

Unravelling the Potential of Curcumin in Cancer Treatment: A Comprehensive Exploration

Anjana Vidya Srivathsa¹, Harish Kumar DR², Hareesh Kumar P³

¹M S Ramaiah University of Applied Sciences, MSR Nagar, Bangalore, India
Email: [anju.srivathsa\[at\]gmail.com](mailto:anju.srivathsa[at]gmail.com)

²M S Ramaiah University of Applied Sciences, MSR Nagar, Bangalore, India
Email: [drhkshs\[at\]gmail.com](mailto:drhkshs[at]gmail.com)

³MSRCASC, College of Arts, Science and Commerce, MSR Nagar, Bangalore, India

Abstract: *The potential use of curcumin, a naturally occurring substance produced from turmeric, as a medicinal agent in the treatment of cancer is examined in this study. New treatment strategies are essential since cancer is a worldwide health concern. High incidence and death rates for cancer still exist despite advances in therapy, especially in lower - and middle - income nations. Because side effects frequently make traditional cancer therapy unworkable, experts are looking for other approaches. In addition, this research explores the chemistry of curcumin, emphasizing its spectral properties, solubility, and structure. Although its safety profile has been established, problems such as low solubility in water still exist. To improve efficacy, techniques such encapsulation in nano - formulations and structural alteration are investigated. More than 160 clinical trials demonstrate the increasing interest in the therapeutic effects of curcumin, especially in the treatment of cancer. Furthermore, this study investigates the chemistry of curcumin, focusing on its structure, solubility, and spectral characteristics. Despite having a well - established safety profile, it nevertheless has issues including limited water solubility. Techniques including structural modification and encapsulation in Nano formulations are being researched to increase effectiveness. The growing interest in curcumin's therapeutic properties, particularly in the treatment of cancer, is reflected in the more than 160 clinical studies that have been conducted.*

Keywords: Cancer, heterocyclic curcumin derivative, cell line study, anti - proliferative

1. Introduction

Cancer is the second biggest cause of mortality worldwide, making it one of the most prevalent and difficult public health issues. In India alone, there were nearly 600, 000 cancer - related deaths and 1.8 million new instances of the disease in 2018. [1] Over the past three decades, there has been a depressing lack of drop in cancer incidence and fatality rates, despite major advancements in cancer therapy. The need to understand the complex molecular mechanisms behind the onset and spread of cancer emphasizes how important it is to expand our knowledge in order to develop preventative and therapeutic measures that work.

Epidemiology landscape, with almost 10 million deaths from the disease and 19 million new cases predicted for 2022, the burden of cancer is immense. By 2040, there are expected to be a startling 47% rise in new cases, or 30 million. [2 - 5] The nations with lower and intermediate incomes bear a disproportionate amount of this cost. Currently, immunotherapy, chemotherapy, radiation, and surgery are included in the standard cancer treatment regimen. But possible side effects including exhaustion, anorexia, and organ damage, as well as psychological impacts like worry and sadness, limit their effectiveness. [8]

Natural Remedies for Cancer Treatment, to shed light on this, there is a rising desire to investigate alternative strategies, especially those based on the natural world. Researchers are interested in some natural items because they may be useful in managing and preventing cancer. These include fruits, vegetables, tea, and spices. One of the most promising candidates was found to be Curcumin, a naturally occurring

substance derived from the rhizome of turmeric (*Curcuma longa L.*), has attracted a lot of interest. [9, 10] Curcumin was first used in food as a natural colouring and fragrant agent, but it has since developed into a molecule recognised for its wide range of biological properties, such as antibacterial, anti - inflammatory, antioxidant, and anticancer properties. Curcumin's anticancer potential has been thoroughly studied in relation to a number of cancer types, including gastric, liver, lung, breast, and prostate cancers. It is an interesting topic for research because of its adaptability in addressing many aspects of cancer genesis and progression. Curcumin's potential as a weapon in the fight against cancer is highlighted by the National Cancer Institute's recognition of it as a third - generation cancer chemo - preventive agent [11].

Mechanisms of Action, Curcumin's anticancer properties are ascribed to its capacity to regulate many molecular pathways implicated in the development of tumours. It has been demonstrated to suppress the growth of cancer cells, cause apoptosis, or programmed cell death, prevent the development of new blood vessels to promote the growth of tumours, and prevent metastasis. Moreover, curcumin's antioxidant and anti - inflammatory qualities help to create an environment that is unfavourable to cancer cells.

Clinical Consequences and Difficulties Although the preclinical research has shown encouraging outcomes, there are obstacles in converting curcumin's promise into successful clinical applications. To improve its effectiveness in human trials, factors including formulation optimisation, pharmacokinetics, and bioavailability must be carefully taken into account. However, further clinical study is needed to fully understand curcumin's function in combination

therapies and its potential to supplement traditional treatments. [12 - 17] This review paper summarizes the effects and mechanisms of curcumin on different cancers based on the results from cell models published in the last five years

Chemistry of curcumin

Curcumin, IUPAC designation (1E, 6E) - 1, 7 - bis (4 - hydroxy - 3 - methoxyphenyl) - 1, 6 - heptadiene - 3, 5 - dione, is a symmetric chemical also referred to as diferuloyl methane, has a molecular weight of 368.38 g/mol and a formula of $C_{21}H_{20}O_6$. The α , β - unsaturated β - diketone moiety is formed by two aromatic ring systems with *o* - methoxy phenolic groups linked by a seven - carbon linker, which define its chemical structure. [15]

Structure and Tautomerism Curcumin's di - keto group demonstrates keto - enol tautomerism, displaying several conformers based on the surroundings. Curcumin has a *cis* - enol configuration in its crystal form, which is maintained by hydrogen bonding aided by resonance. The enol form is more stable than the keto form in the majority of solvents. [19] The prolonged conjugation in curcumin's structure keeps an electron cloud at π across the whole molecule. It takes on *cis* - *trans* isomers in solution, with the *trans* - form being somewhat more stabilized than the *cis* - form.

