University "St. Kliment Ohridski" - Bitola, Republic of North Macedonia
Faculty of Technology and Technical Sciences - Veles

Book of proceedings of the 1st International Scientific Conference - Food Science, Nutrition, Innovative Technologies and Sustainability

Veles, North Macedonia
February 2026

University "St. Kliment Ohridski" - Bitola, Republic of North Macedonia

Faculty of Technology and Technical Sciences - Veles

Book of proceedings of the 1st International Scientific Conference - Food Science, Nutrition, Innovative Technologies and Sustainability

Veles, North Macedonia
February 2026

Publication Title: Book of Proceedings of the 1st International Scientific Conference - Food Science, Nutrition, Innovative Technologies and Sustainability

Publisher: University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences - Veles

Editor-in-chief: Assoc. Prof. Dr. Sc Vezirka Jankuloska, Faculty of Technology and Technical Sciences - Veles, University “St. Kliment Ohridski” – Bitola, Republic of North Macedonia

Editor: Prof. Dr. Sc Vesna Knights, Faculty of Technology and Technical Sciences- Veles, University “St. Kliment Ohridski” – Bitola, Republic of North Macedonia

Technical Editor and Graphic Design: Tanja Stojanovska, Jordan Martinovski, Faculty of Technology and Technical Sciences - Veles, University "St. Kliment Ohridski" - Bitola, Republic of North Macedonia

All papers included in this volume were peer-reviewed by members of the Scientific Committee and Reviewers from a relevant scientific field.

Edition: e-edition

Year of publication: 2026

CIP - Каталогизација во публикација
Национална и универзитетска библиотека "Св. Климент Охридски", Скопје

613.2(062)
616-083.2(062)
606:663/664(062)

INTERNATIONAL Scientific Conference - Food Science, Nutrition, Innovative Technologies and Sustainability (1 ; 2025 ; [Veles])
Book of proceedings of the 1st International Scientific Conference - Food Science, Nutrition, Innovative Technologies and Sustainability [Електронски извор] / [editor-in-chief Vezirka Jankuloska]. - Veles : University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences, 2026

Начин на пристапување (URL): https://ttfv.uklo.edu.mk/2026/02/20/book-of-proceedings-of-the-1st-international-scientific-conference-food-science-nutrition-innovative-technologies-and-sustainability/.
- Текст во ПДФ формат, содржи 193 стр., илустр. - Наслов преземен од екранот. - Опис на изворот на ден 09.03.2026. - Фусноти кон текстот. - Библиографија кон трудовите

ISBN 978-608-67527-0-5

а) Храна -- Квалитет -- Собири б) Исхрана -- Здравствени аспекти -- Собири в) Храна -- Биотехнологија -- Собири

COBISS.MK-ID 68355333

ORGANIZING COMMITTEE

Vezirka Jankuloska, PhD, Dean, University “St. Kliment Ohridski” – Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Vesna Knights, PhD, Vice-Dean for Science and International Cooperation, University “St. Kliment Ohridski” – Bitola, Faculty of Technology and Technical Sciences - Veles, Republic of North Macedonia

Aleksandar Stanković, PhD, Vice-Dean for Science and International Cooperation, Faculty of Applied Sciences – Niš, University of Economics Academy in Novi Sad, Serbia

INTERNATIONAL SCIENTIFIC COMMITTEE

Vesna Knights, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Anka Trajkoska Petkoska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Vezirka Jankuloska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Gorica Pavlovska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Valentina Velkovski, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Tatjana Kalevska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Daniela Nikolovska Nedelkoska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Viktorija Stamatovska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Tatjana Blazhevska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Nevena Gruevska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Sanja Sazdovska, PhD, University "St. Kliment Ohridski" - Bitola, Faculty of Technology and Technical Sciences – Veles, Republic of North Macedonia

Namik Durmishi, PhD, University of Tetova, Faculty of Food Technology and Nutrition, Tetovo, Republic of North Macedonia

Gafur Xhabiri, PhD, University of Tetova, Faculty of Food Technology and Nutrition, Tetovo, Republic of North Macedonia

Ismail Ferati, PhD, University of Tetova, Faculty of Food Technology and Nutrition, Tetovo, Republic of North Macedonia

Vladimir Kitanovski, PhD, Mother Teresa University, Skopje, Republic of North Macedonia

Aksu Samet, PhD, International Balkan University, Faculty of Dental Medicine, Skopje, Republic of North Macedonia

Ljupcho Mihajlov, PhD, "Goce Delchev" University, Faculty of Agriculture, Shtip, Republic of North Macedonia

Emilija Arsov, PhD, "Goce Delchev" University, Faculty of Agriculture, Shtip, Republic of North Macedonia

Frosina Babanovska-Milenkovska, PhD, "Ss. Cyril and Methodius" University – Skopje, Faculty of Agricultural Sciences and Food, Republic of North Macedonia

