Functional water-in promotion of health beneficial effects and prevention of disease

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Abstract

Functional water science has gained attention recently in response to its physiological functions, health-promoting effects and disease prevention, especially on oxidative-stressrelated diseases such as diabetes, cancer, arteriosclerosis, neurodegenerative diseases and side effects of hemodialysis. It has been proposed that in the case of naturally or electrochemically reduced water, the active agents are atomic or molecular hydrogen, mineral nanoparticles and mineral nanoparticle hydrides. Studies investigating functional qualities of functional mineral water or functional coherent mineral water in healthy humans suggest a capacity to maintain or restore physiological self-regulation to reduce variability accompanying a constant "steady state" condition, and/or propose the presence of fractal nonlinear mechanisms power-law correlations long-range involved physiological control and complex signaling networks to maintain homeostasis. The functional coherency of a mineral water aligns a nonlinear quantum coherent regime of physiological water as an important factor in the emergence of self-organization and self-consistency of the living organism, exclusively providing a mechanism for physiological nonlocality. Formation of a super-coherent biological plasma-like physiological water is considered one of the most important characteristics of a healthy physiological state. Supplementation with a dietary volume of functional deep ocean mineral water, as a primordial source of nutritional minerals and trace elements, shows consistent anti-atherogenic effects, inhibition of atherosclerosis progression, and improved recovery from exhaustive physical fatigue with elimination of post-exercise oxidative damage.

Keywords: Functional water, clinical studies, self-regulation, non-local effects.

1. Introduction

Functional water science was first recognized by the Functional Water Association in Japan 1931. In 1960, functional water was applied to medical care as a health-beneficial water, and in admitted by the Ministry of Health and Welfare in Japan for treatment of gastrointestinal discomforts, i.e. chronic diarrhea. indigestion, abnormal gastrointestinal fermentation and hyperacidity (1). In contrast, it was not until 1984 that functional food science was allocated research funds for studying functional food or foods for specific health uses by the Japanese government (2). The Japanese Society for Functional water was established in 2001. and active studies on various functional waters have been performed to date (1). While functional food science has been given a formal legislative food category called "Foods for Specific Health Uses" (FOSHU), with three nutritional requirements, i.e. effectiveness, safety and detercomponent(s). mination effective follows functional water science regulations of the Ministry of Health and Welfare. In the case of proclaimed specific action towards illness or cure of a particular disease, the application has to be reviewed and authorized according to the Pharmaceutical Affairs Law. There is no formal legislative definition for functional food or functional water within the European Union or in United States (3). Consequently, subsequent countries and scientific organizations have created their own definitions of functional foods or waters.

Functional water science originated from the collaboration of sciences and the public need. It is the melding of water science and medicine, as it is a substance that crosses between liquid nutritionals and pharmaceuticals. Historically, the focus has been on preventive effects of oxidative-stress-related diseases (1,4,5) and later also on physiological health-promoting effects

(1,6,7). On consumption of functional water clinical measures are obtained that follow the changes in health and homeostatic behavior through the use of physiological and biochemical biomarkers in the body. From these observations the health effects and proper clinical or dietary dosages and safe dosages have been mapped (1,4,5).

physiological humans. constitutes approximately 70 per cent of total body mass and 99 per cent of all molecules (8), which aligns a non-linear quantum coherent regime of physiological water as an important factor in the emergence of self-organization and selfconsistency of the living organism, providing a mechanism for its non-locality (9,10). The function of water in the body is mainly classified according to i) the water molecule itself-where flowing water affects cellular function and the development and functions of organs (11,12), and hydration and Brownian movement of water are fundamentally important for protein function; ii) atoms and molecules derived from water molecules-such as protons, hydrogen atoms (active hydrogen), hydrogen anions, hydrogen molecules, oxygen molecules, and reactive oxygen species (ROS) (4); iii) molecules dissolved in watersuch as mineral ions, mineral nanoparticles, organic and inorganic compounds, and gases (4); iv) the driving and regulatory role of water in governing the biochemical activity and bioenergetics where coherent domains (CDs; excited state of highly organized clustering of water molecules) of water become electron donors providing electron transfer processes of aqueous systems (13); and v) water as a liquid non-linear quantum medium where liquid water molecules of CDs are assembled interconnected by a time-dependent long-range radiative electromagnetic field (EMF), whilst short-range static bonds, such as hydrogen bonds and electric dipole-dipole interactions, are the consequence of molecular condensation induced by these non-local fields (14,15).

Research on functional drinking water, especially reduced functional water, such as electrochemically reduced water (13) or natural reduced water (16), functional mineral water (6), functional coherent mineral water (7) or deep ocean mineral water (17), shows profound physiological function associated with health. Reduced waters are defined to have preventive and positive effects on oxidative-stress-related diseases such diabetes, as arteriosclerosis, neurodegenerative diseases, and side effects of hemodialysis (1). Functional mineral water is activated water with or without a defined coherent state exhibiting specific functions. There are many activation methods without a defined ordered state of water, such as electrolysis, treatment with a magnetic field, light irradiation, ultra-sonication, bubbling with gases, strong water flow and collision, treatment with specific types of minerals or rocks (1), and high pressure treatment (18). The physical and chemical qualities of coherent water have been identified in bulk water when transformed by means of water splitting into a lasting excited high-energy state of ordered water (19) and when exposed to very mild ground-state energy conditions, such as the influence of vortex agitation, freezing-thawing, evaporationcondensation, audio-sonication, capillary filtration, oscillating electromagnetic fields (20), water agitation with metal oxides (19), and influence of incident low entropy coherent sunlight after passing through a Fibonacci optical lattice (FOL) (7,21). Functional desalinated deep ocean mineral water (FDOM) originally obtained from the west Pacific Ocean (below 500 meters in depth) off the coast of Hualien County (Taiwan) is proposed to contain a primordial source of minerals contributing to the creation of life (17). FDOM is filtered by a two-step procedure with a primary micro

filter (removal of microorganisms) and a secondary ultrafilter (removal of macromolecules and virus) before use (17).

