Passionflower and Sage for Mental Health

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Abstract

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. In this review we focus on *Passiflora incarnat*a and *Salvia officinalis.*

Keywords: **Evidence based Medicine, Herbal Medicine, Mental health, *Passiflora incarnate, Salvia officinalis***

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Introduction

Indeed, clinical trials of herbal medicines are feasible much in the same way as for other drugs [1]. 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. 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 [1].

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 [1].

Passionflower (*Passiflora incarnata*)

Passionflower is a woody, hairy, climbing vine. The medicinal parts are the whole or cut dried herb and the fresh aerial parts. The axillary pedicle grows up to 8 cm and bears 1 flower. The flowers are androgynous and rayed with a diameter of 5 to 9 cm and have an involucre. The 5 sepals are green on the outside, white on the inside and tough. The 5 petals are white to pale red.

The passionflower is a perennial vine on a strong stem reaching up to about 10 m in length. The vine is initially angular, later, gray and rounded with longitudinally striated bark. The plant contains flavonoids (up to 2.5%), cyanogenic glycosides and volatile oil (trace). Passionflower is used internally for depressive states such as hysteria, general nervous agitation, insomnia and nervous gastrointestinal complaints. The herb is used externally for hemorrhoids and as a bath additive for nervous agitation [1, 2].

Anxiety

Several species of *Passiflora* have anti-anxiety effects. *P. incarnata* has been most widely studied in this context. Chrysin, a *Passiflora* extract, was shown to decrease anxiety-like behaviors in rats [3]. In a double-blind randomized study comparing the effect of *P. incarnata* extract 45 drops/day and oxazepam 30 mg/day on 36 patients with generalized anxiety disorder both drugs were equally effective in treating anixety. *P. incarnata* showed a delayed onset of action compared to oxazepam, whereas more impairment of job performance were seen with oxazepam [4]. A combination of Ballota, Passiflora, Valeriana, Crataegus, Cola, and Paullinia were used to treat adjustment disorder with anxious mood in a multi-center double-blind placebo controlled study. By week four, 43% of patients in the herbal drug group and 25% in the placebo group achieved a score of less than 10 [5].

P. incarnata not only was used to treat generalized anxiety, but also was used as a calming agent before surgery. In a study, sixty patients randomly received oral *P. incarnata* (500 mg) or placebo, 90 minutes before outpatient surgery. Patients in the *Passiflora* group showed significantly lower anxiety scores than the control group. No significant difference was observed in psychological measures and psychomotor function between the two groups [6]. In a study, 30 minutes

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prior to spinal anesthesia, sixty patients were randomly assigned to *P. incarnata* extract or placebo. Patients in the *Passiflora* group showed significantly lower anxiety levels prior to induction than the placebo group, whereas no impairment of psychomotor function was observed in either group. Mechanism of action of *P. incarnata* seems to be mediated through GABAergic system. *P. incarnata* extract prevented [(3) H]-GABA uptake into rat cortical synaptosomes without affecting GABA release or transamination. The extract modulated both GABA-A and B receptors without interacting with the ethanol- and the benzodiazepine-site of the GABA-A receptor. It should be noted that some studies showed antagonistic effect of flumazenil on *P. incarnata* action on anxiety. Importantly, one study reported anxiogenic rather than anxiolytic effects of the five extracts of the *Passiflora* using elevated plus maze model [7-9].

Sleep

Some animal studies have shown sleep-enhancing effect of Passionflower either alone or in combination with Chamomile or Kava kava [10]. A double-blind placebo-controlled study assessed the efficacy of *P. incarnata* herbal tea on sleep in 41 participants. The authors showed significantly better sleep quality in the passionflower group than the placebo group [11]. Further controlled studies in human are indicated to replicate this finding.

