






# A Review of *Curcuma Longa* And Its Potential Benefits In Traumatic Brain Injury Recovery

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**Abstract:** Traumatic brain injury (TBI) poses a significant global health burden, often resulting in persistent cognitive and physical impairments. Despite advances in acute care, effective long-term treatments for TBI remain limited. *Curcuma longa* (turmeric) and its active compound, curcumin, exhibit promising neuroprotective properties, including antioxidant, anti-inflammatory, and neurogenic effects. This systematic review evaluates the potential benefits of *Curcuma longa* in TBI recovery. A systematic literature search was conducted in Scopus, PubMed, and Crossref databases, identifying studies from 2019 to 2024. Using the PRISMA guidelines, 237 articles were screened based on inclusion criteria, and 15 studies were selected for analysis. Key data on curcumin's therapeutic mechanisms, efficacy, and delivery innovations were extracted and synthesized. *Curcuma longa* demonstrates multiple therapeutic mechanisms in TBI recovery. Curcumin reduces oxidative stress via Nrf2 activation, modulates inflammation by inhibiting NF-κB signaling, and promotes neurogenesis through enhanced BDNF expression. Emerging delivery systems, such as nanoparticles and phytosomes, significantly enhance the bioavailability of curcumin, thereby addressing limitations in its clinical application. Compared to conventional treatments, curcumin offers a comprehensive approach that targets both secondary injury mechanisms and promotes recovery at the cellular level. *Curcuma longa* holds significant potential in advancing TBI management through its multifaceted therapeutic properties and innovative delivery systems. Future research and clinical trials are crucial for validating its efficacy and optimizing its application in clinical settings.

**Keywords:** *Curcuma longa*; traumatic brain injury; neuroprotection; curcumin; systematic review.

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## 1. Introduction

Traumatic brain injury (TBI) is a significant global health issue, with an estimated incidence affecting between 69 million and 74 million individuals annually worldwide [1–3]. TBI often leads to long-term cognitive, behavioral, and physical impairments. Studies indicate that approximately 30% of TBI survivors experience cognitive and behavioral declines, which can persist for years following the injury [4].

Traumatic brain injury (TBI) primarily results from accidents, falls, and other incidents. The World Health Organization estimates that TBI contributes to approximately 30% of all injury-related deaths, making it a leading cause of mortality and disability worldwide [5]. The Disability-Adjusted Life Year (DALY) index reflects the substantial burden of TBI, with millions of years lost due to disability and premature death attributed to this condition [6]. Despite advancements in acute care and rehabilitation techniques, effective treatment options for facilitating recovery and mitigating long-term damage from TBI remain limited.

*Curcuma longa*, commonly known as turmeric, has been widely recognized in traditional medicine and increasingly explored for its therapeutic properties, particularly in managing inflammatory and neurodegenerative conditions. The primary bioactive compound in turmeric, curcumin, exhibits a wide range of pharmacological effects, including anti-inflammatory, antioxidant, and neuroprotective properties, which make it a valuable candidate for treating various health issues [7, 8]. One study demonstrated that curcumin suppresses the inflammatory response in TBI models via the p38/MAPK signaling pathway, effectively reducing the activation of inflammatory mediators that contribute to neuronal damage [9]. Furthermore, curcumin has been reported to enhance the expression of brain-derived neurotrophic factor (BDNF), which is crucial for neuronal survival and plasticity, thereby supporting recovery following TBI [10].

Given the rising interest in natural therapies and the potential neuroprotective effects of *Curcuma longa*, it is essential to systematically examine the available literature to evaluate its role in TBI recovery. This systematic literature review aims to provide a comprehensive analysis of current findings on *Curcuma longa*'s potential in TBI recovery, highlighting its mechanisms of action, therapeutic benefits, clinical implications, and practical considerations of *Curcuma longa* in TBI recovery.

## 2. Methods

### 2.1. Review protocol.

The protocol was developed in accordance with the guidelines established by the Cochrane Collaboration for systematic reviews and aligns with the recommendations set forth in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) Statement [11].

