Unlocking the Potential of Curcumin-encapsulated Nanoparticles in Alzheimer's disease Management: A Mini Review

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Abstract

Alzheimer's disease (AD) poses a significant global health challenge, characterized by progressive cognitive decline and neuropathological changes. Current treatment options offer limited efficacy, necessitating the exploration of novel therapeutic approaches. Curcumin, a natural polyphenol derived from turmeric, has garnered attention for its potential neuroprotective properties in AD. However, its clinical utility has been hindered by poor bioavailability and limited brain penetration. Recent advancements in nanotechnology have led to the development of curcumin nanoparticles, offering improved solubility, stability, and bioavailability. This mini review examines the therapeutic potential of curcumin nanoparticles in AD treatment. We discuss the multifaceted mechanisms of action of curcumin, including anti-inflammatory, antioxidant, and neuroprotective effects, and explore how nanoparticle formulations enhance its pharmacokinetic profile. Furthermore, we review preclinical and clinical studies evaluating the efficacy and safety of curcumin nanoparticles in AD models and patients. Emerging evidence suggests that curcumin nanoparticles hold promise as a promising therapeutic strategy for AD, with enhanced blood-brain barrier penetration and improved neuroprotective effects compared to conventional curcumin formulations. Future research efforts should focus on elucidating the optimal dosing, formulation, and therapeutic regimen of curcumin nanoparticles to maximize their clinical benefits in AD management.

Key words: Alzheimer Disease, Nanocurcumin, Therapeutics, Nanotechnology

Introduction

The World Health Organization states that dementia has grown to be a major global health concern with far-reaching social, economic, and health concerns. The cognitive function that affects memory, reasoning, direction, comprehension, computation, learning capacity, language, and judgment gradually deteriorates. Alzheimer's disease is the most prevalent cause of dementia, although there are other conditions that can also cause dementia, including frontotemporal dementia, Lewy body dementia, and vascular dementia. Dementia has a significant impact on many different areas worldwide. Globally, the prevalence of dementia is increasing, mostly as a result of aging populations.

According to estimates from the World Health Organization (WHO), 50 million people globally have dementia in 2020; if effective interventions are not put in place, this figure is expected to rise to 152 million by 2050 (Prince et al., 2015). The number of them is rising annually. A new case of dementia is predicted to be recorded every four seconds worldwide, or around 7.7 million new cases (WHO Report 2017). An enormous financial burden of dementia exists for individuals, families, and society as a whole. Medical and social care expenses are considered direct costs; productivity loss and caregiver load are considered indirect costs. In 2018, it was anticipated that dementia care would cost $1 trillion worldwide (Wimo et al., 2017). The World Health Organization (WHO) has declared dementia to be a public health emergency and has urged more action, research, and understanding to address the dementia's expanding effects on people as well as communities. The most prevalent type of dementia, accounting for less than 60–80% of cases, is Alzheimer disease (AD). Statistics show that the number of cases of Alzheimer's disease is rapidly rising, and by 2050, one in five people will likely have the condition. Given the effects of Alzheimer's, a number of worldwide projects and advocacy campaigns, including those led by the Alzheimer's Association and Alzheimer's Disease worldwide (ADI), are vital to the coordination of these efforts (Alzheimer's Disease International 2021). The aging population in India is the primary cause of the rising prevalence of Alzheimer's disease. Research shows that the number of individuals affected by dementia is rising; estimates place the number at over 4 million in the nation (Shaji et al., 2009; Shaji et al., 2002). Alzheimer's disease diagnosis rates in India are still poor for a number of reasons, such as stigma, insufficient awareness, and a dearth of specialized diagnostic facilities (Dias et al., 2014). Late diagnosis frequently prevents prompt support and actions. India's caretakers bear a heavy burden from Alzheimer's illness. Family caregivers, who are frequently spouses or adult children, face financial, emotional, and physical difficulties. Developing legislation and healthcare infrastructure to meet the growing prevalence of Alzheimer's disease presents issues for India (Mukherjee & Haldar 2015; Shaji, & Nair 2013). There is still a lack of access to resources and specialized services for dementia care. Study in India has examined the contribution of both hereditary and environmental factors to the vulnerability of the Indian population to Alzheimer's disease, recognizing the need for study tailored to the specific needs of the region.

