

# Food, Medicine, Poison & Molecular Multitasking: *Novel Conceptual and Clinical Tools for the Botanical Treatment of Cancer*

Jonathan Treasure

## Introduction

Patients confronting a diagnosis of advanced (stage 4) cancer face the statistical reality that conventional chemotherapy can effect a cure in only a tiny minority (between 1-3% depending on the malignancy) of all such cases. More often than not, the reasonable impulse of these patients to investigate alternative treatment options such as herbal medicine is met with negative responses from oncologists. As a result, consumer-patients challenged with cancer seeking herbal medicine resources may resort to unreliable products promoted on the Internet or via multi-level-marketing which offer dubious herbal “cures”. Patients may also be less willing to disclose any use of these products to their physicians.

The emerging integrative model of cancer treatment recognizes the importance of botanical medicine. However, despite extensive positive research data from experimental and preclinical studies, and the anecdotal clinical experience of many practitioners, patients and cancer survivors, its potential in this field remains largely untapped and large scale clinical trials are generally unavailable. The reasons for this are multifactorial, and include historical, political, and cultural factors – and almost invariably a misunderstanding of the core principles of herbal medicine itself.

## Herbs and Herbal Medicine in the USA

An important but often overlooked distinction exists between herbal *medicine*, (the practice) and herbal *medicines* (the plant based remedies used in the practice of herbal medicine).<sup>1</sup> The current trend of presenting so called “scientific information” about herbs divorced from the context of herbal medicine that defines their medical use is rather like presuming that knowledge of needles will

provide an understanding of acupuncture. It is only the specific discipline of herbal medicine that enables a therapeutic understanding of medicinal herbs.<sup>2</sup>

In Europe, herbal medicine (also known as phytotherapy) is a legally recognized healthcare delivery system, and herbal medicines are considered a distinct regulatory category. In the United States, neither herbal medicine (the practice) nor traditional herbal medicines (the remedies) are recognized as such by the legal and regulatory frameworks that determine healthcare provision and the availability of medicines for American citizens.

Herbs are regulated in the US under DSHEA (1994) as “Dietary Supplements”, as opposed to the European traditional medicine category. This separate category for herbs is important for two reasons: it legitimizes the obvious fact that herbs have medicinal properties (in the US medical claims are not allowed for “dietary supplements”) and it also asserts that a valid form evidence and support for efficacy and safety derives from empirical (traditional) use over many years. Traditional use evidence does not replace scientific or clinical trial data, but is a unique category of evidence, which separates herbs with many years of medicinal use from modern engineered nutraceutical products that are promoted as “natural” dietary supplements. A good example would be the traditional herb ephedra, used safely for centuries in Chinese medicine, as opposed to modern “fat burning” dietary supplements combining ephedrine alkaloids, aspirin and caffeine that were promoted as “natural” weight loss aids.

Secondly, herbal medicine as a professional practice is technically illegal in the United States, an anomaly among English speaking countries (such as England, Australia, New

Zealand and Canada). This is the legacy of active political suppression in the early 1900s, by an alliance between the then recently formed American Medical Association (AMA) and emerging pharmaceutical companies. At that time there were between 30-40,000 physicians (MDs) across the US trained by the Eclectic Botanical Medicine movement. They used botanical and natural remedies as their primary method of treatment, and over 50% of the drugs listed in the United States Pharmacopoeia then were botanicals. The AMA used the Rockefeller financed Flexner Report in 1910 to shut down the national network of botanical medical schools, on the pretext of inadequate laboratory facilities, particularly for anatomy.<sup>3</sup> By 1934, there was not a single remaining botanical medical school in the US, and the percentage of botanicals in the USP had dropped from over 70% to 30%. (Today the proportion of botanical substances in the USP is <1%).<sup>4</sup>

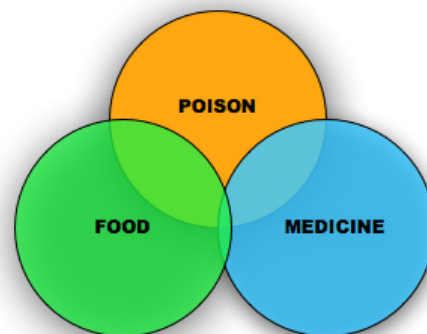
The legacy of this suppression remains today, and herbalists who diagnose and treat medical conditions are vulnerable to the felony charge of practicing medicine without a license - in several states this has proven to be a more than theoretical concern. In some states, licensed Naturopathic Physicians (NDs) may legally prescribe and dispense herbs, and Licensed Acupuncturists (LAc) may dispense Chinese herbal remedies. There is also a small but significant number of experienced herbal practitioners in the US, most of whom are professional members of the American Herbalists Guild (AHG). AHG professional members operate within a framework of informed consent, offering consultations about how botanicals can be used safely and effectively by their clients.

