

ORIGINAL



UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION

In the Matter of)
)
)
DANIEL CHAPTER ONE,)
a corporation, and)
)
JAMES FELJO,)
individually, and as an officer of)
Daniel Chapter One.)
_____)

Docket No. 9329

PUBLIC DOCUMENT

**COMPLAINT COUNSEL'S MOTION AND MEMORANDUM IN
SUPPORT OF THEIR MOTION TO EXCLUDE THE TESTIMONY AND
REPORT OF RESPONDENTS' EXPERT WITNESS SALLY LAMONT**

I. INTRODUCTION

Complaint Counsel hereby moves to exclude the expert testimony of Sally LaMont, N.D. ("LaMont") from the trial scheduled for this case regarding the alleged deceptive advertising engaged in by Respondent Daniel Chapter One ("DCO") and its principal, Respondent James Feijo ("Respondents") in their sale of Bio*Shark, GDU, 7 Herb Formula and BioMixx ("DCO Products"), which they claim prevent, treat, or cure cancer, because this testimony fails to meet the criteria for admissibility of expert testimony established in *Daubert*.

Respondents have tendered LaMont as "an expert in naturopathic medical, herbal medicine, functional medicine ... [and] as an expert on nutritional supplements and botanical medicines in the prevention and treatment of illness and as an expert in reviewing the evidence that supports the functional issues of the four products that are the challenged products"

(Lamont Deposition Transcript, dated February 17, 2009 (“LaMont Tr.”), at 7: 1.20 - 8: 1.2)¹.

LaMont is a naturopathic doctor who specializes in “health promotion...disease prevention and the treatment of disease with...natural therapies that strengthen the body’s innate healing capacities” (LaMont Tr. 9: 1.9-18). In her report, LaMont opines that there is a “reasonable basis” for Respondents to claim:

1. “[T]hat the ingredients of GDU contain bromelain, a source of natural proteolytic enzymes from the pineapple, which helps digest unwanted proteins. GDU also contains turmeric, feverfew and quercetin (sic), which help to reduce inflammation and relieve pain. Next, it is reasonable to claim that these ingredients as a whole may be used as an adjunct to cancer therapy, and that the ingredients possess a wide range of actions as anti-inflammatory agents.
2. [T]hat the ingredients of 7 Herb Formula fight tumor formation, and fight pathogenic bacteria.
3. [T]hat the ingredients of BioMixx boost the immune system, build lean body mass and support healing...[and that] these ingredients assist the body in fighting cancer, cachexia and . . . the destructive effects of radiation and chemotherapy treatments.
4. [T]hat pure skeletal tissue of sharks provides a protein that inhibits angiogenesis - the formation of new blood vessels. It is also reasonable to claim that angiogenesis has been demonstrated to inhibit tumor growth in some studies.”

(Expert Report of Sally LaMont, N.D., L.Ac., dated February 4, 2009, p. 40) (“LaMont Rpt.”), attached hereto as Exhibit A).

As set forth below, the Court should exclude LaMont’s report and testimony from the trial in this action because she lacks the knowledge, skill, experience, training or education required to testify on the serious cancer claims at issue here. Further, the Court should exclude

¹Complaint Counsel refers the Court to the two copies of the deposition transcript of Sally LaMont which were previously filed with the Court, 1) as an exhibit to the Motion for Summary Decision and 2) as a proposed trial exhibit. Therefore, in consideration of not burdening the Court with additional copies and in order to preserve natural resources, the pages are not attached hereto.

LaMont's opinions because they are irrelevant to the issues of this case and/or are unreliable as they are not grounded on sufficient facts and data.

II. LEGAL STANDARD FOR THE ADMISSIBILITY OF EXPERT TESTIMONY

Commission Rule of Practice 3.43(b) requires that evidence must be relevant, material and reliable in order to be admitted. Rule of Practice 3.43(b). With respect to expert witness testimony, a witness "qualified as an expert, by knowledge, skill, experience, training or education" Fed. Rule of Evid. 702, may testify if: "(1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case." *Id.*; *see also*, *Daubert v. Merrell Dow Pharmaceuticals*, 509 U.S. 579 (1993) and *Kumho Tire Co. Ltd. v. Carmichael*, 526 U.S. 137, 153-54 (1996). Respondents as the proponents of the expert testimony, have the burden of proving its admissibility. *Graf v. Baja Marine Corp., et al.*, 2009 U.S. App. LEXIS 1986 at *21 (11th Cir. Feb. 2, 2009), *citing U.S. v. Frazier*, 387 F.3d 1244, 1260 (11th Cir. 2004).

Moreover, this Court has the authority to exclude expert testimony of any nature, whether it is based on "scientific, technical, or other specialized knowledge," if it lacks appropriate indicia of helpfulness to the fact finder. *Kumho Tire*, 526 U.S. at 141. In exercising what has been characterized as "general 'gatekeeping' authority," *id.*, the Court may reject expert testimony that will not "assist the trier of fact to understand the evidence or determine a fact in issue." *Daubert*, 509 U.S. at 591. Indeed, the law is well-established that "[e]xpert testimony that does not relate to any issue in the case is not relevant and, ergo, non-helpful." *Id.*

Respondents cannot meet their burden under the Commission's Rules of Practice, FRE

702 and the principles set forth in *Daubert* of demonstrating that the expert report and testimony of LaMont is admissible for the following reasons explained more fully below: she is not qualified to testify as an expert about cancer; her testimony is irrelevant; and her testimony is not based upon sufficient facts and data. Consequently, the Court should exclude her report and testimony from any trial in this case.

III. LAMONT'S TESTIMONY IN THIS MATTER SHOULD BE EXCLUDED

A. Lamont is not Qualified to Testify as an Expert in this Case.

LaMont is not qualified to testify about the serious claims that Respondents have made that the DCO Products prevent, treat, or cure cancer or tumors. LaMont has never served as an expert witness in any capacity (LaMont Tr. 54: 1.9-12). LaMont is neither a trained medical doctor nor an oncologist. She herself has no training in naturopathic oncology although there are naturopaths who practice oncology (LaMont Tr. 12: 1.7-11). Instead LaMont has kept her "practice very general" (LaMont Tr. 11: 1.20 - 12: 1.2).

According to LaMont, "cancer must be treated with conventional therapies" (LaMont Tr. 15: 1.1-4). LaMont believes that even though plant foods have powerful effects, "patients with cancer...[should not] abandon using the most effective methods" available to treat their disease (LaMont Rpt. p.6). In her own practice, she refers any patient with "a diagnosis that looks like cancer" to a traditional physician for treatment because conventional therapies are the best treatment available for cancer patients. LaMont always encourages her patients suffering from cancer to work with "their oncologist and utilize protocols that are proven to be most effective for their cancer" (LaMont Tr. 49: 1.19-25). At most LaMont will work with the physician to "comanage" a cancer patient's care (LaMont Tr. 10: 1.16-22).

Apart from having no education or experience as an expert or as a health professional

treating cancer, LaMont has never conducted a scientifically controlled study of any kind (LaMont Tr. 184: 1.12-14) that might assist her in evaluating whether there was a scientific basis for Respondents' cancer claims. LaMont has neither the experience, training nor expertise in the cancer treatment area to render opinions in this case. Accordingly, LaMont is not qualified to testify about the cancer claims at issue in this case, and her testimony should be excluded. *See e.g., U.S. v. 99.66 Acres of Land*, 970 F.2d 651, 657 (9th Cir., 1992)(expert testimony concerning residential appraisals properly excluded where witness had no appraisal experience and “personal unfamiliarity” with underlying data).

B. LaMont's Testimony Should be Excluded as Irrelevant.

LaMont's testimony is irrelevant for several reasons and should be excluded.

First, her testimony focuses on “traditional use evidence” i.e. the way in which plant medicine has been used in cultures for centuries (LaMont Rpt. p. 7), rather than analyzing the science available to support Respondents' claims. LaMont's opinion is limited to “traditional use” of these supplements, e.g., “GDU helps digest unwanted proteins” (LaMont Rpt. p. 40) or “BioMixx boosts the immune system” (LaMont Rpt. p. 40), without addressing how the products can prevent, treat or cure cancer. Thus, LaMont's opinion simply does not address the serious claims that Respondents make and should be excluded as irrelevant.

Secondly, LaMont's opinions on policy issues regarding the relative importance of pharmaceuticals versus natural medicines are not relevant. In LaMont's view, the fact that foods and plants have been used as medicine for “millenia” without evidence of serious harm should not be ignored (LaMont Rpt. p. 7). LaMont also opines that plant chemicals are difficult to study in a standard fashion because plants have multiple agents that work together to treat disease (LaMont Rpt. p. 7). Thus, according to LaMont it can be difficult and costly to try and

isolate “a single agent affecting a single target” so that it can be studied. *Id.* LaMont also opines that it is wrong that cancer patients currently “are denied the opportunity to [use] natural therapies in a clinical setting until they have failed conventional therapies” (LaMont Rpt. p. 7).

Respondents’ effort to rely on LaMont’s testimony represents another attempt to deny the fact that Respondents make disease claims. LaMont’s opinions about the ease of testing plant chemicals, or how or when herbal remedies are made available to cancer patient are irrelevant to this case which focuses solely on Respondents’ claims that their products prevent, treat, or cure or cancer. LaMont’s opinion will not assist the Court in evaluating whether there was competent and reliable scientific evidence to support Respondents’ claims about the DCO Products. As noted above, this Court may exclude expert testimony, whether “scientific, technical, or other specialized knowledge,” if it lacks appropriate indicia of helpfulness to the fact finder. *Kumho Tire Co.*, 526 U.S. at 141 (1999). Accordingly, the opinions should be excluded.

C. Lamont’s Opinion Lacks Sufficient Facts and Data and Should be Excluded as Unreliable.

Finally, Lamont’s opinions are not based on sufficient facts and data as required under FRE 702 and *Daubert* as to make them reliable. The paucity of facts and data underlying her opinions was made clear in her deposition through her admission that she had only “limited knowledge of the DCO Products” and so could not defend them (LaMont Tr. 78: 1.1-8).

LaMont’s opinions are grounded on insufficient facts or data to render a reliable opinion here.

LaMont confirmed her lack of foundation when she testified more specifically about the DCO products. LaMont had never heard of Bio*Shark, 7 Herb Formula, GDU, and BioMixx until being engaged as an expert in this case (LaMont Tr. 34: 1.5-7). LaMont has never reviewed

the medical records of any patient who has taken the products to treat or cure their cancer (LaMont Tr. 185: 1.3-5). She acknowledged that there have been no clinical studies performed on the DCO Products (LaMont Tr. 48: 1.21-23) and that she herself has not specifically studied the products (LaMont Tr. 78: 1.18), beyond reading their labels (LaMont Rpt. p. 4).

