Applying the principles of the Five Phase (Wu Xing) model to inform good practice for studies of Chinese herbal medicine

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A B S T R A C T

Introduction: There is a need for a structured approach to defining good practice of herbal medicines. This will enable a more targeted and efficient researching of individual herbs and herbal combinations. We explore the Five Phase model as a means of defining good practice of Chinese herbal medicines (CHM) which can be applied during clinical research.
Methods: The Five Phases (Wu Xing) are a traditional model used in Chinese culture and medicine to describe cycles of change and development. We have adapted this model to provide a multifaceted approach to describing good practice, so that each phase in this cycle represents a specific stage of enquiry relating to good practice. These phases include reflective practice, basic CHM theory, in vitro and in vivo research, reference to classical texts, and the development of professional consensus. This approach was applied to defining good practice for a clinical trial of CHM for Recurrent Urinary Tract Infections (RUTIs).
Results: The Five Phases provided an iterative and inclusive model for exploring the knowledge base of CHM. Each phase generated different insights into the practice of CHM which contributed to the development of standardised and individualised treatments for RUTIs.
Conclusions: The Five Phases offer a useful conceptual model that we believe can be applied to CHM, and possibly other medical systems, to elicit diverse sources of data and to integrate these data in a meaningful and practical manner that can inform clinical practice.

1. Introduction

1.1. The current view

Recent years have seen a renewed interest in exploring the potential contributions of traditional herbal medicines to mainstream health care. There are several factors underlying this. Probably the most pressing is the development of microbial resistance to antibiotics that is threatening to undermine our management of infectious diseases [1–3]. The complex regulatory structures and vast costs of developing and then purchasing new pharmaceuticals, including novel antibiotics, inhibit the provision of replacement therapies and place great strain on healthcare systems around the world [4,5]. In these instances where conventional medicine has become ineffective or unaffordable, herbal medicines are being considered as possible alternatives.

The standard pharmaceutical approach to identifying potentially medicinally useful plants has relied on large screening programmes, coupled with a more targeted focus on how plants are actually used by traditional healers. The end point of these 'bioprospecting' endeavours is usually to extract a single active compound found within a plant that can then be synthesised, standardised and developed into a new pharmaceutical drug. This pathway has, in some instances, been productive and it has been estimated that natural products and their derivatives contribute more than 50% of drugs currently used worldwide, with least 25%

of these developed from higher plants [6]. This process is on going and not just a historical phenomenon, with over 70% of new anti cancer drugs originating from a natural source [7].

However there are disadvantages to this pharmaceutical model. The process of screening and testing large numbers of plant compounds can be inefficient, expensive and is frequently unproductive [8,9]. The emphasis on the identification, extraction and concentration of a single, highly potent, compound may also increase the risks of unwanted adverse effects, influence bioavailability, and will exclude potential synergies of compounds that can occur both within a herb, and between herbs in a herbal formula that typically comprises of several different plants. These synergies may contribute to therapeutic effectiveness and also provide intrinsic buffering systems to reduce these side effects. In Chinese medicine, for example, the potential of compounds from the herb Ban Xia (*Pinellia ternate*) to irritate and inflame the gastrointestinal membrane is significantly reduced by preparing this herb together with ginger (*Zingiber officinale*) [10].

1.2. A 'good practice' approach

An alternative approach is to embrace the 'whole system' model of herbal practice used by traditional healers around the world, who combine relatively un-refined parts of plants (such as roots, rhizome, bark, stems, leaves, flowers and seeds) into complex herbal formulae. In these instances no attempt is made to identify a single active compound. Instead the end point is a complex poly-pharmacy comprising of numerous physiologically active compounds and synergies. These herbal practices are predicated on long histories of traditional use where herbs and combinations of herbs are reported as being helpful for certain conditions. Treatments in these instances are frequently individualised, and are often prepared as herbal teas, soups, or alcohol based tinctures. Herbal medicine is commonly used across the globe either independently or as an adjunct to bio-medicine and it has been estimated that up to 80% of the population in developing countries still relies on these medical practices as a form of primary healthcare [11].

