

Pathways to Plausibility: When Herbs Become Pills

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Abstract

Herbal medicine has long been contrasted to modern medicine in terms of a holistic approach to healing, vitalistic theories of health and illness, and an emphasis on the body's innate self-healing capacities. At the same time, since the early twentieth century, the cultivation, preparation and mass production of herbal medicines have become increasingly industrialized, scientificized and commercialized. What is more, phytochemical efforts to identify and isolate particular 'active ingredients' from whole-plant extracts have intensified, often in response to increasing regulatory scrutiny of the safety and quality of herbal medicinal products. In this article, I examine whether describing these developments in terms of a biomedical 'colonization' of herbal medicine, as has been common, allows us to sufficiently account for the mundane collaborative efforts of herbalists, botanists, phytochemists, pharmacologists, toxicologists and clinicians to standardize and develop certain herbal remedies. By focusing on recent efforts to industrialize and scientifically develop a 'Western' (St John's Wort) and a Vietnamese (Heantos) herbal remedy, I suggest that herbal medicine has come to be not so much colonized as normalized, with herbalists, phytochemists and pharmacologists working to develop standardized production procedures, as well as to identify 'plausible' explanations for the efficacy of these remedies.

Keywords colonization, herbal medicine, mechanisms of action, normalization, paradigm, plausibility

In June 1997, the Vietnamese government and the UN Development Programme (UNDP) signed a three-year agreement to finance and support a project entitled the 'International Scientific Development of the Anti-drug Medication Heantos'. The agreement followed a series of reports about this 13-plant herbal tonic's efficacy in the treatment of opiate addiction, especially anecdotal news of a trial on 110 morphine-addicted war invalids at the

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Hoàng Long Rehabilitation Centre from 1994 which suggested that following treatment with Heantos, up to 80 percent of these invalids had stopped picking up their free monthly rations of morphine provided to them by Vietnam's health authorities. The herbal tonic had itself been developed by traditional herbal practitioner Tran Khuong Đan following experimentation during a series of self-inflicted addiction withdrawals. Dr Ha Anh, Head of the Institute of Orthopedics Science and Rehabilitation of Wounded Veterans and Invalids, who had followed the treatment of the group of invalids, concluded in a report to the Ministry of Health that the 'importance of Heantos is its ability to prevent re-addiction and to appease the patient's craving for drugs' (Vietnam Institute of Orthopedics Science and Rehabilitation for Wounded Veterans and Invalids, 1996). Heantos has since been subjected to two controlled clinical trials in Vietnam which have concluded that 'Heantos supports the alleviation of withdrawal from drug addiction [and] has effects that reduce cravings, reduce paraesthesia, reduce symptoms of digestive disorder, recover the patients' sleep habits and help the patients recover their health rapidly as well as clear their minds' (Vietnam Institute of Chemistry, 1999: 43).

Around the same time, a full-page article in the health section of the 22 September 1997 issue of *Time* magazine was asking whether St John's Wort, a folk remedy made from the plant *hypericum perforatum*, was 'Nature's Prozac?' (Nash and Cray, 1997). This and numerous other media stories cited a string of recent clinical trials as well as pre-clinical pharmacological experiments that had been carried out in Germany. Especially highlighted was a meta-analysis of 23 trials by Linde and colleagues which suggested 'there is evidence that extracts of *hypericum* are more effective than placebo for the treatment of mild to moderately severe depressive disorders' (1996: 253). And while there has since been a lot of debate about the merits of the growing number of clinical trials that have been carried out on St John's Wort, in the closing years of the twentieth century St John's Wort became a herbal 'blockbuster' throughout Europe and America.¹

Both Heantos and St John's Wort have in recent decades been the object of steadily increasing scientific scrutiny through phytochemical, pharmacological and clinical research. At the same time, production of these two remedies has been industrialized and standardized such that both of these 'natural' remedies are now available in pill or capsule form. These processes have involved collaborations between practitioners of herbal medicine, botanists, chemists, pharmacologists, toxicologists and clinicians who have had to negotiate and balance quality, safety and batch consistency requirements on the one hand, and an insistence on preserving 'whole plant' or 'multiple pot' extracts (as opposed to isolating and synthesizing single active ingredients) on the other.

In this article, I will suggest that accounting for efforts to standardize and industrialize St John's Wort and Heantos in terms of a 'scientific colonization' or 'cooptation' is at best an oversimplification. While such descriptions certainly do capture important elements of these processes—e.g. phytochemical elucidation of active ingredients, commercial commodification of herbal medicine—they do not adequately take into account the complex interactions

¹ The sales figures for the US market were spectacular in the final years of the 1990s, with some estimates suggesting that sales jumped 190 percent from \$48 million in 1997 to \$140 million in 1998. In Europe, sales figures for 1998 have been estimated at \$6 billion. And in Britain, an estimated 2 million people were using St John's Wort in 2000. Ironically enough, increased attention to St John's Wort also resulted in a number of media reports suggesting that St John's Wort negatively interacted with a number of commonly used conventional drugs, which resulted in an almost immediate sales decline in Europe and America (Blumenthal, 1999; Kelly, 2001; Lawson, 2000).

and co-circulations of concepts and practices that constitute the microphysics of herbal medicinal product development.

I begin by suggesting that the colonization hypothesis, which has become common in accounts of the scientificization and industrialization of herbal medicines (and other forms of traditional or alternative medicine), is rooted in Kuhnian incommensurability. I will then go on to propose that Canguilhem's notion of normalization is better suited when accounting for these processes. The bulk of the paper will examine the microphysics of efforts to standardize and industrialize St John's Wort and Heantos, focusing especially on three key problems: how to accurately identify medicinal plant species and record their traditional medicinal uses; how to ensure 'batch-to-batch' consistency in the production of 'whole plant' (in the case of St John's Wort) and 'multiple pot' (in the case of Heantos) extract herbal products; and how to establish 'plausible' explanations for the suggested efficacy of these treatments. In conclusion, I will argue that while the transformation of raw herb materials into pills certainly constitutes a normalization of herbal medicine, this normalizing is the result of a complex co-circulation of herbal, biomedical, phytochemical, pharmacological and botanical concepts and practices.

From colonization to normalization

Throughout the world, there has been a growing interest in herbal medicine in recent decades. As ancient as the practice of medicine itself, the use of plants to heal—whether by traditional healers, herbalists, apothecarists or pharmacologists who isolate active compounds from plant extracts—has been a consistent part of medical practice in all corners of the world. In some countries it is estimated that up to 80 percent of the population continue to rely primarily on medicines from plants for their healing needs (WHO, 2002). At the same time, while herbal medicine has long been a commercialized field of patent medicines and/or medicinal plant markets, over the past century or so it has transformed into a highly technologized, multi-million dollar industry. Inspired by the pioneer work of German natural products chemists and companies in the 1920s and 1930s,² the industrialization of medicinal plants into what have come to be known as 'phytomedicines' or 'herbal medicinal products' has developed into a global activity with supply chains spanning all the world's continents. Indeed, the late twentieth-century 'boom' in herbal medicine, often cited as evidence of the growing popularity of alternative and traditional medicines, refers in large part to rapid rises in the sales figures for phytomedicines throughout the 1980s and 1990s (see Gaedcke and Steinhoff, 2002; Richter, 2003).