Mishela Temkov, PhD, "Ss. Cyril and Methodius" University – Skopje, Faculty of Technology and Metallurgy, Republic of North Macedonia

Dimitar Nakov, PhD, "Goce Delchev" University, Faculty of Agriculture, Shtip, Republic of North Macedonia

Ljubica Karakashova, PhD, "Ss. Cyril and Methodius" University – Skopje, Faculty of Agricultural Sciences and Food, Republic of North Macedonia

Jasenka Gajdoš Kljusurić, PhD, University of Zagreb, Faculty of Food Technology and Biotechnology, Zagreb, Croatia

Tamara Jurina, PhD, University of Zagreb, Faculty of Food Technology and Biotechnology, Zagreb, Croatia

Jasmina Lukinac, PhD, Josip Juraj Strossmayer University of Osijek, Faculty of Food Technology, Osijek, Croatia

Marko Jukić, PhD, Josip Juraj Strossmayer University of Osijek, Faculty of Food Technology, Osijek, Croatia

Aleksandar Stanković, PhD, University of Economics Academy in Novi Sad, Faculty of Applied Sciences – Niš, Serbia

Filip Cvetković, PhD, University of Economics Academy in Novi Sad, Faculty of Applied Sciences – Niš, Serbia

Jasminka Gligorijević, PhD, Faculty of Applied Sciences – Niš, University of Business Academy in Novi Sad, Serbia

Sanja M. Petrović, PhD, University of Niš, Faculty of Technology – Leskovac, Serbia

UDK: 615.322:547.979.4

CURCUMIN AND ITS STRUCTURAL ANALOGUES: A REVIEW OF SYNTHETIC STRATEGIES, ANALYTICAL METHODS AND PHARMACOLOGICAL POTENCIAL

Zlatko Lozanovski[1][0009-0009-9228-893X], Valentina Velkovski[2][0000-0003-4978-5710], Angelka Jankulovska [1][0000-0002-4840-0308], Daniela Petkovska [1][0009-0002-9389-7023], Denis Arsovski [1][0000-0003-4992-686X], Gabriel Zhivkovikj[1]

[1]Higher Medical School – Bitola, University "St. Kliment Ohridski" - Bitola, Republic of North Macedonia
[2]Faculty of Technology and Technical Sciences - Veles, University "St. Kliment Ohridski" - Bitola, Republic of North Macedonia
E-mail: zlatko.lozanovski@uklo.edu.mk

Abstract
Curcumin, a polyphenolic compound extracted from *Curcuma longa*, has attracted considerable attention for its traditional use in medicine and its wide-ranging biological activities. It has shown therapeutic potential in various conditions, including cancer, autoimmune diseases, metabolic disorders, neurodegenerative diseases, and chronic inflammation. However, despite its promising pharmacodynamic profile, curcumin's clinical relevance remains limited due to its poor chemical stability and low bioavailability.These limitations stem primarily from its keto-enol tautomerism, rapid metabolism, poor water solubility, and the chemical reactivity of its β-diketone and methylene groups. These electrophilic sites, although crucial for biological activity, also make the molecule highly unstable above pH 6.5, leading to rapid degradation in physiological environments. This review focuses on the exploration and critical evaluation of synthetic structure-based modelling strategies including the elimination of reactive sites (e.g., phenolic and enolic hydroxyl groups), the introduction of stabilizing functional groups, and the design of novel analogues with enhanced metabolic resistance and target selectivity. Special attention is given to derivatization approaches that improve chemical stability, solubility, and systemic delivery. Furthermore, emphasis is placed on the analytical characterization of these analogues through advanced techniques, including spectroscopic and chromatographic methods, in order to validate their structural integrity and potential pharmacological relevance. Overall, the review highlights the potential of curcumin-derived scaffolds in drug development and supports further investigation into optimized analogues for clinical use.

Keywords: Curcumin, Structural Analogues, Molecular Modelling, Synthetic Strategies, Pharmacological Potential.

1. Introduction

Curcumin, the principal curcuminoid found in the rhizomes of Curcuma longa (turmeric) *fam. Zingiberaceae*, is a lipophilic polyphenolic compound renowned for its bright yellow pigmentation. It primarily originates from Tropical Asia, namely India, which is considered the largest producer (about 80% of total production) and exporter to other parts of the world. Its cultivation spread to the coast of China, East and West Africa, while the Arabs, along with the development of trade in the 13th century, brought it to European soil (Parry, 1969).

Although seemingly similar to saffron, turmeric was used in Indian medicine as a

"powerful" medicine known as *Ayurveda* against various diseases. A drink made from a mixture of turmeric and boiled milk was used against respiratory diseases, a combination of turmeric, ginger root, honey and boiled milk was one of the magical drinks among women from northern India who were in the postpartum period. The famous curcumin paste was used to speed up the healing of guts, eye infections and to alleviate the side effects of hallucinating after using hashish (Sharifi-Rad et al., 2020; Goel et al., 2008; Aggarwal et al., 2007).