Symptoms of substance withdrawal

Due to its anxiolytic effects, *P. incarnata* should hypothetically alleviate anxiety associated with drug and alcohol withdrawal. In a study the effects of clonidine plus *passiflora* extract (60 drops/day) were compared to clonidine (maximum of 0.8/day) plus placebo on 65 patients with opioid addiction. The authors showed significantly greater improvement in mental symptoms in the combination therapy than in the monotherapy group. A benzoflavone moiety of *P. incarnata* has been useful in treatment of withdrawal symptoms of morphine, cannabinoids, alcohol, and nicotine in addicted mice [12].

Sexuality

The investigation of the effect of Passionflower on the sexuality is limited to the animal studies. Thirty-day use of Chrysin extracted from *P. caerulea* and a benzoflavone moiety (BZF) extracted from *P. incarnata* in 2-year-old male rats resulted in a significant improvement in overall sexual functions (only in the bioflavonoid group), libido, sperm count, and greater fertilization potential. The novel benzoflavone moiety of the *P. incarnata* not only enhanced sexuality in healthy adult rats, but also prevented the deleterious effects of chronic alcohol, nicotine, and Delta 9-Tetrahydrocanabinol consumption in sexuality of the male rats [13].

Toxicity

A paper reported development of gastrointestinal symptoms, drowsiness, prolonged QTc, and episodes of ventricular tachycardia following self-administration of therapeutic doses of *Passiflora incarnata* in a young female [14].

Sage (*Salvia officinalis*)

Salvia officinalis is a member of the family Lamiaceae and is an evergreen, perennial

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subshrub, with grayish leaves, woody stems, and blue to purplish flowers. The medium-sized, pale violet, white or pink labiate flowers are in 6- to 12- blossomed false whorls, which are arranged above each other in 4 to 8 rows. The calyx is 10 to 14 mm long, funnel-shaped-campanulate, downy, glandular punctate and bilabiate. It is native to the Mediterranean region, although it has naturalized in many places throughout the world. The plant contains volatile oil (1.5-3.5%), caffeic acid derivatives, diterpenes, flavonoids and triterpenes. Many biological activities, including antibacterial, fungistatic, virostatic, astringent, secretolytic, and perspiration-inhibiting effects have been attributed to this plant [1, 2].

Dementia

Sage inhibits cholinesterase, exerts anti-inflammatory and anti-oxidative effects, and improves mood and cognition in animals and healthy human subjects [15]. Sage showed neuroprotective effect in amyloid-beta peptide (Abeta)-induced toxicity in rat pheochromocytoma (PC12) cells. This herb and its active constituent, rosmarinic acid exerted beneficial effects against formation of oxygen free radicals, lipid peroxidation, DNA damage, molecules of apoptosis pathway, p38 mitogen-activated protein kinase, and tau hyperphosphorylation induced by Abeta in PC12. In a 4-month randomized double-blind placebo-controlled study, efficacy and tolerability of sage extract (60 drops/day) was compared to placebo in patients with mild to moderate Alzheimer's disease. Patients in the sage group showed a significantly better outcome on cognitive performance and less agitation than the placebo group [16].

Adverse event and toxicity

The short and medium-term use of sage have been generally associated with good tolerability profile. Sage like several other aromatic plants contains a substance called thujone which potentially can cause severe nervous system symptoms such as convulsion and hallucination. Therefore an acceptable daily intake of 0.11 mg/kg bw/day of thujone has been suggested (2 - 20 cups of sage tea) to avoid side effects [17]. Tonic clonic seizure following accidental use of sage oil has been reported in children. A case of allergic contact dermatitis due to use of *S. officinalis* extract has also been reported [18].

Conclusion

The paper reviewed the use of passionflower and sage in mental health setting. Passionflower has shown promising effects for the treatment of sleep and anxiety disorders. It has also been successfully used as a calming agent prior to surgery and as adjunct to clonidine in the treatment of substance withdrawal. Sage improved symptoms of dementia in one study, even though the study needs replication. Although additional research is needed for all of the herbs, the risks are generally low enough that they may be useful for patients with mild symptoms, those who cannot tolerate prescription medications, or individuals who prefer herbal to traditional remedies [19 - 25].

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