

Preliminary Case Series of Artemisinin for Prostate Cancer in a Naturopathic Practice

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ABSTRACT

Objective: To determine if oral artemisinin is safe and has a short-term effect on prostate specific antigen (PSA) kinetics in patients with prostate cancer (CaP).

Design: Retrospective case series.

Setting: A private naturopathic urology clinic in Seattle, WA.

Patients: All artemisinin-treated CaP patients were identified retrospectively between 2005 and 2008. A total of 15 patients were identified who had taken artemisinin and included in the study, comprising 5 patients who had previously undergone radical prostatectomy (RP) and were having biochemical recurrences as well as 10 patients with no prior conventional therapy for CaP.

Interventions: High-dose, pulsed oral artemisinin 300–400 mg three times a day every other week for 3–24 months (median 9.5 months, IQR 5–12 months). All patients were treated with an array of other naturopathic therapies.

Outcome measures: The primary outcomes were the PSA doubling time and velocity; secondary outcome measures were signs and symptoms of metastasis and survival.

Results: Of those patients who have previously undergone RP, 2/5 (40%) had improved PSA kinetics after artemisinin therapy. Of those with no prior RP, 5/10 (50%) had improved PSA kinetics. No patient developed signs of metastasis and no patients died. There were no reported adverse effects.

Conclusions: This pilot study provides preliminary evidence to suggest that high-dose, pulsed oral artemisinin therapy may have activity in patients with CaP. A larger controlled trial is warranted to confirm these preliminary beneficial effects.

Keywords: Prostate cancer; Artemisinin; PSA doubling time; PSA velocity; Naturopathic medicine

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INTRODUCTION

There is a lack of information about natural treatment options for men diagnosed with prostate cancer (CaP). In men with localized CaP as well as post-prostatectomy patients, the life expectancy is more than 10 years, and so providing safe, effective, and affordable therapies is important because current therapies are too invasive and expensive, particularly for low-grade prostate cancer. Whereas ultimately a whole system naturopathic approach is likely the most important aspect of care for men with CaP, either alone or adjunctive to conventional therapies, the efficacy of individual components of such an approach are still of interest.

Artemisinin (Figure 1) is a sesquiterpene lactone isolated from *Artemisia annua* (sweet Annie, qing hao) herb. Artemisinin and its semi-synthetic congeners are well known as schizontocides for malaria. Artemisinin has been shown to have antineoplastic properties against CaP cell lines.¹ Moreover, limited data suggest that artesunate may also have beneficial effects in the treatment of laryngeal squamous cell carcinoma. A case study of a patient with laryngeal squamous cell carcinoma treated with artesunate, an artemisinin analog, and iron showed 70% tumor shrinkage after 2 months with improved quality and duration of life.² Quercetagenin 6,7,3',4'-tetramethyl ether, a flavonoid from *Artemisia annua*, has also been shown to be cytotoxic *in vitro* against several cancer cell lines.³

Indeed, artemisinin (Figure 1) has been shown in preclinical studies to have antineoplastic activity against CaP cell lines. However, given the lack of clinical data regarding the role of artemisinin in CaP, a retrospective case series is presented here from a single naturopathic practice.

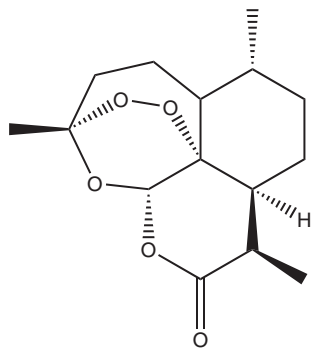


Figure 1: Artemisinin.

METHODS

All patients with biopsy-proven CaP or prostatic intraepithelial neoplasia (PIN) seen in private practice at Northwest Naturopathic Urology (Seattle, WA) were identified by a search of an in-house database as well as a search of electronic medical records. Only those treated with oral artemisinin between January 2005 and December 2008 and either had undergone radical prostatectomy (RP) or had no prior conventional therapy were included. The artemisinin came from the same commercial supplier (purchased from Allergy Research, Alameda). There was no restriction based on age, grade, stage, race, or previous natural treatment. Owing to insufficient numbers of patients who had undergone radiation or androgen deprivation, they were not included.