Due to its specific taste and smell, turmeric was used daily in cooking, as a spice and additive (today it is an integral part of curry spice), and due to its yellow color it was also used in the textile industry as a natural dye for fabrics and textiles (Han et al., 2005; Reddy et al., 2013). The strong yellow color found application in cosmetics among Indian women in the process of skin rejuvenation, protection against various bacteria, temperature regulation and thus protection from daily harmful solar and ultraviolet rays, as well as in the fulfillment of daily ancient rituals accompanied by body and face painting (Tilak et al., 2004). In the last three decades, it has been intensively studied to demonstrate its therapeutic effects against malignant diseases, autoimmune diseases, metabolic, neurological, cardiovascular, pulmonary diseases, and various other inflammatory diseases (Aggarwal et al., 2009; Kannappan et al., 2011; Urošević et al., 2022; Hewlings et al., 2017).

The curcumin molecule is symmetrical and known as diferuloylmethane. It is characterized by two benzene rings containing ortho-methoxy phenolic OH groups linked to a C7 carbon chain representing a bis-*α,β*-unsaturated *β*-diketone, with the chemical formula $C_{21}H_{20}O_6$, molecular weight of 368.37 g/mol and melting point of 183 °C, figure 1.

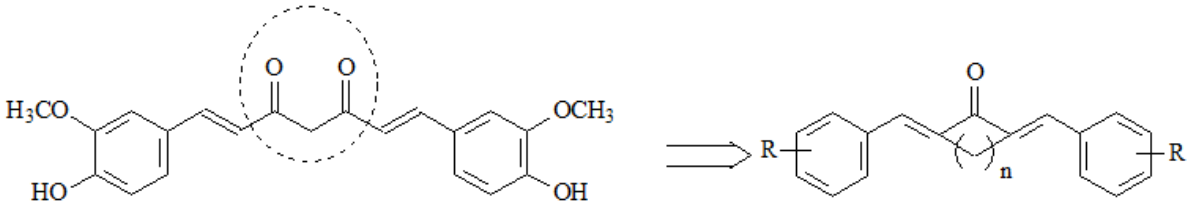

Figure 1: Curcumin (left), Elimination of the reactive β-diketo group and transformation into a monocarbonyl analogue of curcumin (right).

However, despite its promising pharmacodynamic profile, curcumin's clinical relevance remains limited due to its poor chemical stability and low bioavailability. These limitations stem primarily from its keto-enol tautomerism, rapid metabolism, poor water solubility, and the chemical reactivity of its β-diketone and methylene groups. These electrophilic sites, although crucial for biological activity, also make the molecule highly unstable above pH 6.5, leading to rapid degradation in physiological environments (Tabanelli et al., 2021; Sohn et al., 2021; Anand et al., 2007).

In order to increase the bioavailability of curcumin, improve its chemical stability and reduce its rapid metabolism, and in order to improve its systemic delivery in the body, modification of the structure of curcumin is necessary. Modification and "fine tuning" of the structure of curcumin contributes to the newly synthesized analogs possessing better anti-carcinogenic, anti-inflammatory and antioxidant properties, better chemical stability and better bioavailability (Liang et al. 2009). Since the *β*-diketo component is responsible for its chemical instability, the elimination of one keto group as well as increasing the electrophilicity of the enone is approached, figure 1.

Despite extensive research, an integrated overview of the synthetic strategies, analytical methods, and pharmacological potential of curcumin and its analogues is still lacking. Previous studies address individual aspects without providing a comprehensive perspective. This review aims to summarize synthetic approaches, analytical techniques, and pharmacological profiles of

analogues in comparison with native curcumin, offering directions for future clinical development.

2. Literature Review

2.1. Synthetic strategies for curcumin analogues

The literature generally mentions several types of synthetic strategies:

Elimination of potential oxidation sites (phenolic and enol hydroxyl groups) thus preventing radical formation and chemical degradation. Substitution of phenolic hydroxyl groups with methoxy groups (as in dimethoxycurcumin) is characterized by a significant improvement in chemical stability (Liang et al., 2009), figure 2.