These developments have led a number of scholars to suggest that herbal medicine is in the process of being colonized or co-opted by 'Western' biomedicine. For example, in the context of traditional Chinese medicine, Ted Kaptchuk has argued that efforts to modernize traditional medicine:

... are aimed at separating out the effective components of Chinese medicine and introducing them into the framework of modern Western medicine... Yet, although this

² See Timmermann (2001) and Kenny (2002) for discussions on how companies like Madaus, supported by the National Socialist regime took the lead in researching and industrially developing herbal medicines.

knowledge, with its use of traditional herbs and acupuncture, has the veneer of Chinese medicine, the actual application and methodology are clearly Western in orientation. The theory of Yin and Yang and other traditional concepts are left behind. (1983: 24)

In an article on the ‘crisis of traditional medicine’ in Tibet, Janes argues that traditional Tibetan medicine is currently at risk of being ‘co-opted by the medical establishment and distributed without concern for (or understanding of) possible iatrogenic consequences’ (1999: 1804). In relation to what they see as an increasingly global herbal medicine, Jagtenberg and Evans suggest that:

... with its emphases on mass production, biochemistry and standardization, global herbalism provides an antithesis to the magic of the local...[,] the physical and biomedical science’s dismissal of metaphysics, spirituality and value judgments marks a basic paradigm divide between traditionally based natural healing modalities and biomedicine and the physical sciences. (2003: 328)

And finally, Barry argues that such a process of scientificization is complete ‘when the [alternative] therapy has mutated into a medicalized version and divested itself of its alternative philosophy’ (2006: 2648).

And so it is in contrasting ‘frameworks’, ‘establishments’, ‘paradigms’ or ‘philosophies’ that a divide between an authentic traditional herbal medicine and a modernized global herbal medicine is posited. There is a clear sense of loss in these accounts—of the traditional, the magical, the natural or the metaphysical—and as such they chime well with classic modernization critiques. There are also more or less explicit references to what Thomas Kuhn described as ‘incommensurable ways of seeing the world and of practicing science in it’ (1962: 4). In Kuhn’s famous view there is an emphasis on the single, ‘winning’ paradigm— ‘paradigms gain their status because they are more successful than their competitors’ (1962: 25)—and as such, if two paradigms come into competition (e.g. a ‘vitalistic’ herbal medicine and a ‘mechanistic’ biomedicine), one of them will eventually prevail. And it is exactly in the context of such a competition of paradigms that the colonization hypothesis has been enunciated.

Now, while such a hypothesis can certainly be used to address how particular rationalities and practices of validation, standardization and control in herbal medicine (and the various commercial, political or ideological ‘interests’ seen to underpin these) gain their authority and legitimacy, its emphasis on a one-sided colonization makes it very difficult, as we will see, to account for often innovative collaborations between herbal practitioners, phytochemists and pharmacologists when it comes to standardizing and industrializing herbal remedies (see also Kim, 2006). Instead, what I will show in the following by examining efforts to modernize St John’s Wort and Heantos, is how we might understand these processes in terms of a *normalization of herbal medicine*, by which I mean the appropriation of herbal medicine as a distinct object of expert bodies of knowledge which inform and organize practices of standardization, commodification and industrialization. As we will see: traditional or folk knowledge about medicinal plants is considered to be a rich resource yet one about which there is, at best, ‘inconsistent knowledge’, at worst, ‘profound ignorance’; plants are considered ‘living laboratories’ yet ones that are notoriously inconsistent in the production of active ingredients; and vitalistic theories about how medicinal herbs work have been described by some as ‘incongruent with scientific thought’. As a result, if

herbal medicine is to be standardized then it must be normalized, where, as Canguilhem has suggested, norms are ‘that which can be used to right, to square, to straighten’ and ‘to normalize, is to impose a requirement on an existence, a given whose variety [and] disparity with regard to the requirement, present themselves as a hostile’ (1989: 238).

There are three distinctive features of the normalization of herbal medicine that I will highlight in the following sections: the first concerns a kind of *ethno*-scientific taming of the countryside; the second concerns attempts to standardize herbal formulas at a molecular, bio-chemical level; and, finally, the third concerns a search for ‘plausible’ mechanisms of action. What I will demonstrate throughout this analysis is how so-called ‘vitalistic’, ‘reductionist’, ‘alternative’ and ‘mainstream’ concepts and practices have all co-circulated within and informed practices of ethno-botanical taxonomizing, phytochemical standardization and preclinical pharmacological research.

Taming the countryside

The closing decades of the twentieth century saw what Parry (2004: 150) has described as a ‘resurgence of interest in collecting biological materials’ from the ‘wild’ for medicinal or industrial use. There is of course nothing new in the fact that medicinal firms and practitioners look to plants in their quest for novel compounds to fight disease (take, for example, morphine, aspirin and digitalis), but what has been especially characteristic of this more recent resurgence of what has come to be known as ‘bio-prospecting’ is the systematized role that traditional knowledge—as handed down or recorded through the generations—has come to play in the initial identification and/or screening of suitable plant leads when faced with an incredibly lush global biodiversity.³ In Vietnam, efforts to revitalize Vietnamese herbal medicine since the mid 1950s have first and foremost relied on a comprehensive mapping out effort that took organized teams of herbalists, botanists and other scientists to the rural areas of Vietnam in an attempt to record the experiences and knowledge of traditional practitioners (see Wahlberg, 2006). Their task was to standardize the different vernacular names of plants used by traditional practitioners by using botanical taxonomies as well as to record the most common medicinal uses of different plant species. As such, this was in many ways what the nineteenth-century botanist John Harshberger, as one of the first, would have called an ethno-botanic project—a ‘study of plants used by primitive and aboriginal people’ (1896)—albeit unequivocally stripped of Harshberger’s outmoded evolutionary assumptions. To explain the launching of the Vietnamese government’s national ethno-botanic programme, Minister of Health Pham Ngoc Thach argued that:

The scorn of Western-trained physicians for traditional medicine derives from an erroneous conception of science and a profound ignorance of the results obtained by traditional medicine... I would like to draw attention to the extreme richness of the vegetal pharmacopoeia of traditional medicine. Naturally, one cannot experiment on all these vegetal varieties one after another. The age-old experience of the people and physicians of the traditional school comes into play here... There is a danger

³ Of the world’s 250,000 or so species of higher plants only 6 percent have been investigated for their biological activity (Heinrich *et al.*, 2004: 289).

of letting this age-old knowledge of medicine disappear rapidly, because if we don't cultivate it those who practice it will have disappeared after ten or twenty years. (Pham, 1965: 13–15)

In other words, this was not a national study of how 'primitive' peoples used plants, rather it was a case of what in more recent times has come to be described as ethnopharmacology and ethnopharmacognosy. These latter two ethno-sciences concern the study of all 'biologically active agents traditionally employed or observed by man' (Heinrich *et al.*, 2004: 52), especially for medicinal purposes. What makes them 'ethno' sciences is their systematized focus on culturally transmitted traditional knowledge, not only as a matter of cultural heritage but also as an important ally in the search for ecologically, industrially and/or medically relevant active compounds in the face of the 'extreme richness' of the wild.