It should be noted that while many of the leading medical schools in the country have now formed “integrative medicine” departments, the faculty of these units is invariably composed of physicians lacking specific training in botanicals or herbal medicine, whilst herbalists and naturopathic physicians are conspicuously absent from the roll-call. This is, at present, more a cosmetic exercise in response to patient pressure and prospective-student demand; at the same time various medical professionals, institutions and

organizations continue to launch poorly-informed attacks on herbs and herbal medicine, often so explicitly inaccurate that their political motivation is transparent. Last, but far from least, the international pharmaceutical corporations have extended their quest for profits to influence every level of modern healthcare, from so called “peer-reviewed” journal studies through to consumer ads for prescription drugs on cable TV. Pharmaceutical companies have little interest in herbal medicines, because plants are not inherently patentable, and freely available to all. The resultant effect of these various historical cultural political and economic factors is that the real principles of herbal medicine are not well-known, yet at the same time its tools, herbal medicines, are subject to extensive misrepresentation and negative publicity.

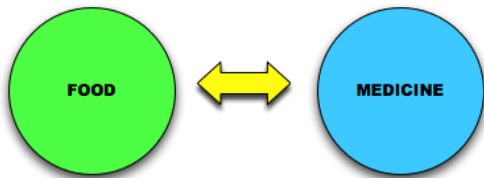
#### **Food as Medicine - Medicine as Food: The Basics.**

The principles underlying herbal medicine are relatively simple, but are quite distinct from those of conventional medicine. They start from the common sense view, originating in prehistory and still universal among indigenous cultures, about how to classify the different substances that humans ingest, based upon how the body responds or uses them. Accordingly, everything we consume falls into three broad groups: - food, medicine and poison. These are distinct yet overlapping categories.



Hippocrates, the father of Western medicine, advised his followers to “*let food be your*

*medicine and medicine your food*". All human cultures have understood this intimate link between food and medicine, just as most people today can intuitively understand the connection between diet and health: this is also the key to understanding herbal medicine. A "food" model of herbs is in fact at the core of herbal medicine. It is quite opposed to the mainstream view of botanicals whose "drug" model of herbs is based upon conventional "silver bullet" pharmacological understanding. Foods (and herbs) are complex, contain many different constituents, and furnish materials that are used by the body to nourish, support and reproduce its vital activities. The body "acts" upon foods, through digestion and assimilation to produce and reproduce itself; for maintenance, sanitation, repair and renewal. Food and medicine are theoretically and in reality closely connected.

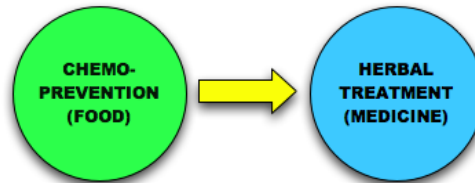


Population studies have shown that people in South East Asian countries have far lower risks of developing most cancers compared to those in North America, and it is considered that the consumption of foods such as garlic, ginger, cayenne, turmeric, soy and cruciferous vegetables play a key role in this "chemoprevention". Chemoprevention involves the inhibition of multiple aspects of the tumorigenic process. Chemopreventive agents are dietary ingredients, which being food derived, are considered pharmacologically safe. These dietary ingredients contain bioactive molecules such as organosulfur compounds from garlic, polyphenols from green tea and curcumin from turmeric, which exert the chemopreventive influences.

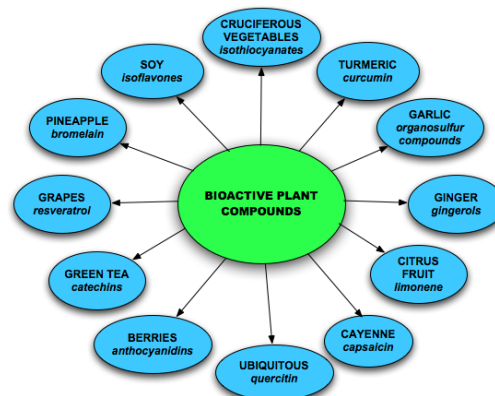
For herbalists, the ultimate difference between food and medicine is arguably one of intention. Herbalists have long used extractive techniques to concentrate the medicinal qualities of plants; by applying these time-

tested methods to chemopreventive agents, these are transformed into therapeutic tools with anticancer activity. The same compounds, when intentionally deployed by practitioners as botanical medicine, transform prevention into treatment.<sup>5, 6</sup>

