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REVIEW ARTICLE

# Curcumin's Potential as A Drug Delivery Method and Anticancer Treatment

**Leesha Varshney, Poonam Yadav, Pallavi Lavahle, Reema Sinha, Anupam, Payal Kesharwani**

## ABSTRACT

This abstract explores the potential of curcuma as both a drug delivery method and an anticancer treatment. *Curcuma*, a natural compound derived from turmeric, has gained attention for its bioactive properties. As a drug delivery method, curcuma's lipophilic nature allows it to encapsulate various therapeutic agents, enhancing their solubility and bioavailability. Moreover, curcuma's inherent anti-inflammatory and antioxidant characteristics contribute to its potential as an effective anticancer treatment. This abstract reviews recent research on curcuma-based drug delivery systems and its mechanisms of action against cancer cells, highlighting its promising role in advancing drug delivery strategies and cancer therapies. Certainly, in recent years, researchers have focused on harnessing the unique properties of curcuma for drug delivery purposes. Its ability to form stable complexes with hydrophobic drugs, along with its biocompatibility, makes it an attractive candidate for improving the delivery of poorly water-soluble drugs. By encapsulating these drugs within curcuma-based nanoparticles or micelles, researchers aim to enhance drug stability and release kinetics, ultimately leading to more effective treatments with reduced side effects. Additionally, curcuma's potential as an anticancer treatment has been extensively investigated. Its active compound, curcumin, exhibits multifaceted effects on various cancer cell types. Curcumin has been shown to modulate signaling pathways involved in cell proliferation, apoptosis, and angiogenesis. Moreover, curcumin's ability to target tumor cells while sparing normal cells makes it a promising candidate for combination therapies that enhance the effectiveness of traditional chemotherapy agents.Clinical studies have explored curcuma's role in reducing cancer growth, metastasis, and even improving patients' response to chemotherapy. However, challenges such as low bioavailability and rapid metabolism of curcumin have prompted innovative approaches, including nanoparticle formulations and co-administration with absorption-enhancing agents .In conclusion, the combined potential of curcuma as a drug delivery method and an anticancer treatment opens up exciting possibilities for the future of pharmaceutical research. By addressing its limitations and further exploring its mechanisms of action, curcuma-based therapies could revolutionize drug delivery strategies and contribute to more targeted and effective cancer treatments.

**Keywords:** *Curcuma*, Drug delivery, Anti-cancer, Enhancing, hydrophobic drugs, Bio-compatilbility, Clinical studies, Nano-particles, Therapies.

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## INTRODUCTION

As a potential anticancer agent, curcumin, which is derived from the spice turmeric, has attracted a lot of interest. This organic polyphenol has a long history of use in traditional medicine and has proven to have a number of positive effects, such as anti-inflammatory, antioxidant, and anticancer characteristics.

Curcumin has been extensively studied for its anticancer activity, including its capacity to inhibit tumour growth, cause cancer cells to undergo programmed cell death (apoptosis), and prevent the establishment of new blood vessels that support tumour development (angiogenesis). Curcumin is a desirable option for the creation of cutting-edge cancer treatments because of these mechanisms.

The ability of curcumin to target a variety of signalling pathways involved in the development and progression of cancer is one of its key benefits. Curcumin prevents cancer metastasis by interfering with a variety of molecular targets, including transcription factors, growth factors, cytokines, enzymes, and cell cycle regulators.

Curcumin also exhibits little toxicity to healthy cells, making it a possible safer alternative to traditional chemotherapeutic treatments. Additionally, by sensitizing cancer cells, it has demonstrated the capacity to improve the efficacy of radiation and chemotherapy. Numerous cancer types, including breast, lung, prostate, colon, and pancreatic cancer, have shown this synergistic impact.

By preventing cell growth and inducing apoptosis, curcumin demonstrates anticancer effects. The dose, length of therapy, and particular cell type all affect curcumin's ability to inhibit cell proliferation. Curcumin stops the cell cycle at low dosages and produces apoptosis at higher ones. The family of cyclin and cyclin-dependent kinases, whose expression is closely linked to cancer is one of the cell cycle-regulating proteins that regulates cell proliferation .

According to a recent study curcumin can make lung cancer cells more susceptible to anoikis by post-translationally altering Bcl-2 through the ubiquitin-proteasome pathway.

Through a variety of signaling mechanisms, such as MMP-9, MMP-2, and COX-2, curcumin also works as a negative regulator of cancer cell migration and invasion.

Curcumin research has been thoroughly examined in both animal and human investigations. Curcumin significantly reduces the growth of skin tumours that are produced by DMBA and TPA in mice. Administering curcumin dramatically lowers the rate of breast cancer metastases to the lung in a xenograft model. Oral administration of curcumin was demonstrated to be well tolerated and to have no dose-limiting toxicity in phase 1 clinical investigations .

Curcumin treatment demonstrated a significant improvement in the precancerous lesion in patients with intestinal metaplasia.Cheng *et al*. confirming the clinical use of curcumin as a cancer prevention treatment agent.

