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## Complementary and Alternative Medicine in the Treatment of Anxiety and Depression

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### Abstract and Introduction

#### Abstract

**Purpose of Review:** There is well documented evidence for the increasing widespread use of complementary and alternative medicine in the treatment of physical and psychiatric symptoms and disorders within Western populations. Here we provide a review of the recent literature on evidence for using such interventions in the treatment of anxiety and depression.

**Recent Findings:** With regard to herbal treatments, kava is effective in reducing anxiety symptoms and St John's wort in treating mild to moderate depression. The association of kava with hepatotoxicity, however, is a significant concern. Promising data continue to emerge for the use of omega-3 fatty acids in managing depression. Evidence for the use of acupuncture in treating anxiety disorders is becoming stronger, although there is currently minimal empirical evidence for the use of aromatherapy or mindfulness-based meditation.

**Summary:** The evidence base for the efficacy of the majority of complementary and alternative interventions used to treat anxiety and depression remains poor. Recent systematic reviews all point to a significant lack of methodologically rigorous studies within the field. This lack of evidence does not diminish the popularity of such interventions within the general Western population.

#### Introduction

Interest in complementary and alternative medicine (CAM) continues to grow as an increasing number of people, including health care professionals, look at ways to improve their own lives and those of others by using a variety of alternatives to conventional medicine. There are difficulties in reviewing research in CAM because of the diversity of practices included under the term and the various ways in which it is applied across different cultures. The World Health Organization refers to the increase in the use of nonconventional medicine, meaning traditional, complementary and alternative medicine, in countries all over the world in its Traditional Medicine Strategy 2002-2005.<sup>[1]</sup> Some authors group complementary medicines into herbal remedies (food supplements that include vitamin preparations and other organic and inorganic substances, such as omega-3 fatty acids),<sup>[2]</sup> whereas others list individual therapies such as acupuncture, aromatherapy, herbal therapy, homeopathy, iridology, naturopathy and reflexology under the umbrella of CAM.<sup>[3-6,7\*,8\*,9]</sup> There is ongoing debate regarding the level of evidence required by the scientific community and appropriate methodological approaches in CAM research, including the feasibility and complexities of using randomized controlled trials (RCTs) and difficulties in identifying suitable placebos.<sup>[10]</sup>

Kessler *et al.*<sup>[11]</sup> reported data on the use of complementary therapies to treat anxiety and depression in the USA, which indicate that complementary and alternative therapies are used more than conventional therapies by people with anxiety and severe depression. This large-scale study found depression, anxiety and insomnia to be among the most common reasons for people to use complementary therapies. For example, 53.6% of respondents suffering

from severe depression reported using complementary and alternative medicine for treatment during the 12 months before the survey.

In the UK, estimates of the proportion of the general population using CAM range from 14% to 30%<sup>[12]</sup> and consumer surveys in other European countries indicate positive public attitudes toward the use of complementary therapies, with acupuncture being identified as one of the most popular forms of complementary treatment.<sup>[13]</sup> The findings of a large postal survey conducted in Australia<sup>[3]</sup> showed that people who were experiencing mild to moderate depression chose self-help strategies and complementary therapies such as aromatherapy, St John's wort, meditation and nutritional supplements rather than seeking professional help. In contrast, those with severe depression were more likely to seek conventional professional help and did not tend to use complementary therapies.

Here we review recent research in CAM approaches to the treatment of anxiety and depression, including use of herbal interventions, nutritional and dietary supplements, acupuncture, light therapy, meditation and hypnosis.

## Anxiety

A number of complementary and alternative interventions are currently being used to treat anxiety and anxiety disorders. For the purposes of this review, they will be grouped as follows: herbal interventions, nutritional supplements and aromatherapy; cognitive interventions, including mindfulness-based stress reduction (MBSR) and meditation; and physical interventions such as acupuncture.