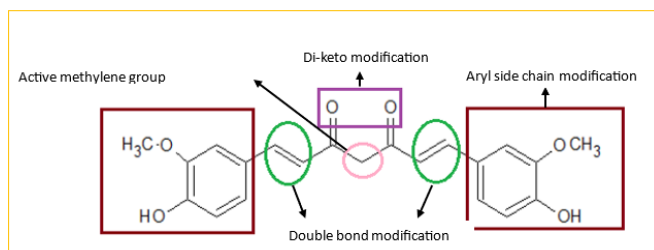


Figure 1: Structure of curcumin and possible points of modification

Curcumin's solubility and spectral characteristics include being hydrophobic (logP value of around 3.0), which means it is nearly insoluble in water but easily soluble in polar solvents such as ethyl acetate, methanol, ethanol, and DMSO. Strong bands may be seen in the visible and ultraviolet sections of its absorption spectra, with peaks around 410–430 nm and 265 nm, respectively. (Li *et al.*, 2019) At 425 nm in methanol, the molar extinction coefficient is $55,000 \text{ dm}^3 \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$

Curcumin has three labile protons, making it a weak Brønsted acid in terms of acid - base properties. For prototropic equilibria, an estimated three pKa have been found, which affects the solubility and colour. In the pH range of 7.5 to 8.5, the first pKa turns curcumin from yellow to red. [30] In alkaline pH (>pH 10) conditions, the completely deprotonated form displays an absorption maximum at 467 nm and a molar extinction value of $53,000 \text{ dm}^3 \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$.

The safety profile and bioavailability of curcumin have been confirmed by pharmacological and toxicological investigations, even at dosages up to 8,000 mg or 12,000 mg per day. Curcumin is 'Generally Recognized as Safe' (GRAS) according to the US FDA. Curcumin's acceptability as a commercially viable medication is hampered, meanwhile, by

issues including poor water solubility, limited bioavailability, and quick bodily excretion. Scholars have put forward techniques to get around these restrictions. There are two main strategies [22 - 25]

- 1) Either curcumin's basic skeletal structure is modified
- 2) It is encapsulated in an appropriate nanoformulation

Studies of modification concentrate on the structure of the molecule, finding reactive areas that may be used to create other variants. Researchers have been captivated by curcumin's preferential symmetric structure, which includes several locations for hydrogen substitution.

Clinical Trials: Despite obstacles, more than 160 active clinical trials are being conducted to determine curcumin's potential therapeutic benefits. Techniques like changing the composition or encapsulating curcumin in Nano formulations show promise for improving curcumin's effectiveness and overcoming its drawbacks. Using surfactants and other chemicals to generate aqueous curcumin solutions opens up new possibilities for the drug's solubility and biological system application. Curcumin is still being thoroughly investigated as research on its potential in a range of medicinal uses progresses.

2. Significance of heterocyclic modified curcumin analogues

In medicinal chemistry, heterocyclic molecules are essential, and it is crucial to include them in curcumin analogues. Heterocyclic rings are found in the architecture of a number of naturally occurring compounds, including vital biological elements such hormones, vitamins, antibiotics, enzymes, nucleic acids (DNA and RNA), hemoglobin, and chlorophyll. These compounds' heterocyclic constitution, which is defined by the inclusion of oxygen, Sulphur, or nitrogen atoms, is responsible for a variety of their physical, chemical, and biological characteristics. [28] To summaries some of the following reasons are listed below

- **Flexibility and Manipulability:** Heterocyclic compounds offer a flexible framework for the synthesis of new compounds, enabling the addition of different reactive functional groups. Because of their versatility, these structures are easily manipulable by researchers, which makes them perfect for integrating certain functionality.
- **Stability and Solubility:** A molecule's capacity to retain its structural integrity depends on the stability that a heterocyclic ring provides. Furthermore, it improves solubility, which is a crucial component of oral absorption and bioavailability and is necessary for a medicinal drug to be effective. (Wang *et al.*, 2021)
- **Benefits of the 1, 3 - Dicarbonyl Site:** In heterocyclic compounds, especially in curcumin's favoured structure, the 1, 3 - dicarbonyl site shows itself to be a good precursor for adding heterocyclic groups. The compound's overall efficacy is increased by the synthesis of stable derivatives with improved characteristics made possible by this location.
- **Overcoming Bioavailability Difficulties:** Research conducted by Liang *et al.* and Liao *et al.* has highlighted the influence of the β - diketone moiety on curcumin's low bioavailability and instability in physiological circumstances. Researchers want to improve curcumin's

stability and bioavailability by making changes to this location. [30 - 33]

- Researchers have analysed the β - diketone chain of curcumin using structure - activity relationship investigations, as demonstrated by Reddy et al. Their research has shown that altering this chain to include hydrazine or a pyrazole ring can result in derivatives with enhanced anti - tumour and anti - proliferative properties.
- Improved Biological Properties of Heterocyclic Derivatives: Studies, like the one by Jankun et al., have shown that the addition of heteroatoms and ring cyclization of curcumin's central region result in the synthesis of derivatives and analogues with stronger anti - angiogenic and anti - tumour properties. Similar to curcumin, the neuroprotective effect of derivatives of curcumin isoxazole and pyrazole has been linked to reduced rotational flexibility, the lack of stereoisomers, and reduced metal - chelation characteristics.
- Stability and Reduced Tautomerism: Chakraborti et al. have highlighted that stability over curcumin is provided by heterocyclic derivatives' lack of tautomerism. The increased characteristics of these derivatives are partly attributed to their stability, which restricts the availability of acidic protons and decreases the nucleophilicity of active methylene carbons.