Pathophysiology of AD

A neurodegenerative ailment that progresses over time, Alzheimer's disease (AD) is typified by the build-up of beta-amyloid plaques, neurofibrillary tangles, and synaptic dysfunction in the brain (Hardy & Higgins 1992). AD is characterized by the extracellular deposition of Aβ peptide and the intracellular accumulation of NFT, or hyperphosphorylated tau proteins (Cummings et al., 2014; Cummings et al., 2019). These histological alterations in the brain of AD patients are eventually identified as Aβ plaques and Neurofibrillary tangles. According to researchers these two occurrences constitute the most prevalent pathophysiological signature of AD. Uncertainty surrounds the molecular mechanism underlying Alzheimer's pathogenesis (Figure 1).

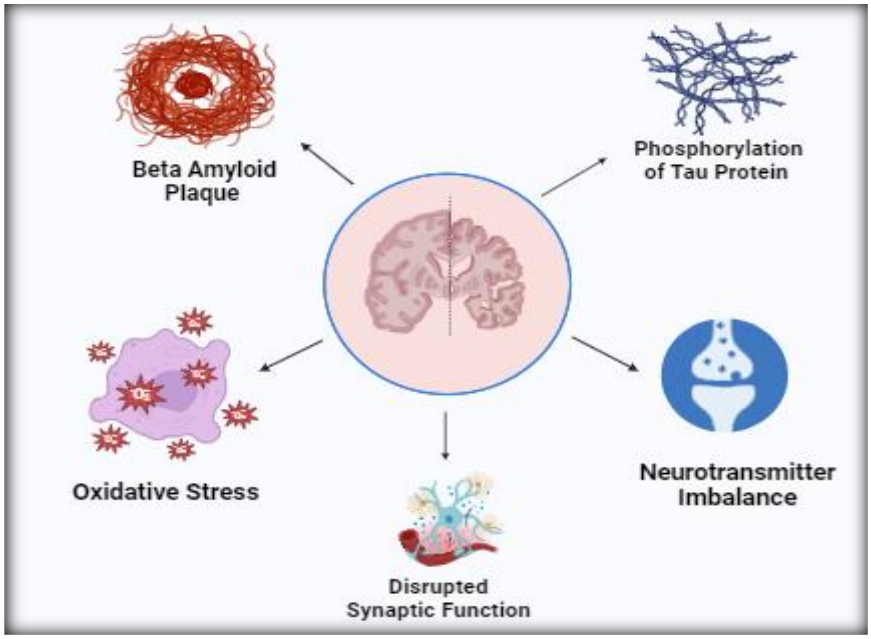

Figure 1 Pathophysiology of alzheimer

Recent approach for the treatment of AD

The development of treatment approaches to alter the course of Alzheimer's disease has been the subject of extensive investigation. Targets for drug discovery initiatives include inflammation, phosphorylation of tau protein, beta-amyloid synthesis, and synaptic dysfunction. A number of medications, such as acetylcholinesterase inhibitors and N-methyl-D-aspartate (NMDA) receptor antagonists, have had their effectiveness evaluated in clinical trials. Novel techniques to treating Alzheimer's disease have been investigated recently, such as precision medicine and disease-modifying medicines. In clinical trials, monoclonal antibodies that target beta-amyloid.Other experimental medications focus on neuroinflammation, synaptic dysfunction, and tau disease. Precision medicine approaches have been made possible by advances in our understanding of the genetic and molecular foundations of Alzheimer's disease. Treating a patient's unique genetic mutations or risk factors enables customized treatment plans. Identification of individuals at risk and customization of interventions are facilitated by genetic testing and biomarker analysis. Several therapy modalities are combined in emerging techniques to address several parts of Alzheimer's pathology at the same time. The goal of combining medication, lifestyle modifications, and precision medicine techniques is to offer more thorough and efficient care. The importance of lifestyle modifications in managing and preventing Alzheimer's disease is being highlighted by research more and more. There is evidence that social interaction, cognitive stimulation, a balanced diet, and regular physical activity can all lower the risk of cognitive decline. At the moment, a variety of pharmaceutical and non-pharmacological therapies are used to treat the disease's wide range of symptoms. Acetylcholinesterase inhibitors, such as galantamine, rivastigmine, and donepezil, are the most often recommended drugs for Alzheimer's disease. These medications increase cholinergic neurotransmission, which temporarily reduces cognitive symptoms and raises the standard of living for Alzheimer's patients. Medications that function as N-methyl-D-aspartate (NMDA) receptor antagonists include memantine (Figure 2).

In certain situations, acetylcholinesterase inhibitors and memantine are used in conjunction to optimize therapeutic advantages. Memantine offers neuroprotection against excitotoxicity and slows cognitive decline in moderate to severe stages of Alzheimer's disease This method presents a more all-encompassing treatment plan by addressing glutamate-mediated neurotoxicity as well as neurotransmitter abnormalities.