### Herbal Interventions, Nutritional Supplements and Aromatherapy

Werneke *et al.*<sup>[2]</sup> conducted an extensive database search and identified 2007 studies of herbal remedies and nutritional supplements in the treatment of psychiatric disorders. The authors found that kava (*Piper methysticum*) was the most researched remedy for anxiety and that there was good evidence for its anxiolytic effect. A Cochrane review reported by Pittler and Ernst,<sup>[14]</sup> which included 11 RCTs involving 645 patients, showed that kava is the only herbal remedy that has been proven to be effective in reducing anxiety. All of these trials showed the anxiolytic effects of kava to be superior to those of placebo. In a recent review, Ernst<sup>[15]</sup> warned that, although it has been shown to be effective in reducing anxiety, kava cannot be recommended for clinical use because of an association with hepatotoxicity, which has led to its withdrawal from the UK market. He emphasized the importance of conducting large, long-term clinical trials to investigate the effects of herbal medicines, which are usually moderate and tend to appear after prolonged periods of use.

Two separate Cochrane reviews investigated the effectiveness and safety of treating anxiety disorders with valerian and passiflora. The valerian review<sup>[16\*\*]</sup> identified one randomized controlled trial involving 36 patients with generalized anxiety disorder that was eligible for inclusion. This study found that patients taking diazepam experienced significantly greater improvement in self-reported anxiety symptoms than those in the valerian and placebo groups, with no significant differences in reported side effects between the three groups. The other review, also conducted by Miyasaka *et al.*,<sup>[17\*\*]</sup> identified two passiflora versus benzodiazepine studies eligible for inclusion with a total of 198 participants, but no findings reached statistical significance. The authors concluded that there is insufficient evidence available to draw any clear conclusions regarding the efficacy or safety of either valerian or passiflora in treating anxiety disorders.

Aromatherapy is concerned with the psychological, physiological and pharmacological effects of essential oils introduced by means of inhalation, olfaction and dermal application. The precise definition of aromatherapy, however, remains problematic. Perry and Perry<sup>[18\*]</sup> consider the terms essential oil therapy or phyto-essential-pharmacology to be more precise than aromatherapy, because effects are not necessarily related to the aromas only. Some practitioners view aromatherapy as holistic medicine, which treats soul, spirit and body, whereas a small number of research groups focus on fragrance compounds and essential oils as medicinal agents and aim to elucidate their modes of action. The pharmacology behind the actions of most essential oils remains uncertain, however. Buchbauer and Jirovetz<sup>[19]</sup> proposed a universal definition of aromatherapy as the therapeutic use of fragrances or of volatile substances to cure and mitigate or prevent diseases, infections and indispositions only by means of inhalation, in the belief that this definition has helped to promote scientific work on aromatherapy and the biological effects of essential oils.

In their review of reports published in English language medical journals, Perry and Perry<sup>[18\*]</sup> found only one small open-label study of aromatherapy in the treatment of psychiatric patients diagnosed with anxiety and depressive

disorders. Aromatherapy was combined with massage and essential oils were individualized.<sup>[20]</sup> The study's author reported that six of the eight participants experienced reduced anxiety and improved mood over an 8-month period of use. It is not possible, however, to distinguish whether this improvement was due to massage, the essential oils chosen, psychotropic medications (which were not standardized), or other factors. The study is also limited by the lack of a control group.

A recently reported study of the effectiveness of aromatherapy in the management of anxiety in patients with cancer<sup>[21]</sup> was carried out in four cancer centres and a hospice in the UK, where 288 patients with cancer and with clinical anxiety or depression were randomly assigned to a 4-week course of aromatherapy massage or usual supportive care. Patients receiving the aromatherapy massage experienced a significant improvement in anxiety and depression symptoms after 2 weeks, and this was maintained at 6 weeks (64% improvement versus 46% in the control group). The difference between the groups disappeared by 10 weeks after randomization. Self-reported anxiety improved more for patients receiving aromatherapy than for patients in the usual care group at 6 and 10 weeks after randomization, whereas there was no significant difference in the improvement of self-reported depression between the group receiving aromatherapy massage and the usual care only arm. Twenty essential oils were used and individualized according to the therapist's choice of oils considered most appropriate for each person. The authors did not report which essential oils were used nor the specific dosages used. The study was unable to demonstrate whether massage or the essential oils, or both, were responsible for the improvement in mood and anxiety of patients receiving aromatherapy.