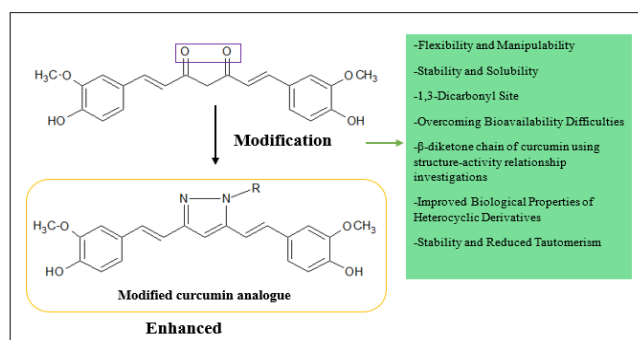


Figure 2: Structural modification on curcumin

Anticancer activity a multitargeted approach

Turmeric contains a bioactive substance called curcumin, which has shown strong anticancer properties by focusing on several molecular pathways connected to inflammation, cancer, and proliferation. Its adaptability is in its capacity to influence different signalling pathways in different types of cancer cells, each of which has unique molecular properties. [32]

NF - KB Pathway Inhibition: Curcumin plays a critical role in the NF - KB pathway. NF - KB controls the transcription of DNA, cell division, and processes linked to the growth of tumours. Curcumin reduces tumour cell proliferation, induces apoptosis, and prevents angiogenesis via blocking NF - KB. Moreover, it stops the epithelial - mesenchymal transition, which promotes distant metastases.

Regulation of the Proteasome Pathway and Cell Cycle: Cell cycle progression is tightly regulated by cyclins and cyclin -

dependent kinases (CDKs). In oncogenesis, losing this control is a crucial stage. By interfering with the ubiquitin proteasome pathway, curcumin stops cell cycle regulating proteins from being degraded. This interference contributes to the antiproliferative effects by causing cell cycle arrest in malignant cells. [34 - 36]

Ubiquitin - Proteasome System Inhibition: Curcumin targets the ubiquitin - proteasome system, which is a regulator of cell proliferation and death. Protease activity suppression stops I κ B α from being broken down, which inhibits NF - KB activation and downstream pathway activation.

Disruption of TGF α - EGFR Signalling Pathway: The TGF α - EGFR signalling pathways that encourage the development and metastasis of cancer cells are interfered with by curcumin. The principal mediators of these signals are receptor tyrosine kinases (RTKs), which include the ErbB family. These RTKs determine the destiny of cells with relation to growth, differentiation, migration, or death. [37]

Microtubule Dynamics Suppression: Curcumin targets the tubulin family of proteins, which are essential for mitosis, intracellular trafficking, and cell migration. Curcumin causes cell death and mitotic arrest by inhibiting microtubule dynamics.

Evading Apoptosis and Controlling Caspase: Curcumin targets molecules that are involved in apoptosis, a process that cancer cells frequently avoid. It promotes cell death by balancing the expression of oncogenes and tumour suppressors through its actions on caspases and upstream regulatory factors.

STAT3 Signalling Inhibition: Many tumours have STAT3 signalling activation. This route is inhibited by curcumin, especially the JAK/STAT signalling, which is known to promote cell division and proliferation.

PRR - Mediated Modulation of Inflammatory Response: Toll - like receptors (TLRs) and other pathogen recognition receptors (PRRs) induce an inflammatory response that curcumin reduces. It suppresses the production of pro - inflammatory cytokines such IL - 6, TNF - α , and IL - 1 β and affects signalling pathways, including NF - KB.

Regulation of Prostaglandins and Leukotrienes: Curcumin controls the levels of lipid autacoids that are generated from arachidonic acid, particularly prostaglandins and leukotrienes. Curcumin's activity on COX isoenzymes and 5 - LOX adds to its anti - inflammatory and anticancer properties. These chemicals play roles in inflammation and homeostasis.

Inhibition of Nitric Oxide (NO) Production: Curcumin inhibits inducible nitric oxide synthase (iNOS), which controls the generation of NO linked to inflammation. The anti - inflammatory and anticancer effects of curcumin are facilitated by this regulatory action. [39]

Table 1: Mechanism of action of promising curcumin derivatives on cancer with current protein

