Nanoscale Glutathione Patches Improve Organ Function

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Abstract **- Glutathione, termed the "ultimate" or "master" antioxidant, is a vital intracellular tripeptide molecule and plays a central role in cellular physiologic functions. Currently the undeniable connection between glutathione and good health is very well established.**

Bioelectrical impedance data indicative of cellular physiologic organ function (status), using an Electro Interstitial Scanning (EIS) system, were acquired from two cohort volunteers. Cohort 1 comprised of 10 subjects: 1 male and 9 females, 18-86 (mean 58) years of age while Cohort 2 were 20 subjects: 4 males and 16 females, 19-80 (mean 54) years of age. Cellular physiologic function in subjects were evaluated in 8 organs (*pancreas, liver, gall bladder, intestines, left and right adrenal glands, hypothalamus and pituitary gland)* while wearing the glutathione patch for a period of 4 weeks. Physiologic function testing was repeated each week. Cohort 1 wore the glutathione patch for 12 hours/day *daily*, while Cohort 2 wore the glutathione patch for 12 hours/day on *weekdays*. Cellular physiologic function baseline data were acquired from all subjects at the beginning of the study period before the glutathione patch was worn. 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 glutathione patch worn 12 hours daily for 4 weeks significantly improves cellular physiologic functional status in different organs.*

The overall data in Cohort 1 in this study demonstrated that glutathione patches worn 12 hours daily over a period of 4 weeks produced a *highly significant* improvement in physiologic functional status of *pancreas, liver, gall bladder, intestines, left and right adrenals, hypothalamus* and *pituitary gland* and *very significant* improvement in *pancreas* with a statistical power of at least 72%. Stated differently all organs achieved *significant* cellular physiologic functional status improvement compared to baseline with a statistical power of at least 91%.

Keywords— **Nanotechnology, Glutathione patch, Cellular physiologic function measurements, Electro interstitial scan (EIS) system, LifeWave.**

I. Introduction

Glutathione is a vital intracellular tripeptide molecule comprised of 3 nonessential amino acids: cysteine, glutamic acid and glycine (g-glutamyl-cysteinyl-glycine abbreviated as GSH). These 3 building blocks in turn are made from different combinations of essential amino acids. The –SH suffix in GSH (reduced form of glutathione) indicates that it contains a sulfhydryl group. This group comes from sulfur-containing amino acids cysteine and methionine. Glutathione is produced naturally in abundance in the body and circulates constantly in the bloodstream neutralizing *free radicals* (dangerous by-products of normal metabolic processes converting food to energy) and removing environmental poisons such as heavy metals, harmful waste products and toxins to protect cells against oxidative stress. Free radicals are unstable oxygen-containing molecules which are hungry for electrons to quench their insatiable desire for cell destruction. Glutathione is a powerful antioxidant (created by the same energy-producing processes that create free radicals), which serves as a built-in defense against the harmful effects of free radicals, by rapidly 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 [1].

Lyons et al, described that glutathione serves diverse physiologic functions such as detoxification of xenobiotics, protection of cells from oxidative stress, and acts as a storage and a transport form of cysteine. They explained that reduced tissue levels of GSH are thought to compromise cell function, promote tissue damage, and increase morbidity under various disease conditions [2].

Wu et al, studied glutathione metabolism and its implications for health. They described that glutathione plays important roles in antioxidant defense, nutrient metabolism, and regulation of a variety of cellular events. They also explained that glutathione deficiency contributes to oxidative stress playing a key role in aging and the pathogenesis of many diseases. These diseases include: seizure, Alzheimer's, Parkinson's, liver disease, cystic fibrosis, sickle cell anemia, human immunodeficiency virus (HIV), acquired immunodeficiency syndrome (AIDS), cancer, heart attack, stroke, and diabetes. They emphasized the need for new understanding of the nutritional regulation of GSH metabolism as a critical step for development of effective health improvement and disease treatment strategies [3].

Townsend et al, provided an overview of the biological importance of GSH at cellular and organism level and showed cause and effect relationships between GSH metabolism and diseases such as cancer, neurodegenerative diseases, cystic fibrosis (CF), HIV, and aging. They also showed how the enzymes involved in GSH regulation and control influence susceptibility and progression of these conditions. They concluded that there seemed to be no harm in supplementing a diet with GSH as "perhaps the product will provide a supply of the constituent amino acids, where, in particular, cysteine may be useful in stimulating gastrointestinal synthesis of GSH" [4].

