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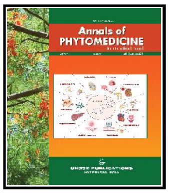

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A comprehensive review of the antioxidative and anti-inflammatory properties of Turmeric (*Curcuma longa* L.)

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Abstract

Turmeric (*Curcuma longa* L.), belongs to the ginger family and is known for its medicinal properties in traditional healing systems such as Ayurveda and conventional medicine. The key bioactive compound in turmeric, curcumin, has drawn significant scientific interest due to its potent anti-inflammatory and antioxidant properties, by modifying important pathways, such as the suppression of cyclooxygenase-2 (COX-2) and nuclear factor kappa B (NF-κB), curcumin reduces the generation of pro-inflammatory cytokines and has anti-inflammatory effects. Additionally, curcumin is a powerful antioxidant that increases the activity of endogenous antioxidant enzymes by scavenging free radicals and activating the Nrf2 pathway, which regulates cellular defense mechanisms. Several clinical studies have demonstrated turmeric's potential in treating inflammation-driven conditions such as rheumatoid arthritis, cardiovascular disease, neurodegenerative disorders, and metabolic syndrome. However, challenges with curcumin's bioavailability limit its widespread therapeutic use. Emerging research on delivery systems such as nanoparticles and liposomal formulations aims to address these limitations. Moreover, combining curcumin with compounds like piperine has been shown to improve its absorption. This review provides an overview of turmeric's anti-inflammatory and antioxidative mechanisms, clinical evidence supporting its use, and future directions to enhance its efficacy and therapeutic potential in modern medicine.

1. Introduction

Turmeric a vibrant yellow-orange spice commonly used in South Asian cuisine (Sivakumar *et al.,* 2022), has been a key component of traditional medicinal systems like Ayurveda and Chinese Traditional Medicine for thousands of years. In these systems, turmeric has been used to treat a variety of ailments, ranging from respiratory issues and skin diseases to digestive disorders and joint pain (Gupta *et al*., 2013; Islam *et al*., 2002). Over the past few decades, turmeric has drawn more focus from modern scientific communities due to its therapeutic properties, especially its potent anti-inflammatory and antioxidative effects.The therapeutic potential of turmeric is primarily attributed to curcumin, its major bioactive compound. Curcumin is a polyphenol known for its wide-ranging biological activities, which include anti-inflammatory, antioxidant, anticancer, antibacterial (Bhavsar *et al*., 2022) and antimicrobial properties (Yuan *et al*., 2011). Research into curcumin has led to a better understanding of how chronic inflammation and oxidative stress are underlying mechanisms in many of the world's most common diseases like diabetes, cancer, cardiac-related issues, metabolic syndromes and neurodegenerative disorders like Alzheimer's disease.

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1.1 Inflammation and oxidative stress: Central pathways to disease

Chronic inflammation is a prolonged and abnormal immune response that leads to tissue damage and disease progression. Inflammation is normally a protective process that helps the body combat infection and repair damaged tissue (Pawelec *et al*., 2014). However, when inflammation persists, it will lead to the emergence of various chronic conditions like arthritis, inflammatory bowel syndrome and even cancer. Conversely, oxidative stress happens when the body's capacity to use antioxidants to detoxify these dangerous chemicals is out of balance with reactive oxygen species (ROS) (Dongre *et al*., 2015). Oxidative stress damages cells, proteins, and DNA accelerating the process of aging and contributing to the onset of ailments such as cardiovascular disease diabetes and neurodegenerative conditions. Since oxidative stress and chronic inflammation are linked and exacerbate each other's negative effects, they are significant therapeutic targets for the prevention and treatment of chronic illnesses.

1.2 Curcumin's role in modulating inflammation and oxidative Stress

Numerous studies have demonstrated that curcumin modulates several key molecular pathways involved in oxidative stress and inflammation (Mokgalaboni *et al.,* 2021). It prevents nuclear factor kappa B (NF-κB), a transcription factor that regulates the expression of numerous pro-inflammatory genes, from becoming activated.

Curcumin decreases the synthesis of inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β), by downregulating NF-κB. This results in a decrease in inflammation and other related symptoms (Chearwae *et al*., 2008).The cyclooxygenase-2 (COX-2) enzyme, which is involved in the synthesis of pro-inflammatory prostaglandins, is also inhibited by curcumin. By reducing COX-2 activity, curcumin helps to alleviate pain and inflammation, making it especially useful in treating conditions like arthritis (Chin 2016; Razav *et al*., 2021). Curcumin's antioxidative properties are equally significant, it scavenges free radicals by neutralizing harmful reactive oxygen and nitrogen species that cause oxidative damage to cells. Moreover, curcumin enhances the antioxidant defenses of the body by upregulating the expression of endogenous antioxidant enzymes such as catalase, superoxide dismutase (SOD), and glutathione peroxidase. This dual approach neutralizing free radicals and enhancing antioxidant defensesmakes curcumin highly effective in combating oxidative stress (Ak and Gülçin, 2008). Furthermore, curcumin activates the Nrf2 pathway, a critical regulator of cellular defense against oxidative damage (Chen *et al*.,1998). Nrf2 activation produces several protective proteins that play a vital role in detoxification, antioxidant defense and cell survival. By modulating these molecular pathways, curcumin helps mitigate the damage caused by both inflammation and oxidative stress, potentially slowing the progression of chronic diseases.

2. Clinical relevance and potential therapeutic applications

Given these mechanisms, turmeric's therapeutic potential has been explored in a variety of clinical settings. Studies have demonstrated its efficacy in managing conditions such as rheumatoid arthritis, inflammatory bowel diseases, and metabolic syndrome. By lowering oxidative damage in the brain, turmeric's antioxidant qualities also protect against neurodegenerative illnesses like Parkinson's and Alzheimer's (Chen *et al*., 2016). However, curcumin's poor bioavailability is because of the compound's difficulty being absorbed or used by the body which restricts its therapeutic application despite its encouraging promise.To address this, researchers have explored various strategies to improve curcumin's bioavailability, including combining it with piperine, an alkaloid from black pepper, and developing advanced delivery systems such as liposomes, nanoparticles, and phospholipid complexes. Turmeric's anti-inflammatory and antioxidative properties offer a natural, complementary approach to modern medicine. As more research is conducted and bioavailability challenges are overcome, turmeric has the potential to play a crucial role in the prevention and management of a wide range of chronic diseases driven by inflammation and oxidative stress (Choudhuri *et al*., 2002). This review explores these mechanisms in depth, with a focus on future therapeutic applications.

3. Bioactive compounds in Turmeric

Curcumin, the most researched and powerful of turmeric's bioactive components, is largely responsible for its therapeutic benefits. Curcumin is a polyphenolic compound that imparts the characteristic yellow-orange hue to turmeric. Curcuminoids are a group of compounds that include curcumin, demethoxy curcumin and bisdemethoxy curcumin. Together, these curcuminoids are responsible for turmeric's broad range of biological activities, including its anti-inflammatory, antioxidative, anticancer, and antimicrobial effects. Curcumin stands out due to its ability to modulate multiple molecular pathways involved in inflammation, oxidative stress, and cell survival (Das *et al*., 2010). Research has shown that curcumin influences several signaling molecules, such as nuclear factor kappa B (NF-κB) and cyclooxygenase-2 (COX-2), which are key players in the inflammatory process. It also acts as a powerful antioxidant by scavenging free radicals and boosting the activity of endogenous antioxidant enzymes. Despite its promising therapeutic potential, curcumin's poor bioavailability has posed significant challenges for its use in clinical applications. Poor bioavailability is primarily due to its low absorption in the gut, rapid metabolism, and quick elimination from the body. As a result, the concentrations of curcumin needed for therapeutic effects are often difficult to achieve through regular turmeric consumption or standard curcumin supplements.To address these limitations, researchers have been exploring various strategies to enhance curcumin's bioavailability. Advanced delivery systems such as liposomes, nanoparticles, and phospholipid complexes have been developed to increase their absorption and stability in the body (El Nebrisi *et al*., 2020). These innovative formulations are designed to enhance curcumin's therapeutic efficacy by improving its pharmacokinetics, making it a more viable treatment option in both acute and chronic diseases.These advances could unlock curcumin's full potential, further validating its use in modern medicine.