Effect	Type of cancer	Mechanism of action	Protein ID and name	
Antiproliferative	Breast	CDK2 decrease	7F4X Joint neutron and X - ray crystal structure of the nucleotide - binding domain of Hsp72 in complex with ADP [40]	
		CDK4 decrease	6GCY Joint neutron and x - ray crystal structure of human carbonic anhydrase IX mimic (saccharin - sugar conjugate complex)	
		Cell cycle arrest at G1 phase	5C8I Joint X - ray/neutron structure of Human Carbonic Anhydrase II in complex with Methazolamide [41].	
		Cell viability decrease	6FJJ Joint neutron and x - ray crystal structure of human carbonic anhydrase IX mimic (saccharin) [42]	
		Cyclin decrease	6SG4 Structure of CDK2/cyclin A M246Q, S247EN [43]	
	Colon	CDK2 decrease	5MHQ CCT068127 in complex with CDK2	
		Cell cycle arrest at G1 phase	4UYA Structure of MLK4 kinase domain with ATPgammaS	
		Cell viability decrease		
		E2F4 decrease		
		P21 and p27 increase		
	Glioma	Cell cycle arrest at G2 phase	6ADI Crystal Structures of IDH2 R140Q in complex with AG - 881	
		Cyclin D1 decrease	6VFZ Crystal Structure of Human Mitochondrial Isocitrate Dehydrogenase (IDH2) R140Q Mutant Homodimer in Complex with NADPH and AG - 881 (Vorasicidib) Inhibitor [44]	
		Egr 1 increase	5SVN Structure of IDH2 mutant R172K	
		foxO1 increase	5I95 Crystal Structure of Human Mitochondrial Isocitrate Dehydrogenase R140Q Mutant Homodimer bound to NADPH and alpha - Ketoglutaric acid	
		P21 increase		
	Gastric	Cell cycle arrest at G0 phase	7TUN Crystal structure analysis of human CKB complex with a covalent compound	
c - myc decrease		6V0Z Structure of ALDH7A1 mutant R441C complexed with NAD		
ODC activity decrease				
P21 increase				
P53 increase				
Pro - apoptotic	Breast	Bad increase	7F4X Joint neutron and X - ray crystal structure of the nucleotide - binding domain of Hsp72 in complex with ADP	
		Bax increase	6GCY Joint neutron and x - ray crystal structure of human carbonic anhydrase IX mimic (saccharin - sugar conjugate complex)	
		Bcl - 2 decrease	5C8I Joint X - ray/neutron structure of Human Carbonic Anhydrase II in complex with Methazolamide	
		FAS inhibition	6FJJ Joint neutron and x - ray crystal structure of human carbonic anhydrase IX mimic (saccharin)	
		GSH decrease		
	Melanoma	Bcl - 2 decrease	51XB Structure of human Melanoma Inhibitory Activity (MIA) Protein in complex with Pyrimidin - 2 - amine	
		JAK - 2/STAT - 3 signaling inhibition		
	Ovarian	Caspase 8 pathway activation	5CG6 Neutron crystal structure of human farnesyl pyrophosphate synthase in complex with risedronate and isopentenyl pyrophosphate	
		Akt signaling inhibition		
		Bcl - 2 and survivin decrease		
lung	P38 MAPK activation			
Antimetastatic	Breast	Ax1 decrease	7F4X Joint neutron and X - ray crystal structure of the nucleotide - binding domain of Hsp72 in complex with ADP	
		CD24 decrease	6GCY Joint neutron and x - ray crystal structure of human carbonic anhydrase IX mimic (saccharin - sugar conjugate complex)	
		miR - 34a increase	5C8I Joint X - ray/neutron structure of Human Carbonic Anhydrase II in complex with Methazolamide	
	Cervical	NF - kB and Wnt pathway inhibition	6IWD The PTP domain of human PTPN14 in a complex with the CR3 domain of HPV18 E7	
		Fascin decrease	4USF Human SLK with SB - 440719	
	Ovarian	JAK/STST3 signalling pathway inhibition	5CG6 Neutron crystal structure of human farnesyl pyrophosphate synthase in complex with risedronate and isopentenyl pyrophosphate	
		miR - 27a decrease	7WLX A novel chemical derivative (53) of THRβ agonist	
	Thyroid	Mtor and Notch 11 pathways inhibition	7B9O Crystal structure of Retinoic Acid Receptor alpha (RXRA) in complexed with S169 inhibitor [45]	

In - vitro studies

Through a number of *in vitro* investigations, the processes and effects of curcumin on molecular pathways have been clarified, providing insight into the compound's potential to treat head and neck cancer. We examine some key discoveries from these investigations here:

NF - κB Activation Inhibition: Curcumin has shown its capacity to inhibit NF - κB activation and thereby limit cell growth and survival in several head and neck cancer cell lines. Oral squamous cell carcinoma cell lines were shown to have constitutively active NF - κB and IκK. Treatment with

curcumin reduced NF - κ B activation, which in turn prevented the cancer cells' proliferation and ability to survive STAT3 Signaling Suppression: Curcumin targeted STAT3, a signaling protein that is overexpressed in head and neck malignancies. It provided a plausible explanation for curcumin's antiproliferative actions by inhibiting the nuclear localization of STAT3 and suppressing the phosphorylation of the protein mediated by IL - 6. [46]

Curcumin showed a preferential effect on cancerous cells relative to normal cells. Research findings indicate that this substance can inhibit the proliferation of squamous cell carcinoma and oral mucosal epithelial cells, with no impact on normal oral epithelial cells. Modulation of Translational Complex Efficiency: Using immortalized oral mucosal epithelial cells and squamous cell carcinoma cells, curcumin's effects on the eIF4F translational complex were investigated. It decreased this complex's effectiveness, which in turn affected the phosphorylation levels of important proteins and decreased the overall amounts of certain chemicals, all of which helped to inhibit the proliferation of cancer cells. [47]

Tumor Suppression and p38 Activation: Curcumin stimulated the promoter activity of two proteins in SAS oral cancer cells: C/EBP α and IGFBP - 5, which are linked to the prevention of head and neck malignancies. In a mouse xenograft model, the activation was mediated by p38 and resulted in a reduction in *in vivo* carcinogenesis. Research conducted on a range of head and neck squamous cell carcinoma cell lines revealed that curcumin's growth - suppressive properties were mainly attributed to its influence on the NF - κ B pathway. [48] It prevented nuclear localization, lowered NF - κ B expression, and decreased the expression of genes that are controlled by NF - κ B, such as cyclin D1, MMP - 9, COX - 2, and anti - apoptotic proteins.

