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# Curcumin as a therapeutic agent in cancer: Progress, mechanism, and clinical prospects

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**Abstract**
Curcumin, a polyphenolic molecule extracted from Curcuma longa, has emerged as a promising adjuvant and therapeutic agent in cancer treatment, demonstrating anti-inflammatory, antiproliferative, and immunomodulatory properties across several malignancies. This review carefully analyzes current progress in curcumin research, clarifies the molecular processes underlying its anticancer effects, assesses therapeutic outcomes in particular cancer types, and addresses problems in clinical translation and prospective avenues for future investigation [1-89].

**Keywords:** Curcumin, cancer therapy, polyphenols, anticancer mechanisms, clinical translation

## Introduction

Curcumin is a major focus of cancer research because it can interact with many molecular targets and cellular signaling pathways that are important to tumor biology, such as those that control cell growth, death, blood vessel growth, invasion, and metastasis. Preclinical studies have shown that curcumin can cause apoptosis in different types of cancer, such as breast, lung, head and neck, prostate, and brain cancers. It does this by suppressing antiapoptotic proteins like Bcl-2 and Bcl-xL and upregulating death receptors DR4 and DR5 on tumor cells, which leads to programmed cell death.

- Stop cells from growing and invading by targeting transcription factors and enzymes such NF-κB, AP-1, COX-2, nitric oxide synthase, STAT3, and matrix metalloproteinase-9 (MMP-9).
- Alter the metabolism of reactive oxygen species in tumor cells, elevating ROS levels beyond thresholds acceptable for cancer cells, therefore inhibiting tumor growth.
  Interfere with important signal transduction pathways, including PI3K/Akt/mTOR, MAPK (Ras-Raf-MEK-ERK), Wnt/β-catenin, Hedgehog, Notch, and JAK/STAT3, which ultimately suppress prosurvival and proinflammatory responses.
- Change cancer-related miRNAs by effectively lowering oncogenic miRNAs and raising tumor-suppressive miRNAs.

There are still a lot of problems that need to be solved before curcumin may be used in the clinic, even though these results are promising. Curcumin is not very soluble in water because it is hydrophobic. This means that it is not very bioavailable when taken orally, it is broken down quickly, and it is not very stable in chemical systems. Curcumin, in its natural form, tends to become stuck in cell membranes because of interactions that make it hydrophobic and hydrogen-bonding, which makes it hard for drugs to reach the cytoplasm and reach therapeutic levels. To tackle these pharmacokinetic issues, researchers have looked into structural changes, nanoformulations (like liposomes and nanoparticles), polymeric carriers, and different adjuvant therapies. All of these are meant to make curcumin more stable chemically, better at targeting specific cells, and easier to deliver throughout the body. Micelle-based, liposomal, and polymeric nanoparticles are all examples of new delivery systems that make curcumin far more bioavailable and stable. This makes it easier for the body to respond to curcumin in vivo and in clinical settings. Moreover, molecular conjugation methods and the combination with chemotherapeutic drugs show promise for overcoming resistance and improving lethal effects, rendering curcumin an increasingly versatile candidate for integrated cancer therapy.

## 2 Molecular Mechanisms of Anticancer Activity

Curcumin exhibits anticancer properties by intricately engaging with and modulating many cell signaling pathways essential for tumor initiation, development, and metastasis. These pathways control things like cell growth, programmed cell death (apoptosis), angiogenesis (the growth of new blood arteries that feed tumors), and the spread of cancer to other parts of the body. Here are further in-depth explanations of these mechanisms, along with proof:

### Inhibition of Pro-Survival and Proliferative Signaling Pathways

**NF-κB Pathway:** Curcumin stops nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling, which is typically turned up in malignancies and helps cells stay alive, inflamed, and resistant to apoptosis. By inhibiting NF-κB activation, curcumin promotes tumor cell apoptosis and reduces inflammatory responses that support cancer cell survival [8, 21, 27].

***EGFR/MAPK Pathway:*** Curcumin inhibits proliferative gene transcription and induces apoptotic death in different cancer cells by targeting elements of the mitogen-activated protein kinase (MAPK) cascade (such as ERK, JNK, and p38) and the epidermal growth factor receptor (EGFR) [14, 57].

**PI3K/Akt/mTOR Pathway:** This pathway helps cells grow and stay alive. Curcumin stops PI3K/Akt signaling, which stops the cell cycle, speeds up apoptosis, and slows down the growth of tumor stem cells. It also increases the levels of tumor suppressor proteins (like PTEN) and decreases the levels of pro-survival factors (like Bcl-2), which makes cancer cells more sensitive to chemotherapy and slows their growth [21, 27, 35].

**STAT3 Pathway:** Curcumin stops gene transcription that is linked to cell growth and immunological evasion by disrupting the Janus kinase (JAK)/signal transducer and activator of transcription (STAT) pathway [21, 27].

**Wnt/β-Catenin Signaling:** Curcumin interferes with Wnt/β-catenin signaling, decreasing the accumulation of nuclear β-catenin, which subsequently downregulates oncogenes such c-Myc and cyclin D1, inhibiting tumor growth and facilitating apoptosis.

### Changing Apoptosis and Cell Death

- Curcumin improves apoptotic signaling through both intrinsic (mitochondrial) and extrinsic (death receptor) mechanisms. This entails the equilibrium of pro- and anti-apoptotic Bcl-2 family proteins, enhancement of mitochondrial membrane permeability, liberation of cytochrome c, and activation of caspases [21, 35, 57].
- Increasing the activity of death receptors (DR4, DR5) and decreasing the activity of anti-apoptotic proteins (Bcl-2, Bcl-xL) makes cancer cells more sensitive to programmed death.

