

# Traditional Chinese Herbal Medicine – East Meets West in Validation and Therapeutic Application

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## 1. Introduction

Chinese herbal medicine has been practiced for thousands of years, and is used increasingly in western countries in conjunction with or in place of allopathic medicine. The earliest extant book of material medica, known as *Shen Nong Bencaojing* (The divine farmer's material medica), appeared in the third century AD. At that time, the Father of Chinese herbal medicine Shen Nong, had classified 365 entities of herbs and drugs (Yang, 2005). The herbal tradition reached its peak some thousand years later, in 1552-1578 AD, of when Li Shi-zhen compiled his Great Herbal *Bencao Gangmu* (Compendium of Materia Medica) of 52 volumes which described 1,892 herbal entities in details (Li, 2003). The World health Organization (WHO) estimates that at least 75% of the world's population utilizes traditional medicines for healing and curing diseases (Robinson & Zhang, 2011). However, the holistic concepts of traditional Chinese medicine (TCM) are far removed from the reductionist principles of the modern day Western approach, and are difficult to express and comprehend in western terms. Western medicine is evidence-based and disease-focused, and relies on the double blinded, randomized, controlled clinical trial as the gold standard to assess clinical utility and safety of treatment, which is usually a pure chemical with a defined pharmacological action. Conversely, TCM is based on history, experience, culture and belief, and most herbal medicines are complex mixtures of largely unknown chemical composition. In western terms, the health benefits of most herbal remedies remain unsubstantiated by scientific evidence in well-designed human studies, and this limits their acceptance by western trained health professionals. In addition to efficacy, the issues of toxicity and of herb-herb and herb-drug interaction that might be additive, synergistic or antagonistic need comprehensive scientific study. In this chapter, we overview the divergence and convergence between the two systems, and explore into nowadays methods used in herbal case-studies representing different stages of herbal use and evaluation. More importantly, the need for and feasibility of performing controlled trials for scientific validation of herbal medicine are discussed, thus repositioning the herbal research, and helping to decide the most favorable direction for East meets West.

## 2. The conceptual divergence between Western and Eastern perspectives

Looking into the world history, modern medicine is known to be originated from the ancient Egyptian medicine, and largely influenced by the Greek medical ideas about anatomy, physiology and practical medicine. Different cultures, from their very beginning, have established their own special ways in the care of the sick (Longrigg, 1997). The earliest written evidences (10,000-2000 BC) have mentioned the practice of Chinese medicine and imhotep in Egypt, which both commonly used medicinal herbs as the treatment modality (Bynum, 2008). Such ancient medical approaches, were largely influence by the cultural and religious beliefs, have later on transformed into scientific disciplines to its own effective and safe practice. The beginnings of true medical science in the West were laid when the reliance on superstition that underpinned tribal medicine was replaced by civilized and rational curiosity about the cause of illness. Modern medicine, at first glance, especially in the past century, is moving from triumph to triumph with the growing number of survivors, it has gained the prevailing acceptance. However, Chinese medicine, holding the key traditional beliefs of healing – holism, is divided into special disciplines e.g. herbalism and acupuncture in the alternative and complementary medicine. Scientific and alternative medical approaches have followed different paths at different speeds. Rational treatment ultimately depends upon properly understanding the true nature of disease. Orthodox and unorthodox practitioners have relied for centuries on ‘tried-and-tested’ methods to ensure the efficacy of empirical remedies. Empiricism has become the general principle to explain the purpose and rationale of therapy (Tong, 2010). The conundrum of east meets west - let’s first look into the theory and thinking of the two perspectives.

### 2.1 The Western perspective

During the last two centuries, western medicine has developed and been practiced both generally and officially in those industrial nations that are collectively known as ‘the West’. The modernization of medicine begun with the taxonomy and classification by grouping of signs and symptoms into disease entities (Bliss, 2011). The anatomic concept has formed the basis of disease identification, explaining and visualizing the cause of illness in the patient’s internal anatomical organs (Duffin, 2010). Later on, disease and environment were bonded upon the discovery of small living organisms, i.e. microorganisms like bacteria and fungi, using microscope (Duffin, 2010). Thus, illnesses are diagnosed based on something so called the “demonstrable pathology”. For cures, chemical drugs and surgery are the main therapeutic lines used to remove specifically the notable causes of the illness (e.g. antibiotics killing pathogenic bacteria, tumor removal in malignant diseases) or at least alleviation of symptoms and distress (Lock, 1997). In simple words, western medicine has a single-minded, materialistic approach that, basically, reduces all bodily function and dysfunction to material causes, mechanical mechanisms and structural flaws that can be thought of and studied in isolation from those who suffer from them – the so called ‘science’, which relies on objective, demonstrable, measurable, and self-evident observations. Western practitioners, at least many of them, are in fact treating the diseases rather than the patients. Empirical beliefs and tried remedies often persist beyond the actual needs of the patients and consequently affect quality-of-life, for example life-term hormone supplementation (with possible side-effects) is needed after the surgical removal of thyroid. Scientific medicine rejects all concepts of ‘vitalism’, the belief on immaterial spiritual or vital forces to explain natural phenomena (Lock, 1997). It has no place for ‘life forces’ or vital principles

distinct from physical and chemical processes, and thus differs from the Eastern medical systems, particularly TCM.

## 2.2 The Eastern perspective

Traditional Chinese Medicine is originated from the culture and lives of the ancient orient, who considered life and death as the meaning of life forces. The underlying philosophy was established based on methods non-differentiable from the western one, namely objective observation, clinical practice, comparison, categorization, production, analysis, integration, and advancement. In other words, TCM is a subject of science specialty. The main difference between Chinese medicine and other medicine lies on “The sages in ancient times who knew the *Dao* (the tenets for cultivating health) who followed the rules of *yin* and *yang* and adjusted *Shushu* (the way to cultivate health)”. According to the earliest text of Chinese medicine (206 BC-220 AD) *Huangdi neijing* (Yellow Emperor’s Inner Canon), the doctrine of *Dao* is drawn from speculations of the two central theories, the creation of the universe (cosmology) and from direct observation of the natural world (Beinfeld & Korngold, 2003). It postulated that all states of being, characteristics and physical phenomena could be categorized as either Yang, which was formless and existed conceptually in an association with heaven, light, heat and masculinity, or Yin, which corresponded to earth, darkness, cold and femininity. The principals of yin-yang suggest that each of these opposites produce the other, however, these verses draw lines of correspondence or association between sets of opposing states (Kaptchuk, 2000; van Wijk et al., 2010). The production of yin from yang and yang from yin occurs cyclically and constantly, so that no one principle continually dominates the other or determines the other (Mann, 2001; Unschuld, 2003). The *Tai Chi* (infinite void) symbol of yin yang (Figure 1) is emblematic of the continual change and renewal (Kaptchuk, 2000). Chinese people believe what the existence of human being is an organic whole which is integrated with the external environment. This idea is known as holism, dispute from the demonstrable anatomy in western medicine, concerning the functional rather than the physical body (Kaptchuk, 2000). Thus, the visceral organs in Chinese anatomy are actually groups of closely related physiological functions, which composed of *jing* (body essence), *qi* (energy), *shen* (spirit) – collectively known as the *San Bao* or ‘three gems’ and allowed the transportation of *qi* within the meridians for health maintenance (Kaptchuk, 2000; Unschuld, 2003). The essential *qi* of the five viscera, further divided into *Zang* (yin organs) and *Fu* (yang organs) are supplied by five corresponding tastes of foods, of each has its corresponding phase (known as five phases theory) (Table 1). The ingestion and storage of the five tastes nourish the five kinds of *qi* (*visceral qi*), however, the harmony of *qi* is essential for the production of *jing* and *shen* in the healthy body (Unschuld, 2003). The concept of five tastes of medicinal foods, derived from the long history of living and clinical experiences, has the direct linkage to the basic theories of yin-yang, five phases, viscera, meridian and collateral, in order to explain the cause of disease and therapeutic principle in TCM. Therefore, medicinal foods including large entities of herbs are commonly used for life nurturing and healing.

