TURMERIC’S HEALING TOUCH: EXPLORING CURCUMIN’S MEDICAL RENAISSANCE

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Abstract
This comprehensive article delves into the multifaceted role of curcumin, a principal component of turmeric, in modern pharmaceuticals, drawing on its long-standing history in traditional medicine systems like Ayurveda and Chinese Medicine.

The core of the article investigates curcumin’s emerging role as a formidable anti-aging agent. Curcumin’s antioxidant and anti-inflammatory properties play a pivotal role in addressing age-related disorders. Its efficacy extends to neurodegenerative diseases, cardiometabolic disorders, cancer, and rheumatoid arthritis, owing to its ability to modulate various cellular pathways, enhance drug susceptibility, inhibit cell proliferation, and foster apoptosis. Notably, curcumin enhances the efficacy of chemotherapy drugs, as evidenced in breast cancer treatments, by modulating drug resistance pathways. The article also emphasizes curcumin’s potential in managing diabetes, cardiovascular diseases, and osteoporosis, highlighting its role in reducing cholesterol levels and improving vascular health, and bone metabolism. Confronting the challenge of curcumin’s low bioavailability, the article explores innovative biotechnological solutions, such as nano-delivery systems, which significantly enhance curcumin’s therapeutic potential.

The harmonious blend of ancient knowledge and contemporary scientific research highlights the lasting significance of curcumin in medicine, setting the stage for its ongoing incorporation into modern healthcare practices.

Keywords: curcumin; anti-ageing; inflammation; antioxidants.

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Key Messages for Research and Practice

- Curcumin, derived from turmeric, targets key aging mechanisms such as oxidative stress and chronic inflammation, showing potential in slowing age-related cellular damage.

- Evidence supports that dietary choices, particularly those high in antioxidants, and consistent exercise contribute significantly to mitigating aging effects.

- Developing nano-curcumin formulations could enhance its therapeutic potential, making it a more effective option for managing age-related conditions.

- Promoting research, accessibility, and education on curcumin’s benefits could form part of a broader strategy to improve the management age-related diseases.
Introduction

The ageing of the global population is a transformative phenomenon with far-reaching implications for society. In recent decades, advancements in healthcare and living standards have contributed to increased life expectancy, leading to a higher proportion of elderly individuals worldwide. According to the United Nations, the number of people aged 60 years or older is projected to double by 2050, reaching nearly 2.1 billion. This demographic shift presents challenges in various sectors, including healthcare, social security, and labour markets [1,2]. As the elderly population grows, there is an increased prevalence of age-related diseases such as Alzheimer’s, cardiovascular diseases, and osteoporosis, which places a significant burden on healthcare systems.

In response to the challenges posed by an ageing population, significant research and development have been dedicated to understanding and mitigating the effects of aging. The public health initiatives promote healthy aging, community engagement, and preventive healthcare as essential in enhancing the quality of life for the elderly [3]. As societies adapt to an increasingly aging population, a holistic approach combining scientific research, lifestyle modifications, and supportive policies will be pivotal in fostering a healthy, active, and productive elderly population [4].

Lifestyle interventions are also crucial in addressing the challenges of an aging population. Diet and exercise have been consistently shown to have a profound impact on healthspan and longevity [5]. Diets rich in antioxidants, such as the Mediterranean diet, and those that promote metabolic health, like intermittent fasting or reduced caloric intake, have been associated with reduced risk of age-related diseases [6].

Curcumin, a natural compound found in spice turmeric, has garnered significant attention in the field of anti-aging research due to its potent antioxidant and anti-inflammatory properties [7]. As a primary active ingredient in turmeric, curcumin is believed to combat aging by neutralizing free radicals and reducing oxidative stress, which are key contributors to the aging process and related diseases [8]. Its anti-inflammatory effects further aid in mitigating chronic inflammation, often linked with age-related conditions. Curcumin also influences several signalling pathways involved in cellular aging, including those related to cellular repair and apoptosis [8].

Therefore, in this article, our objective is to emphasize the key characteristics of curcumin related to anti-aging and its beneficial effects on an organism in case of various diseases.