Although curcumin has shown promise pharmacological benefits and safety both in vitro and in vivo, the molecule has a low bioavailability and tends to accumulate in tissues. It is necessary to conduct more research on proper medication administration, dose optimisation, and biodistribution

Despite these benefits, curcumin has poor water solubility, which results in solubility-limited bioavailability and class II drug status in the Biopharmaceutics Classification System. In addition, due to its quick intestine and 60–70% of an oral dosage of curcumin is processed by the liver and excreted in the faeces

In rats, curcumin (2 g/kg) given as an aqueous suspension reached its peak plasma concentration of 1-g/mL in 1 hour and then rapidly decreased to undetectable levels in 5 hours (24). After giving mice 0.1 g/kg of curcumin intraperitoneally, studies by Pan *et al*. revealed that only around 2.25 g/mL reached the plasma within 15 minutes, and that amount quickly dropped to 0.35 g/mL after 1 hr. About 50% of the curcumin given via parenteral means, such as intravenous, was discovered to be removed in the bile within 5 hours. Even in clinical studies, oral administration of high doses of curcumin (8–12 g daily) led to very low curcumin plasma concentrations (1 g/mL), which were insufficient to exhibit any appreciable pharmacological or therapeutic effect. Despite using high doses of curcumin in several clinical investigations, only a small number of individuals showed positive results. Carroll *et al*.'s fairly recent clinical investigation found that curcumin was significantly more effective at lowering colorectal aberrant crypt foci (ACF) at 4 g/day than at 2 g. When examined by UFLC-UV, neither the plasma nor the biopsy samples from the patients had any curcumin.

## Turmeric Scientific Description

| | |
|---|---|
| Kingdom | Plantae |
| Clade | Tracheophytes |
| Clade | Angiosperms |
| Clade | Monocots |
| Order | Zingiberals |
| Family | Zingiberacae |
| Genus | *Curcuma* |
| Species | *C.longa* |

## Bionomial Name

*Curcuma longa*

## Synonyms

Curcuma Domestica Valeton

## Turmeric Rhizome and Powder

Turmeric powder and rhizome is shown in Figure 1.

## Botanical view of *C. longa*

Botanical view of *C. longa* is shown in Figure 2.

## Extraction and Purification Of Curcumin

The root system of the Asian subcontinental plant known as turmeric, *C. longa*, which belongs to the ginger family, is where curcumin is generated. When first fresh rhizomes are cleaned, washed with deionized water, cut into slices, and dried for a week in the sun before being dried once more for six hours at 50°C in a hot air oven. The dried rhizomes are powdered using an electronic grinder after being chopped into small pieces. Six grammes of the material are exposed to a 12-hour Soxhlet extraction in methanol. A rotary evaporator is then used to concentrate the extract. Curcumin, demethoxycurcumin, and bis-demethoxycurcumin are all present in this crude combination of curcuminoids.

**Figure 1:** Turmeric Powder

**Figure 2:** *Curcuma longa*

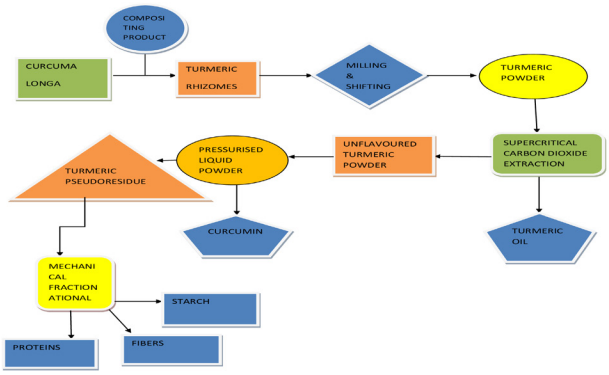


**Figure 3:** Extraction and Purification of Curcumin

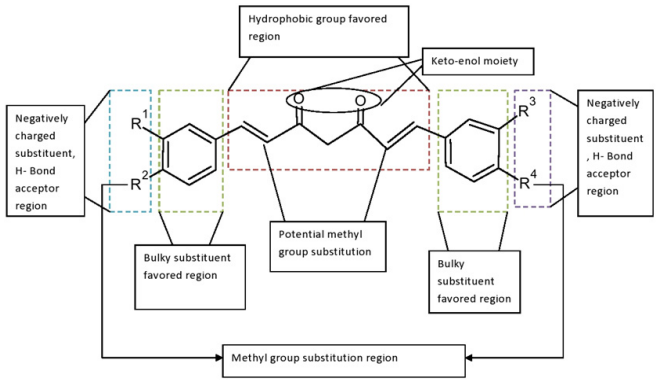


**Figure 5:** Sar of Curcumin

After that, it goes via silica gel column chromatography and is eluted with methanol with increasing polarity, followed by methanol, and chloroform.

All the collected fractions are analyzed by TLC and detected as yellow Spots. Then pure curcumin is collected after recrystallization. It is a golden-yellow solid, with a molecular weight of 368 gmol-1and a melting point of 182°C.

