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Grasping the Abstract:
Integrative Herbal Medicine

Purpose, Intent of QIP

To integrate a combination of lenses in order to make recommendations for future herbal research that will allow for a deeper understanding of the biochemical components and mechanisms underpinning Chinese herbal medicine.

Needs Analysis

Ongoing publications indicate a friction between Chinese medicine and the construct of science. However, the practice of science as laid out by Sir Karl Popper is subject to a philosophical framework that lends itself to a new integration that echoes tenets of the pivotal paper, "Strong Inference." By looking at the intersection between philosophy, plant biology, and experimental design, recommendations emerge that can propel herbal medicinal research.

Target Audience/Group

The target audience for this QIP includes all who are contributing to the body of research focused in Chinese herbal medicine.

Description of Intervention/ End Product

The end product is a paper that first bridges the gap between science as a construct and Chinese medicine as it is taught and practiced. Second, it dives into the biology of plants to piece together the broader picture of how this paradigm perceives this complex system. Next, it presents recommendations that will provide better opportunities for retrospective analyses and propel research going forward.

Method of Sharing

Ultimately, this paper will be expanded into a textbook of single herbs that show up in the Shanghan Zabing Lun.

Summary/Conclusions

The world is changing now more than ever, and the flora is changing alongside it. By making more efficient use of research endeavors simply by using better methods and better documentation, perhaps, research can keep pace with change in spite of limited resources. At the very least, a strong integration of lenses will allow for a better understanding from which all types of experts and practitioners can benefit.

The initial stage, the act of conceiving or inventing a theory, seems to me neither to call for logical analysis nor to be susceptible of it. The question how it happens that a new idea occurs to a man—whether it is a musical theme, a dramatic conflict, or a scientific theory—may be of great interest to empirical psychology; but it is irrelevant to the logical analysis of scientific knowledge… There is no such thing as a logical method of having new ideas, or a logical reconstruction of this process.

— Popper [iv]

There exists a friction between the construct of science and the practice of Chinese medicine.[i,ii] Moreover, as one ventures down the rabbit hole of attempting to integrate a scientific mechanism with the Chinese medicine philosophical model, the road becomes increasingly complex and confounded. Even further, once one incorporates the plant hormone activity both within the life cycle of the plant and within the human body, the infrastructure which we wish to glimpse becomes even more complex with limited methods of testing. With a clear lens and "Strong Inference" methodology, though, methods can be implemented that will propel herbal medicine forward.

At times, an argument is made that the practice of Chinese medicine is equally scientific by comparison to any other investigative course.[iii] In this mindset, the practice of diagnosis is a function of taking in information from the outside world through the five senses followed by asking questions for further understanding and is therefore just another form of scientific observation used to make predictions about a system. However, the birth of Chinese medicine was not nested in Koch's postulates. It was nested in philosophy. Science, in all its glory, is also the pursuit of understanding in order to predict a system and entirely reliant on probability and more nestled in philosophy than most realize.[iv]

We have described the principle of induction as the means whereby science decides upon truth. To be more exact, we should say that it serves to decide upon probability. For it is not given to science to reach either truth or falsity… but scientific statements can only attain a continuous degrees of probability whose unattainable upper and lower limits of truth and falsity.

— Reichenbach [iv]

Moreover, undercurrents of unseen forces affect systems whether directly observed or not. The ability to observe is dependent on the sensitivity of the observer, be it through technology, the five senses, or a combination thereof. Mechanisms of eliminating bias have become the gold standard for establishing evidence capable of supporting a model of understanding predictive of the natural world, from confidence intervals to strong inference models. Even further, when, for every statistically probable event occurrence, a statistically improbable event becomes more likely to occur,[v] the system becomes ever more complicated and even more a matter of philosophy than formalized equations. For scientists and philosophers, the quest is never over, and this understanding leaves very little distinction between science and philosophy, let alone in Chinese medicine. However, for the clinician, applying this understanding is imperative, and it cannot wait for the final destination of the quest. Clinicians must decide the best course of action with the information available. Establishing the merits of the method of practice of medicine has existed since before the powers that be came together to define what would be the official *Huang Di Neijing* in the Han dynasty and later, the official *Shanghan Zabing Lun* in the

Song dynasty. Historically, herbal medicine was considered the least esoteric and preferred in China.[vi] Today, the battle is to prove its worth in evidence in order to be included in the evidence-based medicine model. "Evidence-based medicine (EBM) is defined as 'the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.'"[vii]