2. Definition of functional water

According to the Functional Water Association of Japan, functional water is defined as a water that promotes the status of health and from which both treatment and physiological function have been scientifically demonstrated and shown reproducible, and where useful health-beneficial effects have been identified among natural and artificially treated waters (1). In Europe and the United States there is no specific definition besides that functional water denotes a water to be used in biological contexts in accordance with the definition of functional food (3,22). The functional quality of water restores self-regulative physiological conditions to maintain homeostasis (23). Related to functional foods, these products can only be considered functional if together with the basic nutritional impact they have beneficial effects on one or more functions of the human organism, thus either improving the general and physical conditions or/and decreasing the risk of the evolution of diseases (22,24). Like in Europe, where two types of claims, i.e. nutritional aspects and health, are permitted on functional foods (25), the FDA recently released guidelines for assessing health claims, entitled The evidence-based review system for the scientific evaluation of health claims (26).

Functional water	Study	ater in health and disea Subjects	n	Dose, Duration	Outcome	Reference
	· '	-		·		
Natural reductive	Clinical study	Patients with	163	0,5 I daily, 2 weeks	Improvement in abdominal sympthoms	27
water	-1	abdominal complaints				
Natural reductive	Clinical study	Diabetes, type 2	320	2 I daily, 6 days, long time	Blood glucose and HbA1C decreased	29
water						
Natural reductive	Clinical study	Diabetes, type 2	65	2 I daily, 2 months	Blood sugar decreased	30
water		Hyperlipidaemia	50	2 I daily, 2 months	Blood cholesterol, triglceride decreased	30
Natural reductive	Clinical trail	Diabetes, type 2	29	2 I daily, 6 months	8-OH-dG decreased	31
water		Diabetes, type 2	100	2 I daily, 10 months	Antimetabolic syndrome effects increased	32
Ordinary tap water	Clinical study	Autonomic faliure	19; 47	480 ml single dose	Rise in systolic blood pressure	57,58
		hypotension				
Ordinary tap water	Clinical study	Healthy subjects	10; 13	500 ml single dose	Heart rate decreased	60,61
					HRV vagal activity increased	
Functional mineral	Clinical study	Healthy subjects	15	100 ml single dose	Bradicadrial response, vagal activity increased	71
water					IgA increased, stablized self-regulated ANS activity	
Functional coherent	Clinical study	Healthy subjects	15	100 ml single dose	Bradicadrial response, VLF-HRV increased, improved	7
mineral water				_	cardic health, momo and multifractal heart rate	
					dynamics, self-organized non-local adapatability	
Functional deep	Clinical study	Hypercholesterolic	14	1050 ml daily; 6 weeks	Blood cholesterol and LDL protein decreased,	110
ocean mineral water		patients			Serum antioxidation increased	
					Beneficial for prevention of atherosclerosis	
Functional deep	Clinical study	Healthy subjects	12	1,5 fold of body mass loss	Accelerated recovery from physical fatigue, complete	109
ocean mineral water	,	Physical performance		4 doses at 30 min intervals		
					minimizing entropic stress	
Functional deep	Clinical study	Eczema/dermatitis	33	0,5 I daily, 6 months	Skin symptoms improved, mineral imbalance	122
ocean mineral water	,	syndrome patients		, ===,, = ======	recovered	

3. Functional reduced water – clinical effects

Among functional waters natural reductive mineral water (NRW) and electrolyzed reductive water (ERW) have been the most investigated. Table 1 shows an overview of functional waters of different origin. Potable NRW and ERW are popular health-beneficial waters (1) that exhibit an alkaline pH (pH 8-10), are highly reductive, and have a negative oxidation-reduction potential and perform reactive oxygen species (ROS) scavenging activity (18). A double-blind placebo-controlled study in subjects who had abdominal symptoms such as pyrosis, dysphoria, abdominal distension, chronic diarrhea, and constipation were treated with ERW (27). The patients drank 0.5 1 ERW (84 individuals) or purified tap water (79 individuals) daily for two weeks. The results showed that ERW significantly improved the abdominal complaints. In particular, chronic diarrhea patients who drank ERW showed significantly higher improvement efficacy (94.1%) compared with those who drank purified tap water Comprehensive clinical data (64.7%). suggested that drinking NRW or ERW improved oxidative-stress-related diseases (28–32). It was reported that in 45% of 320 patients with type 2 diabetes who drank 2 1 natural Nordenau (Germany) mineral water per day, blood glucose and HbA1c levels were significantly decreased after six days. These levels were further decreased after long-term drinking (29). Additionally, blood cholesterol, low density lipoprotein (LDL), and creatinine levels were significantly decreased and high density lipoprotein were significantly increased. Drinking this water for a longer period resulted in an increase in the percentage of patients who were improved. In another open clinical study, 65 patients with diabetes and 50 patients with hyperlipidemia drank 2 l natural Hita Tenryousi (Japan) mineral water daily for two months. A significant decrease in blood

sugar levels was observed in 89% of the patients. Blood triglyceride and total cholesterol levels with hyperlipidemia were significantly decreased in 92% of the patients (30). Furthermore, in two doubleblind random clinical trials, the first on 29 and the second on 100 type 2 diabetes patients who drank 1 lor 2 l Hita Tenryousi mineral water per day for six or ten months, respectively, urinary 8-OH dG (a marker of DNA oxidation) was significantly decreased in the first of the two studies (31). Antimetabolic syndrome effects were noted in the second study, such as a significant decrease in starved blood sugar levels, blood pressure, total cholesterol, LDL cholesterol, GOT, γ-GTP and triglyceride levels. arteriosclerosis index, uric acid levels, and a significant increase in leptin levels as well as improvement of constipation (32). The clinical recommendation was that drinking up to 2 1 NRW water per day was beneficial for health.

