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ESSENTIAL OILS AND MINDFULNESS EXERCISES IN INFLUENCING GENE EXPRESSION INVOLVED IN MILD COGNITIVE IMPAIRMENT (MCI): A SYSTEMATIC REVIEW

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ABSTRACT

Mild Cognitive Impairment (MCI) represents a transitional stage between normal cognitive function and dementia, affecting memory and other cognitive abilities. This systematic review explores the impact of essential oils and mindfulness exercises on gene expression involved in MCI. Despite the prevalence of pharmacological treatments, they offer limited prevention of MCI progression to dementia. Non-pharmacological interventions, such as mindfulness exercises, have demonstrated cognitive benefits, albeit with moderate efficacy. Essential oils, used in aromatherapy, show promise in supporting cognitive improvement through their impact on amyloid-beta and cholinesterase pathways. This review synthesizes findings from multiple studies between 2017 and 2024, highlighting that combining essential oils and mindfulness exercises may offer enhanced therapeutic outcomes for individuals with MCI. Further research is needed to establish the efficacy of this integrative approach, which could slow the progression of MCI and improve patients' quality of life.

KEYWORDS *Mild Cognitive Impairment, Essential Oils, Mindfulness, Gene Expression, Non-Pharmacological Therapy, Cognitive Function.*

INTRODUCTION

Mild Cognitive Impairment (MCI) or Mild cognitive impairment is a transitional stage between normal cognitive function and dementia; in this case, a person will experience memory decline and other cognitive impairments to a mild degree and do not interfere with daily activities (Forlenza et al., 2013). The reported prevalence of MCI worldwide varies greatly from 3-42% (Ward et al., 2012). A recent report in the study by Ishikawa et al. (2022) shows that 27.5% of 1,985

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people affected by age-related MCI in communities with below-average social status will increase the risk of MCI twice as much as older people with above-average social status.

Although it does not interfere with activity, MCI, if left untreated, can put you at risk for more serious memory and cognitive function impairments such as dementia and Alzheimer's (Duara et al., 2016; Petersen, 2004). About 10-20% of individuals with MCI develop dementia each year, and the ratio is 10 times more risky than individuals without MCI (Knopman & Petersen, 2014). MCI is categorized into amnestic-MCI, which only impairs memory, and non-amnestic-MCI, which affects other cognitive functions (Van Giau et al., 2019). Most amnestic-MCI will develop into Alzheimer's disease while nonamnestic-MCI more often progresses to dementia (Geda, 2012; Roberts & Knopman, 2013). This means that MCI is indirectly the cause of death and quality decline for individuals aged ≥65 years through the development of dementia and Alzheimer's disease. This problem is a challenge for the health world to overcome cognitive impairment as early as possible.

Pharmacological treatment options such as donepezil, hyperzine A, Vitamin E, and cholinesterase inhibitors have been approved by the FDA for the treatment of MCI. However, these drugs cannot prevent or slow the risk of progression of MCI to dementia and Alzheimer's (Russ, 2014; Yue et al., 2012). So, non-pharmacological or psychotherapeutic therapy is needed, one of which is by the method Mindfulness. Therapy Mindfulness is one of the cognitive exercises that involves the development of consciousness by focusing on the experience that is happening deliberately and non-judgmentally (Kabat-Zinn 2003 in Wong et al., 2017). Mindfullness can be done formally (meditation) or informally by increasing awareness and attention in daily activities (Wong et al., 2017).

Many studies have proven the benefits of therapy Mindfulness in lowering stress, worry, depression and improving the patient's cognitive function (Hofmann & Gómez, 2017; Wells et al., 2019). However, the improvements resulting from the therapy Mindfulness on memory ability, and the ability to plan and solve problems is very small (Huckans et al., 2013; Li et al., 2011; Reijnders et al., 2013; Simon et al., 2012). In Review Rodakowski et al. (2016) explained that the treatment of MCI patients with therapy Mindfulness can have an impact on cognitive changes for the better and support patients' daily activities, but non-pharmacological therapy alone is not enough to provide significant changes to the patient's memory improvement. One of the therapeutic agents that can be chosen is essential oils (essential oil). This journal aims to explain the treatment of MCI using the mindfullness meditation method using aromatherapy from essential oils and evidenced by existing research data.