Recently, numerous reviews of plant derived chemopreventive compounds have identified their potential role in treatment of cancer.<sup>6-8</sup>



Some of the more common chemopreventive compounds derived from dietary ingredients are listed in the following chart:



Of course, a simplistic model of food medicine and poison may have worked well for Paleolithic peoples, but it has become seriously distorted in our advanced industrial societies. Poisons are ubiquitous, in the environment and food chain, and are detectable in large numbers in our bodies.<sup>9</sup> Meanwhile, food, or at least much of what is sold as "food" can arguably be categorized as poison in terms of its industrial processing, synthetic additives, colorings and preservatives, pesticide residues, and a nutrient composition emphasizing "bad" fats and simple sugars and depleted of beneficial

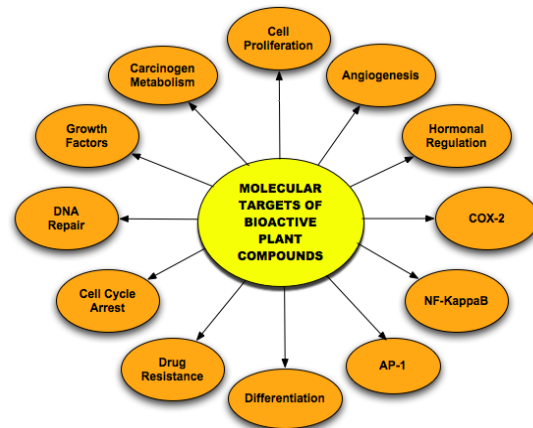
minerals, vitamins and phytonutrients. Finally medicine, that is pharmacotherapy, has in turn become a major killer, quite properly described as poison, and a leading cause of death among US citizens.<sup>10</sup> In our practice, we have found that explaining the food-medicine-poison model to stage 4 cancer patients, (who have already “flunked” prevention) makes it easier for them to grasp the importance of dietary changes: everything they eat from must be “medicine” in order to help reverse progression of their disease.

### Molecular Multitasking

Chemopreventive plant compounds affect all phases of the cancer process, i.e., tumor initiation, promotion and progression. Botanical medicines are complex molecular multitasker mixtures, simultaneously exerting influence on different levels and via different mechanisms.<sup>5</sup> By contrast, pharmaceutical drugs are classically single synthetic compounds, ideally expressed by the silver bullet model, that acts upon a single specific mechanism, whilst minimizing collateral damage (AKA side effects).

Modern research is confirming that many chemopreventive dietary compounds are active at precisely the molecular targets that scientists seek to affect with the newer generation “targeted” biological response modifier drugs, typically the monoclonal antibody agents.<sup>6,11,12</sup> Despite massive investment and effort, only a handful of such drugs have been licensed for cancer to date – examples include Iressa®, Gleevec®, Herceptin® and Avastatin® among others. Yet chemopreventive plant compounds have been shown to engage many of the same molecular targets that have been identified by modern cancer researchers and targeted by these drugs. With an established safety record and a fraction of the cost of conventional chemotherapy, these agents represent an enormous and almost untapped resource for cancer treatment. Some of the molecular targets of plant compounds are illustrated in the diagram below. Most of the chemopreventive compounds influence several of these targets simultaneously and often synergistically. For example green tea compounds act on signal transduction factors,

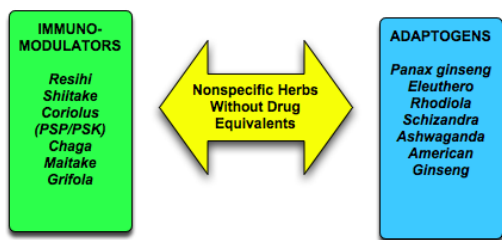
inhibit COX-2, promote cell cycle arrest, increase apoptosis and disable multidrug resistance pumps.



### Immunomodulation

Another key role for plant medicines in cancer is immunomodulation. A common misconception among lay people is the oversimplified idea that “stimulating the immune system” will eradicate a cancer. In fact, cancer evades immune system surveillance because of the low immunogenicity of most tumors. Nonetheless, many patients with advanced malignancy do have lowered levels of innate (Th1) immunity, the branch of the immune system whose cells, such as natural killer (NK) cells, directly kill tumor cells. A variety of herbal medicines and plant compounds directly stimulate this innate immune response. These same agents can be used to help protect bone marrow against the myelosuppressive effects of conventional chemotherapy. The two most important classes of herbs here are the immunomodulating medicinal mushrooms, such as Shiitake, Maitake, and Reishi and the “adaptogens”, including *Panax ginseng*, *Eleutherococcus*, *Rhodiola*, and others.

