TESTING LIFEWAVE ANTI-AGING CARNOSINE PATCHES FOR RESTORING MENTAL DECLINE

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I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study

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DECLINE AND REDUCING STRESS
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Introduction

This study is a test of the effects of carnosine (a known dipeptide commonly produced by the body) on anti-aging in older persons. The interest in carnisone has been promoted by recent evidence that the substance has the recognized properties of protecting the body from the damaging processes of glyosylation, combating cellular damage due to toxins and reversing other aging damages due to oxidative stress such as wrinkled skin, mental decline and other deteriorating signs of aging.

The method of helping the body produce carnosine in this study capitalizes on the one of the newer of sciences—nanotechnology. In research with nanotechnology processes, when atoms/molecules are altered they acquire new properties. In the case of these patches, the inventor has altered amino acids to produce photo receptors of certain frequencies in the bioelectrical system, thus increasing production of desired body functions. The patches to be tested in this study are activated to produce carnosine as the desired outcome (Schmidt & Haltiwanger, 2000; Haltiwanger, 2006).

To test the activation of the bioelectrical system, studies by the company have demonstrated the increase in infra-red activity generated by the mechanisms of the patches (Clark, et al, 2006). Yet additional studies have shown change toward greater balance of the autonomic drive of the heart rate rhythm, not only demonstrating the bioelectrical effect of patches, but also to indicate stress reduction of the heart action (Nazeran, 2007; Budzynski, et al, 2008; Budzynski, et al, 2010).

Two studies have examined the carnosine patch for the effects on the physiologic function of organ systems using an Electro Interstitial Scan to measure the biochemical and hormonal levels of organs for positive changes compared to a baseline (Blake-Greenberg & Nazeran, 2010; Streeter, et al, 2010). The outcome of this present study is to test whether the carnisone patches will reverse changes in the aging process over a month's time through wearing of the patches. Specifically, the study examines the improvement of

memory and other brain activities such as information processing speed and cognitive functioning and cognitive proficiency. Secondarily, the study examines the reduction of stress (by balance of the sympathetic and parasympathetic contribution to the heart beat action).

Background

Anti-aging and Carnosine. The field of anti-aging has entered a new era through the study of the natural substances in the body whose production declines with aging. A key peptide is carnosine whose function in the body is the regulation of metabolism. Through cellular research in animals (predominantly in Russia) many of the properties of carnosine have been discovered which demonstrate the anti-aging actions of this small dipeptide (beta-alanine and L-histidine). It is neuroprotective in its activity as an antioxidant and its antiglycating features. Carnosine acts by countering hydroxyl radicals, one of the more destructive free oxygen radicals produced during oxidative breakdown. It blocks the highly reactive malondealdehyde (MDA) which contributes to atherosclerosis, joint inflammation, cataract formation and aging in general (Hipkiss, 1998; 2001; 2009; Quinn, et al, 1992;).

Carnosine supports the processes of protein metabolism by blocking the more damaging processes such as glycosylation, peroxidation and cross-linking of proteins. Glycosylation produces the *advanced glycosylation endproducts* (AGE's) which are abnormal, cross-linked oxidized products causing extensive damage to the collagen thereby producing the wrinkling features of the aging skin. This oxidative stress leads to poor metabolic regulation and unregulated blood sugar levels. Diabetes is a common outcome.

Additionally, carnosine has a heavy metal chelation effect as well as a pH-buffering ability, lending to its capacities for preventing neurodegeneration and accumulation of senile features. Carnosine has been successfully used to treat patients after stroke by reducing glutamate excitotoxicity and has also augmented Parkinson's drug use to improve its efficiency (Stvolinsky, et al, 1999; Boldyrev, et al, 2010; Shen et al, 2010).

Recently, by examining telomere length as a biomarker, researchers have discovered that the length of telemeres has been found to diminish under oxidative stress and inflammatory conditions. Shorter length of telomeres due to the absence of telemerase

eventually leads to cell death. It has been found that telomere health is improved by addition of carnosine to the body (Babizhayev et al, 2010). Babizhayev (2010) also showed that the progressive accumulation of oxidative damage which causes cataract formation in the lens of the eye is deterred by a topical administration of an ophthalmic carnosine solution. The antioxidant capacities of carnosine appear to reverse the aging action and limit telomere shortening. Thus, carnosine as a critical anti-aging substance shows great promise.