### Stopping Angiogenesis and Tumor Inflammation

- Curcumin inhibits angiogenesis by diminishing vascular endothelial growth factor (VEGF) and its receptor signaling, so obstructing tumor vascularization and restricting food availability to cancer cells [7, 13, 34, 46].
- Curcumin reduces inflammation that promotes tumors by lowering the levels of cytokines including TNF-α, IL-6, and interleukins. This is a major cause of cancer growth.
- Changing the tumor microenvironment and the immune system
- Curcumin changes the tumor microenvironment by stopping inflammatory mediators and fixing immunological dysfunction. It restores anti-tumor immunity by lowering immunosuppressive cytokines, boosting the activity of cytotoxic T cells and natural killer (NK) cells, and messing with immunological checkpoint signaling [7, 13, 34, 46].
- Curcumin's control of both oncogenic and tumor suppressive microRNAs (miRNAs) makes gene expression networks in cancer cells even more precise. For example, it downregulates miR-21 (oncogenic) and upregulates miR-192-5p (tumor suppressive).

### Other Pathways and Interactions

- Curcumin has been demonstrated to influence many pathways, including JAK/STAT, Notch, Hedgehog, and p53, hence augmenting its array of anticancer properties.
- Curcumin may help get around tumor adaptability and resistance that often happen during single-target therapy by working on more than one signaling axis at a time.

Curcumin's ability to control many molecular and cellular targets makes it a one-of-a-kind and flexible natural substance that could stop cancer from starting and spreading in many different types of cancer. Its activity is especially interesting since it affects so many pathways, from cell survival and growth to immune regulation and stopping the spread of cancer.

## 3 Therapeutic Uses in Certain Cancers

### Liver Cancer

Curcumin has been extensively investigated for its therapeutic potential in liver cancer, exhibiting the capacity to inhibit tumor development, induce apoptosis, and regulate critical signaling pathways associated with hepatocarcinogenesis. Consistent findings from systematic evaluations of preclinical and clinical trials demonstrate curcumin's efficacy in suppressing proliferation and inducing programmed cell death in hepatocellular cancer cell lines and animal models [1, 27, 39]. Clinical trials indicate positive safety and acceptability profiles for oral curcumin treatment, with notable enhancements in patient liver function indicators and overall disease progression [70, 77]. Molecular processes encompass the inhibition of NF-κB, STAT3, and PI3K/Akt pathways, with the downregulation of oncogenic miRNAs that facilitate tumor survival [1, 27, 39, 70].

### Prostate Cancer

Several meta-analyses substantiate curcumin's function as an adjunctive medication in prostate cancer treatment, evidencing its ability to diminish tumor burden, lower prostate-specific antigen (PSA) levels, and enhance patient biochemical recurrence rates [4, 21, 30]. Mechanistic investigations demonstrate curcumin's suppression of

androgen receptor signaling, disruption of cell cycle regulatory proteins, and alteration of apoptotic factors that facilitate prostate tumor regression [21, 42, 73]. Curcumin's antioxidant and anti-inflammatory properties mitigate inflammation associated with prostate cancer, improving therapeutic outcomes when used in conjunction with traditional treatments [4, 21].

**Cancer of the colon and rectum**

Dietary supplementation with curcumin is associated with a reduced incidence and development of colorectal cancer through many mechanisms, including anti-inflammatory actions, inhibition of tumor-promoting cytokines, and alteration of gut microbiota composition [6, 23, 32]. Systematic studies have shown that curcumin can lower the size of colorectal tumors and inflammatory indicators including TNF-α and IL-6 in both animal models and real-life situations [44, 75, 82]. Curcumin-enriched foods also make patients' lives better by reducing the negative effects of chemotherapy and boosting their antioxidant defenses [6, 23, 75].

**Cancers of the mouth and head and neck**

Curcumin shows anti-cancer actions at the molecular level in malignancies of the mouth, head, and neck. Experimental investigations demonstrate that curcumin inhibits the expression of genes associated with tumor proliferation and metastasis, including COX-2, MMP-9, and cyclin D1, while enhancing the effectiveness of chemotherapeutic drugs such as cisplatin and 5-fluorouracil [5, 22, 31]. Clinical assessments demonstrate diminished severity of oral mucositis in cancer patients administered curcumin, signifying its preventive and therapeutic advantages [43, 74, 83]. Curcumin also changes the activity of epigenetic regulators and miRNAs that are important for cell growth and death, which helps keep tumors under control [5, 22, 31].

**Lung and Melanoma**

Recent data demonstrates curcumin’s inhibitory effect on non-small cell lung cancer (NSCLC) via cell cycle arrest and the modulation of oncogenic Wnt/β-catenin signaling pathways, leading to reduced tumor development and metastasis [51, 60]. Curcumin inhibits proliferation and causes apoptosis in melanoma by targeting many molecular pathways, such as MAPK and PI3K/Akt, while simultaneously augmenting anticancer immune responses [60, 61]. Preclinical results underscore curcumin's synergistic effects with radiation and immunotherapies, facilitating the development of prospective combination treatments for challenging malignancies [51, 60, 61].

Curcumin exhibits diverse therapeutic potential across multiple cancer types by influencing tumor development, apoptosis, inflammation, and immune responses, as evidenced by systematic reviews and meta-analyses [1-83]. These outcomes highlight the necessity for more clinical studies to enhance curcumin formulations and their incorporation into cancer treatment regimens.

## 4 Improvements in Curcumin Formulations

Curcumin's therapeutic progress has been significantly hindered by its inadequate water solubility, chemical instability, fast metabolism, and resultant limited systemic bioavailability. To address these pharmacokinetic issues, different formulation strategies have been rigorously explored, resulting in the creation of many enhanced delivery systems aimed at improving curcumin's absorption, biodistribution, and therapeutic efficacy.

**Formulations with liposomes**

Liposomal encapsulation of curcumin entails the integration of the molecule into lipid bilayer vesicles, enhancing its solubility, stability, and bioavailability. Liposomal curcumin has a longer circulation period in the blood and is taken up by tumor cells more easily by endocytosis [53, 62]. Research indicates that these formulations enhance curcumin's anticancer and anti-inflammatory properties while diminishing systemic toxicity. Liposomal curcumin has shown enhanced antitumor activity in models of breast, prostate, and liver cancer when compared to free curcumin [24, 53].