Disease diagnose in TCM is based on the pattern identification and syndrome differentiation. Rooting from the doctrine of yin and yang, the ‘eight principles’ were developed as the guiding principle to categorize illnesses into yin and yang, exterior and interior, cold and heat, deficiency and excess (Shiang & Li, 1971; Unschuld, 2003). Signs and symptoms of illness were comprehensively analyzed through the four examinations known as inspection, listening and smelling, inquiry, and palpation. With then, Chinese

practitioners can determine the cause, nature and location of the pathogens, consider the disharmony between the disease and healthy qi, and conclude to identify the pattern of a certain nature following the rules of the eight principles. Upon identifying the disease pattern, a treatment plan, normally using herbal medicine and/or acupuncture, can be determined to rebalance the patient's inner yin and yang energy, and thus treating the root of the illness. Herbs may be prescribed individually or as part of a formula, of which formula are polyherbals including four typical components (Table 2) that promote the effective use of herbs (Covington, 2001). The ultimate aim of Chinese healing is to preserve or restore the healthy equilibrium of the body to adapt to the living environment. Chinese also believed that changing states either of body or of mind could affect the healthy balanced state, and therefore, an excessive emotion might cause a bodily illness or vice versa. Asian healers and practitioners treat consciousness as an organ of the body rather than a separate entity residing within it.

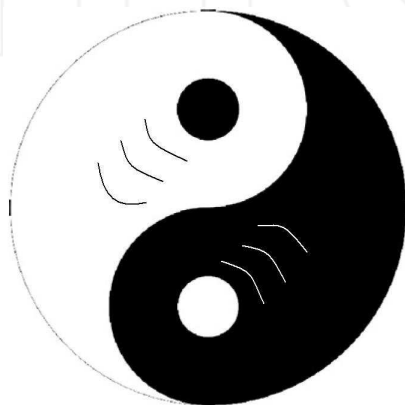


Fig. 1. Taijitu in motion. The forces of yin and yang are expressed in dark and white, respectively, are interdependent and interact constantly to form the integrated whole. Furthermore, the small circles of opposite shading illustrate that within the yin there is yang and vice versa, whereas the dynamic curve dividing them indicates that yin and yang are continuously merging, overall representing yin and yang's ability to create, control, and transform into each other (Yuen & Gohel, 2008).

Phases (Elements)	Tastes	Zang (yin organs)	Fu (yang organs)	Tissues	Sense organs
Wood	Sour	Liver	Gallbladder	Tendons	Eye
Fire	Bitter	Heart	Small intestine	Vessels	Tongue
Earth	Sweet	Spleen	Stomach	Muscles	Mouth
Metal	Pungent	Lung	Large intestine	Skin/hair	Nose
Water	Salty	Kidney	Bladder	Bones	Ear

Table 1. The Five phase theory. The five elements control the corresponding tissues and organs that are also correspondent with the five tastes of foods.

Components	Purpose
Principal	Use to treat the principal pattern of disease.
Associate	Use to assist the principal ingredient(s) in treating the major syndrome or serve as the main ingredient against a coexisting syndrome.
Adjutant	To enhance the effect of the principal ingredient, moderate or eliminate the toxicity of the principal or associate ingredients, or can have the opposite function of the principal ingredient(s) to produce supplementing effects.
Guide	To focus the actions of the formula on a certain meridian or area of the body or harmolize and integrate the actions of the other ingredients.

Table 2. The composition of typical herbal formula in TCM. Each component may consist of more than one herb, and a formula may not consist of all four components.

### 3. Junctions between the two systems of medicine – The dynamic equilibrium of the body as yin-yang interplay

While the maintenance of health and the treatment of disease are expressed in very different terms in the two cultures, the physiological processes and pathological changes that define human health are common in many aspects on each side of the East-West divide. Yet despite how difficult it is being illustrated in the language of modern medicine, the yin-yang theory governs the underlying principle of occurrence and development of diseases in TCM (Kaptchuk, 2000). An algorithmic scoring system is now available to group human subjects quantitatively into broad categories of yin and yang, in accordance to their health conditions expressed in the western terms (Langevin et al., 2004). More recently, a mathematical reasoning model using steady multilateral systems was successfully applied to guide the treatment of diseases based on the “*yin yang wu xing*” principle of TCM (Zhang, 2011). This is an important milestone, in East meets West, expressing the yin and yang entities numerically, which permits the mathematical manipulation and provides quantitative parameters for statistical analysis, which eventually make acceptance of TCM diagnosis to modern medicine with a standardized method and scientific validity. Maintaining yin and yang in harmony is akin to attaining the homeostatic state in modern medicine. However, the logic of yin-yang is often misunderstood as a matter of two complementary opposite qualities only, whereas the compensatory, synthetic and dialectical natures are entirely omitted. On the other hand, researchers have attempted to align the yin-yang concept with different physiological mechanisms of the body.

### 3.1 Oxidation and antioxidation

Reactive oxygen species (ROS), by-products of mitochondrial combustion, are generated alongside the adenosine triphosphate (ATP) during the process of oxidative phosphorylation in metabolism (Halliwell, 2009). ROS are known to be detrimental leading to oxidative damage of DNA, protein and lipid molecules, while the accumulation of such damage has been regarded as an endogenous cause of ageing as well as age-related disorders including cancers (Finkel & Holbrook, 2000; Halliwell, 2009). Fortunately, our body has an antioxidant defense mechanism, in forms of endogenous enzymatic and dietary non-enzymatic molecules, to counteract the harmful activities of ROS *in vivo* (Gutteridge, 1994). Therefore, the balance between antioxidation and oxidation play an important role in health maintenance. The analogy of yin-yang balance with that of antioxidation-oxidation has been suggested by different researchers (Ko et al., 2004, 2006; Ou et al., 2003; Szeto & Benzie, 2006), who come up with a general agreement that yin corresponds to antioxidation and Yang corresponds to oxidation involved in energy metabolism. Researchers (Ou et al., 2003) proposed that, inside the body, yang represents the driving force for energy-generating oxidation processes, while yin exhibits the protective role of antioxidation. Pharmacologically, the 'yang-invigorating' herbs were found to promote ATP-generation capacity through stimulating the mitochondrial electron transport, in rat heart homogenates *ex vivo* (Ko et al., 2004, 2006) and cultured cardiomyocytes *in vitro* (Wong et al., 2011). In TCM, the heart plays a pivotal role in fueling the vital activities in all organs, hence promoting the body function in terms of 'Qi' (Kaptchuk, 2000; Ko et al., 2004). Experimental analysis has demonstrated that yang-herbs processed protective effects on DNA *ex vivo* from hydrogen peroxide challenge (Szeto & Benzie, 2006). Authors of the work then argued that the antioxidation-oxidation relationships are not necessarily obeyed to the opposite nature of yin and yang. In fact, apart from the antioxidant activities derived from the phytochemicals, ROS such as superoxides and nitric oxide, are also present in herbs (Achike & Kwan, 2003; Lin et al., 1995). In general, yin-herbs were found to have higher free-radical scavenging activities than yang-herbs (Ko & Leung, 2007; Szeto & Benzie, 2006). Herbs by themselves are not explicitly absolutely antioxidant or oxidant in nature. Antioxidant and ATP generation (oxidation) actions could be coexisted amongst yang-promoting herbs, while the ATP generation capacity was absence in yin-herbs (Ko et al., 2004). Therefore, it is not surprising that yang-invigorating herbs are able to enhance the antioxidant status of human red cells after ingestion (Mak et al., 2004) and simultaneously protect DNA (Szeto & Benzie, 2006), further supporting the important role of the yin nature of yang-herbs being played in safeguarding the ATP generation process with ROS production. According to the Chinese Materia Medica (Bensky et al., 2004), some single herbs such as *Ganoderma lucidum* (Lingzi), are neutral in nature as they presumably contain complex chemical constituents and so have both yin and yang properties. The differential biochemical analysis of Lingzhi indicated that the water-soluble extract containing higher antioxidant capacities than its ethanol counterpart, were designated as the yin and yang, respectively (Yuen & Gohel, 2008). Functionally, in this study, the former (yin) reduced the carcinogen-induced oxidative DNA damage, while the later (yang) induced the formation of ROS and oxidative DNA damage resulting in apoptosis, in a pre-cancerous cell line (Yuen & Gohel, 2008). The authors anticipated that, even in a single herb, phytochemicals are interacting as yin and yang interplay that may be responsible for its multiple functions-bearing characteristic.

