angiogenesis, and cell division, while promoting apoptosis and cell cycle arrest.

Keywords: Azadirachta indica, Apoptosis, Cancer therapy, Quercetin, clinical trials

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1. Introduction

Neem is a wonder of modern medicine, being utilized extensively in Ayurvedic, Unani, and Homoeopathic treatment. Traditionally, it has been used to treat fever, infections, inflammation, skin conditions, and dental problems. It helps effectively for a number of epidermal dysfunctions, including eczema, psoriasis, and acne. Neem twigs are used to clean teeth, ease toothaches, and act as an oral deodorant. Neem bark has deodorizing and antimicrobial properties [1]. Nimbidin, Nimbin, Nimbolide, Azadirachtin, Gallic Acid, Epicatechin, Catechin, quercetin, and Margolone are the phytochemical compounds found in neem [2]. This tree is approximately forty to fifty feet tall, with a straight trunk and long, spreading branches that form a large, circular head. Its bark is rough and dark brown, with wide longitudinal cracks that are separated by flat ridges [3]. The compound, imparipinnate leaves consist of five to fifteen leaflets per leaf. The complex leaves are changing from one another in sequence. Mostly in the leaf axils, it bears many flowering panicles. The selel has oval, around one-centimetre-long petals that are fragrant and white. Plant grows yellow drupes that are 12–20 mm long, ellipsoid, and globous. The green fruits eventually turn yellow as they ripen, and they smell pleasantly like garlic. In March and April, flowers and new leaves appear. Depending on the region, fruits ripen between April and August [4]. Human intervention has further expanded the neem's distribution. Cultivation and naturalization have facilitated its establishment in Thailand, Malaysia, and Indonesia. More recently, deliberate introductions have broadened its reach to encompass Peninsular Malaysia, Singapore, the Philippines, Australia, Saudi Arabia, tropical Africa, the Caribbean, and Central and South America. The taxonomic classification represents different categories of neem trees, which are particularly brief about neem nomenclature [5].

2. Phytochemicals Present in Different Parts of Neem Tree

Neem is also occasionally referred to as the "storehouse" of many phytochemicals. The neem tree yielded more than 300 phytochemicals [6]. Isoprenoids and non-isoprenoids are the two major types of phytochemicals that have been identified from different portions of neem [7]. Numerous physiologically active substances, including triterpenoids, alkaloids, flavonoids,

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carotenoids, phenolic compounds, steroids, and ketones, may be extracted from the neem tree (Figure 1) [8].

3. Isolation of Que from Neem

Quercetin can be extracted from neem leaves (Azadirachta indica) through a simple solvent extraction process. First, fresh or dried neem leaves are collected, washed, and dried to remove excess moisture. The leaves are then ground into a fine powder using a mortar and pestle or blender. A solvent such as ethanol or methanol (often a 70% ethanol-water mixture) is added to the powdered leaves to dissolve the quercetin, and the mixture is allowed to stand for several hours or up to 24 hours with occasional stirring. Afterward, the mixture is filtered to separate the plant material from the solvent, which contains the extracted quercetin. The solvent is then removed by gently heating the filtrate or using a rotary evaporator to concentrate the extract. For further purification, column chromatography can be employed to isolate quercetin from other compounds. The final extract is dried and stored in an airtight container to preserve its properties.