**Nanoparticles and polymeric carriers**

Nanoparticle-based delivery methods, including as polymeric nanoparticles, solid lipid nanoparticles, and nanomicelles, represent some of the most promising methodologies. Polymeric nanoparticles provide regulated and prolonged release of curcumin, reducing degradation and enhancing bioavailability [64, 67, 68]. Nanoparticles also help with passive tumor targeting by using the increased permeability and retention (EPR) effect to preferentially build up curcumin in tumor tissues [24, 67]. Some formulations are surface-functionalized to actively target tumor-specific receptors, which makes them much more effective [62].

Solid lipid nanoparticles (SLNs) are biocompatible and preserve curcumin from breaking down, which leads to a higher plasma concentration and a longer half-life [24, 62]. Research shows that nanoparticle curcumin is more effective in killing cancer cells than other types of curcumin. This includes colorectal, lung, and melanoma malignancies [53, 67, 69]. Nanoparticle compositions provide combination therapy techniques, including co-delivery with antisense oligonucleotides or chemotherapeutics, thereby augmenting synergistic tumor suppression [67, 68, 69].

**Micellar and Other Colloidal Systems**

Micellar formulations use amphiphilic molecules that come together on their own to form nanoscale carriers. These carriers hold hydrophobic curcumin molecules to make them easier to dissolve and transport throughout the body [53]. This method not only keeps curcumin from breaking down too soon, but it also helps it be absorbed better by the stomach, which leads to higher plasma levels after oral treatment [24, 62].

**Other New Ways to Deliver**

More progress has been made by linking curcumin with polymers and peptides to make it more targeted and easier for cells to take up, as well as by using carriers that respond to tumor-specific circumstances (such pH and enzymes) to release curcumin [64, 67]. Researchers are also looking into nanoemulsions and cyclodextrin inclusion complexes to make things more water-soluble and bioavailable [24, 62].

**Implications for Clinical Practice**

These new formulations work together to fix the main bioavailability problems with native curcumin, which leads to more stable therapeutic levels and stronger anticancer

effects in vivo [53, 64, 67]. Improved delivery systems let curcumin become part of more effective chemopreventive and chemotherapeutic plans. For example, it can be used with standard cancer medications to lower doses and adverse effects while increasing effectiveness [68, 69].

Advanced curcumin formulations, including liposomes, nanoparticles, micelles, and polymer conjugates, significantly enhance solubility, stability, transport, and tumor targeting compared to free curcumin. These developments greatly enhance curcumin's therapeutic efficacy against many malignancies, promote combinatorial therapies, and constitute a vital area of continuing study [24, 53, 62, 64, 67, 68, 69]. This is a more in-depth version with more information and more sources:

**5 Improvements in Curcumin Formulations**

Curcumin's clinical progress has encountered significant obstacles owing to its inadequate water solubility, chemical instability, quick metabolism, and low systemic bioavailability, which restrict its therapeutic concentrations in plasma and tissues. To solve these problems, scientists have devised better delivery systems that improve curcumin's absorption, stability, biodistribution, and anticancer effectiveness in different cancer models.

**Liposomal Formulations**

Liposomal encapsulation means putting curcumin molecules inside phospholipid bilayers, which makes them more soluble and keeps them from breaking down by enzymes. Liposomes enhance curcumin's pharmacokinetic profile by prolonging circulation duration and facilitating more effective tumor cell uptake via endocytosis [53, 62]. In preclinical trials of breast, liver, and prostate malignancies, liposomal curcumin has been demonstrated to have much stronger antitumor effects than free curcumin. You can change the lipid bilayer composition to make it easier for drugs to get to the right places, which helps them build up at tumor sites and reduces off-target damage [24, 53].

**Nanoparticles with Polymeric Carriers**

Nanoparticle-based delivery vehicles, including polymeric nanoparticles, solid lipid nanoparticles, and nanomicelles, show great promise because they can give controlled, long-lasting release and keep curcumin from breaking down and losing its effectiveness too soon. Polymeric nanoparticles made from biocompatible materials improve oral bioavailability and tumor targeting by taking advantage of the increased permeability and retention (EPR) effect in tumors [24, 62, 64]. Adding targeting ligands to the surface of nanoparticles (such folate or antibodies) makes them much more selective and easier for cancer cells to take up [67].

Solid lipid nanoparticles (SLNs) provide the dual advantages of biodegradability and regulated drug release, resulting in elevated plasma curcumin concentrations and extended half-lives compared to native curcumin [24, 62]. Numerous studies illustrate the enhanced tumoricidal efficacy of nanoparticle-based curcumin formulations, markedly impeding tumor cell proliferation and metastasis in colorectal, lung, and melanoma models [53, 67, 69]. Nanoparticles also work as multifunctional platforms for combination therapy, allowing curcumin to be delivered with chemotherapeutic drugs or antisense oligonucleotides to boost their anticancer effects [53, 67, 68, 69].

**Colloidal and Micellar Systems**

Amphiphilic surfactants in micellar formulations self-assemble into nanocarriers that trap hydrophobic curcumin, making it easier to dissolve in water and absorb. This method keeps curcumin stable in fluids in the gastrointestinal tract and makes it easier for the body to absorb it after it is taken by mouth [24, 53, 62]. Micellar curcumin formulations enhance cellular absorption and provide superior anticancer efficacy both in vitro and in animal models.

**Other New Ways to Deliver**

Other cutting-edge methods involve attaching curcumin to polymers or peptides that allow for active targeting and better penetration of tumors. Stimuli-responsive carriers are made to release curcumin only in certain conditions that are particular to tumors, like an acidic pH or high amounts of enzymes [64, 67]. Nanoemulsions and cyclodextrin inclusion complexes efficiently improve curcumin solubility and safeguard it from degradation during transport [24, 62].

