HRG80™ Red Ginseng – An Effective Intervention for Energy, Using CFS, Fibromyalgia, and Post Viral Fatigue as a Model

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Abstract

Aims: To determine the effectiveness of a unique form of red ginseng for improving energy, stamina, and related factors.

Background: Chronic fatigue syndrome and fibromyalgia (CFS/FMS) affects 2.1% of the world's population. It is estimated that 15 to 25% of people who have had COVID-19 illness will have persistent fatigue and debilitation from post-viral CFS. Additionally, disabling fatigue affects about 31% of the adult population.

These combined conditions result in millions of people affected by serious fatigue and in need of effective options to improve function. Clinical experience suggested that a unique hydroponic form of red ginseng, containing very high levels of rare noble ginsenosides, often resulted in marked improvement.

Objectives: The purpose of this initial pilot study was to explore the effects and effectiveness of this unique red ginseng extract (HRG80™).

Method: An open-label prospective study of 188 people with severe CFS/FMS recruited from the principal investigator's (JT) practice and newsletter.

*Inclusion criteria***:** Meeting the CDC diagnostic criteria for CFS or ACR 2010 (amended 2011) diagnostic criteria for fibromyalgia, rating their overall well-being as 5 or less (10 being healthy) on a visual analog scale (VAS). Those with post viral fatigue were allowed to participate.

Interventions: HRG80 Red Ginseng for one month. Subjects were allowed to titrate the dose within preset guidelines to what they found to be optimal.

Outcome measures: The primary outcome measure was the VAS composite score, measured pre- and post-treatment, from a sum of three subscales (energy, well-being, mental clarity).

Secondary outcome measures were changes in sleep, pain, and stamina. Also included was the participant's overall self-assessment of being much worse, worse, no change, better, or much better.

Results: 188 subject patients completed the one-month treatment trial. 60.1% of subjects rated themselves as improved, with 13.3% rating themselves as much better.

Highly significant improvement was seen in all 7 categories. The 60.1% that improved showed a p <.0001 for each outcome measure, with a:

1. 67 % average increase in energy
2. 44 % average increase in overall well-being
3. 48 % average improvement in mental clarity
4. 58 % average composite improvement in the above 3 (primary outcome measure)
5. 46 % average improvement in sleep
6. 33 % average decrease in pain
7. 72 % average increase in stamina

Conclusions: A unique form of Red Ginseng (HRG80) resulted in marked improvement in people with CFS and fibromyalgia. This included the subgroup with post-viral CFS/FMS, whose improvements were similar to the entire group.

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Keywords: fatigue, fibromyalgia, chronic fatigue syndrome, post viral CFS, COVID 19, Long Hauler's Syndrome, ginseng, pain, pain relief.

Introduction

Several factors have combined to create a "perfect storm" of a human energy crisis, including but not limited to:

1. an almost 50% loss of micronutrients in the processed western diet [1]
2. about one third less sleep since lightbulbs were invented [1]
3. numerous chemicals in the environment acting as toxins, including endocrine disruptors [2]
4. the increased speed and stress of modern life.
5. infections triggering chronic fatigue and fibromyalgia

The Sars-CoV-2 virus, responsible for COVID-19 illness, has accentuated this by increasing stress.[3] In addition, it is estimated that 10 to 20% of people who had the virus will have persistent

post-viral chronic fatigue syndrome,[4] making the need for effective support urgent. This is in addition to the 33% of adults who already suffer with severe fatigue.[5]

Historically, in Asian medicine, ginseng has been one of the most valued herbs for overall support of energy and vitality. This has been discussed at length in excellent reviews elsewhere.[6-8] Key hallmarks of CFS/FMS, including post-COVID and post-viral chronic fatigue syndrome include severe fatigue and cognitive dysfunction (called "brain fog").[9] Research suggests that *Panax ginseng* (Meyer) root extracts can help both.[6,8,10] At doses of 4.5-9 gm a day, red ginseng even helped cognition in Alzheimer's.[11-12]

