The use of *Scutellaria lateriflora*: a pilot survey amongst herbal medicine practitioners

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The use of *Scutellaria lateriflora*: A pilot survey amongst herbal medicine practitioners

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Abstract

American skullcap (*Scutellaria lateriflora*) is a popular herb in traditional medicine systems and western *Materia medica* for anxiety and related disorders. It is reported to be one of the most widely used medicinal herbs, with anecdotal evidence for minimal side-effects and with no known toxicity. This article summarises the results of a pilot survey conducted amongst herbal medicine practitioners on their use of *S. lateriflora.*

An email survey was conducted amongst herbal medicine practitioners in the UK and Ireland. It aimed to gather information on the extent of, and indications for, current use of *S. lateriflora*, its perceived effectiveness and its safety. Herbal medicine practitioners were selected from the membership list of the National Institute of Medical Herbalists (NIMH). All members with identifiable email addresses were contacted (n = 377) and responses were received from 62 (a 16% response rate).

The results of the survey suggested that *S. lateriflora* is highly regarded among herbal medicine practitioners as an effective intervention for reducing anxiety and stress and is commonly prescribed for these conditions and related co-morbidities. The results were not conclusive as the response rate was low and respondents were only those with email access.

Keywords

Scutellaria lateriflora; Skullcap; Survey; Anxiolytic herbs; Medical herbalists

1. Introduction

American or Virginian skullcap (*Scutellaria lateriflora*) (Figure 1) is a perennial herb belonging to the *Lamiaceae* (mint) family (also known as *Labiatae*), sub-family *Lamioideae*, and is one of 360 known *Scutellaria* species worldwide (Cole *et al.* 1991; Malikov & Yuldashev 2002), many of which are used medicinally (Joshee *et al.* 2002). It grows on wetlands and is indigenous to North America and Canada where it is widely distributed - from Alaska to Florida and British Columbia to Quebec (the only places it is not found are the North-west Territories, Alberta and Yukon in Canada and Wyoming, Nevada and Utah in the US) (U.S.D.A. 2012). It is grown commercially worldwide, including in Australia and New Zealand (Wills & Stuart 2004).

Figure 1 ***Scutellaria lateriflora*** (© C. Brock)

S. lateriflora is used extensively and has been highly valued in traditional western herbal and ethnobotanical medicines for anxiety, hysteria, phobias, panic attacks, tension, depression, sleep disorders and stress (Felter & Lloyd 1898; Joshee *et al.* 2002). Known as a woman's herb by Native Americans, the Cherokees used it as an emmenagogue, thus promoting menses and aiding expulsion of the placenta following childbirth. Native American women also used it to ensure general menstrual health (Joshee *et al.* 2002) as well as for mastalgia and premenstrual tension (Greenfield & Davis 2004). Some tribes still use it in ceremonies to induct girls into womanhood and for purification rituals (Joshee *et al.* 2002).

The first European to record its use (in 1787) as a medicinal herb was German Physician Johann David Schöpff, who noted its use as a tonic, for fevers and as an abstergent (detergent) (Upton *et al.* 2009). It was mentioned in the first American *Materia medica* in 1785 but had been in longstanding use as a home remedy before then (Lloyd 1911). Dr

Lawrence Van Derveer (1740-1815) studied *S. lateriflora* extensively and used it as a treatment for rabies (hydrophobia); it was then used for this purpose both professionally and as a home remedy. In 1819 Dr Lyman Spalding wrote *'A history of the introduction and use of Scutellaria lateriflora* (scullcap), *as a remedy for preventing and curing hydrophobia, occasioned by the bite … '* (Lloyd 1911; New Jersey Historical Society 2001). Medical doctor Joseph Bates wrote in 1855 in the Boston Medical Journal (Bates 1855) that because *S. lateriflora* was eventually scientifically proved to be utterly useless for this purpose it fell into disrepute and was consequently removed from pharmacopoeias. He nevertheless described using *S. lateriflora* in his practice, claiming a fluid extract had great value in the treatment of nervousness, irritability and restlessness, particularly in children. He also held it in high regard for hysteria and for relieving symptoms of inflammation in patients with arthritis or convalescing from fevers. He prophesied that it would be found to be highly successful in treating many diseases in the future, particularly those for which opium was currently prescribed (Bates 1855). In 1860 it was introduced into the official *United States Pharmacopoeia* as *Extractum Scutellariae Fluidum* (Millspaugh 1892; Upton *et al.* 2009) but was dropped in 1910. It was in the US *National Formulary* in 1916 and removed in 1942 when interest in natural remedies declined. It is not included in the *European Pharmacopoeia* (Upton *et al.* 2009).

Modern herbal medicine's application of *S. lateriflora* appears to be based upon its traditional uses for anxiety states. Greenfield and Davis (2004) for example, suggest it is used most commonly for insomnia, nervous disorders and digestive disturbances. Bergner (2002) proposes its action is primarily as a trophorestorative on the central nervous system (CNS), allowing relaxation following nervous exhaustion (Bergner 2002). It is also prescribed by western herbalists for epilepsy (British Herbal Medicine Association 1983), post-stroke paralysis, atherosclerosis, hyperlipidaemia, allergies, skin conditions and inflammation (Natural Medicines Comprehensive Database 2011).