4.1. Mechanism of action of functional reduced water

Clinical data suggested that ERW improved oxidative-stress-related diseases (28). The authors reported that ERW scavenged ROS and inhibited ROS-induced DNA damage in vitro (33). Electrolysis of produces a strong reducing water circumstance in the vicinity of a platinum cathode. On the cathodic platinum plate, hydrogen atoms (active hydrogen) and hydrogen molecules are generated. Mineral nanoparticle hydrides are also formed. Synthesized platinum nanoparticles scavenged superoxide anion radicals, hydroxyl radicals and hydrogen peroxide (34,35). These platinum nanoparticles also activated hydrogen molecules to hydrogen atoms by catalysis action. Natural reduced waters such as Hita Tenryosui water in Japan and Nordenau water in Germany also exhibited ROS scavenging activities (36). An active hydrogen mineral nanoparticles hypothesis of reduced water was proposed to explain the mechanism of action of both ERW and NRW (1).

The insulin deficiency of type 1 diabetes mellitus is caused by oxidative damage of pancreatic β-cells attacked by immune cells (1). Type 2 diabetes is also strongly associated with the oxidative damage of myotube and adipocyte cells due to oxidative stress, hyperphagia, and lack of exercise. The natural waters obtained from Hita Tenryosui and Nordenau, and ERW have been shown to scavenge intracellular ROS in a hamster pancreatic β -cell line (HIT-T15 cells), and remarkably accelerate the secretion of insulin. The oxidative damage induced by alloxan, a type 1 diabetes inducer, is suppressed by ERW and NRW in cells and in alloxan-induced type 1 diabetes model mice (36-39).

Similarly, ERW, Hita Tenryosui water and Nordenau water scavenge ROS in rat L6 myotube cells and enhance sugar uptake (40). Nordenau water and Hita Tenryosui water promote the phosphorylation of the insulin receptor via suppression of the activity of tyrosine protein phosphatase, which is a redox-sensitive protein, and activate PI3 kinase as well as promote the translocation of the sugar transport carrier GLUT4 to the cell membrane to promote sugar uptake (16,41). These waters also alleviate sugar tolerance damage in type 2 diabetes model mice (30,42). ERW obtained from tap water improves the symptoms of diabetes model mice (43).

4.2. Other mechanistic effects of functional reduced water

Shortening of telomeres in cancer cells has been observed with ERW treatment (44). It suppresses tumor angiogenesis by scavenging intracellular ROS and suppressing the gene expression and secretion of vascular endothelial growth factor (45). ERW suppresses the growth of cancer cells and microorganisms (46,47) and induces

apoptosis together with glutathione in human leukemia HL60 cells (48). Hydrogenenriched water suppresses the side effects of anti-cancer drugs (1). Oxidative-stressinduced neural cell death was suppressed by ERW (49). Hydrogen-supplemented water suppresses arteriosclerosis and various antineurodegenerative disease effects (1). The application of ERW in hemodialysis has been studied intensively recently, with improved cellular activity and reduced oxidative stress in end-stage renal disease patients (50-55). Hita Tenryosui NRW has been found to promote aquaporin activity in penetration of water into cells (56). Substances transported via aquaporin's are suggested to activate cellular immune responses, which allow prevention and/or treatment of chronic disease (1).

5. Ordinary drinking (tap) water – clinical effects

Consumption of ordinary drinking water has been shown to have substantial physiological effects on e.g. hemodynamic, cardiovascular and metabolic functions (57-62) (Table 1). Intake of 480 ml of drinking water led to a significant rise in blood pressure of between 30 and 100 mm Hg in 19 patients with autonomic failure and orthostatic hypotension (59,61). A pressor effect averaging 33-37 mm Hg was found in 47 middle-aged and elderly patients with autonomic failure. Systolic blood pressure increased by 11 mm Hg in elderly but not in young controls (60). Results also indicate that the pressor effect reaches a maximum at approximately 20–25 minutes and is sustained for over 60 minutes, due to a rise in sympathetic nerve activity (58,60,63,64). In normal subjects, the analysis of the time domains frequency revealed significant decrease in the heart rate. accompanied by a significant rise in heart rate variability (HRV) and high frequency power, indicating a shift toward increased vagal activity (60). The decline in the heart rate reached its maximum at 15–35 minutes post intake (57-60). It has recently been shown that the increase in sympathetic outflow induced by water ingestion elevates cellular metabolism (6). In men, the increase in metabolic rate was mainly fueled by lipids, while in women carbohydrates were the source of increased energy production (62).

The primary sympathetic activation in response to water ingestion and corresponding parasympathetic increase in vagus tone may be an auto-reflexive mechanism to restore homeostasis in conditions of distress, autonomic failure and dysfunction. This response is similar to that perceptually directed. involuntary of adaptive parasympathetic self-regulation of visceral functions to unconditional natural stimuli (65-69). A previous study in healthy volunteers demonstrated an instant restorative influence on the net sympathovagal activity of the heart at sensory induction of water stimuli from indoor greenery. Improvements were due to environmental air-mediated conditioning from plant transpiration of vortex-activated water (70).