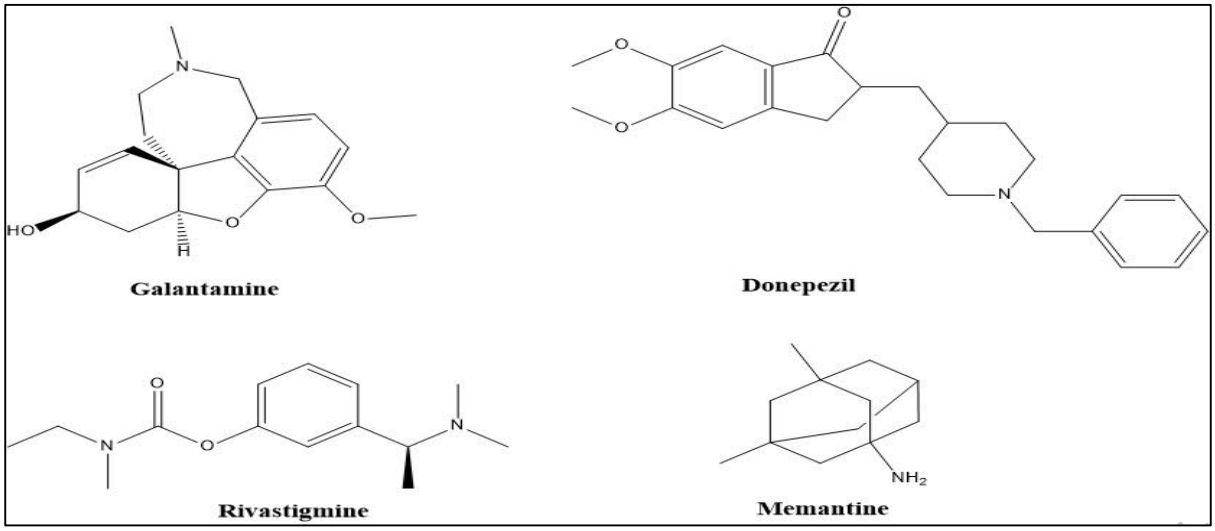

Figure 2 Chemical Structure of FDA- Approved anti-alzheimer Drugs

Antipsychotic medications may be recommended to treat dementia's behavioral and psychological symptoms (BPSD).To find new treatment approaches, ongoing research investigates cutting-edge targets such neuroinflammation, mitochondrial malfunction, and synaptic plasticity. Future developments in Alzheimer's treatment are anticipated to be driven by cooperative efforts, extensive clinical trials, and the incorporation of technological innovations, including artificial intelligence. The field of Alzheimer's disease research and therapy is always changing, with an emphasis on creating novel and potent approaches. A diverse therapy pipeline has resulted from recent advancements in understanding the pathophysiology of Alzheimer's disease, offering promise for better outcomes for those afflicted by this debilitating neurological illness.

Antioxidant Approach for AD

Alzheimer's disease is a neurological disease that progresses over time and presents many difficulties for those who have it as well as those who care for them. The need for efficient treatment approaches grows as the frequency of Alzheimer's disease rises worldwide. However, because of possible adverse effects, their use is closely regulated, highlighting the necessity of a well-rounded approach to Alzheimer's treatment. Non-pharmacological approaches are just as important as pharmacological ones. Notwithstanding encouraging results, there are still obstacles in the way of converting antioxidant therapy into practical AD treatments. The intricacy of antioxidant therapies is influenced by factors like target specificity, bioavailability, and the intricate interaction of several pathways. Subsequent investigations seek to tackle these obstacles and identify new therapeutic targets within the cascade of oxidative stress. Antioxidants are used in therapeutic efforts to reduce oxidative stress in AD. Certain compounds have demonstrated potential in preclinical and clinical trials, including coenzyme Q10, polyphenols, and vitamins C and E.

These compounds also have antioxidant capabilities. These substances may strengthen natural antioxidant defenses, neutralize ROS, and guard against oxidative damage. Numerous recent studies have demonstrated the significance of oxidative stress in the development of Alzheimer's disease. Researchers discovered that Aβ accumulation and neurofibrillary tangle (NFT) deposition in the brains of AD patients are linked to oxidative stress. Thus, antioxidants' ability to scavenge free radicals presents a potentially effective therapeutic approach for the treatment of AD (Halliwell et al., 2001; Domenico et al., 2015 and Lee et al. 2010 Choi et al., 2012). Clinical researchers are currently concentrating on multipotent drugs since they are easy to use, safe, and effective against complex diseases. *Bacopa monnieri, sage (Salvia officinalis), ginsenosides, baicalin, jawar, curcumin, sesamin,* and *kaempferol* are among the plant extracts that have been shown to be beneficial in recent studies on neurodegenerative diseases (Koul et al. 2023, Kaur et al. 2017, Mahomoodally et al. 2013, Bhattacharjee et al., 2020, Singh et al., 2022, and Kuhad et al.,2008).