### 3.2 Immune balance

Given that many antioxidants are immunomodulating. The herb Cordyceps (*Cordyceps sinensis*) enhanced the concanavalin A (Con A)-stimulated splenocytes proliferation and the myocardial ATP generation capacity, which were disseminated in terms of TCM as 'yin-nourishment' and 'yang-invigoration', respectively (Siu et al., 2004). This is consistent with the notion of Ko and Leung (Ko & Leung, 2007) that yin-herbs, in addition to their significant antioxidant capacities, also possess immunomodulatory properties, including mitogen-stimulated proliferation of mouse splenocytes, cytokines secretion, leukocyte migration, and antibody production. In TCM, "Fu-zheng" therapy is one of the basic principles, literally equivalent to the promotion of the natural host defense mechanism, following the immunological balance of yin and yang (Macek, 1984). The Chinese believe that the herbal regimens may not only stimulate host defense but also enhance the vitality of their patients, hence the immune system resembles the yin aspect to support such vital yang aspects as the heart force and energy generation (Ko & Leung, 2007). The immunological yin-yang is considered as the cross-talk between the innate and adaptive arms of the immune system: the former serving to initiate a response of the latter, and the latter amplifying the former, defending the body from pathogens but sometimes exaggerating it certain immunological disorders (Lafaille & Mathis, 2002). The intricate immune network is composed of uncountable pairs of cells with activating/suppressive activities and stimulatory/inhibitory molecules, analogous regulatory interplay (Lafaille & Mathis, 2002; Macek, 1984). No doubt, T-suppressor and T-helper cells are in opposition but are totally interdependent, and an imbalance of either cell population can result in disease (Macek, 1984). Proinflammatory and antiinflammatory processes formed another interplaying pair that must be balanced to maintain health (Mann, 2001; Mills & Bhatt, 2004; Zhang, 2007). The interplay of interferon-gamma (IFN- $\gamma$ ) with other immune components was crucial to the development of autoimmune disease (Zhang, 2007). Hence, the inside views of yin-yang in the system denoted inflammatory process as yang, while its regulation as yin. Once an inflammatory process (yang) is initiated, IFN- $\gamma$  is produced to promote inflammation until reaching the peak level, the inflammation then intensifies and compresses its opposite to activate a regulatory process (yin), and finally resulting in the reduction of inflammation. The differential immunological study of Lingzhi demonstrated that the ethanol extract in yang nature induced the secretion of proinflammatory interleukins (IL)-2, -6, and -8 via nuclear factor-kappaB (NF- $\kappa$ B) pathway in the apoptotic pre-cancer cells, but such effects were not exhibited by the water extract in yin nature (Yuen et al., 2011). This is explained that "yang initiates the expression of yin. Yang controls the origination and enjoys the completion of a process while yin follows the effects produced by yang and completes the work of yang" (Chan, 1969). In viral myocarditis, interleukin 6 (IL-6) played the paradoxical roles in promoting and suppressing the inflammation, to avert deleterious viral effects and to increase tissue destruction, respectively (Mann, 2001). Given that C-reactive protein (CRP) plays critical roles in atherosclerosis central to plaque progression and plaque rupture, the interplay of proinflammation and antiinflammation, that affecting the CRP levels is considered as a determinant for vascular health or illness (Mills & Bhatt, 2004). Such arterial inflammatory process is closely regulated by the local T-helper 1 (Th1)-type and Th2-type responses, with the principal inducers IL-12 and IL-10, respectively (Yang et al., 2010). Previous researches have demonstrated the presence of both IL-12 and IL-10 in atherosclerotic lesions, and the increase of IL-10 secretion led to the reduction in lesion size, that suggesting IL-10 is a counterbalancing factor that exerts its effect on Th1-Th2

cooperation by downregulating IL-12 and IL-18 production and inhibiting the Th1-based immune response, altogether to fully illustrate the yin-yang picture (Yang et al., 2010). The Th1/Th2 imbalance, an expression of yin-yang disharmony, causing the dichotomy between the humoral and cellular arms is related to pathological changes, such that cancerous tumor with Th2 dominant (Witz, 2008) and spontaneous abortion when Th1 reaction is in excess during pregnancy (Wilczynski, 2005).

### 3.3 Hormonal harmony

The biochemical meaning of yin-yang is extendable to the interaction between the immune system and other systems, involving a variety of hormones as key mediators. The endocrine system is known as one of the regulatory machineries to the immune response. Established literatures have documented that high levels of stress elevate the concentration of hormones such as glucocorticoids (cortisol or corticosterone) and catecholamines (epinephrine or norepinephrine), which exert immunosuppressive activities by binding the receptors on lymphocytes and impairing the immune defense, so that overall health will be altered (Kaye & Lightman, 2005; Vegiopoulos & Herzig, 2007). Consequently, certain soluble factors of the immune system, i.e. cytokines and interleukins, are altered to act on the brain and variety of endocrine pathways, to trigger feedback reactions in the Hypothalamic-pituitary-adrenal (HPA) axis (Dunn, 1996). The bidirectional interaction between the immune and the endocrine system is also reflected by its influence on the reproductive system, probably via the hypothalamus-gonadal axis. Gonadal hormone like estrogen involves in the development of the thymus (an important lymphoid organ for lymphocyte differentiation), while the removal of thymus can induce pathologies in ovaries, testes and thyroid endocrine tissues, hence changes in one system will likely influence the other (Ahmed, 2000). The gender differences in brain development and immune response, possibly also in other non-gonadal organs, were explained as the compensatory yin-yang effects between sex chromosome and sex hormone status (Palaszynski et al., 2005). Furthermore, the functions of endocrine glands are explicitly controlled by the antagonizing sympathetic and parasympathetic activities of the autonomic nervous system in response to stimulation. In a recent human psychophysiological study, the decreases of parasympathetic and sympathetic activity were associated with the deficiency of yin and yang, respectively (Taitano et al., 2003). This is exemplified by the cardiac autonomic control that the activation of parasympathetic and sympathetic inputs to the heart in tandem results in greater cardiac output, demonstrating the synergistic and complementary properties of yin-yang interplay (Paton et al., 2005). In patients with hypothyroidism they are classified as having a deficiency of yang in terms of the TCM diagnosis, and the usage of yang tonifying herbs was shown to help in alleviating the symptoms (Kuang et al., 1988). As previously mentioned, yang-herbs actively promote the ATP-generation capacity and cardiac activity, and in hypothyroid rabbits, serum levels of thyroxine ( $T_3$ ) and triiodothyronine ( $T_4$ ) were elevated by intake of selected yang tonifying herbs, following the enhancement of myocardial  $\beta$ -adrenoceptor density and affinity (Min et al., 1998).