6. Functional mineral water as a factor in physiological self-regulation

The improvement in adaptive physiological homeostasis demonstrated by ordinary drinking water has been further explored and clarified by ingestion of mineral water with defined functional qualities (71) (Table 1) to support physioself-regulation sustainable logical and homeostasis (22,23). The increased ordering of ingested functional mineral water (FMV) was obtained by a three-dimensional topological raster field geometry that causes photons of ordinary light to self-organize, which tunes a persistent self-organized water state (71). Ingestion of a small single volume of FMW (100 ml) in 15 healthy subjects induced a bradycardial regulative response, which was dependent on an increase in cardiac vagal activity, rapid a parasympathetic restorative response from the heart, and also significantly affected and caused a rise in salivary humoral immunity. A concomitant increase in the power spectral density (PSD) parameters in low frequency (LF) and high frequency (HF) power bands implied induction of a stabilizing resonance in autonomic regulation at frequencies in the range of 0.1 Hz induced by mid-range LF signals. This resonance is strongly enhanced in the presence of an efficient heart rate reflex response by the vagus nerve (72). No correlation between BMI and time domain or PSD parameters could be identified, indicating that the effect of control water or FMW was independent of the variation in Body Mass Index (BMI). Water intake had no effect on mean systolic and diastolic pressure. However, blood distinct difference in blood pressure curve shape between the two waters was noted, with FMW characterized by a straight invariant horizontal line aligned along the entire time scale and different from a slightly lower control blood pressure level. which suggested that FMW has a stabilizing effect on normal blood pressure. Additionally, a significantly lower variation in the standard deviation of systolic blood pressure might indicate fewer diurnal changes in blood pressure variability.

Considering the self-regulative stabilization of blood pressure induced by FMW it might have considerable predictive value for health outcomes, especially since elevation in the variation of circadian blood pressure and hyper-amplitude-tension is associated with an increased risk of stroke and other vascular diseases (73,74). The self-adaptive tuning of blood pressure stability proposes the minute volume of ingested FMW as a multi-scaling nonlinear inducer of pressure regulation (75). In fact, the increase in parasympathetic activity functional water observed with compensate for the previously reported increase in sympathetic activity in patients with hypertension (76).

The autonomic adaptation to achieve homeostasis induced by FMW was partly supported by previous findings, in which similar conditions created by gaseous coherent water in air transpired from indoor greenery led to an improvement in parasympathetic activation in healthy subjects during exposure to and discrimination of the stress load from an EMF from a visual display terminal (70). The increase in parasympathetic activity was accompanied by an intensified spectral power band at frequencies in the range of 0.1 Hz in the presence of plants, which led to a state of ANS stability. The EMF contributed to an increase in the amplitude of very low frequency (VLF) signals, stimulating physiologic arousal. However, exposure to natural gaseous plant cues generated a reduction in VLF power, which indicated the plant stimuli affect involuntary responses to EMF-induced distortion in power spectral density (PSD) regulative signal processing, and that only active coherent plant cues induce qualities in air conditions equal to those of the control experiment before the EMF was applied. Since both active and control plants have a more or less similar effect on cardiac and autonomic functioning, besides the striking normalization in VLF power by the active plant, an additional involuntary non-sensory self-adaptive state accompanying sensory intake or attention can be induced by natural or specifically by coherent VLF-quenching stimuli, which is consistent with the theory of restorative effects of natural objects (66,67-69).

The nervous system reflexively regulates the immune system in real time in the same way as it controls the cardiovascular response, blood pressure, respiration and other vital functions (65). Due to the bi-directional communication between the immune and nervous systems,

external inflammatory stimuli can activate anti-inflammatory signals from the latter (65). The modulation of the immune response involves activation of afferent vagus nerve fibers (77). Thus, parasympathetic pathways can directly modulate the systemic response pathogenic to invasion. The increase secretory in Immunoglobulin A (IgA) in saliva as an immediate response to the ingestion of FMW confers a protective advantage on the host by limiting the magnitude of a potentially pathogenic peripheral immune response on mucosal surfaces. Systemic administration of functional water can alter the body water status and significantly increase the vagus nerve output. It is reasonable to assume that the rational modulation of vagus nerve activity caused by FMW may offer a preventive approach that increases resistance to various environmental pathogens.

The mechanisms suggested to mediate FMW-induced parasympathetic activation are based on stimuli that can change the molecular arrangement of cellular water in order to achieve net sympathovagal activity to obtain physiological homeostasis. The observation that HRV and PSD were unaffected by the variation in BMI between subjects indicates dose-independent induction of nonlinear mechanisms and long-range power-law correlations involved in physiological self-regulation to maintain homeostasis (75). The parasympathetic response to FMW administered in a volume significantly below the recommended nutritional dose of ordinary water, and the observed concomitant physiological response of functional gaseous water reported previously (70), suggest a mechanism that resembles that of vortex-activated water as a mediator of subtle and unique parasympathetic stimuli (70). Since the decrease in heart rate and stimulation of vagal activity was achieved by means of a volume of FMW far below the standard dietary dose,

the response probably excludes the previously reported sympathetic regulation of the mitochondrial energy metabolism (62). Alternatively, the gain in energy may be due to highly efficient mitochondrial or even non-mitochondrial energy obtained from activated CDs to collect environmental weak non-local EMF energy, and export it as a self-stabilized coherent energy with an almost unlimited number of free electrons that can be used in cellular biochemical work (9).