RESEARCH METHOD

This study uses a systematic review method Through data search using Harzing Publishing (http://www.harzing.com). The process of searching for data in the form of a journal uses three keywords, namely "Mild Cognitive Impairment, Essential Oils, Mindfulness". Furthermore, the three keywords are visualized using the software Vosviewer to see the pattern of relationships. The selected journals are

those that meet the following inclusion criteria: original article, published in English from 2017-2024, the study sample was individuals with MCI, and involved compounds or products containing essential oils. Since meditation is a major component of the practice of mindfulness, studies that explicitly feature forms of meditation as part of the intervention will be considered for data in this study. Exclusion criteria include systematic review journals, meta-analyses, case reports, abstracts, presentations, posters, and editorial letters. The review in this research was carried out in accordance with the guidelines Preferred Reporting Items for Systematic Reviews and Meta Anlyses (PRISMA) (Lomas et al., 2018).

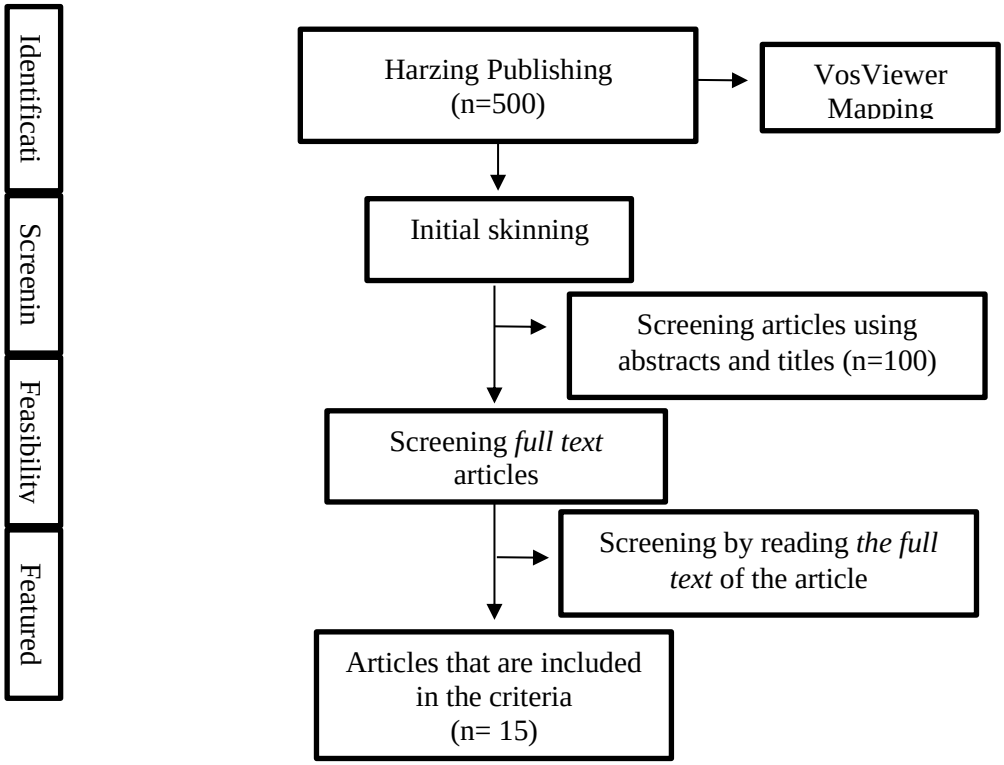

Figure 1. Article Collection Process Flow Char

The quality of the research methodology was assessed using criteria from the Cochrane Risk of Bias Tools method consisting of sample size, demographic characteristics, and study design. The selected journals are those that fall within the medium and high criteria. The criteria must contain the following:

Table 1.
Quality assessment based on the Cochrane Risk of Bias Tools

Criterion	Quality of research		
	Low (0)	Medium (1)	Height (2)
Sample size	No reports on sample size	There was a calculated sample size, but the subjects	The number of samples is calculated and the subject is adequate

		included in the study were not enough because there was a reduction	
Research design (randomization)	The randomizatio n sequence is unclear and it is not reported what method uses	The randomization sequence is obvious but the method is inefficient (e.g. drawn)	Adequate randomization (e.g., computer use Software, Random Number Table and minimization)
Research design (Treatment conditions)	Not using controlled conditions	Using actively controlled conditions (e.g., listening to music)	Suitable care conditions (i.e. dosage and duration, structured, controlling training at home)
Intervention	Lack of detailed explanations About the intervention and protocols	Explaining Mindfullness components such as breathing, meditation, etc.) or interventions using essential oils or aromatherapy	Well explained and comprehensive, such as skills/training sessions structured, meditation using aromatherapy, etc.

RESULT AND DISCUSSION

Article identification using Harzing Publishing obtained as many as 500 articles that mentioned one of the three keywords "Mild Cognitive Impairment, Essential Oils, Mildfullness". Before starting article screening, the three keywords are visualized using Vosviewer to see the network and mapping of the three keywords. The initial screening stage through title and abstract was obtained as many as 100 articles by deleting 400 other unrelated articles. A total of 100 articles were re-screened by reading the entire article (n=50) and then adjusted to the criteria that had been set. The results were obtained as many as 15 articles that met the criteria.

Table 2.
Cochrane Risk of Bias Tools quality assessment results

Research	Sample size	Randomization	Research design	Intervention
(Boiangiu et al., 2020)	2	1	1	2

(Olawuni et al., 2018)	0	0	1	2
(Tang et al., 2022)	2	1	2	2
(Siang et al., 2021)	2	0	2	2
(Guo et al., 2022)	2	1	1	2
(Xu et al., 2017)	2	1	1	2
(Strikwerda-Brown et al., 2022)	2	0	2	2
(Stuerz et al., 2022)	2	1	1	2
(Okuda et al., 2020)	2	1	1	2
(Siang et al., 2020)	2	0	2	2
(Chouinard et al., 2019)	2	1	1	1
(Hung et al., 2022)	0	0	1	1
(Bonan Liu et al., 2020)	2	1	1	2
(Capatina et al., 2020)	2	1	1	2
(Reitano et al., 2023)	2	1	1	2

Mindfulness and Mild Cognitive Impairment (MCI)

Mindfulness is an exercise based on awareness that arises when focusing on the moment we are living without judgment (Schuman-Olivier et al., 2020). The concept of mindfulness was then rearranged and adopted by counseling practitioners as part of the practice of therapy (Hanley et al., 2016). Historically, the practice of mindfulness was considered the cornerstone of contemplative living and was usually practiced in conjunction with other practices to improve quality and benefits (Dahl & Davidson, 2019). Psychological processes such as non-reactive attention and related metacognitive (introspective) skills developed through mindfulness are engaged and built in other forms of meditation including those that develop virtue orientation and self-inquiry.

The therapeutic properties of minfulness have been studied to explain its effect in improving cognitive function both in older adults at risk of dementia and those without. Cohort-based research was conducted on 261 participants by Strikwerda-Brown et al. (2023) during 2017-2019. Data is collected through questionnaires Five Facet Mindfulness Questionnaire (FFMQ) which contains 39 items, cognitive, longitudinal, and amyloid-β. FFMQ consists of five measurement subscales, namely Observing (aware, pay attention, internal and external stimulation), describing (verbally labeling and expressing experiences), acting with awarness (paying conscious attention to what is happening instead of acting automatically), nonjudgment (not judging one's own experience), and nonreactivity (the emergence of experience without reacting to it) (Baer et al., 2006). The analysis was carried out using the Multivariate partial least swuares method to test the relationship between the attributes of mindfulness consisting of decreased cognitive function, amyloid-β, and Tau. The results reported by Strikwerda-Brown et al. (2023) explain that high levels of nonjudgment, describing, and nonreactivity are associated with lower rates of cognitive failure, global cognition, and memory decline. The increase in mindful nonjudgment and nonreactivity levels was associated with a decrease in the tomography signals of Ab and Tau positron emission in the medial temporoparietal and lateral frontal and bilateral regions.

