Human Clinical Trial

Evaluating the Safety and Efficacy of

PANITROL

A Supplement Containing Juniper, Goldenrod, Dandelion, Meadowsweet, Willow, and Whole Grape

In the Treatment of Chronic Arthritis Symptoms

A Randomized, Placebo Controlled Study

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1.0 ABSTRACT

The purpose of this two-group randomized placebo-controlled 30-day study was to evaluate an all-natural herbal dietary supplement product (Investigational Product, or IP) with respect to alleviating chronic arthritis pain using human subjects with a documented history of arthritis.

This IP is an all herbal diet supplement available for use in the control of chronic arthritis pain. The product is composed of extracts of Juniper (*Juniperus communis*), Goldenrod (*Solidago virgaurea*), Dandelion (*Taraxacum officinale*), Meadowsweet (*Filipendula ulmaria*), Willow (*Salix alba*), and whole grape (*Vitis vinifera*)

This was a 30-day, 75-subject study using patients drawn from a large population of chronic arthritis sufferers. The patients were randomized into two groups and took either placebo or active treatment. The direct objective of this investigation is the performance of the test product compared to placebo in reducing chronic severe pain associated with arthritis. Future studies are planned to more accurately elucidate which of these many phytochemicals, and in what combinations, exert the most influence on the chronic arthritis symptom suite.

Daily records were kept by each patient as to their pain level and the number of capsules they took morning and evening, and reviewed by the Fenestra research staff interviewer during follow-ups.

This study was performed by FENESTRA RESEARCH LABS clinical study personnel at Valley Mountain View Hospital in Las Vegas, Nevada. The OPTIMAL WELLNESS TEST portion of this research was done using proprietary devices and methodologies developed by FENESTRA RESEARCH LABS.

2.0 PROTOCOL

2.1 SCREENING and FOLLOW-UP

Following an initial screening at Visit 1 (week 0), subjects entered a 1-week baseline period (subjects were told to refrain from taking any unnecessary OTC's, prescription drugs, or natural products for the remainder of the

study). Subjects who met all inclusion criteria and none of the exclusion criteria during the intake at Visit 2 (week 1) were then provided either the placebo or the IP along with a protocol describing daily dosing to follow for the duration of the study and a patient log for recording date, age, sex, pain intensity, and number of capsules taken. The second evaluation on Visit 3 (week 3) was performed following standard procedures and the study's protocol was again gone over with each subject on an individual basis. Final evaluations of test subjects were completed on visit 4 (week 5) of the study.

Study subjects (18 yrs or older, M/F) had to be in generally good health and have had a history of extreme arthritis pain for a minimum of at least one (1) year prior to the start of the study. A diagnosis of arthritis by a qualified physician was required for entry in the trial. Subjects must have had daily pain which, by their own description, was level 9 to 10 (before pharmaceutical intervention) when using a linear pain scale where level 0 means no pain, a level 1 is the mildest possible pain and a level 10 is the worst imaginable pain. This is the same scale used in the study.

2.2

DOSAGE and PAIN ASSESSMENT

This was a 30-day, 75-subject study drawn from a large population of arthritis patients. The patients were randomized to active treatment (n=49) or placebo (n=26). All subjects in both groups took 3 capsules in the morning and 1 capsule at night for the first 5 days of the study. The dosage was then reduced to 2 capsules in the morning with an optional additional 1 capsule at night. Rescue medications were not allowed in this study.

Arthritis pain was assessed using the widely accepted procedure of self-assessment by the patients using a linear scale from 0 to 10, where 0 represents no pain, 1 represents the mildest possible pain and 10 represents the worst imaginable pain. Daily records were kept by each patient of capsules taken and pain level, and reviewed by the Fenestra research staff interviewer during follow-ups.

In this study "chronic arthritis pain" was defined as a clinical diagnosis of arthritis by a physician and pain every day of level 9 or 10 for one year or more prior to the trial.

2.3 INCLUSION CRITERIA

- A written informed consent consistent with required guidelines and meeting prior to participation in the trial.
- Male/female subjects 18 years of age or older.
- Arthritis and arthritis pain must be chronic, having been present daily for a minimum of at least one (1) year prior to the start of the study. Subjects must have had daily pain which, by their own description, is level 9 to 10 (before pharmaceutical intervention) when using a linear pain scale where grade 1 is the mildest possible pain and grade 10 is the worst imaginable pain. This is the same scale used in the study.
- A diagnosis of arthritis based on typical symptomology, *i.e.* pain, stiffness, etc. by a qualified healthcare professional at least 1 year prior to the start of the study.
- Subjects whose *Optimal Wellness Test* (OWT) indicated they were at least 35% out of balance for standard Wellness with respect to the resistivity, conductivity, and Anabolic-Catabolic Balance (oxidative

stress) indicators (the red zone).

- Subjects who were able to follow the protocol as designed by the manufacturer and Fenestra Research labs.
- Generally good health.