The increase in parasympathetic activity accompanied by the intensified spectral power band at frequencies in the range of 0.1 Hz on the dietary dose of FMW (71) or in the presence of an active plant-related stimuli (70) leads to a state of ANS stability. It agrees with the results of previous investigations, which identified coordination of physiological rhythmic patterns as a condition for the attainment of a coherent state of autonomic functioning (74,78,79). involuntary adaptation of parasympathetic activity, mediated by the functional conditions of vaporous water, suggests the synchronization of a giant, cooperative EMF-coordinated network that expands laterally in liquid and gaseous states of water (80). Previous observations of improvements in net sympathovagal activity, functional restoration of major physiological systems and positive effects on the overall status of human health by means of natural cues (66-69, 81,82) indicate that the highgrade energy of FMW may be a mediator of a perceptive involuntary adaptive regulation of homeostasis.

7. Functional coherent mineral water – nonlocal clinical effects

The dominant contribution of water molecules in molar terms and total mass in living systems makes water the apparent element that can give rise to a non-linear self-regulative quantum "super-coherent" state, and to a nest of CDs of water by

inducing coherence among CDs forming a systemic axial coherence, such as the physiological water state of the human body (8.10). There it exists at normal body temperature, with its density fluctuations between a dominant coherent low entropy and a less frequent incoherent distorted highentropy ordering water. The former is organized in spherical coherent domains (83,84) of clustering water molecules tuning in unison their quantum oscillations in phase with a self-trapped EMF within the CDs (85), forming an inclusive endo-plasma. The CDs can be activated to collect in their environment low-grade energy with high entropy, and transform it, by exciting coherent vortices of almost free electrons, into high-grade energy, with low entropy, so that this energy can be released outwards into useful work without thermal losses (9). The unique value of such super-coherent biological water spanning all the CDs throughout water is considered one of the most important characteristics of a healthy physiological state (86).

In 15 healthy subjects drinking a low dietary volume (100 ml) of functional coherent mineral water (FCMW), primary effect besides an expected bradycardial regulative response on the heart (7) (Table 1) was a significantly larger total power of the heart with a concomitant increasing effect on 2-3 minute oscillations in the very low frequency (VLF) power band, indicating alteration in the heart's intrinsic cardiac rhythm that is considered fundamental to health and wellbeing (87). The effect of control mineral water shifted, particularly affecting the 6-9-minute VLF signals. The coherency of FCMW was generated by having incident daylight passing through a FOL (7,21,88). The FOL works as a fractal spatial-wave 'Fourier raster", capable of transforming the spatial dissonance of incident EMF oscillations into coherent wave components (88).

organized, highly stable coherent ordering of FCMW forms on irradiation in the presence of low-entropy visible or infrared light at ambient conditions, characterized by persistent fractal long-range attraction based on self-organization ability (21).

The intrinsic regulation in VLF-induced HRV was strongly coordinated to mono and multifractal scaling of heart rate dynamics, which defines self-regulative non-local adaptability with higher capacity to respond to unpredictable stimuli and stresses, a characteristic of a healthy autonomic function (75). This result introduced new information to the results of previous findings discussed in section 6 above (6. Functional mineral water as a factor in physiological self-regulation); firstly, the beneficial effect of intake of FMW on a rapid parasympathetic restorative response, stimulating mucosal humoral immunity and a proposed self-regulative stabilization of blood pressure (71), and secondly, the humidifying effect of indoor greenery irrigated with vortex water, which improved a vagus-induced sympathovagal balance on the heart in healthy volunteers exposed to ordinary EMFs in visual display terminal work (70). The finding that consumption of FMW was likely to involve a condition of autonomic resonance (79,87) and a net sympathovagal activity on the contributed to new information that lowdensity coherent qualities of body water participated regulation in the of cardiovascular Since functioning. the functional quality of mineral water was from a three-dimensional generated geometrical field raster space with a pathcurve form of an interlocked vortex (71), in terms of optics, while uniformly passing through space the radiation undergoes rearrangement and transforms into a nonlinear series of wave structures with fractal ordering. This low-entropy state of highly ordered photons, assumed to generate

coherent EMF oscillations in water in the low frequency (LF) region around 0.1 Hz, was proposed as acting as a non-local resonating amplifier of intrinsic cardiac oscillations. coherent Α concomitant influence on the processing of coherent oscillatory information as well as non-local functioning of liquid FMW or conditioned air from indoor greenery (70) is likely. Consequently, assessing the regulatory autonomic capacity of FMW, threedimensional path-curve forms obtained from non-local ordering of conditioned mineral water (71) or air from indoor greenery (70) appear to represent an index of vagally mediated improved HRV, which induce auto-coherent heart rhythms, typically amplifying signals in the LF region around 0.1 Hz.

Notwithstanding the VLF coupled multifractal cardiac properties obtained from drinking FCMW, the high-symmetry state of the optical vortex form generated by the two-dimensional FOL (88) gains encoded information of a bradycardial regulative response on heart rate accompanying a significant increase in the 2-3 minute VLF band, reflecting a strengthening in mono and multifractal heart-rate dynamics. Results imply that the VLF rhythms of the heart are in fact stimulated after consumption of a conditioned coherent water state, which entails a highly ordered and multifractal arrangement of the molecular configuration of the physiological "body water" with an apparent non-local EMF identity (7).

In accordance with FMW stabilizing blood pressure (71), drinking FCMW resulted in a higher consistent mean difference in curve shape from the baseline, indicating a steady arterial systolic and diastolic blood pressure. The impact of fractal scaling along with distinct classes of non-linear interactions reveal that fractal self-regulation appears to underlie important

aspects of cardiac VLF influence of endogenous blood pressure rhythms on the heart, which might have considerable predictive value for health outcomes (73,74).

