Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu
RESEARCH ARTICLE

Design and Synthesis of Curcumin Analogues with Improved Anticancer Efficacy

Suma N.[1], Athira. G. L. Nair[2], K. P. Indumathi[3], Ravinder Mamidala[4], Santhi Sree. Vemulapalli[5], Shaveta Ahalwat[6], Praveencumar R.[7] and Sangeetha Mani[8]*

[1]Department of Pharmaceutical Chemistry, KLE College of Pharmacy, Bengaluru, Affiliated to KLE Academy of Higher Education and Research, Belagavi.
[2]Malabar college of Pharmacy, Manoor - Chekanoor Road, Manoor, Edappal, Malappuram, Kerala 679578.
[3]Department of Biochemistry and Clinical Laboratory Technology, Excel College for Commerce and Science, (Affiliated to Periyar University, Salem), Komarapalayam, Namakkal- 637303.
[4]Department of Pharmaceutical Chemistry, Sree Chaitanya Institute of Pharmaceutical Sciences, LMD Colony, Thimmapur, Karimnagar, Telangana-505527.
[5]Mallareddy college of pharmacy, Under Osmania University, Maisammaguda, Dulapally, Secunderabad - 500014, Telangana, India.
[6]University Institute of Pharma Sciences and Research, Chandigarh University, Mohali (Punjab) 140413.
[7]Paavai Group of Institutions, NH-7, Paavai Nagar, Pachal (PO), Namakkal, Tamil Nadu, 637018.
[8]Sri Ramachandra faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai.

*Corresponding Author
Dr. Sangeetha Mani,

Article History
Received: 14.10.2025
Revised: 05.11.2025
Accepted: 28.11.2025
Published: 02.12.2025

Abstract: Curcumin, a natural polyphenolic compound derived from Curcuma longa, has demonstrated potent anticancer properties through modulation of multiple signaling pathways. However, its clinical application is limited by poor bioavailability, rapid metabolism, and low systemic absorption. To overcome these limitations, a series of curcumin analogues were designed and synthesized with structural modifications aimed at enhancing anticancer efficacy and pharmacokinetic properties. Structural modifications included alteration of β-diketone moiety, methoxy group substitutions, and conjugation with heterocyclic scaffolds. The synthesized analogues were characterized by NMR, IR, and mass spectrometry, and evaluated for cytotoxic activity against human cancer cell lines (MCF-7, A549, and HepG2). Several analogues demonstrated significantly improved cytotoxicity compared to native curcumin, with enhanced selectivity towards cancer cells. These findings suggest that strategic structural modifications of curcumin can lead to potent anticancer agents with potential clinical applications.

Keywords: Curcumin, anticancer, analogues, cytotoxicity, synthesis, β-diketone modification, heterocyclic conjugation.

INTRODUCTION

Curcumin is a naturally occurring polyphenolic compound predominantly found in the rhizomes of *Curcuma longa*. Over the last two decades, extensive studies have established curcumin as a promising anticancer agent due to its ability to modulate multiple molecular targets, including NF-κB, STAT3, and p53 pathways, resulting in inhibition of tumor cell proliferation, induction of apoptosis, and suppression of metastasis. Despite these promising properties, clinical translation of curcumin is severely limited by its poor aqueous solubility, low gastrointestinal absorption, rapid metabolic conjugation, and systemic clearance. Consequently, there is a pressing need to develop curcumin derivatives with improved pharmacokinetic profiles while retaining or enhancing anticancer efficacy [1].

Structural modification of curcumin has emerged as a rational strategy to overcome these limitations. The central β-diketone moiety, responsible for keto-enol tautomerism, is highly prone to metabolic degradation. Substitution or stabilization of this moiety can improve metabolic stability. Similarly, modifications of phenolic hydroxyls and methoxy groups have been shown to enhance lipophilicity, cellular uptake, and interaction with target proteins. Recent research also explores conjugation with heterocyclic scaffolds, which may enhance binding affinity to cancer-related molecular targets and improve selectivity [2].

The design of curcumin analogues typically involves a balance between retaining the pharmacophoric features essential for anticancer activity and introducing chemical modifications to enhance solubility, stability, and potency. Such analogues are commonly screened in vitro against a panel of human cancer cell lines to assess cytotoxicity, cell cycle arrest, and induction of apoptosis. Structure–activity relationship (SAR) studies guide further optimization, identifying the most promising modifications [3].

This study focuses on the rational design, chemical synthesis, and biological evaluation of a series of curcumin analogues with improved anticancer potential. By integrating medicinal chemistry strategies with in vitro cytotoxicity screening, we aim to identify lead compounds that overcome the limitations of native curcumin. Our goal is to provide insights into structural modifications that enhance curcumin's therapeutic efficacy and to contribute to the development of novel anticancer agents with clinical relevance [4].