Red ginseng, produced by steaming and drying P. ginseng before the herb is skinned, has shown increased effectiveness for fatigue and cognition relative to white ginseng. [6,10] It may be especially helpful for stress induced psychological fatigue as well[13]. Importantly, this may be via modulation of the hypothalamic-pituitary- adrenal (HPA) axis,[14] which is significantly impacted in CFS.[15]

The literature suggests that these benefits are amplified by using a unique new hydroponically grown ginseng (HRG80), which has over 7 times higher levels of rare ginsenosides than other ginseng products.[6] Red ginseng powder in HRG80 also contains 15.2% total ginsenosides (approximately 6-fold higher level than white ginseng).[6] [I would change this, because the percentage of total ginsenosides is not that important and looks like a low number. Also, the number we use of 7X more rare ginsenosides is in comparison with white, fermented, and red ginseng—not just white ginseng. I don't think we should keep saying white ginseng—we should be comparing to other red ginsengs]

Oral ginsenosides are poorly absorbed [16] and therefore methods of increasing absorption of therapeutic agents may be helpful. One clinically studied system is the use of a natural plant compound called gamma cyclodextrin[17] which has been combined with HRG80 Red Ginseng in one of the 2 formulations used in this study.

Rare ginsenosides have 17 times higher bioavailability and biological activity than classic ginsenosides.[6] This led the authors to explore the use of HRG80 Red Ginseng in their practice. We found it to be extremely helpful. Therefore, we decided to do an initial pilot study to assess its efficacy in CFS and fibromyalgia, including exploring its effects in post-viral CFS/FMS.

Some ginseng studies required very high dosing (e.g., 4500– 9000 mg/day) to show a benefit. [11-12] This may sometimes limit ginseng's clinical utility. Because of the higher bioavailability of the HRG80, including a chewable tablet with gamma cyclodextrin to enhance absorption of the ginseng, we wanted to further explore what forms and dosing offered the optimal clinical benefit, and whether lower doses could be used.

Materials and Methods

Patient Enrollment

The author (JT) invited patients in his practice as well as readers of his newsletter (available at Vitality101.com) to join in this study. 188 participants qualified for the study by meeting diagnostic criteria for CFS or fibromyalgia, being willing to take the supplement, and completing the pre- and post-study questionnaires. No compensation was given for being in the study, except all participants received the supplement free of charge.

Inclusion Criteria

1. Subjects needed to meet the ACR 2010 (amended 2011) diagnostic criteria for fibromyalgia 9 or the CDC criteria for chronic fatigue syndrome 10. They needed to rate their overall well-being as five or less on the VAS below. Those with post-viral fatigue were also allowed to participate.
2. Subjects needed to live in the United States, be over 18 years of age, and nonpregnant.

Exclusion Criteria

1. Subjects could not be on the blood thinner Coumadin (generic name: warfarin).

Interventions

Participants were given HRG80 Red Ginseng for one month of use. Subjects were sent either Terry Naturally HRG80 Red Ginseng Energy capsules, which contain 200 mg (Panax ginseng) root powder (HRG80) per capsule or Terry Naturally HRG 80 Red Ginseng Chewable tablets, which contain 100 mg of the HRG80. The 100 mg chewable tablets also contained gamma-cyclodextrin (GammaSorb^{TM}) to enhance absorption.

Subjects were instructed to take either one or two tablets or capsules daily. If taking two daily, they could be taken together, or one in the morning and one at lunch. They were instructed to titrate the dosing to what they found to be optimal.

Outcome Measures

The primary outcome measure was the VAS composite score measured pre- and post-treatment from a sum of three subscales below (energy, well-being, mental clarity). Secondary outcome measures were the changes individually in energy, well-being, mental clarity, sleep, pain, and stamina. Also, the person's overall self-assessment of being much worse, worse, no change, better, or much better.

The VAS questions asked were:

Please rate the following on a scale of 1 (near dead) to 10 (excellent):

A) How is your energy?

1 2 3 4 5 6 7 8 9 10
1 = near dead and 10 = excellent

B) How is your overall sense of well-being?

