

Glass Half-full or Half-empty? Final Thoughts on Medicinal Fungi

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Research on macro fungi within the past 30 years has been conducted primarily by Asian scientists (Wasser 2017). Until quite recently however the studies on which initial claims of curing cancer, diabetes and heart diseases have not been the subject of well-organized and randomized double-blind clinical trials in East Asian hospitals (Schilsky 2018). The majority of claims made for the efficacy of native herbs and fungi are based on what happens to human tissue samples in a two-dimensional Petri dish (*in vitro*) (Keiger 2013), in genetically engineered mice or rats, or in small group of patients (Tang, Zang, and Ernst 1999). Most are unrepeatabe. The following is a quote found three years ago from marketers of fungal supplements on the commercial website www.mushroomscience.org:

Thousands of years ago, people in the Far East observed that certain kinds of mushrooms, besides being very tasty sources of food, had a lot of other health benefits (anti-oxidant, healthy skin, immune support, increased energy, liver health, memory and concentration, and stress relief.¹ Ancient cultures all over Asia made these mushrooms a regular ingredient in many traditional recipes for foods and teas. People soon noticed that their overall health improved significantly, and they associated these improvements with their diet. Thus, they were the very first to recognize the mushroom's medicinal value.

Advocates of consuming macro fungi as medicine understandably have been deeply impressed by the high regard in which fungi have been held over the millennia in Asian cultures that adopted and adapted Chinese theories of health, disease and remedies to their own needs. The vast majority of authors of books and articles on medicinal fungi have some basic knowledge of what is called Traditional Chinese Medicine (TCM) and a few are knowledgeable herbalists, teachers and practitioners of Chinese acupuncture (Rogers 2011, 2016). Like their research counterparts in Asia charged with proving the efficacy of TCM and its documented medicines, many espouse the belief that TMC endured for so many years because it was based on empirical

¹ These statements have not been evaluated by the Food & Drug Administration.

evidence. This is also the official stance of the Chinese government, which has taken pride in spreading knowledge of older therapeutic practices employed to care for the emperor and the politically, economically, and socially privileged segments of the population in imperial dynastic times. Their views generally regard employing fungal and herbal preparations as preventative medicine - and as critics of the reductionist approach of biomedicine - mirror the official statements of the Chinese government in its efforts to legitimize its classical medical traditions and pharmaceuticals for use at home for the peasant masses and abroad (Hepeng 2008; Rencun & Hai 2018) since the mid-1950s.

TMC is actually an uneasy ongoing attempt to synthesize modern biomedical knowledge and modified older medical theories and practices that exists under the auspices and direction of the Chinese government for purposes of caring for the basic needs of the rural population. There is little that is 'traditional' about it. In the pre-modern era, all science reflected the views of the elite regarding our connections to cyclical changes inherent in all aspects of life. It was practiced by educated scholar-officials and others obliged by the requirements of filial duty to care for sick family members (Hinrichs 2013). With few exceptions, the scholar-physician did not take on clients unless his services were requested by equals or superiors. His role was not so much to heal, but to advise those dependent upon him on ways to recalibrate and coordinate one's thoughts and behavior to better synchronize with patterns of cyclic change observed in the heavens and on earth. Medical theory and practice were based on a theory of correspondences that incorporated everything known from foods, tastes, textures, odors, daily and seasonal changes in weather and temperature, planetary movements, minerals, gems, colors, musical notes, numbers, and so on. Within the classical system, the exterior and interior of the human body embody a complex of functions that ideally resonate with patterns of cyclic change over time in the heavens, on earth, and in political and social realms. A life unsynchronized with the cosmic order could render one susceptible to a range of emotional and physical aberrations that would manifest themselves in a weakened constitution and possibly disease (Unschuld 1985). The physician's role was to restore the ill to a normal functioning state of health and harmony in tune with nature's laws or patterns (Kaptchuck 2000). He

