This article explores the importance of continued access by researchers to Chinese medicinal herbs via DSHEA, in light of a potential increase in tropical diseases in historically non-tropical regions.

Preserving access to traditional Chinese medicine will become important as tropical diseases gradually become endemic to the United States. As the climate warms and mosquitos proliferate, diseases formerly confined to the tropics are moving north. Simultaneously, the malaria parasite is developing resistance to Artemisinin-based Combination Therapy (ACT), the preferred first line of defense. With the Dietary Supplement Health and Education Act (DSHEA) in place, traditional Chinese herbs remain legally available, making possible continued research into future treatments for malaria and other tropical diseases using Chinese herbal medicine. However, various parties assert that greater regulation of herbal medicine is needed. This article advocates retaining DSHEA as the law governing Chinese herbal medicine to allow researchers to draw upon many options, including all available herbal medicines, to find new treatments for malaria and other resilient diseases. This position is supported by a survey assessing the experiences of professionals in the Chinese herbal medicine field relative to DSHEA and tropical diseases, as well as literature reviews. The outcomes are described below.

**Pressure to Increase Regulation of Herbal Medicine**

There has been great consternation in the media regarding the safety of herbal medicine in the marketplace, leading to ongoing questions and concerns about whether additional regulation should be required and whether herbal medicines should no longer be categorized as supplements under DSHEA regulations. A recent New York Times article reported herbal supplements at four major supply chains did not contain the ingredients claimed on
the label.(5) This claim is being challenged by the American Herbal Products Association (AHPA). (6) AHPA claims the testing of the contents was not adequate, because the DNA barcoding process used does not produce accurate results when used on a processed product vs. the raw plant product. In another article, the New York Times reported substances recalled by the US Food and Drug Administration (FDA) were soon returned to store shelves, still containing the same ingredients.(7) However, most adulterated dietary substances, recalled items and supplements receiving Warning Letters from FDA are not Chinese herbal medicine products. From 1996–2012, out of 122 Warning Letters sent to supplement manufacturers, only 11 pertained to traditional Chinese medicine products. Comparatively, 1,000 Warning Letters were sent during the same time period to pharmaceutical companies.(8)

DSHEA does not require the same clinical trials for herbs as for pharmaceuticals coming into the market. Dietary supplements do not need approval from FDA before they are marketed; however, herbal medicines are, in fact, regulated. (9–11) Traditional Chinese medicine products have a long history of relative safety, as stated in FDA's ruling on ephedra. While most companies and entities are no longer permitted to hold or distribute ephedra, FDA provided an exception: ma huang (aka ephedra) may continue to be used by practitioners of traditional Chinese medicine. The agency stated, “Several ephedra species (including those known as ma huang) have a long history of use in traditional Chinese medicine. These products are beyond the scope of this rule because they are not marketed as dietary supplements.”(12)

Various parties over time have asserted herbs are not in fact regulated and additional regulation should be required.(13,14) DSHEA currently provides parameters for ensuring herbal safety. FDA has the authority to inspect facilities, send Warning Letters and seize dietary supplement products when it deems the manufacturing facility is out of compliance with the law.(15)

Current regulation of Chinese medicinal herbs as dietary supplements permits access to Chinese herbs, including qing hao or artemisinin. Artemisinin in the form of ACT has been and continues to be vital in the treatment of malaria.(16–18) However, according to the World Health Organization (WHO) and others, the malaria parasite is becoming resistant to artemisinin. (19,20) Resistance to treatment will require research to find new effective treatments for malaria. Further, as the climate warms, additional tropical diseases appear likely to migrate to new areas. (21,22) These combined factors call for continued legal access to Chinese herbal medicine so new treatments for malaria and other tropical diseases can be developed.

Brief History of Malaria Treatments

In 2700 BC, malaria as a set of symptoms was described in Chinese medical writings in the Nei Ching, a well-known ancient text. Medical texts found in the Mawangdui Tomb contained descriptions of the qing hao plant, which were attributed to Ge Hong of the East Yin Dynasty in 340 CE. During the construction of the Panama Canal, 21,000 of 26,000 workers contracted malaria over a five-year period, providing the catalyst for increased emphasis on control of malaria in the US. Much of the early work by the Centers for Disease Control (established 1946) focused on malaria eradication and control. The primary control method was spraying dichlorodiphenyltrichloroethane (DDT) on the interior surfaces of homes and sometimes home owners’ properties. Between 1947 and 1949, 4.6 million houses in 13 southeastern states had been sprayed with DDT. Air spraying of insecticides also was used. In 1949, it was declared the US had eradicated malaria as a significant health threat.(23)