## 4. Feasibility of validating Eastern medicine by Western methods

The theory of yin-yang is explanatory to the biochemical activities of various biological phenomena, which supporting the feasibility of using western methods for TCM validation.



Regardless of what treatment principle behind, science and technology provide objective, accurate and reliable platforms for examining the effectiveness and efficacy of traditional therapeutic modalities. Herbal remedies are often marketed as dietary supplements, where they are not required to meet with the stringent clinical testing of pharmaceuticals, even though their usage may be for the same purpose, i.e. treatment of disease. Most herbal-derived medicines are complex mixtures of largely unknown chemical composition. They may be decoctions, infusions or extracts of one or many herbs, the quality and identity of which may vary widely, whose active ingredients are not well defined and whose molecular action is unknown. In light of the increasing globalization of herbal medicines, the WHO-leading authorities have put plenty of efforts to setup guidelines and regulations for the herbal identification and quality control (World Health Organization Special Programme for Research and Training in Tropical Diseases (WHO-TDR, 2005).

#### **4.1 Authentication of herbal identity and quality control of ingredients**

In TCM, herbs are traditionally authenticated by smell, taste and appearance that are totally dependent on the prescriber's experience. Even a famous herb such as ginseng, cases of misidentification have caused adverse reactions after use have been reported (Yap et al., 2008). Right herb possessing the right properties must be given to a right person for the right purpose. Therefore, reliable authentication becomes an important issue to safeguard the efficacy and safety about the usage of herbal medicine. Fingerprint analysis is accepted as the standard methodology for the assessment of natural products (WHO-TDR, 2005). Each herbal species has its unique fingerprint chemical profile containing an array of individual compounds separated and developed by chromatographic technique coupled with suitable detection methods (Schaneberg et al., 2003; Tistaert et al., 2011). There are several chromatographic techniques that can be used for the fingerprint profiling, including *Thin layer chromatography* for fast screening of samples, *High performance liquid chromatography* (HPLC) for high resolution, selectivity and sensitivity, *Ultra-High performance liquid chromatography* for superior sensitivity and resolution to HPLC, *Hydrophilic interaction chromatography* for retention and separation of hydrophilic compounds, and *Gas chromatography* for characterization and identification for volatile compounds (Tistaert et al., 2011). Additionally, there are some pattern recognition methods (some sort of statistical methods), which enable the visualization and further exploratory data analysis on information that is included in the chromatographic profile, are available for addressing the difficult differentiation of some closely related species (Lu et al., 2005; Tistaert et al., 2011; Zhao et al., 2009). The quality of herbs may vary due to the cultivation conditions, breeds and places of origin, for examples, liquid chromatographic coupled with multistage mass spectrometry (HPLC-MS) technique has revealed there to be non-stable and inconsistency of chemical constituents amongst different batches of Lingzhi samples (Chen et al., 2008a). In this regard, the research team (Chen et al., 2008b) has demonstrated the feasibility of employing multiple statistical analyses of HPLC fingerprints of Lingzhi to discriminate samples in accordance of origin of cultivation (Chen et al., 2008b). For fingerprinting the complicated decoctions, multi-herb botanical drug products, multiple chromatographic fingerprinting was suggested, in order to capture the complete picture of chemical profile (Fan et al., 2006). By employing such chromatographic technology, herbs of different species that share the identical bioactive ingredients, or at least a particular chemical fraction, can be merged and classified to facilitate the standardization of herbal products (Xie et al., 2010). In

the past decade, the rapid growth of molecular techniques has also benefited the herbal authentication. Numerous polymerase chain reaction (PCR)-based and sequencing methods using specific probes have shown to be applicable for validating the herbal identities (Chang et al., 2009; Herrero et al., 2010; Law et al., 2011). Particularly, random amplified polymorphic DNA (RAPD) profiling, a newly developed cost-effective PCR-based technique, has extensively used to differentiate large number of medicinal species from their close relatives or adulterants (Khan et al., 2011; Kiran et al., 2010). Not surprising, encouraging outcomes support the development of DNA barcoding technique, which enables the fast screen of botanical identities just like we checking out at the supermarkets (Song et al., 2009).

#### **4.2 Extraction and fractionation of herbs – recovery of the active ingredients**

For pharmaceutical preparation, the technique of HPLC-MS is still promising the characterization and isolation of chemical constituents from medicinal plants (Han et al., 2009; Yang et al., 2009). In addition to polysaccharides and flavanoids which have been commonly identified in many herbs, phytochemical analyses revealed 'marker components' that could be used for quality evaluation and standardization of specific herbs, for example, triterpenoids and  $\beta$ -glucans in *Ganoderma* (Wang et al., 2006), cordycepin and ergosterol in *Cordyceps* (Paterson, 2008), ginsenoside in *Ginseng* (Chen et al., 2009). The complexity of TCM samples, particularly multiple active constituents and low concentration levels of active compounds, poses a big challenge to analytical chemistry for active ingredients recovery (Tang et al., 2009). To solve this problem, researchers have devoted to develop and optimize a wide variety of sample preparation methods for herbs, such as shaking, ultrasonic, soxhlet, boiling, distilling, high/ultrahigh pressure, heat reflux, supercritical-fluid ( $\text{CO}_2$ ), microwave, etc (Chen et al., 2009, 2007; Shouqin et al., 2004). Usually, traditional techniques for extraction are time consuming and with low efficiency in recovery and purification of active ingredients. The technique of high pressure extraction coupled with selective solvents have been suggested in providing cost-effective and time-saving methods for obtaining single components of high purity (Shouqin et al., 2004). With the ultrahigh pressure extraction, not only the yielding of ginsenosides extracted from ginseng roots was increased, but the extract was shown to have enhanced free radical scavenging activity, when compared with other extraction methods (Chen et al, 2009). However, the extraction conditions and solvents being used need to be carefully decided based on the chemical characteristics and physical natures of the target molecules. For Lingzhi as an example it was found that the fraction of polysaccharides and triterpenes, each contains more than 100 molecules, can be simply extracted by water and ethanol (Yuen & Gohel, 2005). The most abundant polysaccharides type found in Lingzhi was  $\beta$ -glucans (Askin et al., 2010; Yuen & Gohel, 2005). The problems with  $\beta$ -glucan are low extraction yielding and poor purity, although various extraction methods using organic solvents have been applied (Askin et al, 2010). Recently, Askin and co-workers (Askin et al., 2010) have used a hydrothermal extraction method with 'subcritical water', conditioned at 473 K temperature at 10 MPa atmospheric pressure, and successfully obtained the maximum total amount (57.4% yielding) of  $\beta$ -glucans from Lingzhi. Besides, extraction of total triterpenes with organic solvents and water have long been practiced, however, isolation of the acidic triterpenes, mainly highly oxygenated triterpenoids which responsible for the bitter taste of the Lingzhi, from the total triterpenes fraction can be achieved with 95% aqueous ethanol under reflux

