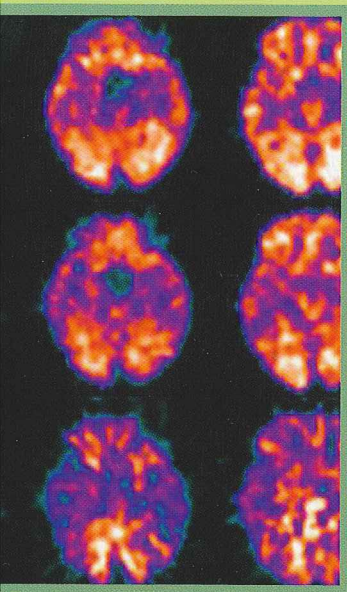
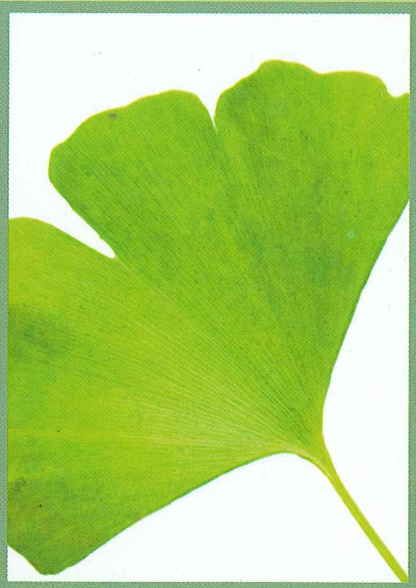
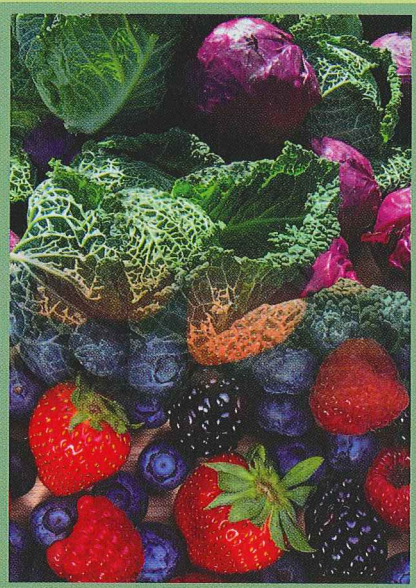
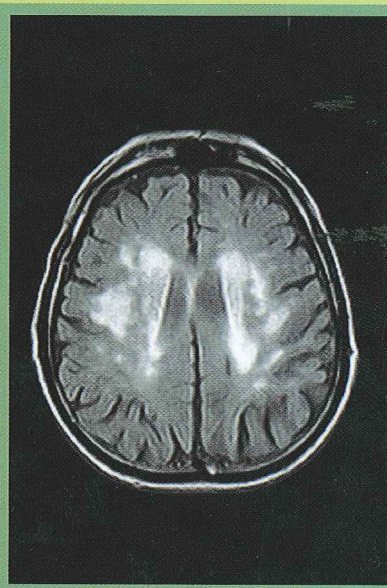
# Diet and Nutrition in Dementia and Cognitive Decline

Edited by
Colin R. Martin and Victor R. Preedy

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Chapter 92

# Ferulic Acid and *Angelica archangelica* Extract in Dementia: Effects on Cognitive Functions and Behavioral and Psychological Symptoms of Dementia

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## LIST OF ABBREVIATIONS

**Aβ** amyloid β-protein
**AD** Alzheimer's disease
**ADAS-Jcog** Japanese version of the cognitive subscale of the Alzheimer's Disease Assessment Scale
**ADL** activities of daily living
**ADNI** Alzheimer's Disease Neuroimaging Initiative
**BPSD** behavioral and psychological symptoms of dementia
**CDR** Clinical Dementia Rating
**ChEIs** acetylcholinesterase inhibitors
**DLB** dementia with Lewy bodies
**FTLD** frontotemporal lobar degeneration
**MCI** mild cognitive impairment
**MMSE** Mini-Mental State Examination
**NPI** neuropsychiatric Inventory
**QOL** quality of life
**WMS-R** Wechsler Memory Scale-Revised