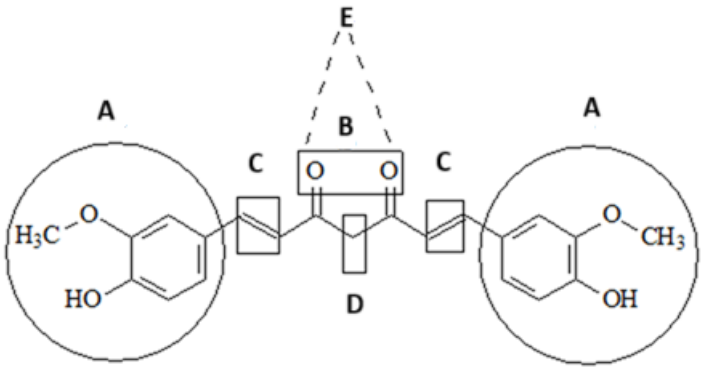

Figure 2: Curcumin, structural modifications in the aryl side group (A), structural modifications in the diketo functional group (B), structural modifications in the double bond (C), structural modifications in the active methylene functional group (D) and modifications for possible metal complexes (E).

Modification of the *β*-diketo group and synthesis of monocarbonyl analogs of curcumin MACs (monocarbonyl analogs of curcumin), figure 2.

Removal of the *β*-diketo group: in cells in vivo, curcumin undergoes enzymatic degradation, and the degradation products themselves enter into reactions with proteins, in order to prevent this enzymatic degradation, the *β*-diketo group is removed (Fuchs et al. 2009; Liang et al. 2009). In vitro tests conducted on mice (after oral administration of several monocarbonyl analogues of curcumin) found that they have a longer retention time in the body compared to curcumin, which directly indicates their improved systemic and chemical stability in the body (Liang et al., 2009).

Enrichment with functional groups or atoms: since the elimination of enol and phenol hydroxyl groups disrupts intermolecular bonds, thereby weakening biological and pharmacological characteristics, the synthesized analogues should be "enriched" with functional groups or atoms that will be capable of maximum electrostatic interactions with target receptors (such as cancer cells), figure 2.

Liang and co-workers found that the electronegativity of carbonyl groups and halogen elements as strong electrophiles (which have the ability to attract electrons) through substitution reactions in the benzene ring improves the cytotoxicity of newly synthesized analogues, also substitution of electron donating groups in the benzene ring such as amines, alkyl and alcohol groups shows better antitumor effects. The most suitable electrophilic groups based on their bonding ability (X···:O) are halogen elements (X = F, Cl, and Br) and haloalkanes that cannot be easily oxidized by oxygen or reactive oxygen species (ROS) with the exception of the hydroxyl radical (·OH) (Fuchs et al. 2009; Liang et al. 2009). Correspondingly weak nucleophilic groups

such as methoxy or alkyl peroxy groups (R-O-O-CH_3) are more cytotoxic than curcumin in the treatment of various tumor cells (Liang et al. 2009).

Since it is insoluble in water, several methods of hydrophobic interactions have been developed using biocompatible substances that are widely used in the food industry, such as lipids, liposomes, polyethylene glycol, biopolymers, cellulose and hydrogels, which facilitate its solubility and thus its bioavailability (Priyadarsini et al., 2009).

2.2. Analytical Methods for Characterization and Bioanalysis

Since curcuminoids are hydrophobic substances and do not dissolve in water, the most commonly used solvents for extraction are alcohol and acetone, with the extraction being characterized by high yields. The most commonly used extraction methods are Soxhlet extraction and ultrasonic extraction. Soxhlet extraction of turmeric precipitate using acetone (for 4 to 5 hours) is characterized by a yield of about 5% consisting of 42% curcuminoids (Paulucci et al. 2013; Lee et al. 2012).

There are a large number of studies on the separation of curcuminoid pigments by thin-layer chromatography (TLC), column chromatography (CC) and high-pressure thin-layer chromatography (HPTLC) on aluminum plates with silica gel as the stationary phase and chloroform-methanol as the solvent. The most commonly used stationary phase is silica gel and the following solvents (mobile phase) are used: benzene, ethyl acetate, ethanol, chloroform, acetic acid, hexane and methanol (Urošević et al., 2022).

The HPLC method has been shown to be quite sensitive, precise and accurate in the detection and quantification of curcuminoids in the extract of the rhizome of Curcuma longa (Lee et al. 2012). Ali and his collaborators described a very precise separation and detection of curcumin from the turmeric mixture using an HPLC method involving a phenyl column and acetonitrile/methanol/water as the mobile phase (Ali et al., 2014).

Kim found that HPLC and LC/MS detect curcumin at trace levels in biological fluids, making them particularly useful methods for monitoring its metabolism, distribution, and elimination from the body (Kim et al., 2013). High-performance liquid chromatography (HPLC) separation was performed on a reversed-phase C18 column and gradient elution with acetonitrile/water or chloroform/methanol (Ali et al., 2014). UPLC coupled to tandem mass spectrometry was used to detect curcumin metabolites in plasma and urine with a detection limit of 2.5 ng/ml (Marczylo et al., 2009). Spectroscopic approaches complement chromatographic methods for structural and stability studies. UV–Vis spectroscopy, for example, has been validated to quantify curcumin in nanoparticle formulations with satisfactory linearity and accuracy (Kotha et al., 2019). In other studies, the reaction between monocarbonyl curcumin derivatives with a cyclohexanone core and thiols, as well as the formation of mono- and bis-adducts, was monitored via UV–Vis spectroscopy (Lozanovski et al., 2023).

