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Corresponding author:
Sasitorn Chusri

sasitorn.chu@mfu.ac.th

Author Affiliation:
Mae Fah Luang University, Chiang Rai, Thailand.

Curcumin and Dementia: A Systematic Review of Its Effects on Oxidative Stress and Cognitive Outcomes in Animal Models

Kehinde, SA; Lin, WP; Lay, BB; Phyo, KY; San, MM; Pattanayaiying, R; Chusri, S.

ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 1 May 2025 and was last updated on 1 May 2025.

INTRODUCTION

Review question / Objective To systematically evaluate the effects of curcumin on oxidative stress and cognitive outcomes in animal models of dementia. This objective aims to assess whether curcumin has neuroprotective properties, particularly its impact on reducing oxidative stress and improving cognitive functions in preclinical studies using animals as models for dementia.

Rationale A systematic review is necessary to synthesize and critically assess the current animal model evidence on curcumin's efficacy in reducing oxidative stress and improving cognitive outcomes. This can clarify its therapeutic potential and support further translational research in the context of dementia.

Condition being studied The condition being studied in the article "Curcumin and Dementia: A Systematic Review of Its Effects on Oxidative Stress and Cognitive Outcomes in Animal Models" is dementia.

METHODS

Search strategy We used descriptors indexed in the Health Science Descriptors and Medical Subject Headings. The terms used in the searches were Curcumin, Curcuma, in vivo, dementia, oxidative stress, neurodegenerative disease, frontotemporal dementia, neurodegeneration, neuroinflammation, mice, rats, synaptic, cognitive impairment, cognitive abilities, cognitive function, synaptic dysfunction, synaptopathies, neuropsychological functions, in English. The Boolean operators "AND" and "OR" were used to combine the descriptors. Both MeSH terms and keywords variations were used and articles limited

to “rodents” and English language” where possible. A comprehensive literature search of electronic databases using US National Library of Medicine and the National Institutes of Health, Pubmed- (http://www.pubmed.gov), SCOPUS (http://www.scopus.com), Allied and Complementary Medicine Database (AMED), AMED (https://www.ebsco.com/products/research-databases/amed) and Latin American and Caribbean Health Sciences Literature, LILACS (https://lilacs.bvsalud.org). These databases were searched for findings published until April, 2024. Only articles about original and experimental studies with rats and mice, and that investigated the antioxidative, anti-inflammatory and cognitive enhancing effects of curcumin/curcuma were considered. In addition, the reference lists of selected articles were manually analyzed to identify other relevant studies that could be included in this review. In studies with multiple interventions, only data from the curcumin/curcumin extract treated and control groups were considered in the systematic review. All the articles from these searches were exported to Ms Excel19 and duplicate records were deleted. Articles were firstly screened by reading titles and abstracts, and irrelevant articles were excluded. The remaining articles were then screened by reading the full text. Articles that were irrelevant or without available full text were also excluded.

Participant or population Animal models used in research to study dementia, typically rodents (such as mice or rats) that are experimentally induced or genetically modified to develop dementia-like symptoms.

Intervention The use of curcumin (a natural compound found in turmeric) administered to animal models to evaluate its impact on oxidative stress and cognitive outcomes related to dementia.

Comparator Vehicle control and positive control.

Study designs to be included The following study designs will be included: Inclusion Criteria Study Designs:1.In vivo experimental studies using animal models of dementia (e.g., Alzheimer’s disease, vascular dementia, or other neurodegenerative models).2.Controlled studies (both randomized and non-randomized) that evaluate the effects of curcumin on: Oxidative stress markers (e.g., MDA, SOD, GSH, ROS). Cognitive outcomes (e.g., performance in memory and learning tasks like the Morris water maze or novel object recognition).3.Intervention studies where curcumin is administered as a treatment or preventive.

Eligibility criteria To be eligible for inclusion in this systematic review, studies had to meet the following criteria: (1) they must be original research articles involving animal models of dementia, including but not limited to Alzheimer's disease, vascular dementia, or mixed pathologies; (2) the studies must have investigated the effects of curcumin, either in its pure form or as a major active component of turmeric, administered through any route and dosage; (3) the research must include assessments of oxidative stress markers (such as malondialdehyde, superoxide dismutase, or glutathione) and/or cognitive outcomes measured through validated behavioral tests (e.g., Morris water maze, Y-maze, or novel object recognition); and (4) the studies must be published in English, in peer-reviewed journals.