Methods of Restoration of Carnosine. The main foci of the field of "Regenerative Medicine" has been that of restoring body substances that are lost due to illness and aging. Rather than injecting drugs for blocking pathological damage, regenerative medicine seeks supplementary methods by which the body's own substances can restore health. The method of restoration of carnosine in this study incorporates the use of the bioelectromagnetic system within the body as a modality for achieving changes in the body. The work of a number of Asian scientists in Korea and Japan as early as 1964 have led to the finding that the body contains a structure of electromagnetic mesh-like channels, called Bongham Ducts (named after the first scientist to produce a dye that allows the visualization of these ducts) (Wijk, et al, 2007; Shin, et al, 2005). This structure is thought to be the carrier for bioelectrical energy by which the body activates various bodily functions. The structure was found to follow the careful discoveries of ancient Chinese meridian charts. Acupuncture points of the meridians are tapped when the meridians emerge more closely to the skin surface. This discovery vindicates much of the skepticism faced by Energy Medicine.

Energy medicine has long known that specific light frequencies such as an infra-red ray can produce changes in the body. As well, other biofrequencies in the body produce specific functional changes. To date. biophysicists have recorded the various specific resonance frequencies controlling the cellular activity of almost every type of cell or bodily function. The inventor of the patch, David Schmidt, has used nanotechnological methods to generate the photoreceptors for signaling the frequencies that produce carnosine. As noted by Brandimarte, et al, "the LifeWave patches use the wide-range infrared radiation, emitted by the human body, as an energy source that activates the nanocrystals ....and

makes them operate as non-chemical, molecular antennae and information transmission centers." (Brandimarte, et al, 2009; Schmidt & Haltiwanger, 2000).

Haltiwanger (2006) notes that while it is well known that the sun emits infra-red radiation, it is less recognized that the human body also does so. The body, in fact, generates a wide band of resonant frequencies in the body. Every molecule carries its own resonance frequency, a concept which the inventor of the patch has used to advantage to develop nanotechnology products that can transmit selected resonant frequencies. Haltiwanger decribes the LifeWave production in the following way:

> "LifeWave patches are manufactured with natural materials *to produce organic molecules that are nanometers in size. The production of small molecular antennae of nanoscale size is the nanotechnology aspect of this technology.* ....These organic materials have been chosen because they have optical (chiral), liquid crystal and semiconductor properties. By using the nanotechnology production process called solution-based self-assembly, these optically active and electrically conductive materials when placed in LifeWave patches, form small nanosize molecular structures that function as molecular antennae. Placing a conducting material in an oscillating magnetic field creates an electrical signal/frequency in the conducting material." (Haltiwanger, 2006).

The patches have been tested independently to be non-permeable, such that no drug is passed through the patch filament (Brown, 2004) and in earlier Olympic trials, were declared by the US and World Anti-Doping Agencies to be categorized as safe, not falling under the WADA list of Prohibited Substances and Methods. The patch has been considered a harmless, safe medical device by the FDA.

Study Design

The design is an experimental, treatment-control design: It is a month long pre-post patch study in which one part addresses the brain functioning of thought processes (measured by the Microcog). The other part of the study is a short test using the Heart Rate Tracker to gather 5 minutes of the heart rate. The purpose is to examine aspects of stress as measured by the balance of stimulation of the heart beat by the sympathetic and parasympathetic components of the autonomic nervous system.

Sampling. A sample size of 20 treatment and 20 control subjects have been obtained, ages 40 and older, who are not incapacitated by an acute disorder. Subjects are accepted if they are not under close monitoring with frequent changes of prescription drugs such as changing cardiac management drugs, drugs for Alzheimer's management or later stages of Parkinson's, as examples. The sample will be diverse, since little is known about carnosine's differences among groups of people, except for recognition of its reduction with aging.