### 2.2. Focus question.

The research question was formulated using the PICO framework, focusing on the following query: "What is the impact of *Curcuma longa* and its potential benefits in traumatic brain injury recovery?". The population targeted is represented by individuals with traumatic head injuries (THIs) or animal models. The intervention refers to the administration of *Curcuma longa* or curcumin in cases of traumatic head injuries. The comparison involves

subjects (human or animal) who received *Curcuma longa* treatment or were given standard treatments without *Curcuma longa* supplementation. The outcome highlights how curcumin and related treatments improve neurological recovery, reduce inflammation, and offer therapeutic potential in both human patients and animal models with traumatic head injuries and in various health conditions.

### 2.3. Search strategy.

This research constituted a systematic literature review investigating the impact of *Curcuma longa* and its potential benefits in traumatic brain injury recovery. The literature search was conducted in November 2024, using articles from well-regarded international journals sourced from the Scopus, PubMed, and Crossref databases. Keywords such as “*Curcuma longa*”, “curcumin”, “turmeric”, “traumatic”, “injuries,” and “effect” yielded 237 documents. Only articles published in English between 2019 and 2024 were considered. Boolean operators and wildcard characters were strategically applied throughout the search process to refine results and capture both singular and plural forms of terms across the databases.

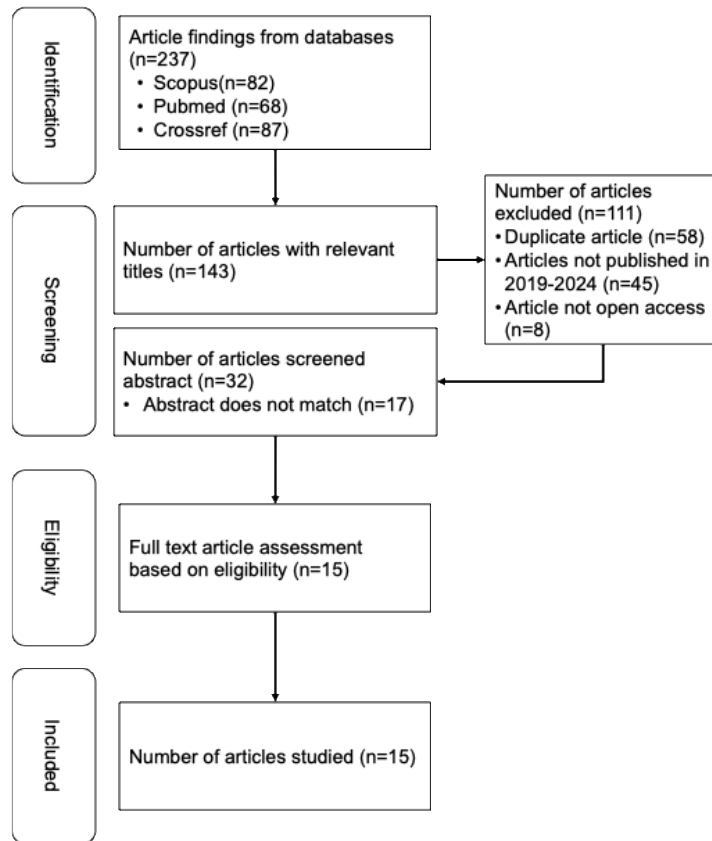
### 2.4. Study selection and eligibility criteria.

The systematic review process began with a comprehensive article search. To minimize errors and potential bias in the selection process, at least two researchers independently reviewed each article. The articles were initially filtered based on their titles and abstracts, followed by a full-text evaluation of those that appeared to be relevant. As a result, 15 articles were selected for inclusion in the review. Relevant data from 15 articles were extracted, including information such as the title, authors, publication year, study objectives, sample characteristics, research methods, and key findings. Subsequently, a narrative synthesis was performed to succinctly summarize the results and identify recurring patterns and themes across the studies.

