

## Review

### Efficacy of aroma therapy for dementia

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#### Abstract

**[Background]** Dementia is characterized by progressive loss of memory and cognitive function, various behavioral and neuropsychiatric disturbances. It is one of the most important care problems in the aging populations. The olfactory limbic system is associated with emotion and memory function. Current pharmacological approaches for dementia are merely palliative. It is increasingly recognized that non-pharmacological options should be pursued.

**[Objective]** The aims are to review systematically English literature on aromatherapy for dementia up to July 2010 and to make clear the efficacy of aromatherapy for dementia.

**[Design]** A randomized control trial regarding aromatherapy for dementia.

**[Method]** The English language literature up to July 2010 were searched by the databases PubMed and ALOIS, and bibliographies. The search terms: aromatherapy, complementary therapy, alternative therapy, essential oil, and dementia were used. The inclusion criteria were existence of informed consent, mention of details of randomized technique, detailed transition of the number of dropouts, justification, standardization of outcome measurements, blind evaluation of the evaluator, and clearly presented outcome indications. The exclusion criteria included studies in non-English publications without English abstract, pharmacological interventions, screening instrument studies, and normal clinical trials without control group. There was no restriction on the length of the intervention trial or number of cases. Cognitive function, quality of life, relaxation were selected as the treatment outcomes.

**[Results]** Seven randomized controlled trials were extracted, of which six researches showed that the aromatherapy intervention had statistically significant treatment outcomes.

**[Discussion]** Although the extracted six studies showed efficacy in treatment outcomes by aromatherapy intervention, the numbers of the patients in those referred six studies were relatively small and the meta-analysis of them could not be performed.

**[Conclusion]** Carefully designed, large-scale randomized controlled trials will be investigated to remedy the current scarcity of evidence regarding aromatherapy, and further evidence for efficacy of aroma therapy for dementia is needed.

**Key words:** systematic review, complementary therapy, essential oil, lavender, lemon balm

## 1. Introduction

Dementia is a loss of cognitive abilities<sup>39)</sup> that leads to impairment in memory, reasoning, planning, and personality<sup>36)</sup> that seriously interferes with daily life. Dementia is a group of symptoms caused by gradual death of brain cells or amyloid deposition<sup>21)</sup>. According to World Alzheimer's Report 2009<sup>42)</sup> (a survey conducted in 2009 by Alzheimer's Disease International), the number of dementia patients will reach to 65.7 million in 2030. The prevalence of dementia is expected to roughly double every 20 years. The treatment, prevention, and care of dementia patients are important health problem in the aging populations<sup>43)</sup>.

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There are several types of therapeutic drugs that inhibit progression. Pharmacological approaches involve neuroleptic or other sedative medication<sup>1)</sup>. No specific therapeutic drug has been developed for improving dementia-related impairment of cognitive function. Current pharmacological approaches for dementia are primarily palliative. It is also known that there have been cases of serious side effects<sup>15)30)</sup>. Therefore, non-pharmacological options might be pursued first. The traditional non-pharmacological treatments include behavioral therapy, reality orientation approach and validation therapy, cognitive therapy, multisensory therapies and aromatherapy<sup>14)</sup>.

Essential oils have been used to treat symptoms and diseases for thousands of years. The term aromatherapy was used by a French chemist Gattefosse who had published a text in 1936<sup>11)</sup>. Aromatherapy is the therapeutic use of essential oil from herbs, flowers, and other plants<sup>31)</sup>. Essential oils have been used in the British National Health Service<sup>35)</sup>, and other western civilized countries.

