



## Aromatherapy in the Treatment of Alzheimer's Disease: A Systemic Review

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### ABSTRACT

Complementary medical therapy has received great interest within the field of dementia treatment and also the use of aromatherapy and essential oils is increasing. Essential oils from plants are used therapeutically for hundreds of years to enhance physical and psychological state, there's very little confirmed scientific proof of their efficacy. Therapeutic uses of essential oils is anticipated to drive the expansion, this is often expected to come up with vast demand for aromatherapy products. This review includes proof from mechanistic, neuropharmacological studies of the results of essential oils in relevant in vitro and in vivo models. It's over that aromatherapy provides a probably effective treatment for Alzheimer's. Clinical trials concluded provide a potentially effective and safe treatment for psychiatric disorders, including Alzheimer's. Aromatherapy has an efficacious non-pharmacological therapy for dementia. Aromatherapy may have some potential for improving cognitive function, especially in AD patients

**Keywords:** Alzheimer's Disease (AD), Aromatherapy, Cognitive function, Dementia.

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### INTRODUCTION

Alzheimer's disease (AD) could be a neurodegenerative disorder that's characterised by global cognitive decline together with a progressive loss of memory, orientation and reasoning.<sup>1</sup> Alzheimer is that the most typical explanation for dementia within the older patient and over thirty five million individuals everywhere the globe are tormented by dementia<sup>2</sup> and, in keeping with the survey created by the world Health Organization (WHO) in 2012, it was found that 54% of all the cases of dementia are AD-related. These data account for the social burden of AD worldwide. Other forms of dementia are vascular dementia, frontotemporal dementia, and Lewy body dementia. AD could be a progressive neurodegenerative disease characterised by cognitive and noncognitive dysfunctions.<sup>3</sup> Alzheimer's disease is characterised by the abnormal deposition of the amyloid  $\beta$  (A $\beta$ ) peptide, intracellular accumulation of neurofibrillary tangles of hyperphosphorylated  $\tau$  protein, loss of synapses and dendritic spines, cholinergic denervation, hypoperfusion and hyperaemia.<sup>4</sup> The  $\tau$  protein, represent mediators of neurodegeneration, that is among the most causative factors of impaired synaptic plasticity, neuroinflammation, a part of vascular reactivity impairment, cholinergic denervation, neurotransmitter imbalance, neuronal loss, nerve fiber alterations and

substantial synaptic loss through oxidative stress.<sup>5</sup> Although these are the basic goal within the future, the foremost frequent issue for individuals with AD remains the management of Behavioral and Psychological Symptoms of dementia (BPSDs)<sup>6</sup> and pain.<sup>7</sup> These pathological changes begin primarily in medial lobe anatomical structure then progress to the association cortices of the frontal, temporal and parietal lobe. Degeneration within the basal neural structure lead to a significant decrement in neocortical and hippocampal levels of the neurotransmitter acetylcholine.<sup>8</sup>

It's the sixth leading cause for all deaths and also the fifth leading cause for death in persons aged  $\geq 65$  years. The incidence in 2050 is expected to reach 1,000,000 persons per year, leading to a complete calculable prevalence of 11 to 16 million affected persons.<sup>9</sup>

Aromatherapy derived its name from the word aroma, which suggests fragrance or smell and medical therapy which suggests treatment. Aromatherapy uses essential oils to promote health and well being. The inhaled aroma is wide believed to stimulate brain function. Essential oil may also absorb through the skin, travel through blood and may promote whole body healing. This medical therapy could be a natural means of healing a human mind, body and soul.<sup>9-11</sup> Essential oils, as the main therapeutic agents, which are said highly concentrated substances extracted from flowers, leaves, stalks, fruits and roots, and also distilled from resins.<sup>12</sup>

Since the atypical antipsychotics should to be used solely in brief term treatment and not over twelve weeks, there has been growing interest within the use of aromatherapy for behavioral and psychological symptoms of dementia handling over the last years. The interest in aromatherapy for the treatment of many disorders like anxiety, mood



disorders, and certain forms of pain registered an excellent growth.<sup>13</sup> Furthermore, aromatherapy has provided the most effective proof, together with psychological treatment, for the management of agitation in Alzheimer disease.<sup>14</sup>

This article reviews the increasing proof in support of psychological interventions or alternative therapies (such as aromatherapy) as a first-line management strategy for agitation, moreover because the potential pharmacological alternatives to atypical antipsychotics.