A systematic review offers a rigorous methodology for addressing research questions and synthesizing evidence from multiple studies. It can provide stronger conclusions regarding the impact of *Curcuma longa* and its potential benefits in traumatic brain injury recovery. The inclusion and exclusion criteria for this study are outlined in Table 1 and Figure 1.

**Table 1.** Inclusion and exclusion criteria.

<b>Inclusion</b>	<b>Exclusion</b>
The article that discusses the impact of <i>Curcuma longa</i> and its potential benefits	Articles that are not related to the impact of <i>Curcuma longa</i> and its potential benefits
Research article English documents Published year 2019-2024 Available in full-text Open access Research conducted in many countries	Non-research article Non-English documents Published outside 2019-2024 Not available full-text Non-open access
Quantitative, qualitative, and experimental research methods	Systematic review method, literature review, non-research



**Figure 1.** Article extraction process flowchart.

### 3. Results and Discussion

#### 3.1. Data extraction from the literature results.

Based on search results using preset keywords and inclusion criteria, 237 potential papers were first obtained from three literature databases: Scopus (n=82), PubMed (n=68), and Crossref (N = 87). Following the title screening process, 143 articles with relevant titles were identified. After removing duplicate papers (n=58), those not published between 2019 and 2024 (n=45), and non-open access articles (n=8). A subsequent screening of abstracts resulted in the review of 32 papers, with 17 abstracts failing to meet the set criteria. A subsequent full-text inspection was performed to determine eligibility, resulting in the inclusion of 15 papers in the study (Table 2).

**Table 2.** Data extraction from literature.

Title, authors, year	Aim	Sample	Method	Result
“Combination of Curcumin with Autologous Transplantation of Adult Neural Stem/Progenitor Cells Leads to More Efficient Repair of Damaged Cerebral Tissue of Rat”[12]	To assess the effectiveness of curcumin combined with autologous neural stem/progenitor cell transplantation for repairing brain tissue after injury.	36 male Wistar rats	Neural stem cell cultivation, brain injury induction, and treatment with curcumin and stem cells.	Combination therapy reduced lesion size and improved neurological status.
“Insights Into the Authentic Active Ingredients and Action Sites of Oral Exogenous Glutathione in the Treatment of Ischemic Brain Injury Based on Pharmacokinetic-Pharmacodynamic Studies”[13]	To investigate the therapeutic effects of oral glutathione on ischemic brain injury and identify its active ingredients.	30 male Sprague-Dawley rats	Methods included I/R model creation in rats, oral GSH administration, and LC-MS/MS for quantitative analysis of metabolites.	Oral GSH significantly reduced infarct size and pro-inflammatory cytokine levels in rats, improving neurological function and cell viability in hCMEC/D3 cells.