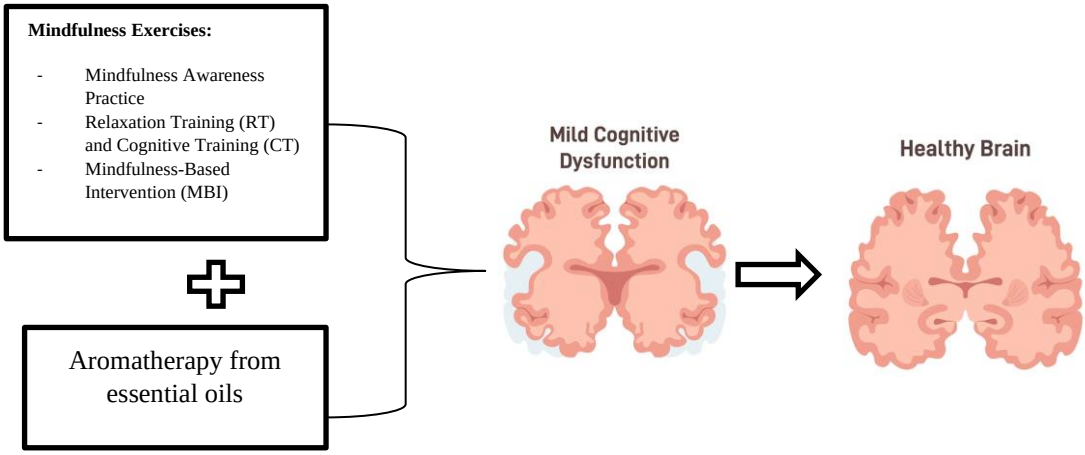

Figure 2. Illustration of Mindfulness and Essential Oils in Overcoming MCI

Mindfulness-based therapy is a therapy that incorporates the concept of mindfulness into therapy to teach mindfulness, ranging from formal meditation (e.g., sitting still for 45 minutes) to informal practice (e.g., bringing mindfulness into daily activities) (Baer, 2014). Types of mindfulness-based therapy consist of MindfulnessBased Stress Reduction (MBSR), Mindfulness-Based Cognitive Therapy (MBCT), Acceptance and Commitment Therapy (ACT), and Functional Analytic Psychotherapy (FAP). This review focuses on mindfulness therapy for MCI disorders regardless of the intervention ethode used.

1. Mindfulness Awareness Practice (MAP)

Mindfulness Awareness Practice (MAP) is a Singapore version of mindfulness intervention method that is modified from the MBCT method by MCBee and is specifically for the elderly (McBee, 2009). This method was used in the research of Siang et al. (2020) and Siang et al. (2021). The selection of this method is based on the type of method that is specifically focused on the elderly, in contrast to MBCT which is aimed at individuals in general. Assuming that the elderly participants can follow the training instructions well and maintain commitment until the end of the training session because of the simpler training model. Each session is led by an instructor who is certified and experienced in teaching MAP. The techniques carried out consist of:

a. Mindfulness exercises by engaging the senses

In this exercise it focuses on the different senses (sight, hearing, and touch) to cultivate focused attention. Participants were asked to pay attention to their body senses when doing daily activities, including brushing their teeth.

b. Breathing exercises with body scan exercises

Participants were asked to sit and be guided to develop kinesthesia by focusing on different parts of their body as relaxation techniques. In more detail, the participants were guided by the instructor to pay attention to one part of their body at a time, while imagining that the breath was directed to each area of the body and relaxed the muscles in certain areas. This process continues to be repeated to all parts of the body, starting from the upper part of the body to the bottom.

c. Movement Nature

Exercises in which students are taught to be aware of flexibility, strength, and confidence in movement. It is based on a method developed by Feldenkrais with the aim of restoring natural coordination and mobility of movements.

d. Visuomotor coordination duties

That is to train participants in mind-body coordination. The participants were guided to perform various cognitive demands involving the visual and motor systems. For example, the participants used one hand to perform a task with an elastic band and then quickly switched to performing the same task using the other hand.

e. Finally, stretching exercises

Aim to relax the muscles, by requiring participants to stretch their muscles mindfully, while sighing and releasing tension.