3.1 Mechanisms of anti-inflammatory action

Curcumin, the principal bioactive compound in turmeric, exerts potent anti-inflammatory effects by modulating several key molecular pathways. Inflammation, a fundamental immune response, becomes harmful when dysregulated or chronic, leading to diseases like arthritis, cancer, and cardiovascular disorders. Curcumin's multi-targeted approach makes it particularly effective in curbing inflammation at the molecular level.

3.2 Inhibition of NF-κB pathway

According to Tabanelli *et al.* (2021), curcumin decreases inflammation mostly by blocking the nuclear factor kappa B (NF-κB) pathway. A transcription factor called NF-κB controls the expression of numerous pro-inflammatory genes, such as those that generate inflammatory cytokines and enzymes. TNF-α, interleukin-6 (IL-6), interleukin-1 beta (IL-1β), and other inflammatory mediators are not transcriptionally triggered by NF-κB accessing the cell nucleus when curcumin is present. Curcumin reduces inflammation by inhibiting NF-κB, which in turn reduces the synthesis of these inflammatory proteins (Shehzad *et al*., 2013; Liczbiñski *et al.,* 2020).

3.3 Inhibition of cyclooxygenase (COX) and lipoxygenase (LOX)

Curcumin also directly inhibits COX-2, an enzyme that produces pro-inflammatory prostaglandins that modulate inflammation and discomfort (Rao, 2007). In addition, curcumin inhibits lipoxygenase (LOX), an enzyme involved in synthesizing leukotrienes, another group of molecules that promote inflammation (Katsori *et al*., 2011). By suppressing COX-2 and LOX, curcumin reduces both prostaglandin and leukotriene levels, effectively lowering inflammation and its associated symptoms, such as pain and swelling (Dey *et al.,* 2022).

3.4 Cytokine modulation

Inflammatory cytokines and chemokines are crucial immune response mediators., curcumin modulates their activity by downregulating the production of pro-inflammatory cytokines, including TNF-α, interleukins, and interferon-gamma (IFN-γ) (Mollazadeh *et al*., 2019). This broad-spectrum cytokine modulation helps curcumin control the immune response and inflammation, making it useful in conditions characterized by excessive cytokine activity, such as autoimmune diseases.

3.5 Modulation of NLRP3 inflammasome

The multiprotein complex known as the NLRP3 inflammasome is responsible for the initiation of inflammatory processes, particularly in response to pathogens and cellular damage (Chauhan *et al*., 2020). The activation of NLRP3 has been implicated in a variety of inflammatory diseases, including gout (Kim 2022; Liu *et al*., 2023), type 2 diabetes (Ding *et al.,* 2019), and Alzheimer's disease(Feng *et al*., 2020; Sorkheh *et al*., 2021. It has been demonstrated that curcumin inhibits the NLRP3 inflammasome's activation, lowering its contribution to the inflammatory cascade and assisting in the prevention of chronic inflammation (Yin *et al.,* 2018; Hasanzadeh *et al.,* 2020). By targeting multiple inflammatory pathways, curcumin exhibits a broad and effective anti-inflammatory action, making it a potential agent for treating ailments rooted in chronic inflammation (Benameur *et al.,* 2023).

Table 1: Mechanisms of action of curcumin

Mechanism	Description	Reference
Inhibition of NF-κB pathway	Curcumin lowers pro-inflammatory cytokines like TNF-α and IL-6 by blocking NF-κB activation.	Jin *et al.* (2007); Ghandadi and Sahebkar (2017); Kumar *et al.* (2017)
COX-2 and LOX inhibition	Curcumin inhibits COX-2 and lipoxygenase pathways, reducing prostaglandins and leukotrienes.	Shishodia (2013); Dey *et al.* (2022); Shah (2023)
Cytokine modulation	Downregulates pro-inflammatory cytokines (TNF-α, IL-1β).	Das and Vinayak (2014); Aggarwal *et al.* (2013)
NLRP3 inflammasome modulation	Inhibits NLRP3 inflammasome activation, reducing inflammation in various diseases.	Olcum (2020); Benameur (2023)
Upregulation of antioxidant enzymes	Enhances the activity of SOD, catalase, and glutathione peroxidase.	Al-Rubaei *et al.* (2014); Yonar *et al.* (2017); Meshkibaf *et al.* (2019)
Activation of Nrf2 pathway	Activates Nrf2, leading to increased production of antioxidant proteins.	Ashrafizadeh *et al.* (2020); Shahcheraghi *et al.* (2021)

4. Antioxidative properties of Turmeric

An imbalance between the body's capacity to neutralize reactive oxygen species (ROS) with antioxidants and the generation of ROS leads to oxidative stress, a significant factor in cellular aging and a variety of disorders (Tanvir *et al*., 2017; Verma *et al*., 2018). According to Labban (2014) and Nasri *et al.* (2014), ROS are linked to the pathophysiology of diseases like cancer, neurological disorders, and cardiovascular diseases. They can seriously harm cells, including proteins, lipids, and DNA. By using several pathways, turmeric's potent antioxidative qualities, especially through its main ingredient curcumin, help lessen the negative consequences of oxidative stress.

4.1 Free radical scavenging

One of the primary antioxidative actions of curcumin is its ability to directly neutralize free radicals (Kebede *et al*., 2021). According to Asouri *et al.* (2013), curcumin can scavenge a wide range of reactive oxygen and nitrogen species, including superoxide anions, hydroxyl radicals, and nitrogen radicals. Lipids and other vital biomolecules may sustain oxidative damage from these free radicals, resulting in lipid peroxidation (Gupta *et al*., 2020), proteins (leading to dysfunction), and DNA (potentially causing mutations) (Agarwal *et al*., 2018). By scavenging these free radicals (Barzegar and Movahedi, 2011), curcumin prevents cellular and molecular damage (Patel *et al*., 2020; Liczbiñski *et al*., 2020), thereby protecting tissues from oxidative stress-induced harm.

4.2 Upregulation of antioxidant enzymes

Curcumin strengthens the body's natural antioxidant defenses by increasing the activity of several endogenous antioxidant enzymes, such as superoxide dismutase (SOD) (Jiang*et al*., 2018;Khayatan *et al.,* 2024), catalase (Najjar *et al*., 2017; Najjar *et al*., 2017), and glutathione peroxidase (El-Barbary 2016; Yonar *et al*., 2017; Ghasemi *et al.,* 2021). These enzymes play a critical role in neutralizing ROS. For instance, SOD converts the superoxide radical into hydrogen peroxide, which is then broken down by catalase into water and oxygen. This upregulation improves the body's overall resistance to oxidative damage, providing a more robust protective mechanism against ROS-related damage.