1 2 3 4 5 6 7 8 9 10
1 = near dead and 10 = excellent

C) How is your mental clarity?

1 2 3 4 5 6 7 8 9 10
1= brain dead and 10= good clarity

D) How is your sleep?

1 2 3 4 5 6 7 8 9 10
1= no sleep and 10 = 8 hours of sleep a night without waking

E) How severe is your achiness/pain? (1 is worst possible pain)

1 2 3 4 5 6 7 8 9 10
1= very severe pain and 10 = pain free

F) How is your stamina?

1 = no stamina and 10 = healthy stamina

2. Each subject's overall subjective feeling after taking the supplement (i.e., much better, somewhat better, no change, somewhat worse, or much worse).

Study Design

The design (a prospective open, unblinded trial) used outcome measures in the form of the Visual Analog Scale (VAS) questionnaire and was kept simple to improve compliance. All patients gave informed consent, and the study was approved by the Practitioner Alliance Network IRB (ID#: PAN-SES 1-2020).

Patients could continue their current treatments during the study. They were asked not to make any changes to their current treatments during the study.

Statistical Analysis

All analyses were performed using the Statistical Package for the Social Science (SPSS) version 27.0 (SPSS Inc., IBM Corp., Armonk, USA). Continuous variables were assessed for normality using visual inspection of histograms and qq-plots. The primary outcome measure was the VAS composite score measured pre- and post-treatment. The composite score was derived from a sum of three subscales (energy, well-being, mental clarity), ranging from 0 to 30, with higher scores indicating better health and functioning. Secondary outcomes were pre- and post-treatment total scores on six VAS subscales (energy, sleep, pain, well-being, mental clarity, stamina) ranging from 0 to 10 with higher scores indicating better health and functioning. Two-tailed, paired samples t-tests were used to examine change in VAS scores following treatment with the alpha level set to .05. Effect sizes were calculated using Cohen's *d* for paired samples t-tests. Effect sizes are interpreted as follows: small: $d = 0.2$; medium: $d = 0.5$; large: $d = 0.8$. To adjust for multiple testing in relation to the secondary outcome analyses, a Bonferonni Correction was applied with the alpha level set to .008 (.05/6). Analyses were performed for the overall sample (N = 188) and repeated in the subsample that self-reported feeling 'better' or 'much better' following treatment (herein referred to as *improvers*; n = 113).

Supplementary analyses were conducted to examine whether change in VAS scores were different between subjects with and without a virus onset of illness. A mixed model ANOVA (analysis of variance) was conducted with treatment entered as a within-subjects factor (i.e., pre- and post-treatment VAS scores) and illness onset status (yes = 76, no = 112) entered as a between-subjects factor. The group by treatment interaction was examined to determine whether the effect of treatment was different between illness onset groups. A second mixed model ANOVA was conducted to examine differences in treatment effects between subjects who took the supplements in capsule (n = 95) versus tablet (n = 93) form. The mode of supplement was entered as the between-subjects factor, and the group by treatment interaction was examined. The assumption of equality of variances was assessed with Levene's test.

Additionally, exploratory analyses were conducted to further understand the effects of different supplement forms and doses. A mixed model ANOVA was run with treatment as the within-subjects factor and dose/form as a four-group between-subjects factor (1 tablet per day = 35; 1 capsule per day = 22; 2 tablets per day = 39; 2 capsules per day = 59). Follow-up analyses were conducted among the subsample of improvers to describe and compare the effectiveness of treatment between specific subgroups using t-tests. A series of chi-square tests were used to examine differences in daily preference for supplement intake. Specifically, the frequencies of

preferred daily dose (1 per day, 2 per day, other) and daily frequency (once daily, twice daily, other) were compared between subgroups who used capsules or tablet form. The alpha level was set to .05 for all supplementary and exploratory analyses.

Results

A total of 188 participants completed the treatment. All continuous variables were normally distributed, and no missing data were observed. The sample characteristics are summarized in Table 1. Briefly, the sample was on average 59 years old with a mean duration of illness of 19 years. Most subjects were female and most met criteria for chronic fatigue syndrome and fibromyalgia. More than half the sample were characterized as improvers.