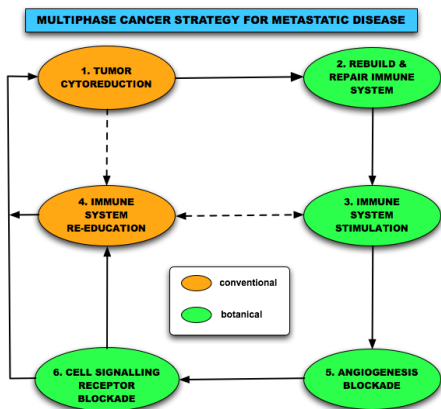
In both cases, we see that the plant medicines have no equivalent among pharmaceutical drugs. The mushrooms contain polysaccharides, which are not only immunostimulating, but have a multitude of anticancer effects, as well as non-specific effects of increasing longevity and reducing stress. The adaptogenic herbs such as Panax



ginseng are even more unique. Adaptogens are non-specific, non-toxic, and “normalizing”. This means the effect they produce varies according to the physiopathological state. For example, ginseng can be angiogenic in wound healing but in cancer, the same herb is *antiangiogenic*.<sup>13</sup> Herbalists consider this apparent paradox is typical of the normalizing properties of adaptogens, (which also have multiple anticancer effects, as well beneficial interactions with conventional chemotherapy and radiation) and illustrative of the wisdom of the body.

### Herbs and Multiphase Treatment Strategy

Advanced cancer is a multifactorial process which demands multifactorial treatment. Integrative strategies for metastatic disease may vary in detail but a working multiphase model is shown below (the phases are may overlap in practice).



The areas where botanical medicines are most effective are shaded (Phase 2, 3, 5 & 6 in the chart). Tumor cyto-reduction or debulking (Phase1) is best effected by conventional surgery or other physical means, or conventional chemotherapy (which should be assay driven<sup>1</sup>). Immune system re-education

<sup>1</sup> “assay driven” refers to live tumor resistance and

(Phase 4) is best performed by dendritic cell or other vaccines, most of these are investigational at this time.<sup>2</sup>

### A Note on Poison

When a poison is ingested, it acts in a harmful way upon the structure-function system of cells, tissues or organs of the body. This is the fundamental difference between medicine and poison. While the *body acts* on food, (and in our definition also upon medicine since food and medicine are interrelated) *poison acts* on (or harms) the body, actively disrupting the vital processes, interfering, interrupting, impairing, in a dynamic manner in contrast to the restorative, curative and yet passive forms of influence provided by medicine.

Although it is often said that the dose makes the poison, which may be relatively true, it is also the case that medicines, according to our fundamental definition, can never be toxic or poisons directly. The one is inherently curative, and the other is inherently damaging. Certain plants have furnished modern medicine with drugs that are used in cancer therapy as cytotoxic agents. Better-known examples among cancer drugs include Taxol from the Pacific yew tree, and the vinca alkaloids from the Madagascar periwinkle. These compounds, unlike the chemopreventive compounds described above, are effective as anti-cancer agents (in some cases) by virtue of their nature as poisons. The importance of this difference is considerable, for very often the fact that plants were the original source of some pharmaceuticals blurs the distinctions between two very different kinds of agents - medicines and poisons. This confusion has now been incorporated at subtle levels into the everyday language shared by herbal and mainstream medicine.

### Herb-Cancer Drug Interactions

There is a significant body of experimental and clinical data supporting a positive role for

sensitivity to chemo therapy drugs assays by test panels such as Weisenthal or Nagourney laboratories.

<sup>2</sup> The author is indebted to integrative oncologist Dr Dwight McKee for the model of multiphase treatment presented here, although it is based upon the work of many researchers and clinicians, both published and unpublished.

botanicals in combination with conventional treatments in oncology. Many chemopreventive compounds are associated with beneficial chemosensitization and radiosensitization, other plant compounds such as flavonoids disable the pumps that cause multidrug resistance. The immunomodulating and adaptogenic herbs described above protect against myelosuppression, which is the dose-limiting toxicity of many chemotherapeutic drugs, as well as increasing the ability of cancer patients to withstand the general stress of both chemo and radiation. Other herbs offer protection against specific organ toxicities of chemotherapy, such as ginkgo for platinum induced renal toxicity.<sup>14,15</sup> Almost invariably these plant medicines are, as described above, “molecular multitaskers”. Ginkgo for example also protects against ototoxicity and neuropathy, and at the same time is a radiation sensitizer by increasing local perfusion rates.<sup>16-19</sup> Green tea compounds not only enhance doxorubicin transport into malignant cells, it protects the myocardium against the cardiotoxic effects of the drug.<sup>20-24</sup> From the integrative perspective, the list of potential beneficial interactions between botanicals and conventional cancer treatments is long and impressive.