4.3 Activation of Nrf2 pathway

It has also been demonstrated that curcumin activates the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, which is a crucial regulator of the antioxidant response in the body. Nrf2 regulates the expression of several detoxification enzymes and antioxidant proteins, including heme oxygenase-1 (HO-1) (Son *et al*., 2013; Xiao *et al*., 2018) and NAD(P)H quinone oxidoreductase 1 (NQO1) (Morales *et al*., 2020), which guards cells from oxidative damage. By activating Nrf2, curcumin enhances the cellular production of these protective proteins, helping cells cope more effectively with oxidative stress (Shin *et al*., 2020; Liao *et al.,* 2020). Through these mechanisms, curcumin's antioxidative properties offer substantial protection against oxidative stress, contributing to the management and prevention of illnesses where oxidative damage is a major factor (Rahmani *et al.,* 2018; Patel *et al*., 2020). This ability to neutralize free radicals, boost endogenous antioxidants, and activate protective pathways underscores turmeric's potential as a therapeutic agent in the fight against oxidative stress-related conditions.

5. Clinical evidence of anti-inflammatory and antioxidative effects

Numerous clinical studies have investigated the efficacy of turmeric, particularly curcumin, in treating diseases that are driven by inflammation and oxidative stress. These studies provide strong evidence for curcumin's potential therapeutic benefits in a variety of conditions:

5.1 Rheumatoid arthritis

The use of curcumin in the treatment of rheumatoid arthritis (RA) is a chronic inflammatory illness marked by joint inflammation (Dongre*et al*., 2021). In a randomized controlled experiment, RA patients who took supplements of curcumin demonstrated notable improvements in symptoms such as joint pain, swelling, and stiffness. These results were comparable to those of patients taking non-steroidal anti-inflammatory drugs (NSAIDs), but without the side effects typically associated with NSAIDs. This demonstrates the potential of curcumin as a natural remedy for RA symptoms (Kou *et al*., 2023)

5.2 Cardiovascular disease

Curcumin's anti-inflammatory and antioxidative properties have been shown to benefit patients at risk of or suffering from cardiovascular diseases (Sureda*et al*., 2020). Clinical studies have demonstrated that curcumin reduces markers of systemic inflammation, such as C-reactive protein (CRP) (Adibian *et al*., 2019; Gorabi *et al*., 2022), in individuals at risk for cardiovascular disease (CVD). Additionally, its antioxidative effects help protect against atherosclerosis by preventing lipid peroxidation and reducing endothelial dysfunction, two key contributors to the advancement of heart disease (Karimian *et al*., 2017; Parker *et al.,* 2017). These results suggest that curcumin may play a major role in preventing or managing cardiovascular conditions.

5.3 Neurodegenerative disorders

Curcumin's potential has been investigated in managing neurodegenerative illnesses like Alzheimer's. Curcumin has been shown in Alzheimer's disease experimental models to decrease inflammation and oxidative stress in the brain, two important processes in the emergence of neurodegenerative diseases. Curcumin's ability to prevent the accumulation of amyloid plaques(Reddy *et al*., 2018), a hallmark of Alzheimer's (Goozee *et al.,* 2016), and reduce neuroinflammation suggests that it could be beneficial in slowing the progression of neurodegenerative disorders (Maiti *et al*., 2015; Bhat *et al*., 2019).

5.4 Metabolic syndrome

Metabolic syndrome, characterized by a combination of insulin resistance, obesity, hypertension, and dyslipidemia, is closely linked to chronic inflammation and oxidative stress (Azhdari *et al.,* 2019). Clinical trials have shown that curcumin supplementation improves insulin sensitivity (Bateni *et al.,* 2021), reduces oxidative stress(Qiu *et al.,* 2023), and decreases inflammatory markers (Jabczyk *et al.,* 2021) in patients with metabolic syndrome. These outcomes demonstrate curcumin's ability to treat metabolic diseases, like type 2 diabetes and problems associated with obesity, offering a natural means of reducing disease progression and enhancing overall health.

As per Table 2, clinical evidence underscores curcumin's potential as a safe and effective therapeutic agent for a wide range of conditions characterized by inflammation and oxidative stress, supporting its integration into conventional treatments for chronic diseases.

Table 2: Clinical applications of curcumin

Disease condition	Study design	Findings	Reference
Rheumatoid arthritis	Randomized controlled trial	Significant reduction in joint swelling and pain.	Javadi *et al.* (2019); Bagherniya *et al.* (2021) ; Zeng *et al.* (2022)
Cardiovascular disease	Observational study	Reduced levels of C-reactive protein (CRP).	Funamoto *et al.* (2016); Shao *et al.* (2017); Silalahi *et al.* (2021); Naghsh *et al.* (2023)
Neurodegenerative disorders	Clinical trial	Reduced inflammation and oxidative stress in the brain.	Monroy *et al.* (2013); Bhat *et al.* (2019); Mohseni *et al.* (2021)
Metabolic syndrome	Randomized controlled trial	Improved insulin sensitivity and reduced inflammation.	Azhdari *et al.* (2019); Hodaei *et al.* (2019); Bateni *et al.* (2021)

6. Synergistic effects of Turmeric with other compounds

Curcumin's therapeutic potential can be significantly enhanced when it is combined with other bioactive compounds, leading to improved efficacy in both anti-inflammatory and antioxidative capacities. These synergistic interactions are particularly valuable in overcoming curcumin's inherent drawback is poor bioavailability, and can amplify its effects in treating diseases associated with inflammation and oxidative stress.

6.1 Piperine

Among the most, well-researched synergistic combinations, piperine an alkaloid found in black pepperhas been revealed to inhibit the metabolism of curcumin in the liver and intestines, thereby increasing its bioavailability by up to 2000%. This enhanced absorption allows curcumin to remain in the bloodstream for a longer period, increasing its therapeutic effectiveness (Liu *et al*., 2020). Together, curcumin and piperine offer potent antioxidative and anti-inflammatory effects

(Kaur *et al*., 2017; Setiawan *et al*., 2021), making this combination a promising natural approach for conditions like arthritis (Thakkar *et al*., 2022), metabolic disorder (Hosseini *et al*., 2023), and cardiovascular problems (Tabaee *et al*., 2021; Tehrani *et al*., 2024).

6.2 Resveratrol

Another compound that works synergistically with curcumin is resveratrol, a polyphenol found in grapes and red wine. Studies indicate that combining curcumin with resveratrol results in additive antioxidative and anti-inflammatory effects, which are greater than the effects of either compound used alone (Banez *et al.,* 2020). This combination strengthens the body's defenses against oxidative stress and may offer additional effective protection against illnesses such as neurodegenerative disorders (Mazzanti and Giacomo, 2016; Fukutomi *et al*., 2021), cardiovascular disease (Banez *et al*., 2020; Imperador *et al*., 2022), and cancer (Arena *et al.,* 2021). The complementary mechanisms of action of curcumin and resveratrol make them a powerful pair for improving cellular resilience against oxidative damage and inflammation.

