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Impact of Mangosteen Peel and Centella Asiatica on Cognitive Function in Healthy Older Adults

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A B S T R A C T

Introduction: The increasing elderly population in Indonesia is accompanied by a growing risk of cognitive decline and dementia. Current pharmacological interventions have limited effectiveness and may cause adverse effects, highlighting the need for safe, natural-based alternatives. Mangosteen peel (*Garcinia mangostana*) and gotu kola (*Centella asiatica*) possess neuroprotective, antioxidant, and anti-inflammatory properties that may enhance cognitive function in older adults. **Objective:** This study aimed to evaluate the effectiveness of mangosteen peel and *Centella asiatica* extract supplementation in improving cognitive function among the elderly. **Methods:** A quasi-experimental pretest–posttest two-group study was conducted among 26 elderly residents at Griya Lansia Garut selected by purposive sampling. The intervention group received combined mangosteen peel and Centella asiatica supplementation for four weeks. Cognitive function was measured using MMSE, TMT-A, and Forward Digit Span, with data analyzed using Wilcoxon and Mann–Whitney tests ($p<0.05$). **Results:** The intervention group showed significant improvements in MMSE scores ($\Delta=2.15$; $p<0.001$), processing speed and attention as measured by TMT-A ($p=0.021$), and working memory as measured by Forward Digit Span ($p<0.001$). Between-group comparisons revealed significant differences in MMSE ($p<0.001$) and TMT-A score changes ($p=0.008$), whereas no significant difference was observed for Forward Digit Span ($p=0.458$). **Conclusion:** Supplementation with mangosteen peel and *Centella asiatica* extracts may improve global cognitive function and attention in elderly individuals. This combined botanical intervention shows promise as a supportive non-pharmacological strategy for preventing cognitive decline; however, larger randomized controlled trials are required to confirm its efficacy and safety.

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1. INTRODUCTION

The number of elderly people in Indonesia shows a significant upward trend. According to a report by CNN Indonesia, data indicate that in 2021 the elderly population accounted for approximately 12 percent of the total population, and this figure is projected to increase to 20 percent by 2045 (Ibrahim, 2025). This increase in the elderly population is a consequence of rising life expectancy and the success of health development efforts (Pinilih et al., 2018). However, the aging process is generally accompanied by physiological and degenerative changes, one of which is a decline in cognitive function.

Cognitive function plays a crucial role in supporting daily activities, encompassing memory, attention, language abilities, and problem-solving skills (Riani & Halim, 2019). Untreated cognitive impairment can progress to mild cognitive impairment (MCI) and eventually dementia. In Indonesia, the prevalence of dementia continues to show an increasing trend. In 2016, an estimated 1.2 million people were living with dementia, and this number is predicted to rise to 2 million by 2030 and more than 4 million by 2050 (Alzheimer Indonesia, 2019). Dementia is characterized by a progressive decline in multiple cognitive domains, including memory, language, orientation, attention, judgment, and decision-making abilities. This condition has a significant impact on daily activities, reducing independence and increasing dependence on others among the elderly (Tadjudin et al., 2024).

One possible approach to preventing or slowing cognitive decline in older adults is the use of natural-based therapies that have been proven to possess neuroprotective, antioxidant, and anti-inflammatory effects. In this regard, natural-based interventions such as mangosteen rind and gotu kola (Centella asiatica) offer a promising and relatively safe solution. Mangosteen rind is known to be rich in prenylated xanthone compounds, with α-mangostin (α-MG) as its main component (Tiang et al., 2020a). Mangosteen rind extract and α-MG have been reported to exhibit various pharmacological activities, including antidiabetic, antioxidant, anti-inflammatory, antitumor, antibacterial, and, most notably, neuroprotective effects (Mahmudah et al., 2024).

Furthermore, the use of mangosteen (Garcinia mangostana) peel extract may support improvements in cognitive function. According to Septiana et al. (2023), one of the main bioactive components in mangosteen peel is α-mangostin, a secondary metabolite successfully isolated from the extract. This compound is known to possess various pharmacological properties, including antioxidant and anti-inflammatory activities, and shows considerable potential in supporting the treatment of Alzheimer's disease. Research has demonstrated a mild improvement in cognitive function among elderly patients with Alzheimer's disease following six months of mangosteen peel extract administration (Muangpaisan et al., 2022).