### Cognitive Interventions

Toneatto and Nguyen<sup>[22]</sup> reviewed controlled studies of MBSR for the treatment of anxiety and depression published before 2007 and found no evidence for the efficacy of MBSR in reliably reducing anxiety symptoms. The reviewed studies that reported a statistically significant reduction in anxiety or depression after MBSR did not include an active control group; positive findings were found only when waiting list or usual treatment groups were used as controls. The authors suggested that nonspecific variables may account for improvements in the MBSR-treated patients and that future studies with improved methodologies are required to test the specific efficacy of the mindfulness component of the intervention.

Meditation has a long history across many cultures. There are many types of meditation, all involving techniques for the focusing of attention. The object of focus can be an image, an idea, a word, a phrase, or one's breath. In their Cochrane review of RCTs in which meditation therapy was used as an intervention for anxiety disorder, Krisanaprakornkit *et al.*<sup>[23\*]</sup> focused on studies published before 2006 in which meditation therapy was compared with conventional treatments, including drugs and other psychological treatments. The review targeted meditation therapies that used concentrative meditation or mindfulness meditation to treat anxiety disorders. The two studies eligible for inclusion in the review included 45 individuals and were conducted in the USA, whereas there were no eligible studies from Eastern countries such as India and China, where many meditation techniques originated. The authors were unable to draw firm conclusions about the effects of meditation in anxiety disorders because of the small number of eligible studies. They did note that dropout rates were high in each of the studies reviewed.

In a study published after these two reviews, Lee *et al.*<sup>[24]</sup> investigated the effectiveness of a meditation-based stress management programme in patients with anxiety disorder. Forty-six patients diagnosed with anxiety disorders were randomly assigned to either the meditation programme (MBSR, which included some education on coping with anxiety, exercise, muscle build up, relaxation and hypnotic suggestion) or the education programme. The education programme focused on the biological aspects of anxiety disorder, with no stress management or behaviour techniques taught. Prescribed medications were not altered during the study. The duration of the programme was 8 weeks, with 60-min sessions provided weekly. There were significant decreases in all anxiety scale scores for the meditation programme group compared with patients on the education programme. No significant improvement in measures of depression, somatization, or obsessive-compulsive symptoms was demonstrated. Limitations of the study include the possible confounding effects of administered medication, the lack of a true placebo control and the absence of any follow-up data. The authors suggest that a larger study taking into account the above limitations is needed to confirm these findings.

### Physical Interventions

Acupuncture is a traditional Chinese treatment using needles which are inserted at specific points of the body and either manipulated or electrically stimulated. Traditional Chinese theory posits that acupuncture corrects the imbalances in yin and yang forces that circulate along channels in the body, and this balance is considered to be essential for good health. Two recent studies are of interest.

A randomized crossover trial conducted by Gibson *et al.*<sup>[25]</sup> found statistically significant differences between acupuncture and breathing retraining, in favour of acupuncture, in a small sample of 10 patients diagnosed with hyperventilation syndrome (HVS). The authors cautioned that, although there appears to be a beneficial effect of using acupuncture to treat HVS by reducing anxiety and hyperventilation symptoms, there may be a carry-over effect after the acupuncture treatment that was not detected because of the small sample size. They suggest that a two-arm randomized trial using an acupuncture placebo might be more appropriate for further investigating the effects of acupuncture on HVS.

Another recently reported RCT evaluated the efficacy and acceptability of acupuncture for treatment of post-traumatic stress disorder (PTSD).<sup>[26]</sup> In all, 84 patients diagnosed with PTSD were randomly assigned to one of three groups, with one group receiving acupuncture, another group receiving cognitive-behavioural therapy (CBT) and the third acting as a wait list control. A total of 61 participants completed the trial and the results suggest that acupuncture might be useful in reducing symptoms of PTSD, depression, anxiety and impairment in people diagnosed with PTSD. Treatment effects in the acupuncture group were similar to those with the group CBT intervention, and both interventions were superior to the wait listed control on all measures. Both groups also expressed high satisfaction with care, and both acupuncture and group CBT were seen as equally acceptable by participants in treating PTSD. Treatment effects were maintained for 3 months after the end of treatment in both the acupuncture and CBT groups. This initial evidence that acupuncture may be effective and acceptable for treating PTSD suggests that a larger study is indicated to evaluate this adequately. The authors suggested that a multisite trial with multiple therapists rather than a single therapist, additional control groups, treatment validation procedures and blinded outcome assessment should be considered.