Essential oils have been defined as non-oily, highly fragrant essences extracted from plants by distillation, which evaporate readily<sup>24)</sup>. They are most commonly used in oil burners, in bath water, or massaged into the skin. Essential oils apply directly to the skin with rapid absorption through the skin into the bloodstream within 10–30 minutes<sup>7)16)</sup>. Essential oils particles travel directly through the olfactory bulb to the limbic system, thus the aroma of the essential oil evaporates and stimulates the olfactory sense<sup>24)</sup>. Essential oils are said to have antifatulence, anticolic properties<sup>34)</sup>, antibacterial<sup>25)</sup> and antifungal activity<sup>41)</sup>. An essential oil can be anticipated to have a strong sedative effect<sup>10)</sup>. Lavender is widely used in behavioral and psychological symptoms of dementia (BPSD) treatment. A number of clinical trials have been conducted on the use of lavender, including Jimbo et al.<sup>26)</sup>, Lee<sup>32)</sup>, Snow et al.<sup>47)</sup> and others<sup>3)–6)8)19)20)–26)28)30)32)38)51)52)53)</sup>. These clinical trials indicated that sedation<sup>23)</sup> and aggravation of dementia<sup>12)</sup> are suspected as major adverse effects of aromatherapy.

There are studies reporting on the high olfactory threshold<sup>27)44)45)</sup> and a decline in olfactory function<sup>13)29)41)46)51)</sup> in Alzheimer's disease (AD). It is certain that olfactory perception declines over time, however the ability to recognize aromas remains<sup>18)</sup>. The majority of patients with AD, the patients do not completely lose their sense of smell<sup>41)</sup>. The nose contains 10–100 million receptors for olfaction<sup>48a)</sup>. Olfactory membranes contain millions of nerve endings causing the sense of smell to be the most acute of all senses. The limbic system of the brain plays a primary role in a range of emotions, including pain, pleasure, docility, affection, and anger<sup>51b)</sup>. It controls more subtle responses of emotion, and memory. The olfactory nerves are directly connected to the limbic system of the brain, thus the stimulation by the aroma causes immediate, physical and emotional responses.

Aromatherapy is comparatively safe and is being tested in medical institutions and rehabilitation facilities for the primary prevention and treatment of dementia. The evidence-based effectiveness of aromatherapy on dementia should be elucidated.

In recent years, progress and innovations in healthcare and other fields are measured by evidence-based medicine, systematic reviews, and meta-analyses. A systematic review is defined<sup>37)</sup> as, “the application of scientific strategies that limit bias by the systematic assembly, critical appraisal, and synthesis of all relevant studies on a specific topic.” A systematic review is a literature review that focused on a single question that tries to identify, appraise, select and synthesize all high quality research evidence relevant to that question. Systematic reviews of high-quality randomized controlled trials are very important for evidence-based medicine<sup>37)</sup>. Systematic reviews are not limited to medicine and are quite common in other sciences such as healthcare.

## 2. Objective

The objectives of this study are to review systematically randomized control trials regarding aromatherapy for dementia up to July 2010 and make clear the efficacy of aromatherapy for dementia.

### 3. Methods

#### 3.1. Study Group

The research group consisted of two physicians, one physiotherapist, and one graduate student.

#### 3.2. Search Strategy

The search strategy included PubMed and ALOIS (a comprehensive, open-access register of dementia studies maintained by the Cochrane Dementia and Cognitive Improvement Group. <http://www.medicine.ox.ac.uk/alois/>) databases for English-language literature, along with hand searching the bibliographies of retrieved articles. Key words included aromatherapy, complementary therapy, alternative therapy, essential oil, and dementia were used to search on randomized control trials (including review articles that contain experiments comparable to randomized control trials [RCT]) on aromatherapy for dementia.

##### 3.2.1. Determination of Extracted Data and Eligibility Criteria for Study Selection.

The data to be extracted from the collected information are items related to the literature (literature numbers, authors, affiliated organizations, titles, journal names, volumes, numbers, pages, and abstracts), items related to the study design and subjects (study designs, objectives, numbers of subjects, male-female ratios, and mean ages  $\pm$  standard deviations), and items related to the study results (2  $\times$  2 contingency tables of the intervention and control groups and odds ratios or sample mean  $\pm$  standard deviation).

After the extraction of data, the study group set up the eligibility criteria for the study selection to be used for data synthesis. For the qualitative evaluation (scoring the quality of the studies), no objective scoring method has been established other than for randomized controlled studies. Therefore, qualitative evaluation was not performed.