## CHEMISTRY OF CURCUMIN

Plants and other animal parts that have been discovered as being physiologically active have been utilized for thousands of years as dietary supplements. Due to their potential to treat and prevent human diseases, these natural substances have drawn a lot of attention. A significant biologically active substance called curcumin (diferuloylmethane) is obtained from the dried rhizome of turmeric, or *C. longa*. Due to its yellow color, it has been widely utilized as a medicinal herb and food additive for ages. Curcuminoids, which include curcumin (curcumin I), demethoxycurcumin (curcumin II), and bisdemethoxycurcumin (curcumin III), are thought to be responsible for its therapeutic effects (Figure 4). A significant portion of commercial curcumin is curcumin I (77%), whereas curcumin II and III make up roughly 17% and 3% of the total.

### Structure Active Relationship of Curcumin

A drug molecule's pharmacokinetics and physiochemical characteristics are also changed by changes to its chemical structure, in addition to its ability to bind to receptors and pharmacological activity . A detailed examination of a drug's natural and synthetic counterparts is required to identify the key pharmacophores inside the molecule . Figure shows the curcumin molecule's chemical make-up. It is made up of two phenyl rings that have been given hydroxyl and methoxyl groups and are joined by a seven carbon keto-enol linker (C7), as can be seen. Curcumin is a naturally occurring substance, however the majority of its derivatives are created through a Aryl-aldehyde and acetylacetone interaction. Several chemical derivatives, such as compounds with alkyl substituents on the middle carbon of the linker (C7 moiety), can be produced using this assembly approach. This derivative showed much more effectiveness than curcumin in reducing endothelial cell growth are both *in-vivo* and *in-vitro* invasion, and it also showed a steric hindrance impact towards metabolising enzymes like alcohol dehydrogenase.Dimethylcurcumin, also known as ASC-J9 (5-hydroxy-1, 7-bis (3, 4-dimethoxyphenyl)-1, 4, 6-heptatrien-3-one), is a recently created derivative of curcumin that promotes the degradation of androgen receptors It has seen utilization to treat prostate cancer. A substantial anti proliferative impact against estrogen-dependent breast cancer cells has been demonstrated by it. Although the molecule's targetability and activity have been improved by methylation, its hydrophobicity has significantly risen In contrast to curcumin, which has decreased the amount that may be administered as part of a cancer treatment.

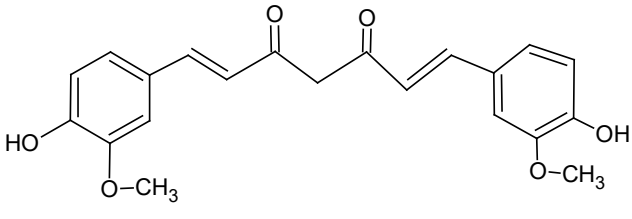


**Figure 4:** Molecular Structure of Curcumin

## MECHANISM OF ACTION OF CURCUMIN

Numerous malignancies, including those of the breast, lung, colorectal, head and neck, gastric, bladder, prostate, thyroid, liver, ovarian, oral, pancreatic, cervical, tongue, and brain, have been the subject of in-depth research on curcumin's anticancer properties. Figure, we'll go into more detail about the fundamental mechanics.

The primary outcomes and mechanisms of curcumin's anti-cancer actions.

- Curcumin may prevent proliferation by slowing the cell cycle by blocking the Wnt/-catenin pathway, Increasing the expression of p53, p21, and p27, while subsequently reducing the levels of CDK4 and Cyclin D1..

- Through inhibition of the TGF-β/Smad2/3 pathway, curcumin has the potential to elevate E-cadherin levels and diminish the presence of N-cadherin, vimentin, fibronectin, slug, and snail, thereby impeding migration and invasion.
- By stimulating the p38 MAPK, JNK, and ERK pathways, curcumin has the potential to enhance the generation of reactive oxygen species (ROS).
- Curcumin has the potential to induce ferroptosis and elevate the levels of TFRC, FTL, and FTH1.
- Curcumin may boost apoptosis by increasing the expression of pro-apoptotic proteins like Bax, Cleaved-caspase-3, Cleaved-caspase-9, and Cleaved-PARP, while concurrently inhibiting the expression of anti-apoptotic protein Bcl-2.
- By enhancing the expression of Beclin1, Atg5, Atg3, and LC3B-II/I, curcumin may help the PI3K/Akt/mTOR pathway induce autophagy.
- Through blocking JAK/STAT3 pathways, curcumin could lower levels of Oct4, Sox2, and Nanog to diminish stemness..
- TLR4/NF-B signaling pathway could be suppressed by curcumin to reduce inflammation (TNF-, IL-6, and IL-1).
- Curcumin can suppress the expression of VEGF, CD31, SMC, iNOS, and COX-2, which can reduce angiogenesis
- By lowering the Firmicutes/Bacteroidetes ratio, curcumin may be able to control the gut microbiota.