2.4 EXCLUSION CRITERIA

- History of head trauma.
- History of serious diseases or illness.
- Moderate to severe renal insufficiency.
- Recent history (<6 months prior to Visit 1) of myocardial infarction.
- Regular use oxygen therapy.
- Active tuberculosis, a history of cancer within the last 5 years (treated basal cell carcinoma allowed), thoracotomy with pulmonary resection within 1 year prior to the trial, currently in a pulmonary rehabilitation program or who have completed a pulmonary rehabilitation program in the 6 weeks prior to the screening visit (Visit 1).
- Current prescription for diuretic medications, cardiac stimulants, or any other medication that may, in the opinion of the Fenestra research staff, alter testing results.

- Use of opiate analgesics, prescribed or otherwise, obtained for recreation or for any treatment reason including migraine.

- History of drug addiction.
- Females who are pregnant, lactating, or nursing or who may become pregnant during the course of the study.
- Diagnosis as HIV-positive, diagnosis of AIDS, or with any neuromuscular condition including CP, MS, ALS, or Huntington's Chorea
- Uncontrolled hypertension (*e.g.* BP>150/100).
- Patients with any condition not previously named that, in the opinion of the investigators or intake staff, would jeopardize the safety of the patient or affect the validity of the data collected in this study.

2.5 PAIN ASSESSMENT

Arthritis pain was assessed using the widely accepted procedure of self-assessment by the patients using a linear scale from 0 to 10, where 0 represents no pain, 1 represents the mildest possible pain and 10 represents the worst imaginable pain. In this study "chronic arthritis pain" was defined as a clinical diagnosis of arthritis by a physician and pain every day of level 9 or 10 for one year or more prior to the trial.

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All subjects in the study were instructed to make no changes to their daily consumption of food or liquid in regards to the amount, volume, or type consumed.

NOTE: Compliance to the protocol was monitored and maintained through bi-weekly phone calls with Fenestra Labs Clinical Studies personnel as well as in-person office visits as described above.

3.0 RESULTS AND DATA ANALYSIS

3.1 Statistical Methods

The statistical model for this study is a two-factor repeated measures experiment with one grouping factor (Treatment, Control) and one repeated factor (Day 1 to Day 30). Subjects reported, *inter alia*, perceived pain on a scale of zero(0) to ten(10), with 0 representing no pain and 10 representing severe pain. Since the pain reports are ordinal and not continuous, and since the responses tended to clump around 10 at the beginning of the study and at 0 for the treated group at the end of the study, non-parametric tests rather than normal theory tests are called for. To compare between groups within day of observation the Mann-Whitney U-test was used. This test determines whether the pain scores in one group were significantly higher or lower than the pain scores in the other group. It ranks scores without regard to group and then compares whether the sum of ranks in one group is different from the sum of ranks in the other group. To compare within groups across days the Friedman Two-way Analysis of Variance by Ranks was used to compare pain

responses in subsequent days to those reported for Day 1. The Friedman test ranks responses within a subject for Day 1 and for the day being compared to Day 1. These ranks are then summed across subjects and then compared to test whether the sum of ranks for Day 1 differ from those of the comparison day. For ordinal data it is usual to report the Median value, which is that value above which 50% of the scores are found, and the Inter-Quartile Range. In the inter-quartile range, 25% of subjects are below the lower value given, while 25% are above the upper value given.

The Results of these statistical analyses are shown in Table 1 below.

Table 1. Median and Inter-Quartile Range Pain Score by Group and Day							
	Placebo			Treated			p[a]
Day	Median	IQ Range		Median	IQ Range		
1	10	10-10		10	10-10		0.0706
4	10	9-10		7 [b]	5-10		<0.001
7	10	10-10		2 [b]	1-4		<0.001
10	10	10-10		0 [b]	0-1		<0.001
14	10	10-10		0 [b]	0-0		<0.001
a) Mann-Whitney U-test between groups							
b) Significantly different from Day 1 by Friedman Test							

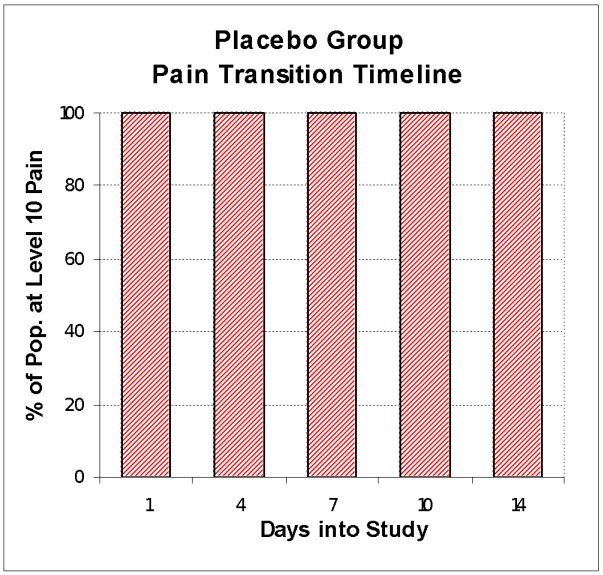
Beginning at Day 1 the two groups were not significantly different by the Mann-Whitney test, with identical medians and inter-quartile ranges. As the study went on, by Day four the active treatment group had significantly smaller median pain scores. This trend continued, until by Day 14 none of the treated group was reporting any pain. Not shown in Table 1 is the fact that from Day 13 on there was no reported pain among the treated group while the placebo group continued the same high pain levels. When comparing responses over time within group using the Friedman test, it was found that the placebo group did not change over time. The treated group showed highly significant decreases in pain scores, starting by Day 3 (data not shown) which continued throughout the study. This effect is shown in Table 1 by the fact that the inter-quartile range converges to zero.