and evaporation under reduced pressure, followed by chloroform extraction under acidic condition (Huie & Di, 2004). Silica gel column chromatography has also been described as an additional purification procedure for such acidic triterpenes (Huie & Di, 2004). To extract the specific triterpenoid saponins from another *Ganoderma species*, microwave-assisted extraction was demonstrated to be superior over other techniques, in terms of high yielding and short extraction time (Chen et al., 2007). Because of its gentle extraction conditions of supercritical CO<sub>2</sub> used with relatively low viscosity, high diffusivity, low extraction temperature, rapid and minimal use of halogenated solvents, supercritical fluid extraction (SFE) is a widely accepted extraction technique, however, its application is largely limited by the non-polar nature of CO<sub>2</sub> (Chen et al., 2011; Tang et al., 2009). Nonetheless, the dissolving and penetrating powers of SFE were employed to aid the breaking of extremely hard and resilient sporoderm of *Ganoderma lucidum* spores, in order to obtain the spore components and easy the subsequent extraction (Fu et al., 2009; Liu et al., 2002). Furthermore, activity-guided fractionation of herbal remedies has remained a hot field in the separation science. Constituents sharing similar chemical structures or physical properties can be isolated together into fraction during the chromatographic separation. Hence, the time-specific fraction can be tested for certain desired bioactivities such as anti-tumor (Li et al. 2010), antimicrobial (Kitzberger et al., 2007), antioxidant (Chen et al., 2009; Kitzberger et al., 2007), and many other activities by using any *in vitro* platforms and animal models. Results will then guide to identify the potent fractions and the effective bioactive ingredients. For example, in the study of Wang et al (Wang et al., 2005), four fractions namely R, F1, F2 and F3 were produced by the SFE of *Cordyceps sinensis* with CO<sub>2</sub>, followed by bioassays that indicated that fraction R was the most active fraction to scavenge free radicals and induce apoptosis on human colorectal and liver cancer cells, while the remaining fractions exhibited only low to moderate levels of scavenging activities but no antitumor effect.

### 4.3 *In vitro* experiments and animal studies

In translational research, tissue culture and animal models serve as convenient tools for drug screening and mechanistic investigation. As presented in a scientific review (Yuen & Gohel, 2005), huge numbers of cancer cell lines and tumor-bearing animal models were used to address the antitumor properties of Lingzhi, its extracts or isolated compounds. By employing a well-established tumorigenic transformation model of uroepithelial cells, a series of chemopreventive properties were demonstrated by the ethanol extract of *Ganoderma lucidum* (GLE) to inhibit the carcinogen-induced tumorigenesis of bladder cancer through the inhibition of growth and cell migration (Lu et al., 2004; Yuen et al., 2008), telomerase-associated apoptosis (Yuen et al., 2008), oxidative DNA damage (Yuen & Gohel, 2008), and stimulation of selected cytokines and neutrophilic migration (Yuen et al., 2011). Meanwhile, an *ex vivo* orthotopic organ culture model is being used to establish the synergistic effects between GLE and other conventional chemotherapeutics. Anticancer effects of Lingzhi were also supported by the induction of cell cycle arrest and apoptosis amongst human and rodent tumor cells of various origins through signaling pathway controlling cell death, inhibition of cell adhesion, invasion and migration in foci formation assays, and stimulation of anti-angiogenesis, anti-metastasis and tumor regression in tumor-bearing rat/mice models (Wachtel-Galor et al., 2011). To delineate the cause-and-effect mechanism of particular genes and/or proteins, sometimes techniques of

cell transfection and transgenic mice will be applied to create overexpression or suppression of certain gene(s), and used to test the herbal products. These experimental models are excellent to study the mechanism of action under the well-controlled microenvironments; however, they also limit on a focused pathway, ignoring the holism, and might not reflect the actual response inside the human bodies, especially issues about bioavailability and drug distribution. On the other hand, animal studies allow the determination of therapeutic and toxic dosage ranges, which are crucial before human trials can be admitted. Furthermore, animal models enable the whole body physiological examination and individual organ tissues can be isolated to study the drug effects as well as toxicities. Some pathological conditions, for example diabetic rats can be induced by intraperitoneal injection of streptozotocin, and was used to establish the mechanism underlying the antioxidant enzyme activity of Lingzhi polysaccharides to diminish pancreatic damage through the bax/bcl-2 modulation (Yang et al., 2010). In another experiment conducted by Tam et al. (Tam et al., 2011), a two-herb formula (with Radix Astragali and Radix Rehmanniae) was designed according to the classical theory of Chinese medicine, that was shown to elicit the actions of fibroblast proliferation, angiogenesis and anti-inflammation which favored the wound healing, in a chemically induced diabetic foot ulcer rat model. Nowadays, advanced molecular technology such as DNA micro-arrays also allowed the rapid high-throughput gene expression screening to conclude the outcomes of herbal remedies when tested on animal and cell culture studies (Hudson & Altamirano, 2006).

#### 4.4 Safety and efficacy issues

For anything being applied inside the human body, regardless it is for treatment or health maintenance purpose, safety and efficacy are the first concerned. Despite the general public perceived herbal products as low risk because of the long history of usage, the current body of scientific evidence is seldom conveyed. In fact, herbal medicines may carry potential harms due to contamination, adulteration, misidentification, as well as unknown interactions with other herbal products, pharmaceutical drugs or even diets (Jordan et al., 2010). Unlike conventional drugs which are single chemical compounds, the complex composition of whole herbs or their extracts contain a myriad of phytochemicals, making the toxicological evaluation difficult, especially the therapeutic effects are also possibly based on the interaction of these different components could hardly be separated (Jordan et al., 2010). In terms of quality control, it is suggested that markers used for Chinese herbal medicine should be strongly correlated with their safety and efficacy, and thus 'marker components' of specific herb should be the 'effective components' which consisting both the active (bioactivity for therapeutic effects) and relative (no specific action but affect the therapeutic effects of active components) components, rather than just the most abundant chemical constituents mentioned in 4.1 as convenient (Li et al., 2011). One more challenge is that, the *in vivo* target sites for herbal remedies are usually unknown because of their complicated natures, and thus antidotes are unavailable in case of adverse reactions occur (Li et al., 2011). Therefore, scientifically, not so much can be done regarding the safety and efficacy concerns of traditional herbal medicine, but only taking the passive role in waiting for the case reports of adverse reaction are inadequate, demanding proper designed randomized controlled trails to conduct.