## Preventing the proliferation of cancer cells

Cancer is characterised by unchecked cell proliferation, making anti-proliferation a crucial treatment strateCurcumin may be able to reduce the multiplication of cancer cells, according to numerous research. For instance, a study found that curcumin could decrease the viability of MDA-MB-231 and MDA-MB-468 triplenegative breast cancer cells. It could also impede colony proliferation by blocking the Hedgehog pathway and the expression of downstream target genes PTCH1, SMO, Gli1 and Gli2 Additionally, curcumin dramatically increased the expression of miR-34a, which inhibited the proliferation of prostate cancer PC3 and DU145 cells Cell development, cell division, and the duplication of genetic materialare all made possible by the cell cycle, a closely controlled procedure Since cyclin is commonly overactive in cancer cells, producing unregulated development of cancer cells, targeting the cell cycle is believed to be one of the objectives of cancer therapy, causing unchecked growth of cancer cells . The cell cycle is divided into four stages: G1 (when cells choose whether to divide and expand or enter the quiescent G0 phase), S (DNA synthesis), G2 (mitosis preparation), and M (mitosis).Human malignancies exhibit abnormal activation of cell cycle proteins, which contributes to the pathogenesis of the majority of tumors . Curcumin was found to target NF-B signaling to produce subG1 population accumulation, cause G2/M arrest, and upregulate the expression levels of p21 in breast cancer MCF-7, MDA-MB-453, and MDA-MB-231 cells. Curcumin has been shown in several in vivo experiments to slow tumor growth. By blocking circ-PRKCA, curcumin, for instance, could diminish the volume and weight of lung tumors in the BALB/c nude mice xenograft model. Curcumin also inhibited the growth of ovarian cancer in xenograft models by increasing Cir-PLEKHM3 In the 4-nitroquinoline-1-oxide-induced head and neck cancer model, curcumin may also lessen tumor growth and a transformational phenotype, and tumor volume was dramatically decreased following curcumin treatment. Another study discovered that curcumin promoted miR34a expression, which in turn significantly decreased tumor weight and tumor size in BALB/c nude mice bearing subcutaneous xenografts of SGC-7901 gastric cancer cells. Additionally, curcumin dramatically reduced the weight and volume of the liver tumor in a HepG2 xenograft mice model.

## Clinical Trial: Evaluation of Efficacy of Curcumin

The effectiveness and safety of curcumin as a preventive therapy agent for various malignancies are now being investigated in a number of clinical studies. Curcumin was demonstrated to be safe even at high dosages in prospective phase I clinical trials (Cheng *et al*., 2001). Patients in this study were given oral curcumin tablets for three months at doses of 500, 1000, 2000, 4000, and 8000 mg daily to treat premalignant lesions brought on by oral leukoplakia, intestinal metaplasia, uterine cervical intraepithelial neoplasia, skin Bowen's disease, and bladder cancer. Even at the maximum dose (8000 mg/day), there was no harm seen in these subjects. The patients, however, rejected this dose because of its large volume. The peak blood concentration of curcumin was 0.51 0.11 M following the administration of 4000 mg, while it was 0.63 0.06 M and 1.77 1.87 M following the administration of 6000 mg and 8000 mg, respectively. A comparable study revealed that healthy volunteers receiving a single dose of curcumin up to 12,000 mg did not experience any harmful effects that were dose-limiting, not even minor side effects like diarrhea (Lao *et al*., 2006).

A second phase clinical trial was carried out in colon cancer patients to further explore the phamacodynamics of curcumin (Sharma *et al*., 2004). Curcuminoid was given orally at doses of 450, 900, 1800, and 3600 mg/day of curcumin for 4 months. It is formulated as a 500 mg soft gelatin capsule containing 450 mg of

curcumin, 40 mg of desmethoxycurcumin, and 10 mg of bisdesmethoxycurcumin. These biomarkers are widely used to assess the efficiency of curcumin because curcumin is known to stimulate glutathione S-transferase (GST), reduce prostaglandin E2 (PGE2) synthesis, and decrease the development of oxidative DNA adducts (M1G). To evaluate the pharmacokinetic parameters, curcumin and its metabolites were taken from plasma, urine, and faeces and analyzed. Except in a few instances when patients experienced a little gastrointestinal upset, the data demonstrated that curcumin was well tolerated by the patients without a dose-limiting toxicity. The outcome also demonstrated that curcumin was appropriate for phase II evaluation at a dose of 3600 mg/day. Since GST and M1G were not affected by curcumin's ability to reduce PGE2, it is possible that these two proteins are not reliable indications of the drug's effectiveness. Curcumin and its glucuronide, sulphate, and other metabolites were also discovered in the plasma and urine. These metabolites' occurrence at all time points suggests that oral administration of curcumin results in inadequate systemic availability. Numerous investigations have shown low systemic bioavailability of curcumin due to poor absorption, quick metabolism, and rapid systemic elimination, which is consistent with the a fore mentioned conclusion Following curcumin treatment, the metabolites of curcumin called glucuronide and sulphate are quickly found in the portal and peripheral circulation . In this trial, Patients with colorectal cancer liver metastases received oral administration of curcumin at doses of 450, 1800, and 3600 mg per day for a week. Since no presence of curcumin or its metabolites in the or hepatic tissue, curcumin cannot be used to treat individuals who have tumors that are far from the absorption site Patients with advanced pancreatic cancer received 8 g/day of curcumin orally for 8 weeks as part of a phase II clinical trial. In addition to successfully lowering tumor size and activating NF-B and COX-2, the medication was well tolerated by the patients and had no adverse systemic effects. According to one mechanism, curcumin causes an overexpression in the p53 tumor tissues, which causes cancer cells to undergo apoptosis.