Nuclear magnetic resonance (NMR) spectroscopy, both conventional and ^{1}H-NMR based techniques, has been increasingly adopted for curcuminoid profiling due to its non-destructive nature and capacity for simultaneous detection and quantification of molecular species (Prasad et al., 2022). Moreover, combining analytical signals from different techniques—such as HPLC-UV, FTIR, ^{1}H-NMR, and chemometric analysis has been used to develop metabolic fingerprinting approaches for sample authentication and discrimination among turmeric cultivars (Vidal et al., 2020).

The extraction of curcumin is also possible using supercritical fluids, i.e. carbon dioxide at a pressure of 25 to 30 MPa and a temperature of 44.8 °C (Chassagnez-Méndez et al., 2000). There are also studies on enzymatic extraction of curcumin, using α-amylase and glycoamylase, where the method is characterized by high yield, but due to the high cost of the analysis, this method is rarely used (Kurmudle et al. 2013).

Nhujak found that microemulsion electrokinetic chromatography using oil droplets and

surfactants was useful in the extraction and determination of curcumin in food and medical samples (Nhujak et al. 2006). Capillary electrophoresis with amperometric detection is also a successfully implemented method for the detection of curcumin in food.

Taken together, these converging analytical methodologies—from chromatographic to spectroscopic to metabolomic platforms—form a robust toolkit for structural validation, quantification, and pharmacological comparison of curcumin and its analogues across various research settings.

2.3. Pharmacological evaluation

Curcumin has the ability to target specific molecular pathophysiologies of certain diseases. Antitumor properties are manifested by blocking: cell proliferation (cyclin D1, c-myc), cell pathways (Bcl-2, Bcl-xL, cFLIP, XIAP, and cIAP1), activation of the caspase cycle (caspase -8, -3, and -9), the tumor suppression cycle (p53, p21), the death receptor cycle (DR4, DR5), all other cell signaling pathways that include the protein kinase cycle (c-Jun N-terminal kinases (JNK), protein kinase B (PKB), also known as Akt, and 50 adenosine monophosphate-activated protein kinase (AMPK), thereby preventing the spread of several types of cancer, including: multiple myeloma, colon, pancreatic, breast, prostate, and lung tumors (Devassy et al., 2015). It is also stated that curcumin increases the effectiveness of radiotherapy and thus leads to a faster outcome of the treatment (Akpolat Ferah et al., 2010).

There are also studies in which monocarbonyl analogs of curcumin have been synthesized - such as B63, through chemical modifications of its structure, which have shown that compared to curcumin, this analog has a higher antiproliferative effect on colon cancer cells (Zheng et al., 2014), figure 4.

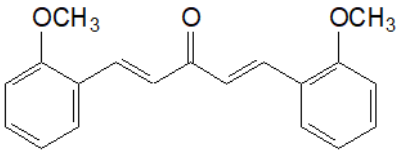

Figure 4: Structural formula of B63 (curcumin derivative).

Thanks to the hydroxyl and methoxy groups in its molecule, curcumin possesses anti-inflammatory and antioxidant properties (Deogade et al., 2015). It provides negative regulation of pro-inflammatory interleukins (IL-1, -2, -6, -8 and -12), cytokines (tumor necrosis factor alpha (TNF-a), monocyte chemoattractant protein-1 causing reduced production of tyrosine kinase and activation of transcription (JAK / STAT).

Curcumin, through the expression of HO-1, activates the Nrf2-dependent antioxidant response, inhibits the synthesis of TNF in vascular and aortic smooth muscle cells, and stimulates the expression of p21 through HO-1. In another study conducted on people with coronary artery disease, it was found that the values of serum triglycerides and cholesterol-LDL and VLDL were significantly reduced in the group of patients who consumed curcumin (Mirzabeigi et al., 2015).

Curcumin plays a key role in: the suppression of the inflammatory response resulting from hyperglycemia, the increase in the expression of the GLUT2, GLUT3 and GLUT4 genes, the increase in glucose uptake into cells and its increased consumption and the activation of AMPK, thereby reducing blood glucose levels and reducing insulin resistance (Ghorbani et al., 2014).