The training was divided into 2 sessions over 9 months. The first session lasted for 3 months, where in this session the intervention with the coach took place once a week with a training duration of 1 hour. The second session is called a booster session which lasts for 6 months. In the intervention booster session with the coach, it is carried out once a month with a training duration of 1 hour. The rest of the participants were asked to practice independently by providing a daily notebook. At the end of the session in the 9th month, the book will be collected. During the intervention process, samples were collected at months 0, 3, and 9 for testing. The test parameters consist of sociodemographic profiles, health screening, physical assessments (Activities of Daily Living and Instrumental Activities of Daily Living), Mini Mental State Examination (MMSE), Depression and Anxiety Screening Test, Clinical Dementia Rating (CDR), neurocognitive tests, MRI scans, blood, urine, feces, and saliva samples. The results of the intervention showed that MAP exercises can improve cognitive function in the elderly with MCI (Siang et al., 2020). Participants who were intervened with MAP showed a decrease in High-sensitivity C-Reactive Protein (hs-CRP) in the 9th month. The decrease in hs-CRP is more significant in women than in men. Meanwhile, the classification based on MCI subtype showed a decrease in hs-CRP only in the amnestic MCI group. Thus MAP improves cogniphytic function in specific MCI groups (Siang et al., 2020). Similar exercises were also carried out in the Reitano et al. (2023) study, where the intervention given to 22 MCI patients was in the form of an MBSR program consisting of body scans (15 minutes), Life review and Autobiograpical memory (15 minutes), and process0based cognitive axercise and metacognitive exercises (15 minutes). The exercise is carried out once a week for 8 weeks. The assessment consisted of the Montreal Cognitive Assessment (MoCA) score and the Beck Depression Inventory II (BDI-II) score. Samples were taken at the time before the intervention and after the intervention. Results showed significant improvements between time points in the global score of MoCA ($x2 = 4,000$, $p = 0.046$), the MoCA memory subscale score ($x2 = 4,571$, $p = 0.033$), and the cognitive BDI-II and affective factors ($x2 = 4,000$, $p = 0.046$) of only patients treated with mindfulness. Reitano et al. (2023) also reported a significant difference between scores before and after the intervention. This suggests that MAP exercises are effective in patients with MCI.

2. Relaxation Training (RT) and Cognitive Training (CT)

Relaxation Training (RT) is one part of the training Mindfulness (Francesco et al., 2019). Relaxation exercises are a modified technique of the method introduced by Jacobson, namely Progressive Muscle Relaxation (PMR) (Jacobson, 1938; Toqan et al., 2023). Stuerz et al. (2022) use this method to provide calm and rest for the nervous system so as to induce the central nervous system's reciprocity mechanism which will reduce stress and muscular tension (Stuerz et al., 2022). Cognitive Training or cognitive training is a pencil-based exercise (pancil Based Training), where participants are given a number of tasks with different levels of difficulty to complete. Cognitive training tasks are instructed by a clinical psychologist and include manual exercises for older adults that focus on creativity, perception, concentration, alertness, information processing, short- and long-term memory, speech fluency, memory retention, problem-solving, and logic (Lehner, 2010). The intervention was carried out on 53 elderly people diagnosed with MCI with MMSE scores ranging from 21-26 points and divided into two groups. Relaxation exercises are assisted by trained instructors and musical aids as a relaxation medium. The training lasts for 6 weeks which is divided into 2 stages. In the first stage, the first 27 group participants received relaxation exercises for 6 sessions that were carried out twice a week for 3 weeks. In the second stage, the first group received a short relaxation exercise combined with cognitive training for 6 sessions conducted twice a week for 3 weeks. While the second group was given cognitive exercises in the first three weeks and a combination of short cognitive exercises with relaxation exercises of the same duration and sessions. At the end of the session, data were collected in the form of sociodemographics, assessment of cognitive effectiveness and emotional status, MMSE, Age Concentration Test (ACT), Clinical Self-Rating Scale (CSRS-AMS), Geriatrci Depression Scale-Short Form (GDS-SF), and Visual Analog Scael (VAS) to assess pain experience. The findings of Stuerz et al. (2022) report that both RT and CT methods combined during the exercise period, respectively, can improve cognitive performance, well-being, decreased mood disorders, depression, and pain distress. The results of the study also showed that those who intervened with RT gave better results in terms of cognitive and emotional status in the elderly with MCI.