For the primary and secondary analyses, there was a significant mean increase in VAS composite and all VAS subscale scores from pre- to post-treatment, with predominately large effects sizes (see Table 2). The same pattern of findings was observed in the subsample of improvers, though all the effect sizes were notably larger (see Table 3). Results of the supplementary analyses examining change in VAS scores by virus onset of illness did not reveal any significant group by treatment interactions (all p values > .05). Likewise, there were no significant group by treatment interactions when examining change in VAS scores by supplement form (capsule vs. tablet, all p values > .05). These findings can be taken to mean that treatment effects were similar across groups. The results of the mixed model ANOVAs are summarized in Tables 4 and 5.

Exploratory analyses examining treatment effects by varying supplement dose and form did not reveal any significant group by treatment interactions in the overall sample (all p values > .05). In other words, there was no statistically significant difference between any of the four subgroups (1 capsule, 1 tablet, 2 capsules, 2 tablets per day) in terms of the degree of change on the VAS scores (composite or subscales). This can be taken to mean that 100mg (in the form of 1 tablet daily) was very clinically effective and statistically significant, and there was no added benefit of taking more than 100mg per day of the red ginseng when it was combined with the gamma-cyclodextrin (only present in the tablet form, not capsules). This is further supported by comparisons between those who took 1 tablet and 1 capsule per day in the subgroup of improvers, which did not reveal any significant differences indicating that most of the highly significant improvement can be obtained with the single tablet of 100 mg of the HRG 80 red ginseng combined with the gamma-cyclodextrin daily (see Table 6 below; additional supporting data is available on request in an Appendix).

Descriptive summary statistics are provided for self-reported daily supplement preferences in Table 7. To briefly summarize, just over half of the sample reported taking two capsules or tablets per day, while 70% of the sample indicated that they preferred to take the supplements

once daily. There was a significant overall difference in preference for daily dose between those who used capsules and those who used tablets ($X^2 = 7.78$, $p = .020$). Specifically, a greater proportion of persons preferred two supplements per day (compared to one) when it was in capsule form, as compared to tablet form. There was no difference between groups in their preference for the frequency of daily dose.

Table 1. Sample Characteristics (N = 188)

Variable	**Value**
Age in years, mean (SD)	58.6 (11.6)
Gender, female %	89.4 (168)
Duration of illness in years, mean (SD)	18.9 (10.6)
Onset with viral illness, % (n)	40.4 (76)
Diagnosis of CFS, % (n)	96.8 (182)
Diagnosis of FMS, % (n)	94.1 (177)
Self-reported feeling post-treatment, % (n)	
Much worse	2.7 (5)
Worse	3.2 (6)
Same	34.0 (64)
Better	46.8 (88)
Much better	13.3 (25)

Note. CFS = chronic fatigue syndrome; FMS = fibromyalgia.

Table 2. Change in VAS Scores with Treatment in Full Sample (N = 188)

Variable	Pre-tx Mean (SD)	Post-tx Mean (SD)	t statistic (p-value)	Effect size (*d*)	Percent Improvement
VAS Composite	12.2 (3.5)	17.1 (4.8)	-14.31 (<.001)	-1.04	40.2
VAS 1. Energy	3.6 (1.3)	5.4 (1.8)	-13.30 (<.001)	-0.97	50.0
VAS 2. Sleep	4.5 (1.7)	6.0 (2.0)	-10.46 (<.001)	-0.76	33.3
VAS 3. Pain	4.6 (1.8)	5.5 (1.8)	-5.84 (<.001)	-0.43	19.6
VAS 4. Well-being	3.9 (1.4)	5.7 (1.9)	-12.89 (<.001)	-0.94	46.2
VAS 5. Mental Clarity	4.7 (1.6)	6.1 (1.8)	-10.18 (<.001)	-0.74	29.8
VAS 6. Stamina	3.3 (1.5)	4.8 (2.1)	-10.04 (<.001)	-0.73	45.5

Note. VAS = visual analogue scale. Effect size = Cohen's *d*.