Table 3: Synergistic effects of curcumin with other compounds

Compound	Mechanism of action	Combined effects	Potential applications	Reference
Piperine	Inhibits curcumin metabolism, increasing bioavailability.	Enhanced absorption and therapeutic efficacy.	Improved outcomes ininflam-matory disease treatment.	Manap *et al.* (2019); Setiawan *et al.* (2021); Saini *et al.* (2023)
Resveratrol	Antioxidant that protects against oxidative damage.	Additive antioxidative and anti-inflammatory effects.	Potential synergy in cancer prevention and treatment.	Majumdar *et al.* (2009); Du *et al.* (2013); Malhotra *et al.* (2014); Schmidt *et al.* (2020)
Quercetin	Flavonoid with anti-inflammatory properties.	Enhanced anti-inflammatory effects and improved bioavailability.	Potential benefits in allergic responses and chronic inflammation.	Güran *et al.* (2019); Schmidt *et al.* (2020)
Gingerol	Anti-inflammatory and anti-oxidative properties.	Combined effects may enhance overall anti-inflammatory action.	Synergistic effects in digestive health and joint pain relief.	ElNebrisi *et al.* (2020); Zhou *et al.* (2022); Adrianta *et al.* (2023)
Omega-3 fatty acids	Anti-inflammatory effects through multiple pathways.	Potential for enhanced cardiovascular protection and reduction of systemic inflammation.	Management of heart disease and arthritis.	Abdolahi *et al.* (2017); Etemadi *et al.* (2021); Rodríguez *et al.* (2024)

These synergistic interactions highlight the potential of combining curcumin with other natural compounds to improve its therapeutic effects, paving the way for more effective and natural treatment options for chronic diseases.

7. Limitations and future directions

Curcumin has well-established anti-inflammatory and antioxidative qualities, but the drawback of low bioavailability limits its usage as a therapeutic agent. This issue restricts curcumin's ability to achieve sufficient concentrations in the bloodstream and target tissues, thereby limiting its overall efficacy in clinical applications (Kunnumakkara *et al.,*2019). Future research must address these challenges to fully harness turmeric's therapeutic potential.

7.1 Improved delivery systems

A major priority for improving the effectiveness of curcumin is the creation of sophisticated delivery methods. Formulations that have been studied to increase curcumin's absorption, bioavailability, and stability in the body include nanoparticles, liposomes, micelles, and phospholipid complexes. These innovative delivery methods increase curcumin's systemic availability and therapeutic potential by shielding it from fast metabolism and improving its passage across cell membranes. Further development and optimization of these delivery methods could make curcumin a more viable treatment option for a wide range of diseases (Tabanelli *et al.,* 2021).

7.2 Larger clinical trials

Although several small-scale studies have demonstrated the positive impacts of curcumin, there is a pressing need for large, well-designed clinical trials to confirm these findings. The majority of recent research is constrained by inadequate controls, small study periods, or sample sizes. Larger trials with rigorous methodologies are essential to validate curcumin's efficacy in treating various diseases, such as arthritis, cardiovascular disease, and neurodegenerative disorders. In addition, standardized dosing regimens and long-term safety assessments are crucial to establishing curcumin as a reliable therapeutic agent in clinical settings.

7.3 Exploration of derivatives

Another promising avenue for future research is the development of curcumin derivatives. These analogs could improve curcumin's bioactivity, stability, and metabolic profile. By synthesizing derivatives with enhanced properties, researchers may create more potent and effective therapeutic agents that overcome the limitations of natural curcumin. For instance, curcumin analogs with better resistance to degradation and improved tissue penetration could treat a broader range of conditions with greater efficacy, while turmeric holds significant therapeutic promise, overcoming its limitations requires a multifaceted approach. Ongoing research into delivery systems, larger clinical trials, and the development of curcumin analogs will be crucial in realizing its full potential in modern medicine.

8. Conclusion

Turmeric (*Curcuma longa* L.), particularly its active component curcumin, has garnered significant attention for its remarkable anti-inflammatory and antioxidative properties. These characteristics make turmeric a valuable candidate for the prevention and treatment of various diseases characterized by chronic inflammation and oxidative stress, including rheumatoid arthritis, cardiovascular diseases, neurodegenerative disorders, and metabolic syndrome.Nevertheless, curcumin's low bioavailability limits its therapeutic use and limits its efficacy in clinical settings. Despite these challenges, ongoing research is focused on developing advanced delivery mechanisms, like nanoparticles and liposomal formulations, that can enhance curcumin's absorption and systemic availability. These technological innovations hold promise for overcoming the bioavailability barrier, allowing for more effective therapeutic use of turmeric in clinical practice. Furthermore, larger and more rigorously designed clinical trials are essential to validate the findings from smaller studies, ensuring that curcumin's efficacy is well-established across various conditions. Additionally, the exploration of curcumin derivatives could result in the identification of novel compounds with improved bioactivity and stability, further expanding its potential applications. Incorporating turmeric and curcumin into modern therapeutic strategies could revolutionize the management of inflammatory and oxidative stress-related illnesses. In modern medicine, turmeric is positioned to play a significant role in improving health and avoiding disease as research continues to reveal its full therapeutic potential.

Authentication of the plant species

In the present review, the plant species *Curcuma longa* L. authenticated as 0792, by Dr. K. Madhava Setty, Plant Taxonomist (IAAT:337), Department of Botany, Sri Venkateswara University, Tirupathi, Andhra Pradesh, India.

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Conflict of interest

The authors declare no conflict of interest relevant to this article.

References

Abdolahi, M.; Tafakhori, A.; Togha, M.; Okhovat, A. A.; Siassi, F.; Eshraghian, M. R. and Djalali, M. (2017). The synergistic effects of ù-3 fatty acids and nano-curcumin supplementation on tumor necrosis factor (TNF)-α gene expression and serum level in migraine patients. Immunogenetics, **69**:371-378.

Abdul Manap, A. S.; Wei Tan, A. C.; Leong, W. H.; Yin Chia, A. Y.;Vijayabalan, S.; Arya, A. and Madhavan, P. (2019). Synergistic effects of curcumin and piperine as potent acetylcholine and amyloidogenic inhibitors with significant neuroprotective activity in SH-SY5Y cells *via* computational molecular modeling and *in vitro* assay. Frontiers in Ageing Neuroscience, **11**:206.

Adibian, M.; Hodaei, H.; Nikpayam, O.; Sohrab, G., Hekmatdoost, A. and Hedayati, M. (2019). The effects of curcumin supplementation on high sensitivity C reactive protein, serum adiponectin, and lipid profile in patients with type 2 diabetes: A randomized, double blind, placebo controlled trial. Phytotherapy Research, **33**(5):1374-1383.

Adrianta, K. A. and Somantara, I. G. (2023). The Curcumin and gingerol combination as an Immune regulator and anti-inflammatory agent of SARS-CoV infection according to a Nutrigenomic approach: A mini-review. The Natural Products Journal, **13**(1):3-12.

Agarwal, A.; Kasinathan, A.; Ganesan, R.; Balasubramanian, A.; Bhaskaran, J.; Suresh, S. and Sivalingam, N. (2018). Curcumin induces apoptosis and cell cycle arrest *via* the activation of reactive oxygen species–independent mitochondrial apoptotic pathway in Smad4 and p53 mutated colon adenocarcinoma HT29 cells. Nutrition Research, **51**:67-81.

Aggarwal, B. B.; Gupta, S. C. and Sung, B. (2013). Curcumin: An orally bioavailable blocker of TNF and other pro-inflammatory biomarkers. British Journal of Pharmacology, **169**(8):1672-1692.

Ak, T. and Gülçin, I. (2008). Antioxidant and radical scavenging properties of curcumin. Chemico-biological Interactions, **174**(1):27-37.

Al-Rubaei, Z. M.; Mohammad, T. U. and Ali, L. K. (2014). Effects of local curcumin on oxidative stress and total antioxidant capacity *in vivo* study. Pakistan Journal of Biological Sciences, **17**(12):1237-1241.

Arena, A.; Romeo, M. A.; Benedetti, R.; Masuelli, L.; Bei, R.; Gilardini Montani, M. S. and Cirone, M. (2021). New insights into curcumin-and resveratrol-mediated anti-cancer effects. Pharmaceuticals, **14**(11):1068.