In all cases, pure artemisinin was dosed on a schedule of 7 days on, then 7 days off. This is based on research showing that artemisinin absorption stops after approximately 5–7 days in men.⁴ This is due to upregulation of intestinal CYP2D6, which completely blocks absorption after a few days. Based on the dosing of artemisinin in malaria patients, a daily dose of 400 mg three times a day (tid) was used during on-treatment weeks. One CaP patient (for simplicity's sake not included in this study as he underwent radiation therapy) developed mild numbness and tingling in the feet at this dose after several months of treatment, and so all subsequent patients to that event were treated with 300 mg tid. No further obvious adverse effects of artemisinin occurred at this dose.

The ideal primary outcome measures for CaP patients are development of symptomatic and/or metastatic disease, deciding to initiate invasive therapy (with attendant potential for decreased quality of life), or CaP-related mortality.⁵ This is a preliminary study to determine whether there is a biological signal to justify future research and the study was not powered to detect differences in these outcomes.

A much less satisfactory surrogate marker is that of serum total prostate specific antigen (tPSA) level.⁶ Screening tPSA has failed in most large double-blind trials to accurately predict CaP-related mortality.⁷ Others have convincingly argued for the overall lack of utility of tPSA as a surrogate.⁸ Some aggressive prostate tumors lose the ability to make PSA, leading

to false negative results.⁹ tPSA is also commonly elevated by common, benign, prostate conditions, creating false positive results.¹⁰ Nevertheless, tPSA and its kinetics are still in wide use clinically and represent the only available, widely-used, affordable, relatively non-invasive marker for CaP at this time. The fact that it is a less-than-ideal surrogate marker does not make it a worthless measure, and it is still a common tumor marker for CaP.¹¹

PSA velocity (PSAV) and PSA doubling-time (PSADT) were used as the primary endpoints for this case series. PSAV and PSADT were calculated from beginning to end of the artemisinin treatment period. PSAV and PSADT are standard outcome measures showing changes in tPSA levels over time.¹² Considerable data support the acceptance of PSA-DT as a marker in clinical trials for the evaluation of oncologic drugs for prostate cancer.^{12,13} A PSAV <0.75 ng/mL/year with a PSADT >1 year, or when the results were negative because of falling tPSA, were considered signs of treatment success. These are relatively conservative cut-off points for success; many use a PSADT >2 years for example.¹⁴

PSADT and PSAV were calculated using the Memorial Sloan-Kettering Cancer Center (MSKCC) website, <http://www.mskcc.org/applications/nomograms/prostate/PsaDoublingTime.aspx>. However, for values of PSA <0.1 (which MSKCC could not calculate), the Prostate Cancer Networking Group of Greater Cincinnati site was used, <http://rommet.com/KAD/pcngcincinnati/psa/calculator.html>.

The measurement of phase angle (PA) during assessment with a bioimpedance analysis device was not completed on sufficient patients to use as a marker throughout the study. This measure, related to fatty acid make-up of cell membranes in the body, has previously been shown to have some

prognostic value in patients with pancreatic cancer and colorectal cancer.^{15,16} For those patients with PA data, they will be presented here to see if there is any basis for the hypothesis that PA might be useful in monitoring CaP progression. A PA >5 degrees and/or rising was considered a favorable outcome whereas a value <5 degrees and/or falling was considered an unfavorable outcome.

Any patient who decided to undergo conventional therapy during the study period, who developed signs of metastatic disease, or who was lost to follow-up, is treated both as a treatment failure and dropped from the analysis, since reasons outside of treatment failure were likely involved in their decisions to discontinue naturopathic care.

Patients were assessed at every visit for a range of adverse effects. New signs or symptoms of any kind were assessed by an oral interview. Most patients had basic serum testing including complete blood counts and chemistry panels conducted at least once while taking artemisinin.

All subjects were simultaneously treated with numerous lifestyle changes and dietary supplements (see Appendix). These were quite varied and no other supplement was used in common by all patients in the study except artemisinin. No single diet was used uniformly among the subjects.

RESULTS AND DISCUSSION

PATIENTS WITH PRIOR RADICAL PROSTATECTOMY

Median artemisinin dosing was for 11.5 months (IQR 9.75–14.75 months) in this group of 5 patients. Patients 7 and 24 had favorable PSA

Table 1: Initial characteristics, prior radical prostatectomy.