Alzheimer's and its management

The medicinal benefits of many plant species, either as extracts or formulations, have been investigated by various authors in an attempt to treat alzheimer disease and associated comorbidities. The conducted studies and their significant outcomes are discussed below.

Adetuyi et al., 2024 screened the antioxidant and anti-acetylcholinesterase effect of methanol leaf extracts of three Nigerian endemic plants, *Spondias mombin*, *Carica papaya* and *Kalanchoe crenata.* The study reported that in every experimental test, the plant's efficacy was as follows: *S. mombin* > *C. papaya* > *K. crenata.* They found highly significant positive relationships between the antioxidant activities and AChE inhibitory activityand total flavonoid and total phenolic contents. They found that these plant species provide significant secondary metabolite that can act as a natural antioxidant and acetylcholinesterase inhibitor, which will be aid in the treatment alzhiemer disease (Adetuyi et al.,2024).

Zavala et al., 2024 evaluate the neuroprotective effect of *Petiveria alliacea* plant species on scopolamine induce mice model. They administrated extract of plant at a dose of 500 or 900mg/kg for 21 days in mice. they reported that plant species exhibited protective effect, show decrease in oxidative stress and regulate cholinergic function in the brain having significant memory enhancing potency *(*Zavala et al., 2024).

Huang et al., 2023 evaluated the potential of methanol extract of *miracle fruit seed* for the treatment of alzheimer on mice model. They administrated 6mg/kg dose for 1 month. They reported that this therapeutic strategy accomplished by increasing the number of surviving neurons and modifying the insulin and Wnt signalling pathways. Furthermore, this finding increases the potential applications of Miracle fruit seed as a medicine and creates new avenues for the application of phytotherapy to treat alzheimer disease (Huang et al., 2023).

Mahnashi et al., 2023 evaluate that assess how the plant species *Desmodium elegans* works on to reduce the amnesia caused in scopolamine-induced animal model of alzheimer's disease. The current study's findings show that *D. elegans* contains pharmacologically active polyphenols, which may be involved in the plant's potential for neuroprotection. During in vitro experiments, DC was discovered to be biologically more active than any other fraction.

The test results of this shows that samples improve cognition performance and memory in animal model (Mahnashi et al., 2023). Shalaby et al., 2023 screened the neuroprotective effect of *ginsenoside Rb1* on the cerebral cortex in a mouse model of alzheimer disease. They administrated 70mg/kg/day to mice and measured all the oxidative parameters. Collected data from this study indicate *ginsenoside Rb1* a potential neuroprotective effect against alzheimer's via suppression of amyloid β and formation of phosphorylated tau protein. It also shows anti-apoptotic effect by minimizing gliosis (Shalaby et al., 2023).

Oyeleke et al., 2022 find out *Bacopa floribunda* plant extract exhibit antioxidant and anti-inflammatory effects on amyloid beta 1-42-induced alzheimer's disease in BALB/c mice. The outcomes of their study indicates that crude saponins and flavonoids from the *Bacopa floribunda* were able to neuroinflammation, microgliosis and oxidative stress. The higher dose of saponins (100mg/kg and 200mg/kg) and flavonoid (100mg/kg) were observed more effective. *(*Oyeleke et al.,2022). Huang et al., 2022 screened the neuroprotective effect of Chinese herbal extract for the treatment of alzheimer through apoptosis signaling pathway. They use 4 chinease herbal extract that has been previously investigated for its neuroprotective properties, including *Curcuma longa, Polygala tenuifolia Willd, Gastrodia elata Blume, and Acorus gramineus Aiton.* The aim of this study was to examine the targeted protein by GPCRAC extract and its synergistic protective effects for the treatment of alzheimer's disease. They discover that administering GPCRAC extracts effectively reduces scopolamine-induced cognitive impairment, possibly via modifying the apoptotic signalling system and dopaminergic synapse (Huang et al., 2022).

