APPLICATION OF CARNOSINE PATCH IMPROVES CELLULAR PHYSIOLOGICAL STATUS IN DIFFERENT ORGANS

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ABSTRACT

Carnosine (β -alanyl-_L-histidine) was first isolated from meat extracts by Russian scholars in 1900. Carnosine is now recognized as an anti-aging chelator/antioxidant with non-enzymatic free radical scavenging properties and serves as an immunomodulator and neuroprotector molecule. It is a naturally-occurring (endogenously synthesized) dipeptide present in brain, cardiac muscle, stomach, kidney, olfactory bulbs and in large quantities in skeletal muscle. As free-radical-induced damage to the cells is an important factor in causing *aging and senile diseases*, carnosine has the potential ability to *prevent and treat* diseases such as atherosclerosis, diabetes, Alzheimer's disease and senile cataract. Recent clinical research shows that carnosine could be used for skin care and smoothing wrinkles and it has the ability to rejuvenate senescent cells and delay eyesight impairment and cataract which are manifestations of the aging process. These results provide valuable data in favor of considering carnosine as a natural *anti-aging* compound.

Bioelectrical impedance data indicative of cellular physiologic organ function (status), using an Electro Interstitial Scanning (EIS) system, were acquired from twenty volunteers (7 males and 13 females, 19-83 years of age, 118-185 lbs in weight, 5-6 ft in height) after giving informed consent. Cellular physiologic function in these subjects were evaluated in 10 organs (pancreas, liver, left and right kidneys, intestines, left and right adrenal glands, hypothalamus, pituitary and thyroid glands) while wearing the carnosine patch for a period of 2 weeks. Physiologic function (EIS) testing was repeated each week. Cellular physiologic function baseline data were acquired from all subjects at the beginning of the study period before application of the carnosine patch. Subjects were instructed to keep well hydrated during the study period. All subjects served as their own control. The hypothesis to be tested was: *The carnosine patch worn 12 hours/day on alternate days for two weeks significantly improves cellular physiologic functional status in different organs*.

Statistical analyses were carried out comparing the cumulative averages of the net changes in cellular physiologic functional status of each organ at the end of the study period with respect to the corresponding baseline data. The results showed a *highly significant* (p < 0.001) improvement with an average statistical power of at least 84% in physiologic functional status of the liver, right kidney, right and left adrenal glands, hypothalamus and thyroid gland. There was a *very significant* (p < 0.01) improvement with an average statistical power of at least 95% in the functional status of pancreas and pituitary gland. The left kidney and intestines did not achieve statistical significance over this period (p < 0.5) probably requiring more time for the carnosine patch to take effect in these organs.

In summary, the overall data in this study demonstrated that the carnosine patch worn 12 hours daily on alternate days (3 days a week: Tuesdays, Thursdays, and Saturdays) over a period of 2 weeks produced a *very significant* (p < 0.01) improvement in the physiologic functional status of the pancreas, liver, right kidney, left and right adrenals, hypothalamus, pituitary and thyroid glands with an average statistical power of at least 95%. Therefore, the *hypothesis was accepted as true*.

Keywords: Carnosine patch, Aging, Antioxidant, Acupuncture points, Electro interstitial scan (EIS) system.

INTRODUCTION

Carnosine termed an "amazing anti-aging nutrient" is a dipeptide molecule comprised of 2 amino acids: beta-alanine and L-histidine. It was first isolated from meat extracts by Russian scholars in 1900 [1]. It is a naturally-occurring (endogenously synthesized) molecule present in brain, cardiac muscle, stomach, kidney, olfactory bulbs and in large quantities in skeletal muscle [2]. Many studies on biological and biochemical effects of carnosine have suggested that it possesses antioxidant and free radical scavenging properties [3]. *Free radicals* are dangerous by-products of normal metabolic processes converting food to energy. Free radicals are unstable oxygen-containing molecules, which are hungry for electrons to quench their insatiable desire for cell destruction. Carnosine like its "dancing partner" glutathione is an antioxidant that serves as an endogenous defense against the harmful effects of free radicals, by quenching the destructive free electrons in these molecules. The balancing act between free radicals and antioxidants could be easily disrupted for any reason such as when the body is under stress, fighting an infection or inflammation or healing from an injury, in which case more free radicals are generated. Free radicals are also created when the body is exposed to cigarette smoke, alcohol, ultraviolet light, heavy metals, air pollution, pesticides, food additives, and other environmental toxins.