3. Mindfulness Based Intervention (MBI)

This method was used in the research of Chouinard et al. (2019). Mindfulness Based Intervention is a method developed by Larouche, Chouinard, et al. (2015) Adapted from the Mindfulness-Based Stress Reduction (MBSR) which has been widely used in the therapy of neurodegenerative diseases (Larouche, Hudon, et al., 2015). The practice of mindfulness is developed through four formal practices, namely body scanning, conscious movement, sitting meditation, and walking meditation, as well as daily informal exercises. Studies conducted so far show that MBI can be done by elderly people with physical or cognitive limitations, is more affordable, and has an impact on reducing Alzheimer's risk factors (Marciniak et al., 2014). The exercise was given to participants with amnestic MCI and lasted for 30-45 minutes, 6 days a week for 8 weeks. The exercise process consists of body scanning, mindful movement, mindful walking, sitting meditation, meta-meditation, and group discussions guided by the instructor. In addition, participants

were also asked to repeat the training session at home for about 30 minutes and were given a CD with a training guide. This method is compared to the exercise method Psychoeducation-based intervention (PBI) in different groups. At the end of the session, an assessment was carried out in the form of psychilogical stress and Carticol Awaking Response (CAR) by taking saliva samples. The results showed a slight decrease in CAR in the MBI group who practiced a lot at home compared to the PBI group. However, both MBI and PBI methods can improve healing and coping strategies.

Essential oils and Mild Cognitive Impairment (MCI)

Essential oils are a mixture of volatile compounds in the form of plant secondary metabolites. Essential oils can be found in plant parts such as leaves, seeds, flowers, roots, and bark (Ayaz et al., 2017). Its main constituents include monoterpene hydrocarbons, sesquiterpene hydrocarbons, oxygenated squiterpenes, oxygenated monoterpenes, and esters (Tongnuanchan & Benjakul, 2014). The benefits of essential oils in overcoming neurodegenerative problems have been widely proven in research. In this review, we focused on the benefits of essential oils against diseases Mild Cognitive Impairment (MCI) as the risk of Alzheimer's formation. In overcoming cognitive problems, it is necessary to study from the multifactorial and complex patiphysiological side. There are two hypotheses currently in use, namely the amyloid hypothesis and the cholinergic hypothesis.

Based on this, the class of drugs used to treat cognitive problems such as MCI, dementia, and Alzheimer's is acetylcholinesterase inhibitors (AChE inhibitors) (Haake et al., 2020). Research also reports that people with MCI and dementia show an increased risk of developing anxiety and depression compared to people with normal cognitive function (Tonga et al., 2020). It has also been proven that oxidative stress is an important factor in the three pathways of Alzheimer's progression, namely macromolecular peroxidation, amyloid-beta (A) metal ion redox potential, and mitochondrial dysfunction, all of which affect cell homeostasis, species reactive oxygen formation (ROS), and regulation of A and p-tau formation (Cassidy et al., 2020).

Essential oils from the plant are reported to restore cognitive function based on both the amyloid and cholinergic hypotheses as summarized in Table 2. Research Boiangiu et al., (2020) using mixed essential oils (MO) from five aromatic plants, namely sweet orange (68%), lemon (30%), lavender (1%), sage (0.5%), and rosemary (0.5%). The test was carried out in vivo involving rats divided into 7 groups, each group had 5 rats. The group consisted of, the control group, 2 groups treated with mixed essential oils (given MO1% and MO3%) without induction, the MCI induction group with scopolamine (Sco 0.7 mg/kg bb), the group given scopolamine + Donepezil (5mg/kg bb), the scopolamine + MO1% group, and the scopolamine + MO3% group. The duration of the study lasted for 23 days, on the 24th day data was taken. During the intervention period, animal habits (behavior analysis) were tested using the Y-Maze, Novel Object Recognition (NOR), and Radial Arm Maze. The test parameters consist of the analysis of chemical components with Gas Chromatography-Mass Spectrometry (GC-MS), Molecular Docking, and test microtiter enzyme to Acetylcholinesterase (AChE) and Butyrylcholinesterase (BChE) inhibitors. The results reported by Boiangiu et al

(2020) in their study were that there were 91.11% limonene compounds in the essential oil mixture used and were proven to have an interaction with the BChE enzyme modulated by the Van Der Walss (vdw) bond between limonene and SER198, HIS438, LEU286, VAL288, and PHE329 residues. In addition, MO may reduce AchE and BChe regulation and improve cognitive function in Scopolamine-induced mice.