The current methods of oral supplementation with glutathione or its amino acid precursors have not been effective in significantly elevating the blood levels of this antioxidant due to stomach acid destruction of L-Glutathione and unpredictability of results with precursor amino acids. Direct daily injection of glutathione has been more effective in producing short term elevation of glutathione, however this approach is unreliable due to expense and inconvenience. Preliminary clinical data from blood and urine samples collected every 24 hours over a period of 5 days from 15 volunteers wearing the glutathione patch have shown a 3 to 4 fold increase in blood levels of glutathione compared to baseline levels [5].

This is the first study of its kind to investigate the effect of the glutathione patch on organ physiologic function. Bioelectrical impedance data indicative of cellular physiologic function were acquired using and EIS system.

The overall data in this study demonstrated that glutathione patches worn 12 hours daily over a period of 4 weeks caused *highly significant* improvement in physiologic functional status of *pancreas, liver, gall bladder, intestines, left and right adrenals, hypothalamus* and *pituitary gland* and *very significant* improvement in pancreas with a statistical power of at least 72%. Stated differently all organs achieved *significant* cellular physiologic functional improvement with a statistical power of at least 91%.

II. Material and Methods

Subjects: Two cohort of volunteer subjects participated in this study. Cohort 1 comprised of 10 subjects: 1 male and 9 females, 18-86 (mean 58) years old while Cohort 2 were 20 subjects: 4 males and 16 females, 19-80 (mean 54) years old. Cohort 1 wore the glutathione patch for 12 hours *daily*, while Cohort 2 wore the glutathione patch for 12 hours/day on *weekdays* only. After giving informed consent, cellular physiologic function baseline data were acquired from all subjects at the beginning of the study period before the glutathione patch was worn and weekly afterwards for 4 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 glutathione patch 2 inches inferior to the navel (below belly button) or on CV_6 acupuncture point according to manufacture's instructions. Figure 1 shows the glutathione patch and the anatomical position for wearing the glutathione patch.

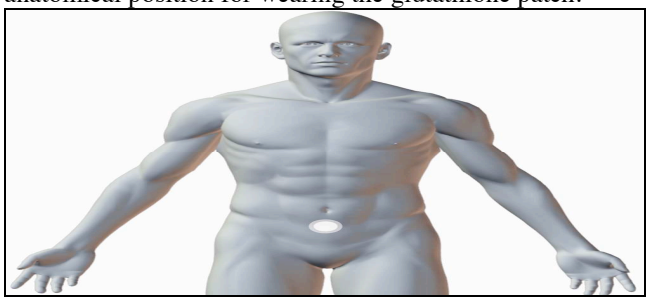

Figure 1. The LifeWave glutathione patch and the anatomical position for wearing it (CV_6).

Glutathione Patch: For this research, the nanoscale glutathione patch (LifeWave, La Jolla, California, USA) was used. The glutathione patch is described as "a new method for increasing glutathione levels by stimulating acupuncture points on the body with a combination of pressure and infrared energy. The LifeWave glutathione patch is a non-transdermal patch that does not put any chemicals or drugs into the body. The LifeWave glutathione patch contains natural nontoxic crystals that absorb body heat to generate infrared signals that cause the body to produce more endemic glutathione. These crystals are active for 12 hours. Clinical studies utilizing blood analyses indicate an average rise of more than triple the blood glutathione over a period of 24 hours" [5]. For a comprehensive discussion of the LifeWave glutathione patch please see reference [6].

Electro Interstitial Scan (EIS) System and Measurements: An EIS system (LD Technology, Coral Gables, Florida, USA), a programmable electro medical device, was deployed to acquire bioelectrical impedance measurements indicative of cellular physiologic functional status in 10 organs. The EIS system is a French device, classified as a Biofeedback Class 2 device in the United States (FDA product Code: HCC). Recently the FDA has approved a number of alternating current (ac) bioelectric impedance (BIM) devices for use in cardiology and oncology [10 -15].