Regarding Bio*Shark, Dr LaMont acknowledged that she did not have any facts or data demonstrating that Bio*Shark actually “inhibits tumor growth (LaMont Tr. 91: 1.15-19). Furthermore, she had no specific information or data on showing the bioavailability, the absorption and distribution of Bio*Shark’s shark cartilage (LaMont Tr. 101: 1.23 - 102: 1.12). LaMont testified that this information would be essential in determining whether Bio*Shark was effective in treating cancer. *Id.*

With respect to 7 Herb Formula, LaMont did not know what the recommended doses of 7 Herb Formula were and thus, could not say if it was given at an effective dosage (LaMont Tr. 104: 1.5-7). Moreover, LaMont did not have facts or data about the amount of cat’s claw in 7 Herb Formula, which information would be necessary in determining whether the product is effective in treating cancer (LaMont Tr. 129: 1.18-22).

Similarly with GDU, LaMont had no information about whether the recommended dose of GDU would, on its own, be effective in eliminating tumors (LaMont Tr. 74: 1.19 - 75: 1.3). Indeed, LaMont found that the dosage of quercetin, a key component contained in GDU, was on the “lower end of the therapeutic spectrum” (LaMont Tr. 67: 1.8-16) putting the product’s effectiveness as a therapeutic agent in doubt.

With BioMixx, LaMont had no data showing that this product had ever gone through clinical trials to support a claim that its use could cure cancer (LaMont Tr. 172: 1.14-20). In fact, LaMont did “not think that as a stand-alone [product], BioMixx [could] cure ... cancer or

probably even effectively treat it” (LaMont Tr. 176: 1.16-22).

Despite her lack of essential information about the products, LaMont still concluded that there was a “reasonable basis” for Respondents to make their claims about the DCO Products. Moreover, LaMont reaches this finding despite the fact that her report cites to no controlled studies of the DCO Products or their components. LaMont’s conclusion clearly was based on speculation and therefore should be excluded as unreliable.

IV. CONCLUSION

Because LaMont is not qualified to testify in this case and her opinions are irrelevant and unreliable because they are not based on sufficient facts and data, Complaint Counsel respectfully requests that the Court enter the proposed order annexed hereto, excluding the LaMont from testifying at trial.

Respectfully submitted,



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Dated: March 16, 2009

Exhibit A

REPORT OF EXPERT WITNESS SALLY LaMONT
In the Matter of Daniel Chapter One
FTC Docket #9329

I. QUALIFICATIONS

As you will see in my curriculum vitae, I am dually licensed in California as naturopathic doctor and acupuncturist. I graduated from the National College of Naturopathic Medicine in Portland, Oregon in 1981 and have been licensed in both Oregon and California to practice naturopathic medicine. I graduated from Emperor's College of Oriental Medicine in 1986 and have been licensed in both California and Oregon to practice acupuncture. I am a member of the American Association of Naturopathic Physicians and the California Naturopathic Doctors Association and the California Society of Oriental Medicine and Acupuncture.

I have practiced naturopathic medicine since 1981, working with diet, nutritional supplements, botanical medicine, and mind-body treatments. Since being licensed as an acupuncturist in California in 1986, I have integrated acupuncture and Chinese herbal medicine into my work. My practice focuses on helping people identify the root causes of their condition, removing the obstacles to cure, and developing personalized natural treatment protocols to resolve symptoms and promote health. I evaluate patients through a variety of state-of-the-art laboratory tests and integrate nutritional medicine with herbal medicine and acupuncture.

Since 2005, I have been on the faculty of San Francisco State University's "Institute for Holistic Healing Studies" within their Department of Health Education. Over the past 4 years, her popular classes include "Naturopathic Medicine and Personal Wellness", "Nutrition and Herbal Medicine" and "The Holistic Health Speakers Series".

In 1998, I joined the board of directors of the California Naturopathic Doctors Association (CNDA). I took a brief sabbatical from my practice in May of 2000 to serve as Executive Director of the CNDA and lead the successful legislative campaign to

license NDs in California. Passage of the Naturopathic Doctors Practice Act resulted in the creation of the Bureau of Naturopathic Medicine within California's Department of Consumer Affairs. Licensure of NDs provides Californians legal access to the care of licensed naturopathic doctors. The established scope of practice in California allows licensed NDs to serve as primary health care providers who treat acute and chronic conditions, in a prevention-oriented approach to healthcare.

For the last 22 years, I have witnessed the tremendous value that changes in lifestyle, diet and the correct use of the nutritional and herbal supplements can provide. During this time in practice I have had the opportunity to provide adjunctive care to patients undergoing conventional cancer treatment, utilizing a range of dietary supplements and botanical medicines that were compatible with their conventional regimen. The body has immense self-healing capacities, which when properly supported can respond and heal from even serious diseases. In my experience, people receiving chemotherapy and radiation fare better, in both the short and long term, when they concurrently use natural therapies and lifestyle to mitigate the side effects and support their overall health.

An additional note: I have had the unusual experience of supporting my first husband, John LaMont, M.D., a family practitioner, through his death from non-Hodgkins lymphoma in 1992. John lived for 16 years with this cancer and as one of the first medical doctors interested in nutrition and natural therapies, he pursued virtually all known conventional and alternative treatment modalities. Together we explored a variety of nutritional interventions including the use of high dose intravenous vitamins, traditional Chinese medical options including acupuncture and variety of Chinese herbal medicine, Ayurvedic medicine including working with Dr. Deepak Chopra in 1991, Dr. Stanislaus Burzynski's antineoplastic therapies and well as 4 rounds of conventional chemotherapy, radiation, monoclonal antibody therapies at Stanford and a bone marrow transplant.

Together, my education and these experiences give me a unique perspective as an expert witness in this case.

II. SCOPE OF WORK

I have been asked by the attorneys representing Daniel Chapter One to provide a opinions on the use of nutritional supplements and botanical medicines in the prevention and treatment of illness, including but not limited to cancer. In addition, I was asked to review the evidence that exists regarding the mechanisms of action of the major constituents of DCO's cited products and to provide an opinion of that evidence for:

- "GDU"
- "7 Herb Formula"
- "BioMixx"
- "BioShark"

Compensation: \$175/hour

Prior expert testimony: see prior disclosures.

III. MATERIALS CONSIDERED

To form my opinion, I have conducted literature searches on PubMed, that includes over 18 million citations from MEDLINE and other life science journals for biomedical articles back to 1948. PubMed includes links to full text articles and other related resources. I also utilized Google, and numerous websites including the website of the Memorial Sloan-Kettering Cancer Center, Dr. Duke's Ethnobotanical and Phytochemical Database and the database of the American Botanical Council. I have utilized several books, including Medicinal Plants of the World (Van Wyk and Wink). In addition, I have drawn from my experience as a practicing naturopathic doctor and acupuncturist who utilizes dietary supplements and botanical medicines in daily practice.

I have also reviewed the information provided to me by Daniel Chapter One, including the Daniel Chapter One Product Labels, Literature provided by Daniel Chapter

One, and the Summary of Medical Evidence provided Daniel Chapter One, all of which I understand have been provided to the FTC by Daniel Chapter One and/or its counsel.

IV. SUMMARY OF OPINIONS ON THE EVIDENCE PRESENTED

Hippocrates, the Father of Medicine, advised his patients to “Let your food be your medicine and your medicine be your food.” Traditional and indigenous cultures naturally understood the connection between plants as both their food and their medicine. Today, there is a growing body of scientific evidence to substantiate the fact that the natural compounds present in plants act in multiple ways to support our innate homeostatic mechanisms, improve physiological function and reduce the expression of disease. “Epidemiological studies consistently indicate that consumption of fruits and vegetables lowers cancer risk in humans and suggest that certain dietary constituents may be effective in preventing (colon) cancer. Plant-derived phenolic compounds manifest many beneficial effects and can potentially inhibit several stages of carcinogenesis in vivo.” *Carcinogenesis* 2000 May; 21(5): 921-7. Many population studies have demonstrated lower incidences of several chronic degenerative diseases in cultures that eat a plant-based diet compared to the Western diet. Campbell, TC, *The China Study* (Dallas, TX: Ben Bella Books 2005); Cordain, L., “Origins an Evolution of the Western Diet: Health Implications for the 21st Century,” *American Journal of Clinical Nutrition* 81, no.2 (2005): 341-54.

Humans have co-evolved with plants and we survive and thrive today because our bodies utilize plants for sustenance. The macronutrients, micronutrients and phytonutrients in food and phytochemicals in plants are biologically active compounds that influence our metabolism. A wealth of information on potential treatments for cancer and other conditions dwells in the clinical knowledge of traditional and indigenous cultures and their Material Medica. Herbalists have long known that herbs are an extension of food and have used the plants of this earth as medicines. They have prepared teas and concentrated extracts to potentiate the therapeutic effects of these phytomedicines. More recently, ethnobotanists and pharmacognocists have worked to identify and catalogue these plants and their bioactive constituents. International researchers have begun the laborious process of isolating the biologically active

compounds and examining their mechanisms of action in order to determine their effect on various aspects of disease, especially carcinogenesis (i.e. the production of cancer or carcinoma).

The biologically active compounds in plant medicines have been termed “secondary metabolites”. Interestingly, the compounds produced by one species to protect them from their environment actually influence the metabolism of another species, and mimic the structure of our hormones, neurotransmitters and other aspects of our metabolism. These biologically active compounds have interacted with and shaped our physiological processes over millennia in a process termed “evolutionary molecular modeling”. One of the advantages of using the phytonutrients present in food and the phytochemicals present in plants is that they exert their influences on multiple molecular targets. “Secondary metabolites usually are multifunctional compounds because most of them carry more than one pharmacologically active chemical group. In addition, secondary metabolites usually occur in complex mixtures. In consequence, the extract of a medicinal plant affects more than one molecular target and it is likely that several targets are affected concomitantly when taking phytomedicines. In complex disorders, the application of such extracts increases the chances of “hitting” one or several relevant targets”. Van Wyk and Wink, *Medicinal Plants of the World*, Timber Press, Portland, Oregon 2003.

In his recent book “Anticancer -- A Way of Life”, oncologist David Servan-Schreiber, M.D., Ph.D., who is himself a two-time cancer survivor, suggests we can approach cancer in this way: “There are certain circumstances under which these savage bands are disrupted and lose their virulence: (1) when the immune system mobilizes against them, (2) when the body refuses to create the inflammation without which they can neither grow nor invade new territories, or (3) when blood vessels refuse to reproduce and provide the supplies the cells need to grow. These are the mechanisms that can be reinforced to prevent the disease from taking hold. Once a tumor is installed, none of these natural defenses can replace chemotherapy—or radiotherapy. But they can be exploited, accompanying conventional treatments, to fully mobilize the body’s resistance to cancer”. Dr. Servan-Schreiber goes on to elucidate the growing body of evidence that a

diet rich in chemoprotective plants can assist us in multiple ways in our fight to prevent and support the treatment of cancer. (Servan-Schreiber, D., *Anticancer—A Way of Life*, Viking Penguin Press, New York, New York, 2008).