Free radicals are the underlying cause of a variety of illnesses in the body [4]. They are also one of most important possible causes of *aging* and senile diseases [5]. The literature shows that the emergence and development of *aging* are closely related to free-radical-induced damage to cells. Free radical damage leads to instability and malfunctioning of the cells, which consequently cause senile diseases such as atherosclerosis, diabetes, Alzheimer's disease, and senile cataract. Research on the biological and biochemical effects of antioxidants and free radical scavenging molecules such as glutathione and carnosine has shown that these compounds have the ability to protect cells from the harmful effects of free radicals and therefore could exert a normalizing function on cell metabolism and therefore serve as endogenous *anti-aging* compounds.

Extensive preliminary research by Russian, Japanese, German and Australian scholars have shown that carnosine has a variety of beneficial effects including an increase in muscle strength and endurance, protection against radiation damage, enhancement of immunity and reduction of inflammation, protection against formation of ulcers and their treatment, treatment of burns, promotion of wound healing after surgery, improvement of appearance, etc.

In a review, Quinn et al [6], suggest that carnosine and its related dipeptides could be considered as the water-soluble counterpart to lipid-soluble anti-oxidants such as vitamin E and serve to protect cells from oxidative damage. They refer to numerous studies that have demonstrated strong and specific antioxidant properties of these compounds both at the tissue and organelle level. They describe that carnosine and its related dipeptides play a number of roles such as neurotransmission, modulation of enzymic activities and chelation of heavy metals. They also describe that these compounds have antihypertensive, immunomodulating, wound healing and antineoplastic effects.

Hipkiss et al [7], present evidence to suggest that carnosine in addition to its antioxidant and oxygen free-radical scavenging activities, also reacts with deleterious aldehydes to protect susceptible macromolecules. They propose that the role of carnosine and its related dipeptides should be explored in pathologies that involve deleterious aldehydes, for example, secondary diabetic complications, inflammatory phenomena, alcoholic liver disease, and possibly Alzheimer's disease. For a more detailed study on carnosine's beneficial effects please refer to the references listed in [8].

The current methods of oral supplementation with carnosine would take 1-4 months to reach steady state and show any significant effects. Marios Kyriazis MD has performed a preliminary experiment using L-carnosine supplements (50 mg daily) on 20 healthy human volunteers, aged 40-75 years, for a period of 1-4 months. He reports "No side effects were reported. Five users noticed significant improvements in their facial appearance (firmer facial muscles), muscular stamina and general well-being. Five others reported possible benefits, for example better sleep patterns, improved clarity of thought and increased libido. The rest did not report any noticeable effects. This is not surprising because supplementation with carnosine is not expected to show any significant noticeable benefits in a short time, but it should be used as an insurance against deleterious effects of the aging process. If any benefits are noted, these should be considered as an added extra bonus. It is worthwhile persevering with the supplementation long term, even if you do not experience any obvious benefits, as you will still be well protected against aging. Carnosine can be used together with vitamin E and/or Co-enzyme Q10 for full antioxidant protection, but even if it is used on its own it should still confer significant protection both against free radicals and against glycosylation." [9]

This is the first study of its kind to investigate the effect of the carnosine patch on organ physiologic function. Bioelectrical impedance data indicative of cellular physiologic function, using an EIS system, were acquired from 20 subjects: 7 males and 13 females, 19-83 years of age, 118-185 lbs in weight, and 5-6 ft in height. Cellular physiologic function in subjects were evaluated in 10 organs (pancreas, liver, left and right kidneys, intestines, left and right adrenal glands, hypothalamus, pituitary and thyroid glands) while wearing the carnosine patch for a period of 2 weeks, 12 hours/day on alternate days of the week (Tuesdays, Thursdays and Saturdays). Physiologic function testing was repeated each week. Each visit was approximately 1 hour in duration for the testing. Physiologic function baseline data were acquired from all subjects at the beginning of the study period before the carnosine patch was worn. Subjects were instructed to keep well hydrated during the study period. All subjects served as their own control.

The overall data in this study demonstrated that the carnosine patch worn 12 hours daily on alternate days over a period of 2 weeks produced a *very significant* (p < 0.01) improvement in the physiologic functional status of the pancreas, liver, right kidney, left and right adrenals, hypothalamus, pituitary and thyroid glands with an average statistical power of at least 95%. Therefore, the *hypothesis was accepted as true*.

MATERIALS AND METHODS

For this research, the carnosine patch (LifeWave, La Jolla, California, USA) was used. The carnosine patch is described as a new method for increasing carnosine levels by stimulating acupuncture points on the body with a combination of pressure and infrared energy. The carnosine patch is a non-transdermal patch that does not put any chemicals or drugs into the body. The carnosine patch contains natural nontoxic crystals that absorb body heat to generate infrared signals that cause the body to produce more endogenous carnosine. The carnosine patch is termed the "dancing partner" of the glutathione patch and seems to nicely enhance and complement its physiological effects.