might prescribe combinations of organic and inorganic ingredients with instructions on proper preparation techniques and guidance on the time of day and duration period to consume them. Classical medicine generally satisfied the needs family members who were not suffering from debilitating illnesses. Despite statements like the one at the top of this essay, Chinese medicine was never intended to cure heart diseases, diabetes, Alzheimer's or cancers. If a scholar-physician's prescription didn't work, dissatisfied patients were free to consult any one of numerous other practitioners, pharmacists or itinerant herbalists that catered to different segments of the urban and rural populations. Other specialists dealt with opening blockages to the movement of chi' through acupuncture or moxibustion, repairing broken bones, giving dietary advice, removing curses, assisting birthing, childhood diseases, women's health, veterinary medicine and caring for military wounds. The range of medical practices was broad and included exorcisms, incantations, wearing of talismans and charms, as well as the use of foods, herbs, insects, parts of exotic and wild and domestic animals, worms, venoms and inorganic ingredients (Gernet 1959). While it is likely that some practices and remedies resulted in healing the sick due to the efficacy of the procedures and medicines employed, by and large patients suffering from many disorders got well on their own. This situation happens to all of us. Most disorders are self-limiting. We eventually recover from most discomforting health problems within a week or two whether or not we take medicines. Some Confucian trained physicians also observed that the body spontaneously healed itself of pathologies through the process of vomiting, sweating, bleeding or excretion of urine or feces (Liu 2015, 26).

In cultures informed by Galenic medicine, bloodletting was a common practice of healers for at least two thousand years (Lawrence 2008). Despite seeing their patients weaken and often die, the practice continued up through the twentieth century even in the 'advanced industrial world'. Therapeutic 'Phlebotomy' continues to be practiced today for two diseases: hereditary hemochromatosis and polycythemia vera (Juergens 2005). The TMC prescriptions used in ancient and in modern China appear for the most part to have been no worse than those employed in the west through the first decades of the twentieth century. On the positive side, the educated physician's recognition that one's psychological or emotional state can have an effect on one's perception of health was unique. The importance given to managing stress through meditative breathing techniques, exercise, massage, acupuncture and other techniques may have been the greatest gift TMC has bestowed on our efforts to incorporate Chinese therapeutic practices into our hospitals'

complementary medical programs for patients suffering from severe and terminal illnesses. An argument could also be made that traditional emphasis on the importance of dietetics (Chang 1977) was beneficial especially for those who could afford to eat a varied diet rich in healthy foods from all parts of the empire and beyond. China's efficient agricultural practices, storage and distribution methods supported continuous population growth beyond that experienced anywhere else in the world despite having far less arable land. Challenges to government order in the nineteenth century resulting from the encroachment of European traders with weaponized ships and missionaries in tow at treaty ports, widespread opium addiction, land shortages, floods (Ye, Fang, and Li 2016), drought, crop failures, famines, peasant revolts, epidemics, and military invasions led to the breakdown and collapse of traditional government institutions designed to protecting the Chinese population from widespread starvation.

Following the collapse and the dissolution of the empire with the abdication of the last emperor in the early twentieth century, influential politicians, intellectuals and reformers began looking outside their borders for inspiration for China's future as an equal among nations. Chinese science and its association with a failed dynastic political system was deemed unsuitable by intellectuals pushing for modernization. Sun Yat-sen, a western trained doctor, ordered the burning of extant ancient medical texts. Chinese medicine was judged to be a stinging remnant of China's feudal past and was abolished in 1929 as unscientific (Unschuld 1985). The few remaining native practitioners familiar with the indigenous scholarly tradition of classical medicine went into hiding in fear of being persecuted.

After the establishment of the People's Republic in 1949, intellectuals who viewed ancient Chinese medicine as a source of national pride gained ascendancy, argued for and supported its official revival and sponsorship by the government under Mao (Chen 2017). He personally did not believe in Chinese medicine (Li 1996), but there simply were not enough Chinese physicians of biomedicine to care for the country's half-billion people. Mao depended on traditional medicine - including the practice of acupuncture, (a therapy most scholar-officials had little use or respect for during the previous two millennia), to treat the masses and particularly the rural peasantry (Zhang 2017). The plan was to modernize and systematize Chinese classical medicine to make it more scientific. To this end, they

removed some ingredients included in pharmacopeias deemed superstitious. They also promoted the use of Chinese drugs deemed equivalently efficacious to conventional, but costly, 'western' drugs. These would be sold at home and abroad as affordable alternatives.