Measurements. The Microcog is a computerized assessment of cognitive functioning. The test is age and education normed, up through ages 80-89. It measures:

Attention/mental control
Reasoning/calculation
Memory
Spatial processing
Reaction time
Information processing speed
Information processing accuracy
General cognitive functioning
General cognitive proficiency

The Microcog test requires from ½ to ¾ hours time. It is repeated at exit from the study a month later. Although test-retest has been reported as valid if the test is not taken again before a month, one hazard is that subjects learn to be more careful, therefore the second try is likely to affect Reaction Time, lengthening the subtest's timing.

The BioCom is an instrument for measuring heart rate activity. The program to be used is the Heart Rhythm Scanner which produces a heart rhythm balance score, determining the balance of the heart's activation through use of the parasympathetic drive and the sympathetic drive. The heart rate is very sensitive to changes in heart rhythm activity and body health due to stress. Activation of the bioelectric system as a response to carnosine will stimulation of the heart by altering the autonomic stimulation and balance.

Study Structure

The study required one month of the subjects' time. Subjects were randomized initially by LifeWave by numbering packets of placebo and carnosine before the packets were shipped to the investigators. At entry all the tests were administered. The subject were given a month's supply of carnosine/placebo patches and instructed to apply one patch each morning just below the umbilicus, wear it for 10 hours and discard it. These patches were to be worn for 5 days each week, then subjects were given a rest for 2 days. The subjects were emailed weekly to see if they were having problems and to urge compliance in maintaining their participation as instructed. At exit time, all subjects were called back for post-testing. Both investigators and subjects were blinded as to which

subjects were in the treatment or control groups. At the end of the post-testing, all subjects were given a 2 month supply of the authentic patches.

In addition to a two month's supply of free patches given at exit, to assure continuation in the study the subjects received $30 at the time of the initial testing for transportation, with the promise of another $30 when they return for the exit testing.

Human Subjects Consent

The Human Subjects Consent Form was reviewed and approved by the Independent Investigational Review Board, Inc. in Florida. The consent form was given to each subject and signed, indicating understanding of the study and willingness to participate. No problems for subjects emerged during the course of the study.

Data Analysis and Results

The data were processed on Strata for statistical analysis. A two-sample T-test with unequal variances was used to compare treatment and control groups. It was necessary to discard 4 from the sample for various reasons: One person did not return for 6 weeks; another was thought to be a controlled diabetic, but suffered a severe hyperglycemic event just before she came for post-testing; a third subject came for post-testing but was quite emotionally overcome by having had her newly-divorced ex-husband commit suicide and a fourth was obviously overwrought, but did not express the reason why.

The sample was evenly dispersed by age: the average age of the treatment group was 57 years and the control group, 61. By gender, the treatment group averaged 35.2% male and 64.71% female; the control group averaged 36.8% male and 63.1% female.

The Microcog differences between Treatment and Control group are presented in Table 1. All differences were significantly different with the exceptions of Spatial Processing, Reaction Time and Processing Accuracy, this latter of which almost reached a significance of $p > .05$.

Table 1. Carnosine Study Report - Microcog Differences between Treatment and Control Groups (Tx=17;Control=19)

Subtest	Pretest		Post-test		Differences		Probability	
	MeanTx	Mean C	Mean Tx	Mean C	Tx	Control		
Attention	99	99.7	107.33	99.9	8.35	0.3	0.022	*
Reasoning	109.5	108.3	116.5	109.5	7.2	1.26	0.051	*
Memory	98.1	107.6	109.2	107.7	10.82	0.52	0.0095	*
Spatial Processing	107.5	110.7	113.9	111.8	6	1.11	0.12	
Reaction Time	97.3	97.8	101.5	92.6	2.94	-5.31	0.131	

Processing Speed	99.4	98.8	105.4	98.2	5.7	-0.63	0.001	*
Processing Accuracy	101.6	108.6	113.4	113.89	11.76	5.26	0.063	
Gen. Cognitive functioning	100.4	104.3	112.4	107.6	12	3.31	0.0004	*
Gen. Cognitive Proficiency	97.9	101.4	112.9	105.7	15.05	4.36	0.0016	*

*p<.05

Table 1 displays all pretest and posttest scores on subtests of the Microcog,
indicating differences between treatment and control groups and levels of significance.