## INTRODUCTION

Dementia is characterized by progressive deterioration of cognitive functions in presenile or senile age. Symptoms of dementia are classified as "core symptoms" and "peripheral symptoms." In 1999, the International Psychogeriatric Association Consensus Group defined peripheral symptoms as the behavioral and psychological symptoms of dementia (BPSD) [1]. Core symptoms are progressive cognitive disability, while BPSD represent a cluster of noncognitive symptoms and behavioral disturbances. Developing an understanding of how to inhibit the progression of cognitive disturbance and control BPSD is the most important problem associated with dementia.

Ferulic acid is a phytochemical that is found in the cell walls of plants. The structure of ferulic acid is based around a benzene ring (Figure 92.1). Phytochemical acids including ferulic acid act as an antioxidant. In other words, ferulic acid exhibits reactivity toward free radicals and reactive oxygen species [2]. This is useful, as such deleterious oxidants have been involved in cancer and accelerated aging. *Angelica archangelica* is a biennial plant from the umbelliferous family *Apiaceae* (Figure 92.2) and has been used for flavor enhancement and in aroma therapy. Extracts prepared from this plant are known to inhibit the action of acetylcholine esterase [3]. These interesting effects led us to investigate the availability of ferulic acid and *A. archangelica* for use in the treatment of dementia symptoms. In this article, we describe the results of this investigation and suggest the therapeutic use of ferulic acid and *A. archangelica* extract to suppress the progression of cognitive disturbance and control BPSD.

**Diet and Nutrition in Dementia and Cognitive Decline.**

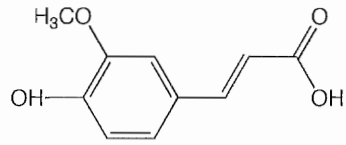


**FIGURE 92.1 Ferulic acid.** Chemical structural formula ($C_{10}H_{10}O_4$).

**FIGURE 92.2** ***Angelica archangelica.*** Wild *Angelica archangelica. With permission from © emer—Fotolia.com.*

## SUPPRESSING THE PROGRESSION OF COGNITIVE DISTURBANCE

Alzheimer's disease (AD) is very common in dementia. Patients with AD suffer from memory disturbance, and then disorientation of time and executive dysfunction, resulting in disturbance of social activity and the daily lives of patients. Patients with AD have been treated with symptomatic therapy using memantine and cholinesterase inhibitors (ChEIs), such as donepezil, galantamine, and rivastigmine. However, the effect of symptomatic therapy for memory disturbance in AD patients is transient and rather limited, resulting in the progression to cognitive disturbance.

The principal neuropathological abnormalities of AD are extracellular deposition of amyloid β-protein (Aβ) (Figure 92.3) and intracellular neurofibrillary tangles (Figure 92.4) containing phosphorylated tau. In accordance with this amyloid cascade hypothesis in AD, many studies have been carried out in the pharmaceutical industry to prevent the production and accumulation of Aβ. However, pharmacological approaches, including the administration of Aβ antigens (active vaccination), anti-Aβ antibodies (passive vaccination), and chemical inhibitors of beta-secretase or gamma-secretase, have not been successful. Once patients were diagnosed with dementia, it was discovered that amyloid and phosphorylated tau pathologies had already accumulated, and a great number of neurons had already disappeared in the brain. The pharmacological treatment associated with Aβ may, however, be useful for patients if they receive treatment in a prodromal condition of dementia.

The concept of mild cognitive impairment (MCI), developed by Petersen et al. refers to a transitional zone between normal aging and dementia [4]. The criteria for MCI include (1) memory problems, (2) objective memory disorder, (3) absence of other cognitive disorders or repercussions of daily life, (4) normal general cognitive function, and (5) absence of dementia. A person diagnosed with MCI experiences memory problems greater than normally expected with aging, but do not exhibit symptoms that are indicative of AD. However, most of such cases will convert to dementia. It would thus be highly pertinent to identify potential therapies with which to suppress the conversion to dementia. Because MCI is considered to be the prodromal stage, clinical trials of pharmacological treatments that reduce Aβ for MCI patients have begun. However, the efficacy and safety of such treatment strategies have yet to be reported.