A small clinical study assessing acute effects of *S. lateriflora* indicated it has anxiolytic actions with minimal loss of cognition (Wolfson & Hoffmann 2003). The authors assessed the anxiolytic properties of the herb in a double-blind, placebo-controlled crossover study of 19 healthy volunteers. Participants took either 2 placebo capsules, one capsule containing 100 mg of organic freeze-dried *S. lateriflora* extract, two capsules of these, or one capsule of 350 mg organic freeze-dried *S. lateriflora.* Participants' energy, cognition and anxiety were self-rated at various time points up to 2 hours following administration of test or placebo substances, when measurements tended to return to baseline. The three herb tests all had notable effects in reducing subjective anxiety scores when compared to placebo, the most effective being the two 100 mg capsules. There was only a very mild decline in cognition and energy with the herbs, with no adverse reactions or side-effects, suggesting that *S. lateriflora* could be a valuable anxiolytic - as many anxiolytics impair cognitive function and physical performance (Wolfson & Hoffmann 2003). It is unclear whether the results were statistically significant as this was not determined.

Furthermore, two studies found major skullcap flavonoids, including baicalin, baicalein and wogonin, extracted from *S. baicalensis* but also found in *S. lateriflora,* had affinities for the benzodiazepine binding site of gamma-aminobutyric acid A ($GABA_A$) receptors, suggesting anxiolytic properties for these flavonoids (Liao *et al.* 1998; Hui *et al.* 2000). Ligands binding to the benzodiazepine site of the $GABA_A$ receptor decrease the likelihood of action potentials by excitatory neurotransmitters such as adrenalin and noradrenalin, implicated in anxiety and stress (Rabow *et al.* 1995; Paladini *et al.* 1999). Another study found both hot water and 70%

ethanol extracts of whole aerial parts of *S. lateriflora,* as well as six major isolated flavonoids (baicalin, scutellarin, wogonin, lateriflorein, ikonnikoside I and dihydrobaicalin), bound to serotonin-7 (5-HT_7) receptors, suggesting the potential of *S. lateriflora* for attenuation of negative mood states (Gafner *et al.* 2003).

Modern pharmacology research has demonstrated anti-tumour, anti-inflammatory, anti-viral, antibacterial and hepatoprotective effects of individual compounds, particularly the flavonoids, found in the *Scutellaria* genus (Shang *et al.* 2010). In common with all *Scutellaria* species studied *S. lateriflora* is rich in flavonoids, a group of phenolic compounds that are highly active physiologically, with a wide range of pharmacological actions (Malikov & Yuldashev 2002; Shang *et al.* 2010; Li *et al.* 2012). Baicalin, baicalein and wogonin are considered to be major active flavonoids in *S. lateriflora* and have been researched extensively because of their presence also in *S. baicalensis* (Joshee *et al.* 2002; Li *et al.* 2012).

Since 1998 a large number of compounds have been isolated from *S. lateriflora* (Shang *et al.* 2010), which could have far reaching implications for research into its actions and indications. Most recently (Li *et al.* 2012), using a sensitive method of HPLC with ultraviolet photodiode array and electrospray ionization tandem mass spectromic detection (HPLC-DAD/ESI-MS), six more flavonoids were isolated from methanolic extracts of authenticated *S. lateriflora* aerial parts. The flavonoids identified in this species for the first time are norwogonin-7-*O*-glucoronide, wogonin-7-*O*-glucoronide, 5,7-dihydroxy-6,8-dimethoxy flavone-7-*O*-glucoronide, dihidrooroxylin A-7-*O*-glucoronide, galangin-7-*O*-glucuronide, and 5,6,7-trihydroxy-flavanone-7-*O*-glucuronide (Li *et al.* 2012).

More than one species within a genus may possess exactly the same or similar flavonoids. For example, in common with many other *Scutellaria* species, *S. lateriflora* and *S. baicalensis* have similar phytochemical constituents, although in different ratios and quantities, which may explain the differing traditional uses amongst *Scutellaria* species (Cole *et al.* 2008). Using HPLC, Cole *et al.* (2008) quantitatively compared the content of flavonoids scutellarin, wogonin, baicalin and baicalein in aerial parts of *S. lateriflora, S. baicalensis* and *S. racemosa* grown in identical conditions. *S. lateriflora* contained the highest amount of baicalein while *S. baicalensis* contained 800 times more scutellarin than the other two herbs. Of the three herbs *S. racemosa* had the highest wogonin content. Baicalin content was similar for the three herbs (Cole *et al.* 2008), which differs from the findings of Makino *et al.* (2008) who found baicalin content in the leaves and stems of *S. baicalensis* was insignificant in comparison to *S. lateriflora*. There was slightly more baicalin in *S. baicalensis* root than in *S. lateriflora* leaves (Makino *et al.* 2008). Interestingly, of five skullcap species analysed (*S. baicalensis, S. lateriflora, S. racemosa, S. tormentosa and S. wrightii*), Islam *et al.* (2011) found a greater baicalin content in the roots of *S. wrightii* than in root, stem or leaf of the other species and 5-fold higher than in *S. baicalensis* root. The authors also demonstrated that *S. wrightii* and *S. tormentosa*, previously uncharacterised species, are good sources of the flavonoids scutellarin, baicalin, baicalein and wogonin. As these flavonoids are also found in *S. lateriflora* there are implications that these species also have medicinal properties. It is possible that differences in flavonoid concentration between studies may have been due to differences in growing conditions.