#### 3.3. Inclusion criteria and exclusion criteria<sup>24)</sup>

The inclusion criteria were existence of informed consent, mention of details of randomized technique (selection bias), detailed transition of the number of dropouts (attrition bias), details, justification, standardization of outcome measurements, blind evaluation of the measurer (measurement bias), and clearly presented outcome indications (valid statistics). There was no restriction on the length of the intervention trial or number of cases.

The exclusion criteria included studies in non-English publications, pharmacological interventions, screening instrument studies, and normal clinical trials. There was no restriction on the length of the intervention trial or number of cases.

### 4. Results

One hundred and fifty-five research articles (1985–July, 2010) on RCT that studied dementia and aromatherapy, complementary therapy, alternative therapy or essential oil, were searched. Out of 155 trials, seven studies<sup>2)6)17)18)26)33)46)</sup> were met the eligibility criteria that include cognitive function, quality of life, and relaxation in the treatment outcomes. All studies were quantitative. Three studies were conducted in the United Kingdom<sup>2)6)46)</sup>, two studies in Japan<sup>17)26)</sup>, and other studies in China (Hong Kong)<sup>33)</sup> and the United States of America<sup>18)</sup>. Sample sizes ranged from four to 71. Targeted symptoms included not only BPSD: behavioral and psychological symptoms of dementia<sup>6)17)</sup>, behavioral disturbance<sup>18)46)</sup> or, excited agitation<sup>33)</sup> but also cognitive functions<sup>26)</sup>. Used essential oils were lavender in six studies<sup>5)7)17)18)33)46)</sup>. Intervention included five aromatherapy and control<sup>2)17)18)26)33)</sup> or two massage with aromatherapy<sup>5)46)</sup>. The effects on symptoms were assessed by measuring behavior categories<sup>46)</sup> and TDAS (the Touch Panel-type Dementia Assessment Scale) immediately before and after treatments.

The method used were, one double blind RCT study, one single blind RCT study, two parallel or

placebo control trials, one single-case study design study, one single blind crossover study and one crossover study.

The table provides a summary of the characteristics of seven aromatherapy studies for dementia. In three studies<sup>7)18)46)</sup>, researchers found significantly reduced excessive motor behavior. In the other three studies<sup>2)26)33)</sup>, researchers found improved test scores such as Cohen-Mansfield agitation inventory (CMAI), CCMAI: the Chinese version of CMAI score (CCMAI), examination neuropsychiatric inventory (NPI) score, the Chinese version of NPI, revised Hasegawa's dementia scale HDS-R, mini-mental state (MMSE) and so on<sup>26)</sup>. The Functional Assessment Staging of Alzheimer's disease test (FAST) is a functional scale designed to evaluate patients at the more moderate to severe stages of dementia when the MMSE no longer can reflect changes in a meaningful clinical way. In one study conducted by Gray et al.<sup>18)</sup>, researchers found no efficacy in aromatherapy.

A single-blind, case-controlled study<sup>44)</sup> investigated the effects of lavender essential oil on disordered behaviour in patients with severe dementia. Twenty-one patients were randomized to receive massage only, lavender essential oil administered as massage or lavender oil administered via inhalation plus conversation. Of the three patient groups, those receiving the essential oil massage showed a significantly greater reduction in the frequency of excessive motor behaviour.

In the largest double-blind, placebo-controlled study<sup>2)</sup>, 72 patients with severe dementia displaying agitation in the National Health Service (NHS) continuing care were randomized to receive either lemon balm essential oil (n = 36) or sunflower oil (n = 36) in addition to patients' existing psychotropic medication. Lemon balm oil (sunflower oil was used as placebo oil) was mixed with a base lotion and applied to the patients' face and arms. There were no side effects. Clinically significant changes in agitation (as assessed using the Cohen-Mansfield Agitation Inventory: CMAI) and quality of life indices were compared between the two groups over a 4-week period of treatment. Of the patients who received the treatment, 60% (21/35) had a 30% drop in Cohen-Mansfield agitation inventory (CMAI) score, compared to 14% (5/36) of those who received the placebo. An overall improvement in excited state (an average drop in CMAI score) was seen in 35% of patients who were treated with the lemon balm oil, while improvement was seen in 11% of those receiving the placebo (Mann-Whitney U test; Z = 4.1, p < .0001). Quality of life indices showed greater improvement in patients treated with the essential oil (Mann-Whitney U test; percentage of time spent socially secluded: Z = 2.6, p = 0.005; percentage of time spent engaged in constructive activities: Z = 3.5, p = 0.001). The odds ratio was 3.09.