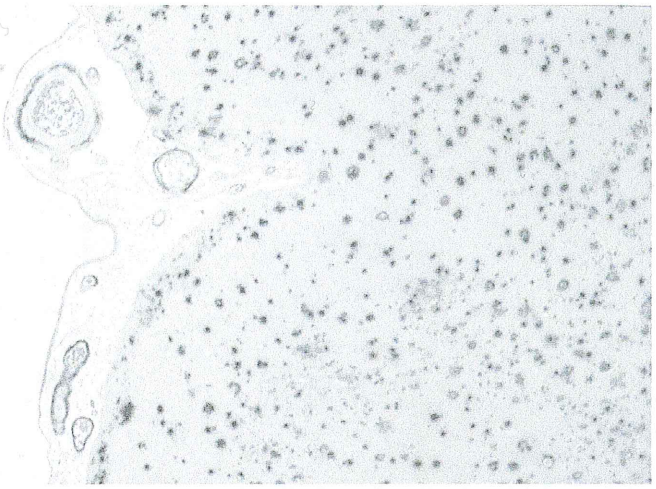

**FIGURE 92.3 Deposits of Aβ in brain tissue from a patient diagnosed with AD.** Black plaques are deposits of Aβ.

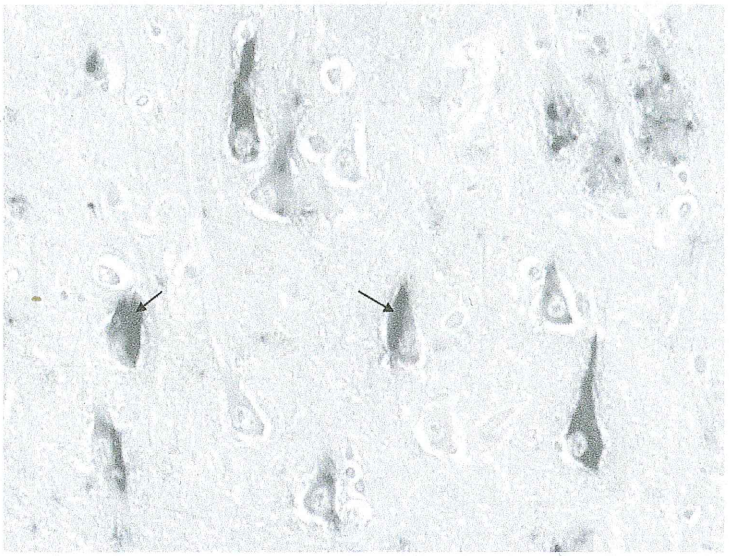

**FIGURE 92.4 Neurofibrillary tangles in neurons within the brain tissue from a patient diagnosed with AD.** Neurofibrillary tangles are marked by the arrows.

Recent studies have indicated that ferulic acid inhibits free radicals, chronic inflammation, and neurotoxic action of Aβ in the brain [2,5,6] and that *A. archangelica* reduces the activity of acetylcholine esterase [3], suggesting an effect of ferulic acid and *A. archangelica* in suppressing the onset of cognitive disturbance. Based on these data, we speculated that ferulic acid and *A. archangelica* extract (Feru-guard®) may delay conversion from MCI to dementia. In order to investigate this hypothesis, we performed an open-label study.

MCI was diagnosed according to the following criteria: (1) Mini-Mental State Examination (MMSE) score over 24 points; (2) Clinical Dementia Rating (CDR) score under 0.5 points; and (3) Wechsler Memory Scale-Revised (WMS-R) logical memory score under 13 points. Twenty-eight patients with MCI (14 male) were enrolled and prescribed a dose of 3.0 g/day (b.i.d. [morning and evening]) Feru-guard® for 1 year. At baseline and 1 year after the start of treatment, MMSE and the Japanese version of the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-Jcog) were used to evaluate cognitive function. Patients whose CDR score exceeded 1 point were considered as being demented.