## Depression

Complementary and alternative treatments for depression and depressive disorders discussed in this report are grouped into the following categories: herbal interventions, nutritional supplements and aromatherapy; cognitive interventions, including hypnotherapy, CBT and mindfulness-based cognitive therapy; and physical interventions, including acupuncture and light therapy.

### Herbal Interventions, Nutritional Supplements and Aromatherapy

A recent review reported by Ernst<sup>[15\*]</sup> indicated that St John's wort (*Hypericum perforatum*) is the only herbal remedy found to be effective as a treatment for mild to moderate depression. The author discussed a previous meta-analysis published in German language by Roder *et al.*<sup>[27]</sup> In five trials involving 2231 patients that compared St John's wort with conventional antidepressants, Roder *et al.* found both approaches to be equally effective. St John's wort was significantly effective when compared with placebo in 25 trials involving a total of 2129 patients. Ernst cautioned against using St John's wort with other medications because it can increase the plasma levels of a range of drugs and there is a possibility that it can occasionally trigger psychosis in patients who are using selective serotonin reuptake inhibitors.

Thachil *et al.*<sup>[9]</sup> conducted a review of the evidence for complementary therapies used in depression by searching the literature for studies on CAM as monotherapy. Nineteen reports were reviewed, yielding grade 1 evidence (strong evidence from at least one systematic review of multiple well designed RCTs) for the use St John's wort, tryptophan/5-hydroxytryptophan, S-adenosyl methionine, inositol and folate in depressive disorders. None of these findings was conclusively positive, and folate had a significant effect only when combined with an antidepressant. The review found grade 2 evidence (strong evidence from at least one properly designed RCT of appropriate size) for the use of saffron in mild to moderate depression, but the results are inconclusive and large-scale trials are warranted to investigate further its potential as an effective treatment.

Mischoulon<sup>[28\*\*]</sup> reported that the results of recent studies of omega-3 fatty acid supplementation, including the use of eicosapentaenoic acid (EPA), are promising in treatment of depression. In addition, the omega-3 fatty acids have been shown to be safe and might be useful in specific populations, such as the elderly, pregnant or lactating women, and people with medical co-morbid conditions. A number of controlled trials and a few open studies have suggested that supplementation with doses of EPA and docosahexaenoic acid (DHA) that are about five times higher than the standard dietary intake in the USA may have antidepressant or mood-stabilizing effects. Mischoulon described as compelling the evidence for the efficacy and safety of omega-3 fatty acids to treat patients with depression, but recommended that more well designed controlled trials be conducted in larger patient populations. He suggested that, although the data remain inconclusive, patients with mild depression or those who are unresponsive to conventional antidepressants might be the best candidates for alternative treatments such as St John's wort and

omega-3 fatty acids.

Clayton *et al.*<sup>[29]</sup> reviewed the evidence for the rationale and benefit of omega-3 fatty acids in the treatment of psychiatric disorders in children and adolescents, and found some evidence of likely benefit in the treatment of unipolar depression. The authors emphasized the importance of conducting further well designed research, taking into account the importance of blinding patients and researchers to treatment and choosing appropriate placebos and omega-3 fatty acids (EPA and DHA.)

Aromatherapy research was recently reviewed by Perry and Perry.<sup>[18\*]</sup> They discussed the antidepressant properties of essential oils such as bergamot (*Citrus bergamia*) and geranium (*Pelargonium graveolens*) in a report offering clinical and neuropharmacological perspectives of aromatherapy in managing psychiatric disorders. Although some studies have shown an association between aromatherapy and improvement in mood in healthy adults, there is a notable lack of methodologically sound trials in clinically depressed populations. No conclusions can be drawn regarding the efficacy of aromatherapy in treating depression until such trials are conducted. The authors arrived at the overall conclusion that, based on relevant neuropharmacological and limited clinical evidence, aromatherapy is a treatment with major but relatively unexplored potential in the field of clinical psychiatry.