The US continues to apply controls to prevent mosquito infestation by encouraging removal of standing water and use of clothing and body sprays as deterrents, as well as biological larvicides in aquatic habitats of mosquitoes and government use of pesticide applications during maximum adult mosquito activity in urban residential areas.(24) However, despite such efforts, the US Environmental Protection Agency (EPA) acknowledges there has been an increase in diseases which were formerly considered tropical, especially in the southwest US.(25)

Because millions of malaria cases occur in more than 90 countries annually, efforts to discover new treatments have been ongoing for decades.(26) Yet, ACT therapy is still
the most effective treatment available to modern medicine. WHO recommends ACT as the first line of defense for uncomplicated *P. falciparum* malaria. Artemisinin or qing hao has been used for centuries in China to treat “steaming bone disease.” The modern use was “discovered” in the 1970s in China. At that time, the chemical constituents were believed to be more effective than the plant itself. Now, after four decades, studies indicate the raw plant may be more effective in combating malaria than the extracted chemical constituents. Thus, further discoveries about the contents of raw herbs may provide additional useful information about beneficial treatments in the future.

Bringing ACT to market involves using effective substances from both Eastern and Western medicine to maximize health benefits for the patient. ACT combines artemisinin-based compounds artesunate, artemether and dihydroartemisinin with companion drugs, which include amodiaquine chlorproguanil/dapsone lumefantrine, mefloquine, piperaquine and sulfadoxine/pyrimethamine. ACT had been adopted by most countries in the southern hemisphere by 2007 and was approved for use in the US by FDA in 2009.

**Analyzing the Effectiveness of DSHEA**

**Survey of Chinese Herbal Medicine Experts**

The continuing use of ACT demonstrates the importance of keeping Chinese herbal medicines available to researchers, especially in view of an expected increase in tropical disease cases in non-tropical areas. This calls for maintaining DSHEA oversight at its present level.

To determine whether DSHEA provides satisfactory parameters for Chinese herbal medicine to address malaria and other tropical diseases, a survey was created and literature reviews were conducted to assess the experiences of professionals in the Chinese herbal medicine field relative to DSHEA and tropical diseases.

An anonymous survey of practitioners of Chinese herbal medicine was conducted in March 2015 requesting: 1) feedback on the adequacy of DSHEA both as it stands and relative to potential use in developing future treatments for tropical diseases; and 2) information about treating tropical diseases in the US. The data collection tool Survey Monkey was used, with 35 respondents. Four CEOs of Chinese herbal medicine companies in the US were interviewed in March 2015 and asked the following questions:

- Do you believe DSHEA could be improved by allowing more-specific information on labels and product information?
- Do you believe DSHEA could be improved in other ways?
- Do you believe there are any possible benefits to the trade in Chinese herbs from a premarket approval process?
- Do you believe having DSHEA in place will afford the Chinese herbal medicine community the opportunity to address malaria and other tropical diseases as they become endemic in the United States?

Survey results revealed the majority (72%) of respondents believe DSHEA provides an appropriate framework to support future research of Chinese herbs to address malaria and other tropical diseases. Those who did not agree expressed: 1) concerns about western science labs’ using only the chemical constituents of the herbs, therefore bypassing the potential healing value of using the entire herb plant in research; 2) concerns that those interested in profit would work to eliminate practitioner access and attempt to market directly to the consumer, potentially causing problems when consumers are not fully advised by licensed, qualified practitioners of traditional Chinese medicine; and 3) interest in changing the law to eliminate direct-to-public distribution, so consumers would be able to purchase herbs only from a practitioner of traditional Chinese medicine, rather than over the counter at natural food stores or online.

In the personal CEO interviews, 75% responded that requiring premarket approval of herbal medicines would be a disadvantage to both the herb industry and the consumer due to high costs of implementation. One CEO felt premarket approval would be helpful to the herb industry and to consumers if structured in a way traditional herbal medicine companies could afford, thus passing on reasonable costs to consumers, and if FDA approval of herbs would encourage insurance companies to more fully reimburse patients. One-quarter
of practitioners surveyed reported seeing tropical diseases in their clinics contracted in the US, and three of those had had visits from patients with US-contracted malaria.

CEOs of traditional Chinese medicine companies generally agreed **DSHEA provides a better regulatory framework than existed prior to its passage in 1994, but the current statute leaves room for improvement.** Two CEOs emphasized traditional Chinese medicines have thousands of years of demonstrated efficacy and safety when prescribed by licensed, qualified practitioners; one indicated this information should be strongly considered by the US as it creates laws and regulations relative to Chinese medicine.

Both the CEO groups interviewed and the professionals surveyed strongly agreed the current framework of premarket approval required by pharmaceutical companies would not be a fit for the herbal industry. Several practitioners and one industry CEO suggested Canada’s regulatory framework provides a potential example of a more effective and relevant statute specific to traditional Chinese medicine, as opposed to its current US categorization under supplements.