Commercial herbal products have been found to contain significant variations in phytochemical profile within a species. Such variation may be according to geographic region, biodiversity, ecological variations, cultivation, seasonality, harvesting, and storage

time affecting stability; processing method, marc to menstruum ratio and alcohol concentration (Ciddi 2006; Gao *et al.* 2008).

Notwithstanding these variations, another problem is whether or not the herb is the correct species. Studies have shown wide variations in phytochemical profile of herb claimed to be *S. lateriflora.* Zhang *et al.* (2009), for example, discovered a wide variation in individual and total phenolic content in 10 different commercial preparations of *S. lateriflora* (analysed by HPLC and compared with *S. baicalensis* and whole, freeze-dried extract). Baicalin content, for example, varied from 0.48% to 10.10% (compared to 18.95% for whole extract). Total phenolic content for these two preparations was 1.11% (extract – type not described) and 20.55% (fine powder in a capsule) respectively (41% for whole extract) (Zhang *et al.* 2009).

Another HPLC analysis (Gao *et al.* 2008), of seven commercial preparations (obtained from five companies), which compared baicalin, baicalein and wogonin content of *S. lateriflora* (four samples of *S. baicalensis* were also analysed), also found wide variations in individual and total content of these flavonoids. One sample contained no baicalin, baicalein or wogonin. Of all three flavonoids, µg/ml ranged from 180, 280 and 97.5 to 12,700, 629 and 152 respectively (Gao *et al.* 2008). One commercial *S. lateriflora* tincture tested by Gao *et al.* (2008), which had the highest flavonoid content (12.66 mg/ml), was extracted in 45% ethanol, whereas the others were extracted in 25% ethanol. When the investigators later compared extraction in 25% and 45% ethanol from the same batch of *S. lateriflora* plant material they found that 45% ethanol yielded around five times more flavonoids than 25% ethanol (Gao *et al.* 2008).

Quality control and correct identification may be of particular importance in the case of *S. lateriflora* because of the large number of *Scutellaria* species (Malikov & Yuldashev 2002) and frequent substitution or adulteration with other skullcaps or potentially harmful herbs such as germander (*Teucrium*) (Wolfson & Hoffmann 2003). Respondents to the practitioner survey said they used a variety of suppliers, mainly for price, convenience or habit but it is important to ensure the herb has been authenticated.

Anxiety, stress and related disorders are problems treated most frequently in the herbal medicine clinic (del Mundo *et al.* 2002). As *S. lateriflora* is reported to be one of the most used herbs in western materia medica (Bergner 2002) it is likely that this is the herb of choice by western medical herbalists for these conditions. The purpose of the survey was to provide further evidence for its popularity in relation to other herbs used for the same conditions, to gather anecdotal evidence of its effectiveness and to gain information about prescribing practices such as dosage and duration of treatment, why it is prescribed and any reported issues in using it. The results may help to inform treatment protocols in clinical studies. A brief version of the survey was reported previously (Brock *et al.* 2010) along with a more detailed scientific basis for the use of *S. lateriflora*.

2. Materials and methods

UK and Ireland herbal medicine practitioners with an email address identifiable from the register of the National Institute of Medical Herbalists (NIMH) were contacted. NIMH members are qualified herbalists who have undergone several years' rigorous scientific training, following which they take consultations with patients with a wide range of conditions, using the same diagnostic skills and examination techniques as orthodox doctors. This organisation was chosen as it is the largest organisation representing medical herbalists in the UK. As a number of herbalists belong to more than one representing organisation there

was a risk of some receiving a survey questionnaire twice if more than one register was used. Each of the 377 practitioners selected received an electronic letter and survey questionnaire form.

A mixed methods approach was used with mainly open questions in order to gather as much information as possible about practitioners' experiences with, and beliefs about, *S. lateriflora.* Respondents were asked:

- Whether they regularly prescribe *S. lateriflora* and, if not, reasons for not doing so;
- what they thought were its main actions and indications;
- what they prescribed it for and for how long;
- the length of time in which they expect to see a response in patients and what responses they expected to see;
- what patients reported from its use;
- whether there have been any reported side-effects and what were perceived contra-indications;
- type of preparation used and reasons for choices;
- dosage and strength;
- whether used alone or in combination;
- What was their favourite herb for anxiety?
- They were also asked how long they had been in practice and to add any additional comments should they wish to do so.

3. Results and discussion

Of 377 questionnaires sent, 62 practitioners responded (16%). Of all responders, 57 (92%) said they regularly prescribe *S. lateriflora.* Length of time in practice and experience varied widely but generally the responders comprised a group of highly experienced herbal practitioners. The average length of time in practice was 9.03 years (SD = ± 7.14) and the average time spent with patients per week was 10 hours per practitioner.