Nine patients dropped out of the present study on their own accord. There were no adverse effects or significant changes in the physical findings or laboratory data. One (4.8%) out of 21 patients converted to dementia within 1 year. MMSE scores at baseline and 1 year after the start of treatment with Feru-guard® were $26.67 \pm 1.32$ and $26.90 \pm 2.59$, respectively. ADAS-Jcog scores at baseline and 1 year after the treatment were $8.66 \pm 2.72$ and $7.70 \pm 3.48$, respectively. Treatment with

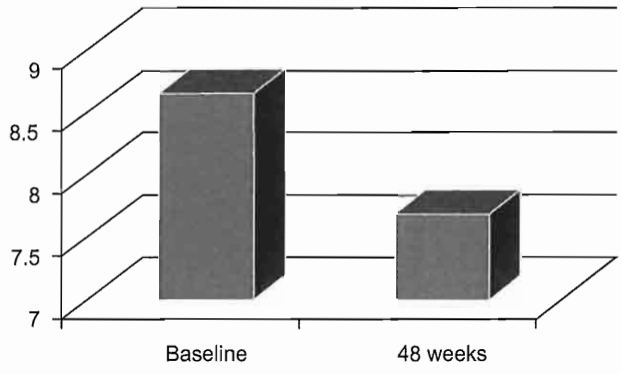


**FIGURE 92.5 Changes in Alzheimer's Disease Assessment Scale scores 48 weeks after Feru-guard® treatment in 21 patients with MCI.** Using the Japanese version of the cognitive subscale.

Feru-guard® led to reduced ADAS-Jcog scores in 15 (71.4%) out of the 21 patients and significantly reduced ADAS-Jcog scores overall ($P < 0.04$) (Figure 92.5).

Studies reported by the Alzheimer's Disease Neuroimaging Initiative (ADNI) showed that over 18.3% of MCI patients converted to dementia within 1 year [7], whereas the Japanese ADNI study calculated the rate of conversion from MCI to dementia within 1 year as being 29.6% [8]. Several researchers have assessed whether drugs for symptomatic therapy to AD such as ChEIs and memantine delay the progression of cognitive disturbance in MCI. Winblad and colleagues showed that galantamine failed to significantly influence the conversion to dementia [9]. Furthermore, Feldman and colleagues revealed that there was no significant benefit of rivastigmine on the progression rate to dementia [10]. In a recent clinical trial, MCI patients who received ChEIs and/or memantine showed a greater decline in cognitive disturbance [11]. In this particular study, 150 (84.7%) of the 177 patients who received ChEIs used donepezil. The magnitude of decline was more than twofold greater in patients treated with ChEIs and memantine than in those treated with ChELs only. Considering these findings collectively, we can hypothesize that ChEIs and/or memantine are not effective in inhibiting the conversion to AD in MCI patients.

In our study, 4.8% of patients treated with ferulic acid and *A. archangelica* extract became demented within 1 year, showing that the rate of conversion from MCI to dementia within 1 year was 4.8%. Hence, it is possible that ferulic acid and *A. archangelica* extract could suppress the conversion from MCI to dementia. Furthermore, our study showed that treatment with ferulic acid and *A. archangelica* extract led to reduced ADAS-Jcog scores in 15 (71.4%) of 21 MCI patients, and to significantly reduced ADAS-Jcog scores overall. ADAS-Jcog score is a clinical rating instrument that measures cognitive function in demented patients and can characterize the effects of pharmacological treatment on symptoms [12]. Therefore, the improvement of ADAS-Jcog induced by ferulic acid and *A. archangelica* extract is highly notable. Our evaluation using ADAS-Jcog suggests that treatment with ferulic acid and *A. archangelica* extract not only suppressed, but also improved, cognitive disturbance associated with MCI.