Ashrafizadeh, M.; Ahmadi, Z.; Mohammadinejad, R.; Farkhondeh, T.and Samarghandian, S. (2020). Curcumin activates the Nrf2 pathway and induces cellular protection against oxidative injury. Current Molecular Medicine, **20**(2):116-133.

Asouri, M.; Ataee, R.; Ahmadi, A. A.; Amini, A. and Moshaei, M. R. (2013). Antioxidant and free radical scavenging activities of curcumin. Asian Journal of Chemistry, **25**(13):7593.

Azhdari, M.; Karandish, M. and Mansoori, A. (2019). Metabolic benefits of curcumin supplementation in patients with metabolic syndrome: a systematic review and meta analysis of randomized controlled trials. Phytotherapy Research, **33**(5):1289-1301.

Bagherniya, M.; Darand, M.; Askari, G.; Guest, P. C.; Sathyapalan, T. and Sahebkar, A. (2021). The clinical use of curcumin for the treatment of rheumatoid arthritis: A systematic review of clinical trials. Studies on Biomarkers and New Targets in Aging Research in Iran: Focus on Turmeric and Curcumin, 251-263.

Banez, M. J.; Geluz, M. I.; Chandra, A.; Hamdan, T.; Biswas, O. S.; Bryan, N. S. and Von Schwarz, E. R. (2020). A systemic review on the antioxidant and anti-inflammatory effects of resveratrol, curcumin, and dietary nitric oxide supplementation on human cardiovascular health. Nutrition Research, **78**:11-26.

Barzegar, A. and Moosavi-Movahedi, A. A. (2011). Intracellular ROS protection efficiency and free radical-scavenging activity of curcumin. PloS One, **6**(10):e26012.

Bateni, Z.; Rahimi, H. R.; Hedayati, M.; Afsharian, S.; Goudarzi, R. and Sohrab, G. (2021). The effects of nano curcumin supplementation on glycemic control, blood pressure, lipid profile, and insulin resistance in patients with the metabolic syndrome: A randomized, double blind clinical trial. Phytotherapy Research, **35**(7):3945-3953.

Benameur, T.; Frota Gaban, S. V.; Giacomucci, G.; Filannino, F. M.; Trotta, T.; Polito, R. and Panaro, M. A. (2023). The effects of curcumin on inflammasome: Latest update. Molecules, **28**(2):742.

Bhat, A.; Mahalakshmi, A. M.; Ray, B.; Tuladhar, S.; Hediyal, T. A.; Manthiannem, E. and Sakharkar, M. K. (2019). Benefits of curcumin in brain disorders. Biofactors, **45**(5):666-689.

Bhavsar, S. K.; Humbal, B. R.; Sadariya, K. A. and Baria, T. R. (2022). Evaluation of the *in vitro* antibacterial activity and minimum inhibitory concentration of *Curcuma longa* L., *Ocimum sanctum* L. and

Piper nigrum L. ethanolic and aqueous extracts. Ann. Phytomed., **11**(1):455-464.

Chauhan, D.; Vande Walle, L. and Lamkanfi, M. (2020). Therapeutic modulation of inflammasome pathways. Immunological Reviews, **297**(1):123-138.

Chearwae, W. and Bright, J. J. (2008). 15-Deoxy-Ä 12, 14-prostaglandin J 2 and curcumin modulate the expression of toll-like receptors 4 and 9 in autoimmune T lymphocyte. Journal of Clinical Immunology, **28**:558-570.

Chen, H. W. and Huang, H. C. (1998). Effect of curcumin on cell cycle progression and apoptosis in vascular smooth muscle cells. British Journal of Pharmacology, **124**(6):1029-1040.

Chen, J.; Chia, N.; Kalari, K. R.; Yao, J. Z.; Novotna, M.; Paz Soldan, M. M. and Mangalam, A. K. (2016). Multiple sclerosis patients have a distinct gut microbiota compared to healthy controls. Scientific Reports, **6**(1):1-10.

Chin, K. Y. (2016). The spice for joint inflammation: Anti-inflammatory role of curcumin in treating Osteoarthritis. Drug Design, Development and Therapy, 3029-3042.

Choudhuri, T.; Pal, S.; Agarwal, M. L.; Das, T. and Sa, G. (2002). Curcumin induces apoptosis in human breast cancer cells through p53-dependent Bax induction. FEBS letters, **512**(1-3):334-340.

Das, L. and Vinayak, M. (2014). Curcumin attenuates carcinogenesis by down-regulating proinflammatory cytokine interleukin-1 (IL-1α and IL-1β) *via* modulation of AP-1 and NF-IL6 in lymphoma bearing mice. International Immunopharmacology, **20**(1):141-147.

Das, R. K.,]; Kasoju, N. and Bora, U. (2010). Encapsulation of curcumin in alginate-chitosan-pluronic composite nanoparticles for delivery to cancer cells. Nanomedicine: Nanotechnology, Biology and Medicine, **6**(1):153-160.

Dey, R.; Dey, S.; Samadder, A.; Saxena, A. K. and Nandi, S. (2022). Natural inhibitors against potential targets of cyclooxygenase, lipoxygenase and leukotrienes. Combinatorial Chemistry and High Throughput Screening, **25**(14):2341-2357.

Ding, S.; Xu, S.; Ma, Y.; Liu, G.; Jang, H.; and Fang, J. (2019). Modulatory mechanisms of the NLRP3 inflammasomes in diabetes. Biomolecules, **9**(12):850.

Dongre, P. R.; Bhujbal, S. S. and Kumar, D. (2015). The bronchodilatory activity of *Curcuma longa, Zingiber officinale* and *Alpinia galanga* based herbal formulation (AHF). Oriental Pharmacy and Experimental Medicine, **15**:341-346.

Du, Q.; Hu, B.; An, H. M.; Shen, K. P.; Xu, L.; Deng, S. and Wei, M. M. (2013). Synergistic anticancer effects of curcumin and resveratrol in Hepa1-6 hepatocellular carcinoma cells. Oncology Reports, **29**(5):1851-1858.

El Nebrisi, E.; Javed, H.; Ojha, S. K., Oz, M. and Shehab, S. (2020). Neuroprotective effect of curcumin on the Nigrostriatal pathway in a 6-hydroxydopmine-induced rat model of Parkinson's disease is mediated by α7-nicotinic receptors. International Journal of Molecular Sciences, **21**(19):7329.

El-Barbary, M. I. (2016). Detoxification and antioxidant effects of garlic and curcumin in Oreochromis niloticus injected with aflatoxin B 1 with reference to gene expression of glutathione peroxidase (GPx) by RT-PCR. Fish Physiology and Biochemistry, **42**:617-629.

Etemadi, S.; Barhaghi, M. S.; Leylabadlo, H. E.; Memar, M. Y., Mohammadi, A. B. and Ghotaslou, R. (2021). The synergistic effect of turmeric aqueous extract and chitosan against multidrug-resistant bacteria. New Microbes and New Infections, **41**:100861.

Feng, Y. S.; Tan, Z. X.; Wu, L. Y.; Dong, F. and Zhang, F. (2020). The involvement of NLRP3 inflammasome in the treatment of Alzheimer's disease. Ageing Research Reviews, **64**:101192.

Fukutomi, R.; Ohishi, T.; Koyama, Y.; Pervin, M.; Nakamura, Y. and Isemura, M. (2021). Beneficial effects of epigallocatechin-3-O-gallate, chlorogenic acid, resveratrol, and curcumin on neurodegenerative diseases. Molecules, **26**(2):415.