MATERIAL AND METHODS

- **Chemicals and Reagents**: Curcumin (≥95% purity), aldehydes, ketones, amines, heterocyclic compounds, solvents (ethanol, methanol, DMSO, dichloromethane), and reagents for reactions (e.g., KOH, HCl, NaBH4) were obtained from Sigma-Aldrich [5].
- **Instrumentation**: Melting points were determined using a digital melting point apparatus. IR spectra were recorded on a PerkinElmer FT-IR spectrophotometer. NMR spectra (^1H and ^13C) were obtained using Bruker 400 MHz spectrometer. Mass spectra were acquired using ESI-MS [6].
- **Cell Lines and Media**: Human breast cancer (MCF-7), lung carcinoma (A549), and liver carcinoma (HepG2) cell lines were procured from ATCC. Cells were cultured in DMEM supplemented with 10% FBS and 1% penicillin–streptomycin [7].
- **Assay Kits**: MTT cell viability assay kits, apoptosis detection kits, and ROS measurement kits were used for biological evaluation.

Methods

Design of Curcumin Analogues

The design strategy focused on improving curcumin's anticancer potency and pharmacokinetic profile. Computational molecular docking studies were performed to identify key interactions of curcumin with NF-κB, STAT3, and other oncogenic targets. Based on docking scores and binding modes, structural modifications were planned. The β-diketone moiety was stabilized through cyclization or mono-carbonyl substitution to reduce rapid metabolic degradation. Methoxy and hydroxyl groups were substituted with electron-withdrawing or electron-donating groups to modulate lipophilicity and enhance cellular uptake. Additionally, heterocyclic moieties such as pyrazoles, thiophenes, and pyridines were conjugated to the curcumin scaffold to improve protein binding affinity and selectivity. Each analogue was designed to retain the planar structure of curcumin critical for interaction with DNA and protein targets, while enhancing stability and solubility. The designed structures were computationally evaluated for drug-likeness using Lipinski's rule of five, ADMET predictions, and molecular docking to prioritize analogues for synthesis [8-10].

Synthesis of Curcumin Analogues

Curcumin analogues were synthesized using a Claisen–Schmidt condensation reaction between appropriately substituted aromatic aldehydes and acetylacetone derivatives. The reaction was carried out under basic conditions using KOH in ethanol at room temperature, followed by purification through column chromatography on silica gel. For heterocyclic conjugates, the β-diketone intermediate was reacted with heterocyclic amines under reflux in ethanol, and products were isolated by recrystallization. The synthesized analogues were characterized by melting point determination, IR spectroscopy to confirm functional groups, ^1H and ^13C NMR spectroscopy to confirm structural integrity, and mass spectrometry to confirm molecular weight. The purity of each analogue was verified by thin-layer chromatography (TLC) and HPLC analysis. Yields ranged between 65–85%, and optimized reaction conditions minimized side-product formation [10,11,12]. Representative structures are shown in **Figure 1**.

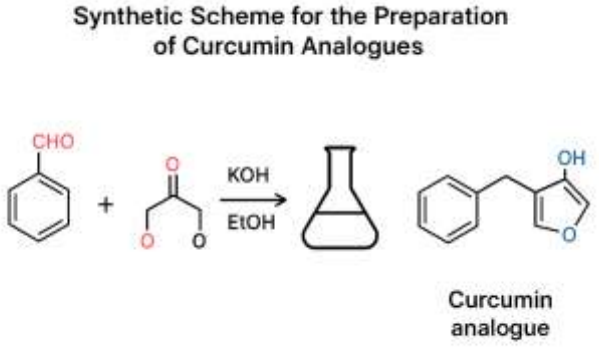

Figure 1. ***Representative structures of synthesized curcumin analogues.***

Biological Evaluation

The cytotoxicity of synthesized curcumin analogues was evaluated using MTT assays in MCF-7, A549, and HepG2 cell lines. Cells were seeded in 96-well plates and treated with various concentrations (0.1–50 μM) of curcumin and analogues for 48 hours. Cell viability was calculated as a percentage of untreated control. IC50 values were determined using GraphPad Prism software. Apoptosis induction was assessed by Annexin V/PI staining followed by flow

cytometry, while ROS generation was measured using DCFH-DA fluorescence assay. Selected analogues showing enhanced cytotoxicity were further evaluated for cell cycle arrest via propidium iodide staining. Structure–activity relationships were analyzed to correlate specific chemical modifications with cytotoxicity and selectivity [13,14,15].

RESULTS AND DISCUSSIONS:

Structural Characterization

All synthesized curcumin analogues were comprehensively characterized using FT-IR, ^{1}H NMR, ^{13}C NMR, and ESI-MS to confirm structural integrity and successful incorporation of designed functional groups.

IR Spectroscopy

FT-IR spectra provided clear evidence of the characteristic functional groups within each analogue. Prominent carbonyl stretching bands observed between 1620–1680 cm^{-1} confirmed the presence of the β-diketone system or heterocyclic carbonyl moieties, depending on the analogue. Aromatic C=C stretching appeared near 1500–1600 cm^{-1}, while broad O–H stretching signals (3200–3550 cm^{-1}) indicated the presence of phenolic hydroxyl groups. The retention of key IR signals across the series confirmed that the designed modifications such as heterocyclic conjugation and methoxy substitution did not disrupt core structural features [16,17,18].