With limited resources available, mid-twentieth century Chinese physicians and scholars were forced to rely on Japanese translations of original Chinese texts or on the translations of western sinologists to rediscover their own medical traditions. To satisfy skeptics trained in conventional biomedicine, physicians of biomedicine and Chinese medicine were required to prove that TCM was as scientific as 'western' medicine. To this end, they were commissioned to find descriptions of diseases in the historical literature which appeared to match modern disease conditions (Unschuld 1986). They were ordered to find prescription ingredients mentioned in the imperial pharmacopeias to effect cures of these disease conditions. Government directives were not conducive to encouraging an unbiased examination of its medical texts, therapies or prescriptions. Lacking proper training in conducting clinical trials, it is not surprising that the majority of studies published suggested that TCM was highly effective in preventing diseases that 'western' medicine continued to find challenging.

By the mid-to-late 1950's Mao's regime began promoting world-wide use of TCM. Claims were made that it was founded on a long monolithic and empirically valid tradition of diagnosis, disease determination, and knowledge of thousands of efficacious pharmaceutical ingredients. In being holistic and patient-centered rather than organ-centered, it was deemed superior but complementary to conventional biomedicine. In reality, Chinese medical theories, practices and medicines changed constantly over the previous two millennia (Sivin 1987). But this political analysis facilitated the easy export of TCM and acupuncture to spread and become firmly established around the world. It also sanctioned the uneasy preservation of TCM to exist side-by-side with modern conventional medicine in China.

Despite attempts to make TCM conform to the mechanistic concepts of disease in the West, the overall result has been disappointing for many. Equating modern ideas of health with older ones is historically inaccurate and has led many inside and outside China to believe that pre-moderns understood the dynamics of heart diseases and cancers as well as a trained heart specialist or oncologist - just in a more 'holistic' and gentle way. Western researchers, writers and manufacturers of herbs and fungal products continue to espouse the fiction that TMC was practiced for all members of society and that physicians in pre-modern China appeared to comprehend the complexities of the immune system, the role of free radicals and the value of antioxidants. Certainly, the theoretical foundations of TMC were generally reflective of the desire to depart from the superstitious beliefs of the uneducated regarding the causes of disease. Some health prescriptions were undoubtedly based on experiential knowledge that served to change the patient's condition for the better. Remedies for wounds, and common conditions like sleeplessness, listlessness, constipation, diarrhea, hemorrhoids, fevers, coughs, certain urinary conditions, skin diseases, erectile dysfunction and pain were discovered and used successfully. But with some notable exceptions (Anderson 2014), the elite medical practitioners of the past selected specific materials for a prescription based largely on esoteric criteria that conformed to idealist theoretical considerations. Thus, *Ganoderma lingzhi* being reddish was associated with the functions of the heart (cognition, consciousness and mental states), blood, the emperor as ruler, fire, late summer, south, Mars, heat, weddings, happiness, laughter, certain musical notes, red cinnabar, particular foods including chickens and beans, scorched odors, flavors, scents, bitter tastes, the tongue, small intestine, and magical numbers 2 & 7 (Maciocia 2015, 19-26, 107-116). Chinese scholars who practiced or dabbled in classical medicine were usually no more inclined to consider questioning the veracity of their belief in knowable patterns of nature's cyclic changes than astrologer-astronomer Johannes Kepler would question the literal truth of Pythagoras' belief in the harmony of the spheres. If a theory, therapy or medicine didn't behave as expected, discrepancies might be attributed to any of a number of causes. On the other hand, a prescription that seemed to work once for any one patient, might be declared, boldly promoted and marketed as a 'proven remedy' (Sivin 1987, 19). Despite decades of ongoing attempts to establish a scientific basis for the ingredients employed in prescriptions for various disease descriptions, so far only one - artemisia - has been found medically efficacious for treating a serious disease common in many regions in the world - malaria. It was used in early China in combination with several other ingredients for fever. In any case, the Chinese government's propaganda that drug therapy in

historical China was analogous to the empirical science of modern medicine does not appear to be able to withstand scrutiny (Crozier 1976, 354).

