NUTRITIONAL SUPPLEMENT TO COMPLEMENT CANCER THERAPY

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Background

Infinimin® Immunity multivitamin, an integrative medicine product of Infinitum Health, LLC, has garnered significant anecdotal customer testimonials regarding cancer. A formal research program has begun to understand the mechanisms and clinical opportunity of this unique multivitamin. Historically, 47% of cancer drugs approved on the market were originally from a natural origin, recent research has highlighted more effective and efficient methods than our classical synthetic methods[1]. Reviewing these medical frameworks, demographic data across countries, and detailed statistical analysis of publicly available data, we have created a formulation that appears to have significant properties to integrate with traditional cancer therapy to help prevent, mitigate, and/or extend the life of cancer diagnosed patients.

Our combination takes into account key polysaccharides such as Fucoidans (from specific seaweed species), β-glucans (from specific mushroom species), antioxidant properties (from the specific fruit, *euterpe oleracea*), and a base multivitamin panel that appears to have dramatic anticancer properties.

Fucoidan, found in seaweeds, has been used in Traditional Chinese Medicine (TCM) for millenia[2]. It shows a wide range of biological activities including anticoagulant, anti-inflammatory[3], antidiabetic[4], procoagulant[5], anticancer[6], and antiviral activities[7]. It has low toxicity[8], good biocompatibility[9], and encouraging results in preclinical and sporadic early-stage clinical trials[10,11]. Moreover, it appears to complement and enhance traditional chemotherapy protocols[12,13].

B-glucans, from mushrooms, has also been used in TCM, has shown antitumor[14], immunomodulating, antioxidant, radical scavenging, cardiovascular, antihypercholesterolemia, antiviral, antibacterial, antiparasitic, antifungal, detoxification, hepatoprotective, antidiabetic effects, as well as complement traditional chemotherapy protocols.[15,16,17,18,19,20,21,22, 23].

Acai, has dramatic antioxidant capability which seems to suggest supporting healthy cells to stay alive. This support is shown by what is know as the oxygen radical absorbance capacity, or ORAC. It measures both the degree and speed with which a certain food inhibits the action of an oxidizing agent, then integrates these two measurements into a single value, producing an accurate assessment of different types of antioxidants of different strengths[24]. Acai is one of the most potent antioxidants available and has strong marketing potential.

The essential vitamin complement panel increases activity, specifically, tumor inhibition and suppression (Vitamin C & Fucoidan; Vitamin C and Maitake) and increases the absorption of larger polysaccharides like those from Reishi and Maitake)[22]

Finally, the "multivitamin" is a known market space and accepted supplement delivery model by the lay population and is the reason why this formulation is branded under this category. [24, 25].

Having disclosed this information, while all of these extracts have great potential, individually, no comprehensive formulation has been developed to optimize their effect against cancers, specifically. Infinimin® was developed with this in mind and has recently been awarded a patent for its unique formuliation[26]. Our label of ingredients is shown below.

SUPPLEMENT FACTS

Serving Size: 3 Capsules **Servings per Container: 30**

Amount per Serving		%Daily Value
Vitamin A (as Vitamin A Acetate)	5000 IU	100%
Vitamin C (as Ascorbic Acid)	60 mg	100%
Calcium (as Calcium Carbonate)	45 mg	5%
Vitamin D3 (as Cholecalciferol)	400 IU	100%
Vitamin E (as DL-Alpha Tocopheryl Acetate)	30 IU	100%
Thiamin (as Thiamin HCl)	1.5 mg	100%
Riboflavin	1.7 mg	100%
Niacin	20 mg	100%
Vitamin B6 (as Pyridoxine HCl)	2 mg	100%
Folic Acid	400 mcg	100%
Vitamin B12 (as Cyanocobalamin)	6 mcg	100%
Pantothenic Acid (as d-Calcium Pantothenate)	10 mg	100%
Infinimin® Patented Blend:	2000 mg	†
Brown Seaweed, Kombu (Laminaria Japonica) 85% Fucoidan		
Wakame (Undaria Pinnatifida)		
Maitake Mushroom (Grifola Frondosa)		
Reishi Mushroom (Ganoderma Lucidum)		
Bladderwrack (Fucus Vesiculosus) (Thallus)		
Cordyceps (Cordyceps Sinensis) (Mycelium)		
Acai (Euterpe Oleracea) (Berry)		