Lin et al.'s research<sup>33)</sup> was conducted on the effects of English lavender aromatherapy on the Chinese elderly suffering from dementia with clinically significant behavioral disturbance. This study showed marked improvement in violence resulting from dementia. The change in aggregate the Chinese version of examination, neuropsychiatric inventory (NPI) (CNPI) and the Chinese version of CMAI (CCMAI) score after aroma treatment (lavender inhalation) was considerable compared to the placebo control (sunflower inhalation) from 24.68 (SD: 10.54) to 17.77 (SD: 7.52), (p < 0.001). Although the majority of interventions are normally given during the daytime, they placed an aromatic diffuser next to the patients' pillows for a minimum of one hour while they slept.

Fujii et al.<sup>17)</sup> utilized lavender aromatherapy for peripheral symptoms in 28 dementia patients (18 patients with AD, four patients with vascular disease (VD)<sup>44)</sup>, and six AD with cerebrovascular disease (CVD). NPI, mini-mental state examination (MMSE), and Barthel index tests were implemented. All scales were examined at the baseline and in the fourth week of intervention. The NPI, MMSE, and Barthel index results were analyzed using the Wilcoxon paired comparison test. The p < 0.05 result indicates a statistical significance. The application criterion was diagnosis of dementia according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV). The intervention implemented lavender aromatherapy three times a day, one hour after meal (n = 14), while the control group was randomized (n = 14). Observations were made for four weeks. Two drops of lavender oil

were applied to the collar of the hospital gown. The control group showed no significant changes in NPI scores (from  $32 \pm 11$  to  $27 \pm 12$ ). A significant improvement was recognized in the scores for the intervention group (from  $31 \pm 10$  to  $18 \pm 12$ ;  $p < 0.01$ ). Neither group showed significant change in Barthel Scale and in MMSE scores (intervention group: from  $9 \pm 8$  to  $9 \pm 7$  versus control group: from  $8 \pm 8$  to  $8 \pm 7$ ).

Jimbo et al.<sup>26)</sup> treated 28 elderly dementia patients, 17 of whom suffered AD. After a 28-day control period, aromatherapy was conducted over 28 days followed by a 28-day period of no aromatherapy. In the morning, rosemary and lemon essential oils were used, and lavender and orange were used in the evening. To determine the effects of the aromatherapy, patients were evaluated four times-before the control period, after the control period, after the aromatherapy, and after the period of no aromatherapy, using the Japanese version of the Gottfries-Brane-Steen Scale (GBSS-J), Functional Assessment Staging of Alzheimer's Disease (FAST), Hasegawa's Dementia Scale-Revised (HDS-R), and the touch-panel method for the screening of dementia (TDAS: the Touch Panel-type Dementia Assessment Scale). After treatment, all patients showed significant improvement in personal orientation related to cognitive functions in both the GBSS-J and TDAS. In particular, significant improvement was seen in the FAST 3-5 AD (mild-moderate AD) group ( $p < 0.05$ , GBSSJ-A-13 score (abstract function)).

## 5. Discussion

Sensory stimulation to patients with dementia decrease agitation, restlessness, and sleeplessness (insomnia)<sup>9)</sup>. Sensory stimulation is considered as stimulation to one of five senses: vision, hearing, taste, touch and smell<sup>9)</sup>. Aromatherapy has a long history and shows the early results.