Methods

A comprehensive literature search was conducted across multiple databases, including Scopus, MEDLINE/PubMed, and CENTRAL, utilizing a variety of search terms. The keywords selected for this search encompassed «turmeric», «curcumin», «anti-aging», «inflammation», «cellular ageing», and «gerontology». Each identified article was rigorously evaluated for relevance. Furthermore, the bibliographies of these articles were scrutinized to uncover any supplementary pertinent sources. The scope of this review was limited to articles published in English over the past decade, encompassing both human and animal studies that shed light on the subject. To enhance the reliability and relevance of the literature review, specific exclusion criteria were imposed after the initial search phase, including: lack of an abstract; document types such as book chapters, conference proceedings, and errata; articles that have been retracted; studies that fail to explore the anti-aging properties of curcumin or its role in addressing age-related conditions.

Curcumin: Possible role in aging pathways

Curcumin has been recognized for its potential role in anti-aging within the pharmaceutical sector due to its antioxidant and anti-inflammatory effects. These properties have garnered interest from the scientific and medical communities for curcumin’s ability to shield biomolecules against oxidative damage and inhibit the production of detrimental compounds like malondialdehyde and nitrotyrosines. [9]. Additionally, it demonstrates antioxidant capabilities by neutralizing diverse reactive oxygen species like superoxide, hydrogen peroxide, and nitric oxide radicals, alongside preventing lipid oxidation. This effect stems from boosting the activity of antioxidant enzymes including SOD, CAT, GPx, and OH-1, and elevating GSH levels through the upregulation of glutathione transferase [8]. Moreover, curcumin impedes enzymes responsible for producing reactive oxygen species, such as LOX, COX, and xanthine oxidase, making it an effective chain-breaking antioxidant, capable of scavenging peroxyl radicals due to its hydrophobic nature [7].

Several studies have indicated curcumin’s capacity to: block key pro-inflammatory transcription factors like NF-κB and AP-1 [10]; lower levels of several pro-inflammatory cytokines, including TNFα and various interleukins [11] suppress inflammation-promoting enzymes such as 5-lipoxygenase and

**Cardiometabolic disorders**

Higher cholesterol, fluctuations in blood pressure and obesity increasing in society at a very fast pace due to changes in our lifestyle, environment, and dietary habits like eating most processed food. According to statistical data by WHO (World Health Organisation) around 1.7 billion people above the age of 30 years were suffering from high cholesterol levels in their blood. And according to different surveys around 1 billion people suffer from high blood pressure and around 1.9 billion people suffer from being overweight and it’s continuously rising. With the rising population of aged people, these trends have become a global epidemic as these have arisen due to the changes in physiology associated with ageing.

As the incidence of diabetes increases, it becomes increasingly important to develop more advanced prevention and treatment plans. Studies on curcumin have shown promising results, and it is one of the most promising phytobioactive compounds concerning its metabolic benefits. Studies on animals have shown that curcumin can improve β-cell function, prevent β-cell death, reduce hyperglycemia, lower insulin resistance, and delay the onset of type 2 diabetes [12]. Clinical trials on diabetic patients have also shown that those who consume curcumin experience significantly reduced levels of glycosylated haemoglobin (HbA1c) and fasting plasma glucose [13].

In various experiments and clinical studies, curcumin is effective in treating cardiovascular disorders due to its anti-atherogenic effect, which helps to suppress the accumulation of cholesterol [14]. It has also been found to lower both plasma and hepatic cholesterol levels [15]. A meta-analysis conducted by Qin and colleagues has discovered that the supplementation of turmeric extract or curcumin can significantly reduce serum low-density lipoprotein (LDL-C) and triglyceride levels, thereby reducing the risk of cardiovascular disorders [16]. In another recent meta-analysis, it was found that curcumin can increase adiponectin levels and decrease BMI, waist circumference, and weight [17]. Based on these and other research findings, many authors regard curcumin as a safe, well-tolerated, and efficient dietary adjunct for cardiovascular disorders.