†Daily Value Not Established

Other Ingredients: Gelatin Capsule, Cellulose, Magnesium Stearate

Materials and Methods

To understand more about the mechanisms by which these customers are stating benefits, we designed an MTT Screening Assay using four cancer cell lines to aid in understanding cell viability and apoptosis. The effects of Infinimin® on cancer cell viability was tested on the following 4 cell lines;

A-172, glioblastoma
A-375, malignant melanoma
A-549, lung
DU-145, prostate

The test product was prepared for addition to cell cultures in vitro in the following manner; 0.5g dry product was added to 5ml of phosphate-buffered saline (PBS). The samples were allowed to sit at room temperature for an hour under gentle agitation, and were then sterile-filtered through a 0.22 micron cellulose-acetate syringe filter. These filtrates were the 1:1 stock solutions, corresponding to 100g/L product. Serial dilutions were prepared in PBS. Adding each dilution to cell cultures results in a further 10-fold dilution. This protocol was followed for preparation of product fresh on each test day, so that prepared extracts were used on the same day of preparation.

Viability testing was performed using the MTT screening assay. The MTT assay utilizes a dye that changes color dependent on mitochondrial function, which is directly related to cellular metabolic activity and viability. This assay is commonly used for cytotoxicity testing of drug compounds. The MTT assay is frequently used as a first step when starting work on the biological effects of complex natural products and is a very recognized assay used in determining cellular viability and metabolism. Changes in metabolic activity can trigger changes in MTT results while the number of viable cells is actually constant.

In the MTT bioassay, chemical reactions triggers a specific color development based on cellular functions:

- When a reduction in color is measured, this is linked to a reduced cellular viability, either as a result of direct killing or inhibition of mitochondrial function leading to cell death.
- When an increase in color is measured, this has two possible explanations: 1) Increased cell numbers (growth); 2) increased mitochondrial function (energy production).

The test product was evaluated across a broad dose range (0.02 to 2 g/L).

Results

Four different cancer cell lines were used to test serial dilutions of test products for their effects on cell viability in 48 hour cultures. Eight 2-fold serial dilutions were tested for each product, starting at 2 g/L. Testing conditions were performed in triplicate and cultures maintained at 37oC, 5% CO2 for 48 hours. The viability of cells exposed to product dilutions was compared to the viability of untreated cells cultured under the same culture conditions. Results are Summarized below:

A-172, glioblastoma - Treatment of Glioblastoma cells with the 6 highest doses of Infinimin ® PBS led to **statistically significant**, dose-dependent reductions of cell viability.

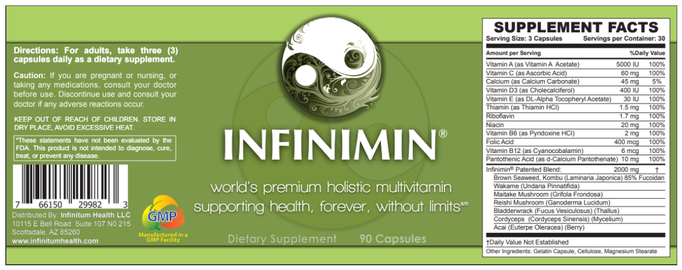
A-375, malignant melanoma - Treatment of Malignant Melanoma cells with the 4 highest doses of Infinimin® PBS led to a slight reduction of cell viability that was **statistically significant** at the 2g/L concentration.