Patient	Age	Race	Clinical stage	Gleason score(s)	Cores positive	RP Date	Baseline tPSA, post-RP
7	61	W	T2a	4+3, 4+4	5/12	11/04	0.03 (11/05)
24	54	W	T1c	3+3	1/6	8/03	0.03 (ustPSA) (7/04)
25	68	AA	T1c	Unknown	6/6	5/06	0.6 (5/06)
26	63	W	T1c	3+3	Unknown	3/03	0.2 (6/03)
31	51	W	T2b	5+4	Unknown	9/07	0.47 (10/07)

AA, African-American; FOC, first office call; RP, radical prostatectomy; us, ultrasensitive; W, White.

Table 2: Outcome measures, prior radical prostatectomy.

Patient	Artemisinin dose	Duration of Tx (months)	Pre-Tx PSA	Post-Tx PSA	PSADT; PSAV begin to end of Tx	Other markers
7	300 mg tid	11	0.11 (11/07)	0.09 (10/08)	Negative; negative	PA 6.4 (2/08), 6.8 (6/08)
24	300 mg tid	6	0.17 (7/08)	0.20 (10/08)	1.07 year; 0.12 ng/mL/year	–
25	400 mg tid	>1	0.9 (8/06)	Unknown	Unknown	–
26	Variable (200–1200 mg tid)	23	1.36 (2/07)	6.9 (11/08)	0.75 year; 3.17 ng/mL/year	–
31	300 mg tid; 1 month 400 mg tid	12	0.46 (1/08)	1.8 (11/08)	0.38 year; 1.77 ng/mL/year	–

LTF, lost to follow-up; PA, phase angle; tid, three times per day; Tx, treatment.

Patients with positive outcomes are listed first, then those with negative outcomes.

kinetics (measured from baseline to end of therapy with artemisinin, defined as PSADT >1 year and PSAV <0.75 ng/mL/year); see Tables 1 and 2. Two patients in this group met the primary outcome measure. If the one patient (25), still alive and well as of 10/1/09, but who provided no follow-up PSA data, is excluded, then 2/4 patients (50%) had favorable outcomes. No patient was known to have required additional radiation or hormone therapy. There was no evidence of metastatic disease or other severe outcomes in the any of these patients.

One patient (number 7) had PA data improved by this marker with a rise from 6.4 to 6.8 degrees over the treatment period. This correlated with the improvement in his PSA kinetics.

Patient 26 stated he made numerous errors in dosing artemisinin. He estimated that he took less than 200 mg three times per day for most of the treatment period, varying from 100 mg three times per day to 600 mg three times per day. He also took artemisinin continuously at first, though he did eventually realize his mistake and start doing intermittent dosing.

PATIENTS WITH NO PRIOR CONVENTIONAL THERAPY

Median artemisinin dosing was 7 months (IQR 4.5–10.5 months) in this group of 10 patients. Among those patients who did not have prior conventional

Table 3: Initial characteristics, patients with no prior conventional therapy.

Patient	Age	Race	Clinical stage	Gleason score	Cores positive	Other tests	Baseline tPSA, just pre-bx
2	47	AA	T1c	3+4	2/12	BS neg 7/07	8.0 (3/07)
9	51	W	T1c	3+3	3/12	CT neg 2/08	3.12 (12/07)
30	55	W	T1c	3+3	2/6	n/a	3.86 (4/07)
3	59	W	T1c	3+3	4/12	n/a	4.5 (6/07)
32	50	W	T1c	3+3	1/13	CT neg (5/06)	3.04 (2/06)
28	55	W	T0	PIN	1/12	n/a	4.5 (2/07)
12	75	AA	T1c	3+3	1/18	CT, BS neg (2/00)	16 (1997)
20	70	W	T1c	3+3	2/12	n/a	9.5 (7/05)
21	50	W	T2b	3+3, 4+3, 4+4	8/12	MRI neg (10/08)	4.48 (10/08)
33	55	W	T1c	4+4	unknown	CT, BS neg (1/08)	36 (1/08)

AA, African-American; BS, bone scan; bx, biopsy; CT, computer tomography; FOC, first office call; MRI, magnetic resonance imaging; PIN, prostatic intraepithelial neoplasia; W, White.

Table 4: Outcome measures, patients with no prior conventional therapy.