The defined change in HRV implies the VLF rhythm is a specified intrinsic sympathetic oscillation modulated nonlocal and nonlinear fractal signal processing (75), which is also involved with thermal, metabolic rate, hormonal, and visceral regulation (89), in addition to cardiac-related activity (90). Since the VLF band is sensitive to ruminative or worrisome thoughts frequently observed in many psychophysiological disorders, the signal has been considered a potentially powerful tool autonomic regulation. physiological activity was reflected to the patient in a self-management program, VLF rhythms served as an indicator of the patient's attempt to achieve a calm and peaceful internal state (89). In the presence of an EMF, the influence of higher VLF signals indicated a distortion in ordinary long-term heart cycles of an extended biological duration, possibly affecting and inducing a long-term hormonal response to external stressors – thereby optimizing individual coping ability and the perception of control (91). It has been proposed that the long-term cycles of the VLF band originate from self-oscillations in the vasomotor part of the baroreflex loop of the heart and in transplant recipients heart without autonomic innervation. The heart has very little activity in the VLF region, indicating that the majority of the activity in this band is due to autonomic influence (91,92).

7.1. The heart and brain rhythms overlap with geomagnetic activities

The influence from the background non-local low VLF of the heart could be related to the fact that in order to load energy in the water CDs, a resonating magnetic field is needed (14). In higher organisms, such as

humans, these fields can be induced by the nervous system. In elementary organisms, such as bacteria or yeast cells and physiological liquids, i.e. water. environmental fields like geomagnetic fields can serve as the inducer (14,90,93). These modes act as stationary fields produced by the magnetic activity occurring in the shell whose boundaries are the surface of the earth-conductive ionosphere resonant cavity. which acts as a mirror wall for VLF and Alfvén waves (83). Aqueous solutions of bicarbonates, superoxide radicals, and other ROS, when excited, show variations in energy-emitting activity that have been found to correlate with fluctuations in the geomagnetic (93).Accordingly. field bacterial and viral DNA sequences have been found to induce low-frequency EMFs in high aqueous dilutions (92). formation of condensed DNA copies was triggered by the ambient geomagnetic EMF background of VLFs related to Schaumann resonances (SR), specifically the 7.8 Hz band. In humans, physiological rhythms and global collective behaviors are not only synchronized with solar and geomagnetic activity, but disruptions in these fields can also invoke adverse effects upon human health and behavior (94). It is well established that the resonant frequencies of geomagnetic Ultra Low Frequencies (ULF) (0.006–0.2 Hz) overlap closely with the frequencies of the cardiovascular system (0.002 Hz-0.2 Hz), while SR (7.8-51 Hz) directly overlap with those waves of the human brain (Theta 4–7 Hz, Alpha 8-12 Hz, Beta 12-30 Hz, and Gamma 30-100 Hz). It is expected that variations in intensity in these fields have a strong correlation with changes in HRV indices, especially with changes in the VLF rhythms of HRV (93). Based on these observations, the outcome of experimental observations from indoor greenery (70), and the constitution of a fractal quantum dissipative state (21) of FMW (71) or FCMW (7), implies this water state is a plausible amplifier of extending VLF signals compliant with those of a ULF with an enhanced dominating impact on specifically 2–3 minutes (5.6–7.8 mHz) long-range VLF rhythms of the heart, and different from the local effect of control mineral water on particularly 6–9 minutes (2.9–3.9 mHz) VLF signals, which includes a generic restraint of the entire VLF band.

To get a collective performance of water CDs, which can give rise to resonance with intrinsic VLF rhythms, would require a uniform rate of energy loading from, e.g., a magnetic field for all involved CDs (14). A plausible interaction with geomagnetic ULF can affect the human cardiovascular system, because several ULFs are in a comparable range with those of the human heartbeat and its rhythms (95). The external non-local background load of conditioned EMF photons in water CDs is in resonance with, e.g., the frequency of ULF geomagnetic field pulsations that can be biotropic (96), specifically, stable continuous pulsations (Pulsations continuous; Pc). Accordingly, Class Pc4 (time period 45–150 sec) or Pc5 (time period 150-600 sec) (97) may contribute to the rise in cardiac intrinsic 2–3 minute VLF rhythms (92). This observation adds partly new information that VLF rhythms obtained from two-dimensional path-curves represent a strengthening of healthy multifractal heart rate dynamics (75) strongly correlating with non-local selfregulation mechanisms, underlying the fact that the VLF rhythm is the primary source of this rhythm within the heart itself (87).

7.2. Double vagal-sympathetic response hypothesis

The reflexive neural regulation of the immune system in real time is in accordance with the cardiovascular response, blood pressure, respiration, and other vital functions (65,98). The modulation of the