*A. archangelica* is known to reduce the activity of acetylcholine esterase and increased levels of acetylcholine in the brain [3]. Because acetylcholine is critically involved in cognitive function, one of the mechanisms by which treatment with ferulic acid and *A. archangelica* extract improves cognitive function in patients with MCI may be the increased levels of acetylcholine in the brain. However, this hypothesis does not concur with the non-efficacy of ChELs in MCI patients. On the other hand, MCI patients who were amyloid-positive to positron emission tomography using Pittsburgh compound B were more likely to convert to AD than amyloid-negative patients [13], suggesting that inhibition of amyloid burden in the brain of MCI patients is important in the suppression of the conversion. Mori and colleagues showed that ferulic acid reduced the deposition of an oligomer of Aβ and inhibited β-secretase production in the brain [14]. In addition, Hiratsuka and colleagues reported that ferulic acid suppressed neuronal loss derived from endoplasmic reticulum stress [15]. These actions of ferulic acid might be associated with the improvement of cognitive function in patients with MCI.

## CONTROL OF BPSD

BPSD are an integral part of the disease process and are commonly associated with reduction in the quality of life (QOL) for patients as well as their caregivers [16] and increased levels of caregiver stress [17] and in the cost of care [18]. Frontotemporal lobar degeneration (FTLD) and dementia with Lewy bodies (DLB) are characterized by prominent behavioral and psychological symptoms [19,20]. BPSD in FTLD include aggression, disinhibition, stereotyped behavior, dietary

changes, and apathy, while those in DLB include visual hallucination, delusion, depression, anxiety, and rapid eye movement sleep behavioral disorder. These symptoms in FTLD or DLB place a heavier burden on caregivers than the symptoms of AD or vascular dementia. Although antipsychotic drugs have been used to reduce such symptoms, their adverse effects (e.g., arousal disturbance, ileus, tardive dyskinesia, malignant syndrome, and rhabdomyolysis) reduce the patients' ability to perform activities of daily living (ADL) and reduce their QOL. Therefore, establishing a safe therapy for BPSD without using antipsychotic drugs is highly necessary for patients with dementia and their caregivers.

An earlier study demonstrated the possibility that ferulic acid and *A. archangelica* extract are effective against BPSD [21]. We also reported two patients with DLB showing good responses to Feru-guard® [22]. Given these findings, we hypothesized that Feru-guard® is highly likely to be useful for the treatment of serious BPSD in FTLD or DLB. To assess this hypothesis, we designed a prospective, open-label study.

FTLD or DLB was diagnosed according to the clinical diagnostic criteria for FTLD [19] or consensus guidelines for the clinical and pathologic diagnosis of DLB [20], respectively. Ten patients with FTLD (3 males) and 10 patients with DLB (1 male) were enrolled. Subjects were prescribed a dose of 3.0 g/day Feru-guard® for 4 weeks. During this period, there were no changes in medication, rehabilitative regimen, hospitalization, or care environment. A trained psychologist evaluated BPSD using the Japanese version of the Neuropsychiatric Inventory (NPI) [23] at baseline and 4 weeks after treatment.

There were no adverse effects observed. Treatment with Feru-guard® led to reduced NPI scores in 19 (95.0%) out of 20 patients and to significantly reduced NPI scores overall ($P < 0.001$) (Table 92.1). Treatment also led to significantly reduced NPI subscale scores ("delusions," "hallucinations," "agitation/aggression," "anxiety," "apathy/indifference," "irritability/lability," and "aberrant behavior" [Table 92.1]). Feru-guard® treatment also significantly reduced NPI scores in both the FTLD and DLB groups (Table 92.1). Our analysis of the differences in the improvements in NPI subscale scores between the two groups revealed that "disinhibition," "irritability/lability," and "aberrant behavior" were more significantly improved in FTLD, and "hallucinations" and "depression" were more significantly improved in DLB. A multiple regression analysis was performed using age, sex, education period, diagnosis, baseline MMSE score, and baseline NPI score as dependent variables, along with improvement of NPI score as the independent variable. The independent variable was selected by stepwise regression. Consequently, the baseline MMSE score was significantly positively correlated with improvement in NPI score (Pearson's correlation coefficient: $r = 0.466$, $P = 0.022$), and predicted the improvement of NPI significantly ($\beta = 0.466$, $P = 0.044$).