I κ K Activity Inhibition: I κ K activity was shown to be inhibited by curcumin, which resulted in the reduction of the NF - κ B pathway. Reduced phosphorylation of I κ B - α and sequestration of NF - κ B in the cytoplasm were the results of this inhibition. Furthermore, the administration of curcumin led to a dose - dependent reduction in IL - 6 and IL - 8 through I κ K inhibition.

AKT - Independent Inhibition of I κ K: Curcumin was observed to inhibit I κ K in head and neck squamous cell carcinoma (HNSCC) cell lines without requiring activation of AKT. This finding is noteworthy. Given that curcumin's mechanism of action is distinct from those of other treatments that target the EGFR/AKT signaling cascade, including cetuximab, this result has practical implications. Curcumin with other medications, such as cetuximab, may provide a supplemental strategy for the treatment of head and neck malignancies. To conclude, *in vitro* research demonstrates curcumin's complex actions on head and neck cancer, including selective effects on cancer cells, blockage of important signalling pathways, and modification of translational complexes. These results highlight curcumin's possible therapeutic benefit in the fight against head and neck malignancies and point the way for further study and clinical implementation.

3. Future Prospects of Heterocyclic Curcumin Derivatives

Heterocyclic curcumin analogues have a bright and varied future ahead of them, with several research and development fields demonstrating the possibility of medicinal uses. An explanation of the potential paths and future directions is provided below:

Enhanced Activity and Stability: The curcumin scaffold's integration of a heterocyclic ring structure solves the compound's chemical instability and static residual complexity problems. This change has the potential to increase the molecule's overall activity manifold and stability.

- Applications: Heterocyclic compounds of curcumin have shown potent antibacterial action, occasionally even outperforming the effectiveness of conventional antibiotics. The restricted investigation of antifungal activity points to a possible direction for more study in this area, broadening the range of potential uses.
- Possessing Antimicrobial and Antimalarial Properties: When compared to curcumin, heterocyclic curcumin analogues have demonstrated greater anti - mycobacterial efficacy. The notable activity seen suggests a route for future study to investigate these compounds as possible antimalarial drugs, despite the paucity of data on their antimalarial potential. [49]
- Antioxidant Activity: Curcumin - pyrazole and curcumin - isoxazole have demonstrated a constant higher level of antioxidant potential. Potential antioxidant medicines might be made possible by doing further animal trials to evaluate their efficacy *in vivo*.
- Anti - tumor and anti - inflammatory properties: *In vitro* studies using a variety of cell lines have demonstrated the better anti - inflammatory and anti - tumor effectiveness of many heterocyclic analogues. To evaluate these results and convert them into possible therapeutic approaches, future research may concentrate on particular *in vivo* testing and investigations. [Click or tap here to enter text.](#)
- Neuroprotective Potential: It has been demonstrated that several heterocyclic curcumin analogues, including CNB001, have neuroprotective properties. In - depth research is necessary to perhaps transform these analogues into acknowledged neuroprotective medications, especially in neurological conditions like Parkinson's and Alzheimer's illnesses.
- Investigating Novel Domains: Limited research has been done in areas including anti - viral, anti - adipogenesis, and anti - diabetic properties. To fully understand the potential of heterocyclic curcumin analogues and their uses in a variety of therapeutic fields, future study might go deeper into these regions.
- Preclinical studies and In Vivo Experiments: Since many research have been carried out predominantly *in vitro*, more specialized testing, *in vitro* experiments, and ultimately clinical trials are required. *In vivo* models and human studies will be essential in confirming the safety and effectiveness of heterocyclic curcumin analogues as medicinal agents.
- Cross - Domain Research: Numerous studies have alterations that don't just match to the diketo site, or they fall within numerous domains. These multi - domain

studies provide opportunities for thorough examinations, delving into the varied functions and possible uses of these analogues in a range of therapeutic contexts

4. Conclusion

Curcumin is a very promising clinical molecule that has shown therapeutic effects for a number of chronic illnesses, including cancer therapy. It has a well-established capacity to regulate genes involved in cell proliferation, apoptosis, and metastasis as well as growth factors, cytokines, and transcription factors. Its quick elimination, limited solubility, and poor absorption have prevented its early use as a medicinal agent, despite its low toxicity. Many curcumin formulations, including synthetic derivatives, analogues, nanoparticles, liposomes, phytosomes, micelles, and natural adjuvants like piperine, have been developed in an attempt to overcome these obstacles. Improved distribution of curcumin to target tissues and increased bioavailability, absorption, and retention duration have all been demonstrated by these formulations.

Although curcumin's anticancer action has been demonstrated in several in vitro studies, further research is necessary to validate and confirm curcumin's utility in the treatment and prevention of cancer, particularly in epidemiological and clinical trials involving large cohorts. Research has examined several groups and their quantitative structure - activity relationships (QSAR) in the field of synthetic approaches for curcumin derivatives. Certain curcumin compounds have proven to be more efficacious than curcumin itself. Strong antioxidants are essential since free - radical oxidation is linked to conditions including cancer, Alzheimer's, Parkinson's, and cardiovascular problems.

There are insufficient thorough pharmacokinetic and pharmacodynamic research for curcumin, its analogues, and derivatives, despite their potential biological activity. The ongoing investigation of curcumin analogues provides a useful foundation for the logical creation of antioxidant agents with enhanced characteristics. All things considered, curcumin has a lot of promise, but further study and clinical trials are required to fully realize this potential and find new avenues for its application in a variety of medical diseases.