Another way of looking at these results is to examine the percentage of the test group that experienced a certain level of relief from chronic arthritis pain within a certain time after the start of the trial.

3.2 Results

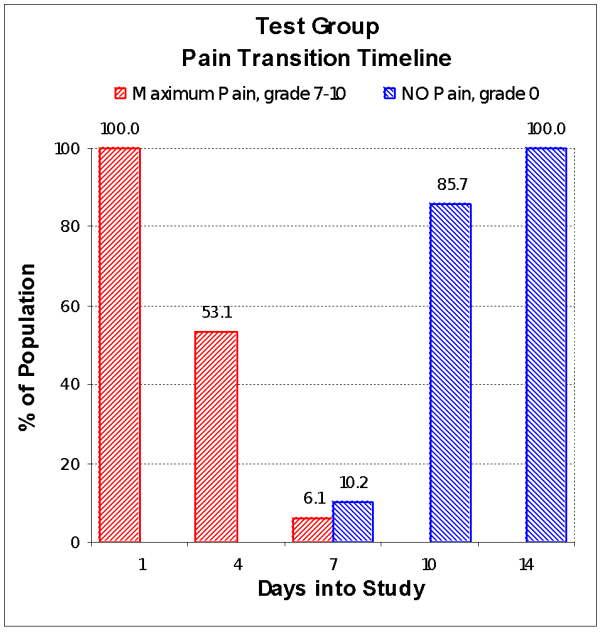
Placebo Group —

- All Placebo subjects started study at pain=10
- **No** change in pain level during study



Test Group —

- All Test subjects started study at pain = 9 to 10
- By Day 4 only 53.1% of patients were at pain = 9 to 10
- By Day 7 only 6.1% of patients were still at pain = 9 to 10, and 10.2% of patients reported NO PAIN AT ALL
- After Day 7 no patients (0%) of patients were at pain = 9 to 10
- By Day 10 85.7% of patients were reporting NO PAIN AT ALL
- By Day 14 100% of patients were reporting NO PAIN AT ALL



5.0 OPTIMAL WELLNESS TEST DATA ANALYSIS

Certain physiologic parameters indicative of various states of oxidative stress, electrolyte imbalances, and hydration were measured during this study using OWT apparatus and calculation algorithms. OWT apparatus and calculation algorithms are proprietary and were developed by Fenestra Research Labs. All measurements were taken at baseline (Visit 0) and at the study's end.

Parameters measured in both urine and saliva included:
pH, rH_2 (a derived index of oxidative stress), ORP (redox potential), and r (resistivity).

Parameters measured only in urine in addition to the above included:
Surface tension, specific gravity, NO_3^-, NH_3, deg. Brix, and conductivity.

Generally speaking, these parameters were chosen because they relate to ionic content and balance between the plasma, the cells, and the extracellular fluids, the presence of reduced or oxidized biomolecules, and the first, in some cases even pre-symptomatic, stages of degeneration. Measuring parameters in saliva and urine can be indicative of the state of hydration in tissues and the body's ability to absorb nutrient and palliative chemicals and to get rid of toxins, metabolites, and tissue degradation residues, many of which stimulate further inflammation and pain. Hydration can be particularly important in the case of joint tissues such as articular cartilage which become prone to mechanical injury and degradation upon loading when dry.

There was no statistically significant change in any parameter measured for the placebo group.
A simple non-paired t-test comparing the differences between baseline and final parameter values for placebo and live product groups showed small but statistically significant changes in salivary ORP and resistivity, and in urinary specific gravity, ammonia, and conductivity.

Additional studies are planned to elaborate the clinical significance of these changes (in light of symptomatic relief achieved with the test product) and to further refine their diagnostic and predictive utility, especially with regard to joint tissue health.

6.0 CONCLUSIONS

Statistical analysis of these data shows a consistent picture between treatment groups over time. The Placebo group showed no reduction in pain to speak of for the entire duration of the test, meaning that there was no measurable placebo effect. This can be attributed in part to the high level of pain at the start of the trial. The Treatment group had a uniformly and dramatically more favorable response and achieved that response in a relatively extremely short time. The reduction in pain in this group did not depend on the length of time chronic pain had existed prior to the study (inclusion criteria was one year or more) and was both sex and age independent. No adverse events whatsoever were reported during the study.

Based on these clinical comparisons and the complete lack of known adverse side effects, interactions, or contra-indications from the herbal ingredients in the IP was shown to be a safe and highly effective means of eliminating or substantially reducing arthritis pain and the frequency of attacks while also reducing or eliminating other side effects of the syndrome without impacting various internal organ systems or the CNS, thus making it a viable replacement for pharmaceutical approaches to arthritis pain control.