3.1. Actions and indications attributed to *S. lateriflora*

The majority of respondents provided more than one indication and/or action and use of *S. lateriflora* (Table 1). There was some confusion over the difference between actions and indications and most common conditions for which it is prescribed. For example, 77% (n = 48) of respondents said they would prescribe it for anxiety but only 35% (n = 22) suggested it has an anxiolytic action and only 18% (n = 11) gave anxiety as an indication for the herb. For simplicity, 'indications' and 'reasons for prescribing' have been amalgamated in Table 1. The confusion between actions and indications and reasons for prescribing is interesting and deserves consideration by herbalists generally; it calls into question how a misunderstanding of the language might potentially impose restrictions to the way in which herbs are used. If so, such an impediment may impact upon herbal practice as a whole. Rigorous scientific research could explore this issue.

3.2. The practitioners' choice for anxiety

Results indicate the principal use of *S. lateriflora* is for relief of anxiety, stress or associated conditions with most 77% (n = 48) survey respondents stating they would prescribe it specifically for anxiety and all said they would prescribe it for anxiety-related co-morbidities.

When asked what is their preferred herb for anxiety, twenty five 25 (40%) chose *S. lateriflora* (Figure 2). It is interesting to note that one respondent indicated their preferred anxiolytic as being *S. baicalensis* as, although *S. baicalensis* root is most commonly used for inflammation (Joshee *et al.* 2002), it is reported to have been used as a sedative (Liao *et al.* 1998). Conversely, *S. lateriflora* is reported to have been traditionally used for inflammation. The Iroquai tribe, for example, used it 'to keep the throat clear' (Joshee *et al.* 2002). Additionally, both *S. lateriflora* and *S. baicalensis* have been found to inhibit cyclooxegenases *in vitro* (Gafner *et al.* 2004; Jia *et al.* 2007).

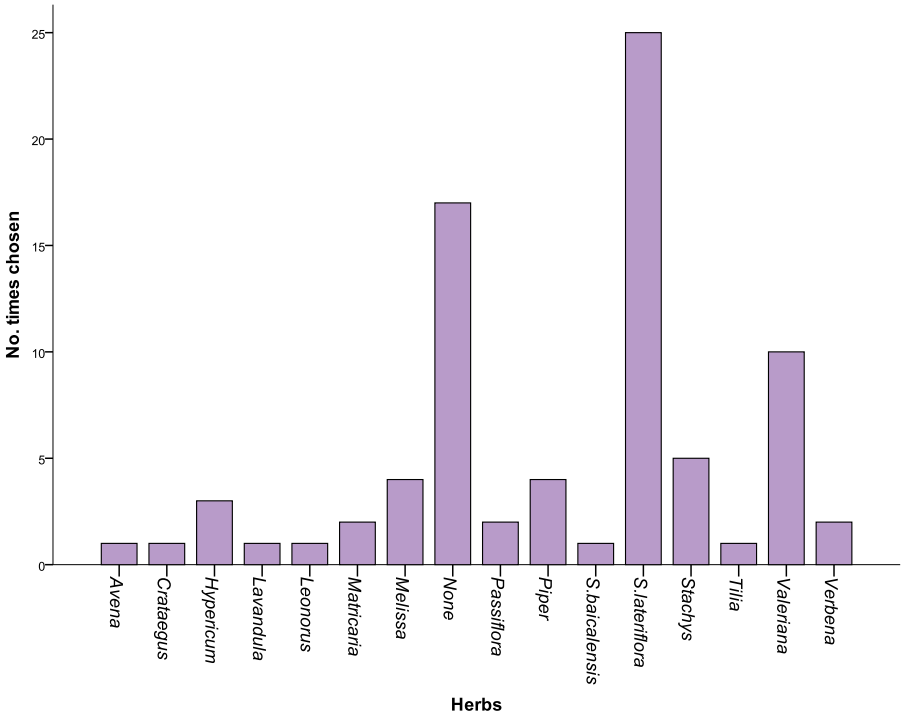
Common reasons for prescribing *S. lateriflora* are provided in Table 1. All respondents who regularly prescribe *S. lateriflora* (92%) identified use for anxiety as distinct from depression and whilst some reported it useful also in depression, two respondents reported it as unsuitable for significant depression (described as "mentally depressed states" and "severe depression") as in their opinion it tended to exacerbate it. Usefulness for insomnia and sleep-related disorders was reported by 33 (53%) respondents. Practitioners who prescribe for poor sleep invariably described it to be related to an overactive mind, obsessive or racing thoughts, worry and anxiety.