Table 3. Change in VAS Scores Among Subsample Who Self-Reported Improvement (N = 113)

Variable	Pre-tx Mean (SD)	Post-tx Mean (SD)	t statistic (p-value)	Effect size (*d*)	Percent Improvement
VAS Composite	11.9 (3.2)	18.8 (4.3)	-17.71 (<.001)	-1.67	58.0
VAS 1. Energy	3.6 (1.4)	6.0 (1.7)	-14.86 (<.001)	-1.40	66.7
VAS 2. Sleep	4.4 (1.7)	6.4 (1.8)	-11.95 (<.001)	-1.36	45.5
VAS 3. Pain	4.5 (1.9)	6.0 (1.7)	-7.36 (<.001)	-0.90	33.3
VAS 4. Well-being	3.8 (1.2)	6.3 (1.6)	-15.63 (<.001)	-1.74	43.6
VAS 5. Mental Clarity	4.4 (1.3)	6.5 (1.7)	-12.80 (<.001)	-1.45	47.7
VAS 6. Stamina	3.2 (1.4)	5.5 (2.0)	-12.48 (<.001)	-1.41	71.9

Note. VAS = visual analogue scale.

Table 4. Results of Mixed Model ANOVAs Examining Change in Primary and Secondary Outcomes by Illness Onset Status (N = 188)

Outcome Variable	F-statistic (p-value)
VAS Composite	
Treatment	204.57 (<.001)
Treatment*Group	1.57 (.212)
VAS 1. Energy	
Treatment	172.22 (<.001)
Treatment*Group	0.26 (.614)
VAS 2. Sleep	
Treatment	113.03 (<.001)
Treatment*Group	2.77 (.098)
VAS 3. Pain	
Treatment	31.47 (<.001)
Treatment*Group	0.33 (.567)
VAS 4. Well-being	
Treatment	168.03 (<.001)
Treatment*Group	2.03 (.156)
VAS 5. Mental Clarity	
Treatment	104.74 (<.001)
Treatment*Group	1.49 (.224)
VAS 6. Stamina	
Treatment	103.65 (<.001)
Treatment*Group	2.37 (.125)

Note. VAS = Visual analog scale.
Group: Onset with viral illness - yes (n = 76), no (n = 112).

Table 5. Results of Mixed Model ANOVAs Examining Change in Primary and Secondary Outcomes by Supplement Form (N = 188)

Outcome Variable	F-statistic (p-value)
VAS Composite	
Treatment	203.65 (<.001)
Treatment*Group	0.04 (.844)
VAS 1. Energy	
Treatment	220.65 (<.001)
Treatment*Group	2.44 (.120)
VAS 2. Sleep	
Treatment	109.70 (<.001)
Treatment*Group	1.19 (.277)
VAS 3. Pain	
Treatment	33.91 (<.001)
Treatment*Group	0.58 (.447)
VAS 4. Well-being	
Treatment	165.39 (<.001)
Treatment*Group	0.02 (.891)
VAS 5. Mental Clarity	
Treatment	103.00 (<.001)
Treatment*Group	0.18 (.676)
VAS 6. Stamina	
Treatment	100.85 (<.001)
Treatment*Group	1.82 (.179)

Note. VAS = Visual analog scale.
Group: Supplement form - capsules (n = 95), tablet (n = 93).

Table 6. Percent Improvement in Each Symptom (in Improvers) with Each Dose and Form

Outcome Variable (% Improvement in Improvers)	One Tablet (n = 25)	One Capsule (n = 16)	Tablet vs. Capsule t Statistic (p-value)	Effect size (*d*)	Two Tablets (n = 24)	Two Capsules (n = 39)
VAS Composite	60.6	69.0	0.56 (.581)	.18	70.7	68.3
VAS 1. Energy	70.9	78.4	0.31 (.757)	.11	92.1	96.5
VAS 2. Sleep	62.5	78.8	0.64 (.531)	.23	59.4	60.9
VAS 3. Pain	45.5	67.0	0.90 (.375)	.29	36.2	67.2
VAS 4. Well-being	68.5	80.6	0.61 (.547)	.20	79.6	80.1
VAS 5. Mental Clarity	56.4	67.9	0.70 (.490)	.22	55.0	58.7
VAS 6. Stamina	74.7	123.7	1.41 (.168)	.45	87.8	105.1

Note. VAS = Visual analog scale.