**Literature Review**

The Johns Hopkins online library database Knowledgenet/ProQuest was consulted for the literature reviews.

A review of literature on treatment resistance in malaria from 2010–2015 was conducted. 234 peer-reviewed articles relevant to whether the parasite malaria is becoming resistant to artemisinin were reviewed. 100% of articles reviewed were in agreement that resistance is being developed by the malaria parasite to current forms of drug treatment.

Peer-reviewed articles seeking a new treatment for malaria were reviewed in 2010–2015 to assess verifiable progress in finding a new and effective treatment for malaria in the face of artemisinin resistance development. Of the resulting 84 articles, 71 included the key word search preference and were reviewed. Of these articles, only three articles advocated progress was made in research, but did not involve active treatments utilizing either drugs or herbs. Sixty-eight articles reviewed did not offer specific solutions for the future treatment of malaria as artemisinin resistance grows. A review of literature on **DSHEA** as an effective or ineffective law relative to Chinese herbal medicine was conducted. Thirty peer-reviewed articles were reviewed. 18 articles were relevant to the topic and supported **DSHEA** as an effective law

One author’s opinion directly reflected participants in the survey of Chinese medicine professionals stating, “For dietary supplement manufacturers, a compromise on relatively low-cost measures, including enhanced labeling, registration, and disclosure of adverse event reporting, might prove a feasible and far less burdensome outcome.”(33)

This approach is in contrast to premarket approval for herbal products, which has been frequently advocated by opponents of **DSHEA**. Other articles contained partially inaccurate information about **DSHEA**: one stated, “No manufacturing standards regulate the quality and production of herbal remedies.”(34) In fact, FDA’s website states: “Manufacturers and distributors of dietary supplements and dietary ingredients are prohibited from marketing adulterated or misbranded products. This means the firms are responsible for evaluating the safety and labeling of their products before marketing to ensure they meet all the requirements of **DSHEA** and FDA regulations. FDA is responsible for taking action against any adulterated or misbranded dietary supplement product after it reaches the market.”(35)

Another author, in suggesting **DSHEA** does not provide enough oversight, argued Chinese herbal medicines are dangerous based on an unfortunate series of incidents in Belgium in the early 1990s; however, the information provided was incomplete. Fang ji was being sold there as a slimming agent, resulting in serious adverse events.(36) These incidents were not related to traditional Chinese medicine practices, which do not use fang ji for weight loss.

These commentaries provide insight into the degree to which the relationship between **DSHEA** and traditional Chinese medicine is understood by the public. Interestingly, the papers advocating the relative ineffectiveness of **DSHEA** often provided constructive feedback agreeing with the opposite side of the discussion. One paper indicated “Other nations, too, are looking at issues related to botanical supplement safety. Both the European Union and Canada have added a new ‘traditional medicine’ category for products having a history of use in the literature without adverse reactions.”(37) The same
author goes on to point out DSHEA does currently empower FDA to enforce the law: “FDA and other agencies have become more vigilant in enforcing laws pertaining to supplements.” (38) Thus, it appears parties opposed to DSHEA and those in support of DSHEA as an effective law governing traditional Chinese medicine may actually be in relatively close agreement. In the 220 peer-reviewed articles, 100% agreed some degree of resistance to current forms of drug treatment is being developed by the malaria parasite: discussion was based on how the resistance is developing.

Further, 71 articles were reviewed to assess verifiable progress in finding a new and effective treatment for malaria due to artemisinin resistance development. Of those where researchers were not using artemisinin in their testing, three said progress was made in research, but did not involve active treatments utilizing either drugs or herbs. Suggested solutions included applying pesticides on the interior of homes and using insecticide-treated mosquito nets (39) and hammocks. Sixty-eight articles reviewed offered no specific herb or drug treatment based on verifiable data for the future treatment of malaria.

These findings underline not only the need for new, effective treatments for malaria, but also for identifying the method by which the parasite is acclimating to currently available drugs including ACT. The malaria parasite is developing resistance to artemisinin and ACT in multiple countries and evidence suggests resistance to insecticide spray as well. (40) This is likely to remain a challenge for the US government, and new solutions are needed for malaria and other diseases as they become endemic in the US.

Conclusion

Like artemisinin, quinine and atovaquone are antimalarial drugs derived from herbal plants. (41) Herbs and plants in other parts of the world have long been used to address the symptoms of malaria: in the Chipinge district in Zimbabwe, 28 plants from 16 plant families are used by the local healers. (42) Thus, keeping DSHEA as the law governing Chinese herbal medicine will enable exploration of as many options as possible, including all available herbal medicines, to find new treatments for malaria and other resilient tropical diseases.

References


25. Ibid.


39. About the Author

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