Abdallah et al., 2022 evaluate the effect of phenolic compound oleuropein (OLE) extracted from oleuropein rich olive leaf extract they aim to evaluate the effect of this phenolic compound at a low dose and observed their beneficial effects against the Aβ pathology of alzheimer disease in the homozygous 5xFAD mouse model. Findings demonstrated that OLE reduce the neuroinflammation by inhibiting NF-κB pathway and by activating RAGE/HMGB1 and NLRP3 inflammasomes (Abdallah et al., 2022.)

Nashar et al., 2022 evaluate the neuroprotective effect of Artichoke-Based nanoformulation against alzheimer induce mice model. Significant improvements in cognitive abilities and healing of spatial memory were noted, along with a significant decrease in the levels of tau protein, β-amyloid, and TNF-α, three inflammatory biomarkers. Mice administered free artichoke extract or artichoke-loaded SLNs demonstrated a considerably higher degree of neuroprotective effectiveness in dentate Gyrus sub-regions. The findings will affect the prospective medical picture for artichoke bracts, which were previously thought to be an agricultural waste product, and demonstrate the great potential of the extract as a botanical anti-AD medication (Nashar et al., 2022).

Anwar et al., 2021 screened A Leaf Extract of *Harrisonia abyssinica* and find out their neurobehavioural, histological and biochemical activity against aluminum chloride induce alzheimer disease in rat model. They administrated the *H. abyssinica* high dose of 200mg/kg /b.w in rat . In order to determine the neurobehavioural, histological, and biochemical activities of *Harrisonia abyssinica* leaf extract against aluminium chloride-induced alzheimer disease in rat models, Anwar et al., 2021 tested the extract. They gave rats a high dose of 200 mg/kg /b.w. of *H. abyssinica*. The adequate potential of the *H. abyssinica* extract component to block the AChE and ERK2 active sites was demonstrated by molecular docking (Anwar et al., 2021).

Rakesh et al., 2021 evaluate the ameliorative effect of myrcene in alzheimer disease induce mouse model. They give 100mg/kg/b.w dose via intraperitoneal route for 30 days . results of behavioural and oxidative stress indicate the significantly neuroprotective effect of myrcene. The best result in their study was obtained from a combination of drug myrcene and donepezil. It was found that in a both combinations alone and as a combined drug myrcene show potency for the treatment of alzheimer (Rakesh et al., 2021).

Luo et al., 2021 evaluate the effect of garlic extract against cognitive impairment and alzheimer disease. Analysis of their study shows that garlic extract could reduce the level of amyloid beta at cerebral brain region of animal model (Luo et al., 2021).

Shariare et al., 2020 evaluate the liposome based drug delivery system of *Aphanamixis polystachya* leaf extracts and their neurobehavioural activity in mice model. Data from an in-vivo neurobehavioural investigation showed that the liposomal batches significantly improved cognitive function, locomotion activity, and mobility performance of dementia-induced mice in contrast to the A. polystachya leaf extract alone (Shariare et al., 2020).

Shiekh et al., 2020 evaluate the potency of *Hibiscus sabdariffa* L plant extract as a neuroprotective agent against streptozotocin induce alzheimer disease in mice model. The histopathology immunohistochemistry, behavioural test and oxidative stress parameter results shows that extract prevent memory impairment, amyloidogenesis and neuroinflammation (Shiekh et al., 2020).

Lin et al., 2020 screened synergetic effect of *berberine* and *curcumin* on improving cognitive function in an alzheimer induce mice model. They reported that the mice's cognitive performance improved more with the combination *berberine* and *curcumin* treatment than with the single medicine, indicating the synergistic benefits of the two treatments. Furthermore, they discovered that the administration of both curcumin and *berberine* together had noteworthy synergistic effects on lowering the synthesis of soluble amyloid-β-peptide (1-42) (Lin et al., 2020).

Matthews et al., 2020 evaluate Caffeoylquinic Acids in *Centella asiatica* and their reverse cognition mechanism in Male 5XFAD alzheimer's disease mice model. This study assessed the role of caffeoylquinic acids (CQA) and triterpenes (TT), which are usually regarded as CA's active components, in the cognitive effects of CA water extract (CAW) in 5XFAD mice, an alzheimer's disease model. These findings support CQA's involvement in CAW's cognitive effects (Matthews et al., 2020).

Stefanescu et al., 2020 review the inhibitory property of various plant secondary metabolites against beta amyloid aggregation on transgenic mouse model of alzheimer disease. In their studies they conclude that that luteolin, myricetin, silibinin, and epigallocatechin-3-gallate can reduce aggregation to less than 40% (Stefanescu et al., 2020).