Table 7. Daily Supplement Intake Preferences

	Full Sample (n = 188)	Subgroup: Capsule (n = 95)	Subgroup: Tablet (n = 93)
Daily dose, % (n)			
1 per day	30.3 (57)	23.2 (22)	37.6 (35)
2 per day	52.1 (98)	62.1 (59)	41.9 (39)
Other	17.6 (33)	14.7 (14)	20.4 (19)
Daily frequency, % (n)			
Once per day	70.2 (132)	74.7 (71)	65.6 (61)
Twice per day	17.6 (33)	16.8 (16)	18.3 (17)
Other	12.2 (23)	8.4 (8)	16.1 (15)

Discussion

This study provides preliminary data on a potentially effective herbal intervention for chronic fatigue syndrome and fibromyalgia, including following viral infections. It is very promising that this safe and low-cost intervention was able to significantly improve patients' clinical outcomes, with 60.1% of subjects improving.

The group that improved reported an average 67 % increase in energy, 72% increase in stamina, and 48% improvement in mental clarity, which is a dramatic improvement for a single agent. This makes it a powerful addition to our S.H.I.N.E.® Protocol, which optimizes Sleep, Hormonal function, Immunity, Nutritional support, and limited Exercise as able. In our earlier RCT, S.H.I.N.E.® resulted in an average 91% improvement in quality-of-life in those with CFS/FMS, [18-19] making these conditions highly treatable.

Research has now advanced to the point where fatigue, brain fog, and other health conditions associated with CFS and fibromyalgia can be significantly, and often dramatically, improved.

This study has several weaknesses, the key one being the lack of randomization and a placebo control group. The other is that outcomes were all subjective. However, given that the primary debilitation from these illnesses is via subjective effects rather than lab test changes, these subjective measures are critical in these conditions.

In addition to supporting the effectiveness of ginseng, the study also adds important information on the use of unique forms of the herb, and strategies to increase absorption. A significant problem in the use of ginseng is the high dosing sometimes required to achieve optimal benefits.

Clinically, we found much lower doses of HRG80 to be effective. This was confirmed by a recent study[6] showing that the effective total daily dose of HRG80 ginseng in treating day-to-day fatigue was 418 mg, 10-fold lower than sometimes used effective doses of red ginseng (4500-9000 mg per day).

Although marked clinical and statistical improvement was seen in all groups taking the HRG 80 Ginseng, most of the statistically significant clinical improvement was able to be obtained with a single tablet containing just 100 milligrams of the red ginseng, when combined with gamma-cyclodextrin (GammaSorb) to enhance absorption. Increasing the HRG80 red ginseng dose from 100 mg to as high as 400 mg (without the gamma-cyclodextrin) resulted in clinically modest but statistically insignificant improvements relative to the 100 milligram tablets. However, what form and dose were optimal varied with each individual, as is usual in clinical practice. Overall, this study shows that even low doses of 100 mg can deliver optimal benefits when combined with gamma cyclodextrin to improve absorption.

It also points the importance of the forms and amounts of ginsenosides used for treatment. In this study, using a form of ginseng that has 7 times higher levels of rare ginsenosides than common red ginseng resulted in people requiring only 1 – 3% of a standard ginseng dose. This highlights the benefit of combining new natural technologies with old wisdom.

Conclusions: A unique form of red ginseng (HRG80), resulted in marked improvement in energy levels, sleep, mental clarity, pain relief, and overall well-being in those with CFS and fibromyalgia, including those with post-viral CFS/FMS.

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