### Cognitive Interventions

Alladin and Alibhai<sup>[30]</sup> compared the effectiveness of the combination of hypnosis and CBT, which they termed cognitive hypnotherapy, with that of standard CBT in 84 patients with major depression. Patients were randomly assigned to the two treatment groups, which were run over 16 weeks. The investigators found that treatment outcomes were significantly enhanced when CBT was combined with hypnotherapy. Patients from both groups exhibited significant improvements compared with baseline scores, with greater reductions in depression, anxiety and hopelessness in the cognitive hypnotherapy group than in the CBT group. This improvement was maintained at 6 and 12 months of follow up. The authors suggested that further expanded studies across multiple settings are required to replicate these findings. In addition, they propose the use of a dismantling design to clarify which subcomponents of the hypnotherapy intervention are most important.

In their wide-ranging review of complementary treatments for depression, Pilkington *et al.*<sup>[8\*]</sup> concluded that two recent trials suggest that mindfulness-based cognitive therapy, which integrates aspects of CBT with components of MBSR programmes, may be useful in preventing relapse in people who have recovered from depression. In more general terms, the authors found that, although use of complementary medicine for the management of depression is widespread, there is currently a rather limited evidence base for the efficacy of CAM treatments compared with that for antidepressants or CBT, and that the findings reported remain inconclusive because of small sample sizes, inadequate follow up, limited information on attrition and lack of blinding.

### Physical Interventions

The first systematic review of RCTs investigating the efficacy of acupuncture in treating depression was that conducted by Leo and Ligot.<sup>[31]</sup> They examined nine RCTs, five of which were considered to be of poor methodological quality, and found that acupuncture tended to be as effective as antidepressants in treating depression in the limited studies available for comparison. The authors stated, however, that the overall evidence remains inconclusive because of the varied methodology and study designs used, but that further research investigating the use of acupuncture in treating depression is warranted.

MacPherson and Schroer<sup>[32\*]</sup> attempted to resolve the problem of variability in application of acupuncture treatment, which makes it difficult to test the effectiveness of this intervention empirically. They described acupuncture as a complex intervention because of the difficulty in precisely defining what the active ingredients are and how they relate to each other. The authors reported the process of implementing a consensus method to develop a standardized treatment protocol in preparation for a RCT of acupuncture to treat depression. Components likely to be essential to the intervention that would need to be incorporated into the protocol were identified and rated over two rounds of evaluation by 15 practitioners. Such standardization is an important step towards improving the methodological rigour of clinical trials conducted using CAM interventions.

Light therapy is another physical intervention that is used to treat depression and depressive disorders. It exposes patients to a bank of bright lights for a variable number of hours per day, usually between 1 and 3 h. Patients can read or engage in other activities during the period of exposure. In a recent paper that reviewed CAM therapies in the treatment of depression in children and adolescents, Jorm *et al.*<sup>[7\*]</sup> found good evidence for the efficacy of light

therapy in winter depression. There was no evidence that it would be effective for nonseasonal depression because of the very limited data available, suggesting that further research is warranted.

## Conclusion

There is significant and growing interest in the use of CAM to treat psychiatric disorders across Western and non-Western societies. We review the current evidence regarding CAM treatments for anxiety and depressive disorders with a focus on recent studies and reviews. With regard to the use of herbal interventions, kava has efficacy for reducing anxiety but is linked to hepatotoxicity. St John's wort is the only demonstrably effective herbal treatment for mild to moderate depression. There are now some promising published data for the omega-3 fatty acids EPA and DHA, supporting their role as adjunct treatments in mild to moderate depressive states. There is currently minimal evidence for the use of pure aromatherapy in alleviating the symptoms of anxiety or depression, but the evidence for acupuncture in treating anxiety disorders, including PTSD, is a little more robust. Regarding cognitive interventions, MBSR currently has very little empirical basis but initial research into the combination of hypnotherapy with CBT appears promising in treating depression.

The well documented popularity of CAM interventions for anxiety and depression is not reflected in the current evidence base, which is very limited. There is a paucity of high-quality studies in the field. Until a reasonable number of methodologically sound studies are completed across these varied treatment modalities, it will remain difficult to draw any substantive conclusions regarding their usefulness to the clinician.

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