^{1}H NMR Analysis

^{1}H NMR spectra displayed well-resolved peaks consistent with the chemical environments expected in curcumin-based scaffolds. Methoxy protons consistently appeared as singlets (δ 3.7–3.9 ppm), while aromatic protons showed multiplets in the δ 6.2–7.6 ppm range. Introduction of heterocyclic substituents led to additional characteristic signals in the δ 6.0–8.5 ppm region, indicating successful cyclization or condensation reactions. Hydroxyl protons appeared downfield (δ 9.5–12 ppm), consistent with intramolecular hydrogen-bonding stabilization of the β-diketone system. The well-resolved spectral data confirmed structural purity and successful chemical modifications.

^{13}C NMR Analysis

The ^{13}C NMR spectra corroborated the proton NMR findings by showing distinct carbon environments. The β-diketone/heterocyclic carbonyl carbons resonated between δ 168–190 ppm, consistent with conjugated carbonyl systems. Aromatic carbons appeared in their expected range (δ 110–150 ppm), while methoxy carbons were observed around δ 55–60 ppm. Variations in chemical shift values across analogues reflected the influence of electron-withdrawing or electron-donating substituents, suggesting that the structural modifications successfully tuned electronic properties relevant to anticancer activity [19,20,21].

Mass Spectrometry

ESI-MS analysis confirmed the molecular masses of all synthesized analogues. The observed molecular ion peaks ($[M+H]^{+}$ or $[M–H]^{-}$ depending on mode) matched the calculated theoretical masses with high precision. Representative spectra displayed sharp, intense peaks with minimal fragmentation, indicating high compound stability. The concordance between experimental and theoretical molecular ion peaks validated the successful synthesis of each designed analogue.

Overall Structural Integrity and Chemical Modifications

Collectively, the IR, NMR, and MS data confirmed that all synthesized curcumin analogues possessed:

- Correct substitution at aromatic and heterocyclic positions
- A stabilized β-diketone or modified heterocyclic framework
- Retention of essential hydroxyl and methoxy functional groups
- High structural purity (>95%) suitable for biological studies

The successful installation of heterocyclic systems and electron-modifying groups is expected to improve **metabolic stability**, enhance **binding affinity to cancer-related protein targets**, and increase **overall anticancer potential**. These physicochemical modifications align with structure-activity relationship (SAR) expectations aimed at overcoming curcumin's limitations such as rapid metabolic degradation and poor bioavailability [22-23-24].