Essential oils from plants Piper nigrym L and Monodora myristica has been reported to have a similar mechanism against AChE and BChE enzymes and can improve cognitive function by Olawuni et al. (2018). The research focuses on the invitro method using Electric eel acetylcholinesterase (AChE) and serum Butyrylcho-linesterase (BuChE) from horses. In addition, 02 ml essential oil intervention (concentration 50, 100, 200 mg/kg BB p.o) was carried out on mice that had been induced with scopolamine (0.4 mg/kg BB) for 7 days. The animals are assessed for their performance by measuring Step-Through Latency Time (SLT) and Escape Latency Time (ELT). The cholinesterase activity of mice was assessed by extracting their brain tissue at the end of the study. The results showed that M. myristica Dominated by compounds α-phellandrene (18.13%), while P. nigrum Dominated by β-pinene (5.92%) and caryophyllene (4,55%). Both essential oils produced significant inhibitory activity ($p>0.05$) at a concentration of 416 μg/ml, where M. myristica shows stronger inhibition against AChE and BuChE than P. nigrum. This trend was also shown significantly ($p>0.05$) in ELT and SLT when compared to the group that was only given scopolamine (Olawuni et al., 2018).

The effects of essential oils from different plants on AChE enzymes are reported by Hung et al. (2022). Essential oils extracted from Callicarpa sinuata, Callicarpa petelotii, Callicarpa nudiflora, Callicarpa erioclona and Vitex ajugifolia. Reported results show that Essential oil Callicarpa candicans showed resistance to AChE at IC50 values between 45.67 and 58.38 g/mL. Essential oils Callicarpa sinuata, Callicarpa petelotii, Callicarpa nudiflora, Callicarpa erioclona and Vitex ajugifolia showed good resistance activity at IC50 values between 28.71 and 54.69 grams/mL. Meanwhile, essential oils from lemon (LEO) were reported by Bonan Liu et al., (2020). Testing was performed on Alzheimer's mice Double Transgene APP/PS1, in which the mice showed significant memory deficits and synaptic density before being treated with essential oils. Test parameters using test Morris Water Maze (MWM), Novel object recognition, and correlative indicators, including neurotransmitters (acetylcholinesterase, AChE), nerve growth factors (Brain-derived neurotrophic factor, BDNF), postsynaptic marker (PSD95), and Presynaptic Markers (Synapsin-1and Synaptophysin). Administration of lemon essential oil showed an increase in postsynaptic marker (PSD95) and synaptic density as well as a decrease in acetylcholinestery rates in APP/PS1 mice (Bonan Liu et al., 2020).

Using different test animals, essential oils Rosmarinus officinalis reported to inhibit AChE enzyme in scopolamin-induced zebrafish (Capatina et al., 2020). Rosmari essential oil (concentration 25, 150, and 300 L/L) is given by soaking zebrafish (Danio rerio) once daily for eight days while induction of scopolamine (100 M) is administered 30 minutes before treatment. The test is assessed by the Novel Tank Diving Test (NTT) and the Y-maze test. The results showed that

rosemary essential oil could improve brain damage, memory, and cognitive function caused by scopolamine. In addition, AChE activity decreases after administration of essential oils (Capatina et al., 2020).