This was exactly the approach chosen by herbalist Tran Khuong Đan as he traversed Vietnam from south to north in the 1980s, looking for possible leads that could help him in his efforts to develop a herbal remedy against addiction. Travelling off the beaten track, Đan trekked the length of Vietnam's 2,000 or so kilometres, visiting rural communes and villages where opium cultivation and use had been a part of daily life for centuries. In these villages, Đan sought out traditional herbalists to discuss and exchange ideas on treating opium dependency. By the end of the 1980s, Đan settled down to digest and organize the experiences and knowledge he had amassed during his travels. He also began scouring traditional Chinese and modern medical texts to learn as much as he could about addiction as well as methods of treatment. It was from this broad base of knowledge, spanning the traditional practices of village herbalists and the theoretical underpinnings of Sino-Vietnamese traditional medicine, that Đan developed Heantos, a 13-plant herbal remedy for addiction (Tran, 1999). This remedy was presented to the health authorities in 1990 and Heantos has since undergone a series of clinical trials in Vietnam, as well as receiving the support of the United Nations in efforts to further scientifically develop it. One of the first tasks of Đan's collaborators at the Institute of Chemistry in Hanoi was to botanically identify and categorize each of the 13 plants in the remedy since, as explained in the United Nations project document:

... a common problem in literature [about Vietnamese medicinal plants] is a lack of precise species identification (according to Latin names denoting *species*, *genus* and *family*). The result is that a single species can have up to 20 different local or Vietnamese names in various books, depending on the source. It is therefore critical for the standardization of Heantos that each plant is identified and taxonomized according to botanical categories. Ethnopharmacognostic studies will also be prepared by Vietnamese scientists with the assistance of traditional practitioners throughout Vietnam. (UNOPS, 1999: annex III)

In many 'Western' countries, processes of industrialization and urbanization are also seen as a threat to local knowledge about the healing properties of plants. For example, when a group of herbal practitioners, botanists and remedy producers launched an 'Ethnomedica' group in 1999 to 'Research the Herbal Traditions of Britain', their rationale for doing so was not unlike that of the Vietnamese government:

150 years ago Britain was still mainly a rural society. Lives and activities were defined by the seasons and everyone knew the names and uses of several common wayside

plants. Within two generations of the industrial revolution most of the population had moved into cities. As people developed an urban lifestyle they lost contact with the land and their practical herbal traditions. Not just forgotten but no longer accessible—where was the nearest dandelion, dock, healing tree or stream for watercress? . . . The loss of local knowledge—be it about plants or anything else—is one of the side-effects of globalisation and rapidly changing societies. While this issue is recognised in the tropics, and is receiving a lot of attention from those concerned with development and the conservation of cultural and biological diversity, it is not the case here at home. The UK has long been industrialised and ranks among the most developed of regions. Yet studies have shown that fragments of knowledge passed down through a long oral tradition still exist among older people. Its value increases the more it is lost as time passes. (Ethnomedica, 1999: n.p.)

In the three-year period 2003–2006, over 1,000 records of medicinal plant use gleaned from interviews and survey cards that had been carried out by a group of 13 researchers as well as by Kew Gardens, were collated and organized. Scientists at Kew Gardens have also been able to use the information gathered as a means of screening potential plant candidates for further phytochemical research into therapeutically active compounds. In this way, traditional knowledge of the ‘folk’ uses of plants has been instrumental in collaborations to collect, organize and investigate plant medicines.

St John’s Wort (*hypericum perforatum*) is a case in point. Native to Europe, this plant has a long history of medicinal use dating back to the third century BC. In 1630, Italian iatrochemist Angelo Sala reported that ‘St John’s Wort has a curious, excellent reputation for the treatment of illnesses of the imagination . . . and for the treatment of melancholia, anxiety and disturbances of understanding’. In 1652, one of the ‘founding fathers’ of organized herbal medicine practice in Britain, Nicholas Culpeper, classed the very yellow-flowering St John’s Wort ‘under the celestial sign Leo, and the dominion of the Sun’ in his *English Physitian*. And in 1814, Robert John Thornton explained in his *Family Herbal* how ‘formerly it was supposed, and not without reason, that madmen were possessed of the devil, and this plant was found so successful in that disorder, that it had the title *Fuga daemonum*, as curing demoniacs’ (cited in Rosenthal, 1998: 202). It was with reference to exactly these kinds of recorded ‘folk uses’ of St John’s Wort found throughout Europe that, in 1984, Commission E (made up of physicians, pharmacists, naturopathy practitioners, pharmacologists, toxicologists and biostatisticians) of the German Federal Institute for Drugs and Medical Devices listed ‘psychovegetative disturbances, depressive moods, anxiety and/or nervous unrest’ as possible treatment uses for *johanniskraut*, while noting that ‘a mild antidepressant action of the herb and its preparations has been observed and reported by numerous physicians’ (Heilpflanzen-Welt, 2005). Since then, a series of clinical trials have been carried out in Germany, USA and the United Kingdom on the efficacy of this plant in the treatment of depression (see Wahlberg, 2008).

And so, in both European and Vietnamese contexts, ethno-sciences have been deployed as a specific means to document, organize and archive for posterity the kind of information about the medicinal uses of plants that is otherwise seen as at risk of being lost as yet another side effect of globalization and modernization processes. They have also been deployed to right what is considered a ‘profound ignorance’ of the traditional or folk use

of plants for healing purposes on the one hand, and a ‘lack of precise species identification’ on the other. What has made these projects distinct is how the systematized recording of traditional or folk knowledge—whether gained through interviews, surveys or historical literature reviews—has interacted with botanical, phytochemical and pharmacological research. In both Vietnam and Western countries such as the UK and Germany, such ethno-scientific projects have involved collaborations between traditional herbal practitioners, pharmacologists, botanists and phytochemists.