Gotu kola (Centella asiatica) contains key triterpenoid compounds such as asiaticoside, madecassoside, and asiatic acid, which exhibit neuroprotective properties. Pharmacologically, gotu kola has been shown to increase cerebral blood flow, thereby optimizing the delivery of oxygen and nutrients to neurons, as well as stimulating neurogenesis and synaptic plasticity that support memory and concentration (Gray et al., 2016; Matthews et al., 2019a; Speers et al., 2021a). In vitro and animal studies have demonstrated cognitive-enhancing effects of Centella asiatica extract in mice (Gray et al., 2016). Changes in gene expression induced by Centella asiatica extract suggest an influence on mitochondrial biogenesis, which, together with the activation of antioxidant response genes, may contribute to improved cognitive function.

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From a mechanistic perspective, the combination of mangosteen rind and gotu kola has the potential to provide synergistic effects. Xanthones in mangosteen rind suppress inflammatory pathways and neutralize reactive oxygen species (ROS) (Catorce et al., 2016; Cho & Chin, 2016; Tiang et al., 2020b), while triterpenoids in gotu kola enhance mitochondrial biogenesis, activate endogenous antioxidant responses via the Nrf2 pathway, and support synaptic plasticity (Matthews et al., 2019b; Speers et al., 2021b). This synergy of antioxidant, anti-inflammatory, and mitochondrial function–enhancing effects may improve neural network integrity and enhance cognitive performance in older adults experiencing age-related physiological decline. Therefore, the combination of these two ingredients theoretically offers greater benefits than their individual use.

However, to date, the efficacy of combining mangosteen rind and gotu kola has not been scientifically established and requires further research to determine its safety, optimal dosage, and mechanisms of action in humans, particularly among older adults. Most existing studies have been conducted in animals and have examined only single ingredients in isolation, thus failing to provide a comprehensive understanding of their effectiveness in improving cognitive function in humans. Therefore, the purpose of this study is to evaluate the effectiveness of combining mangosteen peel and gotu kola in improving cognitive function in the elderly.

2. METHODS

Research Design

This study was designed as a quasi-experimental study employing a pretest–posttest control group design. This design was selected due to practical limitations in the field that prevented full randomization of participants, particularly among the elderly population at Griya Lansia Garut. Despite the absence of randomization, this approach allows for the evaluation of intervention effectiveness by examining changes in cognitive function scores before and after treatment in the intervention group and by comparing these changes with those observed in the control group.

Data analysis was conducted using nonparametric inferential statistics due to the relatively small sample size and the absence of an assumption of normal data distribution. The Wilcoxon Signed-Rank test was employed to assess differences in cognitive function scores before and after the intervention within each group. The Mann–Whitney U test was used to compare changes in cognitive function scores between the intervention group and the control group. The results of these statistical analyses were used to support claims regarding the effectiveness of the combined mangosteen peel and gotu kola extract intervention in improving cognitive function among older adults, with the level of statistical significance set at $p < 0.05$.

Population and Sample

In this study, the population consisted of all elderly residents of Griya Lansia Garut, aged 60-90 years, who met the inclusion criteria. A total of 87 elderly residents were registered at the institution. However, after a selection process with inclusion and exclusion criteria, the eligible population was confirmed to be smaller, thus increasing the homogeneity and relevance of the research data. Focusing on a specific population that meets these criteria is crucial for obtaining accurate research results and aligning with the research objectives regarding the cognitive function of the elderly.

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The purposive sampling method was used in this study as a sampling technique to select the most suitable individuals based on certain criteria, so that the selected sample has relevant characteristics in accordance with the research objectives (Borgstede & Scholz, 2021). The selected sample size consisted of 26 elderly individuals, divided into two groups: an intervention group comprising 13 elderly individuals who received supplementation with a combined extract of mangosteen peel and gotu kola, and a control group consisting of 13 elderly individuals who did not receive supplementation. The inclusion criteria for participants were elderly individuals aged 60 years or older, without severe hearing or vision impairment, and not suffering from advanced neurodegenerative diseases, to ensure valid and representative data (Mardiana & Sugiharto, 2022; Agnes Fridolin et al., 2022; World Medical Association, 2013). To assess the presence or absence of hearing impairment, an initial MMSE score screening was conducted. Elderly individuals were included in the sample if their initial MMSE score fell within the following ranges: 27-29 (pre-dementia), 18-26 (mild dementia), and 10-17 (moderate dementia).