Funamoto, M.; Sunagawa, Y.; Katanasaka, Y.; Miyazaki, Y.; Imaizumi, A.; Kakeya, H. and Morimoto, T. (2016). Highly absorptive curcumin reduces serum atherosclerotic low-density lipoprotein levels in patients with mild COPD. International Journal of Chronic Obstructive Pulmonary Disease, **11**:2029-2034.

Ghandadi, M. and Sahebkar, A. (2017). Curcumin: An effective inhibitor of interleukin-6. Current Pharmaceutical Design, **23**(6):921-931.

Ghasemi, M.; Khorsandi, K.; and Kianmehr, Z. (2021). Photodynamic inactivation with curcumin and silver nanoparticles hinders Pseudomonas aeruginosa planktonic and biofilm formation: Evaluation of glutathione peroxidase activity and ROS production. World Journal of Microbiology and Biotechnology, **37**(9):149.

Golzari-Sorkheh, M.; Brown, C. E.; Weaver, D. F. and Reed, M. A. (2021). The NLRP3 inflammasome in the pathogenesis and treatment of Alzheimer's disease. Journal of Alzheimer's Disease, **84**(2):579-598.

Goozee, K. G.; Shah, T. M.; Sohrabi, H. R.; Rainey-Smith, S. R.; Brown, B.; Verdile, G. and Martins, R. N. (2016). Examining the potential clinical value of curcumin in the prevention and diagnosis of Alzheimer's disease. British Journal of Nutrition, **115**(3):449-465.

Gora, I. M.; Ciechanowska, A. and Ladyzynski, P. (2021). NLRP3 inflammasome at the interface of inflammation, endothelial dysfunction, and type 2 diabetes. Cells, **10**(2):314.

Gorabi, A. M.; Abbasifard, M.; Imani, D.; Aslani, S.; Razi, B.; Alizadeh, S. and Sahebkar, A. (2022). Effect of curcumin on C reactive protein as a biomarker of systemic inflammation: An updated meta analysis of randomized controlled trials. Phytotherapy Research, **36**(1):85-97.

Gupta, N.; Verma, K.; Nalla, S.; Kulshreshtha, A.; Lall, R. and Prasad, S. (2020). Free radicals as a double-edged sword: The cancer preventive and therapeutic roles of curcumin. Molecules, **25**(22):5390.

Gupta, S. C.; Sung, B., Kim, J. H.; Prasad, S.; Li, S. and Aggarwal, B. B. (2013). Multitargeting by turmeric, the golden spice: From kitchen to clinic. Molecular Nutrition and Food Research, **57**(9):1510-1528.

Güran, M.; Þanlýtürk, G.; Kerküklü, N. R.; Altundað, E. M. and Yalçýn, A. S. (2019). Combined effects of quercetin and curcumin on anti-inflammatory and antimicrobial parameters *in vitro*. European Journal of Pharmacology, **859**:172486.

Hasanzadeh, S.; Read, M. I.; Bland, A. R.; Majeed, M.; Jamialahmadi, T. and Sahebkar, A. (2020). Curcumin: An inflammasome silencer. Pharmacological Research, **159**:104921.

Hodaei, H.; Adibian, M.; Nikpayam, O.; Hedayati, M. and Sohrab, G. (2019). The effect of curcumin supplementation on anthropometric indices, insulin resistance and oxidative stress in patients with type 2 diabetes: A randomized, double-blind clinical trial. Diabetology and Metabolic Syndrome, **11**:1-8.

Hosseini, H.; Ghavidel, F.; Panahi, G.; Majeed, M. and Sahebkar, A. (2023). A systematic review and meta analysis of randomized controlled trials investigating the effect of the curcumin and piperine combination on lipid profile in patients with metabolic syndrome and related disorders. Phytotherapy Research, **37**(3):1212-1224.

Hu, S.; Maiti, P.; Ma, Q.; Zuo, X.; Jones, M. R.; Cole, G. M. and Frautschy, S. A. (2015). Clinical development of curcumin in neurodegenerative disease. Expert Review of Neurotherapeutics, 15(6):629-637.

Imperador, C. H. L.; Scarim, C. B.; Bosquesi, P. L.; Lopes, J. R.; Cardinalli Neto, A.; Giarolla, J. and Chin, C. M. (2022). Resveratrol and curcumin for Chagas disease treatment-A systematic review. Pharmaceuticals, 15(5):609.

Islam, F.; Karim, M. R.; Shahjahan, M.; Hoque, M. O.; Alam, M. R. and Hossain, M. A. (2002). Study on the effect of plant spacing on the production of turmeric at farmers field. Asian Journal of Plant Sciences. pp:24.

Jabczyk, M.; Nowak, J.; Hudzik, B. and Zubelewicz-Szkodzińska, B. (2021). Curcumin in metabolic health and disease. Nutrients, 13(12):4440.

Javadi, M.; Khadem Haghighian, H.; Goodarzy, S.; Abbasi, M. and Nassiri Asl, M. (2019). Effect of curcumin nanomicelle on the clinical symptoms of patients with rheumatoid arthritis: A randomized, double blind, controlled trial. International Journal of Rheumatic Diseases, 22(10):1857-1862.

JIN, C. Y.; LEE, J. D.; Park, C., Choi, Y. H. and KIM, G. Y. (2007). Curcumin attenuates the release of pro inflammatory cytokines in lipopolysaccharide stimulated BV2 microglia 1. Acta Pharmacologica Sinica, 28(10):1645-1651.

Katsori, A. M.; Chatzopoulou, M.; Dimas, K.; Kontogiorgis, C.; Patsilinakos, A.; Trangas, T. and Hadjipavlou-Litina, D. (2011). Curcumin analogues as possible anti-proliferative and anti-inflammatory agents. European Journal of Medicinal Chemistry, 46(7):2722-2735.

Kaur, S.; Sharma, R.; Sarangal, V.; Kaur, N. and Prashar, P. (2017). Evaluation of anti-inflammatory effects of systemically administered curcumin, lycopene and piperine as an adjunct to scaling and root planning:A clinical study. AYU (An International Quarterly Journal of Research in Ayurveda), 38(3-4):117-121.

Kebede, B. H.; Forsido, S. F.; Tola, Y. B. and Astatkie, T. (2021). Free radical scavenging capacity, antibacterial activity and essential oil composition of turmeric (*Curcuma domestica*) varieties grown in Ethiopia. Heliyon,7(2):e06239

Khayatan, D.; Razavi, S. M.; Arab, Z. N.; Hosseini, Y.; Niknejad, A. Momtaz, S. and Sahebkar, A. (2024). Superoxide dismutase: A key target for the neuroprotective effects of curcumin. Molecular and Cellular Biochemistry, 479(3):693-705.

Kou, H., Huang, L; Jin, M.; He, Q.; Zhang, R. and Ma, J. (2023). Effect of curcumin on rheumatoid arthritis: A systematic review and meta-analysis. Frontiers in Immunology, 14:1121655.

Kumar, P.; Sulakhiya, K.; Barua, C. C. and Mundhe, N. (2017). TNF-α, IL-6 and IL-10 expressions, responsible for disparity in action of curcumin against cisplatin-induced nephrotoxicity in rats. Molecular and Cellular Biochemistry, 431:113-122.

Kunnumakkara, A. B.; Harsha, C.; Banik, K.; Vikkurthi, R.; Sailo, B. L.; Bordoloi, D. and Aggarwal, B. B. (2019). Is curcumin bioavailability a problem in humans: Lessons from clinical trials. Expert Opinion on Drug Metabolism and Toxicology, 15(9):705-733.