Scientific research, a selection of which follows in this report, demonstrates that the phytonutrients and phytochemicals present in plants have the capability to act at the precise molecular targets that scientists are seeking to affect with the new generation of biological response modifiers:

- Immunostimulatory effect: astragalus and medicinal mushrooms
- Anti-inflammatory effect: curcumin and bromelain
- Anti-angiogenic effect: green tea and ginseng

Some examples of how plant phytochemicals act as “biological response modifiers” to affect our physiological process are detailed here in this report:

- Watercress: rich in glucosinolates that inhibit carcinogenesis and induce apoptosis
- Turmeric rich in curcuminoids that inhibit COX2
- Bromelain: proteolytic and anti-inflammatory effect
- Quercetin (ubiquitous in plants): inhibits tumor growth, alters cell cycle regulation
- Green tea (EGCG): signal transduction, inhibits COX2 and induces apoptosis,

Knowledge of this kind of information should empower us to use these compounds as our food and as our medicine. The awareness of the powerful chemoprotective effects of plant foods and medicines should not influence patients with cancer and other serious diseases to abandon using the most effective methods that modern medicine has to offer. Furthermore, such knowledge does not diminish the need for further research but instead should hasten its pace.

“Phytomedicines often contain a mixture of substances that have additive or even synergistic effects, so that the health benefits are difficult to test or verify. Plant medicine

or phytochemicals may have subtle effects of several different biochemical pathways and receptors in the mind-body continuum that may all contribute directly and indirectly to restore equilibrium and balance. It is hard to dismiss medical claims of safety and efficacy when a plant medicine has been used in traditional cultures for centuries without evidence of serious side effects. Research results generated over the last few decades have given us a much better understanding of the scientific rationale behind many natural remedies.” Van Wyk and Wink, *Medicinal Plants of the World*, Timber Press, Portland, Oregon 2003.

Without a doubt, research is urgently needed to elucidate the mechanisms of action of phytonutrients and phytochemicals in the prevention and treatment of disease. The very complexity of these compounds presents immense challenges for research since they do not occur, nor do they act in isolation. One challenge with this approach is that it reduces the naturally occurring agent, which contains multiple compounds affecting multiple targets, to a single agent affecting a single target. While it is urgent that we understand the secondary metabolites and their actions, developing a new drug from that information is not the only worthwhile path. Adding to the challenge is the fact that research dollars are limited when natural agents can't be patented and their sale will never recover the cost of the research. As pharmaceutical scientific research works to identify new potential drugs from natural agents, it tends to diminish or dismiss the therapeutic value of the former.

Traditional use evidence does not replace human clinical trials. There are real limits to our current understanding of plant-based medicines that rests mostly on cultured cell lines and animal models. But many would argue that it is not essential that we wait to recommend the use of the original plant compound until all the evidence has been collected. The current situation is that cancer patients in particular are denied the opportunity to utilize natural therapies in a clinical setting until they have failed conventional therapies. In our rush to identify and utilize the most biologically active components of food and botanical medicines, we must respect the fact that for millennia mankind has used these foods and plants without evidence of serious harm.

V. ANAYLSIS AND FINDINGS

A. GDU

The four main ingredients in GDU are reviewed in this document.

- 1) Bromelain
- 2) Turmeric
- 3) Feverfew
- 4) Quercetin

SCIENTIFIC NAME: ANANAS COMOSUS (BROMELIACEAE)

Common name: Bromelain

Historical use: Bromelain belongs to a group of plant-derived proteolytic enzymes isolated from the stem and core of the pineapple. It has been used in the Chinese Materia Medica, other Asian cultures and by Western herbalists for a wide range of applications including but not limited to traumatic injury and arthritis and cancer.

Clinical Summary:

Bromelain has many in vitro and in vivo studies and its properties include: 1) the ability to interfere with growth of malignant cells; 2) inhibit platelet aggregation; 3) fibrinolytic activity; 4) anti-inflammatory action; 5) skin debridement properties. These biological functions of bromelain, a non-toxic compound, have therapeutic values in modulating a) tumor growth; b) blood coagulation; c) inflammatory changes; d) debridement of third degree burns; 3) enhancement of absorption of drugs. J Ethnopharmacol. 1988 Feb-Mar; 22(2):191-203.

Biochemically active constituents and known mechanisms of action:

Chemical constituent: Sulphydryl proteolytic enzyme, cysteine-proteinase. Bromelain also contains a peroxidase, acid phosphatases, several proteases inhibitors and organically bound calcium. Alt Med Rev 1: 243-257.

In addition, CCS and CCZ are two novel constituents (proteases) that and bind the growth of a broad range of tumor cells including breast, colon, lung, ovarian and melanoma. Med Res News 2005; <http://www.qimr.edu.au>

Bromelain has been demonstrated to:

- Reduce platelet aggregation and adhesion of platelets to blood vessel endothelial cells.
Cell Mol Life Sci 2001;58:1234-45.
- Act as anti-inflammatory agents in various forms of arthritis and inflammatory states via reduction in PGE2 and TXA2. Ethnopharmacology 22:191-203
- Down-regulate immunosuppressive cytokine TGF-beta, inhibits tumor cell growth, modulation of immune cell function, modulation of cell adhesion molecules and the effects on platelet aggregation and thrombosis. Cancer Chemother Pharmacol 2001; 47: S10-5 & Cell Mol Life Sci. 2001 Aug;58(9):1234-45
- Systemic enzyme therapy (including bromelain) significantly decreased tumor-induced and therapy-induced side effects and complaints such as nausea, gastrointestinal complaints, fatigue, weight loss, and restlessness and obviously stabilized the quality of life.
Integr Cancer Ther. 2008 Dec; 7(4):311-6
- The anti-metastatic effect of bromelain occurs with or without its proteolytic and anticoagulant activity: Journal of Can Res Clin Onc. 1998; 114: 507-508
- Bromelain treatment alters leukocyte expression of cell surface molecules involved in cellular adhesion and activation. Clin Immunol. 2002; 104:183-190
- Pretreatment with bromelain of human T cells cleaves CD44 surface adhesion molecules and markedly enhances CD2-mediated T cell activation. J Immunol 1992; 149:3809-16

- In addition, in vitro studies have shown that bromelain can:
 - inhibit the cytokines IL 4, IL2, gamma interferon
 - reduce cell surface receptors CD44 which is associated with leukocyte migration and induction of proinflammatory mediators
 - reduce CD4 lymphocytes (primary effectors in animal models of inflammation)
 - block growth of a broad range of tumor cells including breast, lung, colon, ovarian and melanoma via two proteins, CCS and CCZ discovered in 2005 by researchers at Queensland Institute for Medical Research.

Pakistani Journal of Nutrition Review 7 (4); 513-520, 2008

- Inhibit the first step of metastasis by diminishing the expression of intracellular compounds that degrade the intracellular matrix and allow migration of metastatic cells through tissues. Cell Mol Life Sci. 2001 Aug;58(9):1234-45
- Bromelain reversibly inhibits invasive effects on glioma cells; These results indicate that bromelain exerts its anti-invasive effects by proteolysis, signaling cascades, and translational attenuation.

Neoplasia. 2001 Nov-Dec;3(6):469-79

Adverse reactions: diarrhea, GI disturbance, allergic reactions (to pineapple). Cell Mol Life Sci. 2001 Aug;58(9):1234-45

Herb/Drug Interactions:

Bromelain may increase blood and urine levels of antibiotics.

Bromelain may change the effect of drugs such as 5-FU and vincristine.

Bromelain may increase the risk of bleeding due to its antithrombotic effects.

<http://www.mskcc.org/mskcc/html/69152.cfm>

SCIENTIFIC NAME: RHIZOMA CURCUMA LONGA

(ZINGIBERACAE)

Common Name: Turmeric, Indian saffron

History of use: Turmeric is a yellow-pigmented spice with a long history of use in Asian cooking and as Traditional Chinese and Ayurvedic medicine. It is part of the ginger family and has been used as an anti-inflammatory. It has been used for centuries in the Asian countries without any toxic effects. *Curr Pharm Des.* 2002; 8(19):1695-706

Clinical summary: A growing body of research suggests that curcumin has a potential for the prevention and treatment of cancer. Preclinical trials have shown that curcumin can both inhibit the formation of tumors in animal models and act on a variety of molecular targets involved in cancer development. In vitro studies have shown that curcumin induces apoptosis and some degree of selectivity of cancer cells. Clinical trials have revealed that curcumin is well tolerated and may produce antitumor effects in people with precancerous lesions or who are at high risk for developing cancer. This seems to indicate that curcumin is a pharmacologically safe agent that may be used in cancer chemoprevention and therapy. Both in vitro and in vivo studies have shown, however, that curcumin *may* produce toxic and carcinogenic effects under certain circumstances and specific conditions and may alter the effectiveness of chemotherapy and radiotherapy.

Mol Nutr Food Res. 2008 Jun; 52 Suppl 1:S103-27

Human clinical trial: Oral curcumin is well tolerated and, despite its limited absorption, has biological activity in some patients with pancreatic cancer. *Clin Can Res.* 2008; 14(14): 4491-4499.

Turmeric has demonstrated anticarcinogenic effect in cultured cell lines and animal models, at all phases of cancer growth including initiation, post-initiation, promotion, and progression, allowing it to be useful in secondary prevention. *Cancer Research.* 1999 Feb 1 (59): 597-601

The current science indicates multiple mechanisms of action to support the intake of such a level of turmeric along with other dietary sources of flavonoids (quercetin) as a reasonable suggestion for individuals who are fighting cancer.

Biochemically active constituents and known mechanisms of action:

To date, at least 94 biologically active compounds have been isolated from turmeric (Dr. Duke's Phytochemical and Ethnobotanical Database (accessed 1/09).

The plant derived phenolic compound curcumin (diferuloylmethane) is the most active constituent.

Curcumin functions as a potent COX 2 inhibitor with anti-inflammatory, anti-oxidant and multiple anticancer activities in dozens of vitro studies and some human clinical trials, a selection of which follows:

Mol Nutr Food Res. 2008 Jun;52 Suppl 1:S103-27

- Curcumin induces apoptosis (programmed cell death) in both androgen-dependent and androgen-independent prostate cancers. Prostate Cancer and Prostatic Diseases. 2000 Aug; 3(2):84-93 PMID: 12497104
- Curcumin has a chemoprotective and growth inhibitory action against a variety of cancer cell lines. Curcumin works in concert with TNF-related inducing ligand (TRAIL) and sensitizes androgen sensitive human prostate cancer cells lines to trigger apoptosis. Mol Cancer Ther. 2003 Jan;2(1): 95-103
- Curcumin inhibits:
 - Lipoygenase activity and the leukotrienes the follow
 - COX 2 expression and the proinflammatory prostaglandins that follow.
 - The initiation of carcinogenesis by inhibiting cytochrome p450 enzymes and increases glutathione S-transferase
 - The promotion and progression of carcinogenesis (S,G2/M cell cycle phase and induction of apoptosis)
 - The growth of DNA mismatch repair of defective colon cancer cells.