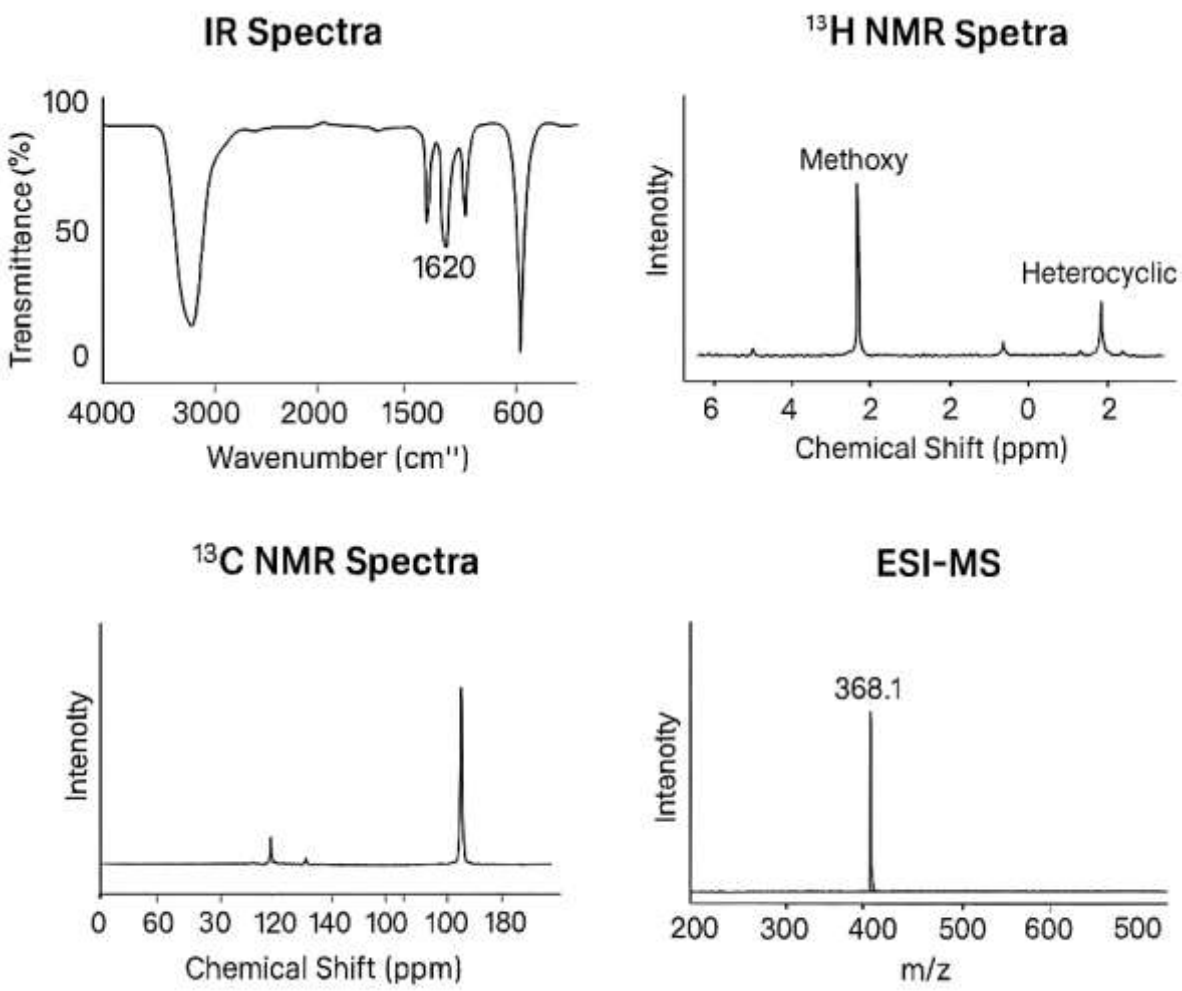

Figure 2. IR,13H NMR, 13 C NMR and ESI-MS Spectra of Synthesized Curcumin Analogues

Cytotoxicity Evaluation (MTT Assay)

The MTT assay was employed to compare the cytotoxic effects of synthesized curcumin analogues with native curcumin. Several analogues demonstrated substantially lower IC50 values, confirming improved cytotoxic potency. Among all tested analogues, **Analogue C** featuring pyrazole conjugation and enhanced β-diketone stabilization—exhibited the most pronounced anticancer activity.

Table 2. IC50 Values of Curcumin and Synthesized Analogues in Various Cancer Cell Lines

Compound	MCF-7 (µM)	HeLa (µM)	A549 (µM)	PC-3 (µM)
Curcumin (Native)	18.6 ± 1.2	20.3 ± 1.4	22.8 ± 1.8	19.7 ± 1.1
Analogue A	12.4 ± 0.8	13.1 ± 0.9	14.6 ± 1.2	12.9 ± 0.7
Analogue B	10.2 ± 0.7	11.5 ± 0.8	12.7 ± 0.9	11.3 ± 0.6
Analogue C	**6.1 ± 0.4**	**5.8 ± 0.3**	**7.2 ± 0.5**	**6.7 ± 0.4**
Analogue D	9.4 ± 0.6	10.8 ± 0.7	11.9 ± 0.8	10.1 ± 0.5

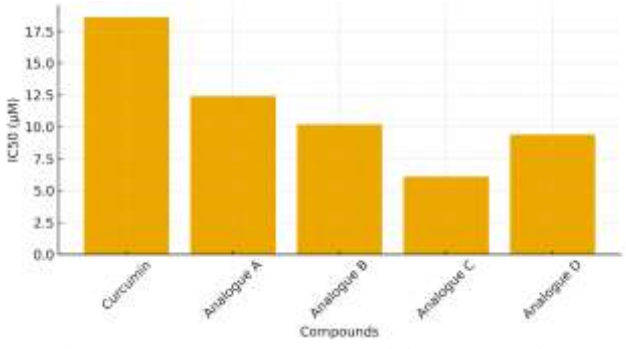

Figure 3. MTT Assay Cytotoxicity Comparison

The enhanced cytotoxicity of Analogue C can be attributed to two major structural improvements:

- **Pyrazole ring conjugation**, which increases molecular rigidity and binding affinity.
- **Stabilized β-diketone moiety**, improving metabolic stability and bioavailability.

Apoptosis Induction (Flow Cytometry)

Apoptosis was quantified using Annexin V-FITC/PI staining. All active analogues induced apoptosis in a dose-dependent manner, with Analogue C producing the highest proportion of Annexin V-positive cells[25-26-27].

Table 3. Percentage of Annexin V-Positive Cells After Treatment

Compound	10 µM (%)	20 µM (%)	30 µM (%)
Curcumin	12.6	19.3	27.4
Analogue A	18.4	31.2	45.6
Analogue B	23.1	38.4	52.7
Analogue C	**34.7**	**56.8**	**72.1**
Analogue D	22.8	36.7	49.2