There are several difficult issues that need to be addressed when researching any 'natural' remedy. The number of compounds in fungi (and herbs) with medicinal potential is huge. Figuring out which help or hinder health in a particular situation is fraught with difficulties, not the least of which is the fact that the levels of various compounds and their therapeutic activity vary greatly from one fruiting body to the next of the same species. Processing procedures are not uniform from one manufacturer to another. Some manufacturers use mycelium combined with preferred growing medium. Some swear by the medicinal activities of fungal spores, while others prefer powdering the entire fruiting body. Hot water and alcohol extracts are considered more potent than powders by some, although in China the preference is to employ hot water extracts. Complicating matters is the fact that prescriptions are not administered to patients as single ingredients, but in combination with several other substances for their alleged moderating or enhancing effects as defined by classical theory. In the hospital environment, for example, a patient is treated with conventional drugs along with concoctions of up to 20 or more other ingredients used by TCM practitioners. As a result, it is impossible to know whether an improvement in a patient's health is due to the standard medicines or the synergistic actions of the entire formula. Needless to say, it is not surprising that scientists are now working to identify and isolate specific compounds and study precisely what they may be doing in the human body.

It is notable that researchers of macro fungi having potential to affect changes in health conditions currently view their properties as having mostly an indirect rather than a direct impact on various disease conditions. Earlier claims for the miraculous ability of fungi to cure all diseases from the common cold to cancers have dampened considerably among scientists throughout the world. But macro fungi continue to be marketed as curative of numerous diseases in countries that do not require evidence-backed proof of their efficacy. As 'functional foods' they may serve to stimulate the immune system to target and fight imbalances that might become pathological in patients whose immune systems have been suppressed. This may be why macro fungal remedies are mainly employed

these days as adjunctive therapies for patients who have been cured of diseases using modern conventional treatments. It is reported that they may enable patients to recover more quickly and with less discomfort. Nonetheless, I find it rather strange that a revised and updated edition of *Cancer Management with Chinese Medicine: Prevention and Complementary Treatments* by Yu Rencun and Hong Hai, makes no mention of studied macro fungi, such as *Ganoderma* or *Cordyceps*, as being employed as either a preventative, curative, or adjuvant remedy for treatment of any kind of cancers! The only fungal foods mentioned that are said to have anti-cancer effects include the oyster mushroom, the white jelly and black jelly fungus (Rencun and Hai 2018, 185-244).

It would be interesting to know whether a non-fungal diet rich in nutrients found in medicinal mushrooms might have comparable effects on the immune systems of patients or if there are potent compounds unique to fungi that make them more therapeutic (Martel 2017). Avoidance of disease through informed nutrition is a hot topic of research among nutritionists and not surprisingly, of Chinese researchers looking to find natural ways to prevent and cure diseases. Various studies propose that a number of foods besides fungi might be used to treat and prevent liver cancer including grapes, asparagus, pomegranates, French beans, tomatoes, black currants, ginger, garlic and others (Zhou 2016; Friedman 2009). We are all aware of magazine, newspaper and online articles espousing the virtues or vices of consuming particular foods. In any case, most existing studies on the subject of prevention or cure of specific diseases through food are *suggestive* of topics and studies that need to be investigated further. None, so far, are reflective of concern for meeting the high standards of evidence-based medicine. As with fungi, the majority of studies indicating anticancer, immunomodulating, antimicrobial, hepatoprotective, antioxidant, antidiabetic and anti-inflammatory properties are reflective of *in vitro* observations (Zhang 2016). The majority of studies employing human subjects have been of poor quality (Chung 2015), with the result that it is impossible to either support or refute the efficacy of using Chinese fungal or herbal medicines to treat specific disease conditions (Wang 2014).