- Curcumin exerts its anti-carcinogenic properties by inducing modulation of the cell cycle and apoptosis by inhibiting proliferation and inducing apoptosis in specific gastric and colon cancer cell lines. *Anticancer Research*. 2001 Mar-Apr; 21(2A):873-8
- Curcumin inhibits human colon carcinoma (Lovo) cell proliferation in a dose dependent manner, and induces apoptosis in colon cancer cells and arrests the cell cycle in S, G2/M phase. *Anticancer Res*. 1999 Sep-Oct;19(5A):3675-80.
- Curcumin decreases the number (and size) of AOM-induced tumors in mice, as well as the percent of mice that get tumors; decreases the numbers of papillomas and squamous cell cancers of forestomach and adenomas and adenocarcinomas of the duodenum and colon
Cancer Research. 1994 Nov 15; 54(22): 5841-7
- Curcumin has a chemoprotective effect in mice with AOM induced colon cancer in various stages of tumorigenesis. *Cancer Res*. 1999 Feb 1; 59(3):597-601
- Curcumin suppresses Apc (gene mutation) that causes intestinal adenomas in animal models *Carcinogenesis*, 2000 May;21(5): 921-7
- Curcumin is known to down regulate Cyclin-D1 expression through activation of both transcriptional and post-transcriptional mechanisms in various prostate, breast and squamous cell lines. *Oncogene*. 2002 Dec 12;21(57):8852-61
- Curcumin can suppress tumor initiation, promotion and metastasis-found to be safe, with no toxicity up in human clinical trials at a dose of up to 10 grams per day.
Anticancer Research 2003 Jan-Feb; 23(1A):363-98

Adverse effects: none known. <http://www.mskcc.org/mskcc/html/69401.cfm>

Herb Drug Interactions:

Anticoagulants / Antiplatelets: Turmeric *may* increase risk of bleeding

Brinker F. Herbal Contraindications and Drug Interactions, 2nd ed. Sandy (OR): Eclectic Medical Publications; 1998

Camptothecin: Turmeric inhibits camptothecin-induced apoptosis of breast cancer cell lines in vitro. Cancer Res 2002;62:3868-75.

Mechlorethamine: Turmeric inhibits mechlorethamine-induced apoptosis of breast cancer cell lines in vitro. Cancer Res 2002;62:3868-75.

Doxorubicin: Turmeric inhibits doxorubicin-induced apoptosis of breast cancer cell lines in vitro. Cancer Res 2002;62:3868-75.

Cyclophosphamide: Dietary turmeric inhibits cyclophosphamide-induced tumor regression in animal studies. Cancer Res 2002;62:3868-75.

SCIENTIFIC NAME: TANACETUM PARTHENIUM (COMPOSITAE)
(PREVIOUSLY IT WAS KNOWN AS CHYRSANTHEMUM PARTHENIUM)
(ASTERACEAE)

Common name: Feverfew, Bachelor's button, wild chamomile

Historical use: Feverfew has been used for centuries as a febrifuge and for the treatment of migraines and arthritis. Other historical uses have been in the treatment of anemia, earache, dysmenorrhea, dyspepsia, trauma and intestinal parasites. More recently, it has been used in gardens to control noxious pests (its pyrethrin component is an effective insecticide and herbicide). Duke JA, Handbook of Medicinal Herbs. CRC Press, Boca Raton, FL, 1985 p.118

Clinical summary: Derivatives from the leaves of the plant have been used primarily to treat migraine headaches. Parthenolide extract has been shown to reduce the frequency of migraine attacks. Another constituent of feverfew has antioxidant activities. A few in

vitro studies have shown that feverfew exhibits anticancer effects. See <http://www.mskcc.org/mskcc/html/69219.cfm> and below.

Biochemically active constituents and known mechanisms of action:

To date, 46 biologically active constituents have been isolated from *Chrysanthemum parthenium*.

(Dr. Duke's Phytochemical and Ethnobotanical Databases (accessed 1/09 but dated 1992. Since this time, the botanical name has evolved to be listed as *Tanacetum parthenium*).

Parthenolide, a sesquiterpene lactone, has been isolated from the leaf of *Tanacetum* and has been the most studied constituent for its anti-inflammatory action. Additional constituents include

Parthenolide has demonstrated effectiveness against cancer by inhibiting NF Kappa B activity:

- Parthenolide has been used in conjunction with Sulindac, an NSAID, in the treatment of pancreatic cancers, demonstrating decreased NFkappaB DNA binding and transcriptional activities in cells treated with the combination compared with the single agents, demonstrating cooperative targeting of the NF-KB pathway. These data provide preclinical support for a combined chemotherapeutic approach with NF-KB inhibitors and NSAIDs for the treatment of pancreatic adenocarcinoma. *Mol Cancer Ther.* Apr 2005;4(4):587-594
- Transcription factors such as NF-KB provide powerful targets for drugs to use in the treatment of cancer. In this report parthenolide (PT), a sesquiterpene lactone of herbal remedies such as feverfew (*Tanacetum parthenium*) with NF-kB inhibitory activity, markedly increased the degree of human leukemia HL-60 cell differentiation when simultaneously combined with 5 nM 1D₅, 25-dihydroxyvitamin D₃ (1,25-(OH)₂D₃). PT by itself did not induce HL-60 cell differentiation. In addition, These results indicate that PT strongly potentiates the 1,25-(OH)₂D₃-induced HL-60 cell differentiation into monocytes *via* the inhibition of NF-KB activity and provide evidence that inhibition of NF-KB activation can be a pre-requisite to the efficient entry of promyelocytic leukemia cells into a

differentiation pathway. *British Journal of Pharmacology* (2002) 135, 1235-1244

- Parthenolide is a major sesquiterpene lactone derived from feverfew (*Tanacetum parthenium*) with known anti-inflammatory activity. Moreover, the anticancer potential of this compound was suggested. In this study, we determined the effect of parthenolide on proliferation of three human cancer cell lines: human lung carcinoma (A549), human medulloblastoma (TE671), human colon adenocarcinoma (HT-29) and human umbilical vein endothelial cells (HUVEC) in vitro. Parthenolide inhibited proliferation of all three types of cancer cells (A549, TE671, HT-29) and HUVEC with the following IC(50) values (in μM): 4.3, 6.5, 7.0 and 2.8, respectively. Thus, the antiproliferative potential of parthenolide was confirmed. *Pharmacol Rep.* 2007 Mar-Apr; 59(2): 233-7
- Parthenolide is an active sesquiterpene lactone present in a variety of medicinal herbs and is well known for its anti-inflammatory activity. The antimicrotubular and antiproliferative effects of parthenolide, well-known microtubule-stabilizing anticancer agent, may influence paclitaxel activity. The tubulin/microtubule system may represent a novel molecular target for parthenolide, to be utilized in developing new combinational anticancer strategies. *Chemico-Biological Interactions* 149 (2004) 165–173
- Parthenolide, an active ingredient of herbal remedies such as feverfew (*Tanacetum parthenium*) mimicked the effects of I κ B α by inhibiting NF- κ B DNA binding activity and Mn-SOD expression, and increasing paclitaxel-induced apoptosis of breast cancer cells. These results suggest that active ingredients of herbs with anti-inflammatory properties may be useful in increasing the sensitivity of cancers with constitutively active NF- κ B to chemotherapeutic drugs. *Oncogene* 2000 (19) 4159-4169

Adverse reactions: Patients allergic to ragweed, chrysanthemum, marigold or other members of the Compositae family may have cross-reactivity to feverfew. Minor GI distress may occur. Mouth ulcerations have been reported from chewing fresh feverfew

leaves. Cases of airborne contact dermatitis have also been reported.

<http://www.mskcc.org/mskcc/html/69219.cfm>

Withdrawal: Muscle stiffness, anxiety, and moderate pain usually occur following cessation of long-term feverfew use (post-feverfew syndrome). Br Med J (Clin Res Ed). 1985 Aug 31; 291(6495): 569–573 and Br J Dermatol. 2007 Mar;156(3):510-5

Herb/Drug interactions: Theoretically, feverfew may have additive effect with anticoagulants and antiplatelet drugs. <http://www.mskcc.org/mskcc/html/69219.cfm>

SCIENTIFIC NAME: QUERCETIN (3,3',4',5,7-pentapentahydroxyflavone)

Common name: Quercetin

Clinical summary: Quercetin is a phytonutrient that is a member of the polyphenolic flavonoid family, constituting the major bioflavonoids in the human diet. The glycoside form is readily available in dietary plants such as *onions, apple, buckwheat, red wine and teas*. Quercetin has a number of biological activities such as antioxidant, anti-inflammatory, and anti-allergy. Quercetin is being used for the treatment of allergic rhinitis, cardiovascular disease, inflammation, cancer prevention and treatment.

<http://www.mskcc.org/mskcc/html/69346.cfm>

Biological activities and known mechanism of action:

Quercetin is a flavonoid molecule ubiquitous in nature. A number of its actions make it a potential anti-cancer agent, including cell cycle regulation, interaction with type II estrogen binding sites, and tyrosine kinase inhibition. Quercetin appears to be associated with little toxicity when administered orally or intravenously. Much in vitro and some preliminary human data indicate quercetin inhibits tumor growth. Altern Med Rev. 2000 Jun; 5(3): 196-200

What follows is an overview of the research on quercetin and cancer from Alternative Medicine Review 2000 Jun; 5(3): 196-200:

- Quercetin was found to down regulate expression of mutant p53 protein to nearly undetectable levels in human breast cancer cell lines. Lower concentrations gave less reduction. The inhibition of expression of p53 was found to arrest the cells in the G2-M phase of the cell cycle.
- Quercetin has been found to inhibit the expression of the p21-ras oncogene in cultured colon cancer cell lines. Mutations of ras proto-oncogenes are found in over 50% of colon cancers, as well as many other tumor types.
- Radiotherapy: Quercetin showed a significant but mild enhancement of the cytotoxic effect of radiation on rat hepatoma cells when added to the medium. A human study showed topical and oral administration of quercetin to reduce skin damage during radiotherapy in patients with head and neck cancers.
- Chemotherapy: Quercetin has been shown to increase the therapeutic efficacy of cisplatin both in vitro and in vivo in mice. An in vitro study using human ovarian and endometrial cancer cell lines found that addition of quercetin to cisplatin caused a potentiation of the cytotoxic effect of cisplatin
- Quercetin has been shown in vitro to protect normal renal tubular cells from cisplatin toxicity.