The six placebo controlled trials (a double blind RCT study, a single blind RCT study, a placebo control trial, a single-case study design study, a single blind crossover study and a crossover study) reported significant beneficial effects on BPSD and/or cognitive function. There are some reports of the effects of aromatherapy on the central features of dementia. Jimbo and his colleagues<sup>26)</sup> showed that aromatherapy improved cognitive function significantly on both the Japanese version of the Goofries, Barene, Steen scale and Touch Panel-type Dementia Assessment Scale in patients with Alzheimer's disease.

A meeting of experts coordinated by the British Association for Psychopharmacology stated that aromatherapy was supported by type 1a evidence (evidence from randomized controlled trials which means one of the highest level of scientific evidence)<sup>10)</sup>. Lavender and lemon balm are two essential oils of particular interest in aromatherapy. In the seven aromatherapy studies for dementia (Table), six trials used lavender and two trial used lemon balm. Jimbo<sup>26)</sup> used rosemary and lemon essential oils in the morning and lavender and orange in the evening. A number of clinical trials of aromatherapy, principally using either lavender or lemon balm demonstrated a significant impact on behavioral problems in patients with dementia. Holmes and Ballard<sup>22)</sup> stated that as mechanisms of action of aromatic essential oils, the individual's perception of the pleasantness of an odor and the individual's past association with an odor were considered from psychological aspects, and that inhibition of glutamate binding, GABA augmentation, and acetylcholine receptor binding were focused from petrochemical effects.

Most patients with severe dementia will lose meaningful sense of smell due to early loss of olfactory neurons<sup>49)</sup>. The pharmacological mechanism by which aromatherapy produces its effects is not thought to involve any perception of odor. The active compounds are thought to enter the body (by absorption through the lungs or olfactory mucosa) and delivered to the brain via the bloodstream, where they elicit direct actions. Diminished olfactory function<sup>51)</sup> may be responsible for the lack of aromatherapy treatment effect particularly in patients with AD<sup>13)29)40)46)</sup>. However, most agree that the majority of patients with AD do not completely lose their sense of smell<sup>40)</sup>. Snow et al.<sup>47)</sup> questioned this olfactory hypofunction theory, and stated that treatment incorporating the act of smelling essential oils with a

Table Characteristics of Seven Aromatherapy Studies for Dementia

Source	diagnosis of dementia	study participants (female)	mean age +/- SD	symptom	essential oil	method	groups	duration	evaluation method	efficacy
Smallwood <sup>(46)</sup> 2001	by a consultant psychiatrist	21 (12)	66.8 +/- 11.5	behavioral disturbance	lavender	RCT single blind	aromatherapy & massage/plain oil massage/conversation & aromatherapy	two weeks	behavior categories*	significant decrease of excessive motor behavior
Ballard <sup>(2)</sup> 2002	CMI, NPI & CDR	72 (43)	78.5 +/- 8.1	excited agitation	Melissa (lemon balm)	RCT, double blind	aromatherapy/control	four weeks	CMAI, NPI, Barthel Index	improvement in 35% of patients (average drop of CMAI score)
Gray <sup>(18)</sup> 2002	chosen volunteers by nursing staff	13 (6)	not described	behavioral disturbance	lavender, orange, tea tree	RCT, parallel-group,	aromatherapy/control	not described	Mean frequencies of resistive behaviors	no efficacy
Fujii <sup>(17)</sup> 2008	DSCM-IV	28 (19)	78 +/- 10	BPSD	lavender	Placebo control trial	aromatherapy/control	four weeks	NPI, MMSE, Barthel Index	significant improvement of NPI score (31 +/- 10 ~ 18 +/- 12, p < 0.01)
Brooker <sup>(5)</sup> 1997	residents on a continuing care ward for severe dementia	4 (3) AD: 2, AD + Parkinson: 1, frontal lobe disorder: 1.	80.3 +/- 7.5	BPSD	lavender	RCT, single-case study design	aromatherapy/massage/aromatherapy & massage/control	three months	individualized scales of agitated behavior	improvement by aromatherapy & massage
Lin <sup>(3)</sup> 2007	DSCM-IV	70 (41)	78.3 +/- 9.4	excited agitation	Tasmanian lavender	RCT single blind crossover	aromatherapy/control	eight weeks	CNPI and CCMAI	marked improvement in violence
Jimbo <sup>(26)</sup> 2009	DSCM-IV + NINCDS-ADRDA, DSCM-IV + NINCDS-AIREN	AD 17 (1), VaD 3 (3), Others 8 (8)	86.3 +/- 6.4, 89.7 +/- 5.5, 84.5 +/- 8.3	cognitive functions of	rosemary & lemon in the morning, lavender & orange in the evening	crossover	aromatherapy/control	112 days	the Japanese version of GBSS, **FAST and HDS-R for efficacy of aromatherapy, and TDAS for the screening of dementia	significant improvement in both GBDD-J and TDAS of all patients, in particular, of mild-moderate AD group