The amyloid hypothesis associated with a decline in cognitive function was reported by Okuda et al., (2020). This amyloid mechanism pathway is influenced by the administration of essential oils. In a study conducted by Okuda et al., (2020), the essential oils used came from a mixture of lemon + rosemary and lavender + orange essential oils. The research model used SAMP8/TaSlc mice whose cognitive function had been damaged. The first cycle of mice is exposed to a mixture of 15 μL of lemon and 30 μL of rosemary essential oil at night (from 8:00 p.m. to 8:00 a.m., group A) or a mixture of 30 μL of lavender and 15 oranges during the daytime (from 8:00 a.m. to 8:00 p.m., group B). In the second cycle, the mice were exposed to a mixture of 15 μL of lemon and 30 μL of rosemary at night (from 8:00 p.m. to 8:00 a.m.) and into a mixture of 30 μL of lavender and 15 μL of orange essential oil during the day (from 8:00 a.m. to 8:00 p.m.; group C). Each oil mixture is impregnated on a 10 cm filter paper and placed at a distance of about 30 cm from the cage. The research cycle lasted two consecutive days with a break of 2 days next for 9 weeks. At week 10, measurements of amyloid beta (Aβ) levels, abnormal phosphorylation of Tau, and Brain-Derived Neurotropic Factor (BDNF). The results reported that brain levels of abnormal Tau phosphorylated Aβ were much lower in the aromatherapy group, while BDNF levels were slightly higher. These results suggest that aromatherapy using aromatic essential oils is beneficial for the prevention and treatment of cognitive function (Okuda et al., 2020).

In addition to amyloid and cholinergic mechanisms, prevention of cognitive decline in MCI and Alzheimer's disease patients can also be done through other mechanisms. The content of amino acid neurotransmitters such as glycine and aspartate fluctuates in learning models and memory impairment (Wu & Zhang, 2018). It has been found in the urine of mice with Alzheimer's induced with traditional Chinese compounds Shengmai-San, the metabolism of glyoxylate and dicarboxylate (Yi et al., 2017). Research conducted Tang et al. (2022) found that citric acid in the group of mice induced cognitive impairment was lower than in the normal group. Citric acid is a substance contained in the mitochondrial tricarboxylic acid metabolic cycle, mitochondrial dysfunction is one of the pathological pathways of memory disorders and Alzheimer's (Perez Ortiz & Swerdlow, 2019). In addition, Tang et al. (2022) also reported the presence of glycine and azelaic acid in plasme samples, as well as aspartic acid in brain tissue samples of mice induced by cognitive impairment. Such metabolites are involved in biosynthesis (phenylalanine, tyrosine, arginine, aminoacyl-tRNA and tryptophan) and metabolism (phenylalanine, alanine, aspartate, beta-alanine, glyoxylic acid, dicarboxylates and glutamate, arginine. Administration of essential oils Cinnamomun camphore It has been shown to alter the megabolism of amino acids and changes in neurotransmitters and improve memory (Tang et al., 2022).

Research Guo et al., (2022) found that in mice induced aging with D-galactose, there were changes in the amino acids thymol and donepezil, as well as changes in the activity of AChE, superoxide dismutase (SOD), Glutathione peroxidase (GSH-PX), and Malondialdehyde (MDA). The pathophysiological

mechanism of cognitive impairment has also been found to occur through the activation of the protein kinase pathway (MAPK) and nuclear factor E2 related Factor 2 (NrF2). The results of the intervention carried out with Monarda didymal essential oil treatment showed that the thymol component in the essential oil can improve learning ability and memory impairment through the MAPK and NrF2 pathways (Guo et al., 2022). Meanwhile, lavender essential oils (100 mg/kg) and linalool (100 mg/kg) can inhibit the decrease in superoxide dismutase (SOD), glutathione peroxidase (GPX) activity, as well as inhibit the increase in AChE and malondialdehyde (MDA). In addition, lavender and linalool essential oils can also significantly protect the expression of NrF2 and heme oxygenase-1 (HO-1) and improve cognitive function in D-galactose and AlCl3-induced mice (Xu et al., 2017).

CONCLUSION

Essential oils that pharmacologically alter the regulation of AChE and amyloid-beta (A) related to cognitive function. Meanwhile, mindfulness exercises provide a boost to psychological improvement in MCI patients. Based on the above review, it can be concluded that essential oil compounds that have aromatherapy can be added to mindfulness exercise interventions to improve better therapy outcomes.

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