In the present study, treatment with ferulic acid and *A. archangelica* extract led to significantly improved NPI scores in FTLD and DLB patients. NPI is a clinical rating instrument that measures neuropsychiatric symptoms in demented patients [23,25]. Our evaluation using NPI indicated that treatment with ferulic acid and *A. archangelica* extract improved BPSD associated with FTLD or DLB. We investigated the differences between improvements in NPI subscale scores in FTLD and DLB groups. This investigation showed more significant ameliorations of "disinhibition," "irritability/lability," and "aberrant behavior" in FTLD and of "hallucinations" and "depression" in DLB. Because these symptoms are characteristic of each of those respective dementias, treatment with ferulic acid and *A. archangelica* extract is considered to be more effective in treating the characteristic symptoms of FTLD and DLB than other symptoms. Our multiple regression analysis indicated that the baseline MMSE score was associated with the improvement of symptoms. Thus, we could anticipate a clinical response to ferulic acid and *A. archangelica* extract in a patient by determining whether his or her baseline MMSE score is high.

Dealing with BPSD can cause caregiver distress and exhaustion. Antipsychotic drugs have been used to reduce such symptoms. The adverse effects of these drugs reduce patients' ADL and QOL. A meta-analysis of randomized placebo-controlled trials found a significantly higher risk of death due to atypical antipsychotic drug treatment for dementia [26], leading to the recommendation of the US Food and Drug Administration that atypical antipsychotic drugs should not be prescribed for the control of BPSD. Because it was recently shown that donepezil and Yokukansan were effective in treating BPSD [27–30], these drugs have been used to treat BPSD instead of antipsychotic drugs. However, even these drugs cause various adverse effects in elderly patients. Donepezil induces gastrointestinal disturbance [31] and torsades de pointes with QT prolongation [32] and exacerbates chronic obstructive pulmonary disease [33] and psychotic symptoms [34]. A major ingredient of glycyrrhiza radix (licorice) in Yokukansan is glycyrrhizin, which occasionally induces pseudoaldosteronism [35]. Based on our clinical experience, Yokukansan causes hypokalemia and loss of appetite in demented patients [30]. These medicines, as well as antipsychotic drugs, might be especially harmful for demented patients who are 80 years old and over. In our subjects taking ferulic acid and *A. archangelica* extract, there were no adverse effects or significant changes in the physical findings or laboratory data. The results suggest that treatment with ferulic acid and *A. archangelica* extract in FTLD or DLB might be safer than other pharmacological treatments.

An imbalance of neurotransmitters in the central nervous system putatively induces anxiety and excitement and consequently induces BPSD. The mechanism by which treatment with ferulic acid and *A. archangelica* extract improves BPSD

**TABLE 92.1** Changes in Neuropsychiatric Inventory Scores 4 Weeks After Feru-guard® Treatment in 20 Patients with Frontotemporal Lobar Degeneration or Dementia with Lewy Bodies