Therapeutic application of Curcuma longa for the treatment of AD

Curcuma longa (turmeric) is a perennial herbaceous plant that belongs to the Zingiberaceae family. It grows through rhizomatous growth. In South Asian civilizations spanning hundreds of years, turmeric has a rich historical and cultural legacy. Its medicinal qualities have led to its use in traditional chinese medicine, ayurvedic medicine, and other traditional healing systems. Most tropical locations, including sections of africa and the caribbean, china, india, and indonesia, cultivate turmeric.

In many religious customs, ceremonies, and activities, turmeric is used as a symbol of spiritual safeguards, success, and cleansing. Turmeric's flavour and scent are derived from the monoterpene and sesquiterpene essential oils it possesses. Turmeric essential oil mostly consists of α-turmerone, β-turmerone, α-phellandrene, and ar-turmerone. The nutritional value and functional qualities of turmeric are attributed to the presence of carbohydrates in its rhizomes, specifically starch, fibre, and oligosaccharides. Proteins and amino acids found in turmeric are vital for both human diet and for the proliferation and maturation of plants. Turmeric rhizomes are extracted using a variety of techniques, such as maceration, Soxhlet extraction, ultrasound-assisted extraction, and supercritical fluid extraction, to separate the bioactive components (Zhang et al., 2018).

Curcuminoids and volatile oils in turmeric extracts are frequently analysed qualitatively and quantitatively using high-performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS), and thin-layer chromatography (TLC). The spectroscopies of nuclear magnetic resonance (NMR), infrared (IR), and ultraviolet-visible are employed to characterise and clarify the structure of the phytochemicals found in turmeric.

Traditionally, people have taken turmeric to help with gastrointestinal issues like indigestion, bloating, and flatulence. Due to its anti-inflammatory qualities, turmeric is used to treat rheumatism, arthritis, and other inflammatory diseases by reducing pain and inflammation. When used topically to bruises and wounds, turmeric helps to minimise inflammation, halt infection, and speed up the healing process. Turmeric is used as a vasodilator and antibacterial to relieve respiratory problems such colds, coughs, and asthma. Turmeric's antibacterial and anti-inflammatory properties are used in skincare products to treat a range of skin issues, including psoriasis, eczema, and acne. The active ingredients in turmeric known as curcuminoids are believed to be responsible for its therapeutic effects. Curcumin, demethoxycurcumin, and bisdemethoxycurcumin are collectively known as curcuminoids. Curcuminoids have anti-inflammatory, antibacterial, anti-oxidant, and anti-cancer effects. The major bioactive compounds present in turmeric rhizomes. This yellow color compound curcuminoids isolated from turmeric rhizomes (kumari et al., 2021).

Curcumin is a polyphenolic compound with a distinctive chemical structure. Curcumin’s chemical structure is made up of two aromatic rings connected by a seven-carbon chain in the middle that has two hydroxyl (-OH) and two methoxy (-OCH3) groups. Curcumin's distinctive anti-inflammatory, antioxidant, and other pharmacological properties are imparted by this structure. There are three different isomeric forms of curcumin: curcumin I, which is the most common type, curcumin II, and curcumin III. Furthermore, a range of curcumin derivatives and analogues have been synthesized to improve the drug's stability, bioavailability, and therapeutic effectiveness. Examples are bisdemethoxycurcumin and demethoxycurcumin, which are respectively devoid of both and one methoxy group. When compared to curcumin, these analogues can have different pharmacological characteristics. Curcumin's biological actions are attributed to its pharmacophores, which includes curcumin's β-diketone moiety, which is present in the Enone form, is crucial for its antioxidant and metal-chelating characteristics, which allow it to scavenge free radicals and prevent oxidative stress. Hydroxyl groups: Curcumin's hydroxyl groups support both its antioxidant properties and its capacity to alter signalling pathways linked to inflammation, apoptosis, and cell division.

Unsaturated carbonyl groups: Curcumin's unsaturated carbonyl groups interact with nucleophilic amino acid residues in proteins, enzymes, and transcription factors to modify their behaviour and function (figure 3).