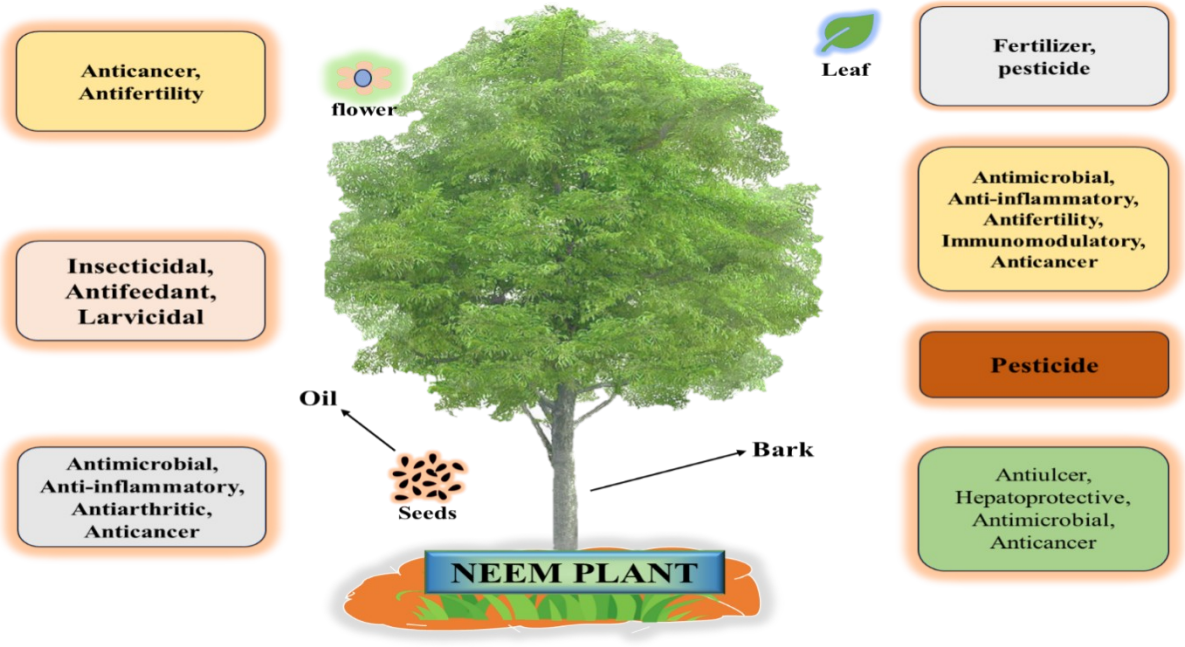

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Figure 1: Illustrating neem plant indicating the therapeutic potential of different parts of this plant.

4. Pharmacological Effects of Que

4.1 Proliferative effect of Que

Qu suppresses the G1 phase and triggers apoptosis by down-regulating cyclin D1, P21, and Twist [9]. It has been stated that Qu significantly inhibits Twist expression via the P38MAPK pathway [10]. Qu acts as an anti-proliferative by inhibiting the phosphorylation of P38MAPK as an indicator of cell proliferation [11]. The drug demonstrates the anti-proliferation of HER2-overexpression through caspase-dependent extrinsic apoptosis induction and inhibition of STAT3 [12]. Yang et al. investigated the Qu causing inhibition in the proliferation of EC cells (endometrial cancer). CCK-8 assay was used to assess the cell proliferation in different groups. Notably no significant difference in proliferation rate was found between the LV-NC groups and the normal ($P>0.05$). That indicates cells were not damaged by the transduction process. Also, cell proliferation was remarkably reduced in the quercetin [13]. Ruonan et al. investigated the activity of Qu in NSCLC by IncRNA SNHG7 miR-34a-5p pathway. The study performed RT-PCR and collected data to check lncRNA and miRNA levels. The study also performed a transwell assay to check the invasiveness ability of cells. In NSCLC, one molecule named SNHG7 was present in high levels, whereas another molecule, namely miR-34a-5p, was present in low levels. Qu lowered the levels of SNHG7 and raised the levels of miRNA-34a-5p in cancer cells [14].

4.2 Anti-inflammatory activity of Quercetin

Quercetin, a flavonoid found in plant foods like onions and berries, displays potent anti-inflammatory activity by inhibiting the generation of pro-inflammatory cytokines and regulation of critical inflammatory pathways, particularly through inhibition of the NF-κB activation that is at the center of inflammatory process regulation within the body; essentially, Qu inhibited inflammation by blocking the inflammatory processes [15]. Haleagrahara et al. investigated the

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anti-inflammatory effects of Qu when administered in combination with methotrexate. They established an arthritis model in C57/bl6 mice by intradermal administration of chicken c11. Qu (30mg/kg) and methotrexate (0.79 mg intra-peritoneally twice a week) were given. Que significantly alleviated joint inflammation by lowering the circulating cytokines and MMP levels. TNF-α and MMP gene expressions also decreased. Results proved that Que has an anti-inflammatory effect [16].

4.3 Anti-angiogenesis effect of Que

Que is an angiogenesis inhibitor in that it blocks the formation of new blood vessel tumors required for growth and spread, foremost by inhibiting the VEGF pathway of signaling and curtailing the transcription of VEGF which plays a pivotal role in angiogenesis [17]. Jin et al. investigated Qu's role in inhibiting angiogenesis. Reporter gene assays of minimal reporters that have hypoxia response elements demonstrated that the activities of HIF-1α and AP-1, important transcription factors for VEGF gene transcription, were inhibited by quercetin. Chick Chorioallantoic membrane assays demonstrated that the enhanced angiogenesis intensity of TAMR-MCF-7 cells was also suppressed significantly by Qu [18].

4.4 Anti-metastasis activity of Que

Both *in-vivo* and *in-vitro* studies have shown that Qu can induce anti-tumor activity by modifying cell cycle progression, inhibiting cell proliferation, inducing apoptosis, inhibiting angiogenesis and metastasis development, and modifying autophagy [19]. Dhanaraj et al. investigated Qu's role in tumor metastasis in ovarian cancer. Assessment of molecules involved in the P13K/Akt pathway. Further PA-1 cells were given a control treatment with the vehicle, concentrations of Qu 50 and 75µM for 24h to analyze the expression of proteins in the P13K/AKT signaling pathway. The treatment resulted in decreased levels of mRNA expressions. The study revealed the anti-metastatic activity of Qu in human metastatic ovarian cancer [20]. Lei et al. studied the role of Qu when given in combination with other anti-cancer drugs on factors associated with metastasis in gastric cancer cells. Both in vitro and in vivo studies were done. Qu is given

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in combination with Irinotecan (CPT-11) which is an anti-cancer drug. Results demonstrated that Qu in combination with the lower dose of irinotecan metabolites SN-38 had similar effects in inhibition of tumor cell growth and increasing apoptosis as those of high dose SN-38 [21].