Title, authors, year	Aim	Sample	Method	Result
“Long-Lasting Exendin-4-Loaded PLGA Nanoparticles Ameliorate Cerebral Ischemia/Reperfusion Damage in Diabetic Rats” [14]	The study aimed to assess the efficacy of Exendin-4-loaded PLGA nanoparticles in reducing cerebral ischemia/reperfusion damage in diabetic rats	The study involved 8 groups of rats.	The methods included administering Exendin-4 or PEx-4 via subcutaneous injection, inducing global cerebral ischemia, and conducting various biochemical and histological analyses.	PEx-4 showed a more sustained hypoglycemic effect and reduced brain edema more effectively than Ex-4 in diabetic rats.
“Long-Lasting Exendin-4-Loaded PLGA Nanoparticles Ameliorate Cerebral Ischemia/Reperfusion Evoked Brain Injury and Voiding Dysfunction in Diabetic Rats” [15]	To assess the effects of Exendin-4-loaded PLGA nanoparticles on brain injury and voiding dysfunction in diabetic rats.	80 female Wistar rats, including control and diabetic groups.	Bilateral carotid occlusion, treatment with Ex-4 or PEx-4, and assessments of oxidative stress and voiding function.	PEx-4 showed improved antioxidant activity, reduced brain edema, and enhanced voiding function compared to Ex-4 in diabetic rats.
“Neuroprotective Effects of Curcumin Through Autophagy Modulation” [16]	To explore curcumin's neuroprotective effects via autophagy modulation	Rats with traumatic brain injury and diabetes mellitus	Methods include in vitro assays and in vivo experiments to assess autophagy markers and neuroprotection	Curcumin enhanced autophagy markers and provided neuroprotection in various models
“Oxygen-Loaded Microbubble-Mediated Sonoperfusion and Oxygenation for Neuroprotection After Ischemic Stroke Reperfusion” [17]	To evaluate oxygen-loaded microbubble-mediated sonoperfusion for neuroprotection after ischemic stroke reperfusion	5 samples per group for the normal, S/R, CMB +, and OMB + groups, with some groups having 5-9 subjects	Methods included sonoperfusion, immunohistochemical staining, enzyme-linked immunosorbent assay, and quantitative polymerase chain reaction	Results showed an 87 ± 3% reduction in brain infarction and improved limb coordination after OMB treatment, with enhanced anti-inflammatory and anti-apoptotic responses
“Anticancer Efficiency of Curcumin on Ovarian Cancer” [18]	Evaluate curcumin's anticancer effects on ovarian cancer by assessing its impact on cell proliferation and migration	ONCO-DG-1 ovarian adenocarcinoma cell line cultures	The methods included cell culture, curcumin treatment, proliferation assays, and wound healing assays	Curcumin inhibited cell proliferation and migration in the ONCO-DG-1 cell line, with an IC50 of 17 µM
“Diarylidene-N-Methyl-4-Piperidone and Spirobibenzopyran Curcumin Analogues as Antioxidant and Anti-Inflammatory Pharmacophores” [19]	To evaluate the antioxidant and anti-inflammatory properties of curcumin analogs and improve their solubility and bioavailability.	30 compounds were synthesized: twenty-one diarylidene-N-methyl-4-piperidones, four diheteroarylidene-N-methyl-4-piperidones, and five spirobibenzopyrans.	Synthesis of compounds via alkali and acid-catalyzed reactions, followed by characterization using UV-Vis, FT-IR, NMR, and mass spectrometry.	The synthesized compounds exhibited significant antioxidant and anti-inflammatory activities, with improved solubility compared to curcumin.
“Anti-Inflammatory Effect of <i>Curcuma longa</i> and <i>Allium hookeri</i> Co-Treatment via NF-κB and COX-2 Pathways” [20]	To investigate the anti-inflammatory effects and mechanisms of <i>Curcuma longa</i> and <i>Allium hookeri</i> co-treatment.	Extracts of <i>Curcuma longa</i> and <i>Allium hookeri</i> .	Methods included cell viability assays, cytokine analysis, and HPLC/GC analysis for active compounds.	Results showed that co-treatment significantly inhibited NF-κB and COX-2 expression, reducing inflammation.
“Incorporation of Standardised Extract of <i>Curcuma longa</i> Linn Into Phytosomes and Its Evaluation for in Vitro Anti-Inflammatory Potential and	To incorporate <i>Curcuma longa</i> extract into phytosomes and evaluate its anti-inflammatory and cytotoxic effects.	<i>Curcuma longa</i> Linn extract	Maceration, Soxhlet extraction, phytochemical analysis, and FTIR compatibility studies	Phytochemical presence confirmed; anti-inflammatory and cytotoxic effects observed.