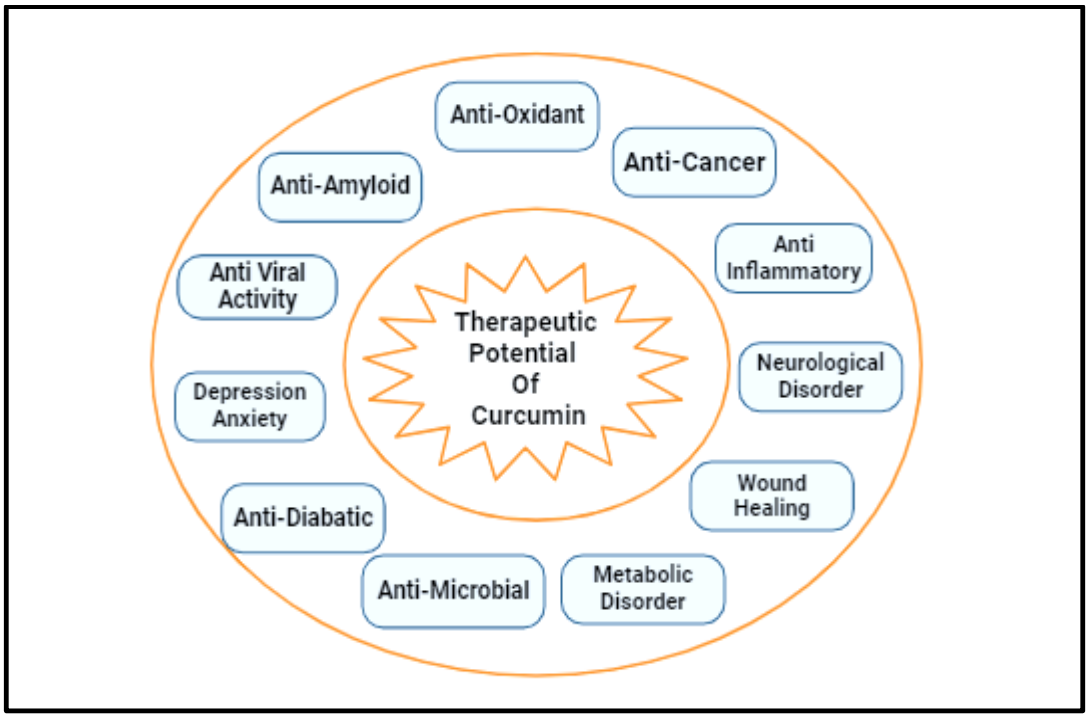

Figure 3 Therapeutic application of curcumin in various disorders

Several molecular targets and signalling pathways are used by curcumin to produce its pharmacological actions, including curcumin inhibits nuclear factor-kappa B (NF-κB), a crucial regulator of immunological responses and inflammation, which reduces inflammation and associated diseases. Nuclear factor erythroid 2-related factor 2 (Nrf2) pathway is activated by curcumin, which increases the expression of cytoprotective proteins and antioxidant enzymes that lessen oxidative stress and support cellular defence mechanisms. MAPK modulation: Curcumin inhibits proliferation and promotes apoptosis via controlling mitogen-activated protein kinases (MAPKs), including p38, JNK, and ERK, which are involved in cell division, growth, and apoptosis. The action of inflammatory mediators such as cyclooxygenase-2 (COX-2), lipoxygenase (LOX), and inducible nitric oxide synthase (iNOS) is inhibited by curcumin. This results in a decrease in the synthesis of pro-inflammatory prostaglandins, leukotrienes, and nitric oxide (Singh et al., 2019; Tønnesen et al., 2002).

Pharmacological activity of curcuma longa

Curcumin has strong pharmacological effects, but its low solubility in water, quick metabolism, and restricted absorption in the gastrointestinal system make it poorly bioavailable. After being taken orally, curcumin is extensively metabolised in the intestine and liver, producing glucuronides, sulphates, and reduction products, among other metabolites. Adjuvants, nanoparticle formulations, and structural changes to improve curcumin's pharmacokinetic characteristics are methods to increase its bioavailability. Researchers' comparative analysis of curcumin encapsulated in nanoparticle foam sheds light on the effectiveness, stability, and bioavailability of this innovative formulation. Even though every study is different in terms of technique and results, a comparison highlights the developments and trends in this sector.

Several researchers looked into the stability and release kinetics of foam nanoparticles loaded with curcumin. The stability of the nanoparticle foam was assessed by the researchers based on a number of variables, such as pH, temperature, and storage conditions. Additionally, they investigated the curcumin release profile from the foam nanoparticles in physiologically simulated settings. The results made clear how crucial formulation factors are for regulating stability and release kinetics and achieving the best possible therapeutic outcomes. Here, the comparative investigations conducted by different researchers are displayed in Table 1, which emphasizes the potential of curcumin foam nanoparticles as a promising drug delivery strategy for enhancing curcumin's therapeutic efficiency.