**Implications for Clinical Practice**

These delivery platforms have greatly improved the pharmacodynamics of curcumin, resulting in greater and more stable plasma/tissue levels that lead to better anticancer effects in vivo [53, 64, 67]. Curcumin can be used in therapeutic regimens, frequently with chemotherapy, to cut drug doses and side effects while increasing patient outcomes [68, 69]. This is because it can improve selective tumor targeting and lessen systemic toxicity.

In short: Liposomal, nanoparticle, micellar, polymeric, and other novel curcumin formulations overcome intrinsic bioavailability restrictions to greatly boost its medicinal effectiveness. These advances are key to unlocking curcumin's full therapeutic potential in cancer treatment by making it more stable, allowing for tailored distribution, and enabling multimodal combination therapies [24, 53, 62, 64, 67, 68, 69].

**6 Impact on health and safety**

Curcumin has attracted significant interest due to its preclinical anticancer potential and its promising clinical efficacy and safety profile as a supplemental or adjunct therapy to conventional cancer therapies. Numerous meta-analyses and comprehensive reviews have methodically assessed curcumin's efficacy, tolerability, and impact on patient-centered outcomes across various cancer types and therapeutic contexts.

**Effectiveness as an Adjunctive Treatment**

Meta-analyses demonstrate that curcumin supplementation improves the overall therapeutic efficacy when used in conjunction with standard oncological treatments, including chemotherapy, radiation, and immunotherapy [10, 12, 16, 33, 55]. Curcumin has been demonstrated to enhance the sensitivity of tumor cells to chemotherapeutic drugs, hence increasing response rates and diminishing treatment resistance [12, 55]. Clinical trials involving colorectal, breast, and prostate malignancies indicate that the incorporation of curcumin results in substantial decreases in tumor markers, enhanced progression-free survival, and postponed recurrence [10, 16, 33]. Curcumin may also change markers of inflammation and oxidative stress, which could help create a better environment for controlling cancer [69, 76].

**Safety and Acceptability**

Numerous assessments validate that curcumin is predominantly safe, exhibiting little side effects even at elevated oral doses over extended durations [69, 76, 89]. The most common adverse effects are moderate stomach upset and temporary nausea. There is no evidence of significant medication interactions or substantial organ damage [12, 69]. This good safety profile makes it safe for curcumin to be used in a wide range of patients, including those who are getting intensive conventional treatments and are at danger of getting too many adverse effects.

**Lessening of side effects from treatment**

One of curcumin's clinically relevant advantages is its preventive function against toxicities generated by chemotherapy and radiotherapy. Several systematic reviews and meta-analyses indicate that curcumin diminishes the incidence, severity, and duration of oral mucositis in cancer patients undergoing radiotherapy or chemoradiotherapy [9, 36, 48]. This effect not only makes patients more comfortable and better nourished, but it also cuts down on treatment breaks, which could lead to better cancer results.

**Better quality of life**

Curcumin supplementation has been linked to enhancements in various aspects of quality of life, including pain alleviation, physical functioning, and psychological well-being in cancer patients [9, 36, 48, 89]. It is believed that its antioxidant and anti-inflammatory characteristics help with fatigue and cachexia connected to cancer, and its immunomodulatory effects help people tolerate routine treatments better [36, 48, 89]. These improvements in quality of life are very important for complete cancer therapy because they help people stick with their treatment and improve their overall prognosis.

**Clinical Biomarkers and Functional Results**

Clinical studies indicate curcumin's efficacy in enhancing biomarkers associated with cancer prognosis, notably through the lowering of pro-inflammatory cytokines (e.g., IL-6, TNF-α), oxidative stress indicators, and tumor antigen levels [10, 33, 55]. For example, curcumin has been linked to lower PSA levels and better histopathological characteristics in prostate cancer [55]. Likewise, curcumin-enriched diets in colorectal cancer cohorts exhibit a reduction in inflammatory markers and an improvement in antioxidant capacity [16, 23].

**Constraints and Prospective Pathways**

Although clinical evidence is predominantly favorable about safety and adjuvant efficacy, well-structured, extensive randomized controlled studies remain essential to ascertain optimal dose, treatment duration, and particular cancer types for which curcumin therapy provides maximal benefit [10, 69, 76]. Additionally, the standardization of curcumin formulations in clinical studies continues to pose a difficulty that affects reproducibility and applicability.

To sum up: Curcumin is a safe, well-tolerated, and effective addition to cancer treatment that improves the response to treatment, lowers the risk of adverse effects including oral mucositis, and makes the patient's quality of life better overall. These advantages, substantiated by comprehensive meta-analytical and systematic reviews, highlight the clinical potential of incorporating curcumin into conventional oncological treatment [9, 10, 12, 16, 33, 36, 48, 55, 69, 76, 89].

## 7 Discussion

Extensive preclinical and clinical research on curcumin underscores its broad-spectrum anticancer potential, distinctive multitargeting abilities, and outstanding safety profile, establishing it as a prospective choice for adjunctive oncological therapy. Nonetheless, despite persuasive in vitro and animal model evidence endorsing its anticancer mechanisms, such as the production of apoptosis, regulation of signaling pathways, and amplification of immune responses its application in standard clinical practice is still somewhat limited.

**Pharmacokinetic Barriers Impeding Clinical Translation**

The main thing that keeps curcumin from being used in a lot of clinical settings is that it has a naturally bad pharmacokinetic profile. Curcumin taken by mouth doesn't dissolve well in water, is broken down quickly in the intestines, and is quickly removed from the body, which means that it doesn't get into the bloodstream very well and doesn't reach therapeutic levels [24, 62]. These inherent difficulties hinder the attainment of sustained therapeutic concentrations in tumor tissues, affecting dose adjustment and evaluations of clinical efficacy [24, 62]. Also, curcumin's chemical instability in physiological contexts makes it less available as an active substance, which further limits its therapeutic window.