References

- [1] Adamczak, A., Ożarowski, M. and Karpiński, T. M. (2020) 'Curcumin, a natural antimicrobial agent with strain - specific activity', *Pharmaceuticals*, 13 (7), pp.1–12. Available at: <https://doi.org/10.3390/PH13070153>.
- [2] Adiwidjaja, J., McLachlan, A. J. and Boddy, A. V. (2017) 'Curcumin as a clinically - promising anti - cancer agent: pharmacokinetics and drug interactions', *Expert Opinion on Drug Metabolism and Toxicology*, 13 (9), pp.953–972. Available at: <https://doi.org/10.1080/17425255.2017.1360279>.
- [3] Anand, P. *et al.* (2007) 'Bioavailability of curcumin: Problems and promises', *Molecular Pharmaceutics*, 4 (6), pp.807–818. Available at: <https://doi.org/10.1021/MP700113R>.
- [4] Busari, Z. A. *et al.* (2017) 'Antiplasmodial activity and toxicological assessment of curcumin PLGA - encapsulated nanoparticles', *Frontiers in Pharmacology*, 8 (SEP). Available at: <https://doi.org/10.3389/FPHAR.2017.00622>.
- [5] Chen, Ciqiong *et al.* (2018) 'Antifungal activity, main active components and mechanism of Curcuma longa extract against Fusarium graminearum', *PLoS ONE*, 13 (3). Available at: <https://doi.org/10.1371/JOURNAL.PONE.0194284>.
- [6] Dosoky, N. S., Satyal, P. and Setzer, W. N. (2019) 'Variations in the volatile compositions of Curcuma species', *Foods*, 8 (2). Available at: <https://doi.org/10.3390/FOODS8020053>.
- [7] Ghasemi, F. *et al.* (2019) 'Curcumin inhibits NF - kB and Wnt/ β - catenin pathways in cervical cancer cells', *Pathology Research and Practice*, 215 (10). Available at: <https://doi.org/10.1016/J.PRP.2019.152556>.
- [8] He, Y. *et al.* (2018) 'Bioactivities of EF24, a novel curcumin analog: A review', *Frontiers in Oncology*, 8 (DEC). Available at: <https://doi.org/10.3389/FONC.2018.00614>.
- [9] Jagetia, G. C. (2021) 'Antioxidant activity of curcumin protects against the radiation - induced micronuclei formation in cultured human peripheral blood lymphocytes exposed to various doses of γ - Radiation', *International Journal of Radiation Biology*, 97 (4), pp.485–493. Available at: <https://doi.org/10.1080/09553002.2021.1876948>.
- [10] Jamwal, R. (2018) 'Bioavailable curcumin formulations: A review of pharmacokinetic studies in healthy volunteers', *Journal of Integrative Medicine*, 16 (6), pp.367–374. Available at: <https://doi.org/10.1016/J.JOIM.2018.07.001>.
- [11] Jennings, M. R. and Parks, R. J. (2020) 'Curcumin as an antiviral agent', *Viruses*, 12 (11). Available at: <https://doi.org/10.3390/V12111242>.
- [12] Karthikeyan, A., Senthil, N. and Min, T. (2020) 'Nanocurcumin: A Promising Candidate for Therapeutic Applications', *Frontiers in Pharmacology*, 11. Available at: <https://doi.org/10.3389/FPHAR.2020.00487>.
- [13] Kim, M. J. *et al.* (2020) 'The inhibitory effect of curcumin via fascin suppression through JAK/STAT3 pathway on metastasis and recurrence of ovary cancer cells', *BMC Women's Health*, 20 (1). Available at: <https://doi.org/10.1186/S12905-020-01122-2>.
- [14] Kotecha, R., Takami, A. and Espinoza, J. L. (2016) 'Dietary phytochemicals and cancer chemoprevention: A review of the clinical evidence', *Oncotarget*, 7 (32), pp.52517–52529. Available at: <https://doi.org/10.18632/ONCOTARGET.9593>.
- [15] Kunnumakkara, A. B., Bordoloi, D., Harsha, C., *et al.* (2017) 'Curcumin mediates anticancer effects by modulating multiple cell signaling pathways', *Clinical Science*, 131 (15), pp.1781–1799. Available at: <https://doi.org/10.1042/CS20160935>.
- [16] Kunnumakkara, A. B., Bordoloi, D., Padmavathi, G., *et al.* (2017) 'Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases', *British Journal of Pharmacology*, 174 (11), pp.1325–1348. Available at: <https://doi.org/10.1111/BPH.13621>.
- [17] Kuttikrishnan, S. *et al.* (2019) 'Curcumin induces apoptotic cell death via inhibition of PI3 - kinase/Akt pathway in B - precursor acute lymphoblastic