Normalizing living laboratories

Yet it is not only through an ethno-botanic mapping of the countryside with the aid of field notes, literature searches, databases and nomenclatures that the normalization of herbal medicine is taking place. It is also increasingly taking place in chemistry laboratories filled with high-tech extraction apparatus, chromatographs and nuclear magnetic resonance spectrometers. It is in these laboratories that the biomass plant samples collected and taxonomized by herbalists and ethno-scientists are subject to labour-intensive phytochemical scrutiny—soaked in extraction solvents, percolated, centrifuged, filtered, dried, partitioned, separated, elucidated and finally characterized in their chemical multiplicities. As argued by Vietnam’s Health Minister Pham, plants are great chemists:

Take for instance the medicinal plants. . . . What is the extract of a plant, if not a complex body, the product of complicated synthesis? Thus, we have either ready-made medicines or products from which we can make higher synthesis, a good part of which process has already been made by those living laboratories: the plants. . . . [With] traditional medicine, we have at the same time clinical indications to choose the plants for experimentation, and the products of a total or partial synthesis. These are the real short cuts offered us by traditional medicine [and] we are working systematically in this direction. (1965: 15)

Notwithstanding such short cuts, the phytochemical partitioning and mapping out of these living laboratories is not only necessary for subsequent pharmacological research on the mechanism of action, it is equally necessary for those regulatory initiatives that seek to assure consumers, as best they can, that they can expect some kind of standardized quality, not to mention safety, from the industrialized herbal products they purchase. For, if there is one thing that is characteristic of phytochemistry, it is that it is a science of ranges that seeks to apply some kind of consistency to the notoriously inconsistent chemists that plants have been shown to be.

Whatever disagreements herbalists and scientists may have over specific mechanisms of action as well as concepts used to account for these mechanisms (more on this later), there is broad agreement that it is the chemicals found in a plant that have a therapeutically significant effect on the body’s physiological functioning when ingested—as put by ‘Western’ herbalist Simon Mills: ‘it is the nature of the material, the character of the remedies, that is the determining factor’ (1993: 150). There is also agreement that the amount and quality of chemicals found in an extract of a particular plant species is dependent on growing conditions (soil, climate, weather conditions, pesticide use), time of harvest (before or after

flowering, early morning or evening), which part of the plant is used (flower, leaves, stem, bark), extraction processes (drying, grinding, boiling, solvent used), as well as storage conditions (humidity, light, temperature). And while all this can be complicated enough with a single-plant like St John's Wort, it becomes even more complex when working with a 13-plant herbal remedy like Heantos.

Plants may well be superb chemists, but the exploitation of the chemicals they produce is dependent on both the conditions in which they 'naturally' produce them and the expertise in extracting them from the plants into a form suitable for ingestion—e.g. tinctures, teas or pills. And so, while sustainable cultivation practices are increasingly being developed with the aim of optimizing growing conditions for medicinal plant species, phytochemistry has been harnessed in the industrialization of herbal medicine production to help reduce batch-to-batch inconsistencies, by breaking down plant or remedy extracts into identifiable single chemical compounds that can be isolated, chemically characterized and thereby used as markers in the standardization of herbal products. These optimized cultivation practices and standardized chemical markers, it is argued, can then replace a herbalist's traditional organoleptic evaluation of medicinal herbs (taste, smell, texture, appearance) when controlling for quality in industrially produced herbal medicinal products. The goal is to ensure 'a consistent content of therapeutically active constituent(s)... irrespective of the year of harvest and the year of production' (Gaedcke and Steinhoff, 2002: 16) by standardizing production procedures.⁴

This of course means that, in order to be able to standardize a herbal medicinal product according to a defined range of therapeutically active constituents, a manufacturer requires not only a clear understanding of what is to be standardized (i.e. which chemical compounds), but also an understanding of how to ensure more-or-less controlled cultivation and harvest, of appropriate production methods which will not damage or degrade chemical constituents excessively during extraction, and of acceptable ranges of constituent content in the final plant extract products. These are the specific problems related to the production of whole-plant extract based products as opposed to single active compound drugs.

St John's Wort is a single-plant remedy, even if very often used by herbalists in combination with other medicinal plants: 'as a nervine, *hypericum* is usually prescribed with three or four other herbs that reflect the individual needs of a patient' (Chevallier, 1999: 92). And not only has it become one of the most clinically studied herbal remedies in the world, it has also become one of the most phytochemically and pharmacologically analysed plants in the past few decades. With a long history of documented medicinal use, as we saw earlier, St John's Wort (*hypericum perforatum*) has recently been described as a 'prolific producer of secondary metabolites' (Müller, 2005: 5). One of the first of these to have been isolated and characterized is the naphthodianthrone hypericin, a red pigment long known for secreting when the yellow flowers of St John's Wort are squeezed by hand. It has also been found to be the culprit in causing hypericism (a disease that leads to potentially lethal photosensitization) in cattle that feed off of the plant, and as a result it has been described as defence agent of the plant. Perhaps not so surprisingly then, it was also hypericin that became one of

4 As Gaedcke and Steinhoff (2002) point out, it should be underscored that in far from all herbal plants and remedies have therapeutically active constituents been pharmacologically identified. For these herbal medicinal products, 'standardization' refers to the implementation of standardized Good Manufacturing Procedures, which can ensure some kind of batch-to-batch consistency where marker compounds are not necessarily therapeutically active.

the first lead candidates in the phytochemical search for active compounds that might explain its anti-depressant effects. But *hypericum perforatum* has since been found to contain many more classes of secondary metabolites, including phloroglucinols (mainly hyperforin and adhyperforin), flavonoids (quercetin, rutin and hyperoside), biflavonoids (biapigenin), xanthenes, proanthocyanidins (catechin), acid phenols (p-coumaric, ferulic and caffeic acids) and essential oils (including 2-methyloctane, limonene and myrcene). To date, pharmacological studies have singled out hypericin, hyperforin, quercetin and rutin as candidate compounds when accounting for the anti-depressant action of St John's Wort.

As much as is now pharmacologically known about the active constituents and possible mechanisms of action which might account for any experienced anti-depressant effects, it remains very difficult to devise standardization procedures for St John's Wort products. To begin with, comparisons of the composition of eight key chemical constituents in different St John's Wort plant specimens have shown variations of as much as 700 percent in individual constituent content measured in micrograms/flowers (Müller, 2005: 16). And while the German Commission E monographs (published in the 1980s) recommend that products be standardized according to a range of hypericin content (1–0.2 mg of total hypericin per 2–4 g of herbal drug), more recent research has suggested that hyperforin is more prominent in generating anti-depressant pharmacologic action. Moreover, hyperforin has been shown to be so chemically unstable (due to a liability to oxidative degeneration) that standardization according to hyperforin content requires very sophisticated and costly extraction techniques. With so many variables at play, it is little wonder that an *LA Times*-commissioned chemical analysis of ten St John's Wort brands from 1998 found considerable discrepancies between what was promised on labels in terms of hypericin content and what was found to be present in sample capsules (three brands contained no more than half the listed amount and four had less than 90 percent of the listed amount; Monmaney, 1998).