Beleen et al. investigated the role of Qu in inducing apoptosis in a human hepatoma cell line (HepG2). The cells were grown in DMEM F12 supplemented with fetal bovine 2.5% and some antibiotics. Several techniques and assays were used including cytotoxicity assay, determination of ROS, and western blot analysis. The study investigated the effect of Qu on the activation of the apoptotic pathway in a human HepG2 cell line treated with Qu for 18h, which resulted in cancer cell death in a dose-dependent manner [22]. Altundaz et al. investigated and studied the antiproliferative effect of Qu on the human body. By using different concentrations of Qu to induce apoptosis and measure cell viability. Determination of apoptosis and cell cycle was done by flow cytometry. The result showed that Qu downregulated the level of HSP90, thus promoting apoptosis in cancerous cells. Overall study showed Quas a potential treatment for thyroid cancer [23].

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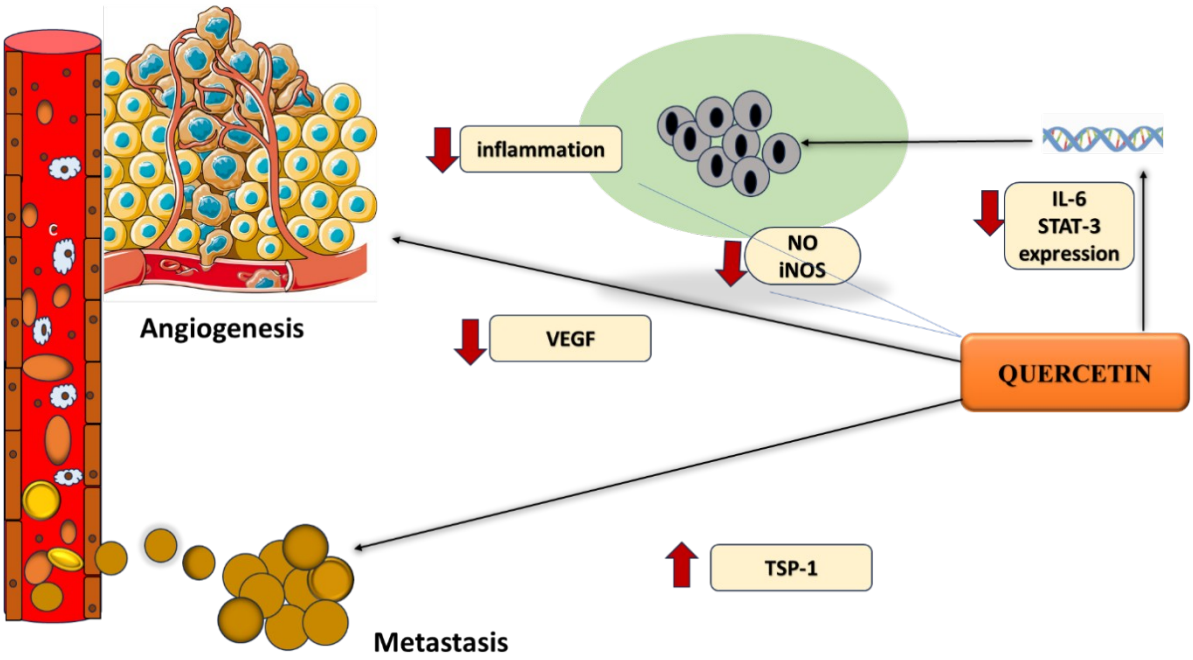

Figure 2: Representing the various mechanisms of anticancer effect of quercetin

4.5 Antioxidant activity of Que

Medical treatment has emphasized the significance of the protection of cells from the damaging effect of oxidation. Oxidative cell injury has been identified as closely related to tumorigenesis. Public and medical interest has in recent times been drawn to foods possessing antioxidant and free radical scavenging activity, which are the significant natural characteristics of QU. The link between CYP genetic variants and cancer risks has been extensively documented. Dong Xu et al. studied the antioxidant activities of QU. Studied the biological and chemical research. Found that the QU therapy in renal ischemia/reperfusion [I/R] increased GSH levels. The effect increased the anti-oxidant capacity in rats, and QU given in higher doses affects the GSH balance. QU also affected signal transduction pathways. QU modulates the enzymes or anti-oxidant substances, that increase anti-oxidant properties [24].

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5. Que as Cancer Therapy

5.1 QUE in Oral Cancer Treatment

Lai et al. examined anti-cancer activity of QUE or SAS cell lines. The result of the study indicated the increased wound healing by inhibiting MMP-2/MMP-2/MMP-9 level. Furthermore, QUE also reduced the level of VEGF, NF-KB, p65 and COX-2. This overall activity helps in the management of oral cancer. Sinta et al. evaluated the combined effect of resirotol and QUE on various cell lines, val33, SCC-15 and JFK-293 cell line. The study showed a synergistic effect of the concentration of the 10um. Additionally, the combined effect also showed inhibition of cancerous cells, DNA damage, ultimately helping in oral cancer treatment. Lei et al. evaluated anti-cancer effect of QUE in SN-38 cell line and Bulb/c nude mice. The result of the study indicated increased cell survival rate by 2-fold when treated with QUE and SN38 as compared to QUE/ SN38 alone. Furthermore, an in-vivo study showed decreased tumour volume by 2.9-fold when treated with QUE in combination with IRI as compared to a control group. Tubtimsri et al. examined the anti-oncology effect of QUE on KON oral cancer cell line. The result of the cell line study showed a decrease in IC50 when treated with QUE by 3.3-fold after 24 hrs. Furthermore, QUE also reduced BCL-

2/BCLXL value.