Instrument

Cognitive function in this study was assessed using three standardized and validated instruments commonly applied in clinical and gerontological research: the Folstein version of the Mini-Mental State Examination (MMSE)**,** the Trail Making Test–A (TMT-A)**,** and the Forward Digit Span (FDS)**.**

The MMSE is a cognitive screening tool with a maximum total score of 30 points, designed to assess multiple cognitive domains, including: Orientation to time and place (10 points), Registration or immediate memory (3 points), Attention and calculation (5 points), Recall or delayed memory (3 points), Language and visuospatial construction abilities (9 points) (Folstein et al., 1975; Salis et al., 2023).

MMSE scores in this study were interpreted as follows: Scores of 27–29 indicate borderline cognitive function or pre-dementia, Scores of 18–26 indicate mild dementia, Scores of 10–17 indicate moderate dementia. Higher MMSE scores reflect better cognitive functioning.

The TMT-A was used to evaluate cognitive processing speed, visual attention, and basic executive function. Participants were instructed to sequentially connect numbers from 1 to 25 as quickly as possible. Performance was recorded in seconds, with shorter completion times indicating better cognitive performance (Reitan, 1958; Bowie & Harvey, 2006).

The Forward Digit Span assesses attention, concentration, and working memory capacity. Participants were asked to repeat a sequence of numbers in the same order as presented by the examiner. Scores were based on the longest correctly recalled digit sequence, with higher scores indicating superior working memory performance (Wechsler, 2008; Henderson et al., 2023).

To ensure consistency and objectivity in data collection, a standardized assessment checklist was implemented, which included: Adherence to standardized administration procedures, Maintenance of a controlled and distraction-free testing environment, Standardization of instructions provided to participants, Accurate score recording in accordance with official guidelines, and independent verification of assessment results by the researcher. The use of this checklist aimed to minimize measurement bias and enhance data reliability.

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Mangostic preparation

Mangosteen peel and Centella asiatica extract (Mangostic) were obtained from the Drug Industry, PT Berkah Alam Nusantara, Garut. Each capsule contains 500 mg. Mangostic was given 1,000 mg twice daily for four weeks, while the control group received nothing.

Research Procedures

The research procedure began with respondent screening. Forty-three elderly residents of Griya Lansia Garut met the inclusion criteria. They were then asked about their willingness to participate. Of the 43, 26 agreed. A pre-test was then conducted on three cognitive function questionnaires: the MMSE, TMT-A, and FDS. They were then divided into two groups: the intervention group and the control group. The intervention group consumed two mangosteen capsules every morning and two capsules every afternoon. Meanwhile, the control group continued their daily activities as usual. After four weeks of intervention, a post-test was conducted on the same three questionnaires. Data analysis was then conducted.

Data analysis

SPSS version 25 was used to analyze the data. The Wilcoxon test was used to examine the pre- and post-treatment samples. The Mann-Whitney test was used to compare variables between the two groups.

Ethics Approval

This research has received approval from the Ethics Commission of PPNI STIKEP West Java with number III/110/KEPK-SLE/STIKEP/PPNI/JABAR/XI/2023.

3. RESULT

The research results are presented in the table below. The results consist of respondent characteristics and outcomes before and after the mangosteen intervention. The study shows significant differences between the mangosteen peel and control groups in age (p = 0.440) and education level (p = 0.187), indicating relatively comparable characteristics. However, there was a significant difference in gender distribution (p = 0.030), with a male predominance in the mangosteen peel group (Table 1). Therefore, gender is a potential contributing factor and needs to be controlled for in further analyses.

Table 1. Respondents Characteristics

No	Variable	Mangosteen peel (n=13)	Control (n=13)	p
1	Age, mean (SD)	69.15 (5.11)	70.62 (6.46)	0.440
2	Sex, n (%)			
	Male	12 (92.3)	8 (61.5)	0.030*
	Female	1 (7.7)	5 (38.5)	
3	Education, n (%)			
	Elementary school	7 (53.9)	11 (84.6)	0.187
	Junior high school	3 (23.1)	0 (0)	
	Senior high school	2 (15.3)	0 (0)	
	College	1 (7.7)	2 (15.4)	

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Table 2. Comparative Study of Cognition Between Mangosteen Peel and Control Among Healthy Elderly