- leukemia', *Frontiers in Oncology*, 9 (JUN). Available at: <https://doi.org/10.3389/FONC.2019.00484>.
- [18] Li, W. *et al.* (2019) 'The curcumin analog EF24 is a novel senolytic agent', *Aging*, 11 (2), pp.771–782. Available at: <https://doi.org/10.18632/AGING.101787>.
- [19] Ma, Z. *et al.* (2019) 'Pharmaceutical strategies of improving oral systemic bioavailability of curcumin for clinical application', *Journal of Controlled Release*, 316, pp.359–380. Available at: <https://doi.org/10.1016/J.JCONREL.2019.10.053>.
- [20] Mortezaei, K. *et al.* (2019) 'Mechanisms of apoptosis modulation by curcumin: Implications for cancer therapy', *Journal of Cellular Physiology*, 234 (8), pp.12537–12550. Available at: <https://doi.org/10.1002/JCP.28122>.
- [21] Nocito, M. C. *et al.* (2021) 'Antitumoral Activities of Curcumin and Recent Advances to Improve Its Oral Bioavailability', *Biomedicines*, 9 (10). Available at: <https://doi.org/10.3390/BIMEDICINES9101476>.
- [22] Olotu, F. *et al.* (2020) 'An Update on the Pharmacological Usage of Curcumin: Has it Failed in the Drug Discovery Pipeline?', *Cell Biochemistry and Biophysics*, 78 (3), pp.267–289. Available at: <https://doi.org/10.1007/S12013-020-00922-5>.
- [23] Patel, S. S. *et al.* (2020) 'Cellular and molecular mechanisms of curcumin in prevention and treatment of disease', *Critical Reviews in Food Science and Nutrition*, 60 (6), pp.887–939. Available at: <https://doi.org/10.1080/10408398.2018.1552244>.
- [24] Rahmani, A. H. *et al.* (2014) 'Curcumin: A Potential Candidate in Prevention of Cancer via Modulation of Molecular Pathways', *BioMed Research International*, 2014. Available at: <https://doi.org/10.1155/2014/761608>.
- [25] Sandur, S. K. *et al.* (2007) 'Curcumin, demethoxycurcumin, bisdemethoxycurcumin, tetrahydrocurcumin and turmerones differentially regulate anti-inflammatory and anti-proliferative responses through a ROS-independent mechanism', *Carcinogenesis*, 28 (8), pp.1765–1773. Available at: <https://doi.org/10.1093/CARCIN/BGM123>.
- [26] *The antioxidant activity of vitamin C, DPPD and L-cysteine against Cisplatin - induced testicular oxidative damage in rats. | Sigma - Aldrich* (no date). Available at: [https://www.sigmaaldrich.com/IN/en/tech-docs/paper/265283?msclid=2fd8d38a4c4519a4b7adb6f247aa90bb&utm_source=bing&utm_medium=cpc&utm_campaign=all%20product_dsa_NA_\(bing%20ebizpfs\)&utm_term=product%20&utm_content=all%20products](https://www.sigmaaldrich.com/IN/en/tech-docs/paper/265283?msclid=2fd8d38a4c4519a4b7adb6f247aa90bb&utm_source=bing&utm_medium=cpc&utm_campaign=all%20product_dsa_NA_(bing%20ebizpfs)&utm_term=product%20&utm_content=all%20products) (Accessed: 12 December 2023).
- [27] Tomeh, M. A., Hadianamrei, R. and Zhao, X. (2019) 'A review of curcumin and its derivatives as anticancer agents', *International Journal of Molecular Sciences*, 20 (5). Available at: <https://doi.org/10.3390/IJMS20051033>.
- [28] Wang, H. *et al.* (2021) 'Curcumin Regulates Cancer Progression: Focus on ncRNAs and Molecular Signaling Pathways', *Frontiers in Oncology*, 11. Available at: <https://doi.org/10.3389/FONC.2021.660712>.
- [29] Yallapu, M. M. *et al.* (2015) 'Therapeutic Applications of Curcumin Nanoformulations', *AAPS Journal*, 17 (6), pp.1341–1356. Available at: <https://doi.org/10.1208/S12248-015-9811-Z>.
- [30] Zia, A. *et al.* (2021) 'The role of curcumin in aging and senescence: Molecular mechanisms', *Biomedicine and Pharmacotherapy*, 134. Available at: <https://doi.org/10.1016/J.BIOPHA.2020.111119>.
- [31] Adamczak, A., Ożarowski, M. and Karpiński, T. M. (2020) 'Curcumin, a natural antimicrobial agent with strain-specific activity', *Pharmaceuticals*, 13 (7), pp.1–12. Available at: <https://doi.org/10.3390/PH13070153>.
- [32] Adiwidjaja, J., McLachlan, A. J. and Boddy, A. V. (2017) 'Curcumin as a clinically promising anti-cancer agent: pharmacokinetics and drug interactions', *Expert Opinion on Drug Metabolism and Toxicology*, 13 (9), pp.953–972. Available at: <https://doi.org/10.1080/17425255.2017.1360279>.
- [33] Anand, P. *et al.* (2007) 'Bioavailability of curcumin: Problems and promises', *Molecular Pharmaceutics*, 4 (6), pp.807–818. Available at: <https://doi.org/10.1021/MP700113R>.
- [34] Busari, Z. A. *et al.* (2017) 'Antiplasmodial activity and toxicological assessment of curcumin PLGA-encapsulated nanoparticles', *Frontiers in Pharmacology*, 8 (SEP). Available at: <https://doi.org/10.3389/FPHAR.2017.00622>.
- [35] Chen, Ciqiong *et al.* (2018) 'Antifungal activity, main active components and mechanism of Curcuma longa extract against Fusarium graminearum', *PLoS ONE*, 13 (3). Available at: <https://doi.org/10.1371/JOURNAL.PONE.0194284>.
- [36] Dosoky, N. S., Satyal, P. and Setzer, W. N. (2019) 'Variations in the volatile compositions of Curcuma species', *Foods*, 8 (2). Available at: <https://doi.org/10.3390/FOODS8020053>.
- [37] Ghasemi, F. *et al.* (2019) 'Curcumin inhibits NF- κ B and Wnt/ β -catenin pathways in cervical cancer cells', *Pathology Research and Practice*, 215 (10). Available at: <https://doi.org/10.1016/J.PRP.2019.152556>.
- [38] He, Y. *et al.* (2018) 'Bioactivities of EF24, a novel curcumin analog: A review', *Frontiers in Oncology*, 8 (DEC). Available at: <https://doi.org/10.3389/FONC.2018.00614>.
- [39] Jagetia, G. C. (2021) 'Antioxidant activity of curcumin protects against the radiation-induced micronuclei formation in cultured human peripheral blood lymphocytes exposed to various doses of γ -Radiation', *International Journal of Radiation Biology*, 97 (4), pp.485–493. Available at: <https://doi.org/10.1080/09553002.2021.1876948>.
- [40] Jamwal, R. (2018) 'Bioavailable curcumin formulations: A review of pharmacokinetic studies in healthy volunteers', *Journal of Integrative Medicine*, 16 (6), pp.367–374. Available at: <https://doi.org/10.1016/J.JOIM.2018.07.001>.
- [41] Jennings, M. R. and Parks, R. J. (2020) 'Curcumin as an antiviral agent', *Viruses*, 12 (11). Available at: <https://doi.org/10.3390/V12111242>.
- [42] Karthikeyan, A., Senthil, N. and Min, T. (2020) 'Nanocurcumin: A Promising Candidate for Therapeutic Applications', *Frontiers in Pharmacology*, 11. Available at: <https://doi.org/10.3389/FPHAR.2020.00487>.

