ORIGINAL

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION

In the Matter of	)	
DANIEL CHAPTER ONE, **a corporation, and**	)	**Docket No. 9329**
JAMES FEIJO, **individually, and as an officer of** **Daniel Chapter One.**	)	**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: l.20 - 8: l.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: l.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 quercitin (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

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[1]Complaint 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: l.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: l.7-11). Instead LaMont has kept her "practice very general" (LaMont Tr. 11: l.20 - 12: l.2).

According to LaMont, "cancer must be treated with conventional therapies" (LaMont Tr. 15: l.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: l.19-25). At most LaMont will work with the physician to "comanage" a cancer patient's care (LaMont Tr. 10: l.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: l.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: l.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: l.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: l.3-5). She acknowledged that there have been no clinical studies performed on the DCO Products (LaMont Tr. 48: l.21-23) and that she herself has not specifically studied the products (LaMont Tr. 78: l.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: l.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: l.23 - 102: l.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: l.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: l.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: l.19 - 75: l.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: l.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: l.14-20). In fact, LaMont did "not think that as a stand-alone [product], BioMixx [could] cure ... cancer or

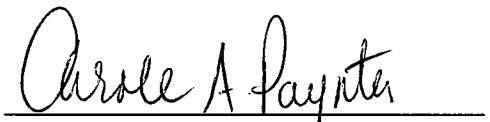
probably even effectively treat it" (LaMont Tr. 176: l.16-22).

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 pharmocognocists 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
- Quercitin (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 Immonol 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 (quercitin) 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:
  - Lipoxygenase 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.

Curr Pharm Des. 2002; 8(19): 1695-706

- 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 turmorigenesis. 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, dysmenorrheal, 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 sesquiterpine 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 1D:,25-dihydroxyvitamin Di (I,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 muM): 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 IkBa by inhibiting NF-kB DNA biding 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-kB 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