Adverse reactions: Human studies have not shown any adverse effects associated with oral administration of quercetin in a single dose of up to 4,000 mg (Eur J Clin Pharmacol 1975; 9:229-234) or after one month of 500 mg. twice daily. (Urology 1999; 54: 960-963)

Herb/Drug interactions:

Chemotherapeutic agents: See above for chemotherapeutic agents

Papain and Bromelain: May assist the absorption of Quercetin in the intestine. Herr, SM. Herb-Drug Interaction Handbook. Chuch Street books. 2nd ed. Nassau NY 2002

Quinolone antibiotic: Quercetin may compete for DNA gyrase binding sites on bacteria. Urology 1999;54:960-3.

B. 7 HERB FORMULA

Ingredients of Daniel Chapter One's "7 Herb Formula" are listed and a selection of the scientific evidence of the activity of their constituents is presented.

SCIENTIFIC NAME: ARCTIUM LAPPA (Asteraceae):

Common Names: Burdock, Greater Burdock, Gobo and Nui bang zi (pin yin)

Historical use: Burdock has a long history of use dating from the Chinese Materia Medica, Native Americans, and Eclectic herbalists as an alterative, anti-inflammatory, antimicrobial, cholegogue, diuretic, diaphoretic, hypoglycemic, and a "blood purifier." Arctium lappa was an original herb in Renne Caisse's "Essiac Tea", which has been used to support the immunity of those with cancer. According to the Journal of Ethnopharmacology, Essiac tea possesses potent antioxidant and DNA-protective activity, properties that are common to natural anti-cancer agents. J Ethnopharmacology. 2006 Jan 16;103(2): 288-96.

Biologically active constituents and proposed mechanisms of action: To date, at least 119 secondary metabolites have been isolated from Arctium lappa (Duke's Phytochemical and Ethnobotanical Database) accessed 1/09. Arctium lappa contains many polyphenolic acids and flavonoids with potential chemoprotective effects.

Below is a list of five of Arctium lappa's most active constituents:

- **Arctigenin:** extract of Arctium lappa showed potent antiproliferative activity against B cell hybridoma cell, MH 60 through apoptosis *Planta Medica*. 2006 Feb; 72(3):276-8
- **Arctigenin** potently inhibits the activity of MKK1 in vitro, thus inhibiting phosphorylation of MAP kinases http://www.proteinkinase.de/html/map_kinase_inhibitors.html#arctigenin
- **Chlorogenic acid:** this study found chlorogenic acid to have anticancer properties via inhibition of microsomal G6P transferase in glioma cells. *Cancer Cell International*, 2006, 6: 7:dol.10.1186/1475-2867-6-7
- **Inulin:** a plant fiber/sugar that reduced carcinogenesis in rats *Carcinogenesis*. 2002 Nov. 23 (11): 1953-60

Clinical summary: *Arctium lappa* contains numerous compounds that possess antipyretic, antimicrobial, antimutagenic, anti-oxidant, antitumor, cholegogue and desmutagenic activities. *Chemoprevention of Cancer*, CRC Press, 1995 Nixon D

Adverse effects: hypoglycemia. Some potential for allergic reaction/contact dermatitis if sensitive to chrysanthemum; it should be avoided by pregnant and lactating women because it may cause uterine stimulation. *JAMA* 1978; 239: 2157

Herb/drug interactions: none discovered

SCIENTIFIC NAME: RHEUM PALMATUM (Polygonaceae)

Common name: Chinese rhubarb (da huang), Turkey Rhubarb

Historical use: Rhubarb has been used in the Chinese Materia Medica for centuries for the treatment of inflammatory diseases; as a purgative/laxative in both Chinese, Western, European herbal medicine; *Rheum palatum* was an original herb in Renne Caisse's "Essiac Tea", which has been used to support the immunity of those with cancer. According to the *Journal of Ethnopharmacology*, Essiac tea possesses potent antioxidant and DNA-protective activity, properties that are common to natural anti-cancer agents. *J Ethnopharmacology*. 2006 Jan 16;103(2); 288-96.

Biologically active constituents and proposed mechanisms of action:

Contains 30 biologically active chemicals (Dr. Duke's Phytochemical and Ethnobotanical Databases) accessed 1/09

- Anthroquinone derivatives are its major active constituents and it is derivatives of these compounds that that play a substantial role in inhibiting angiogenesis.

Journal of Ethnopharmacology. 2009 Jan 21: 121 (2): 313-7

- **Aloe-emodin:** (anthroquinone) possesses anti-tumor properties *Med Research Review*. 2007 Sept; 27(5): 609-30
- **Emodin:** is the most abundant anthroquinone in *Rheum*. It is capable of inhibiting cellular proliferation, induction of apoptosis, prevention of metastasis...through induction of protein kinases, phosphoinositol 3 kinase (P13K), protein kinase C (PKC), NF-Kappa B (NF-KappaB), and mitogen-activated protein kinase (MAPK) signaling cascades. Its anti-proliferative properties are through the p53 and p21 pathways.

Med Res. Review. 2007 Sept; 27(5): 609-30

- **Emodin:** inhibits protein kinase p65 lck; acts on a number of molecular targets within the cell; Inhibits mammalian cell cycle modulation in specific oncogene over expressed cells; induces apoptosis; is used in combination with chemotherapy to reduce toxicity and enhance efficacy; inhibitory effects on angiogenic and metastatic properties make it a sensible candidate as a specific blocker of tumor-associated events. *Medical Research Review*. 2007 Sep; 27 (5): 591-608
- **Quercetin:** is the flavonoid molecule that is ubiquitous in nature, although no research on its action in Rheum is available.
- **Rhein:** (anthroquinone) inhibits the proliferation of various human cancer cells; this study demonstrated that rhein induced cell cycle S-phase arrest on human hepatocellular carcinoma BEL-7402 cells, via downregulation of oncogene c-Myc and apoptosis through the caspase-dependent pathway. *American Journal of Chinese Medicine*. 2008; 36(4):805-13

Clinical Summary: Rhubarb has been used for a variety of conditions including cancer, immunosuppression, constipation, diarrhea, ulcers, hypertension and chronic renal fatigue. The anthroquinone and tannins are thought responsible for the laxative and constipating effects, respectively. Although animal studies have confirmed antitumor effects, limited human clinical data is available. Memorial Sloan-Kettering Cancer Center
<http://www.mskcc.org/mskcc/html/69357.cfm>

Adverse reactions: Intestinal cramps, nausea, vomiting and diarrhea have been reported due to the laxative effect. Long-term use can result in potassium loss due to diarrhea. Do not use long term. Memorial Sloan-Kettering Cancer Center <http://www.mskcc.org/mskcc/html/69357.cfm>

Herb/Drug Interactions: Diuretics: Potassium loss due to the stimulant laxative effect can increase potential risk for hypokalemia. Digoxin: stimulant laxative effect can increase potential risk for hypokalemia. Brinker F. *Herb Contraindications and Drug Reactions*, 3rd edition.

SCIENTIFIC NAME: RUMEX ACETOSELLA (Polygonaceae)

Common name: Sheep sorrel

Historical use: Sheep sorrel historically has been used as a salad green and spring tonic. Rumex acetosella was an original herb in Renne Caisse's "Essiac Tea", which has been used to support the immunity of those with cancer. According to the Journal of Ethnopharmacology, Essiac tea possesses potent antioxidant and DNA-protective activity, properties that are common to natural anti-cancer agents. J Ethnopharmacology. 2006 Jan 16;103(2): 288-96.

Biologically active constituents and proposed mechanisms of action:

Contains 33 biologically active chemicals (Dr. Duke's Phytochemical and Ethnobotanical Databases) accessed 1/09.

- Glycosides: Hyperoside, quercitin
- Anthroquinones: emodin, aloe-emodin, rhein, physcion (Memorial Sloan-Kettering Cancer Center Database (<http://www.mskcc.org/mskcc/html/69375.cfm>))

Clinical summary: Sheep sorrel is extremely nutrient-rich, containing high levels of calcium, iron, magnesium, silicon, sulfur, copper, iodine, manganese, zinc and vitamin C in addition to vitamins A, B complex, D, E, K, P and U. It also contains rutin, the flavones glycosides hyperin and hyperoside, carotenoids, organic acids and Anthroquinones. Sheep sorrel tea has been used traditionally to treat inflammation, fevers and cancer. Though anthraquinones are known to have antioxidant and antitumor activity, the anthraquinones in sheep sorrel have not been tested for these effects beyond anecdotal reports. American Botanical Council HerbClip™

Adverse effects: Sorrel contains oxalate (oxalic acid), which may be toxic in large doses. Reports of organ damage and one report of death following ingestion of a concentrated sorrel soup have been published. Sorrel may also cause kidney stones, precipitation of drugs taken concomitantly, and malabsorption of minerals, such as calcium, iron, or zinc. <http://www.naturalstandard.com/index-abstract.asp?create>

Herb/Drug interactions: none known

SCIENTIFIC NAME: ULMUS RUBRA (Ulmuceae)

Common Name: Slippery Elm, Red elm, Indian elm

History of use: Ulmus rubra has been historically used for gastrointestinal disorders, skin ulcers or abscesses, cancers, coughs, fevers and inflammation. Its primary constituent is mucilage, which is responsible for the demulcent, emollient and antitussive properties, which form a viscous material following oral administration or for topical use. (Memorial Sloan-Kettering Cancer Center database: <http://www.mskcc.org/mskcc/html/69381.cfm>).

Ulmus rubra was an original herb in Renne Caisse's "Essiac Tea", which has been used to support the immunity of those with cancer. According to the Journal of Ethnopharmacology, Essiac tea possesses potent antioxidant and DNA-protective activity, properties that are common to natural anti-cancer agents. *J Ethnopharmacology*. 2006 Jan 16;103(2); 288-96.

Biologically active constituents and proposed mechanisms of action:

Contains 50 biologically active chemicals (Dr. Duke's Phytochemical and Ethnobotanical Databases) accessed 1/09. It is comprised mainly of mucilage, phytosterols, fatty acids and tannins, none of which have been studied for cancer.

Adverse reactions: none known

Herb/drug interactions: Theoretically, the mucilage and fiber content may slow the absorption of concomitantly administered oral medications, though no interactions have been reported. No human or animal studies have been performed to evaluate the efficacy of any proposed claims.

SCIENTIFIC NAME: UNCARIA TOMENTOSA (Pedaliaceae)

Common name: Cat's Claw, Garabato amarillo, Una de Gato

Historical use: Cat's Claw is a vine native to South America, specifically the Peruvian rainforest, where it has been a traditional medicine. It is a very popular immune-enhancing supplement and is known to help digestive complaints, arthritis and is considered to have an anti-inflammatory effect and anti-tumor effects.