### Result of Clinical Trials

To evaluate the impact of curcumin on malignancies, Numerous clinical trials have been conducted. For instance, 40 cervical cancer stage IIB-IIIB patients were enrolled in a quasi-experimental manner, who simultaneously received radiation therapy and curcumin (4 g/day) or a placebo for 7 days. According to the findings, ingestion of curcumin reduced the anti-apoptotic protein surviving in 15 individuals (75%) while raising it in five patients (25%). In contrast, 12 patients (60%) increased their chance of survival, compared to 8 patients (40%) in the placebo group. According to the findings, curcumin was an efficient radiosensitizer when used to treat cervical cancer patients

In addition, 150 women who had advanced or metastatic breast cancer had a 12week intravenous treatment regimen consisting of curcumin (300 mg/week) plus paclitaxel (80 mg/m2 body surface area) or a placebo plus paclitaxel (80 mg/m2 body surface area). The findings revealed that curcumin increased patient self reported performance status and objective response rates, while also reducing fatigue and maintaining quality of life.

Additionally, the rise of prostatespecific antigen was decreased during the time that 97 patients with prostate cancer received curcumin who took 1.44 g of curcumin daily for 6-36 months. In several instances, curcumin had no appreciable impact. For instance, a randomised controlled research revealed that supplementing with nanocurcumin (120 mg/day) did not significantly improve outcomes in prostate cancer patients receiving radiation therapy Furthermore, metastatic castration-resistant prostate cancer did not significantly benefit from six weeks of curcumin (6 g/d) therapy. Further investigation is required since the contradictory outcomes could be caused by the complex components participating in clinical trials.

## CURCUMIN DRUGS DELIVERY SYSTEM

Cancer is a complex disease with over 100 different types, characterized by the uncontrolled growth of abnormal cells and their ability to spread to other parts of the body. This uncontrolled growth is often caused by tumor suppressor genes are turned off while oncogenes are activated. Risk factors for cancer include genetic causes, unhealthy habits and lifestyle choices, exposure to carcinogens, ethnicity, diet, and exposure to infectious agents.

According to projections, there would be over 13.2 million cancer-related deaths and more than 20.3 million new cancer cases worldwide by 2030. Developing nations are particularly affected, accounting for approximately 63% of total cancer deaths Currently, cancers can be treated utilizing both conventional tonic methods (i.e., surgery, chemotherapy, and radiation therapy) and nonconventional or complementary therapeutic approaches, including hormone therapy , immunotherapy, nanotherapy, etc However, modern therapeutic approaches have side effects and mainly cause distress for healthy cells, tissues, and organs. For instance:

- Surgery is the prompt solution in many cases. Yet, there are important concerns about its underlying side effects including blood clotting, blood loss, pain, infections, and impairment of tissues.

- The precisely targeted treatment of cancerous tissues by radiotherapy is necessary to minimize the damage to the surrounding normal tissues. However, the insensitivity and intrinsic resistance of some cancer cells is responsible for tumor recurrence after radiotherapy. Its damaging effects on the DNA of nearby healthy tissues , as well as ovarian failure and infertility, are further downsides.
- The main disadvantage of chemotherapy medications is their toxicity and the possibility of harm to the nearby healthy cells. The most common adverse complications are bleeding, gastritis, loss of appetite due to damaged cells in the gastrointestinal tract, pain ,problems in swallowing due to sore throat and oral ulcers , hair loss and microbial infections due to suppressed immunity .

Moreover, over time, cancer cells can show resistance to antitumor drugs, and this is the primary reason for chemotherapy failure .

Given all of these details, there is rising interest in creating cutting-edge, potent cancer therapies based on nanotechnology.There have been numerous attempts to solve the shortcomings of the therapeutic approaches using nanoparticles (NPs) that are now in use.which have a variety of physico-chemical properties that result from their small size and high surface-to-volume ratio NP-based drug delivery systems offer correct pharmacokinetics and precise targeting, which have demonstrated considerable benefits in the treatment of cancer, diminished drug resistance and reduced side effects . The carrier effect, the positioning impact of the targeting substance after absorption, and triggering cell death by releasing the therapeutic payload in the tumor site are the three main functions of NPs in cancer therapy.

Additionally, NPs offer a platform that makes it easier to encapsulate some insoluble medications and distribute them through the bloodstream. Nano-carriers can increase the half-life of drugs and contribute to their accumulation in tumor-bearing tissues. These desirable impacts are attributed to their size and surface properties as well as their ability to boost retention and permeability. As of right now, the targeting system shields healthy cells from medication cytotoxicity, minimizing the adverse effects of cancer therapy.