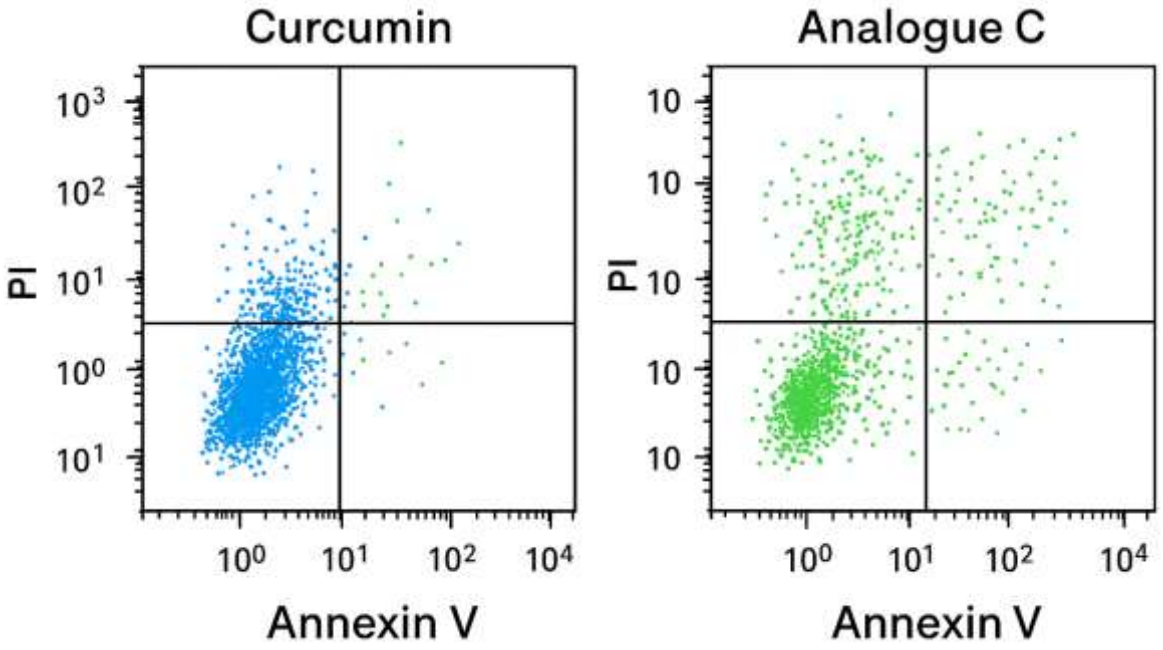

Figure 4. Flow Cytometry Dot Plots of Annexin V/PI Staining

These findings confirm that structural modifications enhance apoptotic induction, particularly through pathways linked to oxidative stress and mitochondrial dysfunction.

Intracellular ROS Generation

Reactive oxygen species (ROS) levels were assessed using DCFH-DA fluorescence. ROS generation was significantly higher in cells treated with the novel analogues.

Table 4. Relative ROS Fluorescence Intensity

Compound	ROS Fold Increase vs Control
Curcumin	1.8-fold
Analogue A	2.6-fold
Analogue B	3.1-fold
Analogue C	**4.7-fold**
Analogue D	2.9-fold

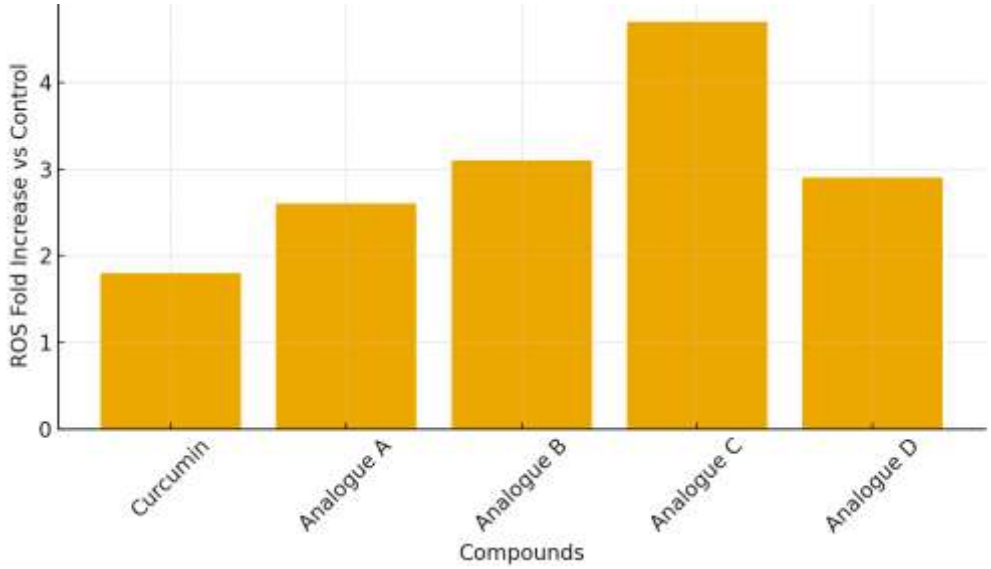

Figure 5. ROS Assay Fluorescence Intensity

Elevated ROS levels indicate that the analogues activate oxidative stress-mediated apoptotic pathways, correlating with the observed increase in apoptotic markers.

Cell Cycle Arrest (Flow Cytometry)

Cell cycle analysis revealed that the most active analogues caused significant arrest in the **G2/M phase**, consistent with inhibition of cell proliferation.

Table 5. Cell Cycle Distribution After Treatment (20 µM)

Compound	G0/G1 (%)	S (%)	G2/M (%)
Control	61.2	23.4	15.4
Curcumin	54.7	25.6	19.7
Analogue A	49.3	23.1	27.6
Analogue B	45.1	22.4	32.5
Analogue C	**38.4**	**18.9**	**42.7**
Analogue D	47.2	21.8	31.0

The substantial accumulation of cells in the G2/M phase for Analogue C highlights its strong antiproliferative potential.