Table 1: Actions and indications attributed to *S. lateriflora*

Actions attributed to *S. lateriflora* (n = 62)	**N**	**Indications/reasons for prescribing *S. lateriflora* (n= 62)**	**N**
Nervine/ nerve trophorestorative	40	Anxiety	59
Anxiolytic	22	Insomnia and other sleep-related disorders	33
Relaxant	20	Stress	21
Mildly sedative	14	Migraine and other types of headaches	13
Calming	8		
Antispasmodic or spasmolytic	8	Depression	9
Cooling	4	Drug withdrawal and addiction	8
Tranquilising	4	Nervous and muscular tension	7
Anti-inflammatory	3	Panic attacks	7
Anti-stress	2	Fear and phobias	7
Mood lifting	2	Eczema, psoriasis/stress-related skin conditions	6
Anti-allergy	2	Physical and mental exhaustion	5
Parasympathetic	1	Excessive thought processes	5
Anti-panic	1	Hypertension	5
An emotional balancer	1	Palpitations	5
Antidepressant	1	Irritability	3
Supporting	1	Twitches and spasms of nervous origin/convulsions	2
Digestive tonic	1	Premenstrual syndrome (PMS)	2
Sustaining	1	Allergies	2
Anti busy brain	1	To put things into perspective	2
Bringing focus	1	Nervousness	2
		Chronic fatigue syndrome	2
		Irritable bowel syndrome	2

N = number of practitioners stating actions and/or indications/reasons for prescribing.

Other anxiety-related conditions given by practitioners as reasons for prescribing included for: 'those who sigh a lot', frustration, menopausal mood swings, despondency, neuralgia, nerve weakness, emotional instability, shock, feelings of not coping, tinnitus, debility, hot flashes triggered by stress, low mood, grand mal, Attention Deficit Hyperactivity Disorder, Obsessive Compulsive Disorder, "liver heat rising" and to "relax constriction where there is heat."



Key: Avena = *A. sativa* (oats); Crataegus = *Crataegus* spp. (hawthorn); Hypericum = *H. perforatum* (St John's wort); Lavandula = *Lavandula* spp. (lavender); Leonorus = *L. cardiaca* (motherwort); Matricaria = *M. recutita* (German chamomile); Melissa = *M. officinalis* (balm); None = no preference; Passiflora = *P. incarnata* (passion flower); Piper = *Piper methysticum* (kava-kava); *S. baicalensis* (baical skullcap); *S. lateriflora* (American skullcap); Stachys = *S. betonica* (wood betony); Tilia = *Tilia* spp (linden); Valeriana = *Valeriana officinalis* (valerian); Verbena = *Verbena officinalis* (vervain).

NB: Many survey respondents gave more than one choice but overall the herb of choice *was S. lateriflora*.

Figure 2 Anxiolytic herbs as preferred by survey respondents

3.3. Duration of treatment

The survey respondents reported the herb as being used over a range of time periods from immediate short-term use to several years, with positive response expected to be experienced by the patient within the first two weeks and persisting throughout the period of use.

According to 8% (n = 5) of respondents who did not state a timescale this is dependent on the health of a patient, the condition presented by a patient and its severity, how long they have been ill and patient compliance. In the words of one practitioner: 'as long as it takes'. All other respondents gave a lower and/or an upper limit. Rarely, it may be prescribed as a one-off but in general the minimum length of time it is prescribed is for 1 or 2 weeks (11%; n = 6). At least 30% (n = 17) of user respondents consider prescribing it long-term (6 months or more), sometimes for years (9%; n = 5), although some stated 'long term' without being explicit about the timescale. Those who stated 'several months' were not included as long-

term prescribers as it is unknown whether this could mean up to 6 months or more than 6 months. Of those who set an upper limit on treatment length 31% (n = 18) stated they would treat for up to 4 months. It is difficult to ascertain average treatment length as many replies were not explicit. What is clear, however, is that it ranges from one-offs to several years.

3.4. Responses looked for in patients

Sleep quality was a major factor in assessing mental state improvement with 53% (n = 30) of *S. lateriflora* prescribers stating they would expect patients to sleep better; for example by sleeping longer, with less waking in the night, an ability to get to sleep and feeling refreshed in the morning. Many (37%; n = 21) felt they would be likely to notice that their patients were better able to cope with the stresses daily life. A reduction in anxiety and feeling calmer would be looked for in patients by 33% (n = 19) and 32% (n = 18) of practitioners respectively. In general, respondents expected their patients to feel happier, less depressed or tearful, calmer, more relaxed, less irritable, less stressed, tense or nervous and more in control of their emotions with elevated mood. They also expected a concomitant resolution or reduction of stress- and anxiety-related physical symptoms such as headaches, digestive disturbances, PMS, inflammatory skin conditions, twitches and spasms, and cardiovascular problems such as hypertension, tachycardia and palpitations.

3.5. Benefits reported by patients

The benefits most often reported by patients to their practitioners were feeling calmer, improved sleep patterns and sleep quality, and better able to cope in stressful situations. Other positive effects were mood elevation, increased energy, being more focused and feeling generally more relaxed. Some user respondents (19%; n = 11) answered that it is difficult to determine what patients have reported from using *S. lateriflora* as they never prescribed it as a single herb but always mixed it with others.

3.6. Effectiveness response time

When asked: “after what length of time would you expect to see a response?” answers were again often implicit rather than explicit. Most provided a range of timescales e.g. “one to two weeks”. Some practitioners did not provide a minimum or maximum timescale, only ‘one month of treatment for every year they have been ill’ or ‘longer term’ and many responded to the question with ‘few days or ‘few weeks’. One said it was difficult to say as they always prescribe *S. lateriflora* in combination with other herbs and therefore values for neither the average nor minimum and maximum expected response time could be ascertained.