Labban, L. (2014). Medicinal and pharmacological properties of Turmeric (*Curcuma longa*): A review. International Journal of Pharma Biomedical Science, 5(1):17-23.

Li, H.; Sureda, A.; Devkota, H. P.; Pittalà, V.; Barreca, D.; Silva, A. S. and Nabavi, S. M. (2020). Curcumin, the golden spice in treating cardiovascular diseases. Biotechnology Advances, 38:107343.

Li, S.; Yuan, W.; Deng, G.; Wang, P.; Yang, P. and Aggarwal, B. (2011). Chemical composition and product quality control of turmeric (*Curcuma longa* L.).2:28-54

Li, W.; Jiang, Z.; Xiao, X.; Wang, Z.; Wu, Z.; Ma, Q. and Cao, L. (2018). Curcumin inhibits superoxide dismutase-induced epithelial-to-mesenchymal transition via the PI3K/Akt/NF-κB pathway in pancreatic cancer cells. International Journal of Oncology, 52(5):1593-1602.

Liao, D.; Lv, C.; Cao, L.; Yao, D.; Wu, Y.; Long, M. and Jiang, P. (2020). Curcumin attenuates chronic unpredictable mild stress induced depressive like behaviors via restoring changes in oxidative stress and the activation of Nrf2 signaling pathway in rats. Oxidative Medicine and Cellular Longevity, 2020(1):9268083.

Liczbiñski, P.; Micha³owicz, J. and Bukowska, B. (2020). Molecular mechanism of curcumin action in signaling pathways: Review of the latest research. Phytotherapy Research, 34(8):1992-2005.

Liu, Y. R.; Wang, J. Q.and Li, J. (2023). Role of NLRP3 in the pathogenesis and treatment of gout arthritis. Frontiers in Immunology, 14:1137822.

Liu, Z.; Smart, J. D. and Pannala, A. S. (2020). Recent developments in formulation design for improving oral bioavailability of curcumin: A review. Journal of Drug Delivery Science and Technology, 60:102082.

Majumdar, A. P.; Banerjee, S.; Nautiyal, J.; Patel, B. B.; Patel, V.; Du, J.and Sarkar, F. H. (2009). Curcumin synergizes with resveratrol to inhibit colon cancer. Nutrition and Cancer, 61(4):544-553.

Malhotra, A.; Nair, P. and Dhawan, D. K. (2014). Study to evaluate molecular mechanics behind synergistic chemo-preventive effects of curcumin and resveratrol during lung carcinogenesis. PloS One, 9(4):e93820.

Mazzanti, G. and Di Giacomo, S. (2016). Curcumin and resveratrol in the management of cognitive disorders: what is the clinical evidence?. Molecules, 21(9):1243.

Meshkibaf, M. H.; Maleknia, M.and Noroozi, S. (2019). Effect of curcumin on gene expression and protein level of methionine sulfoxide reductase A (MSRA), SOD, CAT and GPx in Freund's adjuvant inflammation-induced male rats. Journal of Inflammation Research, 241-249.

Mohseni, M.; Sahebkar, A.; Askari, G.; Johnston, T. P.; Alikiaii, B. and Bagherniya, M. (2021). The clinical use of curcumin on neurological disorders: An updated systematic review of clinical trials. Phytotherapy Research, 35(12):6862-6882.

Mokgalaboni, K.Ntamo, Y.; Ziqubu, K.; Nyambuya, T. M.; Nkambule, B. B.; Mazibuko-Mbeje, S. E. and Dludla, P. V. (2021). Curcumin supplementation improves biomarkers of oxidative stress and inflammation in conditions of obesity, type 2 diabetes and NAFLD: Updating the status of clinical evidence. Food and Function, 12(24):12235-12249.

Mollazadeh, H.; Cicero, A. F.; Blesso, C. N.; Pirro, M.; Majeed, M. and Sahebkar, A. (2019). Immune modulation by curcumin: The role of interleukin-10. Critical Reviews in Food Science and Nutrition, 59(1):89-101.

Monroy, A.; Lithgow, G. J. and Alavez, S. (2013). Curcumin and neurodegenerative diseases. Biofactors, 39(1):122-132.

Naghsh, N.; Musazadeh, V.; Nikpayam, O.; Kavyani, Z.; Moridpour, A. H.; Golandam, F. and Ostadrahimi, A. (2023). Profiling inflammatory biomarkers following curcumin supplementation: An umbrella meta analysis of randomized clinical trials. Evidence Based Complementary and Alternative Medicine, 2023(1):4875636.

Najjar, F. M.; Ghadari, R.; Yousefi, R.; Safari, N.; Sheikhhasani, V.; Sheibani, N. and Moosavi-Movahedi, A. A. (2017). Studies to reveal the nature of interactions between catalase and curcumin using computational methods and optical techniques. International Journal of Biological Macromolecules, 95:550-556.

Najjar, F. M.; Taghavi, F.; Ghadari, R.; Sheibani, N. and Moosavi-Movahedi, A. A. (2017). Destructive effect of non-enzymatic glycation on catalase and remediation *via* curcumin. Archives of biochemistry and biophysics, **630**:81-90.

Nasri, H.; Sahinfard, N.; Rafieian, M.; Rafieian, S.; Shirzad, M. and Rafieian-Kopaei, M. (2014). Turmeric: A spice with multifunctional medicinal properties. Journal of HerbMed Pharmacology, **3**(1):5-8.

Olcum, M.; Tastan, B.; Ercan, I.; Eltutan, I. B. and Genc, S. (2020). Inhibitory effects of phytochemicals on NLRP3 inflammasome activation: A review. Phytomedicine, **75**:153238.

Patel, S. S.; Acharya, A.; Ray, R. S.; Agrawal, R.; Raghuwanshi, R. and Jain, P. (2020). Cellular and molecular mechanisms of curcumin in prevention and treatment of disease. Critical Reviews in Food Science and Nutrition, **60**(6):887-939.

Patiño-Morales, C. C.; Soto-Reyes, E.; Arechaga-Ocampo, E.; Ortiz-Sánchez, E.; Antonio-Véjar, V.; Pedraza-Chaverri, J. and García-Carrancá, A. (2020). Curcumin stabilizes p53 by interaction with NAD (P) H: quinone oxidoreductase 1 in tumor-derived cell lines. Redox Biology, **28:**101320.

Pourhabibi Zarandi, F.; Shojaei Zarghani, S. and Rafraf, M. (2021). Curcumin and rheumatoid arthritis: A systematic review of literature. International Journal of Clinical Practice, **75**(10):e14280.

Qiu, L.; Gao, C.; Wang, H.; Ren, Y.; Li, J.; Li, M.and Zhang, J.(2023). Effects of dietary polyphenol curcumin supplementation on metabolic, inflammatory, and oxidative stress indices in patients with metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials. Frontiers in Endocrinology, **14**:1216708.

Rahmani, A. H.; Alsahli, M. A.; Aly, S. M.; Khan, M. A. and Aldebasi, Y. H. (2018). Role of curcumin in disease prevention and treatment. Advanced Biomedical Research, **7**(1):38.

Rao, C. V. (2007). Regulation of COX and LOX by curcumin. The molecular targets and therapeutic uses of curcumin in health and disease, 213-226.

Razavi, B. M.; Ghasemzadeh Rahbardar, M. and Hosseinzadeh, H. (2021). A review of therapeutic potentials of turmeric (*Curcuma longa*) and its active constituent, curcumin, on inflammatory disorders, pain, and their related patents. Phytotherapy Research, **35**(12):6489-6513.