An EIS (Electro Interstitial Scan, U.S. patent No. US 61/194,509) system was deployed to acquire bioelectrical impedance data indicative of cellular physiologic functional status in 10 organs. The EIS system is a hardware/software computerized system that deploys precise algorithms and proprietary formulas to generate on-screen, 3-D modeling representations of the human body's systems; with specific

intended uses. EIS system is a French electrochemical device, classified as a medical device in Europe and the United States. Its main functions are to read the different processes going on in the body, hyperactivity and hypo-activity in the organs. The EIS system measures the biochemistry and hormone levels. It also measures pH, body composition and the sympathetic and parasympathetic influences of the autonomic nervous system. Even emotional traumas can be detected by measuring the biochemistry and cellular activity in various areas of the brain. By application of harmless, low voltage signals with specific frequencies to 6 electrodes connected to the body bioelectrical impedance (or its inverse tissue conductivity) measurements are made. The computer software calculates the organ responses to the stimulating signals based on changes made to these signals as they pass through the body. Most measurements are done on the extracellular fluids, which constitute the environment of all cells. This is where the biochemistry is most important, and where cellular activity can be measured by looking at what goes into and out of the cells. The EIS system scans the whole body in 3 minutes. It is a biofeedback device in the United States with pending FDA approval.

Inclusion criteria for participation in this study were functional normal individuals who were willing to wear the carnosine patch and participate in the study for a period of two weeks. Participants also agreed not to start with any other new therapy or methods of healing and/or make any major changes in their daily life that could alter the efficacy of the study. Subjects must not have worn the carnosine patch prior to the study. Subjects were recruited from the local area of Palos Verdes and may or may not have been previous patients of Health Integration Therapy. 20 volunteer subjects: 7 males and 13 females, 19-83 years of age, 118-185 lbs in weight, and 5-6 ft in height participated in this study. They wore the carnosine patch for 12 hours *daily*, on alternate days of the week (Tuesdays, Thursdays and Saturdays). After giving informed consent, cellular physiologic function baseline data were acquired from all subjects at the beginning of the study period before the carnosine patch was worn and weekly afterwards for 2 weeks. Subjects were instructed to keep well hydrated during the study period. All subjects served as their own control. The subjects were instructed to place the carnosine patch 2 inches inferior to the navel (below belly button) or on CV_6 . For more information on the carnosine patch and applicable anatomical positions for wearing it please refer to LifeWave website.

RESULTS

The Electro Interstitial Scan (EIS) System used in this investigation measured cellular physiologic function on a scale of -100 to -20 for under-function and 20 to +100 for over-function. A reading in the - 20 to + 20 range is indicative of normal values for organ function.

Table 1 shows typical EIS system readings (cellular function physiologic status) for a female subject, while Table 2 shows typical EIS system recordings for a male subject as examples. Functional physiological status changes in different organs from Week1 compared to baseline were designated as Δ_1 while changes from Week 2 to Week 1 were designated as Δ_2 . Δ_{avg} shows the average value of the changes for the 2-week period, and Δ_T represents the average total physiologic change after 2 weeks and Δ_{T-base} is indicative of total change at the end of the 2-week period with respect to baseline measurements. Table 3 shows the overall mean values and standard deviations for baseline and total change (Δ_T) in physiologic function for each of the organs (n = 20).

| Date | ORGAN NAME | | | | | | | | | | |
|-----------------------|------------|-------|----------------|-----------------|-----------|------------------|-----------------|---------|-----------|---------|--|
| | Pancreas | Liver | Left Kidney | Right Kidney | Intestine | Right Adrenal | Left Adrenal | Hypoth. | Pituitary | Thyroid | |
| Baseline | -58 | -3 | -9 | 0 | -59 | -67 | -51 | -21 | -66 | -58 | |
| Week 1 | -50 | -21 | -25 | -33 | -53 | -60 | -40 | -2 | -55 | -50 | |
| Week 2 | -3 | 14 | 3 | 13 | -43 | -47 | -27 | -21 | -25 | -3 | |
| Δ_1 | 8 | -18 | -16 | -33 | 6 | 7 | 11 | 19 | 11 | 8 | |
| Δ_2 | 47 | 35 | 28 | 46 | 10 | 13 | 13 | -19 | 30 | 47 | |
| Δ_{T} | 55 | 17 | 12 | 13 | 16 | 20 | 24 | 0 | 41 | 55 | |
| Δ_{T-base} | 113 | 20 | 21 | 13 | 75 | 87 | 75 | 21 | 107 | 113 | |

Table 1. Typical Electro Interstitial Scan (cellular function physiologic status) data for a female subject. Age: 30. Weight: 125 lb. Height: 5 ft. 5 inches.

