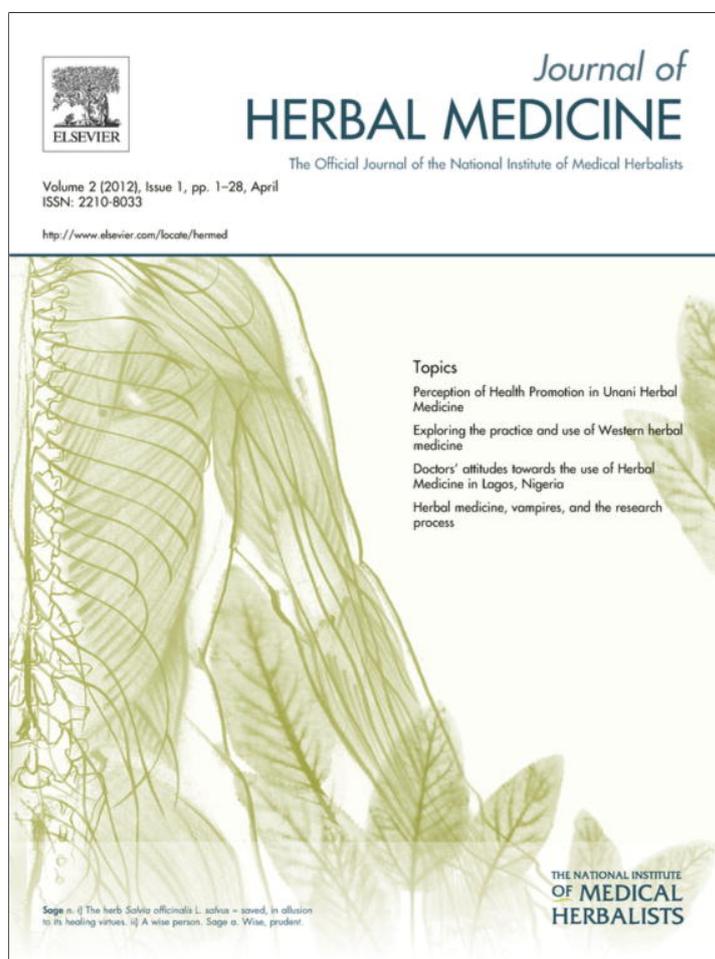


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Opinion Piece

Becoming a stakeholder: Herbal medicine, vampires, and the research process

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For some herbal practitioners research is considered a vital process that the profession has to engage with in order to gain credibility, establish its place within mainstream healthcare and test theories of practice that rest upon a rather rickety anecdotal evidence base. To others research represents a Faustian pact with the dark forces of reductive scientific materialism that undermines and distorts the complex, individualised and profound way in which herbal medicine can facilitate the healing process. Both views, as is often the case, have a large dollop of truth in them but can we predict or influence which of these truths will prevail over time?

The rationale for why herbalists need to engage in the research process has an obvious logic to it. We live in an evidence based culture particularly when it comes to medicine and to turn our backs on the methodologies employed to test the validity of our treatments is to reject the possibility of finding a meaningful and substantial role within the dominant health care system. Without evidence demonstrating the benefits of herbal medicines any risk from these treatments will be considered unacceptable. Thus kava (*Piper methysticum*) is banned whilst most of the drugs that lead to an estimated 197,000 drug related deaths a year in the EU (Archibald et al., 2011), remain in regular usage by maintaining an acceptable 'risk: benefit' ratio (known in James Bond parlance as 'license to kill'). Professional status is also predicated to some extent on our ability to prove that what we do is scientifically rational, biologically plausible, effective and safe. In order to do this we need to subject herbal medicines to a transparent and rigorous scrutiny. What does this actually mean?

Most of us are now aware of the notion of a research hierarchy that begins with anecdotal evidence and proceeds through increasing degrees of rigour through an 'observational' phase (e.g. case series and cohort studies) to an 'exper-

imental' phase of controlled trials that use randomisation and blinding to minimise the effects of various forms of bias and confounding factors in order to focus on testing the specific effect of an intervention. The apex of this evidence hierarchy is the synthesis of these trials into a systematic review that may, if studies are sufficiently similar, be able to generate the mouth-watering prospect of a statistical meta-analysis. The underlying logic of this demanding and immensely expensive process is that larger numbers of patients, treated under controlled conditions, increase the ability of the outcomes of clinical trials to reflect what will be 'true' for the general population. In medical research the numbers involved increase the power of the study to either detect a treatment that works or to identify one that does not. In this instance, it appears, size matters. However in medical research, as well as other aspects of life, it is not quite so simple.

The design of a double-blinded randomised controlled trial (RCT) is clever and potentially highly revealing. By randomly assigning participants to two or more treatment arms without either the patient, the practitioner or the researcher knowing which individual has been allocated to what group, the RCT allows for a dispassionate comparison of the intervention being tested against either an inert treatment (placebo controlled trials) or a similar treatment (equivalence trials). Data from this experiment can then be analysed and may be shown to be significant statistically (unlikely to be a chance occurrence) and clinically important (by achieving pre-agreed and measurable improvements in symptoms). Smart, rigorous and powerful. So what's the problem?