Patient	Artemisinin dose	Duration of Tx (months)	Pre-Tx PSA	Post-Tx PSA	PSADT; PSAV begin to end of Tx	Other markers
2	300 mg tid	5	8.0 (3/07)	5.1 (12/08)	Negative; negative	PA 8.2 (9/07), 7.4 (1/09)
9	400 mg tid	10	3.12 (12/07)	2.24 (10/08)	Negative; negative	–
30	300 mg tid	12	4.02 (11/07)	3.93 (6/08)	Negative; negative	PA 6.5 (1/08), 6.8 (7/08)
3	300 mg tid	9	4.3 (2/08)	4.5 (12/08)	12.7 year; 0.24 ng/mL/year	PA 7.5 (3/08)
32	300 mg tid	5	2.917 (2/07)	3.104 (8/07)	5.53 year; 0.38 ng/mL/year	PA 8.7 (4/07), 9.3 (1/08)
28	400 mg tid	3	4.5 (2/07)	6 (6/07)	0.79 year; 4.57 ng/mL/year	Neg pr bx 9/07
12	400 mg tid	3	15.86 (2/07)	LTF	LTF	LTF
20	300 mg tid	14	9.5 (7/05)	not measured	n/a	–
21	300 mg tid	3	4.48 (10/08)	RP, 0.01 (2/09)	n/a	Neg surgical margins, T2c N0
33	300 mg tid	>1	36 (1/08)	LTF	LTF	LTF

LTF, lost to follow-up; neg, negative; PA, phase angle; pr bx, prostate biopsy; surg, surgical; tid, three times per day. Patients with positive outcomes are listed first, then those with negative outcomes.

therapy, 3/10 (2, 9, 30) had PSADT and PSAV kinetics that were negative numbers thus favorable; see Tables 3 and 4.

Two additional patients (3, 32) had favorable therapeutic and overall PSADT and PSAV. Thus, 5/10 patients (50%) who had not undergone prior conventional therapy had significantly beneficial PSA-based outcomes.

Two patients (12, 33) were lost to follow-up and are considered here, conservatively, to be treatment failures despite lack of PSA data post-treatment. Both patients were confirmed to be alive and well as of 2010. One patient (20) who did not live in Seattle was not lost to follow-up but failed to provide results of subsequent tPSA testing. He stated repeatedly that he was doing well but had decided to pursue other natural treatments because of a slowly rising tPSA (though he never remembered the exact results when contacted).

Patient 28 did not meet the strict criteria for improvement based on PSA kinetics set out here. However, he had concomitant, biopsy-proven, symptomatic prostatitis throughout this period. In October 2007, after a course of oral ciprofloxacin, his tPSA was documented at 0.1 ng/mL. tPSA was therefore impossible to correlate with prostate neoplasia in this patient. Furthermore, patient 28 underwent a repeat prostate needle biopsy soon after completing artemisinin, and there was no detectable cancer or intraepithelial neoplasia present. This is a much better outcome and arguably indicates patient

28 was a treatment success. Nevertheless, for this conservative analysis based on PSA kinetics he was treated as a treatment failure.

One patient (21) decided to undergo RP because of his relatively young age (50 years), relatively large and severe CaP on biopsy, and anxiety. A prior pelvic MRI did not show any extraprostatic extension or abnormal lymph nodes, and no other testing suggested his cancer had spread. At operation, the surgical margins were clear, supporting that he had localized cancer. He is still treated as an artemisinin failure for the purposes of this conservative analysis.

No patient in the non-RP group, beyond the possibility of the two patients who were lost to follow-up, developed any signs of metastatic disease and all were alive at the end of the study period.

Three patients had before-and-after PA data in this group (2, 30, 32). All values were >5 degrees. Two of the three had rising numbers during the treatment period, one had a small decline. PSA kinetics were favorable in all three patients.

None of the patients in this trial developed any adverse effects that could be attributed to artemisinin. No new signs or symptoms developed in any patient related to taking artemisinin. No adverse changes in or abnormal results for serum transaminases, serum creatinine, complete blood count, blood glucose, or other basic parameters on a chemistry panel were seen in any patient.