**Neurodegenerative disorders and neuroprotection**

The neurodegenerative disorder is characterized by impaired cognition and dementia in older persons [18]. Neuropathologically this disorder arises due to the aggregation of amyloid-β (A β) proteins in senile plaques and the accumulation of hyperphosphorylated tau proteins in neurofibrillary tangles in the brain [19]. It has been discovered through research that the dysregulation in non-neuronal cells, such as glia, immune cells, and blood vasculature, plays an important role in the pathology of Alzheimer’s disease (AD) [20]. Therefore, there is convincing evidence to suggest that the administration of modified curcumin can improve vascular health, endothelial function, arterial compliance, and all other vascular hemodynamic indexes [21] by affecting the nitrous oxide bioavailability, oxidative stress, and structural protein in the arterial wall. Curcumin provides anti-inflammatory effects on microglial cells [22,23]. It also activates mechanisms of neurogenesis and synaptogenesis, which provide anti-AD effects. This is done through tau and amyloid β-binding inhibition and metal chelation [24]. In several mouse models of Alzheimer’s Disease, curcumin has been shown to enhance the clearance of tau and improve synaptic function [25]. Other mouse models have also shown that curcumin elevates the expression of the TREM2 gene, which is known to decrease the risk of Alzheimer’s Disease and control the neuroinflammatory gene network by controlling the TyroBP gene [26]. These pieces of evidence suggest that consuming modified curcumin regularly can significantly reduce a country’s health budget for neurological disorders.

Parkinson’s disease (PD) is a prevalent neurodegenerative disorder that ranks second only to Alzheimer’s. It occurs due to the gradual loss of dopaminergic neurons in the substantia nigra, which controls movement. The disease’s hallmark features include resting tremor, bradykinesia, and rigidity [27]. Research indicates that oxidative stress is responsible for the changes in the brain region leading to Parkinson’s [28]. Promisingly, potent antioxidant compounds have shown potential in reducing oxidative stress in PD patients [29,30].

The currently available FDA-approved therapeutic drugs for PD only provide temporary relief from symptoms. Therefore, more innovative approaches are needed in pharmacology research. Recent investigations, both in vivo and in vitro, have shown that phytochemicals like curcumin, which possess neuroprotective properties, can counter oxidative stress and inflammation, prevent
aggregation of α-synuclein (a protein associated with the pathogenesis of PD) and fibrillation, and inhibit monoamine oxidase B [31]. In a meta-analysis conducted by Wang and colleagues on the toxin-based animal model [32] and many other studies, it has been found that curcumin’s strong antioxidant activity provides therapeutic potential in PD and found that to protect substantia nigra neurons and improves the level of dopamine and reduces neuronal apoptosis.

Cancer and the role of turmeric

Cancer ranks as the second most common cause of mortality in advanced nations. A contributing factor to the uncontrolled growth of cancer cells in the tumour environment is their ability to become resistant to contemporary treatments. To combat this, a chemical agent capable of targeting various cancer cell pathways at once is needed. Curcumin has shown promise in this area, as it influences multiple cellular pathways to slow down cell division and inhibit drug efflux transporters, thereby increasing cell sensitivity to medications.

In-depth preclinical research has revealed curcumin’s effectiveness in arresting the cell cycle in cancerous cells, thus inhibiting their growth and spread [33]. It also triggers autophagy in cancer cells [34] by regulating specific kinases, enzymes, transcription and growth factors, inflammatory cytokines, and apoptosis-related proteins through either upregulation or downregulation [35]. For instance, studies have shown that curcumin, when combined with solid lipid nanoparticles, can increase the efficacy of doxorubicin (Dox) tenfold in TNBC, influencing the p65/p50 NF-kB mediated transcriptional activation of the P-glycoprotein transporter [36,37]. Several Phase I and Phase II clinical trials have been launched recently to assess curcumin’s anti-cancer properties. A considerable number of these trials have concentrated on pancreatic cancer [38,39]. The results of these trials, especially Phase II trials, indicate that curcumin is well-tolerated and exhibits potent anti-inflammatory and anti-neoplastic activities in patients with advanced pancreatic cancer [40]. This shows that curcumin has the potent ability to treat the cancer.

Osteoporosis

Osteoporosis is a pathological condition that occurs as people age. It leads to a decrease in bone mass and impairs the bone microstructure. As a result, the chances of osteoporotic fractures increase, especially in elderly women after menopause as oestrogen is the primary hormone regulator of bone metabolism [41]. Pathologically it is commonly mediated by an elevated level of expression of proinflammatory cytokines.