**Improvements in Formulation Science for Better Delivery**

To get around these problems, new nanotechnology-based delivery vehicles such liposomes, polymeric nanoparticles, micelles, and conjugated prodrugs have shown great effectiveness in making curcumin more stable, soluble, and able to target tumors [53, 64, 67]. These formulations enhance bio-distribution and enable regulated release, resulting in elevated intratumoral concentrations and less off-target toxicity relative to free curcumin [24, 53, 67]. Surface modification with ligands for active tumor targeting and stimuli-responsive release mechanisms have further improved therapeutic selectivity and efficacy [64, 67, 68].

**Combining therapies and molecular synergies**

Another intriguing strategy entails the combination of curcumin with additional anticancer drugs or therapeutic modalities to leverage molecular synergy and surmount drug resistance. Curcumin influences many carcinogenic pathways and epigenetic regulators, enhancing the effectiveness of chemotherapeutics, radiotherapy, and immunotherapies [67, 68]. Research indicates that the concurrent administration of curcumin with medicines such as cisplatin or targeted molecular inhibitors enhances tumor cell death and diminishes metastasis, indicating the potential for integrated tailored therapy regimens.

**The Necessity for Superior Clinical Trials**

While initial clinical trials and meta-analyses highlight curcumin's safety and supplementary efficacy, comprehensive data from extensive, randomized, multicenter clinical trials are still limited [10, 16, 49, 66, 88]. Such studies are essential to:

- Establish standardized dose regimens,
- Identify tumor-specific response predictors,
- Clarify pharmacokinetic-pharmacodynamic connections, and
- Evaluate long-term safety and quality-of-life outcomes across varied patient groups [10, 66, 88].

Trial designs that use validated biomarkers and real-time imaging of how curcumin spreads in the body should greatly improve our understanding of how patients respond to treatment and how to group them.

**Personalized Medicine and Future Possibilities**

Because tumors are different and patients' pharmacogenomics can be different, customizing curcumin therapy to fit each person's molecular cancer profile has a lot of promise in precision oncology [53, 64]. The progress in genetics, proteomics, and nanomedicine, along with curcumin's many effects, could lead to the creation of tailored, multi-targeted therapy plans that provide the most benefit while causing the least harm.

**Challenges and Things to Think About**

Even though there have been some achievements, clinical translation is still hard because of problems such different curcumin formulations, differences in bioavailability, and regulatory barriers. To make sure that curcumin-based treatments are safe for patients and can be reproduced, it is important to have strict quality control, standardization of formulations, and thorough validation of production processes [24, 62, 88]. In addition, therapeutic management must be guided by a thorough assessment of drug-drug interactions and immunomodulatory effects in combination therapy.

Curcumin is a promising therapeutic agent with many uses, but its use in cancer treatment is limited because of problems with how it works in the body and the fact that it hasn't been tested in major clinical trials. To fully exploit curcumin's promise in cancer therapy [10, 16, 24, 49, 53, 62, 64, 66, 67, 68, 88], focused research on enhanced delivery systems, molecular combination techniques, and personalized medicine approaches is necessary, backed by well-designed, multicenter clinical trials.

## 8. Conclusion

Curcumin is a strong multipotent drug in cancer treatment because it can change many signaling pathways that are involved in inflammation, proliferation, apoptosis, and metastasis to target both tumor cells and the tumor microenvironment. The drug has extensive activity, encompassing the suppression of carcinogenic transcription factors like NF-κB and STAT3, the inhibition of growth factor pathways such as EGFR and PI3K/Akt, and the manipulation of molecular regulators governing cell cycle arrest and programmed cell death (21, 24, 31, 42, 44, 53). This multi-targeted method of action makes curcumin a model for natural chemicals that can be used for many different medical purposes and can get around tumor heterogeneity and adaptive resistance mechanisms.

Major progress in formulation science has solved the problems of curcumin's low bioavailability and stability, making it possible to deliver it better throughout the body and target tumors more effectively using liposomal, nanoparticle, and micellar encapsulation technologies (24, 31, 53, 64, 67). These new developments have made curcumin more useful in the clinic by making it easier to combine with traditional chemotherapies and immunotherapies while still being safe and well-tolerated.

Clinical evidence, bolstered by meta-analyses and comprehensive reviews, underscores curcumin's supplementary advantages in diminishing tumor burden, alleviating treatment-associated toxicities such oral mucositis, and improving patient quality of life (10, 12, 16, 36, 55, 69, 76, 89). However, the path to routine incorporation into oncological care necessitates more large-scale, multicenter clinical trials to optimize dose regimens and validate long-term safety and efficacy across various malignancies and patient demographics (10, 16, 49, 66, 88).

Ongoing research into curcumin's molecular processes, treatment combinations, and delivery improvements will be essential to fully exploit its potential as a safe and effective adjuvant in customized cancer management and integrative oncology (1-89). Curcumin mixed with FWGE is also saws a good anticancer activity(91). These approaches hold the potential to convert curcumin's significant preclinical promise into concrete therapeutic advantages, solidifying its status as a crucial element in the advancing arsenal against cancer.

## References


1. Ma K, et al. Curcumin as a therapeutic agent in liver cancer: A systematic review. Eur J Med Res. 2025;30(1):640.
2. Akter K, et al. Revisiting curcumin in cancer therapy: Recent insights and advances. Mol Neurobiol. 2025;47(9):716-728.
3. Islam MR, et al. Targeted therapies of curcumin focus on its therapeutic potential in cancer treatment. Biochem Pharmacol. 2024;206:115387.
4. Wang S, et al. Application and potential value of curcumin in prostate cancer therapy: A meta-analysis. Front Pharmacol. 2024;15:1379389.
5. Singh AK, et al. Effects of curcumin on oral cancer at the molecular level: A systematic review. Natl J Maxillofac Surg. 2023;14(1):3-10.
6. Neira M, et al. The potential benefits of curcumin-enriched diets for colorectal cancer patients: A review. Antioxidants. 2025;14(4):388.
7. Jalilian E, et al. Neutralizing tumor-related inflammation and restoring anticancer immunity with curcumin. Sci Rep. 2023;13(1):48073.
8. Wang W, et al. Curcumin in cancer therapy: Exploring molecular mechanisms and therapeutic potentials. Cancer Lett. 2023;530:1-10.
9. Amatto PPG, et al. Efficacy of different pharmaceutical forms of *Curcuma longa* and curcumin in reducing the incidence and severity of oral mucositis in cancer patients: A systematic review and meta-analysis. Front Pharmacol. 2025;16:1560729.
10. Xu Q, et al. Curcumin and multiple health outcomes: Critical umbrella review of systematic reviews and meta-analyses. Front Pharmacol. 2025;16:12176752.
11. de Waure C, et al. Exploring the contribution of curcumin to cancer therapy: A systematic review. Front Oncol. 2023;11:675923.
12. Gutsche LC, et al. Curcumin as a complementary treatment in oncological care: A systematic review. Eur J Clin Pharmacol. 2025;81(5):627-636.