CONCLUSION

This retrospective case series presents some data to suggest that short-term artemisinin may have some benefits based on the surrogate marker of PSA kinetics in patients with CaP (2/5 patients with prior RP and 5/10 of patients without prior conventional therapy had favorable improvements PSA kinetics). Unfortunately, this type of real-world setting involves bias and a large number of potential confounders. However, the main purpose was to provide preliminary evidence in support of mounting a clinical trial of artemisinin in CaP patients, including that artemisinin is safe in this population. This case series is too preliminary to determine whether artemisinin has the potential to fill the gap between lower-force naturopathic interventions such as dietary changes and high-force definitive therapies such as prostatectomy and radiation therapies.

There are many weaknesses in this analysis that limit the ability to come to conclusions from the data presented. The mean duration of therapy for all 15 subjects was just nine months (range 3–24 months). This is too short to truly be expected to show a definitive impact on CaP outcomes that matter. However, the fact that so many patients had distinct lowering of their PSA levels so quickly suggests that artemisinin may have a rapid onset of action in a significant fraction of men in this population.

The lack of standardization of other treatment may have clouded the outcomes. No other single treatment besides artemisinin was consistently used between the subjects, however, so it is not possible that a single other agent could account for the benefits seen here. It is entirely possible that multiple other treatments were accounting for the benefits seen in these patients though. Clearly a rigorous, controlled trial with a control group would

be necessary to know for sure. Still, this case series provides a preliminary evidence base supporting funding such a controlled trial.

The lack of a reasonable surrogate marker or ability to detect outcomes that truly matter to patients with CaP are a serious problem, and they affect most research on CaP. The loss to follow-up of several patients severely hampered the ability to detect the truth in what outcomes were achieved. Many efforts were made to contact all subjects included in this trial but complete data could not be obtained.

Preliminary evidence is presented here on PA as a potential clinical marker for outcomes in CaP. It was very safe at the doses used with no detectable adverse effects. Much more work remains to be done in longer-term, controlled trials, but they can build upon the initial groundwork begun here.

The effects on PSA kinetics seen here suggest artemisinin may warrant further assessment in men with CaP, both when it is localized and after RP.

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DISCLOSURE OF INTEREST

Dr. Yarnell reports a financial interest in Heron Botanicals, outside the submitted work. The author has no affiliations with Allergy Research.

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APPENDIX: ADDITIONAL INDIVIDUALIZED TREATMENTS

Abbreviations: bid, twice per day; DU, dose unknown; hs, at bedtime; qd, daily; tid, three times per day.

Patient 2: pescovegan diet with daily intake of immunomodulating mushroom as food, *Eleutherococcus senticosus* 500 mg bid, Essiac Herbal tincture formula DU, PC Hope (suspected to contain estrogen) DU, Chinese Herbal tincture formula DU, Cell Advance (ingredients unknown) DU, *Serenoa repens* DU.

Patient 3: pescovegan diet, increased exercise, avoidance of ethanol, melatonin 20 mg hs, Herbal tincture formula with *Oplopanax horridum*, *Schisandra chinensis*, *Passiflora incarnata*, *Mahonia aquifolium*, *Catharanthus roseus*, *Hypericum perforatum*, and *Taxus brevifolia* 1 tsp tid; Herbal tincture formula with *Oplopanax horridum*, *Schisandra chinensis*, *Annona muricata*,

Catharanthus roseus, *Piper methysticum*, *Mahonia aquifolium*, *Rheum palmatum*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Phytolacca americana*, *Dicentra formosa*, *Zingiber officinale* 1 tsp tid, Multivitamin, flax oil 2–3 tbsps qd.

Patient 7: pescovegan diet, *Cinnamomum zeylanicum* 0.5 tsp with meals, PectaSol 1 bid, IP6 400 mg 1 qd, 1 bid every other day (Cellular Forte), AHCC 500 mg 1 qd, Lycopene 20 mg qd, Ginger 250 mg, Vit C 1000 mg bid, Prostate 51x (*Serenoa*, *Camellia*, *Urtica* root) 1 qd and 1 bid every other day, Multivitamin 1 qd, Zyflamend 1 qd, Host Defense mushroom blend 1 qd, Holy Basil 300 mg 1 qd, GingerForce 150 mg 1 qd, Green and White Tea 500 mg 1 qd, Turmeric Force 400 mg 1 qd, Bio E Gamma Plex 400 IU E, 200 μ g Se, tocopherols 1 qd, Quercetin 500 mg 1 qd, Jarro-Dophilus+FOS 1 qd 3.4 billion species not stated, Vitamin D3 1000 IU, Zinc aspartate 15 mg, Glutamine 750 mg, Lys 1000 mg, Anti-Aging Formula 1 qd, Niacinamide 250 mg, Pomegranate Plus 250 mg, Folic acid 800 μ g, Selenium 100 μ g, Garlic Force 240 mg