Prevailing models have been those with the seemingly clearest answers, and models that easily fit into accepted paradigms of research. Even though unexplained side effects of pharmaceuticals with supposedly straightforward mechanisms are common, the active constituent model perseveres. Pharmaceutically, regulations are in place to look for adverse reactions in the research process at the macro level and to look for purity and safety of the compounds, such as careful handling of chiral compounds at the micro level after the tragic course of Thalidomide.[viii] Yet, systems biology mechanisms are largely left to biologists in the lab. The final destination is so distant from the impetus of direct care, and what one of the greatest philosophers of science, Sir Karl Popper, would describe as the path of demarcation has already been completed. The methods of research have already been accepted. The production of pharmaceuticals pushes forward without the philosophical debate of how evidence becomes valid. In Chinese medicine, the same paradigms of research are problematic often leading to a renunciation of the current research model that forms the foundation of modern clinical research.[ix] This friction spills over to the herbal medicine pedagogy. In Chinese medicine, pattern differentiation is still rooted in philosophy, while textbooks are peppered with the active constituents of single herbs, some with actions that do not entirely match that of their established natures.[xxi] It becomes a question of integration, a word very familiar to the Chinese medical community.

> *Thus, anyone who envisages a system of absolutely certain, irrevocably- ably true statements9 as the end and purpose of science will certainly reject the proposals I shall make here. And so will those who see 'the essence of science . . . in its dignity', which they think resides in its 'wholeness' and its 'real truth and essentiality'.10 They will hardly be ready to grant this dignity to modern theoretical physics in which I and others see the most complete realization to date of what I call 'empirical science'.*
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> — Popper [iv]

Sir Karl Popper held that scientific theories were creative and abstract in nature. He held that a scientist could only test the system by reference to its implications in hopes of glimpsing the system. If one were to consider the system of an axon and an action potential, the mechanism of depolarization in neural firing is a function one and a testable one. Deeper though, each individual channel may behave inconsistently, and so it is not in the minutia but in the summation of an abstract understanding of the system and probability that allows for the framework to emerge both as fluid and a testable. If this mentality is applied to Chinese medicine, Strong Inference, which arose out of a challenged ability to test molecular biological mechanisms intersecting with an understanding of just how complex the system was that they wished to test. Strong Inference, in a sense, is reductionist, yet it never eliminates the premise of complexity nor supposes a final destination. One must maintain the abstract system and find key points that can be tested with the goals of producing more experiments and opportunities to devise alternative hypotheses and disprove any hypothesis already accepted as true. It warns against the dangers of the single hypothesis, which does not propel research and instead, promotes bias.[xii] With these elements in mind, the question arises of what is the complex, abstract system that herbal medicine presents.

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First, there were yin and yang. There are yang patterns and yin patterns that can be seen throughout the natural world. Patterns of yin and yang are seen in growth patterns of plants. Yin and yang are seen in the patterns of existence of people. At a deeper level of zoom, there are natures of plants that have patterns of activity in mammalian systems. One study suggests that these natures show themselves at the molecular level in mechanisms of histone modifications. Of course, also, in the lens of herbal pharmacology, there exist the so-called active constituents that can be seen to overlap some with the natures of the plant. The common classes of active constituents are alkaloids, glycosides including saponins, organic acids, volatile oils, tannins, phytochromes, and various proteins. Some of these constituents have corresponding flavors. Glycosides tend toward being sweet. Organic acids tend toward sour, and flavor in Chinese medicine, yields a function. Plant hormones, no doubt part of this system, but are they consequential from a medicinal standpoint? Phytochromes are already considered common active constituents, typically purgatives. Jasmonic acid is already showing an augmenting influence over tissue regeneration.[xiii] Gibberellic Acid shows damaging actions to genetic material, which follows with its role in germination in which one genome must prevail.[xiv] Auxin, a growth hormone appears to signal ß-glutathione transferase, participating in mechanisms of subduing inflammation.[xv] Because these hormones affect growth patterns, the growth patterns and stages of the flora in the pharmacopeia is relevant to the system.

In 2015, Tu You You was awarded the Nobel prize for showing that Qing Hao can treat malaria, but through an aromatic compound that must be extracted via cold water. This presents two additional elements of the system. First, decoction method is relevant to any investigation of herbal medicinal properties. As well, the background information leading to this discovery was an investigation of the classics. Whereas some may criticize the adherence to classics over research, if one is to embrace the totality of the natural world in the understanding of herbal medicine, it is not enough to choose one over the other. Classics must be thoroughly investigated as profound opportunities to glean clinical expertise. To look at classical understanding of yin and yang, one would see direct vertical growth as yang and lateral irregular growth as yin. Stem segments of Ma Huang are yang and the response they elicit in the body is yang in nature, increased heart rate, sweating, etc. Another principal herb, Bo He, grows laterally, irregularly, and with many leaves. It is yin in nature and yin in effect. It also contains ample auxin from its growth pattern. Integrating the information hidden at the different layers of zoom to understand, though indirectly, the complex, abstract system.