Abbreviations: AD: Alzheimer's disease, BPSD: behavioral and psychological symptoms of dementia, CDR: the Clinical Dementia Rating Scale, CMAI: Cohen-Mansfield agitation inventory, CCMAI: the Chinese version of CMAI, CNPI: the Chinese version of NPI, DSM-IV: the Diagnostic and Statistic Manual of Mental Disorders, Fourth Edition, MMSE: mini-mental state examination, GBSS-J: Japanese version of the Gottfries-Brane-Steen Scale, HDS-R: Revised Hasegawa's dementia scale, NPI: examinationneuropsychiatric inventory, Others: mixed dementia and other dementia, RCT: randomized controlled trial, SD: standard deviation, TDAS: the Touch Pencil-type Dementia Assessment Scale, VaD: cerebrovascular dementia.

\* behavior categories by Bowie and Mountain (1993), \*\* The FAST (Functional Assessment Staging of Alzheimer's disease) scale is a functional scale designed to evaluate patients at the more moderate-severe stages of dementia when the MMSE no longer can reflect changes in a meaningful clinical way.

sedative effect could be effective even in people who have a severely impaired sense of smell. They stressed the pharmacological effect from inhalation into the blood<sup>47)</sup>. Meanwhile, there is almost no consensus on the mechanism of olfactory deficits. Though there are studies reporting on high olfactory threshold in AD<sup>27)44)45)</sup>, a study also exists that recognized normal threshold<sup>29)</sup>. There is a need to research the causal relationship between an impaired sense of smell and cognitive deterioration.

Rush Alzheimer's Disease Center in Chicago conducted a five-year study involving 589 people on the relationship between olfactory perception and impairment of cognitive function<sup>50)</sup>. In the study, participants were asked to smell aromas: American grass, pineapple, gasoline, and pizza and identify the smell. Compared to participants who correctly answered 11 questions out of 12, those that could only answer eight were reported to have a 1.5 greater risk for mild cognitive impairment (MCI). In other words, as a prodromal symptom of AD, cognitive deterioration of olfactory perception is greater than a decline in olfactory function.

Moreover, it is certain that olfactory perception declines over time, even when the ability to make discriminations is lost in the elderly with dementia, however the ability to recognize aromas remains<sup>18)</sup>. This discrimination disorder has been reported to determine the deterioration of the cognitive condition, and there is a significant possibility that deterioration of the cognitive condition is not due to olfactory perception<sup>18)</sup>.

Although many case-based evidences suggesting the efficacy of aromatherapy in improving sleep, agitated behaviours and resistance to care in dementia, placebo-controlled, randomized studies of adequate size in this area are insufficient.

The followings should be investigated in the future studies:

- 1) Different forms of dementia may respond differently to aromatherapy.
- 2) Neurochemical differences between essential oils may be considered.

Properly conducted, well-designed, randomized, controlled trials are required before firm conclusions regarding the efficacy and safety of essential oils could be drawn.

## 6 Conclusion

Aromatherapy seems to be safe and effective and may have an important role in managing behavioral problems in people with dementia. Despite these preliminary evidence, the mechanism of action of essential oils remains unclear<sup>11)</sup>. Carefully designed, large-scale randomized controlled trials should be investigated.

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