### History of Aromatherapy

Although it should seem to be a newly discovered line of treatment, historic proof shows that aromatherapy dates back to as early as 1555 B.C. In Greece, Hypocrites, the father of medicine studied essential oils and suggested massages with aromatic oils and scented baths when treating his patients.<sup>15</sup> Modern aromatherapy originated in Germany within the sixteenth century. Hieronymus Braunschweig a German surgeon and botanist, wrote a book on distillation of oils from plants that included 25 oils.<sup>16</sup>

The aromatic oils are used for over 5000 years; ancient Egyptians used them as perfumes.<sup>17</sup> Gattefosse, a French chemist, investigated the bactericide and healing properties of essential oils during World War I to treat wounded soldiers and Valnet, a French army surgeon, further revived the appliance of aromatherapy during World War II.<sup>18</sup> India features a whole branch of ancient medication that is currently used as a holistic approach known as Ayurveda. It principally deals with massaging essential oils.<sup>15</sup>

### How Aromatherapy Works?

For centuries, the essential oils have found importance as a curative potential on the body, mind and spirit. These aroma molecules are very potent organic plant chemicals that create the environment free from disease, bacteria, virus and fungus.<sup>19-20</sup> These oils are well-known for their energy specific character, as their efficiency isn't lost with time and age. The stimulation properties of those oils lay in their structure which are closely in likeness with actual hormone.<sup>21</sup> The emotional significance of an odour is provided by the role of the amygdala within the cerebral analysis.<sup>22</sup> Therefore there's increasing interest in any pharmacological action of aroma therapeutics and therefore the terpenes found in aromatherapy essential oils, for example there are results regarding the flexibility of essential oils to boost neurotransmission by inhibiting acetylcholinesterase and increasing acetylcholine in cholinergic neurons to delay the neurological degeneration and cognitive decline that's characteristic in dementia. The penetration potential of those oils to achieve the connective tissue tissues is one in all the necessary characters of this medical therapy.<sup>23</sup> The mechanism of their action involves integration of essential oils into a biological signal of the receptor cells within the nose when inhaled. The signal is transmitted to limbic and

hypothalamus parts of the brain via olfactory bulb. These signals cause brain to release neuro messengers like serotonin, endorphin etc., to link our nervous and other body systems assuring a desired change and to provide a feeling of relief. Serotonin, endorphin and noradrenaline are released from calming oil, euphoric, and stimulating oil respectively to give expected effect on mind and body.<sup>24-25</sup>

### Complementary Approach Through Aromatherapy

Efforts to search out a cure for AD are dissatisfactory, and therefore the medication presently available to treat the disease address only its symptoms and with restricted effectiveness. The underlying pathogenesis could be a loss of neurons within the hippocampus, cortex, and subcortical structures.<sup>26</sup> Two categories of medication are currently approved by the U.S. Food and Drug Administration (FDA) to manage AD, as well as the AchE Inhibitors (AChEIs) like tacrine, donepezil, rivastigmine, and galantamine as well as the noncompetitive N-Methyl-D-Aspartate (NMDA) receptor antagonist, memantine.<sup>27-29</sup> Unfortunately, long-term use of these drugs are costly and have considerable side effects. Moreover, duration of their efficacy is limited and above all, a definitive cure could not be achieved.<sup>30</sup>