Since Alzheimer's disease is characterized by inflammation and oxidative damage to cells, abnormal protein synthesis followed by mutations in genes - curcumin with its antioxidant, anti-inflammatory properties helps in the fight against this disease by improving cognitive functions, reducing beta-amyloid plaques and microglia formations and slowing neuronal

damage. The antioxidant properties of curcumin are especially useful in Parkinson's disease as one of the most common neurodegenerative diseases characterized by the loss of dopaminergic neurons in the gray matter of the brain (Monroy et al., 2013)

Curcumin derivatives also show important antimicrobial properties. Cyclopentane analogues (A1–A17) demonstrated stronger activity than curcumin, especially A12 and A14. The cyclohexanone analogue C09 exhibited potent effects against both Gram-positive and Gram-negative bacteria, surpassing curcumin and ampicillin in strains such as *S. saprophyticus*, *S. aureus*, and *Micrococcus luteus*. These results suggest that the presence of a furan ring within the cyclohexanone scaffold markedly enhances antimicrobial bioactivity (Liang et al., 2008).

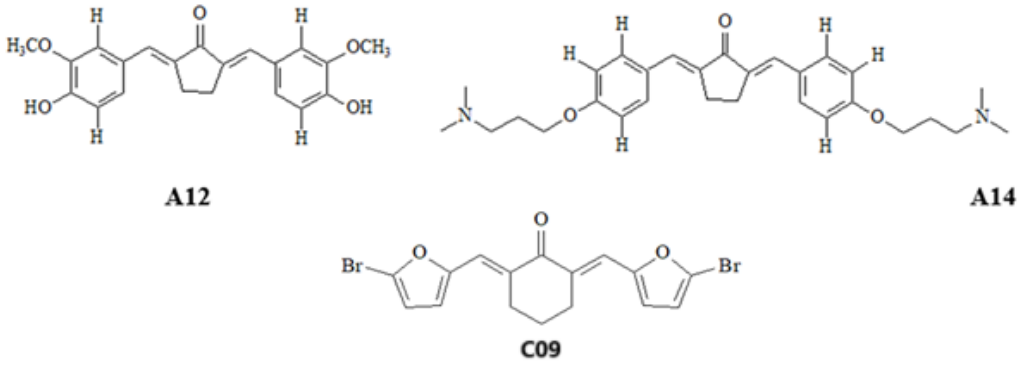

Figure 5: Monocarbonyl analogs of curcumin with a cyclopentane core, analogs A12 and A14, and analogs with cyclohexanone core C09 (Guang Liang et al., 2008)

3. Conclusion

Curcumin is one of the most studied natural polyphenols, known for diverse biological effects but limited by poor solubility, instability, and rapid metabolism. Structural modifications, particularly targeting the β-diketone moiety and aromatic substituents, have produced analogues with improved stability, bioavailability, and pharmacological potency. Analytical methods such as HPLC, LC–MS/MS, UV–Vis, FTIR, and NMR remain essential for their reliable characterization. Pharmacological studies confirm anticancer, anti-inflammatory, neuroprotective, and antimicrobial effects, with several analogues surpassing curcumin in preclinical models.

In conclusion, curcumin and its structural analogues offer strong potential for developing new medicines. Future research should focus on using standardized analytical methods, studying how these compounds behave in the body, and conducting well-designed clinical trials to confirm their effectiveness and safety.

References

Aggarwal, B. B., & Harikumar, K. B. (2009). Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. *The International Journal of Biochemistry & Cell Biology, 41*(1), 40–59. https://doi.org/10.1016/j.biocel.2008.06.010

Aggarwal, B. B., Sundaram, C., Malani, N., & Ichikawa, H. (2007). Curcumin: The Indian solid gold. In B. B. Aggarwal, Y.-J. Surh, & S. Shishodia (Eds.), *The molecular targets and therapeutic uses of curcumin in health and disease* (Advances in Experimental Medicine and Biology, Vol. 595, pp. 1–75). Springer. https://doi.org/10.1007/978-0-387-46401-5_1

Akpolat Ferah, M., Topçu, Y. T., Uz, Y. H., Sapmaz Metin, M., & Kizilay Özfidan, G. (2010). Kanser tedavisinde curcuminin yeri [The role of curcumin in cancer treatment]. *Yeni Tıp Dergisi*, *27*(3), 142–147.

Ali, I., Haque, A., & Saleem, K. (2014). Separation and identification of curcuminoids in turmeric powder by HPLC using phenyl column. *Analytical Methods, 6*(8), 2526–2536. https://doi.org/10.1039/C3AY41987H

Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2007). Bioavailability of curcumin: Problems and promises. *Molecular Pharmaceutics, 4*(6), 807–818. https://doi.org/10.1021/mp700113r

Baliga, M. S., Joseph, N., Venkataranganna, M. V., Saxena, A., Ponemone, V., & Fayad, R. (2012). Curcumin, an active component of turmeric in the prevention and treatment of ulcerative colitis: Preclinical and clinical observations. *Food & Function, 3*(11), 1109–1117. https://doi.org/10.1039/c2fo30097d

Chassagnez-Méndez, A. L., Corrêa, N. C. F., França, L. F., Machado, N. T., & Araújo, M. E. (2000). A mass transfer model applied to the supercritical extraction with CO_2 of curcumins from turmeric rhizomes (*Curcuma longa L.*). *Brazilian Journal of Chemical Engineering, 17*(3), 315–322. https://doi.org/10.1590/S0104-66322000000300007

Deogade, S. C., & Ghate, S. (2015). Curcumin: Therapeutic applications in systemic and oral health. *International Journal of Biological & Pharmaceutical Research, 6*(4), 281–290.