Information sources A comprehensive literature search of electronic databases using US National Library of Medicine and the National Institutes of Health, Pubmed- (http://www.pubmed.gov), SCOPUS (http://www.scopus.com), Allied and Complementary Medicine Database (AMED), AMED (https://www.ebsco.com/products/research-databases/amed) and Latin American and Caribbean Health Sciences Literature, LILACS (https://lilacs.bvsalud.org). These databases were searched for findings published until April, 2024.

Main outcome(s) This review critically examines a wide body of literature, encompassing studies that investigated curcumin’s potential as a therapeutic agent for dementia, a condition closely linked with oxidative stress and neuroinflammation.
The review synthesizes results from various animal studies, exploring different administration protocols, dosages, and treatment durations. One of the main findings across the studies is that curcumin consistently exhibits antioxidant properties, which are crucial in reducing oxidative stress, a key factor in the pathogenesis of dementia. In particular, curcumin was found to significantly reduce markers of oxidative damage, such as malondialdehyde (MDA), while increasing the levels of antioxidants like glutathione and superoxide dismutase (SOD). These findings support the hypothesis that curcumin might mitigate oxidative stress, which could contribute to slowing down the progression of dementia.
In terms of cognitive outcomes, a majority of the studies included in the review reported positive effects of curcumin on memory and learning tasks. For example, animals treated with curcumin performed better on tests such as the Morris Water Maze (MWM) and the Y-maze, which are used to assess spatial memory and cognitive flexibility, respectively. These improvements were observed

even with relatively short treatment durations, ranging from a few days to several weeks.
The review also emphasizes the variability in outcomes depending on the dosage and administration route of curcumin. Studies with higher doses or longer treatment periods tended to show more pronounced cognitive improvements and better reduction in oxidative stress markers. However, it also noted the challenges of curcumin's poor bioavailability, which may limit its effectiveness in vivo.
Overall, the review concludes that curcumin shows potential as a neuroprotective agent against dementia-related oxidative stress and cognitive decline in animal models. However, it stresses the need for more rigorous studies, including clinical trials, to fully establish curcumin's efficacy and optimal usage parameters for dementia.

Additional outcome(s) Not applicable.

Data management The review employs a well-defined mechanism for data collection and management, including identifying relevant studies through databases such as PubMed, Scopus, LILACS and AMED. Researchers initially set specific inclusion and exclusion criteria for studies related to curcumin's impact on oxidative stress and cognitive outcomes in animal models, ensuring that only the most pertinent data was collected.
Once the studies were identified, detailed records of each study's methodology, sample size, and outcomes were meticulously extracted and organized. Data management tools, such as spreadsheets were likely used to catalog and systematically store this information for analysis. Key variables, including the type of dementia model, curcumin dosage, duration of treatment, and cognitive assessments used, were documented to facilitate comparison across studies.
To ensure consistency, all data was reviewed by multiple researchers to minimize biases and discrepancies. This peer review process helped verify that the records accurately reflected the findings of the individual studies. The researchers also assessed the quality of the studies included in the review by using standardized scales, which helped to identify any potential limitations in the data or methodology of the studies.
The extracted data was then synthesized and analyzed to draw overarching conclusions about curcumin's potential in managing oxidative stress and improving cognitive function in dementia. Throughout this process, the review maintained detailed logs of all data points, references, and analyses, providing transparency and reproducibility for future research. By managing records in this structured and rigorous manner, the review ensures that its findings are both reliable and scientifically valuable.

Quality assessment / Risk of bias analysis The quality of the evidence across studies was assessed according to the Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies (CAMRADES), whose purpose is to improve the design, conduct, and reporting of preclinical studies in systematic reviews and meta-analyses. This assessment involved consideration of the risk of bias within studies, directness of evidence, precision of effect estimates, heterogeneity, and risk of publication bias. The risk of bias for included studies was evaluated using a checklist from the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE), based on the Cochrane Collaboration RoB Tool It consists of ten items within six main domains, namely selection bias, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias. The answer for the judgment of bias was either "Yes" to indicate a low risk of bias, "No" to indicate a high risk of bias, or "NC" to indicate an uncertain level of bias because of insufficient information. For each item, one point was given for "Yes". Two of us independently rated the studies as having "low", "unclear", and "high" risk of bias in six dimensions: sequence generation, baseline characteristics, allocation concealment (selection bias), random housing and blinding (performance bias), random outcome assessment and blinding (detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other sources of bias (other). Following the assessment of all studies, authors reported their respective results and discussed any differences to reach the final conclusion. Disagreements in scores were resolved through discussion with a third reviewer.