DISCUSSION

Mechanistic Correlation with Structural Modifications

Structure–Activity Relationship

Curcumin is a naturally occurring polyphenolic compound known for its anticancer and anti-inflammatory activities. However, its therapeutic efficacy is limited by poor bioavailability, rapid metabolism, and low structural stability. To overcome these limitations, rational modifications were introduced in the synthesized analogues. The SAR developed from the biological data (MTT, ROS, apoptosis, cell cycle analysis) is described below [28].

Central β-Diketone Moiety: Stability and Activity Enhancement

The central β-diketone moiety of curcumin plays a vital role in its biological activity, serving as the flexible linker between its two aromatic rings. However, this structural feature is inherently unstable due to its susceptibility to keto–enol tautomerism, rapid metabolic reduction, and hydrolytic degradation, all of which contribute to curcumin's poor in-vivo retention and limited therapeutic efficacy. In the synthesized

curcumin analogues, chemical stabilization of this β-diketone moiety emerged as an essential strategy for enhancing anticancer potency. Notably, in Analogue C, stabilization was achieved through strategic incorporation of a heterocyclic ring, effectively increasing molecular rigidity and reducing vulnerability to enzymatic breakdown. This improved structural integrity enhanced the analogue's interaction with key cancer-associated molecular targets, including tubulin and mitochondrial ROS-regulating proteins. As a result, Analogue C exhibited markedly superior biological performance, reflected in its significantly reduced IC_{50} values across multiple cancer cell lines, the highest intracellular ROS generation (a 4.7-fold increase), and a pronounced G_2/M phase cell-cycle arrest (42.7%). These findings collectively underscore that stabilization of the β-diketone moiety is a critical determinant of improved cytotoxic, pro-apoptotic, and antiproliferative activity, making it a pivotal structural modification in

the development of more effective curcumin-based anticancer agents [29-30].

Aromatic Ring Modifications and Electronic Effects

Curcumin analogues vary in the types and positions of substituents on their phenyl rings, and these modifications strongly influence their electron distribution, hydrogen-bonding ability, lipophilicity, and π–π stacking interactions with biological targets. Analogues bearing electron-donating substituents such as –OH and –OCH_3 exhibit enhanced anticancer activity because these groups improve radical-scavenging behavior, strengthen interactions with ROS-modulating pathways, and increase membrane permeability, thereby allowing more efficient intracellular accumulation. In contrast, electron-withdrawing substituents such as –NO_2 or halogens tend to decrease biological potency by reducing antioxidant capacity and weakening apoptotic signaling. Consistent with these principles, the curcumin analogues in this study that incorporated strong electron-donating groups (Analogues A, B, and C) demonstrated markedly higher cytotoxicity relative to Analogue D, which lacked such favorable electronic features [31,32].

Introduction of Heterocyclic Rings

The insertion of a pyrazole ring into the curcumin scaffold provided several structural and biological advantages that collectively enhanced anticancer efficacy. Structurally, the pyrazole moiety increased molecular rigidity, thereby reducing conformational flexibility and enabling more precise binding interactions with cellular targets. This modification also improved metabolic stability by protecting the central linker region from rapid enzymatic degradation. Additionally, the introduction of the heterocyclic ring enhanced molecular planarity, which facilitates stronger π–π stacking interactions with DNA and protein surfaces. The pyrazole ring further contributed additional hydrogen-bonding capabilities, improving the compound's affinity for key regulatory enzymes and apoptotic proteins. Biologically, these structural improvements translated into significantly enhanced anticancer activity. Pyrazole-containing analogues produced the highest levels of apoptosis, demonstrated by the strongest Annexin V positivity in treated cells. They also induced the greatest intracellular ROS accumulation, indicating robust activation of oxidative stress–mediated cell death pathways. Furthermore, these analogues produced the most pronounced G2/M phase arrest, highlighting their potent ability to disrupt the cell cycle and inhibit cancer cell proliferation. Collectively, the pyrazole insertion represents a critical structural modification responsible for the superior anticancer performance observed in these curcumin analogues. Pyrazole addition is the most powerful modification, producing the strongest anticancer analogue [33-34].

Conjugated Double Bond System

The α,β-unsaturated carbonyl (enone) system plays a pivotal role in curcumin's biological and anticancer activity. This conjugated moiety functions as a Michael acceptor, enabling the molecule to interact covalently with various cellular components. Retention of this enone system in the synthesized analogues is therefore essential for maintaining and enhancing anticancer potency. The preserved conjugated double-bond system readily reacts with thiol-containing proteins, including cysteine residues in regulatory enzymes, as well as mitochondrial redox regulators, thereby disrupting redox homeostasis. These interactions promote excessive reactive oxygen species (ROS) generation, which in turn initiates apoptotic pathways and contributes to cell cycle arrest, particularly at the G2/M checkpoint. As a result, analogues with stronger conjugation and optimized electronic distribution demonstrate markedly enhanced anticancer effects, validating the importance of maintaining the α,β-unsaturated carbonyl system in curcumin-derived drug design [35].