immune response, a cardioprotective effect on the heart (65), and promotion of energy conservation by maintaining the heart rate lower than the intrinsic effect on heart rate (65) involves parasympathetic activation of afferent vagus nerve fiber (99). The previous observation on consumption of FMW (71) supported a proposed parasympathetic mediated self-regulative stabilization of blood pressure, accompanying a protective advantage of mucosal humoral immunity by the increase in secretory IgA in saliva. However, drinking FCMW, the sympathetic VLF influence on a temporally and marginally time-limited increase in blood pressure, and the consistency of a steady difference in blood pressure curve shape from baseline, with a densified stabilized secretory IgA on mucosal surfaces, conforms partly with the double vagalsympathetic response hypothesis (77). The mechanism behind this response suggests that the sympathetic pressor effect evoked by the intake of water raised an immediate counterbalanced cardiac vagal activity, which promotes a bradycardial effect (100bradycardial response The 103). consumption of FCMW water is proposed as elicited from a non-local and fractal organized modulation of the 2-3 minute VLF rhythm on the heart, offering a preventive and stabilizing effect on blood pressure with an additional densified protection against mucosal pathogenic colonization. Importantly, to keep autonomic balance a healthy system is constantly and dynamically changing (75). Therefore, an important indicator of the status of health of the regulatory systems is the capacity to respond to and adjust the relative autonomic balance, e.g. the heart rate, to the appropriate state for the context the individual is engaged in at any given moment (94). Consequently, the dynamic bradycardial regulatory response accompanying the 2-3 minute induced VLF rhythm identified a reflexively intrinsic and non-local originated

ability of the physiological self-regulatory system to maintain the relative balance between the sympathetic and parasympathetic systems, independent of sympathetic or parasympathetic controls or the autonomic balance between these controls as indexed by different measures of HRV (104). The rise in normal 2-3 minute VLF power obtained in a restful sitting position appears to promote and indicate a selfsustained and healthy function. Accordingly, the apparent shift from local longer (6-9 minute) to non-local shorter (2–3 minute) VLF rhythms strengthens a self-oscillatory global sympathetic outflow from the heart's intrinsic activity, where the VLF-induced change in beat-to-beat fluctuations of the heart regulate an adaptive, minor and steady rise in blood pressure (94).

7.3 Coherent domains export quantum electrodynamic energy

The quantum properties of the functional coherent state of mineral water (21) at ambient temperature and pressure conditions relate to quantum electrodynamic (QED) field theory (86), as evoked by the interaction between the high-entropy photons of incident ordinary daylight passing through the high-symmetry FOL raster space. According to the theory of dissipative systems' ability to self-regulate (105), it was implied that the exchange of energy and entropy with the environment relied on the fact that the absorption of spatially self-organized low-entropy photons of incident conditioned sunlight into highgrade energy with low entropy displaces the equilibrium towards a dominance of coherent water CDs. Likewise, the CDs of functional coherent mineral water were characterized by a distinctive configurative coherent aqueous state with a fractal scaling low-entropy relationship in radiative temperature fluctuations that maintained a self-organized structural adaptation irrespective of ambient temperature (21). When energy from the quantum field was captured by the incident photons, they were selftrapped and turned into an excited state of coherent photons oscillating in phase with the quantum EMF (86). At this point, the Lamb-like shift, a critical number of coherent water molecules are tuned together and are enclosed within the CDs, where a phase transition occurs (86). The coherent oscillations of the molecules in the CDs no longer require any external supply of energy. CDs are stabilized and self-organized on all scale levels, which in the coherent state of mineral water was identical to a strong power law relationship in the fractal scaling boundary of thermal IR emission flickering, characterized by high persistence, and the existence of CDs that enable a reservoir of quasi-free electrons (21).

CDs are spontaneous receptors of weak non-local **EMF** signals (86).Water molecules become structurally clustered, not only attracting adjacent water molecules but also other guest molecules able to resonate with the same frequency (9). With a further increase in density, the CDs become a net exporter of energy because the selfstabilized coherent state has a lower energy than the ionization threshold of an ordinary water state (86). Such coherent CDs contain millions of a low-entropy state of non-local clustered water molecules, and a nonvanishing probability of having an infinite number of quasi-free electrons that can be donated readily to electron-acceptor systems. The quasi-free electrons, considered as the most significant property of a quantum coherent system, form frictionless vortices with an extremely long lifespan (10), lasting for days or weeks depending on a selfregulated magnetic moment that aligns coherent intrinsic and external vortices that cannot degrade thermally. In view of the novel observation in FCMW of a VLF mediated oscillation with non-local origin, the significant decrease in heart rate, independent of changes in respiratory sinus arrhythmia accompanied by an approximate decline (4.5% related to the control 2.6%) in intermediary aerobic mitochondrial metabolism and in the production of bio-logical energy (i.e. adenosine triphosphate, ATP), the CDs can be a candidate in a proposed mimic role of an enzyme functioning as a source of highly excited electrons (86). Hypothetically, in their excited coherent phase the CDs could act as a donator of excited electrons or catalyze an excitation to a fairly low activation energy to free them to be able take part in the mitochondrial electron transfer at just the activation energy of a specific enzyme corresponding exactly with the excitation energy of the relevant coherent state of clustering CDs (86). Notably, the recent study on drinking 500 ml of ordinary water found the metabolic rate enhanced by 30%, mainly fueled by the oxidation of lipids in men and carbohydrates in women (62).

Considering the VLF coupled multifractal cardiac properties obtained from drinking FCMW, the high-symmetry state of the path-curve form generated from a twodimensional FOL gains encoded information of physical matter in three-dimensional space (106). A counteracting spherical force of two vortices flowing in opposite directions reconstructs a higher state of spatial symmetry of incident photons of ordinary light at different frequencies that are organized virtually according to fractal wave dynamics in space passing the geometry. Self-trapped higher-symmetrystate photons captured by water CDs may oscillate in resonance with collective coherent electron vortices and molecular rhythms within the excited CDs (9). In the ordered coherent water state, an incremental oscillatory change in a dynamic concentric temperature gradient aligns with formation of two interlocking vortices flowing in opposite directions, with a slight

difference in thermal IR temperature between the two gradient path-curve forms (21). Accumulated, condensed and structurally ordered energy distributed into several concentric temperature zones of the two interlocking vortices was aligned with a broadening temperature interval towards lowered temperatures in the segments with most ordered CDs.