Some claims for the efficacy of macro fungal in humans are based on results observed in Petri dishes or in inbred or genetically modified rodents. Most preliminary trials that appear to be effective in animals fail to be applicable to humans because they are either

ineffective or dangerous. Thalidomide, prescribed as a sedative for sleeplessness, was considered completely safe even for pregnant mothers and children had no effect on mice or rats (Kim and Sciali 2011). But it caused a world-wide epidemic of unanticipated birth defects. It has been estimated that of the few successes of tested drugs on animals, fewer than 14% are replicated in randomized human trials (Wong 2019, 273-286). Many substances will kill cancer cells in a Petri dish, including peroxide, an observation that has led some alternative health practitioners to treat their cancer patients with it. As long as cancer cells have a steady supply of glucose, they can thrive in low to no oxygen environment (Warburg effect). Some hypothesize that the oxygen delivered by injecting 35% food grade hydrogen peroxide into tumors can flood, kill and prevent low oxygen cancer cells from dividing (Wells 2013). Unfortunately, cancer cells can survive and proliferate with or without oxygen and flooding them with oxygen won't help. In fact, hydrogen peroxide can promote cancer growth and metastasis (Lisanti 2011).

Chinese researchers of TCM pharmaceuticals are becoming more sophisticated in conducting studies on fungi and other ingredients used in traditional medicines, but as of now they have not yet presented sufficient evidence that their test tube or animal studies will work as expected in humans (Chen 2016). In the near term, it is unlikely that the situation will improve. Rather than try to meet the tough standards of the FDA approval requirements to sell their products in the lucrative United States market for prescription medicines, under Chairman Xi testing for efficacy and safety of TMC pharmaceuticals has relaxed. China is doing a booming over-the-counter business selling health 'supplements' that are basically unregulated. Based on preliminary studies, though, unlike vitamin and mineral supplements it does appear that most 'medicinal fungi' purchased from reputable cultivators and distributors are generally safe to take under a physician's supervision. It is the responsibility of each individual to learn what goes into validly conducted scientific research and their health supplements. When researchers indicate there *may* be a positive effect from taking a given amount of a so-called medicinal fungus if you have a particular disease, it does not mean there *will* be a positive outcome.

The desire to identify and harness the positive benefits of incorporating edible macro fungi into our diets has hastened the examination of their use in folk traditions over the course of history. This is a positive development. The foods and medicines of all indigenous

healing traditions need to be studied in hopes of finding new and more effective medicines for numerous diseases we will contract in the present and in the future. But our concepts of disease, no matter how inaccurate or incomplete they may be judged in the future, are still too ‘modern’ for us to easily understand the philosophies of health and disease of our predecessors without years of serious study. One of our biggest mistakes is assuming that humans in the past saw the world the way we do today. We can respect and learn about their beliefs systems, without imposing our own on theirs.

IMMUNOLOGY

Immunology is a growing field of study for scientists, especially after harnessing the tool of gene analysis (Hamers 2017). Researchers are working to understand the activity of the body’s defense strategies as well as those of pathogenic origin (Houlton 2018). However, most arguments supporting the efficacy of myco-medicinals neglect to acknowledge that microbes as well as cancer cells evolve quickly and are often able to avoid detection and an immune response (Casás-Selves and DeGregori 2011). In fact, every tumor is different and often requires a combination of drugs to keep it at bay (Schieszer 2015; Waldolz 2018). This is one reason why medicine is becoming more personalized. Assuming that fungal pharmaceuticals are effective in strengthening the immune system and enabling it to fight diseases, is there any reason to believe that they will be any better at defying the ability of microorganisms and cancers to evolve and evade destruction? We just don’t know yet.

Fungi do not hold a monopoly on producing potentially useful medicines, nor are they necessarily the strongest medicinal organisms. Research on targeting specific genes and types of cancers is being carried out using bacteria (Song, Vuai, and Zong 2018; Wogen 2016; Tores 2017), viruses (Kuperferschmidt 2018), and venoms (Sargent 2017), as well as fungi. Recently it was discovered in a lab setting that the Zika virus kills glioblastoma brain tumor stem cells *in vitro* with marginal effect on normal brain tissue, which are normally resistant to current treatments (Zhu 2017, 2843-2857). Some of the newest research involving engineered immune cells for dealing with certain cancers also looks promising, although continued research is required (Neelapu 2017; Sagiv-Barfi 2018).

