The Trace of Evidence Based Medicine in the Avicenna's Approaches

Kashani L (M.D.)[1], Akhondzadeh S (Ph.D.)[2*]

1- Infertility Ward, Arash Hospital, Tehran University of Medical Sciences, Tehran, Iran
2- Psychiatric Research Center, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, Tehran, Iran
* Corresponding author: Psychiatric Research Center, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, South Kargar Street, Tehran 13337, Iran
Tel: +98-21-55412222, Fax: +98-21-55419113
E-mail: s.akhond@neda.net

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Abstract

Many factors underlie the growing popularity of herbal treatments for a variety of chronic conditions. Interestingly, people who use alternative therapies are not necessarily uninformed. If anything, they are more "culturally creative" (i.e., comfortable with cultural changes) and more highly educated. Many people using herbal medicines find the health care alternatives are more congruent with their own values, beliefs and philosophical orientations toward health and life. Similarly, it seems likely that many people feel that herbal medicines are empowering by allowing them to treat themselves without seeing a physician. (This same attitude may be behind the growing popularity of patient-initiated diagnostic scanning procedures such as whole body scans). The danger is that, many people believe that herbal medicines have no toxicity problems or even side effects. In addition, they are not aware of many possible interactions of herbal medicine with concurrent prescribed medications. In this review we focus on Avicenna's evidence based medicine approaches in herbal medicine.

Keywords: **Alternative Medicine, Avicenna, Evidence Based Medicine, Herbal Medicine**

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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 [1-6]. EBM is the integration of clinical expertise, patient values, and the best research evidence into the decision making process for patient care. Clinical expertise refers to the clinician's cumulated experience, education and clinical skills. The patient brings to the encounter his or her own personal preferences and unique concerns, expectations, and values. The best research evidence is usually found in clinically relevant research that has been conducted using sound methodology. Healthcare in the 21st Century relies not only on individual medical skills, but also on the best information on the effectiveness of each intervention being accessible to practitioners, patients, and policy makers. This approach is known as "evidence-based healthcare" [7-14].

Herbal medicines include a range of pharmacologically active compounds: in some cases it is not well understood which ingredients are important for a therapeutic effect. The supporters of herbal medicine believe that isolated ingredients in the majority of cases have weaker clinical effects than whole plant extract, a claim that would obviously require proof in each case. Generalizations about the efficacy of herbal medicines are clearly not possible. Each one needs systematic research including a variety of animal studies and also randomized clinical trials. Indeed, clinical trials of herbal medicines are feasible much in the same way as for other drugs. 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 [15, 16]. There is currently a vigorous debate about whether botanical medicines are effective, and whether it is ever appropriate to use them in a modern medical setting. Some criticisms have stated that clinical studies of botanicals are of poor quality, limited by factors such as small sample sizes, limited duration of therapy, and poorly characterized products. However, similar criticisms have been directed at clinical trials of pharmaceutical medicines. In fact, one recent study compared the quality of clinical trials using phytomedicines to matched trials using conventional medicines and came to the surprising conclusion that the method and reporting quality of Western clinical trials of herbal medicines was on average superior to that of conventional medicines. Numerous randomized clinical trials of herbal medicines have been published and systematic review and meta-analyses of these studies have been available. Many of today's synthetic drugs originated from the plant kingdom, and only about two centuries ago the major pharmacopoeias were dominated by herbal drugs. Herbal medicine went into rapid decline when basic and clinical pharmacology established themselves as leading branches of medicine. Nevertheless, herbal medicine is

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still of interest in many diseases in particular psychiatric and neurological disorders. There are some reasons for this issue 1) patients are dissatisfied with conventional treatment, 2) patients want to have control over their health care decision, and, 3) patients see that herbal medicine is congruent with their philosophical values and beliefs [15]. It has been reported that most patients with a mental disorder sought herbal medicine treatment for somatic problems rather than for their mental and emotional symptoms and the best example is somatic symptoms of depression. Physicians need to understand the biochemical and evidential bases for the use of herbs and nutrients to diagnose and treat patients safely and effectively, to avoid interactions with standard medications, and to provide patients with the benefits of alternative treatments.