There are a number of challenges facing these traditional practices, including problems of quality assurance, product standardisation, ecological sustainability, cost, and the strong taste of many herbal medicines, which can prove problematic for people whose experience of medicine is a pristine, tasteless tablet or capsule. There are solutions to these issues. For example the application of the new high throughput screening 'omic' technologies, such as metabolomics, proteomics and epigenomics, might be able to map the complexity of components operating within a herbal medicine, and thereby inform the development of true gold standards to enable more reliable quality assurance [12]. There is also some evidence of a welcome development of sustainable farming techniques being implemented in geographical areas that have historically provided herbs picked from the wild [13]. Taste and cost may still be issues but, as the means of herbal production continue to develop, they may become less important.

From the perspective of research programmes with limited time and funding one of the key issues in investigating herbal medicines is to identify which are the most likely candidates that may be developed into successful treatments. It seems reasonable to assume that many ineffective treatments are likely to have been 'weeded out' of herbal practice through the experience and observation of generations of herbalists. This suggests that accepted good practice is a reasonable place from which to start research. However, in order to do this we need a process that could be used to define 'good practice'.

We use the term 'good practice' as opposed to 'best practice' advisedly, because without clear, unbiased, comparative effectiveness data that is simply not available at the present time, it is presumptuous to assume that one particular approach could be defined as the 'best' option. There are two components incorporated within this notion of 'good practice'. The first equates to a form of model validity, which can be defined as 'the likelihood that the research has adequately addressed the unique theory and therapeutic context of the . . . system being evaluated' [14]. Good practice in this sense means that the herbal medicine being tested conforms to a reasonable approach to treatment that is consistent with the logic of its traditional use. It would not be considered 'good practice', for example, if a treatment traditionally used for an exudative type of eczema was tested for a non-exudative variant.

The second component of 'good practice' goes further than just model validity by conveying the sense that a particular treatment is, within the confines of existing knowledge, considered exemplary. Thus the herbal medicine being tested is not only
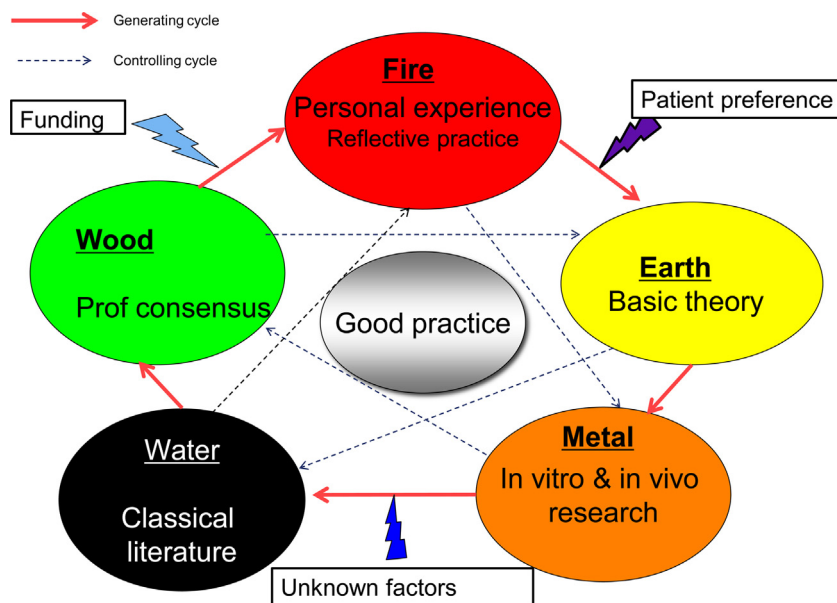

Fig. 1. Five phase model.