As is often the case the strength of something is also its weakness. The very act of controlling and blinding that potentiates RCTs also reduces their relevance to 'real world' medical practice. RCTs usually have a rigorous set of inclusion

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criteria that tend to exclude people who, in addition to the disease being investigated, have co-morbidities, or who are relatively old, or who might get pregnant, or have a history of mental illness, or who don't want to gamble with their health by playing the Russian roulette of receiving a placebo or... I could continue. Do these people seem familiar to you? Yes, that's right, these excluded participants probably represent a significant proportion of the patients you see routinely in your day-to-day practice.

Whilst RCTs have scientific rigour they are starting to look a little wobbly when it comes to clinical relevance. Unfortunately as we delve deeper this wobbliness seems to progress into a full-scale case of vertigo. In addition to using a highly selected, homogenous, and frequently atypical sample population, the design of RCTs tends to distort important aspects of the actual treatment that can be delivered. Medicine (herbal or pharmaceutical) in an RCT should ideally be standardised in constituents, dosage, and over time. This is to ensure blinding, to keep a simple relationship between the intervention and the observed effect of this intervention, and to exclude the messy, impractical (and expensive) business of having someone individualise a treatment. Ideally this medicine should be administered in a bland form that is easy to mimic with the controlled treatment—most frequently a pill or capsule. Does this sound familiar to you? No, I didn't think so. The design of an RCT is very well suited to testing a standardised pharmaceutical drug but it is almost the complete antithesis of what constitutes best practice when it comes to herbal medicine—individualised, changing over time, strong tasting, and often administered as decoctions or tinctures. What we are seeing here, and in the previous instance of an unrepresentative patient sample, is rigour operating at the expense of relevance. RCTs do have the power to accurately test an intervention, but not the kind of intervention that herbalists tend to apply in their clinical practice.

It is not just the remedy that is frequently distorted by the research process; it is also the practice of medicine itself. We know that medicine consists of a rather wonderful and complex relationship between a patient and a practitioner. We also know that this relationship is highly therapeutic and can facilitate an incredibly powerful and mysterious process of self-healing that is frequently dismissed as a 'placebo' response. We don't know exactly what causes this self-healing. It may originate from patient motivation to get well, from the benefits of being 'seen' and 'heard', or as a consequence of the relief at receiving a meaningful diagnosis and treatment. It is probably facilitated by entering into a relationship with a caring 'other', or from some other component of the complex intervention that underlies both complementary and most mainstream medical practice. It is likely to be all these and more. The oldest Chinese character for medicine 'Yi' consists of two parts. The first involves a hand preparing to shoot an arrow in the air? This is thought to be a shamanic ritual to ward off threatening 'pathogenic' spirits. The second is the radical 'Wu' which makes no bones about depicting shamans dancing around a drum.

Medicine was a form of shamanism. Despite the protestations and splutterings of reductive science, much medical practice retains a shamanic aspect. That is its mystery and a significant part of its power to heal. Unfortunately the

RCT is to shamanism what garlic is to a certain Transylvanian Count. The process of blinding and delivering an uncertain remedy undermines the trust that lies at the heart of therapeutic relationship. Conversely the fact that one is partaking in a cutting edge scientific experiment may add potency to a treatment that is not reproducible in the mundane reality of day-to-day clinical practice. The RCT plays with powerful forces at the heart of medicine that further undermines the relevance of its experimental findings.

So, to continue our Transylvanian analogy, does all this drive a stake into the cold heart of scientific research into herbal medicines? How can we engage in this process without turning our living medicine into a compromised, standardised, devitalised, 'un-dead' version of what we know and love? For those of you who are familiar with Buffy the Vampire Slayer—can the archfiend Spike regain his soul?

The answer to my mind, at this point in time, is a qualified yes. But I suspect it will involve a complex and risky process with a sometimes unpalatable, bitter element of compromise. In a way I don't think we have much of a choice. If herbalists don't engage with the research process others will do it for them. If we sit back and let this happen we are faced with the prospect of researchers with little understanding of herbal medicines investigating inappropriate or ineffective herbal treatments and finding that, surprise, surprise, they don't appear work. I am always reminded at this point in the argument about the pleasant 20 min I sat listening to a report of the trial that demonstrated that St John's Wort (*Hypericum perforatum*) did not work for children with Attention Deficit and Hyperactivity Disorder (ADHD). The rather disappointed silence that greeted these results was only slightly disturbed by the herbalist next to me mumbling... "but we don't use St John's Wort for ADHD". As if that had anything to do with it! i.e. well-meaning researchers investigating the wrong treatment and finding it ineffective...