Strategy of data synthesis Two independent reviewers screened titles and abstracts to identify eligible studies. In cases of disagreement, a third reviewer resolved the conflict by determining whether the study met the inclusion criteria. To minimize subjectivity during data collection and entry, three reviewers independently extracted data from the included studies and recorded them in separate databases. Data were abstracted using standardized forms that captured key study characteristics, including first author, publication year, publication country, sample size, animal age, gender, and strain. Additionally, indices such as type of treatment, induction methods, dose, and

duration were also expressed. Physiological indices (oxidative markers, inflammatory markers) and behavioral/cognitive measures (e.g., learning memory, memory performance, locomotor activity, anxiety-like behavior, etc.) and statistical measures for each outcome (means and standard deviations) were documented. When effect sizes could not be extracted or calculated from the published data, corresponding authors were contacted via email for additional statistical information. Finally, the databases were cross-checked, and any discrepancies were resolved through discussion among the reviewers. To enhance the results' visual representation, the data were arranged and depicted with figures, and some were displayed as tables.

Subgroup analysis These analyses focus on specific aspects such as the type of dementia model used, the dose and duration of curcumin administration, and the specific outcomes measured (e.g., oxidative stress markers and cognitive performance). By examining these subgroups, the review aims to understand how different variables impact the effectiveness of curcumin in mitigating oxidative stress and improving cognitive outcomes in various animal models of dementia.

Sensitivity analysis The review examines the variation in the effects of curcumin across different experimental conditions, including different animal models, dosages, and durations of treatment. By conducting this analysis, the authors aim to determine whether the reported effects of curcumin on oxidative stress and cognitive outcomes are consistent and reliable, or if they are influenced by specific study factors.

Language restriction Articles written in English Language only were used for the review.

Country(ies) involved Thailand - Mae Fah Luang University, Chiang Rai, Thailand.

Keywords Curcumin, Curcuma longa, dementia, oxidative stress, neuroinflammation, antioxidant, cognitive function, animal models.

Dissemination plans The dissemination of the findings from the systematic review on curcumin and dementia will focus on reaching both academic and public audiences. First, results will be shared through academic journals, targeting those involved in neurodegenerative research, with particular emphasis on oxidative stress and cognitive function. Presenting the findings at relevant scientific conferences, such as those dedicated to neuroscience or pharmacology, will allow for expert feedback and broader visibility in the research community.

In addition, we will collaborate with research institutions and healthcare organizations to ensure the results are accessible to clinicians, caregivers, and policy makers. This could involve webinars, newsletters, and information leaflets that explain the implications of curcumin's potential in dementia treatment and prevention.

Finally, we aim to engage with the general public by publishing summaries of the findings on health blogs and through media outlets, including social media platforms. This will ensure that individuals affected by dementia, as well as those interested in preventive health, can access and benefit from the research, potentially guiding future clinical trials and treatment approaches.

Contributions of each author

Author 1 - Samuel Kehinde - Funding acquisition, Project administration, Data curation, and Writing – original draft, review, and editing.
Email: samuelabiodun.research@mfu.ac.th
Author 2 - Wai Phyo Lin - Methodology, Data curation, and Formal analysis.
Email: 6431804208@lamduan.mfu.ac.th
Author 3 - Bo Bo Lay - Methodology, Data curation, and Formal analysis.
Email: 6431306113@lamduan.mfu.ac.th
Author 4 - Khin Yadanar Phyo - Methodology, Data curation, and Formal analysis.
Email: 6531804115@lamduan.mfu.ac.th
Author 5 - Myat Mon San - Methodology, Data curation, and Formal analysis.
Email: 6531804120@lamduan.mfu.ac.th
Author 6 - Rinrada Pattanayaiying - Designed the experiments, Validation, and Supervision.
Email: rinrada.pa@ssru.ac.th
Author 7 - Sasitorn Chusri - Designed the experiments, Validation, Funding acquisition, Project administration, Supervision, Data curation, and Writing – original draft, review, and editing.
Email: sasitorn.chu@mfu.ac.th