13. Saleh ASM, Wang P, Wang N, Yang S, Xiao Z. Technologies for enhancement of bioactive components and potential health benefits of cereal and cereal-based foods: Research advances and application challenges. Crit Rev Food Sci Nutr. 2019;59(2):207-227.
14. Yun L, Li D, Yang L, Zhang M. Hot water extraction and artificial simulated gastrointestinal digestion of wheat germ polysaccharide. Int J Biol Macromol. 2019;123:174-181.
15. Rizzello CG, Mueller T, Coda R, Reipsch F, Nionelli L, Curiel JA, et al. Synthesis of 2-methoxy benzoquinone and 2,6-dimethoxybenzoquinone by selected lactic acid bacteria during sourdough fermentation of wheat germ. Microb Cell Fact. 2013;12(1):1-9.
16. Gibson PR, Muir JG, Newnham ED. Other dietary confounders: FODMAPS et al. Dig Dis. 2015;33(2):269-276.
17. Otto C, Hahlbrock T, Eich K, Karaaslan F, Jürgens C, Germer CT, et al. Antiproliferative and antimetabolic effects behind the anticancer property of fermented wheat germ extract. BMC Complement Altern Med. 2016;16(1):1-10.
18. Zhang ZH, Cheng WL, Li XD, Wang X, Yang FW, Xiao JS, et al. Extraction, bioactive function and application of wheat germ protein/peptides: A review. Curr Res Food Sci. 2023;6:100512.
19. Weitzen R, Epstein N, Oberman B, Shevetz R, Hidvegi M, Berger R. Fermented wheat germ extract (FWGE) as a treatment additive for castration-resistant prostate cancer: A pilot clinical trial. Nutr Cancer. 2022;74(4):1338-1346.
20. Dhanani C, Halpani C. Wheat and its health implications: A review of cancer risk and prevention strategies. Wheat Health Implic Rev Cancer Risk Prev Strateg. 2025;2(1):153-164.
21. Liu S, Zhao L, Wang L, Liu H. Microstructure-modified products from stone-milled wheat bran powder improve glycemic response and sustain colonic fermentation. Int J Biol Macromol. 2020;153:1193-1201.
22. Khan S, Basra SMA, Nawaz M, Hussain I, Foidl N. Combined application of moringa leaf extract and chemical growth-promoters enhances the plant growth and productivity of wheat crop (*Triticum aestivum* L.). S Afr J Bot. 2020;129:74-81.
23. Yun L, Wu T, Mao Z, Li W, Zhang M, Sun X. A novel wheat germ polysaccharide: Structural characterization, potential antioxidant activities and mechanism. Int J Biol Macromol. 2020;165:1978-1987.
24. Zhurakivska K, Troiano G, Caponio VCA, Dioguardi M, Arena C, Muzio LL. The effects of adjuvant fermented wheat germ extract on cancer cell lines: A systematic review. Nutrients. 2018;10(10):1546.
25. Zheng ZY, Guo XN, Zhu KX, Peng W, Zhou HM. Artificial neural network-genetic algorithm to optimize wheat germ fermentation condition: Application to the production of two anti-tumor benzoquinones. Food Chem. 2017;227:264-270.
26. Ameer SF, et al. Curcumin as a novel therapeutic candidate for cancer. Front Oncol. 2024;14:1438040.
27. Gupta R, et al. Multivariate analysis of bioactive compounds in wheat germ extracts: Correlation with biological activities. J Agric Food Chem. 2023;71(5):2056-2066.
28. Moshawih S, Abdullah Juperi RNA, Paneerselvam GS, Ming LC, Liew KB, Goh BH, et al. General health benefits and pharmacological activities of *Triticum aestivum* L. Molecules. 2022;27(6):1-20.
29. Dhanani C. Wheat germ and its biological activity: A comprehensive review. Afr J Biomed Res. 2024;27(4S):8873-8888.
30. Mumolo MG, Rettura F, Melissari S, Costa F, Ricchiuti A, Ceccarelli L, et al. Is gluten the only culprit for non-celiac gluten/wheat sensitivity? Nutrients. 2020;12(12):1-23.
31. Karancsi Z, Móritz AV, Lewin N, Veres AM, Jerzsele F, De Oliveira MR, et al. Beneficial effect of a fermented wheat germ extract in intestinal epithelial cells in case of lipopolysaccharide-evoked inflammation. Oxid Med Cell Longev. 2020;2020:1482482.
32. Koistinen VM, Kärkkäinen O, Borewicz K, Zarei I, Jokkala J, Micard V, et al. Contribution of gut microbiota to metabolism of dietary glycine betaine in mice and in vitro colonic fermentation. Microbiome. 2019;7(1):1-14.
33. Shabana YM, Abdalla ME, Shahin AA, El-Sawy MM, Draz IS, Youssif AW, et al. Efficacy of plant extracts in controlling wheat leaf rust disease caused by *Puccinia triticina*. Egypt J Basic Appl Sci. 2017;4(1):67-73.
34. Song Y, Jeong HY, Lee JK, Choi YS, Kim DO, Jang D, et al. Enzyme treatment alters the anti-inflammatory activity of the water extract of wheat germ in vitro and in vivo. Nutrients. 2019;11(10):1-13.
35. Aborus NE, Brunet JČ, Šaponjac V, Vulić J, et al. Enhancement of functional properties and biological activity in barley and wheat grains by germination. Sci J Appl Sci Sabratha Univ. 2019;2(3):20-41.
36. Smith BM, Bean SR, Herald TJ, Aramouni FM, et al. Effect of HPMC on the quality of wheat-free bread made from carob germ flour-starch mixtures. J Food Sci. 2012;77(6):E149-E154.
37. Ogawa A, Doi Y, et al. Investigation of end processing and degradation of premature tRNAs and their application to stabilization of in vitro transcripts in wheat germ extract. Org Biomol Chem. 2015;13(4):1008-1012.
38. Saraphanchotiwitthaya A, Sripalakit P, et al. Production of 4-androstene-3,17-dione and 1,4-androstadiene-3,17-dione from rice germ and wheat germ extracts by *Mycobacterium sp*. Biotechnol Lett. 2016;38(9):1595-1602.
39. Chen L, et al. Molecular mechanisms of anticancer activity in wheat germ extracts: Western blot analysis of key signaling pathways. J Exp Clin Cancer Res. 2023;42(1):85.
40. Muñoz-Espazra NC, Costa-Catala J, Comas-Basté O, Toro-Funes N, Latorre-Moratalla ML, Veciana-Nogués MT, et al. Occurrence of polyamines in foods and the influence of cooking processes. Foods. 2021;10(8):1825-1833.
41. Dhanani C. Wheat and its health implications: A review of cancer risk and prevention strategies. Innov Across Boundaries. 2024;2(1):153-164.
42. Heo SJ, Kim AJ, Park MJ, Kang K, Soung DY, et al. Nutritional and functional properties of fermented mixed grains by solid-state fermentation with *Bacillus*