Patient 9: intermittent pescovegan diet with daily shiitake mushroom ingestion and avoidance of gout-inducing foods, melatonin 10 mg hs, flax meal 1–2 tbsp qd, prostate supplement (*Prunus africana*, *Serenoa*, pyridoxine, zinc) 1 qd, Vit E 400 IU qd, Selenium 200 µg qd, Fish oil 1 g bid, Lycopene 20 mg qd, Soy isoflavones 50 mg bid, Pectasol 1 scoop bid, Bio-D-Mulsion 4000 IU qd, Vit C 1000 mg qd, Goji juice DU, Herbal tincture formula with *Annona muricata*, *Catharanthus roseus*, *Mahonia aquifolium*, *Larrea tridentata*, *Phytolacca americana*, *Rheum palmatum*, *Zizyphus spinosa*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Dicentra formosa*, *Pinellia ternata*, *Trichosanthes kirilowii* 1 tsp tid, Herbal tincture formula with *Catharanthus roseus*, *Artemisia annua*, *Mahonia aquifolium*, *Schisandra chinensis*, *Phytolacca americana*, *Rheum palmatum*, *Zingiber officinale*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Arctium lappa*, *Podophyllum peltatum*, *Trichosanthes kirilowii*, *Rosmarinus officinalis*, *Silybum marianum* 1 tsp tid.

Patient 12: increase vegetables, nuts and fish in diet, moderate alcohol intake, tamsulosin 0.4 mg qd, dutasteride 2.5 mg qd, atorvastatin 10 mg qd, metoprolol 50 mg qd, montelukast 10 mg qd, aspirin 81 mg, melatonin 3 mg hs, green tea extract 800 mg qd, *Ginkgo biloba* standardized extract 60 mg bid, CLA 1000 mg, Odorless garlic of unknown type 1200 mg, Glucosamine HCl 1500 mg, chondroitin sulfate 1200 mg, MSM 900 mg, Multivitamin, Prostate formula (Zn 15 mg, D 200, E 100, B6 50, *Serenoa* 320, *Prunus africanum* 300, *Urtica* root 100 mg, *Cucurbita* 100 mg, Lys 250, Gly 250, Vitamin B 100 mg, Vitamin D 400 IU qd, Boron 3 mg qd, Lycopene 5 mg qd, Resveratrol 50 mg qd, Flax seed oil 1–3 g qd, 80 mg isoflavones qd, Fish oil with 216 EPA and 144 DHA, 4 per day, Herbal tincture formula with *Panax quinquefolius*, *Schisandra chinensis*, *Polygonum multiflorum*, *Mahonia aquifolium*, *Artemisia annua*, *Centella asiatica*, *Fouquieria splendens*, *Rheum palmatum*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Gelsemium sempervirens* 1 tsp tid.

Patient 20: Increase dietary mushrooms, flax powder, garlic, fish, and nuts, Vitamin A 35,000 IU qd, vitamin D 400 IU qd, Vitamin C 2 g tid, Vitamin E 400 IU qd, Prostate formula (Zn picolinate 22.5 mg, Se 200 µg, *Serenoa* 640 mg, *Smilax* 225 mg, *Eleutherococcus* 150 mg, *Equisetum* 150 mg, *Avena*

150 mg, *Cucurbita* 150 mg, *Urtica* root 150 mg, Ala 100 mg, Gly 100 mg, Glu 100 mg, gamma-oryzanol 75 mg per 3 cap) 2 caps bid, Fish oil 1–6 g qd, Herbal tincture formula with *Eleutherococcus senticosus*, *Panax quinquefolius*, *Aralia californica*, *Mahonia aquifolium*, *Catharanthus roseus*, *Rheum palmatum*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Dicentra formosa*, *Phytolacca americana* 1 tsp tid.