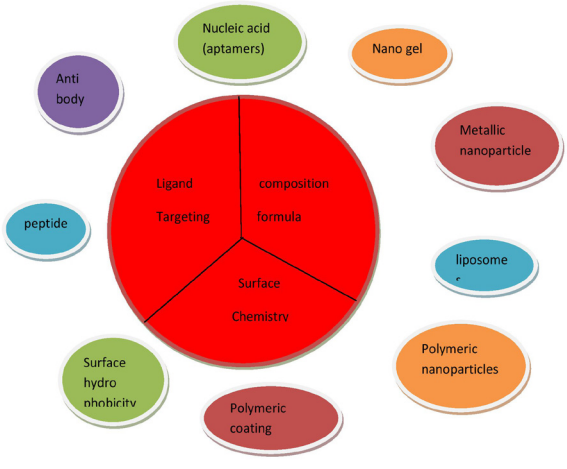


**Figure 6:** Drug Delivery System

Organic nanoparticles (NPs) are a diverse class of materials that have been investigated for decades. Initially, lipid molecules were used as organic substrates or monomers to synthesize polymeric organic nanostructures . Lipids are demonstrated to be excellent drug carriers due to their amphiphilic nature. Biosurfactants like mannosylerythritol lipids form nano-sized micelles above their critical micellar concentration (CMC), and are considered desirable carriers for the delivery of hydrophobic drugs. Liposomes were the first nano-scale medication delivery device authorized for clinical use, which have a core comprising either a hydrophobic or a hydrophilic medication and an exterior lipid layer. By modification of the the lipid layer composition, they can carry out a variety of tasks, including imitation of the living cell biophysical attributes (Examples: deformation and movement). This characteristic can pave the way for more efficient delivery of therapeutic medications Multiple generations of liposomes have been developed as a result of research over the past few decades, providing an effective platform for in vivo delivery of anti-tumor drugs such as paclitaxel and doxorubicin, amongst others additionally to nucleic acids. Following the development of nanotechnology, some nanotherapeutic medications have been marketed and commercialized, and many more have entered the clinical phase since 2010. By enabling medicine combination therapy and impeding the mechanism of drug resistance, nanotherapeutic drugs have advanced the fields of drug delivery and anti-tumor multidrug resistance (MDR).

## Curcumin Delivery System

Curcumin has been packaged and delivered using a range of nano-vehicles, including liposomes, exosomes, micelles, nanoparticles, dendrimers, and hydrogels, leading to improved water solubility, stability, and bioactivity.

## Polymeric Nanoparticles

Numerous polymers have been utilized to make nano formulations of curcumin, which have been shown to boost its biological activity. Biocompatible and biodegradable polymers are preferred in medication delivery systems due to a reduced risk of toxicity. As

a result, natural and synthetic polymers like chitosan and silk fibroin, as well as biodegradable ones like Pharmaceuticals are routinely delivered using PLGA (poly (D, L-lactic-co-glycolic acid). At a 15-fold lower dose, it was discovered to be just as effective as curcumin at decreasing the inflammatory cytokine mRNAs (CXCR3 and CXCL10) and increasing the anti-inflammatory cytokine interleukin-10 (IL-10) in the brain. A rat in vivo investigation revealed that curcumin-PLGA nanospheres had a nine-fold higher bioavailability than unprocessed curcumin given with the alkaloid component piperine.

However, coadministration of curcumin and piperine increased curcumin activity by preventing intestinal and hepatic deactivation. A distinct study examined the anticancer abilities of curcumin-loaded PLGA nanoparticles (CUR-NPs) and curcumin-loaded PLGA nanoparticles conjugated to anti-P-glycoprotein (P-gp) (CUR-NPs-APgp). The latter formulation, compared to CUR-NPs, demonstrated much more specific binding to cervical cancer cells KB-3-1, but with decreased entrapment efficiency. Also created and tested in breast cancer cells were spherical PLGA nanospheres that contained dimethyl curcumin (ASC-J9). The proliferation of estrogen-dependent MCF-7 cancer cells was inhibited as a result of the PLGA nanospheres' ability to release ASC-J9 intracellularly.

## Liposomes

One of the most effective methods for delivering anticancer drugs is nanoscale liposomes. Recent developments in liposome formulations have improved treatment for tumors that are resistant to drugs and reduced toxicity . Since a liposome is made up of an aqueous core and a phospholipid bilayer shell, it is the perfect vehicle for encapsulating both hydrophobic and hydrophilic substances. To encapsulate curcumin, a variety of liposome formulations have been used . Curcumin is soluble in the di hexyl phosphate (DHP), the cholesterol, and the liposomal lipid bilayer of liposomes. It was discovered that this preparation stabilized loaded curcumin proportionately to its amount. Nanoscale liposomes are one of the most effective medication delivery systems.The coating of liposomes with the lipid-polymer conjugate N-dodecyl chitosan-N-[(2-hydroxy-3-trimethylamine) propyl] (HPTMA) chloride was the subject of another study on liposomes. Positively charged nanoliposomes for the delivery of curcumin have been produced using polyethylene glycol (PEG) and cationic polyethyleneimine (PEI). In numerous cell lines, including cervical cancer, human HepG2 hepatocellular carcinoma, A549 lung cancer, and HepG2 hepatocellular carcinoma, this formulation has demonstrated twenty times greater cytotoxic activity than unprocessed turmeric. This is