Devassy, J. G., Nwachukwu, I. D., & Jones, P. J. H. (2015). Curcumin and cancer: Barriers to obtaining a health claim. *Nutrition Reviews, 73*(3), 155–165. https://doi.org/10.1093/nutrit/nuu064

Fuchs, J. R., Pandit, B., Bhasin, D., Etter, J. P., Regan, N., Abdelhamid, D., Li, C., Lin, J., & Li, P.-K. (2009). Structure–activity relationship studies of curcumin analogues. *Bioorganic & Medicinal Chemistry Letters, 19*(7), 2065–2069 https://doi.org/10.1016/j.bmcl.2009.01.104.

Ghorbani, Z., Hekmatdoost, A., & Mirmiran, P. (2014). Anti-hyperglycemic and insulin sensitizer effects of turmeric and its principle constituent curcumin. *International Journal of Endocrinology and Metabolism, 12*(4), e18081. https://doi.org/10.5812/ijem.18081

Goel, A., Kunnumakkara, A. B., & Aggarwal, B. B. (2008). Curcumin as "Curecumin": From kitchen to clinic. *Biochemical Pharmacology, 75*(4), 787–809. https://doi.org/10.1016/j.bcp.2007.08.016

Han, S., & Yang, Y. (2005). Antimicrobial activity of wool fabric treated with curcumin. *Dyes and Pigments, 64*(2), 157–161. https://doi.org/10.1016/j.dyepig.2004.05.008

Hewlings, S. J., & Kalman, D. S. (2017). Curcumin: A review of its effects on human health. *Foods, 6*(10), 92. https://doi.org/10.3390/foods6100092

Kannappan, R., Gupta, S. C., Kim, J. H., Reuter, S., & Aggarwal, B. B. (2011). Neuroprotection by spice-derived nutraceuticals: You are what you eat! *Molecular Neurobiology, 44*(2), 142–159. https://doi.org/10.1007/s12035-011-8168-2

Kim, Y.-J., Lee, H. J., & Shin, Y. (2013). Optimization and validation of high-performance liquid chromatography method for individual curcuminoids in turmeric by heat-refluxed extraction. *Journal of Agricultural and Food Chemistry, 61*(46), 10911–10918. https://doi.org/10.1021/jf402483c

Kotha, R. R., & Luthria, D. L. (2019). Curcumin: Biological, pharmaceutical, nutraceutical, and analytical aspects. *Molecules, 24*(16), 2930. https://doi.org/10.3390/molecules24162930

Kurmudle, N., Kagliwal, L. D., Bankar, S. B., & Singhal, R. S. (2013). Enzyme-assisted extraction for enhanced yields of turmeric oleoresin and its constituents. *Food Bioscience, 3*, 36–41. https://doi.org/10.1016/j.fbio.2013.06.001

Lee, K.-J., Ma, J.-Y., Kim, Y.-S., Kim, D.-S., & Jin, Y. (2012). High purity extraction and simultaneous high-performance liquid chromatography analysis of curcuminoids in turmeric. *Journal of Applied Biological Chemistry, 55*(1), 61–65. https://doi.org/10.3839/jabc.2011.060

Liang, G., Shao, L., Wang, Y., Zhao, C., Chu, Y., Xiao, J., Zhao, Y., Li, X., & Yang, S. (2009). Exploration and synthesis of curcumin analogues with improved structural stability both

in vitro and in vivo as cytotoxic agents. *Bioorganic & Medicinal Chemistry, 17*(6), 2623–2631. https://doi.org/10.1016/j.bmc.2008.10.044

Liang, G., Yang, S., Jiang, L., Zhao, Y., Shao, L., Xiao, J., Ye, F., Li, Y., & Li, X. (2008). Synthesis and anti-bacterial properties of mono-carbonyl analogues of curcumin. *Chemical and Pharmaceutical Bulletin, 56*(2), 162–167. https://doi.org/10.1248/cpb.56.162

Lozanovski, Z., Petreska Stanoeva, J., & Bogdanov, J. (2023). Development of a spectrophotometric method for assessment of the relative reactivity of monocarbonyl analogs of curcumin with 2-(dimethylamino)ethanethiol. *Macedonian Journal of Chemistry and Chemical Engineering*, *42*(1), 13–24. https://doi.org/10.20450/mjcce.2023.2638

Marczylo, T. H., Steward, W. P., & Gescher, A. J. (2009). Rapid analysis of curcumin and curcumin metabolites in rat biomatrices using a novel ultraperformance liquid chromatography (UPLC) method. *Journal of Agricultural and Food Chemistry*, *57*(3), 797–803. https://doi.org/10.1021/jf803038f

Mirzabeigi, P., Mohammadpour, A. H., Salarifar, M., Gholami, K., Mojtahedzadeh, M., & Javadi, M. R. (2015). The effect of curcumin on some of traditional and non-traditional cardiovascular risk factors: A pilot randomized, double-blind, placebo-controlled trial. *Iranian Journal of Pharmaceutical Research, 14*(2), 479–486.

