

## Avicenna and Evidence Based Medicine

Evidence Based Medicine (EBM) is now generally perceived to be the dominant operating system in conventional medicine. It is unsurprising then that some have counseled complementary and alternative medicine practitioners to resist EBM<sup>1,2</sup>. The efficacy of medicinal herbs does need to be established and toxicity, contraindications and side effects also need to be investigated, and this is best done with clinical research and trials that at this time are being conducted almost exclusively on efficacy and are limited in number most probably because of funding. Very little to no attention is being given to the more traditional fresh herbal extracts<sup>3,4</sup>.

Many herbal medicines are now being supported by scientific evidence and have been shown to exert significant effects in the body, relieve symptoms, treat disease and improve everyday function. Any "expert" who still states there's no scientific evidence to support the use of herbal medicines hasn't done their homework. One of interesting example is saffron (*Crocus sativus*) for Alzheimer's disease and depression that has been mentioned by Avicenna in his famous book. Avicenna's famous works is the Canon of Medicine, which was a standard medical text at many medieval universities. The Canon of Medicine was used as a text-book in the universities of Montpellier and Leuven as late as 1650. Avicenna Canon of Medicine provides a complete system of medicine according to EBM. Saffron is the world's most expensive spice, derived from the flower of *Crocus sativus*. Each saffron crocus grows to 20–30 cm and bears up to four flowers, each with three vivid crimson stigmas<sup>3,4</sup>. Indeed, it is a Persian herb with a history as long as the Persian Empire itself. Iran, the world's largest producer of saffron has been investing in research into saffron's potential medicinal uses<sup>3,4</sup>. To date, five published randomized controlled trials have been published about effects of saffron on depression. The first evidence-based study on this subject was published in 2004 showing that saffron was as efficacious as imipramine in the short-term treatment of mild to moderate depression in adults<sup>5</sup>. Importantly, saffron was more tolerable than imipramine (which often causes anticholinergic side effects). Subsequently, saffron was compared to placebo in a six-week randomized controlled trial of 40 adult patients with mild to moderate depression. Saffron resulted in about 12-point reduction on Hamilton Depression Rating Scale (HDRS) compared with only five points seen with the placebo. Tolerability profile of saffron was similar to the placebo<sup>5</sup>. Later, several studies provided evidence for antidepressant effects of different *Crocus sativus L.* constituents compared with both placebo and fluoxetine. Both petal and stigma of *Crocus sativus L.* have shown beneficial effects for treatment of depression<sup>6,7</sup>.

*Crocus sativus L.* is increasingly being studied as a memory enhancer. Saffron can attenuate the deleterious effect of ethanol on memory registration and retrieval, and prevent ethanol-induced inhibition of hippocampal long-term potentiation<sup>3,4</sup>. Crocin seems to be involved in spatial memory and recognition and blocked scopolamine-induced performance deficits in the step-through passive avoidance and radial water maze tests<sup>3,4</sup>. Saffron showed similar protective effects on recognition and spatial memory in chronic stress and hypoperfusion models of memory impairment<sup>3,4</sup>.

In an animal model of Alzheimer's Disease (AD) induced by intraventricular injection of streptozocin, Khalili *et al* showed that administration of crocin resulted in significantly better results in passive avoidance test<sup>3,4</sup>. In a 16-week placebo-controlled study, 46 patients with mild to moderate AD were assigned to saffron 15 mg twice daily or placebo. At the end of the trial, saffron was associated with a significantly better outcome on cognitive function than placebo. Importantly, tolerability of saffron was similar to placebo<sup>8</sup>. In a 22-week donepezil-controlled study, saffron 15 mg twice daily was compared to donepezil 5 mg twice daily. Saffron was as efficacious as donepezil, but was associated with lower frequency of side effects than donepezil<sup>9</sup>. Now if we read again the monograph regarding saffron in the Avicenna's book we will find an evidence based medicine approach.

## References

1. Guyatt G. Evidence-based medicine. ACP J Club 1991;114 (Suppl2):A16.
2. Evidence-Based Medicine Working Group. Evidence-based medicine: a new approach to teaching the practice of medicine. JAMA 1992;268(17):2420-2425.
3. Akhondzadeh S. Herbal medicine in the treatment of psychiatric and neurological disorders. In: L'Abate L, (eds). Low cost approaches to promote physical and mental health: Theory research and practice. New York: Springer; 2007.

4. Akhondzadeh S, Abbasi SH. Herbal medicine in the treatment of Alzheimer's disease. *Am J Alzheimers Dis Other Demen* 2006;21(2):113-118.
5. Akhondzadeh S, Fallah-Pour H, Afkham K, Jamshidi AH, Khalighi-Cigaroudi F. Comparison of *Crocus sativus* L. and imipramine in the treatment of mild to moderate depression: a pilot double-blind randomized trial [ISRCTN45683816]. *BMC Comp Alt Med* 2004;4:12.
6. Akhondzadeh S, Tahmacebi-Pour N, Noorbala AA, Amini H, Fallah-Pour H, Jamshidi AH, et al. *Crocus sativus* L. in the treatment of mild to moderate depression: A double-blind, randomized and placebo controlled trial. *Phytother Res* 2005;19(2):148-151.
7. Akhondzadeh Basti A, Moshiri E, Noorbala AA, Jamshidi AH, Abbasi SH, Akhondzadeh S. Comparison of petal of *Crocus sativus* L. and fluoxetine in the treatment of depressed outpatients: a pilot double-blind randomized trial. *Prog Neuropsychopharmacol Biol Psychiatry* 2007;31(2):439-442.
8. Akhondzadeh S, Sabet MS, Harirchian MH, Togha M, Cheraghmakani H, Razeghi S, et al. Saffron in the treatment of patients with mild to moderate Alzheimer's disease: a 16-week, randomized and placebo-controlled trial. *J Clin Pharm Ther* 2010;35(5):581-588.
9. Akhondzadeh S, Shafiee Sabet M, Harirchian MH, Togha M, Cheraghmakani H, Razeghi S, et al. A 22-week, multi-center, randomized, double blind controlled trial of *Crocus sativus* in the treatment of mild-to-moderate Alzheimer's disease. *Psychopharmacology (Berl)* 2010;207(4):637-643.

***Shahin Akhondzadeh, Ph.D., FBPharmacolS***  
***Editor in Chief***