This is not to say that “adverse” interactions between herbs and drugs are not theoretically possible, but the problem is often vastly overstated, (for a particularly egregious example of this see the review by Sparreboom.<sup>25</sup>) Proper clinical knowledge of both the properties of herbs and drugs is needed to inform appropriate care and management; this will both limit any potential adverse reactions and permit the therapeutic exploitation of beneficial interactions. The food model is once again relevant, particularly since a wide range of dietary ingredients (including grapes, grapefruit and other citrus, broccoli and other vegetables, spices, wine, tobacco, char grilled meat and many more) can alter human drug metabolizing (detoxifying) enzymes. In addition, individual differences in genetic, biochemical, biological and lifestyle demographics contribute enormous variability to drug disposition. Herbal medicine has always considered each individual as a unique

entity, long before the much-heralded “discoveries” of pharmacogenomic variability.

To date, there is not a single verifiable case report in the literature of any harmful interaction between a botanical and conventional antineoplastic treatment. For practitioners of botanical medicine, negative and uninformed secondary articles proclaiming the portentous consequences of interactions between herbs and chemotherapy are sadly predictable.<sup>25</sup> For cancer patients and their advocates their effect is to create fear, and discourages them from employing effective integrative strategies that can enhance therapeutic outcomes.

### **The Wisdom of the Body**

Many questions asked by cancer patients (and care providers) cannot be answered definitively by the available scientific data, making decisions about treatment options hugely challenging. Sometimes enough research has not been done and sometimes the wrong question is asked by research, so the answer is unavailable. A good example is the issue of soy. Pharmaceutical companies have engineered “Roundup™ ready” varieties of GMO soy crops, which are industrially processed into convenience, packaged food, like TVP, frozen soy burgers and sweetened soy milk. Often, unnaturally high amounts of isoflavones (which may be extracted from other legumes) are added. The epidemiological data about soy and chemoprevention has little to do with these products. When in doubt, herbalists recommend the traditional forms of soy, fermented, organic foods like miso and tempeh, taken in moderation, like any healthy dietary ingredient. This is another expression of the principle that the body *acts* upon food and medicine, obtaining the materials that it requires for restorative purposes. The wisdom of the body is a metaphor for the Vital Process, a term disdained by modern medicine. Interestingly, Walter Cannon, regarded along with Claude Bernard as the father of modern physiology, entitled his key textbook, published in 1922, *The Wisdom of the Body*.

So herbalists will trust the wisdom of the body to recognize and make use of food that is organic, unadulterated, unprocessed and prepared in traditional ways. These foods furnish support for the body's nature and self-healing, and these options are invariably safe. Our bodies have co-evolved with plants, both as food and medicine, for billions of years, and there is a deep connection between humans and plants at many levels, from the sacred to the subcellular. The question of how helpful or otherwise soy may be in different clinical scenarios currently has no conclusive scientific answer, and there is no one-size-fits-all solution. In situations like this, where data is unavailable but patients have pressing questions, it is useful to remember the foundation of the food-medicine-poison model. The wisdom of the body and its vital process defines what is food, what is medicine, and what is poison. However, concentrated isoflavone supplements may also have a role in some situations, but in endocrine dependent reproductive malignancies the use of high doses of these materials, unlike food, requires experienced professional management.<sup>26</sup>

## CONCLUSION

Integrative strategies for treatment of cancer must include the benefits of botanical medicines. The difference between the core principles of herbal medicine and the mainstream medical model are profound, yet can be rendered accessible with a food-medicine-poison model of the therapeutic agents. This model is at the theoretical core of modern herbal medicine, and was brilliantly articulated by the US Physiomedicalists at the turn of the 19<sup>th</sup> Century, particularly by William Thurston in his *Philosophy of Physiomedicalism*.<sup>27</sup> The modern science of dietary chemopreventive compounds at the molecular level indicate the durability of this conceptual model as a therapeutic approach which will become increasingly important in the management of cancer, not only in prevention, but in the integrative treatment of advanced disease.

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 Contact [jtreasure@herbological.com](mailto:jtreasure@herbological.com)