5.2 QUE in Stomach Cancer Treatment

Tang et al. evaluated the anti-cancer effect of QUE on SGC7901 cell line. The result of cell line study indicated that Quercetin showed the apoptosis of cancer cells in both in vivo and in vitro cell lines. The phosphorylation level of P13K & AKT significantly decreased. Furthermore, an increased in expression of caspase 3 was also observed. Overall study showed apoptosis of cancerous cells and helps to manage stomach cancer [25]. Huang et al. examined anti-tumor effect of QUE on AGS and MKN45 cell lines as well as on BALB/c mice. The outcome of study showed that Quercetin reduced the tumor volume by 2.5-fold as compared to untreated group. Furthermore, it also reduced the GSH & ROS level in a cell line. Overall, this result indicated

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promising treatment in stomach cancer [26]. Shi et al. evaluated the anti-cancer effect of active herbal on HGC-27 cell line. The result indicated that inhibits proliferation of cells, migration, clonal formation & cell cycle arrest. Overall, it promotes the apoptosis of cancerous cells in HGC-27 cell line. Furthermore, data indicated that Quercetin reduced the MRPK14 mRNA expression and genes related to EMT [27].

5.3 QUE in Colorectal Cancer Treatment

Feng et al. evaluated anti-tumor effect on QUE through NEK7-mediated NLRP3 inflammasome - GSDMD signaling pathway activation. The result of study indicated that pyroptosis was induced in colon cancer by QUE both in vitro and in vivo. Gasdermin-mediated lytic cell death through Quercetin inhibited cancerous colon cells' growth. Additionally, shNEK7 treated group reduced the tumor volume by 1.8-fold as compared to QUE alone group. Furthermore, data showed shNEK7 depressed and restrained NLRP3 inflammation - GSDMD pathway activation [28]. Tang et al. examined the anti-oncology effect of Que on modulating the NRF2/HO-1 pathway through QUE on 5-FU resistance colon cancerous cell line. The outcome of study showed that cell viability was reduced by 5-FU and Que, and apoptosis of colon cancer cells was also induced. Additionally, Que also restrained proliferation, reduced production of ROS and oxidation stress related factors

(CAT, GPx, GR and SOD. Furthermore, combination treatment of Quercetin and 5-Fluorouracil downregulated the NRF2/HO-1 pathway in both colon cancer cells and 5-FU resistance Cancer cells. Overall, these results indicated promising treatment for colon cancer [29]. Trinh et al. evaluated anti-cancer effect of Que on the JNK signaling pathway. The result of the study indicated that QUE was involved in the Invasion & migration of cancerous cells. Extraction of Agrimonia pilosa Ledeb showed the properties like anti-inflammatory and anti-oncology activities. Furthermore, QUE increased the level of E-cadherin, while the vimentin and N-cadherin levels were downregulated through the activation of JNK, p38 and signalling pathway. Overall, data indicated that QUE & quercitrin have an antimetastatic effect on colon cancer [30].

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6. Que loaded Nanoformulation for Cancer Therapy

Nanoformulations are increasingly used in cancer therapy to enhance the delivery and effectiveness of treatment while minimising side effects. These formulations utilise nanoscale carriers such as polymeric nanoparticles, liposomes, dendrimers, micelles, gold nanoparticles, and carbon nanotubes, designed to encapsulate and deliver chemotherapeutic agents or other therapeutic molecules directly to tumour cells [31]. By modifying the surface of these nanoparticles, they can be targeted specifically to cancer cells, improving the solubility, stability, and controlled release of drugs like doxorubicin, paclitaxel, and methotrexate [32]. This targeted approach not only reduces the toxicity to healthy tissues but also increases the drug's therapeutic efficacy. Additionally, nanoformulations can be used for gene therapy, RNA-based treatments, and even imaging, offering a multifunctional strategy for cancer treatment that is both effective and less harmful to the patient (Figure 3). With advancements in nanotechnology, these therapies are becoming a critical component of modern cancer treatment strategies.