#### 4.5 *In vivo* human trails – randomized controlled trails

Human controlled trails that use randomized allocation are the gold standard to restrain bias and confounding in trials evaluating pharmaceuticals. So as for TCM, randomized controlled trials (RCTs) of herbal medicine were not uncommon, at least in China. During 1999-2004, a total of 7,422 RCTs has been identified from 13 randomly selected journals published in Mainland China, and the number is kept increasing (Wang et al., 2007). However, by reviewing these RCTs, outcomes were discouraging, not because of the treatment outcomes themselves, but the poor qualities as assessed by using international standards, i.e. the Jadad score score and the Consolidated Standards of Reporting Trials (CONSORT) checklist, more than 90% of these studies were poorly designed or reported with poor scientific rigor (Gagnier et al., 2011; Wang et al., 2007; Wolsko et al., 2005; Zhong et al., 2010). Some essential RCT components, such as sample size calculation, randomization sequence, allocation concealment, implementation of the random-allocation sequence, analysis of intention-to-treat (ITT), lacking syndrome differentiation of TCM, and the use of placebo was not justified and was ethically contradictory, were not sufficiently described in the methodologies of the studies (Gagnier et al., 2011; Wang et al., 2007; Zhong et al., 2010). Even limiting to the RCTs published in English, many investigators have failed to provide proper characterization to the study herbs such as identity, purity, quality, strength, and composition in their articles (Wolsko et al., 2005). A systemic review has conducted to assess 49 trials which included 3992 cancer patients who have given Chinese medicinal herbs concurrently with conventional cancer treatments (Molassiotis et al., 2009). Majority of the studies has shown positive herbal drug effects in terms of treatment toxicity, quality of life, survival, and tumor regression, however, no clinical recommendation could be concluded because of the poor intervention qualities (Molassiotis et al., 2009). Up to 2005, there were at least 127 Chinese RCTs identified of studying a single compound  $\beta$ -Elemene isolated from the Chinese herb *Curcuma wenyujin*, in order to characterize its efficacy on antitumorigenicity (Peng et al., 2006). Since the middle 1990s, although this chemical component has already been widely used in clinical practice for cancer treatment in China, there were less than two percents of trials performed with the double-blinding in the subject allocation, just four percents have carried out statistical analysis on baseline data, and none have used the intention-to-treat analysis (Peng et al., 2006). On the other hand, an international research team has conducted a series of well-designed RCTs (at phase I/II) on advanced cancer patients, which supported the efficacy of use of Lingzhi as an adjunct cancer therapy where it enhanced the conventional treatment outcome, by improving the immune response, increasing quality of life and survival, and decreasing side effects from conventional treatments (Gao et al., 2002, 2003a, 2003b, 2005). More recently, a perspective, multiple-center, randomized, double-blind, placebo-controlled trial was conducted to study the efficacy and safety of Antiwei granule (with ma huang and Baimaogen as the principals) on infected adults of influenza (Wang et al., 2010). The report provided sufficient evidence to recommend antiwei as an effective influenza treatment based on the positive outcomes, of which increased the patients' recovery by 17% and reduced the severity of illness by 50%. The study was considered as perfectly designed since there was a well characterized herbal prescription, the use of visually indistinguishable starch coupled with a bitter agent as a placebo, fulfillment of all items listed in the CONSORT checklist as an objective outcome measurement using median symptom scores was used, and objective side effects monitored using ECG and vital signs.

## **5. The spectrum of East meets West: The transition from traditional cure to conventional drug really necessary?**

Many folk remedies have maintained their reputation for effectiveness, to be handed on from generation to generation, on the word of the village elders. Faith in the efficacy of a treatment plays a large part in feeling better. Confidence in a remedy is reinforced by word-of-mouth repetition, when everyone tells everyone else in everyday conversation that they simply know it works. Their over-the-counter availability and reputation as natural, 'safe' and effective alternatives to drug treatment makes herbal products attractive to consumers. The great increase in consumption of herbal products is a cause for concern, however, because, in addition to their efficacy, the issues of toxicity and of herb-herb and herb-drug interactions that might be additive, synergistic or antagonistic will require comprehensive scientific study. Scientists all over the world consider herbal species as a rich source for new chemical entities and used them successfully to isolate compounds, such as ephedrine, digoxin, morphine, taxol, atropine and vinblastine, are nowadays conventional drugs in allopathic medicine (Tistaert et al., 2011). To develop a new drug from herbs, the WHO has setup guidelines related on chemical drug development and traditional experience of using herbs. The paradigm of chemical drug development: drug discovery, drug design, pre-clinical studies, and clinical studies. A chemical drug always requires 10-12 years for optimization and evaluation to allow in prescription. Herbal medicine starts with human use and finally become an isolated purified form of chemical(s) for approval to be marketed. Considering the unique features of herbal products are multiple component mixtures and that substantial prior human use precedes their formal investigation, the WHO has issued a set of clear and concise recommendations for preparing well supported clinical trials to evaluate the actual benefits and risks of traditional herbal products being used for clinical purpose (WHO-TDR, 2005). Such operational guidance was built according to the principles of modern clinical sciences with four sets of issues: chemical manufacturing-control (CMC) issues, non-clinical issues, clinical issues, and ethical issues, and considerations have to translate into terms appropriate to support the justification for a clinical trial of a traditional herbal remedy, as summarized in a flowchart (Figure 2). Looking into the recommendations, the WHO has acted supportively in preserving the traditions of herbal medicine, i.e. candidate herbal substance or product should be prepared in accordance with the traditionally-used formulation, where purified chemicals are not required (WHO-TDR, 2005).

## **6. The current positioning: Right or wrong direction of research in traditional Chinese herbal medicine**

In western terms, the health benefits of most herbal remedies remain unsubstantiated by scientific evidence in well-designed human studies, and this limits their acceptance by western trained health professionals. Nonetheless, herbal medicine offers an enormous potential for health promotion and treatment of disease, and several commonly used western drugs have their origins in herbal medicine. On the other hands, the traditional essence of TCM is reconsidered by other investigators, who have used western criteria to validate scientifically the traditional theories and their usage. Based on what are the personal beliefs, the applications of herbal medicine are splitting into either one of the two paths: transition into pure chemicals or holding the traditional way of practice. Right or wrong is always up your decision, or actually there is no answer. However, whatever it is decided will lead the future research direction of herbal medicine very differently.