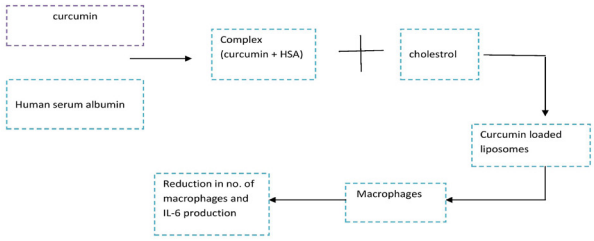


**FIG . 7:** Schematic illustration of curcumin-loaded liposomes that cause a decline in macrophage numbers. Human serum albumin, 1, 2-dipalmitoyl-sn-glycero-3-phosphocholine, and 1, 2-dipalmitoyl-sn-glycero-3-phospho-L-serine are all abbreviations for the same compound. The control, unloaded liposomes, and liposomes loaded with curcumin are represented by the white, grey, and black columns, respectively. Curcumin-loaded liposomes reduce IL-6 synthesis. from Amano and co.

despite having a low encapsulation efficiency (45%). Curcumin was used in an intriguing study by Fujita *et al*. to regulate the release of siRNA during liposomal genedelivery. Because curcumin was added to the liposomal mixture, there was a dose-dependent rise in liposomal permeability, which resulted in a bell-shaped pattern of siRNA release.

We also utilized curcumin-loaded liposomes to stop macrophages from producing IL-6. In order to make the liposomes, a lipid combination containing cholesterol, Curcumin solution and 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) and 1,2-dipalmitoyl-sn-glycero-3-phospho-Lserine sodium salt (DPPS) were combined (HSA) solution. The intended system significantly reduced IL-6 and the overall amount of macrophages.

(A) Schematic illustration of curcumin-loaded liposomes that cause a decline in macrophage numbers. Human serum albumin, 1, 2-dipalmitoyl-sn-glycero-3-phosphocholine, and 1, 2-dipalmitoyl-sn-glycero-3-phospho-L-serine are all abbreviations for the same compound. The control, unloaded liposomes, and liposomes loaded with curcumin are represented by the white, grey, and black columns, respectively. Curcumin-loaded liposomes reduce IL-6 synthesis. from Amano and co.

## Nanogels

Only a few research have looked at the delivery of curcumin using nanogels in cancer therapy, despite the fact that nanogels and hydrogels have drawn a lot of attention as promising drug delivery systems in the last decade. Many polymeric hydrogel nanoparticle systems have recently been developed using synthetic or natural polymers. The most researched natural polymers for creating nanogels for drug delivery include chitin, chitosan, and alginate . Contrarily, the synthetic materials polyvinyl alcohol (PVA), polyethylene oxide (PEO), polyethyleneimine (PEI), polyvinyl pyrrolidone (PVP), and poly-Nisopropylacrylamide (PNIAA) are the

synthetic polymers that are most frequently utilized. Biodegradability and biocompatibility are two key benefits using natural hydrogels for medication delivery rather than manufactured ones. Additionally, the unique properties of nanogels include a porous structure for drug loading and release and a large surface area for drug absorption trapping. A transdermal system containing chitin nanogels loaded with curcumin has been utilized to treat skin cancer, and it has demonstrated more targeted toxicity against human skin melanoma (A375) cells than it has against human dermal fibroblast (HDF) cells without reducing curcumin's anticancer efficacy.

## Peptide and Protein Formulation

As was already mentioned, curcumin medication delivery via polymeric materials and hydrogels has shown promising outcomes. Toxicity of unreacted monomers, postcrosslinking shrinkage or fragility of the polymer gels, and the rapid discharge of a significant amount of the loaded drug during the initial burst release in drug carrier are some drawbacks that have been encountered. Peptides have several benefits when utilized in drug delivery systems, including biocompatibility, desirable hydrophilicity, and simplicity of manufacturing.

A recent study examined the physical characteristics and regarding the therapeutic efficacy of a self-assembling (MAX8) peptide (-hairpin) hydrogel system containing curcumin. By adjusting the level of MAX8 peptide, this newly created approach has integrated several benefits such delivery, stability of the curcumin, and controlled drug release. Another example involves the formation of micelles by an amphiphilic polypeptide (-casein). The hydrophobic centre of the -casein micelles was found to boost curcumin's water solubility by 2500 times. Due to its outstanding biocompatibility HSA, or human serum albumin, is one of the most common employed proteins in the creation of nanoparticles . Aqueous HSA solution with curcumin dissolved in chloroform (to crosslink the HSA molecules) were homogenized to create curcumin-loaded HSA nanoparticles. This formulation increased the solubility of curcumin by a factor of 300, but it only managed a loading efficiency of 7.2%, which was probably caused by curcumin being trapped by hydrophobic interactions within the hydrophobic cavity of albumin. Due to its great biocompatibility and several potential uses in biomedicine, the protein silk fibroin (SF) has recently attracted a lot of attention.