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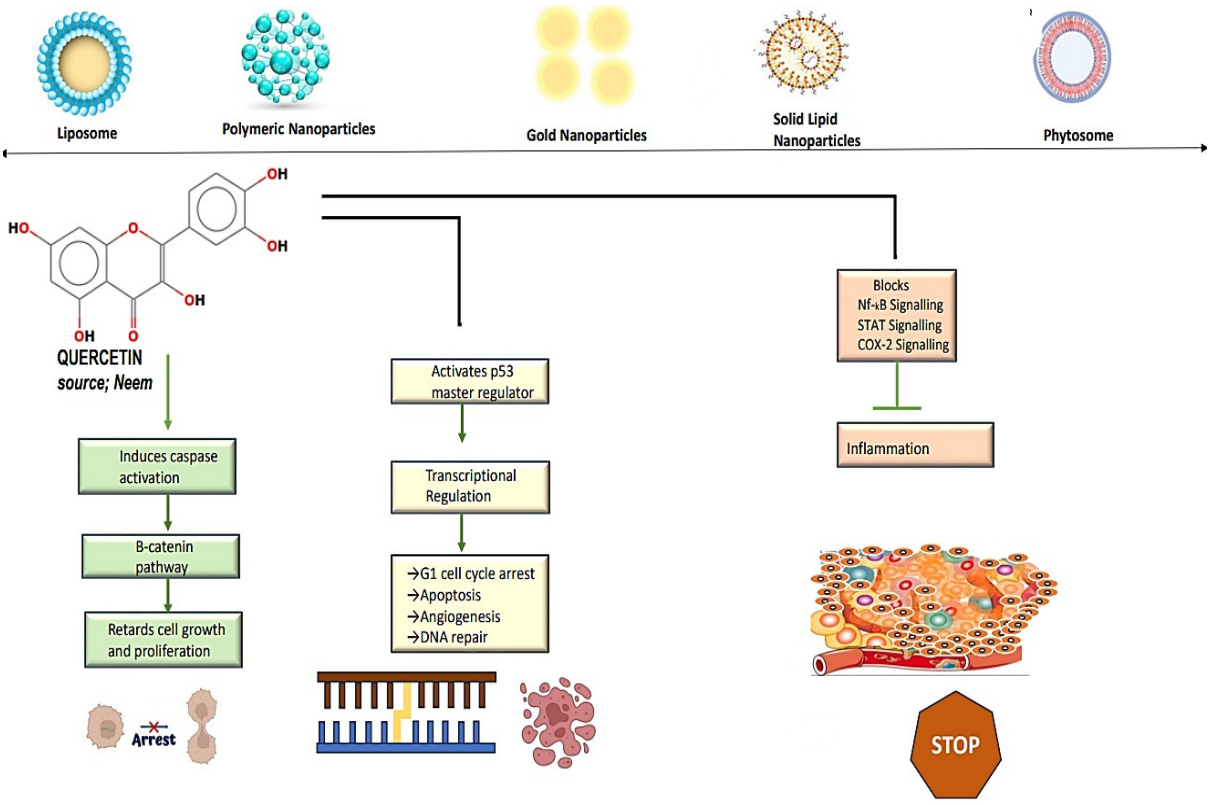

Figure 3: Different nanoformulation indicating various pathways of cancer treatment by incorporating Que.

7. Quercetin application in clinical studies

Although clinical research on quercetin in cancer treatment is still in its early stages, existing studies indicate that it could play a valuable role as a complementary therapy alongside traditional cancer treatments [33]. Quercetin appears to serve a dual function in cancer care: it enhances the effectiveness of chemotherapy and radiation while helping to alleviate common side effects like fatigue, nausea, and oxidative damage. Additionally, quercetin shows potential as a direct anticancer agent, promoting apoptosis (cell death) and slowing the growth of cancer cells [34]. There is growing evidence to suggest that quercetin may be beneficial in treating certain cancers, including breast, prostate, colon, and cervical cancers (Table 1).

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Table 1: Various clinical trials of quercetin reported so far for the management of cancer.

NCT Number	Status	Phase	Enrolment	Study Date Start	Description	Reference
NCT01720147	Completed	1	30	2012-07	The pilot study evaluated the feasibility, pharmacokinetics, toxicity, and effects of oral quercetin in patients with Fanconi anemia (FA) on bone marrow failure (BMF), hematopoiesis, reactive oxygen species (ROS), and insulin sensitivity. After the initial study completion, an expansion cohort was added to further assess the treatment's effects on clinical and biological outcomes over 26 weeks, with an option for patients to continue for up to one year.	[35]
NCT01732393	Completed	I & II	20	2010-01	The research examined how Quercetin, a natural compound found in plants, can help prevent and treat oral mucositis caused by chemotherapy in patients with blood cancers. Participants were given either Quercetin capsules or a placebo to see how effective it was in managing this condition. The study aimed to explore the potential benefits of Quercetin for treating oral mucositis related to chemotherapy.	[36]
NCT01538316	Unknown status	NA	60	2012-03	The double-blind randomized controlled crossover trial compared the efficacy of two dietary supplements with polyphenolic phytochemicals (quercetin and genistein) with a placebo on the increase rate in prostate-specific antigen (PSA). It also sought to determine the incidence of prostate cancer and evaluate oxidative stress markers, malondialdehyde, and protein carbonyls in high-risk patients without systemic treatment.	[37]
NCT03476330	Active, not recruiting	Phase II	48	2018-05	The present study was an open-label, single-arm that measured the effectiveness of quercetin in attenuating buccal micronuclei (DNA damage indicator) and the SCC risk in patients with Fanconi anemia. There were 45 post-HCT and 10 non-HCT patients enrolled and given oral quercetin. It compared its ability to prevent or slow SCC and SCC complications.	[38]
NCT05456022	Unknown status	Phase I	1000000	2022-07	This research explored the anticancer action of free and PLGA-PEG nanoparticle-encapsulated quercetin on a tongue squamous cell carcinoma (TSCC) cell line. It was designed to break the limitations of traditional anticancer therapies by better-targeting cancer cells. Earlier research demonstrated the cytotoxic activity of quercetin against oral squamous cell carcinoma (OSCC), but	[39]