Patient 21: Eat mushrooms regularly, zolpidem, lorazepam, Modified Citrus Pectin 350 mg cap 3 bid, Multivitamin 2 qd, Vit D3 1000–6000 IU qd, *Centella asiatica* tincture 2 droppersful bid, Melatonin 6–10 mg hs, probiotics 50 billion organisms qd, glutamine 1 g, Herbal tincture formula with *Oplopanax horridum*, *Piper methysticum*, *Echinacea angustifolia*, *Centella asiatica*, *Fouquieria splendens*, *Zingiber officinale* 1 tsp tid, *Trametes versicolor* aqueous extract 2000 mg bid, Modified Citrus Pectin 1 scoop bid, Herbal tincture formula with *Annona muricata*, *Catharanthus roseus*, *Mahonia aquifolium*, *Larrea tridentata*, *Phytolacca americana*, *Rheum palmatum*, *Zizyphus spinosa*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Dicentra formosa*, *Pinellia ternata*, *Trichosanthes kirilowii* 1 tsp tid.

Patient 24: ezetimibe/simvastatin 10 mg each qd, aspirin 81 mg qd, Zyflamend 2 tid, multivitamin 2 qd, whey protein DU, creatine 2.7 g after workout, melatonin 3–20 mg with 25 mg theanine hs, fish oil 6 g qd, Herbal tincture formula with *Annona muricata*, *Catharanthus roseus*, *Mahonia aquifolium*, *Larrea tridentata*, *Phytolacca americana*, *Rheum palmatum*, *Zizyphus spinosa*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Dicentra formosa*, *Pinellia ternata*, *Trichosanthes kirilowii* 1.5 tsp bid, red yeast rice 2.4 g qd, açai juice 4–6 oz qd.

Patient 25: pescovegan diet three days per week, eat more vegetables and mushrooms all days, drink green tea, ramipril 0.5 mg, lansoprazole 30 mg qd, tadalafil prn, multivitamin qd, melatonin 20 mg hs, grapefruit juice, Herbal formula with *Panax quinquefolius*, *Withania somnifera*, *Curcuma longa*, *Matricaria recutita*, *Ginkgo biloba*, *Rosmarinus officinalis*, *Catharanthus roseus*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Phytolacca americana*, *Fouquieria splendens*, *Solidago canadensis*, *Mahonia aquifolium* 1 tsp tid, intravenous vitamin C.

Patient 26: aspirin 81 mg bid, USP thyroid 0.75 grain, Provenge, Quercetin 500 mg 5 qd, Acetyl-L-carnitine 620 mg 2 bid, Omega NutriFlax powder 1 tbsp qd, Pomegranate caps 500 mg, 2 qd, Blueberry with pomegranate 1 qd, Super Curcumin 800 mg 1 tid, Grape seed with resveratrol 20 mg, 2 qd, Resveratrol 20 mg 1 tid, NAC 600 mg 1 bid, Super Booster vit C, tocotrienols, lycopene, Se 200 µg, zinc 10 mg, Ginkgo, 1 qd Lactoferrin 300 mg 2 bid, multivitamin 3 bid, Super Zeaxanthin 3.75 mg, Lutein 35 mg, 1 qd, Lipoic acid 150 mg 1 qd, Mega Green Tea Extract polyphenols 725 mg 5 qd, Trimethylglycine 500 mg 1 qd, Mega Silymarin (80%) 900 mg 1 qd, Cruciferous vegetable concentrate extract 1 qd, Omega 3 4–6 qd, Bone Restore per 5 caps D3 1000 IU, Ca 1200 mg, Mg 340 mg, Zn 2 mg, 5 caps qd, Kyolic Aged Garlic 600 mg 1 bid, Mega-C 1000 mg 1 tid, Vitamin E succinate 600 IU, Vitamin D3 10,000 IU qd, CoQ10 100 mg, 1–2 qd, CLA 3000 mg 1 qd, flax oil 2 tbsp qd.

Patient 30: Increase fish, vegetables, mushrooms, and nuts in diet, Coral calcium 3 bid, Vitamin D3 400 IU bid to 2000 IU qd, melatonin 10 mg hs, fish oil 6 g qd.