| | Baseline (Mean ± SD) | Follow-up (Mean ± SD) | *P* Value[a] |
|---|---|---|---|
| **NPI total score** | | | |
| FTLD + DLB | 28.3 ± 9.6 | 17.7 ± 9.7 | <0.001 |
| FTLD | 32.3 ± 11.1 | 22.0 ± 10.2 | <0.01 |
| DLB | 24.2 ± 5.9 | 13.3 ± 7.3 | <0.01 |
| Delusions | | | |
| | 2.2 ± 2.7 | 1.3 ± 2.1 | <0.05 |
| | 2.4 ± 3.4 | 1.5 ± 2.7 | NS |
| | 1.9 ± 2.0 | 1.1 ± 1.3 | NS |
| Hallucinations | | | |
| | 2.8 ± 3.4 | 1.1 ± 2.1 | <0.02 |
| | 0.0 ± 0.0 | 0.0 ± 0.0 | NS |
| | 5.5 ± 2.7 | 2.2 ± 2.5 | <0.02 |
| Agitation/aggression | | | |
| | 4.6 ± 3.2 | 2.5 ± 1.9 | <0.001 |
| | 6.4 ± 2.8 | 3.6 ± 2.0 | <0.02 |
| | 2.7 ± 2.5 | 1.4 ± 1.1 | <0.03 |
| Depression/dysphoria | | | |
| | 1.7 ± 2.9 | 1.2 ± 2.0 | NS |
| | 0.3 ± 0.9 | 0.3 ± 0.9 | NS |
| | 3.1 ± 3.5 | 2.0 ± 2.4 | NS |
| Anxiety | | | |
| | 1.9 ± 2.3 | 1.5 ± 2.0 | <0.04 |
| | 1.6 ± 2.2 | 1.0 ± 1.4 | NS |
| | 2.1 ± 2.5 | 1.9 ± 2.4 | NS |
| Euphoria | | | |
| | 0.2 ± 0.9 | 0.2 ± 0.9 | NS |
| | 0.4 ± 1.3 | 0.4 ± 1.3 | NS |
| | 0.0 ± 0.0 | 0.0 ± 0.0 | NS |
| Apathy/indifference | | | |
| | 5.9 ± 2.4 | 3.3 ± 1.9 | <0.001 |
| | 5.4 ± 2.7 | 3.6 ± 2.6 | <0.03 |
| | 6.3 ± 2.2 | 3.0 ± 0.8 | <0.02 |
| Disinhibition | | | |
| | 1.9 ± 3.1 | 1.8 ± 2.9 | NS |
| | 3.7 ± 3.6 | 3.5 ± 3.4 | NS |
| | 0.0 ± 0.0 | 0.0 ± 0.0 | NS |
| Irritability/lability | | | |
| | 4.0 ± 3.2 | 2.3 ± 2.0 | <0.005 |
| | 5.7 ± 3.4 | 3.2 ± 2.3 | <0.02 |
| | 2.3 ± 1.9 | 1.4 ± 1.2 | NS |
| Aberrant behavior | | | |
| | 3.4 ± 3.4 | 2.6 ± 2.7 | <0.05 |
| | 6.4 ± 1.8 | 4.9 ± 1.8 | <0.05 |
| | 0.3 ± 0.9 | 0.3 ± 0.9 | NS |

[a]*Wilcoxon signed-rank test, with $P < 0.05$ accepted as significant.*
*Abbreviations:* FTLD, Frontotemporal lobar degeneration; DLB, dementia with Lewy bodies; NPI, Neuropsychiatric Inventory; NS, not significant.
*Source:* Kimura et al. [24]. With permission from Geriatrics & Gerontology International.

in patients with FTLD or DLB remains uncertain. Ferulic acid suppresses free radicals and chronic inflammation in the brain [2,5], while *A. archangelica* inhibits acetylcholine esterase and increases acetylcholine in the synapse [3]. Free-radical scavengers might theoretically be utilized as a therapy in FTLD [36], and acetylcholinesterase inhibitors such as rivastigmine and donepezil could alleviate BPSD in DLB [28,37]. These findings may indicate that the suppression of free radicals and acetylcholinesterase derived from ferulic acid and *A. archangelica* extract might lead to the amelioration of BPSD in FTLD or DLB.

## PROBLEMS THAT CONFRONT US

Several limitations of our studies should be considered. First, this study had an open-label design and no control group. Consequently, our results may have been partially due to a placebo effect. Second, our sample size was small. Third, this sample might not represent the whole population of patients with MCI and dementia, since recruitment was from only one outpatient clinic. To overcome these limitations and establish ferulic acid and *A. archangelica* extract as a useful treatment for MCI and dementia, we propose doing double-blind randomized studies with much larger samples.