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					not against TSCC until this research.	
NCT05983224	Recruiting	NA	50	2023-08	The research is examining the influence of quercetin supplementation on glycaemic control, lipid profile, oxidative stress, inflammation, growth factors, adiponectin, sex hormones, and anthropometric markers in women with endometriosis. Participants are being randomly allocated to a quercetin or placebo group and are being treated for 12 weeks. Blood samples are being taken before and after intervention to measure different biomarkers and indicators of health.	[40]
NCT06650891	Completed	Phase III	80	2024-10	The trial evaluated the effectiveness of preoperative quercetin treatment in postoperative pain after a cesarean section. Considering the weakness of opioid analgesics, the study investigated whether quercetin has a role in opioid sparing and enhancement of pain control. Quercetin's anti-nociceptive properties had been established earlier in rodent models, yet its clinical relevance in postoperative pain was unclear.	[41]
NCT05680662	Unknown status	Early Phase I	200	2023-01	The research is investigating the efficacy of quadruple therapy with quercetin, zinc, metformin, and EGCG as an adjuvant to treat early, metastatic, and triple-negative breast cancer (TNBC). This clinical randomized trial is taking 100 patients with breast cancer treated with the compounds and matching with a control of 100 patients. It aims to boost the efficacy of chemotherapy by unveiling new mechanisms by targeting immune and epigenetic pathways.	[42]
NCT06355037	Recruiting	I	10	2024-05	This Phase II, open-label, single-arm trial is assessing the efficacy and safety of dasatinib, quercetin, and chemotherapy combination in mTNBC patients who have progressed on prior chemotherapy. The trial is set to investigate how this combination reverses resistance to chemotherapy, increases sensitivity to chemotherapy, and decreases metastasis and recurrence, offering new treatment options for triple-negative breast cancer patients.	[43]
NCT06615752	Not yet recruiting	I & II	99	2025-03	This Phase I/II study will assess the safety and efficacy of adding green tea and Qu to docetaxel in mCRPC patients. Researchers will pit the pairing of green tea and Qu against a placebo, a so-called look-alike substance free of active medication, with docetaxel. The test will find if the addition of green tea and Quis augmenting docetaxel's therapeutic properties, offering perhaps better mCRPC patient outcomes.	[44]

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8. Future Perspective and Conclusion

The potential of quercetin as a therapeutic agent in cancer treatment is promising, but several challenges remain to be addressed in order to fully realize its clinical application. Future research should focus on conducting well-designed clinical trials to evaluate the safety, efficacy, and optimal dosing of quercetin in cancer patients. Investigating its bioavailability and mechanisms of absorption in humans is crucial, as quercetin's effectiveness may be limited by its poor bioavailability when administered orally. Exploring the use of nanotechnology or other delivery systems could improve the bioavailability of quercetin and enhance its anticancer effects. Additionally, research should aim to identify the specific types of cancers for which quercetin is most effective and determine whether it could be used in combination with conventional therapies, such as chemotherapy, radiation, or immunotherapy, to improve overall treatment outcomes. Understanding the molecular pathways through which quercetin exerts its anticancer effects will also help in optimizing its use as part of personalized cancer treatment regimens. The development of quercetin-based formulations, such as drug conjugates or formulations with adjuvants, could further enhance its therapeutic potential. As research progresses, quercetin may emerge as a promising natural adjunct in cancer therapy, particularly in enhancing the effectiveness of conventional treatments and reducing their side effects.

9. References

1. Sharma A, Paliwal M. An analysis of several medical properties of neem. *Asian Journal of Research in Social Sciences and Humanities* 11(11), 785-791 (2021).
2. Jadhav VP, Suryawanshi YR, Parameswaran S, Wankhede NN. Unveiling the therapeutic potential of neem flower: a phytochemical study for antidiabetic and anticancer properties. *Natural Product Research* doi:10.1080/14786419.2024.2433194 1-17
3. Haji AS, Maurya SR, Shah N. Azadirachta indica A. Juss.: ethnobotanical knowledge, phytochemical studies, pharmacological aspects future prospects. *Plant Environ* 5(1), 1-15 (2023).
4. Mehnaz S, Shamsi Y, Akhtar MW, Mohanty S, Ahmad S. Therapeutic Applications of Neem (Azadirachta indica): A Narrative Review. *Adv Mind Body Med* 38(4), 14-18 (2024).

