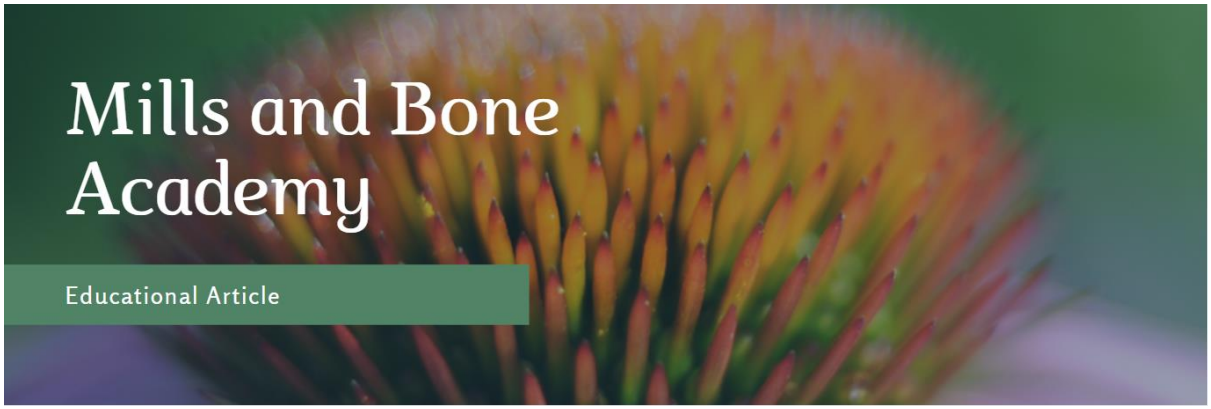

Herbal Alternatives to St John's Wort for Depression –

Kerry Bone

Depression is a common and major health problem in our community. So it is not surprising that many people turn to natural treatments. This was highlighted in a recent survey of 220 women with depression.[i] An amazing 54% reported that they had tried some form of complementary or alternative medicine in the past year. One of the main reasons given by the women surveyed was that they wanted a treatment based on a natural approach. But in the case of depression, what herbs are backed up by clinical evidence?

There is no doubt that St John's Wort is the best and most-proven herbal answer for mild to moderate depression. But unfortunately, St John's Wort has acquired a lot of "baggage" along the way, some of it justified and some not. In particular concerns have been raised about its interaction with a whole range of drugs. There is evidence that St John's Wort decreases the efficacy of these drugs, ranging from digoxin to the contraceptive pill. But probably more concerning in the context of depression are the doubts that it might interact harmfully with antidepressant drugs. There is not a lot of solid evidence, it is more like rumour and propaganda. But the mud has stuck and I now find that many of my depressed patients on conventional medication are reluctant to add St John's Wort to their regime.

In this context it is worthwhile to understand what other herbs might also play a role in managing the blues. There is some encouraging research here which has highlighted some unlikely candidates, namely lavender and saffron. Also, perhaps not unexpectedly, the tonic herb Rhodiola now

has some good evidence for a supporting role in depression.

Lavender has a strong reputation as an herb for the nervous system. In aromatherapy it has been used to calm anxiety and boost mood for a long time. The use of lavender oil in depression is also supported by evidence from clinical studies.[ii] But recently a small double blind clinical trial was conducted to compare the oral use of 60 drops/day (around 3 mL) of a lavender 1:5 tincture with the drug imipramine.[iii] A third group of patients also took both treatments. While the lavender tincture showed some benefit, it was not as effective as the imipramine for depression. Perhaps a higher dose of lavender might have yielded better results, as the dose used in the trial was quite low. But the good news was that the combination of lavender with imipramine worked better than imipramine alone, without any accentuation of the drug's side effects.

The evidence for saffron (*Crocus sativus*) is more extensive, with a number of clinical trials showing promising results, although again these were all small involving around 40 patients. There are trials where it was tested against a placebo and other trials where it was compared to conventional antidepressants, both a tricyclic (imipramine) and an SSRI (fluoxetine).