Patient 31: Eat more mushrooms, garlic, onions, turmeric, ginger, fermented foods, non-tuna fish, nuts and vegetables, Selenium 200 µg qd, Lycopene 20 mg qd, CoQ10 DU, fish oil 1 cap qd, *Serenoa* extract 320 mg qd, Modified citrus pectin powder 1 scoop qd, B complex DU, Emergen-C joint formula 1 qd, *Astragalus membranaceus* tea 1 cup tid, pomegranate, blueberry or cherry juice 4–8 oz qd, melatonin 1 mg hs, *Trametes versicolor* extract 500 mg tid to 1500 mg bid, Herbal tincture formula with *Annona muricata*, *Catharanthus roseus*, *Mahonia aquifolium*, *Larrea tridentata*, *Phytolacca americana*, *Rheum palmatum*, *Zizyphus spinosa*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Dicentra formosa*, *Pinellia ternata*, *Trichosanthes kirilowii* 1 tsp tid, intravenous vitamin C, vitamin D3 5000 IU qd, Herbal formula with *Annona muricata*, *Catharanthus roseus*, *Mahonia aquifolium*, *Artemisia annua*, *Panax quinquefolius*, *Zingiber officinale*, *Taxus brevifolia*, *Rheum palmatum*, *Cephalotaxus fortunei*, *Phytolacca*

americana, *Trichosanthes kirilowii* 1 tsp tid, butyric acid 10 g qd, Herbal formula with *Annona muricata*, *Catharanthus roseus*, *Mahonia aquifolium*, *Camellia sinensis*, *Panax quinquefolius*, *Zingiber officinale*, *Taxus brevifolia*, *Rheum palmatum*, *Cephalotaxus fortunei*, *Phytolacca americana*, *Trichosanthes kirilowii*, *Podophyllum peltatum* 1 tsp tid.

Patient 32: Pancreatic enzymes from Vital Nutrients, 500 mg, 1 tid cc, Super E Complex 400 IU (mixed tocopherols), Selenomethionine 200 µg qd, B complex 50 with 50 µg B12, 400 µg folate, all other Bs 50 µg, 1 qd, Vitamin D3 400–2000 IU qd, vitamin A 1000 IU from fish oil, 5 qd to 1 tid, Kyolic Aged Garlic, 2 caps with Ester C 105 mg, Mushrooms 140 mg, 440 mg AGE, 100 mg astragalus, oregano 100 mg, olive leaf 80 mg, 2 bid, KyoDophilus 1 tid, Zinc citrate 1 qd, Zyflamend 1 tid, LycoPom 1 bid, Antioxidants 23 mg, Hawthorn solid extract, 0.25 tsp bid, PectaSol MCP 1–2 scoops qd, vitamin C 1 g qid, flax meal 2 tbsp qd.

Patient 33: Vit D3 6000 IU qd, ProstaCare 500 mg 2 qd, Beta-glucan 1 qd 500 mg, Amino acids from Twinlabs 2 qd, Turmeric 300 mg 1 qd, OptiZinc 30 mg 4 qd, Mg gluconate 400 mg 1 qd, Ca citrate 1000 mg qd, Phosphatidylcholine 425 mg 1 qd, Iodoral 2 qd, Standard Process CaMg bovine adrenal 3 qd, Perfusia 1 qd, CoQ10 50–300 mg qd, Vit E 400 IU 1 qd, , Quercetin 2 qd, Niacinamide 500 mg 1 qd, Solaray Adrenal, Buffalo liver 2 qd, BioE with Se 400 IU+500 µg 2–6 per day, Potassium 99 mg with amino acids 1 tid, Solaray Mg–K 150 mg+20 mg 3 qd, Folate, B12, 2 qd, OxAbsorb fiber for diarrhea prn, *Calendula* and *Ganoderma* 30 gtt bid, *Selenicereus* and *Crataegus* 10 gtt qd, homeopathic arnica 30C 1 qd, homeopathic leg cramp formula, *Calendula* succus DU, Poly-MVA DU, intravenous vitamin C, copper 1–2 mg qd, Herbal formula with *Annona muricata*, *Catharanthus roseus*, *Oplopanax horridum*, *Mahonia aquifolium*, *Taxus brevifolia*, *Cephalotaxus fortunei*, *Urtica dioica* seed, *Lespedeza capitata*, *Epimedium grandiflorum*, *Juniperus communis*, *Fouquieria splendens*, *Phytolacca americana* 1 tsp tid.