ISSN: 3093-4737

5. Kadir A, Ghosh T, Ilango K *et al*. In-depth review on taxonomy, phytochemistry, traditional uses and pharmacological significance of Azadirachta indica plant. *European Journal of Biomedical* 11(6), 277-284 (2024).
6. Pal D, Sahu P, Sinha P, Dewangan P. Neem (Azadirachta indica) and Hibiscus Seed as Antiproliferative Agents. In: *Seeds: Anti-proliferative Storehouse for Bioactive Secondary Metabolites*, Pal D (Ed.^(Eds).Springer Nature Singapore Singapore 785-810 (2024).
7. Sarkar S, Singh RP, Bhattacharya G. Exploring the role of Azadirachta indica (neem) and its active compounds in the regulation of biological pathways: an update on molecular approach. *3 Biotech* 11(4), 178 (2021).
8. Maji S, Modak S. Neem: Treasure of natural phytochemicals. *Chem Sci Rev Lett* 10(39), 396-401 (2021).
9. Yuan L, Cai Y, Zhang L, Liu S, Li P, Li X. Promoting Apoptosis, a Promising Way to Treat Breast Cancer With Natural Products: A Comprehensive Review. *Frontiers in Pharmacology* 12 (2022).
10. Kim W, Park S, Han S-H *et al*. PRPF4 Knockdown Suppresses Glioblastoma Progression via the p38 MAPK and ERK Signaling Pathways. *Anticancer Research* 45(2), 549 (2025).
11. Veisaga ML, Ahumada M, Soriano S *et al*. Anti-proliferative effect of Annona extracts on breast cancer cells. *Biocell* 47(8), 1835-1852 (2023).
12. Zhang J, Wu Y, Li Y *et al*. Natural products and derivatives for breast cancer treatment: From drug discovery to molecular mechanism. *Phytomedicine* 129 155600 (2024).
13. Yang L, Ma H. Quercetin inhibits the biological activity of endometrial cancer by regulating autophagy: A network pharmacology analysis and cellular experimental validation. *Journal of Functional Foods* 125 106657 (2025).
14. Chai R, Xu C, Lu L, Liu X, Ma Z. Quercetin inhibits proliferation of and induces apoptosis in non-small-cell lung carcinoma via the lncRNA SNHG7/miR-34a-5p pathway. *Immunopharmacology and Immunotoxicology* 43(6), 693-703 (2021).
15. Li Y, Yao J, Han C *et al*. Quercetin, Inflammation and Immunity. *Nutrients* 8(3), 167 (2016).
16. Haleagrahara N, Hodgson K, Miranda-Hernandez S, Hughes S, Kulur AB, Ketheesan N. Flavonoid quercetin–methotrexate combination inhibits inflammatory mediators and matrix metalloproteinase expression, providing protection to joints in collagen-induced arthritis. *Inflammopharmacology* 26(5), 1219-1232 (2018).
17. Yang D, Dang S, Wang Z, Xie M, Li X, Ding X. Vessel co-option: a unique vascular-immune niche in liver cancer. *Frontiers in Oncology* 14 1386772 (2024).
18. Oh SJ, Kim O, Lee JS *et al*. Inhibition of angiogenesis by quercetin in tamoxifen-resistant breast cancer cells. *Food and Chemical Toxicology* 48(11), 3227-3234 (2010).
19. Shahbaz M, Naeem H, Momal U *et al*. Anticancer and apoptosis inducing potential of quercetin against a wide range of human malignancies. *International Journal of Food Properties* 26(1), 2590-2626 (2023).
20. Dhanaraj T, Mohan M, Arunakaran J. Quercetin attenuates metastatic ability of human metastatic ovarian cancer cells via modulating multiple signaling molecules involved in cell survival, proliferation, migration and adhesion. *Archives of Biochemistry and Biophysics* 701 108795 (2021).
21. Lei C-S, Hou Y-C, Pai M-H, Lin M-T, Yeh S-L. Effects of quercetin combined with anticancer drugs on metastasis-associated factors of gastric cancer cells: in vitro and in vivo studies. *The Journal of Nutritional Biochemistry* 51 105-113 (2018).