Title, authors, year	Aim	Sample	Method	Result
Brine Shrimp Lethality Assay” [21]				
“Curcumin Activates Nrf2 Through PKC $\delta$ -mediated P62 Phosphorylation at Ser351” [22]	To investigate how curcumin activates Nrf2 via PKC $\delta$ -mediated p62 phosphorylation.	Multiple samples, including various neuronal cell lines and p62 knockout mouse embryonic fibroblasts (MEFs),	Immunohistochemistry, qRT-PCR, cell culture, transient transfection, and luciferase assay.	Curcumin increased Nrf2 activation and phosphorylated p62 at Ser351, enhancing Nrf2 signaling.
“Liposomal Encapsulated Curcumin Effectively Attenuates Neuroinflammatory and Reactive Astrogliosis Reactions in Glia Cells and Organotypic Brain Slices” [23]	Assess the effects of liposomal curcumin on neuroinflammation and reactive astrogliosis in glial cells and brain slices.	The samples used in the study included human microglial cells (HMC3), human astrocytes (SVGA), and murine organotypic brain slices.	Methods included cell culture, stimulation with LPS and cytokines, treatment with liposomal or free curcumin, and analysis via qPCR, cytotoxicity assays, and immunohistochemistry.	Liposomal curcumin significantly reduced neuroinflammatory cytokine expression and reactive astrogliosis compared to free curcumin and controls.
“ <i>Curcuma longa</i> : Enhances IFN- $\gamma$ Secretion by Natural Killer Cells Through Cytokines Secreted From Macrophages” [24]	Investigate the effect of <i>Curcuma longa</i> on enhancing IFN- $\gamma$ secretion by natural killer (NK) cells through cytokines secreted from macrophages.	The samples used in the study included <i>Curcuma longa</i> extract (CLE), THP-1 macrophages, and NK-92 cells.	The methods included treating THP-1 macrophages with <i>Curcuma longa</i> extract, collecting conditioned media, and measuring IFN- $\gamma$ secretion in NK-92 cells using ELISA.	<i>Curcuma longa</i> extract significantly enhanced IFN- $\gamma$ secretion in NK-92 cells, with a 2.12-fold increase at 100 $\mu$ g/ml, primarily through cytokines secreted by THP-1 macrophages.
“Polymeric Nanoparticles Improved Curcumin Brain Delivery and Its Therapeutic Efficacy Against Intracerebral Hemorrhage” [25]	Enhance curcumin delivery and efficacy in treating intracerebral hemorrhage using polymeric nanoparticles	Samples included Curcumin-loaded polymeric nanoparticles, Madin-Darby canine kidney (MDCK) cells, zebrafish, and C57BL/6 mice.	Methods included anti-solvent precipitation for nanoparticle preparation, in vitro cellular uptake studies, and in vivo biodistribution assessments in zebrafish and mice.	Curcumin-loaded nanoparticles improved cellular uptake, enhanced brain delivery, and showed neuroprotective effects in ICH models.
“Curcumin-Loaded Nanoparticles: A Novel Therapeutic Strategy in Treatment of Central Nervous System Disorders” [26]	To assess curcumin-loaded nanoparticles for CNS disorders and enhance curcumin's clinical use	The review discusses various formulations of curcumin nanoparticles used in in vitro, in vivo, and clinical studies for CNS disorders.	The review analyzes the effects of curcumin nanoparticles through in vitro, in vivo studies, and clinical trials.	Curcumin-loaded nanoparticles improve bioavailability, reduce oxidative stress, and enhance therapeutic efficacy in CNS disorders.

### 3.2. Discussion.

#### 3.2.1. Mechanisms of *Curcuma longa* in TBI recovery.

*Curcuma longa*, commonly known as turmeric, has garnered significant attention in the context of traumatic brain injury (TBI) recovery due to its active compound, curcumin. The neuroprotective mechanisms of curcumin are multifaceted, primarily involving its antioxidant, anti-inflammatory, and neurogenic properties. One of the critical mechanisms by which curcumin exerts its neuroprotective effects is through the modulation of oxidative stress. TBI often leads to an increase in reactive oxygen species (ROS), which can exacerbate neuronal damage. Curcumin has been shown to enhance the expression of nuclear factor erythroid 2-related factor 2 (Nrf2), a transcription factor that regulates the expression of antioxidant proteins. This activation of Nrf2 results in a reduction of oxidative stress and lipid peroxidation, thereby protecting neuronal cells from damage following TBI [22, 27].

Inflammation is another significant contributor to the secondary injury processes following TBI. Curcumin has been demonstrated to inhibit the activation of pro-inflammatory pathways, including the nuclear factor kappa B (NF- $\kappa$ B) signaling pathway, which is often upregulated in response to brain injury [20, 28]. By reducing the expression of inflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF- $\alpha$ ), curcumin can mitigate the inflammatory response that typically follows TBI, thus promoting a more favorable environment for neuronal recovery [28].