Aromatherapy is a type of phytotherapy that uses essential oils, extracted from the various parts of aromatic plants, more often administered via inhalation or topical application and massage for several minor clinical uses.<sup>31</sup> Aromatherapy has long been used for the treatment of BPSD to improve sleep<sup>32</sup>, reduce disturbed behavior<sup>33</sup> and facilitate desirable behavior.<sup>34</sup>

The potential use of natural products has been successfully demonstrated in the field of AD. In recent years, essential oils have attracted special attention. Indeed, the conclusions of several recent studies indicate that essential oils from tea tree oils, medicinal plants, and food crops show significant anti-cholinesterase inhibitory activity. The effects of *Salvia lavandulaefolia* essential oil and some of its constituents on acetylcholinesterase have been reported in vitro and in vivo.<sup>35</sup> Lemon balm is a potential medicinal and aromatic plant grown commonly most of our wild areas. Its essential oil is currently used in medicine and pharmacology of moderate Alzheimer's disease, modulation of mood and cognitive performance.<sup>36</sup> *Zataria multiflora* Boiss oil may be a potentially valuable source of natural therapeutic agents for alleviating cognitive symptoms of AD.<sup>37</sup> Limonene from the essential oil of lemon were tested in scopolamine induced dementia model by applying passive avoidance test and open field test. Limonene and its metabolite perillyl alcohol exhibited significant improvement in memory.<sup>38-39</sup>

Currently available treatments for AD focus on increasing ACh availability, it has been suggested that *S. lavandulaefolia* may provide a novel treatment for Alzheimer's disease.<sup>40-41</sup> A recent parallel-group, placebo-controlled trial reported some protection against declines



in cognitive performance in sufferers of mild to moderate Alzheimer's disease during 4 months administration of *S. officinalis*.<sup>42</sup> Aromatherapy using Bergamot essential oil can improve BPSDs and these effects could be due to the capability of this essential oil of increasing the levels of aspartate, glycine and taurine in a Ca<sup>2+</sup>- dependent manner after systemic glutamate and GABA in a Ca<sup>2+</sup>-independent manner through microdialysis in the hippocampus.<sup>43</sup> A placebo-controlled trial including 15

demented patients affected with agitation, as assessed by the PAS, which reported some effectiveness of 2% lavender oil aromatherapy stream.<sup>44</sup> Fractionation of the crude lemon balm hydroalcoholic extract, demonstrating anticholinesterase activity of most of the fractions, that resulted in being more active than the whole extract. The constituents of the most active fractions are cis- and trans-rosmarinic acid isomers and a rosmarinic acid derivative.<sup>45</sup>