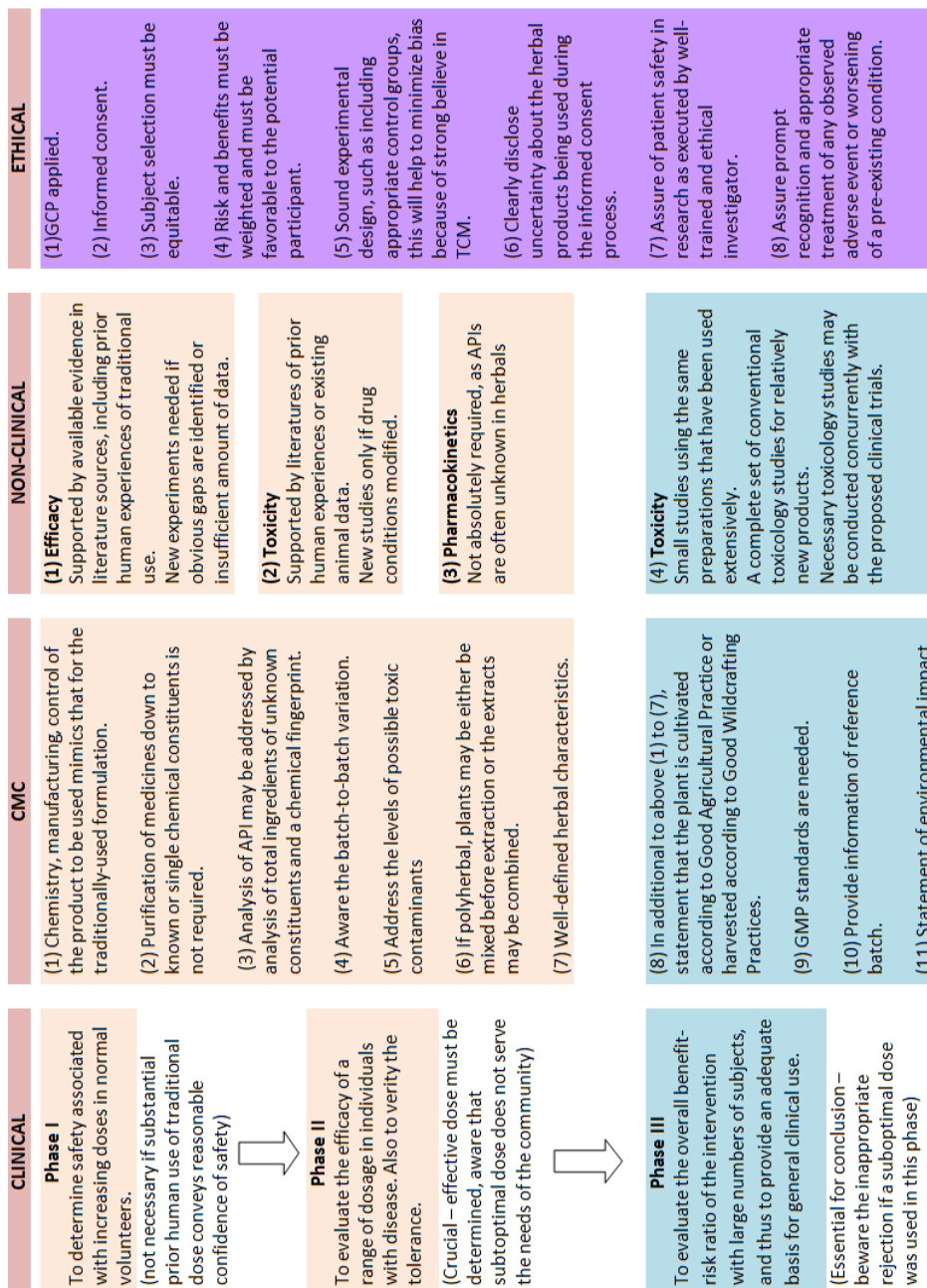


Fig. 2. Recommended information needed to support a clinical trial for an herbal medicine (WHO-I DR, 2005). CMC: chemical-manufacturing-control; API: Active pharmaceutical ingredient; GMP: Good Manufacturing Practices; GCP: Good Clinical Practice.

### 6.1 The transition of herbs into pure chemicals

Referring to the development of plant-derived medicines, the Western approach with clinically effective plant extracts was to ask "what is the active principle?", and then to isolate, purify, determine its structure and produce a standardized dosage form. Herbal medicine has made many contributions to commercial drug preparations manufactured today including ephedrine from ma huang (*Ephedra sinica*) (Gaddum & Kwiatkowski, 1938). Ephedra, which is being used for weight loss, antiasthmatic, or as stimulant for athletic performance, and clinical trials recognized common side effects as increased risk of psychiatric, autonomic or gastrointestinal symptoms, and heart palpitations (Schaneberg et al., 2003; Shekelle et al., 2003). Serious adverse reactions, including death, have occurred; in most cases, the people were abusively taking two or four times the recommended dose (Samenuk et al., 2002). In this relation, one should realize the fact that definite phytopharmaceuticals are highly concentrated that no longer represent the whole herb. In many cases they are vast more effective than the whole herb, but some effects of the herb may be lost and the potential for adverse effects and herb/drug interactions may increase.

In the last 30 years, no plant compounds discovered have generated as much public interest and excitement as has taxol (paclitaxel). Pure taxol, a complex polyoxygenated diterpene, was isolated in 1969 in 0.01% yield from the bark of *Taxus brevifolia* Nutt, following a series of screening experiments for anticancer activity (Kingston, 2007). Later on, taxol was known to be extractable from other *Taxus* species of Yew trees including the Chinese yew Hong Dou Shan (*Taxus chinensis*) grows in china (Siow et al., 2005). Upon the selection of taxol as a development candidate in 1977 and the approval as anticancer drug by U.S. Food and Drug Administration in 1992, efforts were non-stopped to explore methods to enhance its production and synthesis, although the current yielding has achieved over 90% of pure paclitaxel (Khosroushahi et al., 2006; Pyo et al., 2007). The drug is nowadays the first-line treatment for advanced ovarian and breast cancer, the second-line treatment for AIDS-related Kaposi's sarcoma, and used in combination with cisplatin for treating nonsmall-cell lung carcinoma (Siow et al., 2005), however, intensive studies are still underway for its anticancer mechanisms (Varbiro et al., 2001) as well as its toxic side effects (Atas et al., 2006; Rabah, 2010). Nonetheless, according to the *Dongbei Yaozhi zhi* (Records of Plant Herb in Northeast China), TCM used *Hong Dou Shan* to detoxify the body and releases cough (Siow et al., 2005) Perhaps, the traditional use of *Hong Dou Shan* has long been forgotten which attract no more attention at the rear of the successful taxol (Figure 3). Of course, taxol is not the only TCM-derived anticancer drug, but many others such as homoharringtonine from *Cephalotaxus* species, camptothecin from *Camptotheca acuminata*, and vincristine from *Catharanthus roseus*, are all used for cancer chemotherapy in Western medicine (Efferth et al., 2007). This is not East-meets-West, by just turning herbal species into conventional chemical drugs, which contradict the theory and application of traditional medicine.

At edge, Lingzhi is standing at the middle point waiting for you to decide which way to go. Not mentioning it is named to be a superior tonic in the very first pharmacopeia - The divine farmer's material medica, Lingzhi has been used over two thousand years for the promotion of health and longevity. Thousands of studies have been performed with large proportion was focused on its anticancer effects, ranging from experiments *in vitro* and animals to humans' *in vivo*, merely supported its applicability for cancer treatment and prevention (Yuen & Gohel, 2005). Effective and toxic dosages have long been established by animal studies (Kim et al., 1986) in addition to the substantial prior human use. Toxicities were rarely reported, and the safe usage has been convinced by scientific



evidence and history (Mizuno et al., 1995). Several Lingzhi products have already been well characterized by fingerprinting and genotyping techniques for authentication and quality control (Chen et al., 2008a, 2008b). The above conditions explicitly supported the clinical trials at phase I and II. In fact, A New Zealand-based research team (Gao et al., 2002, 2003a, 2003b, 2005) has conducted several phase II trials with advanced cancer patients as mentioned; however, the study aims were just placing Lingzhi as an adjunct therapy, where the outcome measurements were not really the valid disease endpoint. Besides, several isolated compounds, such as ganoderic acids and lucialdehydes, and their efficacy and safety have already characterized by using tissue culture and animal models (Yuen & Gohel, 2005). According to the WHO recommendations (WHO-TDR, 2005), both the crude mushrooms and isolated compounds are justified proceeding to large-scale phase III clinical trials, at least for their anticancer properties. Therefore, the choices are up to your decision, for traditional or conventional? Remember, your determination will lead the future research.