Although a multitude of pharmaceutical agents are available for the treatment of mental disorders, physicians find that many patients cannot tolerate the side effects, do not respond adequately, or eventually lose their response. In comparison, many therapeutic herbs have far fewer side effects. They can provide an alternative treatment or be used to enhance the effect of prescription medications [15].

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. Avivenna’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 [15]. 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 [15, 16].

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 [17]. 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 [15]. Later, several studies provided evidence for antidepressant effects of different *Crocus sativus* L.

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constituents compared with both placebo and fluoxetine. Both petal and stigma of *Crocus sativus* L. have shown beneficial effects for treatment of depression [16, 17].

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 [15]. 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 [15]. Saffron showed similar protective effects on recognition and spatial memory in chronic stress and hypoperfusion models of memory impairment [15].

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 [15]. 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 [19]. 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 [20, 21]. Now if we read again the monograph regarding saffron in the Avicenna's book we will find an evidence based medicine approach. In another words, Avicenna utilized the process of systematically reviewing, appraising and using clinical research findings to aid the delivery of optimum clinical care to patients.

References

1. Sepanjnia K, Modabbernia A, Ashrafi M, Modabbernia MJ and Akhondzadeh S. Pioglitazone adjunctive therapy for moderate-to-severe major depressive disorder: randomized double-blind placebo-controlled trial. *Neuropsychopharmacol.* 2012; 37 (9): 2093 - 100.

2. Salehi B, Imani R, Mohammadi MR, Fallah J, Mohammadi M, Ghanizadeh A, Tasviechi AA, Vossoughi A, Rezazadeh SA and Akhondzadeh S. *Ginkgo biloba* for attention-deficit/hyperactivity disorder in children and adolescents: a double blind, randomized controlled trial. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 2010; 34 (1): 76 - 80.

3. Akhondzadeh S, Fallah J, Mohammadi MR, Imani R, Mohammadi M, Salehi B, Ghanizadeh A, Raznahan M, Mohebbi-Rasa S, Rezazadeh SA and Forghani S. Double-blind placebo-controlled trial of pentoxifylline added to risperidone: effects on aberrant behavior in children with autism. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 2010; 34 (1): 32 - 6.

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[DOR: 20.1001.1.2717204.2016.15.57.6.2]

4. Akhondzadeh S, Malek-Hosseini M, Ghoreishi A, Raznahan M and Rezazadeh SA. Effect of ritanserin, a 5HT2A/2C antagonist, on negative symptoms of schizophrenia: a double-blind randomized placebo-controlled study. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 2008; 32 (8): 1879 - 83.

5. Akhondzadeh S, Gerami M, Noroozian M, Karamghadiri N, Ghoreishi A, Abbasi SH and Rezazadeh SA. A 12-week, double-blind, placebo-controlled trial of donepezil adjunctive treatment to risperidone in chronic and stable schizophrenia. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 2008; 32 (8): 1810 - 5.

6. Akhondzadeh S, Ahmadi-Abhari SA, Assadi SM, Shabestari OL, Kashani AR and Farzanehgan ZM. Double-blind randomized controlled trial of baclofen vs. clonidine in the treatment of opiates withdrawal. *J. Clin. Pharm. Ther*. 2000; 25 (5): 347 - 53.

7. Akhondzadeh S, Naghavi HR, Vazirian M, Shayeganpour A, Rashidi H and Khani M. Passionflower in the treatment of generalized anxiety: a pilot double-blind randomized controlled trial with oxazepam. *J. Clin. Pharm. Ther*. 2001; 26 (5): 363 - 7.

8. Akhondzadeh S, Kashani L, Mobaseri M, Hosseini SH, Nikzad S and Khani M. Passionflower in the treatment of opiates withdrawal: a double-blind randomized controlled trial. *J. Clin. Pharm. Ther.* 2001; 26 (5): 369 - 73.