The challenge for standardizing St John's Wort then, has become one of balancing a need for suitable (preferably therapeutically relevant) bio-chemical markers that can ensure batch-to-batch consistency within an accepted range of marker constituents on the one hand, and on the other to ensure that the entire spectrum of chemicals particular to St John's Wort is present in any whole-plant extract products made from it. Ensuring that a final herbal drug preparation contains a certain constituent within a defined content range, either by adding inert adjustment material (e.g. lactose) or blending extract (of the same plant), can, ironically enough, diminish the quality of the original or so-called 'native extract', and as a result, it is argued, 'the initial question prior to adjustment should always be, if it is considered more important to administer a sufficient quantity of native extract or a defined quantity of the constituent(s) the extract is to be adjusted to' (Gaedcke and Steinhoff, 2002: 17). The answer to this initial question is far from clear-cut, with pharmacologists probably inclined to favour the latter and herbalists the former. For example, medical herbalist Peter Conway argues that 'most herbalists would rather use a St. John's Wort preparation that has a natural balance of constituents, achieved through good growing, harvesting and processing, over one that has unnaturally high amounts of one element, as in many standardised products' (2003: 21). Bearing in mind that 'natural' variation in this 'natural balance of constituents' can be considerable, Conway does suggest that 'it is possible to check the quality of herbal preparations and ensure that there are the right amounts of a broad spectrum of the desirable chemicals present in the product without artificially altering their relative

amounts' (2003: 21).⁵ And so the problem remains of just how to define what is meant by the 'right amounts', a task that invariably will require some kind of 'normal spectrum' marker profiles against which batches can be checked or 'quality controlled'.

As already mentioned, herbal practitioners have in the past relied extensively on organoleptic evaluations of quality, either as they gathered their starting materials from the wild or upon purchasing them from commercial suppliers or at medicinal herb markets. However, new regulations in both Vietnam and the European Union increasingly require laboratory-confirmed quality assurances—especially for industrially produced herbal products, but also for starting materials. And it is in these practices of quality assurance that control profiles based on chromatographic 'fingerprints' have become crucial. By using thin layer (TLC), gas liquid (GLC) and high performance liquid (HPLC) chromatography methods, a plant extract can be broken down into its various chemical constituents, which appear either as bars on a TLC chromatogram or peaks on GLC and HPLC chromatograms. And just as the fingerprints from a crime scene can be checked against a database of past suspects for a match, so too can the chromatograms from a new batch of herbal medicine extract be checked against constituent control 'profiles' to ensure a standard batch-to-batch consistency. For, once chromatographically separated, chemical constituents can be phytochemically identified using nuclear magnetic resonance spectroscopy or mass spectrometry, which allow for three-dimensional structure elucidation of an individual molecule of the chemical constituent under scrutiny. The goal being to identify suitable marker compounds unique to the medicinal herb in question, which can then be used to build chemical reference profiles based on norms of purity and content.

It is also these isolated chemical constituents that can then be individually assayed for possible pharmacologic actions (something we will return to later in this article), and thereby classed into groups of either therapeutically active constituents (i.e. those 'with known therapeutic activity'), active constituents (i.e. those 'which contribute to therapeutic efficacy') or marker substances (i.e. those 'which, according to the state of scientific knowledge, do not contribute to therapeutic activity . . . [yet] are suitable for identification tests and assay (e.g. batch-to-batch control)') (Gaedcke and Steinhoff, 2002: 22–23). Hence the standardization of St John's Wort products today is carried out using not only quantitative content ranges for hypericin and/or hyperforin (expressed in terms of milligrams per daily dose), which have been identified as pharmaceutically relevant constituents, but also qualitative chromatographic standards which reflect an aim to ensure that an extract contains the plant's 'full spectrum' of constituents in relevant amounts.

Now, as we can see, the challenge of standardization in the case of St John's Wort has been a time-consuming, costly and technically sophisticated affair. So much so that one can only imagine the magnitude of such a task when presented with a mixed extract containing all of 13 different plants, such as Heantos. When Tran Khuong Đản approached health authorities in Vietnam with his herbal mixture for the treatment of drug addicts in 1990, his remedy came in the form of a dark, rather earthy-tasting syrup, the result of a complex process of cutting, drying, boiling and mixing. As already highlighted, Đản had spent many years learning from the experiences of fellow traditional practitioners, by

⁵ Mills concurs arguing that 'although there is variability, it is within workable limits, and quality control can reduce it even further' (1993: 262).

travelling throughout the countryside collecting over 100 home-made recipes for treating opium addiction in the 1980s. On the basis of this gathered knowledge, combined with information gleaned from classic medicinal texts (most of which were written in Chinese and Nôm),⁶ Đản began experimenting with various herb combinations and preparation methods. It was at this time, during the late 1980s, that Đản decided to intentionally addict himself to opium in order to personally evaluate the different remedy batches. He would later argue that ‘the only way I could test my medication was to experience the torture of withdrawal for myself’ (Tran, 1999). And so, through a period of two years, Đản would undergo a series of self-inflicted withdrawals, all the while experimenting on himself with the different mixtures he would devise. Đản’s final choice fell on a set of 13 plants and a complex processing protocol which together would produce a herbal remedy for treating addiction with some kind of consistency. It was using this home-brewed syrup that the trial on war invalids described above was carried out in the early 1990s.

Starting in 1995, however, Tran Khuong Đản donned a white laboratory coat in an interesting collaboration with some of Vietnam’s top chemists at Hanoi’s Institute of Chemistry, as part of a UN-sponsored effort to standardize and further develop Heantos. Whereas in the past it was the botanists, ecologists and chemists who had been sent out to the Vietnamese countryside on ethno-scientific missions to liaise with traditional herbal practitioners, in this collaboration a traditional herbal practitioner was invited to join chemists in their laboratories, to assist them in their efforts to identify and characterize the chemical constituents that may be contributing to the therapeutic effects purported to have been witnessed in some 9,000 or so patients who had been treated with Heantos in Vietnam to date. Certainly, Đản’s presence in the laboratory has been far from cosmetic; rather his detailed knowledge of the medicinal properties of each of the plants in Heantos has been instrumental in the transformation of Heantos from its original syrup form into ‘standardized’ capsules. From the identification of the particular medicinal plant species to guidance on the best methods for extracting therapeutic constituents from these plants, Tran Khuong Đản has worked closely with Professor Tran Van Sung over the past decade as a partner in the laboratory. The Institute of Chemistry, in turn, for reasons which will become clear, has enlisted their long-time partners at the Leibniz Institute of Plant Biochemistry in Halle, Germany, to help with ongoing efforts to chemically characterize Heantos, with the ultimate aim of accounting for its therapeutic action.