The Heart Rate Tracker data posed a few difficulties when attempting to examine the total samples on the heart rate variables. The sample showed such a wide variability, it was decided to examine only the upper 1/3 of the two groups who changed the most to compare them on changes in the low frequency (normalized) band which depicts the sympathetic activity. Comparing the upper Terciles of the two groups, the data showed that means of sympathetic activity at pretest(converted to a scale =100 units) between treatment and control were far apart (Tx mean differences = 62.7 as opposed to Control mean differences = 84.4). Nonetheless, because the Standard Error for the treatment group (10.2) was twice that of the control group (5.3) these terciles statistically were not significantly different from each other (p>.1076).

When the upper Terciles of the two groups were compared at post-test, the treatment group mean was 42.1 and the standard error was 10.70. The control group had a mean of 70.55 but the Standard Error was now only 4.42. The p>.05 now showed the terciles to be statistically different, indicating that the treatment group had reduced the stress on their heart beats. (See Table 2).

Table 2. Comparing Low Frequencies (normed) of Heart Beat as Sympathetic
Measure - Pretest and Posttest of Upper Terciles of Treatment/Control
(N=5-Treatment; N=6-Control)

	Mean	Standard Error	Probability
Pretest			
Treatment	62.7	10.23	
Control	84.4	5.38	p>.1076
Post test			
Treatment	42.1	10.7	
Control	70.55	4.42	p>.0543

The same procedure was performed for testing the high frequency (normalized) band which depicts the parasympathetic activity. The tercile was again sectioned out to narrow the wide variability within the total sample. The means for the high frequency normed (converted to a scale of 100), the treatment group had a mean of 37.3, the control, a mean of 15.3. Again the Standard Errors were twice the size in the treatment group (10.23) compared to the control group (5.38) and the groups were found not to be significantly different (p>.1076).

At post-testing of the high frequency (normalized) measures, using the tercile, the treatment group mean was 57.9 with a standard error of 10.70, and the control group mean was 27.5 with a standard error of 5.08. The high frequency changes were now significantly different between the two groups at p>.0442, indicating that the treatment group had changed significantly to improve their parasympathetic measure, showing lower stress effects on the heart beat. (See Table 3).

Table 3. Comparing High Frequencies (normed) of Heart Beat as Parasympathetic
Measure - Pretest and Posttest of Upper Terciles of Treatment/Control
N=5 Treatment; N=6 Control

	Mean	Standard Error	Probability
Pretest			
Treatment	37.3	10.23	
Control	15.3	5.38	p>.1076
Posttest			
Treatment	57.9	10.7	
Control	27.5	5.08	p>.0442

Discussion

Carnosine patches definitively have shown their worth in this study by those in the treatment group having achieving significant improvement in cognitive functioning. In numerous reports of studies in exercise, oxygenation and anti-aging supplements, participants frequently make comments of greater alertness or vigor. Our subjects did not. We did not probe and the subjects did not offer, since neither they nor us knew who had received the carnosine patch rather than the placebo. Three of them had lost about 10 pounds in the course of the study, all of whom turned out to be in the treatment group but they did not attribute the weight loss to the carnosine. Furthermore, we had devised a list of effects, as found in the literature and even those effects were not reported. This study supports the need to use measureable attributes to demonstrate success.

The Microcog gives information and asks for feedback, in the meantime measuring speed, reaction time, accuracy and memory. The test is useful because we were able to probe for more indepth proficiency and processing of information and reasoning. The test showed us that the more complex thought processes were most effectively improved. The manual indicated the validity of the study was maintained if the test was not repeated before one month. However, it seemed that many remembered some aspects of the test

and slowed down their reaction times and speed, so they lost points rather than gained scores due to prior administration (as test-retest reliability would test for).

Individual differences upon entry showed up markedly, indicating that we had a rather diverse sample. This diversity produced a wide variation within traits, especially for tests such as measures of sympathetic and parasympathetic activity. The standard deviations overlapped so widely across groups, it was difficult to test the entire group with the stress measurements as depicted by the sympathetic and parasympathetic activation. By taking the most active responders in both groups, we assumed that we could cut down on the wide deviations. The data were interesting in that in both low and high frequency measures, the two groups were not significantly different at the pretest but were found to be significantly different by posttesting. That would mean that the carnosine patch acts to reduce the stress elements of the heart beat.

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