Before EIS measurements were made on subjects, four operational tests were carried out automatically by the device: power supply test, channel test, volume and conductivity measurement and correspondence tests, as well as cable and precision control tests. Electrodes and electrode application sites were prepared following manufacturer's instructions.

Under software control the hardware delivers a sequence of three 1.28V pulses: 22 ac pulses, 1 second each, at 50KHz (at 0.6 mA, energy/pulse=0.77 mJ); 22 dc pulses, 1 second each (at 0.6 mA, energy/pulse=0.77 mJ); and another set of 22 dc pulses, 3 second in duration for each pulse (at 0.6 mA, energy/pulse=0.77 mJ) to 6 electrodes. These electrodes (2 disposable Ag/AgCl applied to the forehead, 2 reusable polished stainless steel hand electrodes, and 2 reusable polished stainless steel foot electrodes) form 22 different electrode pair (sensing) configurations and measure the intensity of interstitial fluid conductivity (by applying Maxwell's equation) from which on-screen 3-D models of the human body organs are generated. The measurements are scaled on a scale of -100 to +100 [16]. As DC current only passes through the interstitial fluid (16% of the body's total water), the device could measure the composition of interstitial fluid as well as other biochemical parameters and detect ionic abnormalities.

Inclusion Criteria: Inclusion criteria for participation in this study were healthy and functional individuals who were willing to wear the glutathione patch and participate in the study for a period of four 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.

Statistical Analysis: The cellular physiological effect in different organs after 4 weeks of wearing the glutathione patch were compared to baseline data before wearing the patch using the paired t-test. A p value < 0.05 was accepted as statistically significant. Sample size (n), level of significance (α or p), effect size and (mean value of EIS reading after wearing the patch – baseline mean value) and statistical power were related by the following formula.

$$\Phi[Z_\alpha + |\mu-\mu_0| \text{ Sqrt } (n)/\sigma] = \text{Statistical Power} \quad (1)$$

where Z_α is the Z score related to the area under normal distribution curve at the desired level of significance, $|\mu-\mu_0|$ is effect size and σ is the standard deviation and n is sample size.

III. Results

Table 1 shows typical EIS System readings (cellular function physiologic status) for a female subject, while Table 2 shows typical EIS system readings for a male subject as examples. Functional status changes from week to week are designated as Δ_1, Δ_2, Δ_3 and Δ_4, for the 4-week period showing cellular physiologic changes in the organs. Δ_{avg} shows the average value of changes for the 4-week period, and Δ_{total} represents the average total physiologic change after 4 weeks with respect to baseline readings. Table 3 shows the overall mean values and standard deviations for baseline and total change in physiologic function for each of the organs in Cohort 1 (n =10).

Table 1. Typical Electro Interstitial Scan data for a female subject in Cohort 1.

	ORGAN NAME							
Date	Pancreas	Liver	Gall bladder	Intestine	R Adrenal	L Adrenal	Hypoth.	Pituitary
Baseline	-70	-73	-73	-72	-65	-70	-46	-2
Week 1	-42	-43	-43	-49	-34	-32	-22	0
Week 2	-38	-52	-52	-29	-27	-26	-25	0
Week 3	-58	-64	-64	-66	-49	-47	-27	0
Week 4	-55	-61	-61	-58	-32	-29	-26	0
Δ_1	28	30	30	23	31	38	24	2
Δ_2	4	-9	-9	20	7	6	-3	0
Δ_3	-20	-12	-12	-37	-22	-21	-2	0
Δ_4	3	3	3	8	17	18	1	0
Δ_T	15	12	12	14	33	41	20	2
$\Delta_{T\text{-base}}$	85	85	85	86	98	111	66	4

Table 2. Typical Electro Interstitial Scan data for a male subject in Cohort 1.