No	Cognition	Mangosteen peel (n=13)	Control (n=13)	p^b
1	MMSE, score			
	Pre	26.62 (2.26)	23.23 (3.72)	<0.001*
	Post	28.77 (2.13)	22.69 (3.90)	
	Δ	2.15 (1.52)	-1.46 (2.22)	
	p^a	<0.001*	0.131	
2	Trail Making Test-A			
	Pre	231.92 (190.91)	227.85 (64.29)	0.008*
	Post	93.77 (23.52)	216.46 (67.03)	
	Δ	-138.15 (186.78)	-11.39 (76.26)	
	p^a	0.021*	0.600	
3	Forward Digit Span			
	Pre	6.54 (1.05)	5.39 (1.50)	0.458
	Post	7.77 (0.60)	6.08 (1.32)	
	Δ	1.23 (0.93)	0.69 (2.18)	
	p^a	<0.001*	0.273	

Δ: difference pre and post intervention, p^a: Wilcoxon test, p^b: Mann-Whitney test, *Significant

The results shows that the mangosteen peel group showed significant cognitive improvements in MMSE (p<0.001), Trail Making Test-A (p=0.021), and Forward Digit Span (p<0.001) after the intervention, while the control group did not experience significant improvements (Table 2). The difference in change between the two groups was significant in MMSE (p<0.001) and Trail Making Test-A (p=0.008), indicating a positive effect of mangosteen peel on global cognitive function and attention/processing speed. However, improvements in working memory has not shown significant differences between groups.

4. DISCUSSION

The intervention demonstrated statistically significant improvements in cognitive function, particularly in global cognition (MMSE), processing speed (TMT-A), and working memory (Forward Digit Span) in the mangosteen peel group compared with the control group. These findings are promising and suggest that mangosteen peel supplementation may exert beneficial cognitive effects in healthy elderly individuals.

The observed effectiveness can be explained by several plausible mechanisms. Mangosteen peel is rich in xanthones, which have been shown to possess antioxidant, anti-inflammatory, and neuroprotective properties. (Dev et al., 2009; Fitriana, Anggadiredja, et al., 2021; Wattanathorn et al., 2008) These bioactive compounds may reduce oxidative stress and neuroinflammation—two key contributors to age-related cognitive decline—while supporting synaptic function and neuronal survival. Improvements in TMT-A performance further indicate enhanced attention and processing speed, domains that are particularly sensitive to oxidative and inflammatory damage in aging brains.

Cognitive decline is a major public health concern in the aging population, with increasing prevalence of mild cognitive impairment (*MCI*) and dementia. Currently available pharmacological interventions have limited effectiveness and are often accompanied by side effects, spurring interest in novel, multi-targeted, and safer interventions. Traditional medicinal plants, such as *Centella asiatica* (gotu kola) and *Garcinia mangostana (mangosteen*), have long

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been used in Asian medicinal systems to improve memory and brain health. Recent research focuses on their potential to modulate key neurobiological pathways involved in cognitive aging and neurodegeneration, including oxidative stress, inflammation, and mitochondrial dysfunction (Dev et al., 2009; Fitriana, Anggadiredja, et al., 2021; Wattanathorn et al., 2008).

Centella asiatica triterpenes, especially asiatic acid and madecasic acid, play a role in neuroprotection by activating the NRF2 antioxidant pathway through increasing the expression of *HO-1, NQO1, GCLC,* and *GPX4 genes* and decreasing *Keap1* , thereby strengthening cellular antioxidant defenses, suppressing oxidative stress, and protecting neurons from ferroptosis; In addition, *Centella asiatica* also improves mitochondrial bioenergetics and reduces mitochondrial dysfunction which is important for neuronal survival and synaptic plasticity, and increases synaptic plasticity through increasing the expression of AMPA receptor subunits GluA1 and GluA2 in the hippocampus, *BDNF* , and *TrkB* , with activation of *the ERK1/2 pathway* contributing to increased synapse density and learning and memory functions i (Zweig et al., 2021a, 2021b).(Sari et al., 2019; Speers et al., 2021; Wong et al., 2019; Zweig et al., 2021a, 2021b)