In addition to these mechanisms, curcumin's potential to modulate autophagy has been highlighted as a protective strategy against TBI. Autophagy is a cellular process that removes damaged organelles and proteins, and its dysregulation can lead to neuronal death. Curcumin has been shown to induce autophagy, thereby promoting the clearance of damaged cellular components and enhancing neuronal survival [16].

Recent advancements in drug delivery systems, such as the use of nanoparticles, have also been explored to improve the bioavailability of curcumin in the brain, enhancing its therapeutic efficacy against TBI [25, 26]. These innovative approaches aim to overcome the challenges associated with curcumin's poor solubility and bioavailability, thereby maximizing its neuroprotective effects.

In summary, the mechanisms through which curcumin from *Curcuma longa* aids in TBI recovery include its antioxidant properties, anti-inflammatory effects, promotion of neurogenesis, and modulation of autophagy. These combined actions not only protect neuronal integrity but also facilitate recovery processes, making curcumin a promising candidate for therapeutic strategies in TBI management.

#### 3.2.2. Therapeutic benefits of *Curcuma longa* in TBI recovery.

*Curcuma longa*, commonly known as turmeric, has been extensively studied for its therapeutic benefits in the recovery from traumatic brain injury (TBI). The active compound in turmeric, curcumin, exhibits a range of neuroprotective properties that can significantly aid in the recovery process following TBI. These properties include antioxidant effects, anti-inflammatory actions, and the promotion of neurogenesis.

One of the primary mechanisms through which curcumin exerts its neuroprotective effects is by reducing oxidative stress, which is a significant contributor to neuronal damage following TBI. Curcumin has been shown to enhance the expression of antioxidant enzymes,

such as superoxide dismutase and catalase, thereby mitigating oxidative damage in neuronal tissues [22, 27]. Moreover, curcumin's ability to scavenge free radicals directly contributes to its antioxidant capacity, which is crucial in the context of TBI where oxidative stress levels are elevated [20].

In addition to its antioxidant properties, curcumin also plays a vital role in modulating neuroinflammation, which is a common consequence of TBI. Research indicates that curcumin inhibits the activation of the nuclear factor kappa B (NF- $\kappa$ B) pathway, which is responsible for the expression of pro-inflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF- $\alpha$ ) [28].

Furthermore, curcumin has been shown to promote neurogenesis, which is essential for recovery after brain injuries. Studies have demonstrated that curcumin enhances the expression of brain-derived neurotrophic factor (BDNF), a key protein involved in the survival and growth of neurons [16]. This neurogenic effect is particularly important as it may facilitate the repair of damaged neural circuits and improve cognitive functions following TBI [26].

Recent advancements in drug delivery systems, such as the development of curcumin-loaded hydrogels, have also been explored to enhance the bioavailability of curcumin in the brain. These innovative delivery methods aim to improve the therapeutic efficacy of curcumin by ensuring that adequate concentrations reach the target tissues in the central nervous system [25, 29] This approach maximizes curcumin's neuroprotective effects and minimizes potential side effects associated with systemic administration.

In summary, the therapeutic benefits of *Curcuma longa* in TBI recovery are attributed to its multifaceted mechanisms, including antioxidant activity, anti-inflammatory effects, and promotion of neurogenesis. These properties collectively contribute to neuronal protection and recovery, making curcumin a promising candidate for therapeutic strategies aimed at improving outcomes in individuals suffering from TBI.

### 3.2.3. Comparison of *Curcuma longa* to conventional treatments in TBI recovery.

The therapeutic benefits of *Curcuma longa* (turmeric) in the recovery from traumatic brain injury (TBI) have been increasingly recognized, particularly when compared to conventional treatments. Curcumin, the primary active compound in turmeric, exhibits several neuroprotective properties that can complement or enhance the effects of traditional pharmacological interventions.