Table 1: Pharmacological study of *curcuma longa*

Formulation	**Dose concentration**	**Experimental studies**	**Inference**	**Reference**
Nanocurcumin	40mg/kg for 10 days	Chronic constriction injury model of neuropathic pain	Memory impairment improvement Decrease TNF-α and IL-1β in the hippocampal regions, Reduced responsiveness to pain	Saffarpour et al., 2021
Nanocurcumin and Extract of curcumin	2.5 mg/kg Orally for 30 days	Amelioration of deltamethrin-induced hippocampal damage	Antioxidant effect, better improvement found in nanoformulaton as compare to extract	Zaki et al., 2020
Nanocurcumin	Different concentration of 76 mg/ kg/day or 380 mg/kg/day Orally supplemented diets beginning at 4 weeks of age	Mouse model of Pten-defcient prostate cancer	Chemopreventive effect of nanoformulation	Velasco et al., 2020
Nanocurcumin and Extract of curcumin	5 mg/kg/7 days	Mouse model of alzheimer disease	Biocompatible CUR-loaded T807/RPCNP NPs may effectively scavenge ROS, inhibit the death of	Gao et al., 2020

			neuron-like cells, and lower intracellular p-tau levels to slow the progression of AD both in vivo and in vitro	
Curcumin oil	10 mg/kg orally In alternate days, every 48 h, alternate days for 12 days That is, mice were treated at days 2, 4, 6, 8, 10, and 12	Oxidative Stress Induced by b-Amyloid in Mice	Antidepressant-like effect of curcumin-loaded nanocapsules (NLC C) against the Ab25-35-induced neurotoxicity in mice	Fidelis et al., 2019
Curcumin lipid-core nanocapsules	50 mg/kg 14 days	Model Alzheimer's disease induced by β-amyloid 1-42 peptide in aged female mice	Neuroprotective effect	Giacomeli et al.,2019
Curcumin silk nano-microparticles	50 mg CUR/kg 100 mg CUR/kg	Comparative study between oral delivery of curcumin vs silk nano microparticles	Improved CUR bioavailability when silk nanoparticles were used as an encapsulation and delivery carrier as compared to the bare CUR crystals	Wu et al., 2018
Nanocurcumin	low as 2.5 to high as 25 mg/kg	Memory and Hippocampal MMP-2, MMP-9, and MAPKs in Adult Mice	Memory boosting effect was observed at doses as low as 15 and 20 mg/kg	Soukhak et al., 2018
PLGA-Nanocurcumin	(70µg/mg)so in 5 mg it will be 350µg/mg	Degenerative changes in experimental Cerebral Malaria	Better bioavailability of PLGA-curcumin. PLGA-curcumin has potential as an adjunct drug to treat human cerebral malaria	Dende et al 2017

PLGA nanoparticle	2 mg/kg	Mouse model of alzheimer disease	Decreased the level of Aβ, reactive oxygen species (ROS), TNF-α and IL-6, and enhanced the activities of super oxide dismutase (SOD) and synapse numbers	Huang et al., 2017
PLGA nanocurcumin	75 μg/kg/day 150μg/kg/day 300 μg/kg/day	Hemorrhage induced early brain injury in a rat model	Nanocurcumin diminishes leukocyte chemotaxis and subsequent inflammation	Chang et al., 2015
Curcumin Nanocurcumin	15 mg/kg	Lead-Induced Oxidative Stress in Mice	Lead-Induced Oxidative Stress in Mice	Flora et al., 2013

Preclinical research using animal models has shown that nanocurcumin is effective in lowering pathology indicators linked to alzheimer disease and improving cognitive impairments. To further evaluate the effectiveness and safety of nanocurcumin in human beings, clinical trials are now being conducted (Shah et al., 2019).

Conclusion

In conclusion, the utilization of curcumin nanoparticles emerges as a promising avenue in the treatment of Alzheimer's disease (AD). Through its multifaceted mechanisms of action, including anti-inflammatory, antioxidant, and neuroprotective properties, curcumin demonstrates immense therapeutic potential in targeting the underlying pathology of AD. The nanoparticle formulation enhances the bioavailability and stability of curcumin, overcoming the limitations of poor solubility and rapid metabolism, thereby optimizing its efficacy as a therapeutic agent. Additionally, curcumin nanoparticles exhibit improved blood-brain barrier penetration, facilitating direct delivery to the brain and enhancing its neuroprotective effects. Moreover, the safety profile of curcumin nanoparticles underscores its potential as a viable treatment option for AD, with minimal adverse effects reported in clinical studies. As research advances and clinical trials progress, curcumin nanoparticles hold promise as a safe and effective therapeutic strategy for combating the debilitating effects of Alzheimer's disease, offering hope for improved quality of life and better outcomes for patients and their families.

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