## APPLICATIONS TO OTHER DEMENTIAS OR OTHER AREAS OF COGNITIVE DECLINE

Based on the actions of ferulic acid and *A. archangelica* that are described in this chapter, it seems plausible that both ferulic acid and *A. archangelica* may possibly delay aging in the brain and cognitive decline. We have to acknowledge, however, that there have been no published reports suggesting the efficacy of either product in the treatment of patients with dementia or cognitive decline. On the other hand, an open-label study by Nakamura and colleagues showed that when 143 patients with AD were prescribed ferulic acid and *A. archangelica* extract for 9 months, the progression of cognitive decline in these patients was inhibited [38]. The efficacy of ferulic acid and *A. archangelica* extract in other types of dementias remains unknown.

## PRACTICAL ISSUES

We have to acknowledge there are no researches concerning availability of ferulic acid and *A. archangelica* extract for other disturbances and diseases except cognitive dysfunction. On the other hand, recent studies using mice have suggested that each of ferulic acid and *A. archangelica* improves metabolism of glucose and lipid [39–41]. Therefore, we performed two studies including retrospective and prospective studies to investigate how ferulic acid and *A. archangelica* extract affects metabolism of glucose and lipid in human beings.

Retrospective study: We looked over the medical records to know the value of total cholesterol in baseline and after 24 weeks of 17 out of the above-mentioned 21 MCI patients who took Feru-guard®. The values in baseline and after 24 weeks were 200.8 ± 24.9 and 181.8 ± 22.7, respectively. Treatment with Feru-guard® led to significantly reduced total cholesterol ($P < 0.01$).

**TABLE 92.2** Changes in Values of HbA1c, Total Cholesterol, High-Density Lipoprotein Cholesterol, Low-Density Lipoprotein Cholesterol, and Triglyceride 8 Weeks After Feru-guard® Treatment in 6 Healthy Persons

| | Baseline (Mean ± SD) | Follow-up (Mean ± SD) | *P* Value[a] |
|---|---|---|---|
| HbA1c | 5.43 ± 0.34 | 5.12 ± 0.32 | <0.05 |
| T-CHO | 215.0 ± 34.7 | 193.5 ± 45.4 | <0.05 |
| HDL-C | 82.1 ± 31.2 | 83.0 ± 32.6 | NS |
| LDL-C | 117.3 ± 32.2 | 96.2 ± 34.8 | <0.01 |
| TG | 113.8 ± 45.5 | 99.2 ± 45.3 | NS |

[a]*Wilcoxon signed-rank test, with $P < 0.05$ accepted as significant.*
*Abbreviations: T-CHO, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; NS, not significant.*

Prospective study: We designed an 8-week, open-label trial of daily Feru-guard® therapy in six healthy persons. Subjects were prescribed a dose of 3.0 g/day Feru-guard®. We examined the values of HbA1c, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride in baseline and after 8 weeks of the subjects. The result of this study is shown in Table 92.2. Treatment with Feru-guard® led to significantly reduced HbA1c, total cholesterol, and low-density lipoprotein cholesterol ($P < 0.05$).

These findings suggest that ferulic acid and *A. archangelica* extract improved metabolism of glucose, triglyceride, and cholesterol in human beings and prevented or reduced the onset of diabetes and hyperlipidemia. Because diabetes and hyperlipidemia have been enumerated as risk factors of AD [42,43], ferulic acid and *A. archangelica* extract might also reduce the risk of AD by modification of metabolism of glucose and lipid.

## SUMMARY POINTS

- Only one (4.8%) of 21 patients with MCI who were treated with ferulic acid and *A. archangelica* extract converted to dementia within a 1-year study period.
- Treatment led to improvement of scores of the Japanese version of the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-Jcog) in 15 (71.4%) out of 21 patients and significantly improved ADAS-Jcog scores overall within 1 year.
- Treatment improved scores of Neuropsychiatric Inventory (NPI) in 19 (95.0%) out of 20 patients with frontotemporal lobar degeneration or dementia with Lewy bodies.
- Treatment significantly improved NPI scores overall in 4 weeks.
- There were no adverse effects or significant changes in the physical findings or laboratory data.
- Data suggest that treatment with ferulic acid and *A. archangelica* extract delays the conversion from MCI to dementia and controls BPSD.
- Ferulic acid and *A. archangelica* extract are extremely safe and useful for patients with MCI and dementia.

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