There have been two key objectives in the further scientific development of Heantos since the mid 1990s. The first has been to transform Heantos into a stable, so-called ‘multiple pot’ herbal extract. That is to say, to take the first step towards standardization by introducing reproducible extraction procedures, by building on Tran Khuong Đản’s original, perhaps more crude, methods of extraction. In October 1997, the first results of the collaboration between Đản and the Institute of Chemistry came in the form of the first batch of Heantos dry extract capsules. To make things more practicable, Đản and Sung had agreed to divide the plants into three groups, each with a specific therapeutic function as determined by Đản. Each of these three groups of plants was then processed into three individual dry extracts, which were subsequently manufactured into Heantos 1

6 Nôm is a script developed around the tenth century by using and modifying Chinese characters to write Vietnamese.

(for withdrawal), Heantos 2 (a sedative to help patients sleep) and Heantos 3 (to help prevent relapse after withdrawal by keeping cravings at bay) capsules.

The second key objective in the Institute of Chemistry's efforts to develop Heantos further scientifically has been to phytochemically characterize each of the 13 plants included in the original herbal syrup, in much the same way that St John's Wort has been, so as to be able to standardize production procedures. And seeing as this task is a technology-intensive affair (some of which is not available in Vietnam), the Institute of Chemistry called upon their long-time partners at one of Europe's most advanced plant biochemistry institutes in Halle to assist them in this effort. In the period May 2000 to March 2006, Vietnamese and German chemists joined forces to characterize the chemical constituents found in each of Heantos' 13 plants. Starting with literature reviews in Chinese and Vietnamese, as well as international bibliographic databases to map out existing studies on the plants in question, the scientists employed chromatographic methods (thin layer, middle performance liquid and high performance liquid chromatography) to isolate pure compounds from Heantos components, and then infrared, ultraviolet, mass and nuclear magnetic resonance spectroscopy to structure-elucidate these compounds. The goal of these initial phytochemical efforts was 'not to pursue the isolation of single bio-active principles and their synthesizing', but rather 'to contribute to the optimization of the efficacy of Heantos, to its development as a standardized product and to the scientific explanation of the effectiveness of a medication, which has its origin in traditional medicine' (Vietnam Institute of Chemistry, 2001: 5–6).

These efforts were given renewed importance in 2001, when the German government required that analytical techniques for confirming the declared contents of Heantos be developed as a precondition for a randomized controlled trial with Heantos that was due to take place at the University of Essen. As a result, not only has the Institute of Plant Biochemistry assisted fellow Vietnamese chemists with their isolation and characterization work using nuclear magnetic resonance spectroscopy, they have also embarked on an unprecedented effort to develop analytical techniques using mass spectrometric multiple reaction monitoring that would allow for the identification of marker compounds from all 13 plants in what had now become a single dry Heantos extract. A further outcome of the initial phytochemical analyses of the Heantos components has been a rethinking of the strategy of extraction that had initially been developed at the Institute of Chemistry in Hanoi to produce Heantos 1, 2 and 3 capsules. On the basis of the initial literature reviews and chemical characterizations of the Heantos plants, Tran Khuong Đan and Tran Van Sung decided to re-group the plants for extraction, this time not in accordance with therapeutic aims, but rather according to the most prominent group of secondary metabolites found in each of the plants. In doing so, they argued that the amounts of extracted active ingredients could be enhanced as different types of constituents require different extraction methods to optimize yields. Using this new strategy of extraction, the 13 plants⁷ were again divided into three groups that were then submitted to three different extraction methods, using particular solvents, temperatures and extraction times for each group. The resulting mixtures were then evaporated into three different pastes or powders, which were mixed together before a

⁷ Importantly, since the plants of Heantos are not at this stage cultivated, the chemists rely on Tran Khuong Đan's organoleptic evaluation of plant samples before carrying out standard analysis against existing control profiles.

final evaporation was carried out, resulting in a final ‘multiple pot’ powder extract. This was subsequently manufactured into what are now known as Heantos 4 capsules. As a result, therapeutic concerns have become more a matter of adjusting Heantos 4 dosage regimens during the course of treatment than of using different Heantos capsules at different stages (Tran, 2004).

We will recall how complex it can be to develop ‘fingerprint’ control profiles which are faithful to the ‘normal full spectrum’ of constituents in a single plant like St John’s Wort. As put by Professor Ludger Wessjohann of the Institute of Plant Biochemistry, ‘analysing an extract which contains 13 different plants is like being asked to identify an individual fingerprint from a single card which has had hundreds or even thousands of fingerprints messily jammed on top of each other’ (personal communication, 2005). A high-performance liquid chromatogram of a single-plant extract will often produce relatively sharp peaks, indicating the presence of some of the more predominant metabolites in the plant, while a similar chromatogram of a Heantos 4 extract gives a much smoother curve as all the different metabolite peaks ‘hide’ by blending and blurring into each other—an effect that a single bio-active compound approach seeks to avoid by breaking an extract down into the most basic possible chemical denominators and taking it from there. Nevertheless, as scientists in Germany and Vietnam have been committed to working towards a standardization of the entire Heantos mixture, the Institute of Plant Biochemistry has had to enter uncharted territories in their efforts to develop analytical methods that would allow for the confirmation of the presence of all 13 plants in a Heantos 4 extract, in accordance with German national requirements.

Since it was much too early in late 2005 to form any conclusions about what might be the most important therapeutically active constituents, not to mention contributing active ingredients in Heantos, the Institute of Plant Biochemistry has instead focused on searching for unique marker substances from each plant which could be reproducibly identified in the final Heantos 4 extract as a means to confirm their presence in the extract. Chemists at the Institute of Drug Quality Control in Hanoi had already successfully identified 6 out of the 13 plants by comparing high-performance liquid chromatographs of Heantos 4 extracts against control profiles of the 13 plants, but HPLC data was not sufficiently detailed to identify the remaining 7. This task would require submitting Heantos 4 extract to the kind of technology-intensive structure elucidation spectroscopy that is usually reserved for single compounds. Although the resulting data might be described in terms of a lot of ‘noise’ resulting from the thousands of compounds in Heantos 4 extracts, it nevertheless became possible to search for particular patterns in the resulting hydrogen atom spectrums, which might then be used to confirm the presence of previously identified unique marker substances from each of the plants in question.

Searching for plausibility

Much of the debate and controversy surrounding traditional, complementary and alternative medicines, such as herbal medicine, revolves around the question of *whether* or not they work in the treatment of certain conditions (see Wahlberg, 2008). In the cases of St John’s Wort and Heantos, notwithstanding considerable clinical scrutiny, there certainly remain a number of open questions as to whether or not they ‘work’ in the treatment of

depression and addiction respectively.⁸ Nevertheless, as we have seen, there have been sufficient indications to convince chemists and pharmacologists to pursue research into the chemistry and pharmacology of these plants, not only to assist efforts to standardize the production of these remedies as I have shown above, but also to search for pharmacologically plausible mechanisms of action. This search for plausibility in explanations for efficacy is the final route of normalization that I will be accounting for in this article.