- [43] Kim, M. J. *et al.* (2020) 'The inhibitory effect of curcumin via fascin suppression through JAK/STAT3 pathway on metastasis and recurrence of ovary cancer cells', *BMC Women's Health*, 20 (1). Available at: <https://doi.org/10.1186/S12905-020-01122-2>.
- [44] Kotecha, R., Takami, A. and Espinoza, J. L. (2016) 'Dietary phytochemicals and cancer chemoprevention: A review of the clinical evidence', *Oncotarget*, 7 (32), pp.52517–52529. Available at: <https://doi.org/10.18632/ONCOTARGET.9593>.
- [45] Kunnumakkara, A. B., Bordoloi, D., Harsha, C., *et al.* (2017) 'Curcumin mediates anticancer effects by modulating multiple cells signaling pathways', *Clinical Science*, 131 (15), pp.1781–1799. Available at: <https://doi.org/10.1042/CS20160935>.
- [46] Kunnumakkara, A. B., Bordoloi, D., Padmavathi, G., *et al.* (2017) 'Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases', *British Journal of Pharmacology*, 174 (11), pp.1325–1348. Available at: <https://doi.org/10.1111/BPH.13621>.
- [47] Kuttikrishnan, S. *et al.* (2019) 'Curcumin induces apoptotic cell death via inhibition of PI3 - kinase/Akt pathway in B - precursor acute lymphoblastic leukemia', *Frontiers in Oncology*, 9 (JUN). Available at: <https://doi.org/10.3389/FONC.2019.00484>.
- [48] Li, W. *et al.* (2019) 'The curcumin analog EF24 is a novel senolytic agent', *Aging*, 11 (2), pp.771–782. Available at: <https://doi.org/10.18632/AGING.101787>.
- [49] Ma, Z. *et al.* (2019) 'Pharmaceutical strategies of improving oral systemic bioavailability of curcumin for clinical application', *Journal of Controlled Release*, 316, pp.359–380. Available at:
- [50] *The antioxidant activity of vitamin C, DPPD and L - cysteine against Cisplatin - induced testicular oxidative damage in rats.* | *Sigma - Aldrich* (no date). Available at: [https://www.sigmaaldrich.com/IN/en/tech-docs/paper/265283?msclkid=2fd8d38a4c4519a4b7adb6f247aa90bb&utm_source=bing&utm_medium=cpc&utm_campaign=all%20product_dsa_NA_\(bing%20ebizpfs\)&utm_term=product%20&utm_content=all%20products](https://www.sigmaaldrich.com/IN/en/tech-docs/paper/265283?msclkid=2fd8d38a4c4519a4b7adb6f247aa90bb&utm_source=bing&utm_medium=cpc&utm_campaign=all%20product_dsa_NA_(bing%20ebizpfs)&utm_term=product%20&utm_content=all%20products) (Accessed: 12 December 2023).
- [51] Tomeh, M. A., Hadianamrei, R. and Zhao, X. (2019) 'A review of curcumin and its derivatives as anticancer agents', *International Journal of Molecular Sciences*, 20 (5). Available at: <https://doi.org/10.3390/IJMS20051033>.
- [52] Wang, H. *et al.* (2021) 'Curcumin Regulates Cancer Progression: Focus on ncRNAs and Molecular Signaling Pathways', *Frontiers in Oncology*, 11. Available at: <https://doi.org/10.3389/FONC.2021.660712>.
- [53] Yallapu, M. M. *et al.* (2015) 'Therapeutic Applications of Curcumin Nanoformulations', *AAPS Journal*, 17 (6), pp.1341–1356. Available at: <https://doi.org/10.1208/S12248-015-9811-Z>.
- [54] Zia, A. *et al.* (2021) 'The role of curcumin in aging and senescence: Molecular mechanisms', *Biomedicine and Pharmacotherapy*, 134. Available at: <https://doi.org/10.1016/J.BIOPHA.2020.111119>.

Author Profile



Anjana Vidya Srivathsa received the Bachelor's degree in pharmacy from Dayanand Sagar University in 2022, while currently a Research scholar for Master's degree in pharmaceutical chemistry. During the course requirement of this specialization a personal interest in curcumin and its analogues led to the curation of the article.