Monroy, A., Lithgow, G. J., & Alavez, S. (2013). Curcumin and neurodegenerative diseases. *BioFactors, 39*(1), 122–132. https://doi.org/10.1002/biof.1063

Nhujak, T., Saisuwan, W., Srisa-art, M., & Petsom, A. (2006). Microemulsion electrokinetic chromatography for separation and analysis of curcuminoids in turmeric samples. *Journal of Separation Science, 29*(5), 666–676. https://doi.org/10.1002/jssc.200500333

Parry, J. W. (1969). *Spices* (Vol. 2). Chemical Publishing Company.

Paulucci, V. P., Couto, R. O., Teixeira, C. C. C., & Freitas, L. A. P. (2013). Optimization of the extraction of curcumin from *Curcuma longa* rhizomes. *Revista Brasileira de Farmacognosia, 23*(1), 94–100 https://doi.org/10.1590/S0102-695X2012005000117

Prasad, D., Naresh, K. S., Praveen, A., Singam, S. S. R., & Chaudhari, S. R. (2022). Direct ^{1}H-NMR method for simultaneous determination of total and individual curcuminoids. *Food Chemistry Advances, 1*, Article 100020. https://doi.org/10.1016/j.focha.2022.100020

Priyadarsini, K. I. (2009). Photophysics, photochemistry and photobiology of curcumin: Studies from organic solutions, bio-mimetics and living cells. *Journal of Photochemistry and Photobiology C: Photochemistry Reviews, 10*(2), 81–95. https://doi.org/10.1016/j.jphotochemrev.2009.05.001

Reddy, N., Han, S., Zhao, Y., & Yang, Y. (2013). Antimicrobial activity of cotton fabrics treated with curcumin. *Journal of Applied Polymer Science, 127*(4), 2698–2702. https://doi.org/10.1002/app.37613

Sharifi-Rad, J., Rayess, Y. E., Rizk, A. A., Sadaka, C., Zgheib, R., Zam, W., Sestito, S., Rapposelli, S., Neffe-Skocińska, K., Zielińska, D., Salehi, B., Setzer, W. N., Dosoky, N. S., Taheri, Y., El Beyrouthy, M., Martorell, M., Ostrander, E. A., Suleria, H. A. R., Cho, W. C., Maroyi, A., Martins, N. (2020). Turmeric and Its Major Compound Curcumin on Health: Bioactive Effects and Safety Profiles for Food, Pharmaceutical, Biotechnological and Medicinal Applications. *Frontiers in pharmacology*, *11*, 01021. https://doi.org/10.3389/fphar.2020.01021.

Sohn, S. I., Priya, A., & et al. (2021). Biomedical applications and bioavailability of curcumin—An updated overview. *Pharmaceutics, 13*(12), 2102. https://doi.org/10.3390/pharmaceutics13122102

Tabanelli, R., Brogi, S., & Calderone, V. (2021). Improving curcumin bioavailability: Current strategies and future perspectives. *Pharmaceutics, 13*(10), 1715. https://doi.org/10.3390/pharmaceutics13101715

Tilak, J. C., Banerjee, M., Mohan, H., & Devasagayam, T. P. A. (2004). Antioxidant availability of turmeric in relation to its medicinal and culinary uses. *Phytotherapy Research, 18*(10), 798–804 https://doi.org/10.1002/ptr.1553

Urošević, M., Nikolić, L., Gajić, I., Nikolić, V., & Stanković, M. (2022). Biological activities and modern pharmaceutical applications of curcumin. *Antibiotics, 11*(2), 135. https://doi.org/10.3390/antibiotics11020135

Vidal-Casanella, O., Nuñez, N., Sentellas, S., Núñez, O., & Saurina, J. (2020). Characterization of Turmeric and Curry Samples by Liquid Chromatography with Spectroscopic Detection Based on Polyphenolic and Curcuminoid Contents. *Separations*, *7*(2), 23. https://doi.org/10.3390/separations7020023

Zheng, A., Li, H., Wang, X., Feng, Z., Xu, J., Cao, K., Zhou, B., Wu, J., & Liu, J. (2014). Anticancer effect of a curcumin derivative B63: ROS production and mitochondrial dysfunction. *Current Cancer Drug Targets*, *14*(2), 156–166. https://doi.org/10.2174/1568009613666131126115444