ISSN: 3093-4737

22. Granado-Serrano AB, Martiín MA, Bravo L, Goya L, Ramos S. Quercetin Induces Apoptosis via Caspase Activation, Regulation of Bcl-2, and Inhibition of PI-3-Kinase/Akt and ERK Pathways in a Human Hepatoma Cell Line (HepG2)1. *The Journal of Nutrition* 136(11), 2715-2721 (2006).
23. Mutlu Altundağ E, Kasacı T, Yılmaz AM *et al*. Quercetin-Induced Cell Death in Human Papillary Thyroid Cancer (B-CPAP) Cells. *Journal of Thyroid Research* 2016(1), 9843675 (2016).
24. Xu D, Hu MJ, Wang YQ, Cui YL. Antioxidant Activities of Quercetin and Its Complexes for Medicinal Application. *Molecules* 24(6), (2019).
25. Yisha T. Study on the anti-tumor effects of the key component of traditional Chinese medicine nightshade in the treatment of human gastric cancer (SGC7901 cell line). Presented at: *Proc.SPIE*. 2023.
26. Huang J, Chen J, Li J. Quercetin promotes ATG5-mediating autophagy-dependent ferroptosis in gastric cancer. *Journal of Molecular Histology* 55(2), 211-225 (2024).
27. Shi X-F, Yu Q, Wang K-B *et al*. Active ingredients Isorhamnetin of Croci Srigma inhibit stomach adenocarcinomas progression by MAPK/mTOR signaling pathway. *Scientific Reports* 13(1), 12607 (2023).
28. Feng SH, Zhao B, Zhan X *et al*. Quercetin-induced pyroptosis in colon cancer through NEK7-mediated NLRP3 inflammasome-GSDMD signaling pathway activation. *Am J Cancer Res* 14(3), 934-958 (2024).
29. Tang Z, Wang L, Chen Y *et al*. Quercetin reverses 5-fluorouracil resistance in colon cancer cells by modulating the NRF2/HO-1 pathway. *Eur J Histochem* 67(3), (2023).
30. Trinh N-T, Nguyen TMN, Yook J-I, Ahn S-G, Kim S-A. Quercetin and Quercitrin from Agrimonia pilosa Ledeb Inhibit the Migration and Invasion of Colon Cancer Cells through the JNK Signaling Pathway. *Pharmaceuticals* 15(3), 364 (2022).
31. Panthi VK, Dua K, Singh SK, Gupta G, Hansbro PM, Paudel KR. Nanoformulations-Based Metronomic Chemotherapy: Mechanism, Challenges, Recent Advances, and Future Perspectives. *Pharmaceutics* 15(4), 1192 (2023).
32. Haddad R, Alrabadi N, Altaani B, Li T. Paclitaxel Drug Delivery Systems: Focus on Nanocrystals' Surface Modifications. *Polymers* 14(4), 658 (2022).
33. Almatroodi, S. A., Alsahli, M. A., Almatroudi, A., Verma, A. K., Aloliqi, A., Allemailem, K. S., ... & Rahmani, A. H. (2021). Potential therapeutic targets of quercetin, a plant flavonol, and its role in the therapy of various types of cancer through the modulation of various cell signaling pathways. *Molecules*, *26*(5), 1315.
34. Biswas, P., Dey, D., Biswas, P. K., Rahaman, T. I., Saha, S., Parvez, A., ... & Kim, B. (2022). A comprehensive analysis and anti-cancer activities of quercetin in ROS-mediated cancer and cancer stem cells. *International journal of molecular sciences*, *23*(19), 11746.
35. Mehta, P. A., Nelson, A., Loveless, S., Lane, A., Fukuda, T., Teusink-Cross, A., ... & Davies, S. M. (2025). Phase 1 study of quercetin, a natural antioxidant for children and young adults with Fanconi anemia. *Blood Advances*, *9*(8), 1927-1939.
36. Belfiore, E., Di Prima, G., Angellotti, G., Panzarella, V., & De Caro, V. (2024). Plant-derived polyphenols to prevent and treat oral mucositis induced by chemo-and radiotherapy in head and neck cancers management. *Cancers*, *16*(2), 260.

ISSN: 3093-4737

37. Stewart, K. L., & Lephart, E. D. (2023). Overview of BPH: symptom relief with dietary polyphenols, vitamins and phytochemicals by nutraceutical supplements with implications to the prostate microbiome. *International Journal of Molecular Sciences*, *24*(6), 5486.

38. Lee, G. H., Taritsa, I. C., Ruiz, E. S., & LeBoeuf, N. R. (2025). Squamous cell carcinoma. In *Mohs Micrographic Surgery* (pp. 229-254). Cham: Springer Nature Switzerland.

39. Vyas, J., Raytthatha, N., Prajapati, B. G., & Singh, S. (2025). Polymeric Molecular Envelope Technology for Improved Therapeutics Efficacy: A Review. *Current Medicinal Chemistry*, *32*(21), 4176-4191.

40. Khamineh, Y., Ghiasvand, M., Panahi-Alanagh, S., Rastegarmand, P., Zolghadri, S., & Stanek, A. (2025). A Narrative Review of Quercetin's Role as a Bioactive Compound in Female Reproductive Disorders. *Nutrients*, *17*(7), 1118.

41. Mohamed Elmokadem, E., Khaled Abou El Fadl, D., Bassiouny, A. M., Mahmoud, M. M. A. E., Samy, M., & El Said, N. O. (2025). The Adjunctive Effect of Quercetin on Postoperative Pain Management Following Cesarean Section: A Randomized Controlled Study. *Drug Design, Development and Therapy*, 6009-6024.

42. Sirhan, Z., Abu Nada, A., Anabtawi, N., Thyagarajan, A., & Sahu, R. P. (2025). Metformin-based combination approaches for triple-negative breast cancer. *Pharmaceutics*, *17*(5), 558.

43. Nambiar, A., Kellogg, D., Justice, J., Goros, M., Gelfond, J., Pascual, R., ... & Kirkland, J. (2023). Senolytics dasatinib and quercetin in idiopathic pulmonary fibrosis: results of a phase I, single-blind, single-center, randomized, placebo-controlled pilot trial on feasibility and tolerability. *EBioMedicine*, *90*.

44. Wang, Z., Liu, Z., Qu, J., Sun, Y., & Zhou, W. (2024). Role of natural products in tumor therapy from basic research and clinical perspectives. *Acta Materia Medica*, *3*(2), 163-206.