<http://www.mskcc.org/mskcc/html/69166.cfm>

Biologically active constituents and proposed mechanisms of action:

Contains 29 biologically active chemicals (Dr. Duke's Phytochemical and Ethnobotanical Databases) accessed 1/09

The most biologically active compounds in *Uncaria tomentosa* are:

- **Oxyindole alkaloids:** isorhyncholophylline, rhynchophylline and protect against glutamate cell death in cultured cerebellar cells in rats. *Journal Pharm Pharmacol.* 1999 Jun;51 (6): 715-22
- **Oleanolic acid and ursolic acid:** a synthetic triterpenoid based on naturally occurring ursolic and Oleanolic acids induces apoptosis induced by TNF and chemotherapeutic agents through downregulation of expression of NF-Kappa B in human leukemic cells.
Clin Cancer Res. 2006 Mar 15;12(6): 1828-38
- The primary mechanism for cat's claw anti-inflammatory actions appears to be immunomodulation via suppression of TNF synthesis. *Free Radical Biology and Medicine.* 2000 29(1) pp. 71-28
- An aqueous extract of cat's claw induced apoptosis, inhibited lipopolysaccharide induced iNOS expression, cell death and inhibited the activity of NF-Kappa B, providing mechanistic evidence that cat's claw is an effective anti-inflammatory agent. *Alimen Pharmacol Ther* 1998 Dec; 12(12):1279-89
- Another aqueous extract of *Uncaria tomentosa* (C-Med-100) demonstrated a suppressive effect on tumor cell growth through induction of apoptosis. *Anticancer Research* 1998 Sep-Oct; 18(5A):3363-8
- *Uncaria tomentosa* (C-Med-100) demonstrated in a human trial to decrease DNA damage and increase DNA repair. *Phytomedicine* 8(4) pp. 275-282

Clinical Summary: In vitro studies show that the alkaloids from Cat's claw enhance phagocytosis, display immunomodulatory properties, alleviate inflammation, and possess anti-viral activity. Cat's claw is also thought to have anticancer activities and lab results demonstrated growth inhibitory effects on glioma and neuroblastoma cells as well as promyelocytic cells. <http://www.mskcc.org/mskcc/html/69166.cfm>

Adverse reactions: hypotension and diarrhea. <http://www.mskcc.org/mskcc/html/69166.cfm>

Herb/Drug interactions: an additive effect with anti-coagulants or hypotensives is possible but has not been reported. <http://www.mskcc.org/mskcc/html/69166.cfm>

SCIENTIFIC NAME: ELEUTHEROCOCCUS SENTICOSUS (Araliaceae):

Common Names: Siberian ginseng, Eleuthero ginseng, Ci Wu Jia (pin yin);

Acanthopanax senticosus

Historical use: Eleutherococcus senticosus has been used for thousands of years in the Traditional Chinese Materia Medica as a kidney tonic to increase longevity, improve general health and appetite. In 1958, the Russian scientist Brekhman coined the term “adaptogen” as a substances that 1) must be innocuous and cause minimal disorders in the physiological functions of an organism, 2) must have a non-specific action (i.e., it should increase the resistance to adverse influences by a wide range of physical, chemical and biochemical factors), and 3) usually has a normalizing action irrespective of the direction of the pathological state (alterative action). *The Healing Power of Herbs*, Murray; Three Rivers Press, New York, 1995, pp.315-20)

Farnsworth and colleagues reviewed data on an Eleutherococcus senticosus root extract administered to over 2,100 human subjects to assess the adaptogenic effects of ginseng and concluded that it:

1. Increased ability of humans to withstand adverse physical conditions (heat, noise, motion, workload increase, exercise and decompression), and
2. Increase mental alertness and work output, and
3. Improved quality of work produced under stressful conditions, and athletic performance.

Farnsworth and colleagues reviewed data on an Eleutherococcus senticosus root extract administered to over 2,200 human subjects to assess its adaptogenic effect in disease states and concluded that it appears to be effective in:

1. Atherosclerotic conditions in that it can lower serum cholesterol levels, reduce blood pressure and eliminate angina symptoms in human subjects;
2. Improving kidney function and regulating blood pressure in patients with acute kidney infection
3. Improved sense of well-being of psychological complaints (insomnia, hypochondriasis, neuroses) possibly through regulation of biogenic amine content in the brain.

Biologically active constituents and proposed mechanisms of action:

To date, at least 51 biologically active constituents in Eleutherococcus have been identified (Dr. Duke's Phytochemical and Ethnobotanical Database) accessed 1/09. The main active constituents are the eleutherosides, though very little current research is available. Below are some of the highlights:

- Eleutherococcus senticosus demonstrated immunomodulatory properties (enhanced the cellular response of the mouse immunological system (chemokinetic activity of mice spleen cells, GvH reaction), as well as a stimulatory effect of Eleutherococcus on the humoral response (antibody production) in mice. Pol Journal Vet Science 2003;6(3 Suppl):37-9.
- Eleutherococcus senticosus, as part of a formula (AdMax) was evaluated for its effect on ovarian cancer patients. In patients who took AdMax, the mean numbers of 4 T cell subclasses were increased, the mean amounts of IgG and IgM were increased and the results suggest that the combination of extracts from adaptogenic plants may boost the suppressed immunity in ovarian cancer patients who are subject to chemotherapy. Phytotherapy Res. 2006 May; 20(5): 424-5
- Standardized extracts of Eleutherococcus senticosus at generally recommended doses for over-the-counter use are unlikely to alter the disposition of co-administered medications primarily dependent of CYP2D6 or CYP3A4 pathways for elimination. Drug Metab Disp. 2003 5(31): 519-22
- Eleutherococcus senticosus extract was applied to cells in culture resulting in a slight radioprotective effect. American Journal Chinese Medicine. 1981 (9) 48-56
- Eleutherococcus senticosus provided anti-proliferative effects against L1210 murine leukemia cells and suggests that it may be useful for reducing the concentration of conventional anti-metabolites used for their anti-proliferative effects on tumor cells. Journal Pharmacological Science. 1984 Feb; 73(2): 270-2

- Eleutherococcus senticosus aqueous extract of eleutheroside E may have contributed to the anti-fatigue action, recovery of the reduction of NK activity and inhibition of corticosterone elevation induced by swimming stress. *Journal of Ethnopharmacology*. 2004 Dec;95(203):447-53

Clinical summary: Although initial reports from the Soviet Union and reviews of that literature by Farnsworth suggested therapeutic value of *Eleutherococcus senticosus* as an adaptogen, very little current research has been done to substantiate those findings. It is now being recommended that the term “adaptogen” be discontinued and further research be done on this plant to confirm potential therapeutic value in these areas: Anti-oxidant, anti-cancer, immunostimulatory, anti-inflammatory, hypocholesterolemic, cholorectic, anti-pyretic and anti-bacterial actions.

Journal of Ethnopharmacology. 2004 Dec;95(203):447-53

Adverse effects: toxicity studies in animals demonstrated that 33% ethanol extract of *E. senticosus* is virtually non-toxic; it is very well-tolerated in humans and side-effects are quite minimal; very high doses may produce insomnia, irritability, melancholy and anxiety. *Economic and Medical Plant Research* 1, 156-215, Farnsworth, 1985 *The Healing Power of Herbs*, Murray; Three Rivers Press, New York, 1995, pp.315-20)

Herb/drug interactions: none discovered

SCIENTIFIC NAME: NASTURTIUM OFFICINALE (BRASSICACEAE)

Common name: Watercress, Berro

Historical use: Like sorrel, watercress has been used historically as a salad green and spring tonic.

Biologically active constituents and proposed mechanisms of action:

Contains 47 biologically active chemicals (Dr. Duke’s Phytochemical and Ethnobotanical Databases) accessed 1/09. The most biologically active constituent of watercress for cancer is phenethyl isothiocyanate (PEITC). Watercress may have exceptionally good anticarcinogenic potential as it combines a potent inhibitor of Phase I enzymes (PEITC) with at least three inducers of phase II enzymes (PEITC, 7-methylsulfinylheptyl ITC and

8-methylsulfinyloctyl ITC. These compounds act at three stages of carcinogenesis in that they:

1. Inhibit carcinogen activation
2. Induce phase II enzymes and enhance excretion of the potential carcinogens and
3. Induce apoptosis via activation of protein kinase pathway.

The putative anticarcinogenic activity of ITC is consistent with the results of epidemiological studies, which have suggested a reduction in cancer risk through the consumption of cruciferous vegetables. *Carcinogenesis*. 2000 21(11) pp. 1983-88

- PEITC: PEITC selectively affects xenobiotic-metabolizing enzymes in the liver, lung and nasal mucosa and is especially effective in inhibiting the cytochrome p450 dependent oxidation of NNK in the lung and NDMA in the liver of rats. *Carcinogenesis*. 1992 13(12) pp.2205-2210
- PEITC: PEITC was found to be a very potent inhibitor of N-nitrosobenzylmethylamine-induced rat esophageal carcinogenesis. *Cancer Research*. 1991 51, pp. 2063-2068.

Clinical summary: Watercress contains high levels of the glucosinolate, *gluconasturtiin*, which is hydrolyzed to phenethylisothiocyanate (PEITC) upon pulverization of the leaves. It is also a rich source of vitamins A and C, sulfur, iodine, calcium and manganese. Several animal and human studies have demonstrated that PEITC inhibits lung tumors induced by NNK (from tobacco smoke). It also activates detoxification enzymes in cancerous cells. Indoles present in watercress are antiestrogenic and dispose of excess estrogen, which may help prevent hormone related cancers.

American Botanical Council HerbClip™

Adverse reactions: none discovered

Drug/herb interactions: none discovered

C. “BioMixx”

Four of the main ingredients of Daniel Chapter One’s “BioMixx” formula, Whey protein, Astragalus membranaceus, Camellia sinensis and Eleutherococcus senticosus are listed, and a brief selection of the scientific evidence of the activity of their constituents is presented.

WHEY PROTEIN

Whey Protein: Whey is a co-product of cow’s milk in the manufacture of cheese and in recent years has become a functional food. The two primary sources of protein in milk are the caseins and whey. After processing occurs, the caseins are the proteins responsible for making curds, while the whey remains in an aqueous environment. The components of whey include:

Beta-lactoglobulin, alpha-lactalbumin, bovine serum albumin, lactoferrin, immunoglobulins, lactoperoxidase, enzymes, glycomacropetides, lactose, and minerals. Today whey is a popular dietary protein supplement purported to provide antimicrobial activity, immune modulation, improved muscle strength and body composition, and prevention of cardiovascular disease and osteoporosis. *Alt Med Rev.* 2008 Dec; 4(13); 341-7

Whey Protein Constituents:

Whey protein contains all the essential amino acids in higher concentrations than vegetable protein sources. They are efficiently absorbed and utilized relative to free amino acid solutions.