## Complexes of Cyclodextrin

The cyclic oligosaccharides known as cyclodextrins have a lipophilic core and a hydrophilic outer layer. These complexes offer a number of advantageous features for drug delivery, such as greater the loaded medication has

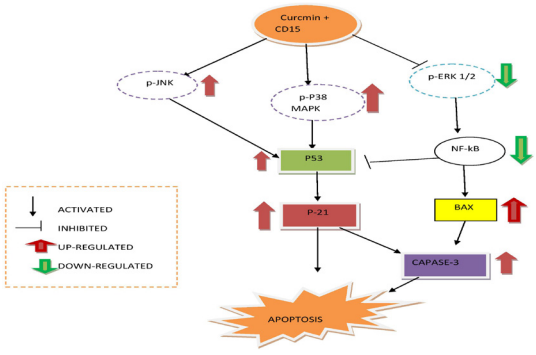


**Fig .8:** Benefits of curcumin complex with cyclodextrins

better stability, solubility, and higher bioavailability. The molecular weight and water solubility of the many forms of cyclodextrins, including natural and, polymerized and chemically altered cyclodextrins, vary Various cyclodextrin complexes exist as well, such as complexes with inclusions and self-assembled cyclodextrins. Cyclodextrins have only sometimes been employed in trials to distribute curcumin to improve bioavailability, stop oxidation, and reduce nonselective toxicity. When compared curcumin that hasn't been processed, a self-assembling combination of -cyclodextrin and curcumin showed greater prostate cancer DU145 taking up curcumin. As shown in Figure 8, cancer cells absorbed cyclodextrincurcumin (CD-CUR) inclusion complexes (CD5, CD10, CD20, and CD30) substantially more quickly than free curcumin.. Another study discovered that curcumin-cyclodextrin complexes have an additional therapeutic benefit for lung cancer. When these complexes were given to animals Having lung cancers inserted orthotopically, curcumin's bioavailability was enhanced, and the tumor size was significantly reduced.

Incorporation of cyclodextrin and curcumin (CD-CUR) and self-assembled complexes. Fluorescence-activated cell sorting (FACS) analysis of the cellular uptake of curcumin and multiple CD-CUR inclusion complexes (CD5, CD10, CD20, and CD30) in DU145 prostate cancer

## Recent Advances in Delivery of Curcumin

Nanoparticle-based delivery systems: Nanoparticles offer a promising platform for curcumin delivery. Various types of nanoparticles, such as liposomes, polymeric nanoparticles, and solid lipid nanoparticles, encapsulate curcumin. These nanoparticles protect curcumin from degradation, enhance its solubility, and improve its shipping to cancerous cells.

Micellar delivery systems: Micelles are self-assembled structures formed by amphiphilic molecules. Curcumin can be encapsulated within these micelles, which can improve its solubility and stability. Micellar delivery systems have shown enhanced Curcumin's anticancer properties in preclinical research.

Lipid-based delivery systems: Lipid-based for-mulations, such as nanoemulsions and lipid nanoparticles, have been investigated for curcumin delivery. These formulations enhance the solubility of curcumin, protect it from degradation, and improve its absorption in the body. Lipid-based systems have showed encouraging outcomes in increasing the bioavailability of curcumin.

Polymer-based delivery systems: Polymers the ability to formulate curcumin into nanoparticles or hydrogels for localized drug delivery. Polymeric nanoparticles can improve the stability and release profile of curcumin, while hydrogels provide a curcumin is released steadily at the tumor site, reducing systemic toxicity. Prodrug approach: Curcumin prodrugs are chemically modified forms of curcumin that are more stable and have enhanced bioavailability. These prodrugs may be created to discharge curcumin in a controlled manner within the body. Prodrug strategies have shown promise in improving the delivery and the effectiveness of curcumin. Combination with other agents: Curcumin can be combined with other agents, such as nanoparticles or drugs, to enhance its anticancer effects. For example, curcumin-loaded nano particles can be mixed with chemotherapy medications to increase their effectiveness and minimize side effects These advances in curcumin delivery systems aim to overcome the limitations associated with its poor solubility and bioavailability, thus enhancing its therapeutic potential as a cancer-prevention tool.. While these strategies show promise in preclinical studies, they require more study to determine their efficacy and safety in clinical settings.

## CONCLUSION

The active component of *C. longa* extract, curcumin, has been the subject of extensive research in recent years for its potential anti-androgenic, anti-cancer, anti-inflammatory, and antioxidant activities. Prostate cancer, breast cancer, colorectal cancer, pancreatic cancer, and head and neck cancer in vitro and in vivo research. Additionally, numerous clinical studies involving human participants have demonstrated its safety and efficacy in cancer patients when used either alone or in conjunction with other anticancer medicines. Curcumin is thought to work through a number of distinct mechanisms to inhibit or induce the production of certain, enzymes, cytokines or growth factors such MAPK, EGF, NF-B, PKD1, COX-2, STAT3, TNF-, and I-K, as well as diverse cellular pathways. However, curcumin's anticancer applicability has been constrained primarily Due to its low water solubility, which also results in low chemical stability, poor oral bioavailability, and limited cellular absorption. various tactics, such as the utilization of drug delivery systems and structural alteration, have been developed to get around these restrictions. The - diketone molecule, the phenyl rings, the hydrogen donor group, and the substituent groups on them are recognised to be the main pharmacophores involved in curcumin's biological activity. These moieties have undergone chemical alteration to produce derivatives of curcumin that are more effective and/or more stable in water.

Many natural or artificial polymers, lipids, or proteins have been employed to transport curcumin to cancer cells or animal xenografts, improving its stability and/ or cellular uptake. A stronger anticancer response has resulted from this.

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