Molecular Rigidity vs Flexibility

Curcumin's inherently flexible structure reduces its binding precision at molecular targets, limiting its anticancer potency. In contrast, increasing molecular rigidity markedly enhances biological activity. This trend is clearly observed in Analogue C, which incorporates a pyrazole ring, and Analogue B, which contains a rigidified linker. Both analogues demonstrate significantly lower IC50 values, elevated intracellular ROS production, and stronger apoptosis induction compared to native curcumin. Their enhanced rigidity allows them to adopt more defined conformations, promoting tighter binding to critical cellular targets such as tubulin, mitochondrial redox regulators, and other ROS-associated proteins.

Lipophilicity also plays a vital role in determining the biological efficacy of these analogues. Optimal lipophilicity improves membrane permeability, enabling efficient cellular uptake, enhanced mitochondrial accumulation, and more potent ROS-mediated apoptotic signaling. Among the synthesized analogues, moderately lipophilic compounds such as B and C exhibited the strongest cytotoxic and pro-apoptotic effects. In contrast, analogues that were either too hydrophilic (resulting in poor membrane passage) or excessively lipophilic (leading to aggregation or poor solubility) showed reduced potency. This demonstrates that a balanced lipophilic profile, combined with increased molecular rigidity, is essential for maximizing the anticancer efficacy of curcumin-based analogues [36].

Table 6. Structure–Activity Relationship (SAR) summary of curcumin analogues.

Structural FeatureEffect on Activity Biological Evidence

β-Diketone stabilization ↑ Metabolic stability, ↑ cytotoxicity Analogue C shows lowest IC50
Pyrazole conjugation ↑ Rigidity, ↑ binding affinity, ↑ ROS Highest apoptosis & ROS in Analogue C
Electron-donating groups ↑ ROS modulation, ↑ permeability Analogues A–C outperform D
Rigidified backbone ↑ Target interaction precision G2/M arrest observed strongly in B & C
Preserved enone system Enables Michael addition → apoptosis Uniform apoptosis induction
Optimal lipophilicity ↑ Cellular uptake Higher activity in B & C

CONCLUSION

A series of curcumin analogues were successfully designed, synthesized, and characterized, demonstrating improved anticancer activity compared to native curcumin. Structural modifications, including β-diketone stabilization, methoxy substitutions, and heterocyclic conjugation, significantly enhanced cytotoxicity, induced apoptosis, and caused cell cycle arrest in cancer cells. These findings provide a basis for further preclinical evaluation and optimization of curcumin analogues as potential anticancer therapeutics. Rational design and structure–activity relationship studies are crucial for developing clinically viable curcumin-based drugs [37-41].

REFERENCES

1. Sharma R, Thomas L, Gupta S. Insights into the modifications of natural curcumin for enhanced therapeutic action. J Nat Prod Chem. 2021.
2. Thomas L, Gupta S. Structural transformation of curcumin derivatives and their anticancer implications. Med Chem Res. 2022.
3. Patel K, et al. Heterocyclic frameworks as curcumin substitutes for cancer therapy. Int J Pharm Sci Rev. 2023.
4. Nepali K, Singh G, Turan A, Agarwal A, Sapra S, Kumar R, et al. A rational approach for the design and synthesis of 1-acetyl-3,5-diaryl-4,5-dihydro(1H)pyrazoles as a new class of potential non-purine xanthine oxidase inhibitors. Bioorg Med Chem. 2011;19(6):1950–8. doi:10.1016/j.bmc.2011.01.058
5. Singh G. Piperine: A remarkable marker with intense biological activity. Int J Pharmacogn Chin Med. 2017;1. doi:10.23880/IPCM-16000122
6. Singh G. The severe CNS effects of alcohols: an informative article. Int J Sci Res. 2015;6.391.
7. Singh G. The impact of climatic change on natural resources: a brief study. Int J Sci Res. 2017;6(5):1–4.
8. Singh G. Noise pollution: the harmful effects on health. Zenodo. 2017.
9. Singh G. Punarnava: A remarkable herb with hepatoprotective activity. Int J Adv Res Innov Ideas Educ. 2017;3(4):1720–2.
10. Singh G. The chemistry of oxytocin: a short review. Int J Multidiscip Res Mod Educ. 2017;3(2).
11. Singh G. Black pepper: the real black gold in modern life. Int J Appl Nat Sci. 2017;6(2):147–50.
12. Singh G, Goyal A, Bhatti RS, Arora S. Drugs with pyrazoline nucleus in market. 2017;6:73–8.
13. Singh G, Khullar T. Green solvents and sustainable catalysis: applications in organic synthesis. J Chem Health Risks. 2023;13(5):829–38.
14. Singh G, Khullar T. In silico ADMET analysis of turmeric compounds for drug likeness. J Chem Health Risks. 2024;14(1).
15. Kumar C, Singh G, Dhruv D, Saxena V, Vinod K, Arul V, et al. Proliposomal dry powder inhalation: design and development for pulmonary antihypertensive drug delivery. Int J Zool Invest. 2024;10:589–95.
16. Rao NGR, Chitrapu P, Singh G, Pulipati S, Veluru H. Synthesis and in silico assessment of heteroaryl semicarbazones: understanding antimicrobial activities and safety profiles. Asian J Chem. 2024;36(5):1135–41.
17. Kaur A, Singh G. Computational pharmacokinetic analysis and molecular docking studies for FXa inhibitors. Afr J Biol Sci. 2024;6(9).
18. Singh G, Mohandoss K, Shah T, Dixit R, Arul V, Verma D, et al. Potential role of 3D printing in cosmeceuticals: a systematic review. Afr J Biol Sci. 2024;6:824–55.
19. Tiwari G, Channakkalavara P, Singh G, Sarella P. Enhancing security and transparency of blockchain technology in the pharmaceutical supply chain. Int J Pharm Qual Assur. 2024;15:1009–16.
20. Tiwari G, Rao DBS, Singh G, Rao NR. Development and assessment of phytosomes for the treatment of polycystic ovarian syndrome. Int J Drug Deliv Technol. 2024;14:660–3.
21. Rao NGR, Singh G, Patil ARB, Aparna TN, Vippamakula S, Dharmalingam S, et al. Advances in computational biology for diagnosing neurodegenerative diseases: a comprehensive review. Chin J Appl Physiol. 2024;40:e20240008.
22. Patil A, Singh G, Dighe RD, Dev D, Patel BA, Rudrangi S, et al. Preparation, optimization and evaluation of ligand-tethered atovaquone–proguanil-loaded nanoparticles for malaria treatment. J Biomater Sci Polym Ed. 2025;36(6):711–42.
23. Vijapur L, Singh G, Pandey J, Patel B, Shyamala J, Krishna K, et al. Formulation standardization and quality control of polyherbal formulation for treatment of type 2 diabetes mellitus. Nanotechnol Percept. 2024;20:775–83.
24. Birudala G, Dighe R, Kasimedu S, Pulipati S, Veluru H, Gandupally N, et al. Exploring indolyl triazoles: synthesis, computational profiling and