9. Akhondzadeh S, Kashani L, Fotouhi A, Jarvandi S, Mobaseri M, Moin M, Khani M, Jamshidi AH, Baghalian K and Taghizadeh M. Comparison of Lavandula angustifolia Mill. tincture and imipramine in the treatment of mild to moderate depression: a double-blind, randomized trial. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 2003; 27 (1): 123 - 7.

10. Akhondzadeh S, Noroozian M, Mohammadi M, Ohadinia S, Jamshidi AH, Khani M. *Salvia officinalis* extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomized and placebo-controlled trial. *J. Clin. Pharm. Ther*. 2003; 28 (1): 53 - 9.

11. Akhondzadeh S, Noroozian M, Mohammadi M, Ohadinia S, Jamshidi AH and Khani M. Melissa officinalis extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomised, placebo controlled trial. *J. Neurol Neurosurg Psychiatry* 2003; 74 (7): 863 - 6.

12. Akhondzadeh S, Abbasi SH. Herbal medicine in the treatment of Alzheimer's disease. *Am. J. Alzheimers. Dis. Other Demen.* 2006; 21 (2): 113 - 8.

13. Farokhnia M, Shafiee Sabet M, Iranpour N, Gougol A, Yekehtaz H, Alimardani R, Farsad F, Kamalipour M and Akhondzadeh S. Comparing the efficacy and safety of *Crocus sativus* L. with memantine in patients with moderate to severe Alzheimer's disease: a double-blind randomized clinical trial. *Hum. Psychopharmacol*. 2014; 29 (4): 351 - 9.

14. Shahmansouri N, Farokhnia M, Abbasi SH, Kassaian SE, Noorbala Tafti AA, Gougol A, Yekehtaz H, Forghani S, Mahmoodian M, Saroukhani S, Arjmandi-Beglar A and Akhondzadeh S. A randomized, double-blind, clinical trial comparing the efficacy and safety of *Crocus sativus* L. with fluoxetine for improving mild to moderate depression in post

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[DOR: 20.1001.1.2717204.2016.15.57.6.2]

percutaneous coronary intervention patients. *J. Affect. Disord*. 2014; 155: 216 - 22.

15. Akhondzadeh S. Herbal medicine in the treatment of psychiatric and neurological Disorders. In: L'Abate L. Low Cost Approaches to Promote Physical and Mental Health: Theory Research and Practice. New York. 2007, pp: 119 - 38.

16. Akhondzadeh S, Fallah-Pour H, Afkham K, Jamshidi AH and 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.

17. Akhondzadeh S, Tamacebi-pour N, Noorbala AA, Amini H, Fallah Pour H, Jamshidi AH and Khani M. *Crocus sativus* L. in the treatment of mild to moderate depression: A double-blind, randomized and placebo controlled trial. *Phytother. Res.* 2005; 19: 25 - 9.

18. 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: 439 - 42.

19. Akhondzadeh S, Sabet MS, Harirchian MH, Togha M, Cheraghmakani H, Razeghi S, Hejazi SSH, Yousefi MH, Alimardani R, Jamshidi A, Zare F and Moradi A. 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: 581 - 8.

20. Akhondzadeh S, Shafiee Sabet M, Harirchian MH, Togha M, Cheraghmakani H, Razeghi S, Hejazi SSH, Yousefi MH, Alimardani R, Jamshidi A, Rezazadeh SA, Yousefi A, Zare F, Moradi A and Vossoughi A. A 22-week, multicenter, randomized, double blind controlled trial of *Crocus sativus* in the treatment of mild-to-moderate Alzheimer's disease. *Psychopharmacology* (Berl) 2010; 207: 637 - 43.

21. Akhondzadeh S. Hippocampal synaptic plasticity and cognition. *J. Clin. Pharm. Ther.* 1999; 24 (4): 241 - 8.

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