Table 2. Typical Electro Interstitial Scan (cellular function physiologic status) data for a male subject. Age: 66 Weight: 168 lb Height: 5 ft 11 inches

| Date | ORGAN NAME | | | | | | | | | | |
|-----------------------|------------|-------|----------------|-----------------|-----------|------------------|-----------------|---------|-----------|---------|--|
| | Pancreas | Liver | Left Kidney | Right Kidney | Intestine | Right Adrenal | Left Adrenal | Hypoth. | Pituitary | Thyroid | |
| Baseline | -14 | -8 | -21 | -25 | -15 | -10 | -16 | -9 | -1 | -13 | |
| Week 1 | -17 | -14 | -23 | -32 | -28 | 3 | -3 | -3 | -1 | -1 | |
| Week 2 | 16 | -2 | -7 | -10 | -16 | -21 | -21 | -21 | 0 | 20 | |
| Δ_1 | -3 | -6 | -2 | -7 | -13 | 13 | 13 | 6 | 0 | 12 | |
| Δ_2 | 33 | 12 | 16 | 22 | 12 | -24 | -18 | -18 | 1 | 21 | |
| Δ_{T} | 30 | 6 | 14 | 15 | -1 | -11 | -5 | -12 | 1 | 33 | |
| Δ_{T-base} | 44 | 14 | 35 | 40 | 14 | -1 | 11 | -3 | 2 | 46 | |

Table 3. Summary of mean and standard deviation values for EIS readings in 10 organs, n = 20.

| | ORGAN NAME | | | | | | | | | |
|--------------------------------|------------|--------|----------------|-----------------|-----------|------------------|-----------------|---------|-----------|---------|
| | Pancreas | Liver | Left Kidney | Right Kidney | Intestine | Right Adrenal | Left Adrenal | Hypoth. | Pituitary | Thyroid |
| Avg Baseline | -13.9 | -23.95 | -4.4 | -12.3 | -3.37 | -33.05 | -36.4 | -23.85 | -3.40 | -28.65 |
| Avg ATotal | 27.39 | 22.13 | 27.36 | 25.38 | 30.85 | 22.67 | 22.23 | 11.86 | 6.27 | 18.52 |
| Avg _{Std} Baseline | 22.05 | 29.95 | 4.4 | 19.1 | 3.1 | 40.4 | 44.75 | 22 | 5.05 | 40.25 |
| Avg _{Std} ∆Total | 46.43 | 41.28 | 40.27 | 37.90 | 39.90 | 39.01 | 40.28 | 22.02 | 10.05 | 35.54 |

DISCUSSION AND CONCLUSION

Statistical analyses were carried out on the EIS system data acquired from these subjects comparing the cumulative averages of the net changes in physiologic functional status of each organ at the end of the 2-week study period with the corresponding baseline data. The results showed a *highly significant* (p < 0.001) improvement in physiologic functional status of all organs tested except in pancreas and pituitary gland that showed a *very significant* improvement (p < 0.01) and left kidney and intestines that did not achieve significance. Average statistical power considering the effect size (% improvement in physiologic function, sample number, and level of significance) was at least 84% in all organs that achieved a *highly significant* improvement in cellular physiologic function. The average statistical power in pancreas and

pituitary gland that showed a *very significant* improvement was at least 95%. Left kidney and intestines did not achieve significance after 2 weeks of exposure to carnosine patch. This could be attributed to the fact that these organs need more exposure time to carnosine patch to significantly improve their physiologic status as a consequence of biochemical changes in their extracellular environment. Considering the fact that supplementation with carnosine or its building blocks may take a month or so to show a steady state effect, this level of impact is still remarkable.

The overall data in this study demonstrated that the carnosine patch worn 12 hours daily on alternate days over a period of 2 weeks produced a *very significant* (p < 0.01) improvement in the physiologic functional status of the pancreas, liver, right kidney, left and right adrenals, hypothalamus, pituitary and thyroid glands with an average statistical power of at least 95%. Therefore, the hypothesis that: *The carnosine patch worn 12 hours/day on alternate days for two weeks, significantly improves cellular physiologic functional status in different organs* was accepted as true.

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