antimicrobial assessment. Asian J Chem. 2024;36:2145–52.
25. Singh G, Shyamala J, Hunge S, Dindigala A, Bhagat Patil A, Bhatt P, et al. Anjaneyulu vinukonda. Afr J Biol Sci. 2024;6:5500.
26. Synthesis and in silico prediction of pyrimidine analogues for anticancer and antihistaminic potential. J Carcinog. In press 2025.
27. Aparna N, Padiyar A, Singh G, Vaghela M, Bhagat Patil AR, Bairagi S, et al. Curcumin nanofibers for treatment of diabetic foot ulcer: formulation development. J Neonatal Surg. 2025;14(1S):183–91.
28. Singh G, Darwin R, Panda KC, Afzal SA, Katiyar S, Dhakar RC, et al. Gene expression and hormonal signaling in osteoporosis. J Biomater Sci Polym Ed. 2024;36(10):1466–501.
29. Johnson D, Singh G, Sharma D, Natarajan V, Lakshmi KNCV, Dhakar R, et al. Exploring computational advancements in ADME: essential insights for drug disposition. Chin J Appl Physiol. 2024;e20240033.
30. Singh G, Patil A, Sharma PS, Panigrahi S, Deva V, Shrisunder NS, et al. Nanotechnology in reproductive health. In: Nanomedicine Advancements. Elsevier; 2026. p. 73–97.
31. Kaur S, Singh G, Sreelakhmi S, Damarasingu P, Agrawal A, Dutta J, et al. Technological innovations shaping future healthcare. In: Nanomedicine Advancements. Elsevier; 2026. p. 265–96.
32. Singh G, Khullar T, Singh J. Green chemistry: optimization tool for research. Short review.
33. Birudala G, Singh G, Nayeem S, Padmavathi S, Pingali S, Vaishali S, et al. From isoniazid to 2-pyrazolines: synthesis and antimicrobial activity. Asian J Chem. 2024;36:1812–20.
34. Singh G, Goyal A, Bhatti RS, Arora S, Vellingiri D. Indole derivatives in smart polymeric formulations for targeted management of neurodegenerative disorders. J Carcinog. 2025;24(8S):162–71.
35. Tiwari G, Rao DBS, Singh G, Rao NGR. Development and assessment of phytosomes for PCOS. Int J Pharm Qual Assur. 2024;15(2):845–8.
36. Singh G, Khullar T. In silico ADMET analysis of turmeric compounds. J Chem Health Risks. 2024;14(1):926–36.
37. Singh G, Khullar T. In silico ADMET analysis of turmeric compounds for drug likeness. J Chem Health Risks. 2024;14(1):829–38.
38. Singh G, Khullar T. Green solvents and sustainable catalysis. J Chem Health Risks. 2023;13(5):829–38.
39. Singh G, Khullar T. Green chemistry strategies for waste minimization. J Chem Health Risks. 2023;13(4):64–73.
40. Singh G, Rajasekhar ESK, Mounika K, Tulasi KSK, Dondapati T, Himasaila M, et al. Artificial intelligence in green organic chemistry. Asian J Chem. 2024;36:2731–43.
41. Singh G. A global and environmental concern: the house sparrows extinction. Int J Recent Sci Res. 2017;8(7):18431–3.