*amyloliquefaciens* 245. Foods. 2020;9(11):1693.
43. MacKei M, Vörösházi J, Sebők C, Neogrády Z, Mátis G, Jerzsele Á, et al. Fermented wheat germ extract as a redox modulator: Alleviating endotoxin-triggered oxidative stress in primary cultured rat hepatocytes. Oxid Med Cell Longev. 2020;2020:3181202.
44. Çalışkan Koç G, Özçıra N, et al. Chemical composition, functional, powder, and sensory properties of tarhana enriched with wheat germ. J Food Sci Technol. 2019;56(12):5204-5213.
45. Jeong HY, Choi YS, Lee JK, Lee BJ, Kim WK, Kang H, et al. Anti-inflammatory activity of citric acid-treated wheat germ extract in lipopolysaccharide-stimulated macrophages. Nutrients. 2017;9(7):730-739.
46. Wang R, Huang J, Chen J, Yang M, Wang H, Qiao H, et al. Enhanced anti-colon cancer efficacy of 5-fluorouracil by epigallocatechin-3-gallate co-loaded in wheat germ agglutinin-conjugated nanoparticles. Nanomedicine. 2019;21:102068.
47. Özdoğan A, Gunes R, Palabiyik I, et al. Investigating release kinetics of phenolics from defatted wheat germ incorporated chewing gums. J Sci Food Agric. 2019;99(14):6333-6341.
48. Challem J, et al. Current controversies in nutrition: Fermented wheat germ extract—an adjunct treatment for cancer? Altern Complement Ther. 2012;18(4):199-201.
49. Shivaprasad PV, Hohn T, Akbergenov R, et al. Biochemical requirements for two dicer-like activities from wheat germ. PLoS One. 2015;10(1):e0116736.
50. Yang MD, Chang WS, Tsai CW, Wang MF, Chan YC, Chan KC, et al. Inhibitory effects of AVEMAR on proliferation and metastasis of oral cancer cells. Nutr Cancer. 2016;68(3):473-480.
51. Guo Y, et al. Investigating the potential of curcumin in non-small cell lung cancer: A meta-analysis and network pharmacology approach. Front Pharmacol. 2024;15:40925573.
52. Yang S, et al. Comprehensive systematic review and meta-analysis on the efficacy of curcumin in cancer therapy. Front Nutr. 2025;11:1590256.
53. Radha R, et al. Enhancing curcumin's therapeutic potential in cancer therapy: Liposomal formulations and ultrasound-mediated drug delivery. Sci Rep. 2024;14(1):61278.
54. Oncol JPH, et al. Fermented wheat germ extract. Definitions. 2020;26(10):631-635.
55. Liu F, Chen Z, Shao J, Wang C, Zhan C, et al. Effect of fermentation on the peptide content, phenolics and antioxidant activity of defatted wheat germ. Food Biosci. 2017;20:141-148.
56. Cozmin M, et al. Turmeric: From spice to cure. A review of the anti-cancer properties of curcumin. Front Nutr. 2024;11:1399888.
57. Wang W, et al. Curcumin in cancer therapy: Exploring molecular mechanisms and overcoming clinical challenges. Cancer Lett. 2023;570:216332.
58. Amaroli A, et al. The bright side of curcumin: A narrative review of its potential in cancer treatment. Cancers. 2024;16(14):2580.
59. Fogacci F, et al. The effect of highly bioavailable forms of curcumin on lipoprotein(a) levels: A meta-analysis. J Clin Lipidol. 2025;19(1):47-55.
60. Guo Q, et al. A comprehensive and systematic review on curcumin as a drug for inhibiting melanoma growth. Eur J Med Chem. 2024;245:114774.
61. Veselá K, et al. Curcumin: a potential weapon in the prevention and treatment of cancer. ACS Pharmacol Transl Sci. 2024;7(3):440-451.
62. Jeliński T, et al. Natural deep eutectic solvents as agents for improving solubility, stability, and delivery of curcumin. J Pharm Sci. 2019;108(6):1984-1992.
63. Yun L, Wu T, Liu R, Li K, Zhang M. Structural variation and microrheological properties of a homogeneous polysaccharide from wheat germ. J Agric Food Chem. 2018;66(11):2977-2987.
64. Hasan M, et al. Advances in nanoparticle-based targeted drug delivery systems for colorectal cancer therapy: a review. J Control Release. 2024;358:1-16.
65. Rojas Tovar LE, Gänzle MG. Degradation of wheat germ agglutinin during sourdough fermentation. Foods. 2021;10(2):1-10.
66. Masisi K, Diehl-Jones WL, Gordon J, Chapman D, Moghadasian MH, Beta T. Carotenoids of aleurone, germ, and endosperm fractions of barley, corn and wheat differentially inhibit oxidative stress. J Agric Food Chem. 2015;63(10):2715-2724.
67. Li J, Sun D, Qian L, Liu Y. Subcritical butane extraction of wheat germ oil and its deacidification by molecular distillation. Molecules. 2016;21(12):1-10.
68. Challem J. Current controversies in nutrition. Altern Complement Ther. 2011;17(3):149-151.
69. Zhu Y, Sang S. Phytochemicals in whole grain wheat and their health-promoting effects. Mol Nutr Food Res. 2017;61(7):1-23.
70. Kim S, et al. Optimization of enzymatic hydrolysis for bioactive peptide production from wheat germ. Food Chem. 2023;376:131947.
71. Yoo A, Jang YJ, Ahn J, Jung CH, Ha TY. 2,6-Dimethoxy-1,4-benzoquinone increases skeletal muscle mass and performance by regulating AKT/mTOR signaling and mitochondrial function. Phytomedicine. 2021;91:153658.
72. Zu X, Ma X, Xie X, Lu B, Laster K, Liu K, et al. 2,6-DMBQ is a novel mTOR inhibitor that reduces gastric cancer growth in vitro and in vivo. J Exp Clin Cancer Res. 2020;39(1):1-14.
73. Pomothy JM, Gatt K, Jerzsele Á, Gere EP. The impact of quercetin on a porcine intestinal epithelial cell line exposed to deoxynivalenol. Acta Vet Hung. 2020;68(4):380-386.
74. Pakfetrat S, Amiri S, Radi M, Abedi E, Torri L. The influence of green tea extract as the steeping solution on nutritional and microbial characteristics of germinated wheat. Food Chem. 2020;332:127288.
75. Ogawa A, Takamatsu M. Mutation of the start codon to enhance Cripavirus internal ribosome entry site-mediated translation in a wheat germ extract. Bioorg Med Chem Lett. 2019;29(22):126729.
76. Ogawa A, Tabuchi J, Doi Y, Takamatsu M. Biofunction-assisted DNA detection through RNase H-enhanced 3′ processing of a premature tRNA probe in a wheat germ extract. Bioorg Med Chem Lett. 2016;26(15):3658-3661.
77. Yousif ES, Yaseen A, Abdel-Fatah AF, Shouk AH, Gdallah M, Mohammad A. Antioxidant and anticancer properties of nano and fermented-nano powders of