Most said it was dependent on the condition being treated and many said that improvement was time and/or dose dependent - practitioners’ own words but suggesting improvement over the minimum response time provided and/or with what they perceive as adequate doses (see Figure 3) - but usually noticeable within a few days; and that continuation of treatment for periods beyond the first signs of improvement was beneficial to the patient. Responses by 12 practitioners suggest, however, that *S. lateriflora* may show an effect immediately or within hours. Twenty practitioners questioned expect to see some results in one or two weeks. Of total expected minimum response times provided (n = 56), only 11 practitioners did not expect *S. lateriflora* to show an effect before 3 weeks. The maximum expected response time was 12 weeks (n = 2) but, as practitioners are very keen to say: “it depends on the individual”.

3.7. Dosing strategies (posology)

The weekly ethanol: water tincture dose of *S. lateriflora* most commonly prescribed (Figure 3) by user respondents is 20 ml (33.3 %) followed by 30 ml (19%). As the average marc: menstruum ratio was 1: 3 in 25% ethanolic extract the most commonly prescribed weekly dose expressed as crude, dried herb was around 7g and10 g respectively. The range of doses represents approximately 1.7-35 g crude, dried or fresh herb in 1:3 ethanol: water (w/v) per week, and the median daily dose is thus 3 ml, which is equivalent to 1 mg at this marc to menstruum ratio. Tinctures are the preferred mode of administration by the majority (96%; n = 55) of respondents who prescribe the herb. The main reasons given were that tinctures are generally more convenient than dried herb and therefore better for patient adherence. There is also a belief that tinctures are more effective than dried herb. Tinctures may be made from either fresh or dried organic and non-organic herb and many user respondents (63%; n = 36) said they prefer to use organic *S. lateriflora* and 42% (n = 24) prefer tinctures made from the fresh herb, believing this to be the most effective.

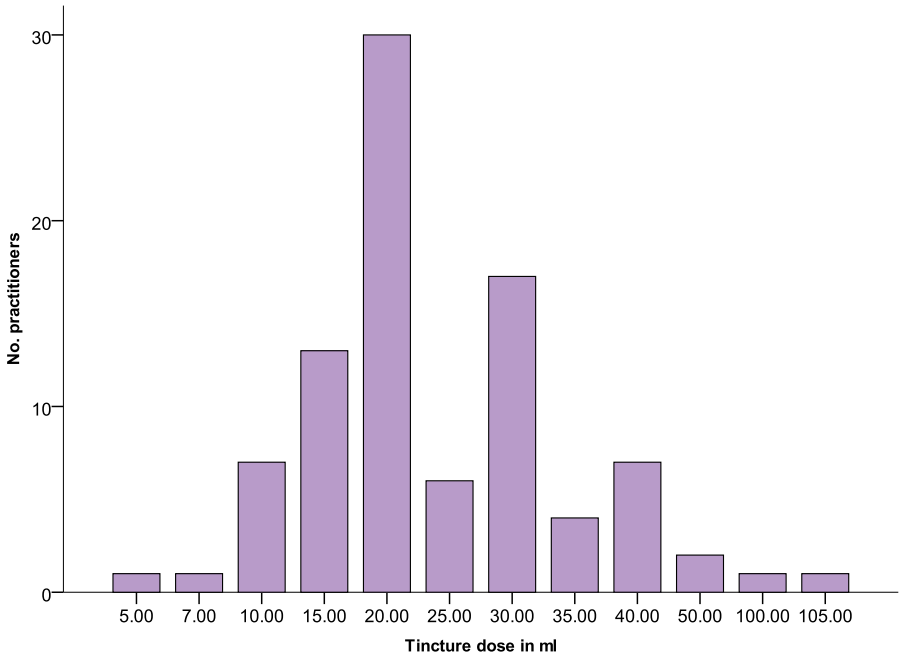


Figure 3 Most commonly administered weekly doses of ethanol: water *S. lateriflora* tincture

All *S. lateriflora* users responding to the survey prescribe the herb in combination with other herbs. Only 9% (n = 5) regularly prescribed *S. lateriflora* as a single herb so it is difficult to draw conclusions about the perceived actions of *S. lateriflora* used on its own. Nevertheless the practitioners appeared to be confident in attributing specific anxiolytic and related actions and responses to *S. lateriflora* as distinct from other herbs in a mixture. Reasons are unclear but this perhaps reflects a combination of empirical, anecdotal and scientific knowledge relating to each of the herbs prescribed simultaneously. Furthermore, respondents (9% of users; n = 5) prescribing it as a single herb reported positive feedback from their patients such as reduced anxiety, fewer and less intense panic attacks, feeling of well-being, feeling more positive, more able to cope. Significantly, a relapse of anxiety symptoms in some patients

was noticed by one practitioner prescribing the herb in combination with other (non-anxiolytic) herbs whenever it was removed from the mixture.

3.8. Contraindications and side-effects

While the majority of respondents (81%; n = 50) did not consider *S. lateriflora* to be contraindicated for any conditions, the other 19% (n = 12) said they would not prescribe it to severely depressed patients, those with bipolar disorder or other specific mental conditions, to those with epilepsy, thyroid conditions, in pregnancy or to children. It may be possible that herbalists are unlikely to prescribe any herbs for situations where safety is unknown.