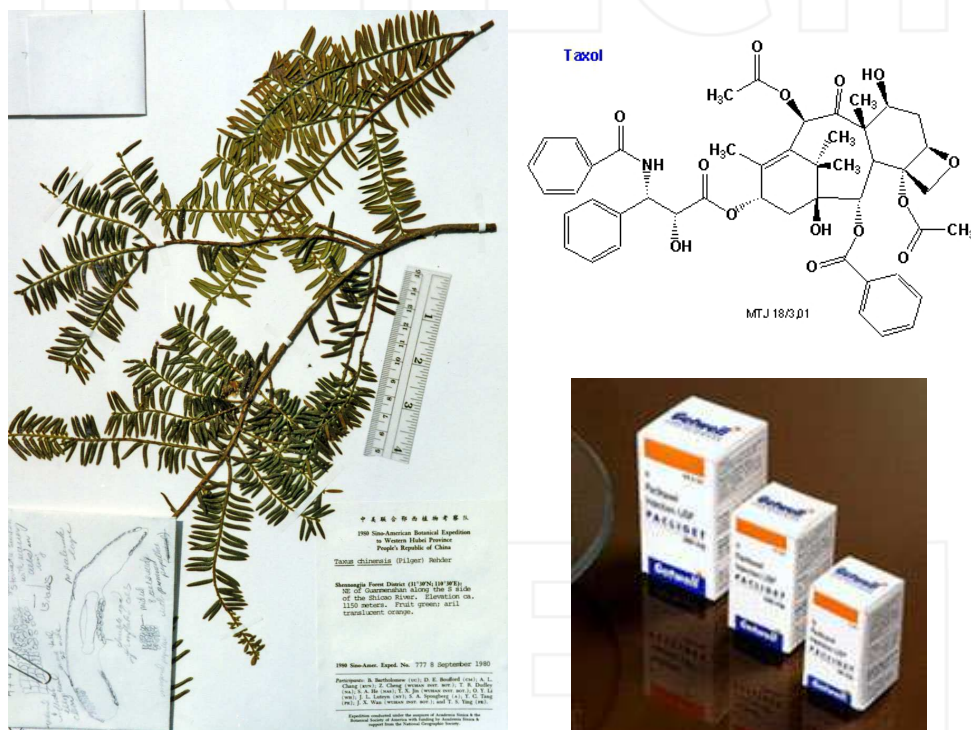


Fig. 3. The chemical structure of taxol in the package of Paclitaxel®, reminding *Hong Dou Shan* (*Taxus chinensis*) available in Hubei China (diagram adopted from © The world Botanical Associates Web page) is one of the herbal sources of taxol.

## 6.2 The validation of holistic application of herbal formulations

We have seen for ourselves herbal medicine's ability both to heal those disorders that often fail to respond to the best of Western medicine, and treat major diseases with methods that

are more sympathetic to the human system and have fewer harmful side effects. The WHO has published a list of ailments and conditions for which treatment or alleviation with Chinese medicine is considered appropriate which include diabetes. In Western medicine, diabetes is deemed as an incurable disease that patients have persistent hyperglycemia associated with high morbidity and mortality due to complications if blood glucose levels are not controlled. In view of TCM, diabetes is referred as *Xiao Ke* which is a syndrome of “wasting and thirsting” (Duan, 2008). The disease is described as the constitutional deficiency of yin of the kidney and lung and associated with the internal heat that consumes fluids, and thus causes wasting and thirst (Covington, 2001; Duan, 2008). There were 13 traditional herbal formulations for treating *Xiao Ke* according to the Yellow Emperor’s Inner Canon, and later on derived into hundreds of prescriptions to aim at different symptoms of diabetes (Duan, 2008; Li et al., 2004). Whilst 33 most frequently used Chinese herbs for clinical treatment of diabetes and its complications were listed (Li et al., 2004). The “Herbal drink to strengthen muscle and control swelling”, which is a six-component formula using *Radix Astragali* (*Astragalus membranaceus*) and *Radix Rehmanniae* (*Rehmannia glutinosa*) as principals, have been shown to promote the healing of diabetic foot ulcers effectively (Chan et al., 2007). Experimental studies revealed that all individual components of the formula were active in modifying tissue glucose homeostasis *in vitro* but inactive to improve glycaemic control of diabetes in diabetic rats *in vivo* (Chan et al., 2007). Focusing on its mechanism for the ulcer healing effects, a chemically induced diabetic foot ulcer rat model was used to establish the *in vivo* anti-inflammatory activities of the two principal ingredients (Tam et al., 2011). This is a typical example of herbal case demonstrating the feasibility of examining the traditionally used cures using of Western approach. More of this caliber should be conducted to eventually place TCM onto the context of modern medicine, and thus East meets West.

## **7. Conclusion – A need for compromise and agreement – A new model for investigation**

The holistic views of TCM generally have no conflicts with the western medicine, perhaps they were just expressed in different terms. Western medicine is usually more concrete in diagnosis and judgment. Treatment is often quicker, particularly in acute cases, and surgery is its strength. Its weak points are that it sees disease as something to be measured and quantified and often ignores the psychological, social and behavioral factors involved in illness. Chinese medicine, on the other hand, can be too flexible and too general where diagnosis and judgment are concerned, and sometimes relies too heavily on the individual practitioner’s experiences. Its strong points are its highly flexible approach, which enabling treatments to be changed as the patient improve, and its emphasis on prevention. The Chinese way tends to treat the whole body rather than to try to isolate a particular infected area. And, finally, the herbs themselves, compared with chemically produced medicines, are relatively cheap and easy to use. They have minimal side-effects, and most have been tried and tested for over many thousand years. Western medicine focuses more on symptomatic management, whereas TCM focuses more on cause and effect. Western medicine is more useful for first-aid and surgical interventions, whereas TCM is more useful in treating internal and chronic illnesses. An ideal health care system should be established to concern

people's physical and mental health, to deal with all personal problems, and to improve people's quality of life. A new model of health care should be composed by a different medical system to provide a holistic approach. TCM, today as an alternative and complementary medicine should be included into the conventional medicine to form the new modern medicine. This is in line with the aim of the WHO to promote recognition of traditional medicine and to support its integration into the mainstream health service. There is space of integration for TCM and modern medicine. A new paradigm for developing medicine is needed, and Chinese medicine could make a significant contribution in this field. To achieve such integration, modern science and technology had to be used to study the action, efficacy and toxicity of Chinese medicines. Although, there are many issues to concern, especially safe and effectiveness, some compromise and agreement are needed. Thus botanicals should be defined, authenticated and documented as to their source and conditions of cultivation using modern methodology. Manufacturing and preparation processes of Chinese medicine should be carefully monitored and standardized. Claims for Chinese medicine should be verified from rigorous controlled trials. Interaction between Western and Chinese medicines should be better studied and information obtained centralized into accessible databases. This would be an enormous undertaking requiring international collaboration and participation of governments worldwide. In fact, the feasibility of herbal validation by using Western methods is well-illustrated. In particular, concerns about identity authentication, quality control, evidences of efficacy and safety of herbal remedies, are being addressed with the modern science and technology, and ultimately allow the gathering of information necessarily to support clinical trials. Along with this route, efforts being played will return with the transition of TCM into a recognized science specialty to fill up the gaps between Eastern and Western medical approaches. In this perspective, it may not be necessary to isolate the active ingredients from herbal remedies or purify them to finally become chemical drugs. To promote the effectiveness, Chinese herbal medicine can remain in formulae but standardizations are needed. Meanwhile, both Chinese and western practitioners should come together and sort out the best treatment they can offer to patients, which very often may be the combination of the modern and Chinese medicine, instead of favoring one over the other. Conventional Western medicine and Chinese medicine should be seen as complementary to each other, rather than as alternatives. Both types of medicine have their advantages and drawbacks, which is why they need to work hand in hand for optimal results. Together, Chinese and Western medicine could form the most effective disease treatment the world has ever known.

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## **Recent Advances in Theories and Practice of Chinese Medicine**

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During the recent years, traditional Chinese medicine (TCM) has attracted the attention of researchers all over the world. It is looked upon not only as a bright pearl, but also a treasure house of ancient Chinese culture. Nowadays, TCM has become a subject area with high potential and the possibility for original innovation. This book titled *Recent Advances in Theories and Practice of Chinese Medicine* provides an authoritative and cutting-edge insight into TCM research, including its basic theories, diagnostic approach, current clinical applications, latest advances, and more. It discusses many often neglected important issues, such as the theory of TCM property, and how to carry out TCM research in the direction of TCM property theory using modern scientific technology. The authors of this book comprise an international group of recognized researchers who possess abundant clinical knowledge and research background due to their years of practicing TCM. Hopefully, this book will help our readers gain a deeper understanding of the unique characteristics of Chinese medicine.

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