Reddy, P. H.; Manczak, M.; Yin, X.; Grady, M. C.; Mitchell, A.; Tonk, S. and Reddy, A. P. (2018). Protective effects of Indian spice curcumin against amyloid-â in Alzheimer's disease. Journal of Alzheimer's Disease, **61**(3):843-866.

S. Karimian, M.; Pirro, M.; P. Johnston, T.; Majeed, M. and Sahebkar, A. (2017). Curcumin and endothelial function: evidence and mechanisms of protective effects. Current Pharmaceutical Design, **23**(17):2462-2473.

Saini, N.; Chopra, B. and Dhingra, A. K. (2023). Synergistic effect of piperine and its derivatives: A comprehensive review. Current Drug Research Reviews Formerly: Current Drug Abuse Reviews, **15**(2):105-121.

Santos-Parker, J. R.; Strahler, T. R.; Bassett, C. J.; Bispham, N. Z.; Chonchol, M. B.and Seals, D. R. (2017). Curcumin supplementation improves vascular endothelial function in healthy middle-aged and older adults by increasing nitric oxide bioavailability and reducing oxidative stress. Ageing, **9**(1):187.

Schmidt, B.; Passos, C. L. A.; Ferreira, C.; Silva, J. D. and Fialho, E. (2020). Synergistic effect of curcumin, piperine and resveratrol in MCF-7 and MDA-MB-231 breast cancer cells. Biomed. Res, **31**:113-118.

Setiawan, P. Y. B.; Kertia, N.; Nurrochmad, A. and Wahyuono, S. (2021). Curcumin in combination: Review of synergistic effects and mechanisms in the treatment of inflammation. Journal of Applied Pharmaceutical Science, **11**(2): 001-011.

Shah, A. J. (2023). Dual Inhibition of Cyclooxygenase and Lipoxygenase by Natural Products. Phytopharmacological Communications, **3**(1):01-01.

Shahcheraghi, S. H.; Salemi, F.; Peirovi, N.; Ayatollahi, J.; Alam, W.; Khan, H. and Saso, L. (2021). Nrf2 regulation by curcumin: molecular aspects for therapeutic prospects. Molecules, **27**(1):167.

Shao, N.; Jia, H.; Li, Y. and Li, J. (2017). Curcumin improves treatment outcome of Takayasu arteritis patients by reducing TNF-á: a randomized placebo-controlled double-blind clinical trial. Immunologic Research, **65**:969-974.

Shehzad, A.; Rehman, G. and Lee, Y. S. (2013). Curcumin in inflammatory diseases. Biofactors, **39**(1):69-77.

Shin, J. W.; Chun, K. S.; Kim, D. H.; Kim, S. J., Kim, S. H., Cho, N. C. and Surh, Y. J. (2020). Curcumin induces stabilization of Nrf2 protein through Keap1 cysteine modification. Biochemical Pharmacology, **173**:113820.

Shishodia, S. (2013). Molecular mechanisms of curcumin action: Gene expression. Biofactors, **39**(1):37-55.

Silalahi, T.; Alwi, I.; Suyatna, F. and Sartika, K. D. (2021). Curcumin's effect on inflammatory response following percutaneous coronary intervention in adult patients with stable coronary heart disease. International Journal of Angiology, **30**(02):132-138.

Sivakumar, P.; Monisha, S.; Selvaraj, K. V.; Chitra, M.; Prabha, T.; Santhakumar, M. and Velayutham, A. (2022). Nutritional value, phytochemistry, pharmacological and *in vitro* regeneration of turmeric (*Curcuma longa* L.): An updated review. Ann Phytomed., **11**(1):236-246.

Son, Y.; Lee, J. H.; Cheong, Y. K.; Chung, H. T. and Pae, H. O. (2013). Antidiabetic Potential of the Heme Oxygenase 1 Inducer Curcumin Analogues. BioMed Research International, **2013**(1):918039.

Tabaee, S.; Sahebkar, A.; Aghamohammadi, T.; Pakdel, M.; Dehabeh, M.; Sobhani, R. and Mirhafez, S. R. (2021). The effects of curcumin plus piperine supplementation in patients with acute myocardial infarction: A randomized, double-blind, and placebo-controlled trial. Natural Products and Human Diseases: Pharmacology, Molecular Targets, and Therapeutic Benefits, 199-211.

Tabanelli, R.; Brogi, S. and Calderone, V. (2021). Improving curcumin bioavailability: Current strategies and future perspectives. Pharmaceutics, **13**(10):1715.

Tanvir, E. M.; Hossen, M. S.; Hossain, M. F.; Afroz, R.; Gan, S. H.; Khalil, M. I. and Karim, N. (2017). Antioxidant properties of popular turmeric (*Curcuma longa*) varieties from Bangladesh. Journal of Food Quality, **2017**(1):8471785.

Tehrani, S. D.; Hosseini, A., Shahzamani, M., Heidari, Z.; Askari, G.; Majeed, M. and Bagherniya, M. (2024). Evaluation of the effectiveness of curcumin and piperine co-supplementation on inflammatory factors, cardiac biomarkers, atrial fibrillation, and clinical outcomes after coronary artery bypass graft surgery. Clinical Nutrition ESPEN, **62**:57-65.

Thakkar, A.; Bhatia, N. and Doshi, G. (2022). Evaluation of curcumin, piperine, and ferrous sulphate combination potential in the adjuvant-induced arthritis model in male Wistar rats. Pharmacognosy Research, **14**(4):483-489.

Velasco Rodríguez, L. D. C.; García, H. S. and Rascón Díaz, M. P. (2024). Curcumin and omega 3 polyunsaturated fatty acids as bioactive food components with synergistic effects on Alzheimer's disease. Psychogeriatrics, **24**(3):701-718.

Verma, R. K.; Kumari, P.; Maurya, R. K.; Kumar, V.; Verma, R. B. and Singh, R. K. (2018). Medicinal properties of turmeric (*Curcuma longa* L.): A review. International Journal of Chemical Studies, **6**(4):1354-1357.

Xiao, Y., Xia, J.; Wu, S., Lv, Z.; Huang, S.; Huang. H. and Ke, Y. (2018). Curcumin inhibits acute vascular inflammation through the activation of heme oxygenase 1. Oxidative Medicine and Cellular Longevity, **2018**(1):3295807.

Yin, H.; Guo, Q.; Li, X, Tang, T.; Li, C.; Wang, H. and Peng, J. (2018). Curcumin suppresses IL-1β secretion and prevents inflammation through inhibition of the NLRP3 inflammasome. The Journal of Immunology, **200**(8):2835-2846.

Yonar, S. M.; Yonar, M. E. and Ural, M. Å. (2017). Antioxidant effect of curcumin against exposure to malathion in *Cyprinus carpio*. Cellular and Molecular Biology, **63**(3):68-72.

Zeng, L.;Yang, T.; Yang, K., Yu, G.; Li, J., Xiang, W. and Chen, H. (2022). **Efficacy** and safety of curcumin and *Curcumalonga* extract in the treatment of arthritis: A systematic review and meta-analysis of randomized controlled trial. Frontiers in Immunology, **13**:891822.

Zhou, X.; Afzal, S.; Wohlmuth, H.; Münch, G.; Leach, D.; Low, M. and Li, C. G. (2022). Synergistic anti-inflammatory activity of ginger and turmeric extracts in inhibiting lipopolysaccharide and interferon-γ-induced proinflammatory mediators. Molecules, **27**(12):3877.

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