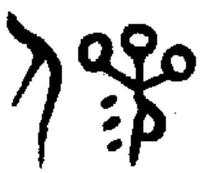
The ultimate aim of this paper is to present recommendations and a status report. Ideally, by establishing agreed upon recommendations, going forward, even if one study does not show a mechanism or medicinal function, an investigator will be able to discern from the methods of evaluation what components and layers may have been at play and/or still require investigation. The following are recommendations for future research and publication for Chinese herbal medicine.

I. For accessibility, all research should include the botanical Latin name for the herb as agreed upon by the International Botanical Congress. For non-Chinese speakers who may not be able to discern between the British romanization and Pinyin, both forms should be used as Mesh terms along with the botanical Latin.
II. To account for variance in growth patterns, three sources should be used with each source origin noted.
III. For raw plant material, grinding of plant tissue leaves much room for variance. While various techniques can be employed, the efficiency can be estimated with nanodrop. Methods are

always diversifying and improving. Therefore, the more sustainable and usable metric is documentation of purity by nanodrop.

IV. For bulk material or granules, all preparations should be documented in detail.
V. Wet bench experiments should be done in triplicate.
VI. All solvents or decoction methods should be noted in detail with duration, pH, and temperature. These will allow for retrospective evaluations to establish whether various biochemical components denatured during processing, including those discovered well after the experiment is conducted.
VII. Recommendations for future research should always be made, and alternative hypotheses should be suggested.
VIII. Possible sources of bias or confounding factors should always be noted.

The model herb used for the evaluation of current method documentation, Ren Shen 人參, Panax ginseng, is often translated as, “man’s root,” is considered the principal qi tonic and tonifies essence. The legend behind this herb is the story of two brothers to go on a hunting trip and are unable to return and run out of supplies. They live entirely off of ren shen and returned in better shape than they were when they left. The pictograph of the characters for Ren Shen, depicted below, shows that even the character, shen 參, comes from a pictograph referential of the constellation Orion. This constellation embodies the quintessential warrior in Chinese culture, and juxtaposed with the legend, it becomes clear that “man’s root” is not a sufficient translation. It is also a uniquely balanced herb, in that it is warm and generates fluids. Its inflorescence is ordered and more yang with a full basal floret which is more yin. Its roots grow deep, which could be seen as yang, while they are also irregular and thick, which can also be seen as more yin natured. It is balanced in morphology and function.


[xvi]

Also, as a widely studied and utilized herb with close to seven thousand results in PubMed, it will serve as an excellent venue for looking at the current state of methods. Are the studies accessible? Can the studies be replicated, can the sources be evaluated, and can the processing be evaluated to establish possible involvement of other components. The methods of the top one hundred resulting peer-reviewed studies in PubMed that were conducted within the last 5 years were analyzed for various components. Reviews were excluded. The results were as follows. Only 2% of the studies evaluated noted both the Latin name and some form of the Chinese name. 84% of the studies noted the source of their herbal material, but 90% did not use an alternate source of material. 76% utilized some form of purity measurement. Only 58% noted the methods used to attain compounds evaluated, whether they were purchased from an outside source or produced in the lab. Moreover, the level of detail ranged from abundant to minimal and redundant.[xvii] “The majority of traditional Oriental herbal materials are decocted with boiling water. Therefore, water extraction was used in the present study.”[lxiii] This investigation, while somewhat superficial brings to light how limited current methods are, and how limited access is for those solely looking for the latest research by searching for the Pinyin. Without changes to our documentation of methods, the acquisition of knowledge from herbal research will be subject to the single hypothesis model warned against by Strong Inference. Moreover, while many of these studies focused on purified ginsenosides, unclear methods preclude future forensic investigations that could establish additional compounds that could be present and confounding results. This is very shortsighted. After all, many discoveries are a result of accidents revealing mitigating factors.

> *…I am interested in science and in philosophy only because I want to learn something about the riddle of the world in which we live, and the riddle of man's knowledge of that world. And I believe that only a revival of interest in these riddles can save the sciences and philosophy from narrow specialization and from an obscurantist faith in the expert's special skill, and in his personal knowledge and authority; a faith that so well fits our 'post-rationalist' and 'post-critical' age, proudly dedicated to the destruction of the tradition of rational philosophy, and of rational thought itself.*
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> — Popper [iv]

By remembering the roots of the modern scientific model in philosophy and by understanding the greater framework within which we operate, we start to see what Sir Karl Popper called the riddles of the world and man's knowledge of the world. With an integrative approach, multiple lenses and multiple levels of zoom can be utilized, which will, hopefully, provide an avenue to better glimpse the larger system in which the Chinese medicine clinicians operate and, ultimately, enhance care for patients.

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