Basic scientific research is necessary in order to develop drugs and therapies that will be better at targeting pathogenic cells than have been used in the past. The entire topic is extremely complicated, and we are just beginning to gain an understanding of some of the issues involved. It seems likely that further exploration of the activities of macro-fungi will ultimately play important roles in both our understanding of the complexities of the immune system as well as provide potent and increasingly less destructive strategies for modifying and living with diseases like cancers.

THOUGHT EXPERIMENT

What is the basis for adding these fungal ingredients to our life-style regimes – when we are not ‘sick’?

Given what is currently known about employing macro fungi to strengthen the immune responses of immune-suppressed patients who have undergone treatments for debilitating conditions, I see no problem with taking macro fungal preparations proven to assist the recovery process under the supervision of a physician. I suspect that there are many other ways of achieving similar results using a combination of nutrient rich vegetables, fruits, beans, nuts and grains with a few different edible fungi thrown in for good measure. Classical Chinese cooking excelled at combining ingredients that were healthy (Cohen 2015, 91-111), varied and capable of ensuring that especially males among the privileged elite, at least, ate well and barring genetic defects, would live a long life. Overindulgence in food, drink and other worldly pleasures led to obesity, diabetes, heart problems and a lifespan that may have exceeded that of most peasants but was significantly shorter than it might have been.

But supposing you are reasonably healthy, would it be wise to take macro fungal supplements or tinctures on a daily basis to prevent any disease? Would you take an antibiotic every day, ‘just in case’? Would you inject yourself with insulin, even if you didn’t have diabetes? Would you consider taking a medicine for treating severe heart disease as a preventative measure, assuming you are free of the disease? Do you think we should undergo radiation therapy or take chemotherapy drugs if we do not have cancer?

If we accept the probability that certain compounds in fungi are effective in boosting the immune system's natural defenses against malevolent intruders in a body that is or has suffered a debilitating disease, what might we expect they will do in a body that is healthy? Most supplements taken by humans are not stored anywhere in the body for use when needed but are expelled as waste. Studies on people with various diseases who take large doses of vitamins, minerals (Dawsey 2014) and antioxidants (Terry 2000) show that contrary to belief, they tend to expire sooner than those who don't take them. We talk about how fungi are closer to humans phylogenetically than we are to plants. As Paul Stamets writes in *Mycomedicinals: An Informational Treatise on Mushrooms*:

Fungal medicines are active against many diseases that afflict humans. A peculiarity of nature is that we suffer from many of the disease organisms that afflict fungi, but in general, are not susceptible to those infecting plants. Many scientists believe that this relationship occurs because we are more closely related to fungi than to any other kingdom, having shared a common ancestor more than 460 million years ago, and thus developed defenses against mutual microbial enemies. For physicians, naturopaths, herbalists, and lay people, medicinal mushrooms may well hold answers for many of today's major health concerns. Increasingly, medicinal mushrooms are valued not only as adjuvant therapies to allopathic practices, but show promise for preventing diseases, including cancer (Stamets and Yao 2002, 5).

I love fungi and appreciate what they do for all of life, including supporting our health and providing defense against many plant diseases. To the extent that some cancers are viral, bacterial or fungal in origin, the possibility that they will have an increasingly greater role to play in our therapies and understanding of cancers in the future seems inevitable. However, based on the results of over 30 years of research I am reluctant to jump to the conclusion that what seems to work in a Petri dish, in rodents, or on a small number of patients in poorly designed clinical trials will necessarily prove to be the secret key to unlock the mysteries of a disease-free long life. For me, the glass is still half-empty. I look forward to learning that today's 'suggested' positive results regarding the medicinal properties of macro fungi will be shown to be tomorrow's curative or preventive medicine based on solid, repeatable evidence.

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