**Table 1:** Evidence Based Aromatherapy

Essential oil	Type of study	Outcome	Reference
<i>Lavandula angustifolia</i> Mill, <i>Salvia rosmarinus</i> and <i>lemon citrus</i>	Human examined the curative effects of aromatherapy in dementia in 28 elderly people, 17 of whom had Alzheimer's disease (AD).	Aromatherapy has some potential for improving cognitive function, especially in AD patients.	46
<i>Lavandula angustifolia</i> Mill. and <i>Melissa officinalis</i>	To summarize the current finding on essential oils tested against neurodegenerative disorders like Alzheimer disease (AD) and dementia	EOs were effective on several pathological targets and have improved cognitive performance in animal models and human subjects	47
<i>Lavandula angustifolia</i> and <i>Lavandula hybrid</i>	To investigate the effects of lavender essential oils on neurological capacity of male Wistar rats subjected to scopolamine induced dementia rat model.	Multiple exposures to lavender essential oils could effectively reverse spatial memory deficits induced by dysfunction of the cholinergic system in the rat brain	48
<i>Pinus halepensis</i> .	To identify the neuroprotective and nootropic effects of <i>Pinus halepensis</i> essential oil in a rat model of acute amyloid beta (1-42) (A $\beta$ 1-42) toxicity.	<i>Pinus halepensis</i> essential oil has nootropic and neuroprotective activities and may be regarded as a therapeutic tool for attenuation of A $\beta$ toxicity and neuronal dysfunction	49
<i>Lavandula angustifolia</i>	Study examines the effects of aromatherapy massage on alleviating agitation and depressive mood in individuals with dementia.	Aromatherapy massage can be an effective and safe intervention to alleviate specific agitated behaviors and depressive mood in individuals with dementia.	50
<i>Tetraclinis articulata</i>	This study investigated the effects of <i>T. articulata</i> essential oil on memory and brain oxidative stress in amyloid- $\beta$ peptide 1-42 (A $\beta$ 1-42)-induced an Alzheimer's disease amyloidosis model.	The study demonstrates that the essential oil could be a potent pharmacological agent against dementia by modulating cholinergic activity and promoting antioxidant action in the rat hippocampus	51
<i>Salvia lavandulaefolia</i>	This study utilised a placebo-controlled, double-blind, balanced, in order to comprehensively assess mood and cognition modulation by <i>S. lavandulaefolia</i>	Results represent evidence that <i>Salvia</i> is capable of acute modulation of mood and cognition in healthy young adults	52
<i>Pimpinella peregrine</i>	The effects of inhaled <i>Pimpinella peregrina</i> essential oil on scopolamine-induced memory impairment in laboratory rats. Y-maze and radial arm-maze tests were used for assessing memory processes.	Studies on the <i>P. peregrina</i> essential oil opens a new therapeutic window for the prevention of neurological abnormalities closely related to Alzheimer's disease	53
<i>Rosmarinus officinalis</i>	To study the effect and mechanism of action of essential oil from <i>Rosmarinus officinalis</i> , which has been suggested to be effective for improving cognitive function, on Alzheimer's type dementia.	The effect of improving cognitive function by inhaled administration of rosemary essential oil, which has been used empirically	54
<i>Mentha longifolia</i>	to evaluate anti-acetylcholinesterase, anti-inflammatory and antioxidant activities of <i>M. longifolia</i> extract for treating the disease	<i>M. longifolia</i> extract and essential oil may have anti Alzheimer effect through their effect as antioxidant agents, anti-inflammatory agents and as acetylcholinesterase inhibitors.	55

<i>Citrus bergamia</i>	Bergamot ( <i>Citrus bergamia</i> ) is a fruit most knowledgeable for its essential oil (BEO) used in aromatherapy to minimize symptoms of stress-induced anxiety and mild mood disorders.	the mode of action of this phytocomplex on nerve tissue under normal and pathological experimental conditions and provide a rational basis for the practical use of BEO in complementary medicine.	56
<i>Origanum majorana</i> L	<i>Origanum majorana</i> L. essential oil (EO) was analyzed by gas chromatography-mass spectrometry (GC-MS) and evaluated for free radical scavenging and anticholinesterase activities	<i>Origanum majorana</i> L essential oil has a significant potential to be used as a natural antioxidant and anti-AChE	57
<i>Artemisia macrocephala</i>	Screening of the essential oil of <i>A. macrocephala</i> for AChE and BChE inhibition potentials	The study confirms the beneficial applications of the oil sample in the treatment of various neurodegenerative disorders including Alzheimer's disease, and all other forms of dementia.	58

## CONCLUSION

There is no doubt that components from EOs are often absorbed through the skin, enter into the circulation then cross the BBB. Therefore, topical application or inhalation of EOs may produce an impact on the nervous system that's not purely psychological. In present study we conclude that aromatherapy an efficacious non-pharmacological therapy for dementia. Aromatherapy may have some potential for improving cognitive function, especially in AD patients. Additional basic research effort is necessary to understand the pharmacological mechanisms underlying aromatherapy. Finally, it's fundamental to hold out clinical research for ensuring an accurate and safe application of aromatherapy.

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