One of the most significant advantages of curcumin is its potent antioxidant activity. TBI is associated with increased oxidative stress, which can lead to secondary neuronal damage. Curcumin has been shown to scavenge free radicals and enhance the activity of endogenous antioxidant enzymes, such as superoxide dismutase and catalase [22]. This antioxidant effect is crucial in mitigating the oxidative damage that occurs post-injury, a benefit that is often not fully addressed by conventional treatments, which may focus primarily on immediate symptomatic relief rather than long-term neuroprotection [27].

In addition to its antioxidant properties, curcumin possesses strong anti-inflammatory effects. It inhibits the activation of nuclear factor kappa B (NF- $\kappa$ B), a key regulator of inflammatory responses, thereby reducing the levels of pro-inflammatory cytokines such as TNF- $\alpha$  and IL-1 $\beta$  [20]. This anti-inflammatory action is particularly beneficial in TBI recovery, as inflammation can exacerbate neuronal injury and hinder recovery. Conventional treatments often rely on corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDs), which can

have significant side effects and may not provide the same level of neuroprotection as curcumin [28].

Recent research has also explored innovative delivery methods to enhance the bioavailability of curcumin, such as curcumin-loaded hydrogels and nanoparticles, which can improve its therapeutic efficacy in the brain [25, 26]. These advancements address one of the main limitations of curcumin, which is its poor solubility and absorption when taken orally. In contrast, conventional treatments often do not have such targeted delivery systems, potentially leading to suboptimal therapeutic outcomes [29].

While conventional treatments for TBI, such as hyperbaric oxygen therapy and pharmacological interventions, have shown promise, they often focus on the immediate management of symptoms and prevention of secondary injuries without addressing the underlying oxidative and inflammatory processes in a holistic manner [18]. In contrast, curcumin offers a multifaceted approach that not only targets these processes but also promotes healing and recovery at a cellular level.

In conclusion, curcumin from *Curcuma longa* presents a compelling alternative or adjunct to conventional treatments for TBI recovery. Its antioxidant, anti-inflammatory, and neurogenic properties provide a comprehensive therapeutic strategy that can enhance recovery outcomes, making it a valuable component in the management of traumatic brain injuries.

#### 3.2.4. Bioavailability challenges and solutions of *Curcuma longa* in TBI recovery.

The bioavailability of curcumin, the active compound in *Curcuma longa* (turmeric), poses significant challenges in its therapeutic application, particularly in the context of traumatic brain injury (TBI) recovery. Despite its well-documented neuroprotective properties, including antioxidant and anti-inflammatory effects, curcumin's clinical efficacy is often limited by its poor solubility, rapid metabolism, and low systemic absorption [19, 21].

The first bioavailability challenge of curcumin is hydrophobic, which limits its solubility in aqueous environments, leading to poor absorption in the gastrointestinal tract [30]. This low bioavailability is a significant barrier to achieving therapeutic concentrations in the bloodstream and, subsequently, in the brain. The second challenge is that once ingested, curcumin undergoes extensive first-pass metabolism in the liver, where it is rapidly conjugated and eliminated [13, 31]. This metabolic process significantly reduces the amount of curcumin that reaches the systemic circulation and the central nervous system (CNS), where it is needed for neuroprotection. The third challenge is that Blood-Brain Barrier (BBB) penetration presents another obstacle to curcumin delivery to the brain. Its tight junctions restrict the passage of many compounds, including curcumin, thereby limiting its neuroprotective effects in TBI [24].

One of the most effective strategies to enhance curcumin's bioavailability is the co-administration of bioenhancers such as piperine, a compound found in black pepper. Studies have shown that piperine can increase curcumin's bioavailability by up to 20-fold by inhibiting its metabolic breakdown in the liver [32]. This combination not only improves absorption but also prolongs the therapeutic effects of curcumin.