Tran Khuong Đan has provided a complex account of the mode of action of Heantos in terms of a therapeutic restoration of the balance of Yin and Yang and the five basic elements in an addict's body using relevant medicinal plants: 'it is by rebalancing Yin and Yang in the body and not by suppressing individual withdrawal symptoms that these symptoms will disappear of their own' (Tran, 1999). At the same time, he has also described how, while developing Heantos, he chose particular plants for his remedy with the specific aim of addressing a 'chronic shortage of drugs in the brain' by normalizing the regulation of endorphins in a detoxified addict (Tran, 1999). Indeed Đan has argued that:

... while traditional medicine was developed over thousands of years, certain aspects still need to be explained scientifically. And so, it tends to be regarded as superstition. Using science to throw light on traditional medicine is imperative. (cited in Impact, 2000)

Similarly, medical herbalist Andrew Chevallier has characterized St John's Wort as a 'nervine', 'having a restorative and tonic or relaxant effect on the ... battered nervous and endocrine systems of people suffering from nervous exhaustion, depression, nerve damage, long-term emotional stress, anxiety, and the like', while also suggesting that it 'markedly increases, to a significant degree, serotonin, noradrenaline and dopamine levels within the synapse, and seems to enhance the tranquilizing activity of GABA and benzodiazepine—all of which are involved ... in the onset or maintenance of depression' (1999: 91, 47). And medical herbalist Peter Conway argues that 'to understand what St John's Wort does exactly, we need first to have a basic understanding of the special chemicals (called neurotransmitters) that are involved in nervous system functions' (2003: 23).

Perhaps the by now very familiar anthropological argument that patients notoriously lack loyalty to any one particular coherent explanatory framework should be extended to practitioners as well. At any rate it does not appear that these herbal practitioners have any trouble maintaining different explanations for efficacy in their accounts of how these remedies work. Should our conclusion be that these herbal practitioners have been 'colonized' and that they have lost touch with a more authentic traditional herbal medicine? If so, it does not appear that this colonization has required these practitioners to discard 'incommensurable', vitalistic explanations—i.e. explanations which are considered by some as 'not congruent with current scientific thought' (Select Committee on Science and

⁸ For example, in a *British Medical Journal* editorial, De Smet and Nolen wrote of the trials included in Linde *et al.*'s (1996) meta-analysis 'although promising, these studies are not sufficient to accept the use of *hypericum* extract in major depression when judged against the criteria of the European Union guidelines for regulatory evaluation of antidepressants' (De Smet and Nolen, 1996: 242) and the largest randomized controlled trial carried out on St John's Wort to date concluded that St John's Wort was less effective than placebo and standard anti-depressants in the treatment of major depression (Davidson *et al.*, 2002). And the UN Drug Control Programme concluded that 'there does not appear to be any evidence that Heantos is more effective than any other products available for a similar "treatment"' (UNDCP, 2001).

Technology, 2000: 4.31)—of how these herbal remedies work. Whatever incommensurabilities are at stake, there seems to be plenty of room for cooperation, even if conclusions are not shared at the end of these collaborations.

What is clear from experiences with St John's Wort and Heantos is that 'plausibility' is something that is to be found through a molecular mapping of the pharmacokinetic and pharmacodynamic pathways that individual chemical compounds found in Heantos and St John's Wort follow as they are absorbed into and then disposed of by the body, and not in explanations which invoke meridian-based pathways of Yin–Yang rebalancing, the vital nourishing of nervous systems or the maintenance of vital rhythms in the organs of the body. Yet, at the same time, as we will see, these differing 'languages of life' have nevertheless co-circulated in recent efforts to unravel pharmacological mechanisms of action. In particular, the concept of 'synergy' has been central to the search for plausibility, a concept that has been described as both 'vitalistic' and 'mechanistic'.

In an article reviewing ten years' worth of pharmacologic research into the mechanisms of action of St John's Wort in the treatment of depression, Butterweck concludes:

Herbal medicines are complex mixtures of more than one active ingredient. Therefore, pharmacological work is complicated by the fact that active compounds are often unknown. Further, synergistic or antagonistic effects of the different compounds cannot be excluded. . . . Today, several compounds from different structural groups and with different mechanisms of action seem to be responsible for the observed antidepressant efficacy of St. John's Wort. Based on recent research, it seems likely that flavonoids, hyperforins and hypericins contribute to the antidepressant efficacy. . . . [Yet] the mechanism of action of the plant is still not fully understood. Our understanding of the mode of action of St. John's Wort is complicated by the fact that the molecular basis of depression itself is still unclear. (2003: 558)

It is amidst this complex of chemical compounds, their synergistic and antagonistic interactions, and their separate yet supplementing pathways of pharmacologic action that explanations for the efficacy of St John's Wort in treating a complex condition like depression has been sought, with the help of *in vitro* receptor binding assays on the compounds found in *hypericum* extract, *ex vivo* studies of rat brains following chronic administration of St John's Wort, and *in vivo* efficacy studies using animal models of depression. The very first pharmacologic investigations from the early 1980s (Suzuki *et al.*, 1981, 1984) had unsurprisingly focused on one of the plant's most conspicuous chemical constituents, mistakenly attributing to hypericin (rather than the whole plant extract) monoamine oxidase inhibiting properties.⁹ Butterweck *et al.* (1998) have argued that hypericin does nevertheless generate anti-depressant activity, but, interestingly, seems to require the services of procyanidins (also present in whole plant St John's Wort extract) in increasing its water solubility and thereby its bioavailability. Most recently, hyperforin (a phloroglucinol unique to hypericum) has emerged as another prime candidate when accounting for the therapeutic efficacy of St John's Wort, this time as an inhibitor of the synaptosomal reuptake of neurotransmitters (Chatterjee *et al.*,

⁹ It has been suggested that the hypericin samples used by Suzuki *et al.* were not 'pure', but contained at least 20 percent of other constituents, notably flavonoids, which would explain why subsequent experiments have confirmed monoamine oxidase inhibiting properties of full plant extracts but not of purified hypericin (Butterweck, 2003: 541–4).