The herb was reported as being well tolerated and with only minor and infrequent side effects (reported by 7 prescribers); including mild digestive upsets, worsening of depression, daytime drowsiness, light-headedness and vivid dreaming. It is uncertain whether any of these side effects could definitely be attributed to *S. lateriflora*. There were no reports of toxicity.

3.9. Survey response rate

It is not clear why there was such a low response rate to the survey questionnaire (despite two follow-ups, an oral presentation alert at a NIMH conference and an advertisement in a NIMH newsletter). Several reasons for low feedback could be postulated. One is that medical herbalists tend to receive a number of survey response requests during any given year, mainly from undergraduates embarking upon their dissertations, and may therefore be suffering from 'survey fatigue'. It could be that some didn't feel the survey was relevant to their practice if they were non-prescribers of *S. lateriflora*. This is difficult to assess but if this was the case then generalisability across herbal medicine practitioners would have been affected by non-response bias (Cummings *et al.* 2001). Some may have been deterred by the length of the questionnaire and the fact that questions were in the main open-ended, requiring considerable time and effort on the part of already busy practitioners, many of whom are doing more than one job or are studying. Studies of response rates to surveys have demonstrated that the more user-friendly a survey is the more likely it is to have a high response rate (LaGarce & Kuhn 1995). A fair amount of typing was required to fully answer the questions so it could not be considered to be as user-friendly as a quantitative scaling method, for example.

3.10. Conclusions

This study has added to the literature in that it has shown that *S. lateriflora* is prescribed for a range of related conditions and its widespread use for sleep disorders has broadened the indications in the British Herbal Pharmacopoeia. Furthermore, the revelation that herbalists ascribe the action of a compound mixture to the herb has provided empirical evidence of its efficacy.

It is recognised that the response rate (16%) for this pilot survey was low and respondents include only those with access to email. It may therefore not be representative of all UK and Ireland herbal medicine practitioners. An advantage of email surveys is that they are fast and cost-effective and provide geographical diversity but exclusion includes those without access to email. Furthermore, responses may have been mainly from those who have had experience of the herb. Non-responders could possibly be mostly non-prescribers. Importantly, it is

possible that those who do not prescribe *S. lateriflora* may not do so because they do not find the herb useful. Although this is speculation it could be a confounding factor. The poor response rate and the propensity of respondents to administer *S. lateriflora* in combination with other herbs make it impossible to rely on evidence regarding the efficacy of the herb from the pilot practitioner survey alone. A future survey could include herbal practitioners from other professional bodies such as the Council of Practitioners of Phytotherapy. In addition, contact with herbalists internationally may provide a more useful indication of the benefits of this herb. Because of the low response rate a future survey could contain fewer closed questions and use a world-wide web electronic format so that respondents could have the option to simply click multiple choices with a computer mouse. Furthermore, it would be helpful to urge survey recipients to respond regardless of whether or not they use the herb.

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References

Bates J. On the fluid extract of Scutellaria lateriflora. The Boston Medical and Surgical Journal 1855; 52:336-7.

Bergner P. Traditional Medicine: Scullcap (*Scutellaria lateriflora*). Medical Herbalism: A Journal for the Clinical Practitioner 2002;13:15-17.

British Herbal Medicine Association. Skullcap. In: British Herbal Pharmacopoeia. Bournemouth, UK: British Herbal Medicine Association; 1983. p 193-4.

Brock C, Whitehouse J, Tewfik I, Towell T. American skullcap (Scutellaria lateriflora): an ancient remedy for today's anxiety? Br J Wellbeing 2010; 1:25-30.

Ciddi V. Withaferin A from cell cultures of *Withania somnifera.* Indian J Pharmaceut Sci 2006; 68:490-2.

Cole IB, Cao J, Alan AR, Saxena PK, Murch SJ. Comparisons of *Scutellaria baicalensis*, *Scutellaria lateriflora* and *Scutellaria racemosa*: genome size, antioxidant potential and phytochemistry. Planta Med 2008; 74:474-481.

Cole MD, Paton AJ, Harleyl RM, Fellows LE. The significance of the iridoid glycoside, catalpol, in *Scutellaria.* Biochem Syst Ecol 1991; 19:333-335.

Cummings SM, Savitz LA, Konrad TR. Reported response rates to mailed physician questionnaires. Health Serv Res 2001; 35:1347-55.

del Mundo WF, Shepherd WC, Marose TD. Use of alternative medicine by patients in a rural family practice clinic. Fam Med 2002; 34:206-212.

Felter HW, Lloyd JU. *Scutellaria lateriflora*. In: King's American Dispensatory. Portland: Eclectic Medical Publications; 1898.

Gafner S, Bergeron C, Batcha LL, Reich J, Arnason JT, Burdette JE et al. Inhibition of [3H]-LSD binding to 5-HT7 receptors by flavonoids from *Scutellaria lateriflora.* J Nat Prod 2003; 66:535-7.

Gafner S, Bergeron C, Russell FE. Extract of mad-dog skullcap. US Patent application US2004/0109906A1. United States: 2004.