Phytosomes are complexes of phytochemicals with phospholipids that enhance the solubility and absorption of herbal extracts. Incorporating curcumin into phytosomes has been shown to significantly improve its bioavailability and therapeutic efficacy in various models, including those related to neurodegenerative diseases [17]. This technology could be particularly beneficial in TBI recovery, allowing for sustained release and enhanced delivery of curcumin to the brain.

Another innovative approach involves the intranasal administration of curcumin, which bypasses the gastrointestinal tract and first-pass metabolism, allowing for direct delivery to the CNS. This method has been shown to significantly increase the concentration of curcumin in brain tissues, enhancing its neuroprotective effects [25].

Hydrogel formulations that allow for sustained release of curcumin can also be employed. These systems can provide localized delivery of curcumin to the site of injury in the brain, potentially improving therapeutic outcomes in TBI [14, 15].

The bioavailability challenges of curcumin from *Curcuma longa* significantly limit its therapeutic potential in TBI recovery. However, innovative strategies such as the use of bio-enhancers, nanoparticle formulations, phytosome technology, intranasal delivery, and hydrogel systems offer promising solutions to enhance its bioavailability and efficacy. Continued research and development in these areas are essential to fully realize the neuroprotective benefits of curcumin in clinical settings.

### 3.2.5. Clinical implications and practical considerations of *Curcuma longa* in TBI recovery.

Curcumin's anti-inflammatory effects are particularly relevant in the context of TBI, where inflammation plays a critical role in secondary injury mechanisms. Studies have demonstrated that curcumin can significantly reduce levels of pro-inflammatory cytokines such as interleukin-1 beta (IL-1 $\beta$ ) and interleukin-6 (IL-6) following TBI, thereby mitigating cerebral edema and neuronal damage [33]. Furthermore, curcumin's ability to inhibit the NF- $\kappa$ B signaling pathway, which is often activated during inflammatory responses, further underscores its therapeutic promise [9].

In addition to its anti-inflammatory properties, curcumin has been shown to promote neuroprotection and enhance cognitive recovery post-TBI. Curcumin has been linked to the activation of neuroprotective signaling pathways, such as the PI3K/Akt pathway, which plays a crucial role in neuronal survival and function [34]. The practical considerations of curcumin administration in TBI recovery also merit attention. The bioavailability of curcumin has historically been a challenge; however, recent advancements in formulation techniques, such as liposomal encapsulation and hydrogel delivery systems, have shown promise in enhancing its bioavailability and therapeutic efficacy [23, 35]. For example, the construction of curcumin-loaded hydrogels has been explored as a method to deliver curcumin directly to the site of injury, potentially improving outcomes in TBI patients [35]. Additionally, combination therapies involving curcumin and other neuroprotective agents, such as neural stem cells, have demonstrated synergistic effects in promoting recovery from TBI [12].

## 4. Conclusions

*Curcuma longa*, particularly its active compound curcumin, demonstrates significant potential in traumatic brain injury (TBI) recovery through its antioxidant, anti-inflammatory, and neurogenic properties. Curcumin reduces oxidative stress, modulates inflammatory responses, and promotes neurogenesis, all of which support neuronal protection and recovery. Despite challenges with its bioavailability, advancements in drug delivery systems such as nanoparticles and hydrogel formulations show promise in enhancing its therapeutic effects. Compared to conventional treatments, curcumin offers a comprehensive, multifaceted approach to TBI management, making it a valuable candidate for improving recovery outcomes.

## Author Contributions

Conceptualization, AT., M.A., and A.A.I.; methodology, AT, P.K.; software, S.N., and A.A.; validation, A.A.I., M.A., and A.A.; formal analysis, S.S.; investigation, AT.; resources, S.S.; data curation, P.K.; writing—original draft preparation, AT.; writing—review and editing, M.A.; visualization, S.N.; supervision, A.A.I.; project administration, M.A. All authors have read and agreed to the published version of the manuscript.

## Institutional Review Board Statement

Not applicable.

## Informed Consent Statement

Not applicable.

## Data Availability Statement

Data supporting the findings of this study are available upon reasonable request from the corresponding author.

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## Conflicts of Interest

The authors declare no conflict of interest.

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