1998; Müller *et al.*, 1998). Pharmacologic studies of hyperforin have suggested that St John's Wort is a broad spectrum reuptake inhibitor of not only serotonin and noradrenaline but also dopamine, GABA and L-glutamate. The precise mechanism of inhibition is yet to be established conclusively, but studies suggest that inhibition is non-competitive—i.e. St John's Wort 'does not inhibit neurotransmitter uptake via direct interaction with the specific binding sites of the neurotransmitter transporter molecules' (Müller, 2005: 38). Instead, the inhibitory mechanism of St John's Wort has been hypothesized in terms of its elevation of intracellular sodium concentration, which in turn reduces the drive for neurotransmitter accumulation within the cell. Studies have also suggested that St John's Wort extract might reduce stress-induced increases in gene transcription as another possible pathway of anti-depressant action.

Tying up the major results to have come out of this flurry of research, a number of reviews of the pharmacology of St John's Wort have been published in the past couple of years. And although one might well have expected these reviews to pinpoint a single compound as responsible for its efficacy as an anti-depressant treatment, conclusions seem instead to point towards a 'synergistic' effect, where multiple compounds act along multiple pathways with multiple targets contributing to a combined efficacy (Butterweck, 2003: 554; Müller, 2005: 26, 81). Interestingly, it is also hypothesized that it is this synergistic combined effect that accounts for St John's Wort's favourable safety profile (in comparison with standard anti-depressant treatments), as, rather than exhibiting a single, highly potent anti-depressant activity, St John's Wort extract exhibits multiple lower potency anti-depressant activities that, when combined, it is argued, can match standard anti-depressants in efficacy while sparing the patient from side effects.

Nevertheless, it is important to underscore that 'synergy' between the various active compounds found in St John's Wort is understood in different ways in the pharmacological literature. On the one hand, synergistic effect is described in a strictly 'additive' sense (Butterweck, 2003: 554), whereby 'various relatively weak effects result in the overall pharmacological effect' (Gobbi and Mennini, 2005: 26), while on the other, it is suggested that 'the pharmacological effects of the single constituents differ when given alone or in combination with other constituents, indicating that the extract is *more* than the sum of the single compounds' (Noldner, 2005: 81). This latter view is congruent with that found in many texts by herbal practitioners who suggest that 'the whole plant is much more than the sum of its parts' (Chevallier, 1999: 17; see also McIntyre, 1988: 53; Mills, 1993: 263). Whatever the understanding of 'synergy', what pharmacological efforts to account for the pathways of action of St John's Wort have shown is that it is at best an oversimplification to suggest that all pharmacologists insist on breaking down plant extracts 'by isolating and synthesising the [single] active principles of herbs to use as drugs' (McIntyre, 1988: 53). Just as Watt and Wood (1988) have argued that there is no monopoly on holism in a clinical context, we might say that neither is there in a pre-clinical context.

Compared to St John's Wort, much less pre-clinical mechanism of action research has been carried out on Heantos to date. It is only very recently that the Institute of Plant Biochemistry in Halle has begun bio-assay testing the biological activity of the many compounds found in the multiple-pot Heantos 4 extract. For this assay testing, the Institute of Plant Biochemistry in Halle has enlisted a polymerase chain reaction-based gene expression profiling method trademarked by the German biotech company Biofrontera as 'Digital

Expression Pattern Display'. This method has been specifically developed 'for the purposes of elucidating pathology pathways of major brain diseases, of analysing the target profiles of drugs presently applied or in development, and of identifying novel targets for drug action' (Maelicke and Lubbert, 2002: 283).

And so we can see how a search for plausibility has brought initial vitalistic explanations of the efficacy of St John's Wort and Heantos (in terms of a nourishing of nervous systems or rebalancing of vital energies) into a so-called 'pre-clinical' pharmacological realm, where balancing and regulating refer to genes, neurochemicals, synapses and receptors. That is to say, when it comes to explanations of how St John's Wort and Heantos work, plausibility relies on a language of receptor regulation, neurotransmission and modulation and not a language of meridians, energy flows and vital rhythms. It might well be tempting to describe this in terms of a 'colonization' of herbal medicine by biomedicine, yet, as we saw, such a one-sided account misses out on the numerous interactions between herbal and modern medicine that, for example, have resulted in scientists resisting the classic 'single-compound' approach that pharmacologists are often charged with blindly following as well as in differing understandings of 'synergy'.

Conclusion

What I have shown in this article is that insisting on the colonization hypothesis makes the task of accounting for the emergence in the 1990s of Heantos and St John's Wort, as two herbal treatments for addiction and depression respectively, very difficult. At best, one would have to conclude that these two herbal remedies are but the latest casualties of modernity's incessant drive to rationalize, commodify, industrialize and colonize 'nature'. What I have described as a normalization of herbal medicine would no doubt be read by some as nothing short of such a 'scientific colonization', an erosion of tradition, a loss of magic. If this is the case, then how should we understand the efforts of doctors, scientists and traditional practitioners alike to standardize and industrialize herbal medicine into capsules and pills? And how should we read the literature by herbal practitioners on St John's Wort and Heantos, which easily incorporates both vitalistic concepts and neuropharmacologic findings into accounts of the efficacy of these remedies in the treatment of depression and addiction? Have they all been co-opted, forced to 'sell out' in the face of market pressures or biomedical 'interests'? And are St John's Wort and Heantos all the worse for it?

Whatever the verdict and notwithstanding the antagonisms that clearly do divide herbal medicine and modern medicine, there does seem to be some kind of common ground at stake—how to demonstrate, account for, consistently ensure and even improve the efficacy of St John's Wort and Heantos. This is not to say that there has been full agreement on how to address these central problems, or indeed on whether or not these treatments have any therapeutic merit whatsoever; this much should be clear from the foregoing analysis. Yet, just as there can be disagreement between herbal and modern medicine practitioners, so too can there be diverging hypotheses amongst herbal practitioners or between pharmacologists or clinicians. Moreover, just as pharmacological concepts of biological 'regulation' have informed accounts of the efficacy of herbal medicines, so too have herbal concepts of 'synergy' or 'polypharmacy' informed possible routes of pharmacological investigation

and standardization. The importance of producing full-spectrum extracts of St John's Wort, as well as sticking to a multiple-pot extract of Heantos (rather than breaking Heantos down into each of its plants), has been underscored rather than undermined in German and Vietnamese pharmacology and chemistry laboratories.

As we have seen then, the normalization of herbal medicine via an ethno-botanical taming of the countryside, a phytochemical effort to molecularly characterize and standardize herbal remedies into capsules or pills, and a pharmacological search for plausible mechanisms of action has relied on an assemblage of concepts (synergy, balance, regulation), objects (plants, extracts, pills, active ingredients, spectroscopes) and norms (plausibility, natural balance of constituents, batch-to-batch consistency), which taken together can account for and standardize the workings of the 'living laboratories' that plants have been shown to be. Normalization has addressed the ignorance, imprecisions, inconsistencies and incongruencies that are seen to surround herbal remedies by attempting to right or square these. And, rather than resulting in some kind of finality or certainty, the process continues to be surrounded and informed by contestation and rectification.

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