So, we have a duty to engage with the research process in order to share our individual and collective experience of herbal medicines. What conditions do you find responsive to herbal treatment? We are not offering a panacea. Herbs are probably better for a chronic cough than for a pneumothorax. In my experience fibroids are difficult to shift but polycystic ovarian syndrome frequently responds well to herbal intervention. We need to identify the areas that herbal medicine consistently treats well and then select those that conventional medicine manages poorly. These constitute an "effectiveness gap" that will include many of the chronic, degenerative problems frequently presenting in primary care such as IBS, recurrent urinary tract infections, allergic disorders, and the kind of disabling symptoms such as fatigue and emotional distress that may slip through the broad disease categories of conventional medicine. Herbal medicine could contribute to filling these gaps. This provides the rationale for funders to firstly research herbal medicines and then, if successful, to justify making these treatments more widely available within mainstream healthcare either as a product or, in my wildest fantasy (sad isn't it), as a service provided by skilled herbal practitioners.

We still have the problem of how we put these treatments to the test without fatally compromising them by employing a reductive RCT. Thankfully the research hierarchy is starting to

blur and change. One of the founding fathers of evidence based medicine has co-written a paper stating that the n-of-1 trial, a kind of RCT involving just one patient, should be at the top of the evidence hierarchy above a systematic review because the data it provides on the impact of an intervention is highly patient specific and more likely to be true for an individual than data inferred from the results of the sample population of a typical RCT (Guyatt et al., 2000). There are other arguments that question the assumption that RCTs provide a more rigorous and precise estimation of the effect of treatment than well designed cohort studies involving large numbers of patients receiving more naturalistic treatments over time without any randomisation or blinding to reduce confounding factors (Concato et al., 2000). These are controversial discussions. Less controversial is the increasing emphasis on pragmatic clinical trials for complex interventions such as physiotherapy, psychiatry and most CAM therapies. Pragmatic trials try to reproduce real world treatments in real world contexts using the kind of varied, complex group of patients that present in day-to-day practice. At Southampton University we conducted a double-blind RCT feasibility study using individualised Chinese herbal decoctions for the treatment of endometriosis. There were problems with the sample of patients we recruited and the small size of the trial but from a methodological point of view it was a success. Best practice of Chinese medicine could be subject to rigorous investigation. Rigour can be successfully combined with relevance (Flower et al., 2011).

Another vital piece of the research puzzle is the growing realisation of the importance of qualitative research to capture the subtle, deep, and frequently unpredictable experiences of people receiving treatment. These findings are often in stark contrast to the monochrome, reductive responses elicited in most quantitative outcomes measures and they shed light on the way in which medicine can facilitate healing at many levels, in domains often far removed from the obvious presenting problem.

The dissatisfaction with a rigid evidence hierarchy is being felt across the research world. New forms of trial methodology that try to capture the complexity of clinical practice are being developed such as multi-factorial, adaptive, expertise based RCTs. Systematic reviews that exclude anything but the most rigorous (and frequently least relevant!) RCTs are being reinforced by more inclusive forms of evidence synthesis that recognise the value of expert opinion, individual case studies, observational studies as well as the importance of well conducted RCTs (Athanasidou and Darzi, 2011). As the old linear hierarchy starts to bend and stretch new models are emerging that describe the production and gathering of evidence in terms of circular models that consider the relative strengths of research designs to answer different questions and contribute to a composite of evidence (Walach et al., 2006), or, my own personal favourite, use the dialectical logic of the yin and yang symbol to capture the constant interplay between the various qualitative and quantitative research methodologies (Scheid and MacPherson, 2012).

There are definitely signs of a growing 'soul' within the corpus of clinical research. However let's not forget those potentially threatening vampiric tendencies. Whilst these

new methodological developments present more subtle and suitable ways of investigating herbal medicines they still have to be paid for. Why should funders interested in GP practices operating as primary care spend scarce resources investigating individualised decoctions that require expensive herbalists and cost a lot of extra money to deliver? Why should phyto-pharmaceutical research companies be interested in what a group of expert herbal practitioners consider to be best practice when they already have their own product they want to test? To my mind this is now the biggest challenge in herbal medicine research. Can we negotiate the requirements and interests of the research funders without compromising the authenticity of our treatments? Can we find ways to justify employing the research designs which ask the kinds of questions that herbalists may be interested in, such as the effect of individualising treatments; the value of traditional methods of administering herbs such as decoctions and tinctures; the importance of the whole system of herbal intervention that may include diet, lifestyle advice, relaxation techniques; what is the optimum dosage range; or which similar herbal products are most effective?

If we don't engage with and try to influence the direction of the research then we stand the real risk of watching from the sidelines as inappropriate remedies are tested and found to be wanting. CAM therapies are very vulnerable to the ebbs and flows of research. Most acupuncturists currently bask in the series of research papers supporting the role of acupuncture in the treatment of infertility, whilst homeopaths have become an endangered species after the concerted effort to undermine the evidence base of their practice. Despite the deep historical and emotional support that underpins herbal medicine each piece of negative research represents another nail in the coffin of herbal credibility and availability. We need to work to keep this lid open, and make sure that the vampire within stays in touch with his new-found soul.

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