Gao J, Sanchez-Medina A, Pendry BA, Hughes MJ, Webb GP, Corcoran O. Validation of a HPLC method for flavonoid biomarkers in skullcap (*Scutellaria*) and its use to illustrate wide variability in the quality of commercial tinctures. J Pharm Pharmaceut Sci 2008; 11:77-87.

Greenfield J, Davis JM. Medicinal Herb Production Guide: Skullcap (*Scutellaria lateriflora* L). USA: North Carolina Consortium on Natural Medicines and Public Health; 2004.

Hui KM, Wang XH, Xue H. Interaction of flavones from the roots of *Scutellaria baicalensis* with the benzodiazepine site. Planta Med 2000; 66:91-93.

Islam MN, Downey F, Ng CY. Comparative analysis of bioactive phytochemicals from *Scutellaria baicalensis, Scutellaria lateriflora, Scutellaria racemosa, Scutellaria tomentosa* and *Scutellaria wrightii* by LC-DAD-MS. Metabolomics 2011; 7:446-453.

Jia Q, Nichols TC, Rhoden EE, Waite S. Identification of free-B-ring flavonoids as potent COX-2 inhibitors. US Patent application US20070135359 A1. United States: 2007.

Joshee N, Patrick TS, Mentreddy RS, Yadav AK. Skullcap: Potential medicinal crop. In: Janick J, Whipkey A, editors. Trends in New Crops and New Uses. Alexandria, VA: ASHS Press; 2002. p 580-6.

LaGarce R, Kuhn LD. The effect of visual stimuli on mail survey response rates. Ind Market Manag 1995; 24:11-18.

Li J, Wang Y-H, Smillie TJ, Khan IA. Identification of phenolic compounds from *Scutellaria lateriflora* by liquid chromatography with ultraviolet photodiode array and electrospray ionization tandem mass spectrometry. J Pharm Biomed Anal 2012. 63:120-7.

Liao JF, Wang HH, Chen MC, Chen CC, Chen CF. Benzodiazepine binding site-interactive flavones from *Scutellaria baicalensis* root. Planta Med 1998; 64:571-572.

Lloyd JU. History of the Vegetable Drugs of the USP. In: Lloyd JU, Lloyd CG, editors. Bulletin of the Lloyd's Library of Botany, Pharmacy and Materia Medica 18. Cincinnati: Lloyd & Lloyd; 1911. p 109.

Makino T, Hishida A, Goda Y, Mizukami H. Comparison of the major flavonoid content of *S. baicalensis, S. lateriflora*, and their commercial products. J Nat Med 2008; 62:294-9.

Malikov VM, Yuldashev MP. Phenolic compounds of plants of the *Scutellaria* L. Genus. Distribution, structure, and properties. Chem Nat Compd 2002; 38:358-406.

Millspaugh CF. *Scutellaria*.In: Medicinal Plants. Philadelphia: John C. Yorston and Company; 1892. p 469-72.

Natural Medicines Comprehensive Database. 2011. Skullcap (*Scutellaria lateriflora*). Stockton, CA: Therapeutic Research Faculty. Available: http://naturaldatabase.therapeuticresearch.com [date accessed 22/11/2011].

New Jersey Historical Society. Manuscript Group 481, Van Derveer Family Papers, 1733-1908. Archives. Newark, N J; 2001. Available: http://www.jerseyhistory.org/findingaid.php?aid=0481[date accessed 21/11/2011].

Paladini AC, Marder M, Viola H, Wolfman C, Wasowski C, Medina JH. Flavonoids and the central nervous system: from forgotten factors to potent anxiolytic compounds. J Pharm Pharmacol 1999; 51:519-26.

Rabow LE, Russek SJ, Farb DH. From ion currents to genomic analysis: recent advances in GABAA receptor research. Synapse 1995; 21:189-274.

Shang X, He X, Li M, Zhang R, Fan P, Zhang Q, Jia Z. The genus *Scutellaria* an ethnopharmacological and phytochemical review. J Ethnopharmacol 2010; 128:279-313.

USDA. Plants profile: *Scutellaria lateriflora* L. (blue skullcap). Plants Database. USA: United States Department of Agriculture Natural Resources Conservation Service; 2012. Available: http://plants.usda.gov/java/profile?symbol=SCLA2 [date accessed 11/7/2011].

Upton R, Graff A, Soria T, Swisher D. American Herbal Pharmacopoeia and Therapeutic Compendium: Skullcap aerial parts. *Scutellaria lateriflora* L. Standards of analysis, quality control and therapeutics. Scotts Valley, California: American Herbal Pharmacopoeia; 2009.

Wills RBH, Stuart DL. Generation of high quality Australian skullcap products. RIRDC Publication No. 04/020. Kingston ACT: Rural Industries Research and Development Corporation; 2004.

Wolfson P, Hoffmann DL. An investigation into the efficacy of *Scutellaria lateriflora* in healthy volunteers. Altern Ther Health Med 2003; 9:74-8.

Zhang Z, Lian XY, Li S, Stringer JL. Characterization of chemical ingredients and anticonvulsant activity of American skullcap (*Scutellaria lateriflora*). Phytomedicine 2009; 16:485-493.