A-549, lung - Treatment of Lung Carcinoma cells with the highest dose of Infinimin® (PBS) led to a reduction of cell viability that was **statistically significant.**

DU-145, prostate - Treatment of Prostate Carcinoma cells with the 7 highest doses of Infinimin® PBS led to reductions of cell viability. This reduction was dose-dependent and **statistically significant** at the 0.125 and 0.5 to 2 g/L concentrations.

These cancer cell lines represent varied genetic profiles for cancer types and the results appear to show a broad spectrum of ability to reduce cancer cell viability using the MTT Assay.

More research is warranted on other cancer cell lines in vitro as well as clinical trial work to prove out efficacy in humans.



Discussion and Conclusion

The data reported here represents the first step to begin to understand the biology behind these clinical benefits reported by customers and the effects of Infinimin® on the viability of 4 different cancer cell lines was studied. Statistically significant reductions of cell viability were seen for all 4 cancer cell lines following treatment with Infinimin® (PBS). Glioblastoma and Prostate Carcinoma cells were the most sensitive to treatment, showing a dose-dependent response. Only the highest dose of Infinimin® (PBS) reduced the viability of Malignant Melanoma and Lung Carcinoma cells. The differences in response of all 4 cancer cell lines to the Infinimin® (PBS) is of strong interest. The cancer cell lines tested here represent a broad range of cancer cell types (brain, skin, lung and prostate) with differing genetic profiles, yet all 4 cancer cell lines had a statistically significant reduction in cell viability (as indicated by reduced mitochondrial function). Certain cancer cell lines (Glioblastoma and Prostate Carcinoma) were more sensitive to Infinimin® treatment than others (Malignant Melanoma and Lung Carcinoma). This is not surprising since each cancer cell line possesses different genetic alterations that lead to differences in response to anti-cancer drugs and therapies[4,5]. This initial pilot work is a first step in beginning to understand how consumption of Infinimin® supports health. In the special case of cancer, the data here suggest that some compounds in Infinimin® could have a direct effect on reducing the growth of cancer cells or enhancing the immune system. With the product proven safe, non-toxic, and complementary effect with traditional chemotherapy, it seems a clear option for healthy patients as a potential prevention to cancer as well as patients diagnosed with these types of cancers to help mitigate effects and/or synergize with therapy plans.

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Figure 1: Description

In the graphs to the right, cell viability is expressed as "Percent viable cells" which is determined by comparing the optical density of cultures exposed to products to that of untreated cultures, which serve as the "100% viability" control.

***indicates significant (p<0.05)**
**** highly significant (p<0.01).**

Dashed line represents the viability of untreated cultures (set at 100%).