Centella asiatica influences synaptic and metabolic pathways by modulating purine, nicotinate/nicotinamide, and glycerophospholipid metabolism that play a role in the pathophysiology of Alzheimer's disease, changes that are associated with improved cognitive performance in animal models, while enhancing neurotrophic support through increasing *BDNF* and related signaling pathways to support neuron growth and survival; Meanwhile, mangosteen xanthones such as α-mangostin suppress neuroinflammation and apoptosis by modulating the PI3K/Akt/GSK-3β pathway thereby reducing tau phosphorylation and amyloid-beta deposition, inhibiting NF-κB activation resulting in decreased proinflammatory cytokines (TNF-α, IL-1β) and oxidative stress, increasing the clearance of tau aggregates through the proteasome system, and increasing *BDNF levels* to support synaptic health and function, so that overall these two botanicals work on complementary neuroprotective pathways, with *Centella asiatica* focusing on antioxidant, metabolic, and mitochondrial support, and mangosteen targeting tau/Aβ pathology and neuroinflammation (Chiang et al., 2025; Pang et al., 2023; Sari et al., 2019; Speers et al., 2021; Wong et al., 2019).

Pharmacokinetically, *Centella asiatica triterpenes* such as asiatic acid and madecasic acid have relatively good bioavailability, detected in plasma and urine, and are able to penetrate the blood-brain barrier, and the development of advanced formulations such as nanoemulsions has been shown to improve bioavailability as well as cognitive effectiveness in animal models; on the other hand, mangosteen xanthones still face limitations in the form of low oral bioavailability and brain penetration, so that although nanotechnology-based delivery systems have been proposed, their clinical effectiveness has not been confirmed through clinical trials (Fitriana, Darmawati, et al., 2021; Fitriana et al., 2024; Khurshid et al., 2018; Muangpaisan et al., 2022).

Overall, *Centella asiatica* is supported by strong preclinical evidence and moderate clinical support in improving cognitive function, particularly memory and executive function, through the mechanisms of NRF2 activation, enhanced mitochondrial function, and increased synaptic plasticity, and shows consistent synergy with aerobic exercise; Meanwhile, mangosteen offers promising mechanistic potential through anti-tau, anti-amyloid beta, and anti-inflammatory

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effects, but its clinical application is still limited due to bioavailability constraints and the lack of clinical trials involving elderly populations, with the note that both botanicals are generally safe to use although potential herb-drug interactions, especially in *Centella asiatica* , need to be considered in elderly patients with polypharmacy (Abdallah et al., 2021; Suhaili et al., 2025).

However, several important limitations must be acknowledged. First, the sample size was relatively small, which limits statistical power and generalizability. Second, the short duration of the intervention precludes conclusions regarding long-term cognitive benefits or sustainability of effects. Third, although statistically significant changes were observed, the clinical magnitude of improvement—especially in individuals with near-normal baseline cognition—requires cautious interpretation. Finally, potential confounding factors such as dietary intake, physical activity, and psychosocial stimulation were not fully controlled.

While short-term cognitive gains were evident, this study did not assess the long-term retention of cognitive improvements after the cessation of the intervention. Cognitive and functional benefits in older adults may diminish over time without continued stimulation or reinforcement. Therefore, future studies should evaluate whether periodic refresher interventions, either through repeated supplementation cycles or combined strategies such as cognitive training and physical exercise, are necessary to maintain cognitive gains. Longitudinal follow-up designs are recommended to determine the durability of effects and to identify optimal intervention frequency and duration.

From a broader perspective, the findings have potential implications for public health and aging-related policy, particularly in low- and middle-income settings where access to pharmacological cognitive enhancers is limited. Mangosteen peel, as a locally available and culturally accepted natural product, could be explored as a supportive, non-pharmacological strategy within community-based healthy aging programs. Integration into policy frameworks would require Collaboration with public health authorities and aging services to ensure safety, standardization, and quality control. Engagement with academic institutions and clinical researchers to generate stronger clinical evidence, Partnership with industry and agricultural sectors to support sustainable production and formulation. Scalability remains feasible given the relative affordability and availability of mangosteen peel; however, standardized dosing, formulation, and regulatory approval are critical prerequisites.

6. CONCLUSION

In conclusion, this study provides preliminary evidence that mangosteen peel supplementation is associated with promising improvements in several cognitive domains among healthy elderly individuals. While the results support its potential role as a supportive cognitive intervention, the findings should be interpreted cautiously due to methodological limitations. Further large-scale, randomized, and long-term studies are required to confirm efficacy, evaluate the sustainability of cognitive benefits, and establish its role within integrated cognitive health promotion strategies for aging populations.

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8. CONFLICT OF INTEREST

None

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