The double-blind placebo-controlled trials found that saffron powder at a dose of just 30 mg per day was significantly better ($p<0.001$) than placebo in improving the mood of patients with mild to moderate depression.[iv,v] There were no more side effects in the saffron group than in the placebo. There was a dramatic drop in the Hamilton Depression rating scale for the patients taking the saffron that kicked in at 2 weeks and continued to drop until the end of the trial at 6 weeks. In all it dropped from around 23 to 9 in the group taking saffron, versus a drop of only around 23 to 18 in the placebo group.

In the comparative clinical trials, saffron was found to be as good as the conventional drugs tested. In the trial comparing saffron with imipramine, patients taking the drug experienced the typical side effects of a dry mouth and excessive sedation.[vi] No such side effects occurred for saffron. Saffron was compared to fluoxetine (Prozac) in two published trials.[vii,viii] The saffron was found to have similar remission rate for depression to the drug, of around 25%. There were no

significant differences between the two patient groups in terms of side effects.

Saffron is a very expensive spice and dye that is commonly used in Indian and Middle Eastern cuisine. The reason why it is expensive is that just a small part of each flower of this attractive Crocus is harvested by hand. This part of the plant is called the stigma and it is bright orange. It takes many flowers to make just a few grams of this exotic spice. So it is just as well that a small dose of only 30 mg per day was effective in the trials.

High quality clinical research from the Swedish Herbal Institute has validated the role of Rhodiola in depression.[ix] In an experimental model of depression Rhodiola performed as well as St John's wort and the antidepressant drug imipramine. The activity was dose dependent and several key phytochemicals in Rhodiola including rosavin were shown to be active.

This research led to a clinical trial of Rhodiola extract in mild and moderate depression. In a randomised, double blind, placebo-controlled model, male and female patients aged 18 to 70 years with Hamilton Rating Scale for Depression (HAMD) scores of 21 to 31 were divided into 3 groups. Over 6 weeks Group A (31 patients) received 340 mg of Rhodiola extract (equivalent to about 7 g of root) per day, Group B (29 patients) received 680 mg/day of extract and Group C (29 patients) were assigned a matching placebo. Both the Hamilton and the Beck Depression Inventory (BDI) were used to assess treatment outcomes at 6 weeks. The BDI is a series of questions developed to measure the intensity, severity and depth of depression.

In terms of overall depression, there were highly significant reductions ($p<0.0001$) in both the Hamilton and BDI scores 6 weeks after Rhodiola treatment that was not evident in the placebo group. The average HAMD score in Groups A and B fell from around 25 to around 18 for both groups, indicating that a dose-response effect was not seen for this outcome. In contrast, a dose-response relationship was observed for the BDI scale, with values falling from around 11 to 8 in Group A and from about 11 to 5 in Group B. In terms of the Hamilton subgroup scores, significant reductions were seen for insomnia, emotional instability and somatisation (physical symptoms caused by mental or emotional factors), but not for self-esteem (except in the high dose Group B). No serious side effects were seen.

In discussing a mechanism of action for Rhodiola, the authors emphasised its adaptogenic (helps you adapt to stress) and antistress activities. In depression it is theorised that stress hormones such as cortisol and indeed the HPA (hypothalamic-pituitary-adrenal) axis are overactivated and do not switch off appropriately via the normal negative feedback. The influence of certain stress chemicals released by cells (stress kinases) is thought to play a key role in this overactivity. In particular they inhibit the sensitivity of receptors in the brain to cortisol. In an experimental model, Rhodiola extract decreased the release of stress kinases and cortisone in response to stress. This suggests that Rhodiola inhibits the stress-induced activation of stress kinases in depressed patients and so restores the impaired sensitivity of their brain receptors to cortisol. This "resistance" of the cortisol receptors is a noted feature in many patients with major depression.

The additional good news is that Rhodiola continues to be validated as an important tonic by new clinical research from Germany.[x] Over 12 weeks it was found that a Rhodiola supplement not only improved physical symptoms such as low energy, decreased libido and exhaustion, it also boosted mental performance and motivation. And the herb may even make you live longer. It is early days yet, but when Rhodiola was given to fruit flies in a laboratory experiment it significantly increased their lifespan.[xi] Some other traditional Chinese tonics also assessed in this study did not exert such a pronounced effect.

What is particularly attractive about Rhodiola in depression is that it is relatively free from side effects. Additionally, since its proposed mechanism of action is quite different to conventional antidepressant drugs, it is unlikely to interact with such drugs. This is a real advantage for this herb.

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