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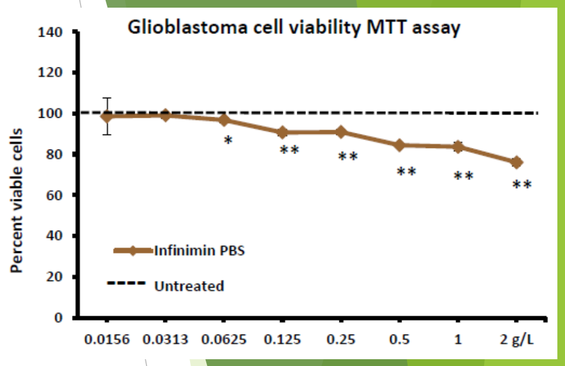
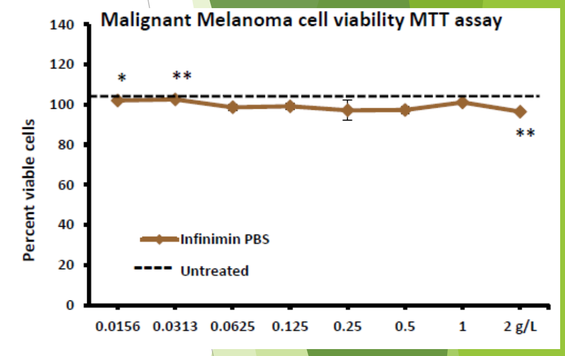
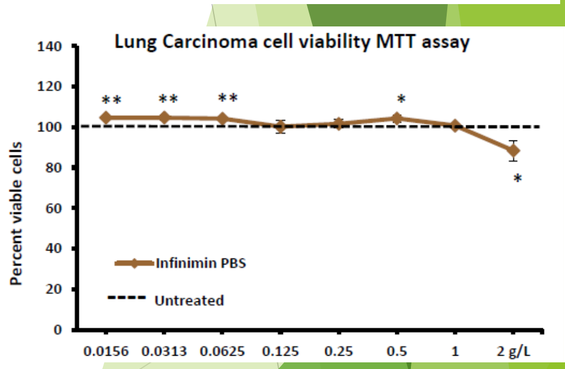
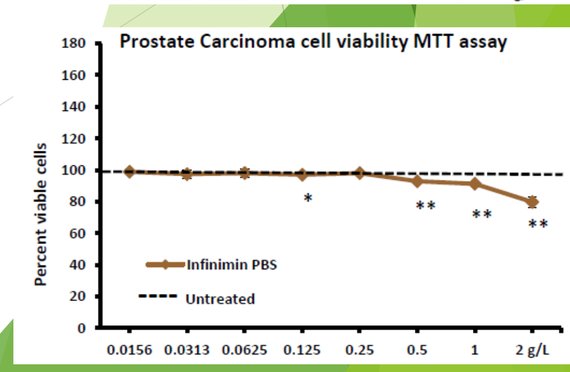
Figure 1: MTT Assay Results









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Congratulations, your abstract (#31) "NUTRITIONAL SUPPLEMENT TO COMPLEMENT CANCER THERAPY" with Kevin Engholdt as the lead author, has been selected for a poster presentation at the 15th Annual Conference of the Society for Integrative Oncology, October 27-29 at the Scottsdale Resort at McCormick Rance, Scottsdale, AZ, USA. Please email info@integrativeonc.org by Monday, August 13, 2018 to confirm your participation as an poster presenter.

A detailed schedule with exact presentation order will be available on the conference webpages by the end of September when the conference program is finalized.

Please check to ensure that the title of your abstract is listed correctly above. This is how it will appear in the program.

Poster Presentation Format
Posters will be open throughout the conference. The Poster Reception will take place on Saturday, October 27 from 5:00 – 6:45 pm MT. You must attend the reception and stand by your poster to be available for discussion as attendees walk through the poster room.

Poster Set-Up time: Saturday, October 27, 2018, 7:00 am – 12:00 pm MT

Poster Removal Time: Monday, October 29, 2018, 7:00 am – 1:00 pm MT
Any posters remaining after 1:00 pm MT will be removed and disposed.

Posters will be allotted one side of a two-sided poster board. The poster number will be on the poster board. The dimensions of the mountable space on the board are 39 inches (100 cm) wide and 39 inches (100 cm) tall. Velcro and/or pins will be provided. It is also recommended that you bring extra copies of your illustrations or a sign-up sheet for people to request copies of your information.

The format of the poster should cover the same information as laid out in the abstract – there should be sections entitled**: Background, Methods, Results, Conclusion.**

Conference Registration
As per the Abstract Guidelines, registration of presenting authors is required for accepted abstracts. Please note that the deadline for registration is Friday, September 4rd, 2018. Online registration is now available; please click here register for the meeting. If you are not registered by the deadline you will not be permitted to present at SIO2018.

Hotel Accommodations
All participants must make their own arrangements for lodging. Conference participants can take advantage of exclusive conference rates at The Scottsdale Resort at McCormick Ranch of $195 per night, plus taxes and fees. Reservations must be made by October 4, 2018, 5:00 pm MT. You can book your reservation online here or by calling (408) 991-9000. The group code is SIO2018.

Questions/Concerns
If you have any questions regarding your presentation at the 15th International Society for Integrative Oncology Conference, please do not hesitate to contact us at info@integrativeonc.org.

Sincerely,

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