FDA-approved drugs which are available in the market accompanied by many side effects and are quite expensive. Therefore, the search for more efficient and safe medicines represents an urgent task as the elderly population rises to treat osteoporosis.

In recent studies, it has been shown that curcumin can be a potential drug candidate for bone-related ageing diseases [42]. Several in vitro and in vivo studies data demonstrate that curcumin can improve various aspects of bone health by affecting the activation and differentiation of osteoclasts and by increasing the mineral density and mechanical properties of the bone. In additional research, it is shown that curcumin inhibits the nuclear factor kappa B (NF-kB) and receptor activator of NF-kB ligand lowers the production of ROS and NO and levels of proinflammatory cytokines such as TNF-α and IL-6 and causes a beneficial change in bone turn over [43,44]. In other studies, it was shown that at high doses of curcumin, the proportion of osteoclasts gets reduced and there is an increase in the number of osteoblasts. Other studies on rat models found that curcumin-loaded nanoformulations can prevent osteoporosis, improve bone density, prevent bone loss, and exert a protective effect against ovariectomy-induced bone loss [45,46,47]. These data overall indicate that curcumin is a promising candidate also for improving the condition of patients suffering from age-related osteoporosis.

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a challenging autoimmune disease that predominantly affects joints and causes discomfort, swelling, and stiffness. RA patients often struggle with daily activities, which can be quite distressing. According to WHO’s latest figures, around 18 million people worldwide are affected by this condition. Interestingly, more than 55% of them are 55 years or older, which shows that RA risk increases with age and peaks between 70-79 years [48] While genetic predispositions like HLA-DR4 and HLA-DR1 alleles may contribute to RA development, environmental triggers, and immune dysregulation are also significant factors.

To manage RA several studies, provide evidence that curcumin can provide therapeutic benefits as it can modulate levels of inflammatory mediators such as nitric oxide, cytokines, chemokines, adhesion molecules, arachidonic acid
and lipoygenase molecules as well as activity of NF-κB signalling [49]. In rat models of collagen-induced arthritis, curcumin was shown to decrease joint swelling by inhibiting the NF-κB signalling and by promoting the apoptosis of macrophages with the alleviation of inflammation and synovial hyperplasia [50].

According to a meta-analysis of randomized clinical trials performed by Daily et al. [51] and other researchers, both curcumin and turmeric may provide relief for arthritis symptoms. However, further research is necessary to develop a properly designed treatment plan. It is imperative to conduct more comprehensive studies to establish the efficacy of these natural remedies in the long term. Therefore, caution should be exercised when considering the use of curcumin and turmeric as therapeutic options for arthritis until further evidence is gathered.

**Modifications to increase the efficiency of curcumin**

The potential benefits of curcumin and its complex chemical structure, which could be useful for the future creation of pharmaceuticals targeting aging. However, the practical application of curcumin is limited by its low bioavailability, which results from its hydrophobic nature, stability issues, poor solubility, and rapid metabolism in the body [52,53]. Addressing these challenges requires innovative biotechnological strategies, such as nano-delivery systems. Research indicates that formulations of nano-curcumin might be more effective than traditional forms of curcumin [54]. Scientists are exploring ways to improve curcumin’s solubility and absorption through modifications with lipids, polymers, nanogels, and metal oxides [55].

Studies show that nanoformulations, such as those using polylactic-co-glycolic acid, enhance curcumin’s absorption in animal models [56], with certain nanoparticle-enhanced curcumin showing increased brain absorption [57,58]. Additionally, curcumin nanocomposites have demonstrated improved anti-inflammatory effects in comparison to its conventional form [59-62].

**Conclusion**

In summary, curcumin is recognized as a useful component in anti-aging research, suggesting its applicability in managing various age-related conditions. Its antioxidant and anti-inflammatory properties, supported by modern delivery methods like nanotechnology, position curcumin as a valuable addition to current healthcare practices. Its role in addressing the challenges of aging contributes to ongoing discussions in medical and wellness communities.

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**CONFLICTS OF INTEREST**

None declared

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