Whey proteins have a high concentration of Branched chain amino acids (BCAA): isoleucine, leucine, valine, which are important factors in tissue growth and repair. Whey proteins are also rich in the sulfur-containing amino acids cysteine and methionine, which enhance immune function through intracellular conversion to glutathione, one of the most important antioxidants in the cell. *Crit Food RevSci Nutr* 2002;42: 353-75

Mechanisms of Action:

Whey has potent antioxidant activity, likely by contributing cysteine-rich proteins that aid in the synthesis of glutathione (GSH), a potent intracellular antioxidant. Crit Food Rev Sci Nutr 2002;42: 353-75

Detoxification:

Practitioners use whey protein as a source of cysteine to increase intracellular glutathione levels. As a detoxifying agent, glutathione peroxidase (GSHPx), which is derived from selenium and cysteine, is an endogenous antioxidant enzyme that converts lipid peroxides into less harmful hydroxy acids. In addition to the above mentioned properties, the alpha-lactalbumin component of whey chelates heavy metals and reduces oxidative stress because of its iron chelating properties. Toxicology 1999; 137:169-184 and J Nutr Biochem 2003; 14:251-8

Immune enhancement:

An *in vitro* study demonstrated that bovine-milk derived IgG suppresses human lymphocyte proliferative response to T cells and conclude that it is likely to confer immunity that could be carried to humans. Int Arch Allergy Appl Immuno 1993;4:231-9
Alpha-lactalbumin also has direct effect on B-lymphocyte function, as well as suppressing T-cell dependent and independent responses. J Nutr 1985;114:1403-8

Clinical indications:

Whey's amino acid profile makes it useful for enhancing body composition, supporting protein synthesis and building lean body mass. For these reasons it has been used in patients with diabetes, obesity, cardiovascular disease, to support pediatric bowel health, and to improve glutathione levels

in individuals infected with HIV and in cancer. Alt Med Rev. 2008 Dec; 4(13); 341-7

- Whey protein concentrates have been researched extensively with respect to cancer prevention and treatment, and glutathione stimulation is thought to be the primary immune-modulating mechanism. Alt Med Rev. 2008 Dec; 4(13); 341-7

- The amino acid precursors to glutathione in whey might increase glutathione levels in tissues, stimulate immunity and detoxify potential carcinogens. *Anticancer Res* 2000; 20:4785-92
- Several animal studies have been assessed the effect whey's immune enhancing components, especially lactoferrin and beta-lactoglobulin. In an animal model of colon cancer, animals given whey components demonstrated significantly lower incidence of tumors and fewer aberrant crypts. *Cancer Epidemiol Biomarkers Prev* 2000;9: 113-7 *Cancer Epidemiol Biomarkers Prev* 2001: 10:555-8 *Jpn J Cancer Res* 1997: 88:523-6
- Fractionated whey had the ability to reduce oral mucositis in hamsters via induction of TGF-beta. *Oral Oncol* 2002; 38: 478-85

Side Effects and Toxicity:

- Individuals with known allergy to milk may not tolerate whey, but many dairy sensitive individuals find that casein is the culprit and not whey, especially if it is hydrolyzed and therefore less allergenic. Most whey proteins have been processed to remove lactose and so those who are lactose intolerant may tolerate hydrolyzed whey protein. *Alt Med Rev.* 2008 Dec; 4(13); 341-7

SCIENTIFIC NAME: ASTRAGALUS MEMBRANACEUS (FABACEAE)

Common name: Yellow root, huang qi (pin yin)

Historical use: Astragalus has been used in Traditional Chinese Medicine for thousands of years as an immune stimulant and qi tonic (adaptogen).

Clinical Summary: Astragalus has been used to support and enhance immune function and is still widely used in China and by acupuncturists for chronic immune conditions like chronic hepatitis and as an adjunctive therapy in cancer. Astragalus extracts have been shown to possess cytostatic properties, inhibit tumor growth and in vitro, animal and anecdotal human data show that astragalus reduces immune suppression resulting from chemotherapy. Astragalus-based herb formulas may enhance the effect of platinum-based chemotherapy. <http://www.mskcc.org/mskcc/html/69128.cfm>

Biochemically active constituents and known mechanisms of action:

To date, 38 biologically active constituents of *Astragalus membranaceus* have been isolated. The most biologically active compounds in *Astragalus* are the triterpene saponins (astragalosides I-X), polysaccharides and isoflavones.

- Because *Astragalus membranaceus* is used as immunomodulating agent in treating immunodeficiency diseases and to alleviate the adverse effects of chemotherapeutic drugs, the anti-carcinogenic effects of *Astragalus* saponin extract were investigated in HT-29 human colon cancer cells and tumor xenograft. Our findings have shown that *Astragalus* saponins (AST):
 - inhibits cell proliferation through accumulation in S phase and G2/M arrest, with concomitant suppression of p21 expression and inhibition of cyclin-dependent kinase activity.
 - promotes apoptosis in HT-29 cells through caspase 3 activation and poly(ADP-ribose) polymerase cleavage, which is indicated by DNA fragmentation and nuclear chromatin condensation.
 - demonstrates an anti-tumorigenic effects in vivo, of which the reduction of tumor volume as well as pro-apoptotic and anti-proliferative effects in HT-29 nude mice xenograft are comparable with that produced by the conventional chemotherapeutic drug 5-fluorouracil (5-FU).
 - reduced the side effects (body weight drop and mortality) associated with the drug combo 5-FU and oxaliplatin are not induced by AST.
 - These results indicate that AST could be an effective chemotherapeutic agent in colon cancer treatment, which might also be used as an adjuvant in combination with other orthodox chemotherapeutic drugs to reduce the side effects of the latter compounds. *Carcinogenesis* 2007 28(6):1347-1355; doi:10.1093/carcin/bgl238

- A partially purified fraction (F3) with an estimated molecular weight of 20,000 to 25,000 derived from the traditional Chinese medicinal herb *Astragalus membranaceus*, was found to possess a potent immunorestorative activity in vitro.

These data indicate that F3 administration markedly enhances the rats' ability to reject the xenogeneic graft and therefore possesses a strong immune potentiating activity in vivo. These preclinical data also provide the rational basis for the use of extracts of *Astragalus membranaceus* in phase I clinical trials among patients suffering from iatrogenic or inherent immune deficiency states. *J Clin Lab Immunol.* 1988 Mar;25(3):125-9.

- **Meta-analysis:** Astragalus has been shown to have immunologic benefits by stimulating macrophage and natural killer cell activity and inhibiting T-helper cell type 2 cytokines. Many published studies have assessed the use of Astragalus and other Chinese herbal medicines in combination with chemotherapy. We sought to evaluate evidence from randomized trials that Astragalus-based Chinese herbal medicine combined with platinum-based chemotherapy (versus platinum-based chemotherapy alone) improves survival, increases tumor response, improves performance status, or reduces chemotherapy toxicity.

Results: Of 1,305 potentially relevant publications, 34 randomized studies representing 2,815 patients met inclusion criteria. Twelve studies (n = 940 patients) reported reduced risk of death at 12 months (risk ratio [RR] = 0.67; 95% CI, 0.52 to 0.87). Thirty studies (n = 2,472) reported improved tumor response data (RR = 1.34; 95% CI, 1.24 to 1.46). In subgroup analyses, Jin Fu Kang in two studies (n = 221 patients) reduced risk of death at 24 months (RR = 0.58; 95% CI, 0.49 to 0.68) and in three studies (n = 411) increased tumor response (RR = 1.76; 95% CI, 1.23 to 2.53). Ai Di injection (four studies; n = 257) stabilized or improved Karnofsky performance status (RR = 1.28; 95% CI, 1.12 to 1.46).

Conclusion: Astragalus-based Chinese herbal medicine may increase effectiveness of platinum-based chemotherapy when combined with chemotherapy. These results require confirmation with rigorously controlled trials.

Journal of Clinical Oncology, Vol 24, No 3 (January 20), 2006: pp. 419-430

Adverse reactions: none known

Herb/Drug Interactions:

- Immunosuppressants: Astragalus may antagonize the effects of immunosuppressants such as tacrolimus and cyclosporine.
- Aldesleukin: Concomitant treatment with astragalus has resulted in a 10-fold potentiation of tumor-cidal activity with decreased side effects.
- Cyclophosphamide: Astragalus may decrease immunosuppression following treatment.

<http://www.mskcc.org/mskcc/html/69128.cfm> (1) (14) (15)

SCIENTIFIC NAME: CAMELLIA SINENSIS (Theaceae)

Common name: Green tea

Historical use: Green tea has been a preferred beverage throughout Asia for millennia. It has a small amount of theophylline that provides a slight stimulatory effect. Its mild flavor allows it to be blended with other components (jasmine flowers) or toasted rice, soy or corn to create a variety of pleasant flavors.

Clinical Summary: Because green tea contains numerous polyphenols, it has potent antioxidant actions its use is associated with cardioprotective, neuroprotective and chemoprotective effects. It has been used to lower cholesterol, lipids, Epidemiologic studies show an inverse relationship between consumption of tea, especially green tea, and development of cancers. Numerous in vivo and in vitro studies indicate strong chemopreventive effects for green tea and its constituents against cancers of various organs.

Biochemically active constituent and proposed mechanisms of action:

The polyphenolic flavonoids are the major biologically active constituents: catechin, epicatechin, epicatechin gallate, epigallocatechin 3-gallate (EGCG), sin catechin, and proanthocyanadins.

Recent studies demonstrate the following clinical outcomes:

- Epigallocatechin 3-gallate (EGCG) is a well-known chemoprevention factor that triggers apoptosis in cells going through the p53 dependent pathway. Cancer Res 2008;68(11);4150-62

- EGCG and EGC are capable of altering AhR transcription and are responsible for most, if not all, of the AhR antagonist activity of GTE, thus offering an insight to how it prevents tobacco related carcinogenesis. Chem Res Toxicol. 2003;16(7);865-872
- ECGC inhibits the growth of human squamous carcinoma, breast carcinoma and colon carcinoma cells and is associated with rapid inhibition of activation of RTKs, EGRF, HERR2 and HER3 inhibition of activation or the expression of several downstream signaling molecules involved in cell proliferation and survival. Therefore, ECGC or Poly E may be useful when used alone or in combination with other agents in the prevention and treatment of colon and other types of human cancer. AACR Conf Front Canc Res Prevent. Nov 12-15, 2006
- ECGC inhibits cancer cell growth through the inhibition of IGF-1 and VEGF receptors, inhibits the Ras/MAPK and P13K/Akt signaling pathways, thereby modulating the expression of target genes, which are associated with induction of apoptosis and cell cycle arrest in cancer cells. Int. J. Mol. Sci. 2008, Volume 9(6), Page 1034-1049

Adverse reactions: Nausea and GI upset have been reported

Herb/Drug Interactions: theoretically, large amounts of green tea may inhibit Vitamin K absorption, thus antagonizing the effects of anticoagulants; may reduce absorption of atropine; may reduce bioavailability of iron and codeine.

