Serial Sevens subtraction task, but increased errors on the Serial Threes task. However, perhaps the most striking finding from this study was of beneficial modulation of mood across the testing sessions, with significantly increased ratings of 'alertness', 'contentedness' and 'calmness' for the 50 µl dose and increased ratings on the latter two measures for the 25 µl dose.

These two initial studies had been undertaken utilising *S. lavandulaefolia* in healthy young participants. Therefore, a further study [28] assessed the effects of four separate single doses (167, 333, 667, 1332 mg) of an ethanolic extract of *Salvia officinalis* with AChE inhibitory properties in an elderly cohort (n = 20, mean age 72.9 years) with presumed, natural, age-related down-regulation of cholinergic integrity [44]. The study used the same methodology and cognitive/mood assessment as the previous study [27]. The results again showed clear improvements in memory performance, in this case largely restricted to the two lower doses, with the 167 mg dose evincing improved 'Secondary Memory' performance at 2.5 and 4 hrs post-dose, whilst the 333 mg dose led to significantly improved 'Secondary Memory' at all post-dose time points, with concomitant improvements on the 'Accuracy of Attention' factor (accuracy of performing three attention tasks). While these effects may be attributed to the extracts' pro-cholinergic properties, other mechanisms outlined above may also be involved.

Chronic Administration in Alzheimer's Disease

To date two studies have also addressed the effects of sage in cohorts suffering from mild to moderate probable Alzheimer's disease. Perry *et al.* [45] conducted a preliminary, open label clinical trial, in 11 participants, primarily assessing the tolerability of 6 weeks oral administration (50 µl twice per day) of an AChE inhibitory (IC50 = 0.116 µl/ml) *S. lavandulaefolia* essential oil, but with several measures of cognitive performance and psychopathology included. Although the trial did not include a placebo condition the results were promising, with excellent tolerability of the extract, and suggestive significant improvements at the 6 week end-point seen on both the accuracy of performing a vigilance task and in dementia psychopathology as assessed by the Neuropsychiatric Inventory (NPI), both in comparison to the outset of the trial.

A double-blind, placebo-controlled trial assessing the effects of 16 weeks administration of a *Salvia officinalis* alcoholic tincture in 39 patients (placebo, n = 20 / *S. officinalis*, n=19) has also been reported [46]. Whilst both placebo and *S. officinalis* groups were reduced to 15 by drop-outs, those in the *S. officinalis* group were shown to have significantly improved scores on the Alzheimer's Disease Clinical Assessment Scale cognitive subscale (ADAS-cog) in comparison to placebo at the study endpoint at 16 weeks. Similarly, clinical ratings (Clinical Dementia Rating) were significantly improved at the end of the study. However, these results require a note of qualification. The extract (60 drops of a 1:1 alcohol:dried leaf tincture per day) was ill defined and no description of the placebo was provided. Furthermore, the pattern of results, with a substantial decline on the ADAS-cog (approximately 7 points over 16 weeks) for the placebo group and a large concomitant rise (approximately 5 points) for the treated group, would not normally be expected in a clinical trial of this duration and nature. To give an example, Le Bars *et al.* [47] conducted a double-blind, placebo-controlled trial of *Ginkgo biloba* extract in a large patient group (N = 236) suffering mild to severe Alzheimer's. They reported a mean decline in ADAS-cog scores of a mere 1.5 points by the 52 week end-point for the placebo group, with a total significant difference of 1.7 points between treatment groups. Whilst the results from Akhondzadeh *et al*'s' trial are promising, it seems most parsimonious to suggest that the magnitude of the treatment effect and decline in ADAS-cog scores for placebo may represent either a product of the low power of the trial (N = 30), or alternatively an interaction with some other factor.

That being the case, this trial does still argue for a concerted effort to establish the efficacy of sage in treating groups suffering a pathological down-regulation of cholinergic function.

MELISSA OFFICINALIS

Historical Perspective

Melissa officinalis (Lemon balm), is a cultivated perennial lemon scented herb. Originating in Southern Europe its cultivation and use spread throughout Europe by the Middle ages.

Records concerning the medicinal use of *M. officinalis* date back over 2000 years with entries in the 'Historia Plantarum' (approximately 300 BC) and the 'Materia Medica' (approximately 50-80 BC). Medicinal use throughout this early epoch include a recommendation by Paracelsus (1493-1541) that balm would completely revivify a man, and indication for "all complaints supposed to proceed from a disordered state of the nervous system" (see: Grieve, 1931). Several early herbal Apothecaries also attributed balm tea not only with general beneficial effects upon the brain, but also with specific mnemonic improvements. These include, from the 17th century, John Evelyn who writes that "Balm is sovereign for the brain, strengthening the memory and powerfully chasing away melancholy"; and the authors of 'The London Dispensary' who recommend Balm for the 'strengthening of the brain'.

Contemporary Usage

Approximately 50 tons of balm leaves are sold each year for medicinal purposes in Germany alone, much of which is cultivated in Eastern European countries and Spain. Contemporary reports suggest that, as well as possessing spasmolytic and antibacterial properties, *Melissa officinalis* can modulate a number of behavioural measures, with indications including administration as a mild sedative, in disturbed sleep, and in the attenuation of the symptoms of nervous disorders, including the reduction of excitability, anxiety, and stress [49, 50]. In keeping with its long history of safe usage no adverse side effects have so far been reported for the herb [51]. *Melissa officinalis* is predominantly sold 'over the counter' as a popular herbal food supplement, most often is combined with other herbs. As an illustration of this, the German pharmaceutical industry's 'Rote Liste' (2001) drug catalogue included 49 products containing lemon balm.