	ORGAN NAME							
Date	Pancreas	Liver	Gall bladder	Intestine	R Adrenal	L Adrenal	Hypoth.	Pituitary
Baseline	-6	-7	-7	-19	-32	-34	-15	-2
Week 1	16	2	2	27	-47	-45	-29	-21
Week 2	23	6	6	31	-43	-48	-26	-21
Week 3	32	0	0	28	-20	-21	-13	1
Week 4	22	14	14	21	14	-13	2	1
Δ_1	22	-5	-5	46	-15	-11	-14	-19
Δ_2	7	4	4	4	4	-3	3	0
Δ_3	9	-6	-6	-3	23	27	13	22
Δ_4	-10	14	14	-7	34	8	15	0
Δ_T	28	7	7	40	46	21	17	3
$\Delta_{T\text{-base}}$	34	14	14	59	78	55	32	5

Table 3. Summary of mean and standard deviation values for EIS System readings in 8 organs in Cohort 1, n = 10.

	ORGAN NAME							
	Pancreas	Liver	Gall bladder	Intestine	R Adrenal	L Adrenal	Hypoth.	Pituitary
$Avg_{Baseline}$	-24.2	-30.9	-30.9	-18.6	-26.8	-30.1	-21.5	-0.8
$Avg_{\Delta Total}$	18.4	31	31	25	35.6	34.5	27.8	1.1
$Avg_{Std\ Baseline}$	18.0	19.6	19.6	32.2	22.4	16.6	12.9	1.3
$Avg_{Std\ \Delta Total}$	29.0	27.1	27.1	38.8	52.2	39.2	22.3	2.64

IV. Conclusions

Statistical analyses were carried out in both cohorts comparing the cumulative averages of the net changes in physiologic functional status of each organ at the end of the study period with corresponding baseline data. The results in Cohort 1 showed a *highly significant* ($p < 0.001$) improvement in physiologic functional status of all organs tested except in pancreas that showed a *very significant* improvement ($p < 0.01$). Average statistical power considering the effect size (% improvement in physiologic function, sample number, and level of significance) was at least 72% in Cohort 1. The results in Cohort 2 showed a *significant* ($p < 0.05$) improvement in physiologic functional status of four organs (adrenal glands, hypothalamus and pituitary gland). Average statistical power considering the effect size (% improvement in physiologic function, sample number, and level of significance) was at least 76% in these tests. No significance improvement in cellular physiologic status was observed in pancreas, liver, gall bladder and intestines in Cohort 2. This could be attributed to placebo effect or the fact that discontinued use and not wearing the glutathione patch for 2 days in a week (about 30% less exposure to glutathione) the subjects in Cohort 2 did not have adequate stimulated detoxification in all organs by glutathione over the study period.

More detailed statistical analyses of the EIS data enabled us to make the following observations:

1. In Cohort 1 (n =10), the average statistical power was more than 72% for all organs showing a *highly significant ($p < 0.001$)* improvement in cellular physiologic function. The average statistical power without considering the pituitary gland was more than 82%. The average statistical power, without considering pituitary and intestine was more than 90%.
2. In Cohort 1 (n = 10), the average statistical power was more than 84% for all organs showing a *very significant ($p< 0.01$)* improvement in cellular physiologic function. The average statistical power without considering the pituitary gland was more than 91%. The average statistical power without excluding the pituitary gland and intestine was more than 97%.
3. In Cohort 1 (n = 10), the average statistical power was more than 91% for all organs showing a *significant ($p< 0.05$)* improvement in cellular physiologic function. The average statistical power without considering the pituitary gland was more than 96%. The average statistical power without excluding the pituitary gland and intestine was more than 99%.
4. In Cohort 2 (n = 20), 4 organs (adrenal glands, hypothalamus and pituitary gland) showed a *significant ($p < 0.05$)* improvement in cellular physiologic function.

In summary, the overall data in Cohort 1 demonstrated that the glutathione patch worn 12 hours daily over a period of 4 weeks produced a *highly significant* improvement in physiologic functional status of *liver, gall bladder, intestines, adrenals, hypothalamus* and *pituitary gland* and a *very significant* improvement in *pancreas* with a statistical power of at least 72%. Stated differently, it could be concluded that the glutathione patch caused a *significant* improvement in cellular physiologic functional status of *pancreas, liver, gall bladder, intestines, adrenals, hypothalamus* and *pituitary gland* with a statistical power > 91%. Therefore, the hypothesis that: *The glutathione patch worn 12 hours daily for 4 weeks significantly improves cellular physiologic functional status in different organs* was accepted as true.

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