<http://www.mskcc.org/mskcc/html/69247.cfm>

SCIENTIFIC NAME: ELEUTHEROCOCCUS SENTICOSUS (Araliaceae):

Common Names: Siberian ginseng, Eleuthero ginseng, Ci Wu Jia (pin yin);

Acanthopanax senticosus

Historical use: Eleutherococcus senticosus has been used for thousands of years in the Traditional Chinese Materia Medica as a kidney tonic to increase longevity, improve general health and appetite. In 1958, the Russian scientist Brekhman coined the term “adaptogen” as a substance that 1) must be innocuous and cause minimal disorders in the physiological functions of an organism, 2) must have a non-specific action (i.e., it

should increase the resistance to adverse influences by a wide range of physical, chemical and biochemical factors), and 3) usually has a normalizing action irrespective of the direction of the pathological state (alterative action). *The Healing Power of Herbs*, Murray; Three Rivers Press, New York, 1995, pp.315-20)

Farnsworth and colleagues reviewed data on an *Eleutherococcus senticosus* root extract administered to over 2,100 human subjects to assess the adaptogenic effects of ginseng and concluded that it:

1. Increased ability of humans to withstand adverse physical conditions (heat, noise, motion, workload increase, exercise and decompression), and
2. Increase mental alertness and work output, and
3. Improved quality of work produced under stressful conditions, and athletic performance.

Farnsworth and colleagues reviewed data on an *Eleutherococcus senticosus* root extract administered to over 2,200 human subjects to assess its adaptogenic effect in disease states and concluded that it appears to be effective in:

1. Atherosclerotic conditions in that it can lower serum cholesterol levels, reduce blood pressure and eliminate angina symptoms in human subjects;
2. Improving kidney function and regulating blood pressure in patients with acute kidney infection
3. Improved sense of well-being of psychological complaints (insomnia, hypochondriasis, neuroses) possibly through regulation of biogenic amine content in the brain.

Economic and Medical Plant Research 1, 156-215, Farnsworth, 1985

The Healing Power of Herbs, Murray; Three Rivers Press, New York, 1995, pp.315-20)

Biologically active constituents and proposed mechanisms of action:

To date, at least 51 biologically active constituents in *Eleutherococcus* have been identified (Dr. Duke's Phytochemical and Ethnobotanical Database) accessed 1/09. The main active constituents are the eleutherosides, though very little current research is available. Below are some of the highlights:

- *Eleutherococcus senticosus* demonstrated immunomodulatory properties (enhanced

the cellular response of the mouse immunological system (chemokinetic activity of mice spleen cells, GvH reaction), as well as a stimulatory effect of Eleutherococcus on the humoral response (antibody production) in mice. *Pol Journal Vet Science* 2003;6(3 Suppl):37-9.

- Eleutherococcus senticosus, as part of a formula (AdMax) was evaluated for its effect on ovarian cancer patients. In patients who took AdMax, the mean numbers of 4 T cell subclasses were increased, the mean amounts of IgG and IgM were increased and the results suggest that the combination of extracts from adaptogenic plants may boost the suppressed immunity in ovarian cancer patients who are subject to chemotherapy. *Phytotherapy Res.* 2006 May; 20(5): 424-5
- Standardized extracts of Eleutherococcus senticosus at generally recommended doses for over-the-counter use are unlikely to alter the disposition of co-administered medications primarily dependent of CYP2D6 or CYP3A4 pathways for elimination. *Drug Metab Disp.* 2003 5(31): 519-22
- Eleutherococcus senticosus extract was applied to cells in culture resulting in a slight radioprotective effect. *American Journal Chinese Medicine.* 1981 (9) 48-56
- Eleutherococcus senticosus provided anti-proliferative effects against L1210 murine leukemia cells and suggests that it may be useful for reducing the concentration of conventional anti-metabolites used for their anti-proliferative effects on tumor cells. *Journal Pharmacological Science.* 1984 Feb; 73(2): 270-2
- Eleutherococcus senticosus aqueous extract of eleutheroside E may have contributed to the anti-fatigue action, recovery of the reduction of NK activity and inhibition of corticosterone elevation induced by swimming stress. *Journal of Ethnopharmacology.* 2004 Dec;95(203):447-53

Clinical summary: Although initial reports from the Soviet Union and reviews of that literature by Farnsworth suggested therapeutic value of Eleutherococcus senticosus as an adaptogen, very little current research has been done to substantiate those findings. It is now being recommended that the term “adaptogen” be discontinued and further research

be done on this plant to confirm potential therapeutic value in these areas: Anti-oxidant, anti-cancer, immunostimulatory, anti-inflammatory, hypocholesterolemic, cholorectic, anti-pyretic and anti-bacterial actions.

Journal of Ethnopharmacology. 2004 Dec;95(203):447-53

Adverse effects: toxicity studies in animals demonstrated that 33% ethanol extract of *E. senticosus* is virtually non-toxic; it is very well-tolerated in humans and side-effects are quite minimal; very high doses may produce insomnia, irritability, melancholy and

anxiety. Economic and Medical Plant Research 1, 156-215, Farnsworth, 1985The Healing Power of Herbs, Murray; Three Rivers Press, New York, 1995, pp.315-20)

Herb/drug interactions: none discovered

D. “BioShark”

History of use: In 1971, Judah Folkman, MD published his work on angiogenesis and cancer in the New England Journal of Medicine. Robert Langer, PhD at MIT followed with the observation that bovine cartilage could inhibit neovascularization of solid tumors. Dr. John Prudden demonstrated that bovine cartilage could inhibit the in vitro growth of osteosarcoma and human myeloma cultured cells. Dr. Prudden developed Catrix, a bovine tracheal cartilage, and began treating end-stage cancer patients in 1972. This therapy exerted a major inhibitory effect on a variety of cancers but did not eliminate them completely. In 1983, Langer began work comparing shark cartilage to bovine cartilage, reporting the same amount of shark cartilage contained 1000 times the quantity of anti-angiogenic factor as did bovine cartilage.

Initial studies in mice by William Lane, PhD showed dramatic results of a decrease in tumor weight of 40% in the treated animals compared to a 2.5 fold increase in tumor weight of the untreated group. Dr. Lane outlined a case report of 8 humans in stage III and IV cancer utilizing 30 grams/day of shark cartilage taken as enemas, which produced very encouraging results. A human clinical trial of 29 patients suffering from stage IV and V cancers that had failed conventional therapies was begun. At the end of 16 weeks

of rectal enemas at a dose of one gram of powdered shark cartilage per 2 pounds of body weight, some patients had marked reduction in tumor size and reduced vascularization of the tumor tissue and tissue adjacent to the tumor. Many patients reported a reduction in pain and an improved sense of well-being.

Townsend Letter for Doctors: Review article Aug/Sept. 1994

In 1994, a Phase 2 human clinical controlled trial was sanctioned by the FDA and conducted by Dennis Miller, MD et al at Cancer Treatment Centers of America. The results of this 60 patient study concluded that under the specific conditions of this study, shark cartilage as a single agent was inactive in patients with advanced-stage cancer and had no salutary effect on the quality of life. *J Clin Oncol.* 1998 Nov;16(11):3649-55.

The challenge with this and other human clinical trials in cancer patients is that the only candidates for therapy are those who are end-stage and have failed conventional treatments. This obviously eliminates candidates who have a strong and functional immune system.

In 2008, researchers isolated two partially purified anti-angiogenesis proteins from shark cartilage that were demonstrated to block microvessel sprouting in the collagen-embedded rat aortic ring assay *in vitro* and inhibition of capillary sprouting in the CAM assay *in vivo*. *Bioscience Reports* (2008) 28, (15–21)

Cartilage in general, and shark cartilage in particular, have demonstrated inhibition of angiogenesis in cell cultures and animal studies. The shark cartilage that has been used in most studies was a highly purified protein derivative. The particularly high doses used, distinct fishy flavor and difficulty with routes of administration present unique challenges with this therapy in humans.

VI. SUMMARY AND CONCLUSIONS

Based on my experience and expertise, as well as the research cited above, I hold the following opinions:

- A. There is a reasonable basis to claim that the ingredients of GDU contain bromelain, a source of natural proteolytic enzymes from the pineapple, which helps digest unwanted proteins. GDU also contains turmeric, feverfew and quercetin, which help to reduce inflammation and relieve pain. Next, it is reasonable to claim that these ingredients as a whole may be used as an adjunct to cancer therapy, and that the ingredients possess a wide range of actions as anti-inflammatory agents.
- B. There is a reasonable basis to claim that the ingredients of 7 Herb Formula fight tumor formation, and fight pathogenic bacteria.
- C. There is a reasonable basis to claim that the ingredients of BioMixx boost the immune system, build lean body mass and support healing. It is also reasonable to claim that these ingredients assist the body in fighting cancer, cachexia and in healing the destructive effects of radiation and chemotherapy treatments."
- D. There is a reasonable basis for the claims that pure skeletal tissue of sharks provides a protein that inhibits angiogenesis – the formation of new blood vessels. It is also reasonable to claim that angiogenesis has been demonstrated to inhibit tumor growth in some studies.

February 4, 2009


Sally LaMont, N.D. L.Ac.

**UNITED STATES OF AMERICA
BEFORE THE FEDERAL TRADE COMMISSION
OFFICE OF ADMINISTRATIVE LAW JUDGES**

In the Matter of)	
)	
DANIEL CHAPTER ONE,)	
a corporation, and)	Docket No. 9329
)	
JAMES FELJO,)	Public Document
individually, and as an officer of)	
Daniel Chapter One)	
)	
)	

[Proposed] ORDER GRANTING MOTION IN LIMINE

On March 16, 2009, Complaint Counsel filed a Motion in Limine to exclude the testimony and report of Respondents' expert witness Sally LaMont from any trial in this case.

IT IS HEREBY ORDERED that Complaint Counsel's Motion in Limine is **GRANTED**.

ORDERED:

D. Michael Chappell
Administrative Law Judge

Dated:

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on March 16, 2009, I have filed and served **COMPLAINT COUNSEL'S MOTION AND MEMORANDUM IN SUPPORT OF THEIR MOTION TO EXCLUDE THE TESTIMONY AND REPORT OF RESPONDENTS' EXPERT WITNESS SALLY LAMONT** and **[Proposed] ORDER GRANTING MOTION IN LIMINE** upon the following as set forth below:

The original and one paper copy via overnight delivery and one electronic copy via email to:

Donald S. Clark, Secretary
Federal Trade Commission
600 Pennsylvania Ave., N.W., Room H-159
Washington, DC 20580
E-mail: secretary@ftc.gov

Two paper copies via overnight delivery to:

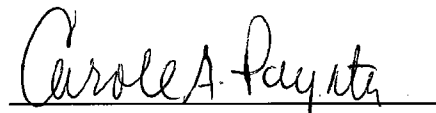
The Honorable D. Michael Chappell
Administrative Law Judge
600 Pennsylvania Ave., N.W., Room H-528
Washington, DC 20580

One electronic copy via email and one paper copy via overnight delivery to:

James S. Turner, Esq.
Betsy Lehrfeld, Esq.
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Complaint Counsel