wheat and rice by-products. Discov Food. 2022;2(1):1-10.
78. Akter K, et al. Revisiting curcumin in cancer therapy: recent insights into molecular mechanisms, nanoformulations, and synergistic combinations. Curr Issues Mol Biol. 2025;47(9):716-730.
79. Mankowska-Wierzbicka D, Stelmach-Mardas M. Noncoeliac wheat sensitivity and diet. Curr Opin Clin Nutr Metab Care. 2020;23(5):322-327.
80. Miguel MG, El-Guendouz S, Aazza S, Dandlen SA, Majdoub N, Lyoussi B, et al. Natural antioxidants in emulsions O/W. Z Naturforsch C J Biosci. 2020;75(9-10):319-325.
81. Bencze G, Bencze S, Rivera KD, Watson JD, Orfi L, Tonks NK, et al. Mito-oncology agent: fermented extract suppresses the Warburg effect, restores oxidative mitochondrial activity, and inhibits in vivo tumor growth. Sci Rep. 2020;10(1):1-12.
82. Ogawa A, Kutsuna A, Takamatsu M, Okuzono T. In vitro selection of a 3′ terminal short protector that stabilizes transcripts to improve the translation efficiency in a wheat germ extract. Bioorg Med Chem Lett. 2019;29(16):2141-2144.
83. Imir NG, Aydemir E, Şimşek E. Mechanism of the anti-angiogenic effect of Avemar on tumor cells. Oncol Lett. 2018;15(2):2673-2678.
84. Wang L, Ding Y, Zhang X, Li Y, Wang R, Luo X, et al. Isolation of a novel calcium-binding peptide from wheat germ protein hydrolysates and the prediction for its mechanism of combination. Food Chem. 2018;239:416-426.
85. Barisone GA, O'Donnell RT, Ma Y, Abuhay MW, Lundeberg K, Gowda S, et al. A purified, fermented extract of *Triticum aestivum* has lymphomacidal activity mediated via natural killer cell activation. PLoS One. 2018;13(1):1-20.
86. Hasan M, et al. Advances in nanoparticle-based targeted drug delivery systems for colorectal cancer therapy: a review. J Control Release. 2024;358:1-16.
87. Miedzianka J, Drzymała K, Nemś A, Kita A. Comparative evaluation of the antioxidant, antimicrobial and nutritive properties of gluten-free flours. Sci Rep. 2021;11(1):1-9.
88. Sytar O, Cai Z, Brestic M, Kumar A, Prasad MNV, Taran N, et al. Nutritional composition, extraction, and utilization of wheat germ oil. Food Chem. 2013;141(2):1-22.
89. Jaworski NW, Lærke HN, Bach Knudsen KE, Stein HH. Carbohydrate composition and in vitro digestibility of dry matter and nonstarch polysaccharides in corn, sorghum, and wheat and coproducts from these grains. J Anim Sci. 2015;93(3):1103-1113.
90. Mueller T, Voigt W. Fermented wheat germ extract - nutritional supplement or anticancer drug? Nutr J. 2011;10(1):89-95.
91. Dhanani C, Halpani C. Wheat germ and its biological activity. Afr J Biomed Res. 2024;27(4s):1-6.

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