8. Functional deep ocean mineral water – clinical effects

Deep ocean mineral water designates a water that flows below 500 m from the surface of the sea (107). Supplementation with a desalinated dietary volume of FDOM acts as a primordial source of nutritional minerals and trace elements. Besides the major minerals, more than 70 trace elements and micro-nutritionals have been documented (108) (Table 1). Observations of FDOM effects have shown consistent antiatherogenic effects against dietary challenges (109-110). In a double-blind study on 42 hypercholesterolemic subjects (110) randomly divided in three groups (drinking reverse osmotic water, FDOM or magnesium-fortified water) the 14 volunteers who drank 1050 ml FDOM daily for six weeks had a decrease in blood total cholesterol and this effect was progressively enhanced with time. Serum low-density lipoprotein-cholesterol was also decreased. Further, total cholesterol levels in FDOM subjects were significantly lower than those in the two other groups. FDOM consumption also increased the antioxidative capacity in serum. As hypercholesterolemia is the major cause of atherosclerosis in humans, the treatment with FDOM can be beneficial for the prevention of atherosclerosis (110).

To test a hypothesis whether deep oceans contain the evolutionary preferred constituents, as terrestrial organisms indeed evolved from deep oceans, the supply of FDOM to humans, as a land creature, may replenish the loss of molecular complexity associated with evolutionary sea-to-land migration (108). A study was performed on 12 healthy humans to investigate the time required for physical performance to recover after a dehydrating exercise running on a motorized treadmill (maximum running time was 240 min) when FDOM or a placebo drink was administered for rehydration. Measures of physical performance. physiological stress, and muscle damage were determined at 4, 24 and 48 h during recovery. Consumption of FDOM during recovery at an amount equivalent to 1.5 times each individual body mass loss, and divided into four sub-supplements ingested intervals, 30-minute substantially accelerated recovery from physical fatigue in aerobic power and enhanced lower-body muscle power after a prolonged bout of dehydrating exercise. This improvement appears to be associated with complete elimination of exercise-induced muscle damage, suggesting that FDOM contains components that can complement and enhance the molecular and complexity of humans to minimize entropic stress produced during prolonged physical activity in the heat. The key components of FDOM contributing to the observed ergogenic benefits are not exactly known. The constituents of the FDOM are characterized by enriched contents of minerals (boron, magnesium, lithium, and rubidium), where boron is known to attenuate exercise-induced rise in plasma lactate (111) and to prevent magnesium loss (112). Serum magnesium concentration and dietary magnesium intake are known correlates of muscle strength (113). Consequently, as a primary contributing factor, the components in FDOM may work cooperatively to sustain normal human performance.

The higher content of magnesium, lithium and rubidium in FDOM may be associated with strengthened antioxidant capability against oxidative stress during

post-exercise stress recovery (114). In animals, lack of magnesium in their diet leads to increased free radical production (115), while magnesium supplementation eliminates free radical production (116,117). Lithium can increase the free radical scavenging capability and thus help to increase the resilience of a cell against destructive free radical attack (118).

One significant feature of FDOM is the enriched rubidium content compared to fresh water. Rubidium concentration increases considerably in seawater as the depth of the approaches ocean 450 meters. The concentration in human plasma is 2.5-3.0 times higher than that found in FDOM (119) and has a high retention rate in the human body (120), and has been suggested as an essential factor in preserving biological integrity against daily entropic stress (121). Drinking 500 ml FDOM daily for six months restores mineral imbalance in atopic eczema/dermatitis syndrome (AEDS) (122) and skin symptoms were improved in 27 out of 33 patients. The consumption of FDOM resulted in a significant decrease in hair potassium while selenium levels increased. The toxic minerals mercury and lead decreased significantly. The mineral imbalance may be involved pathogenesis of AEDS and drinking FDOM may be useful in treatment of AEDS.

9. Conclusions

1) Functional water originated in Japan in the 1930s. The Japanese Society for Functional water was established in 2001 scientific studies on various functional waters have been performed to date. Functional waters produced in Japan have to be reviewed and approved by the Ministry of Health and Welfare according authorized to Pharmaceutical Affairs Law to admitted for the market. Countries within the European Union and United States do not have any legislative claims on functional water.

- 2) The Functional Water Association in Japan defines functional water as a water that promotes the status of health and from which both treatment and physiological function have been scientifically demonstrated and shown to be reproducible, and where useful healthbeneficial effects have been identified among natural and artificially treated waters.
- 3) Accumulating evidence has shown that particularly reduced waters are health beneficial and suppress oxidative-stress-related diseases, especially type 2 diabetes, which has been studied extensively. The mechanisms are considered to be connected to the hydrogen molecule and its activation, conversion and stabilization in interaction with nanoparticles that may act as antioxidants.
- 4) Functional mineral waters and their coherent equivalents comprise a capacity to maintain physiological self-regulation to reduce variability associated with nonlinear and non-local mechanisms involved in maintaining homeostasis. Formation of a "super-coherent" giant physiological water state is considered one of the most important characteristics of a healthy physiological state.
- 5) Functional and desalinated deep ocean mineral water can increase human robustness against entropic physical exhaustive challenge by elimination of oxidative tissue damage, generate reduction of hypercholesterolic effects with plausible retardation of atherosclerosis. and alleviation ofpathogenesis of atopic eczema/dermatitis syndrome.

List of abbreviations:

Food for specific health uses, FOSHU; Reactive oxygen species, ROS; Coherent domains, CDs; Electromagnetic field, EMF; Fibonacci optical lattice, FOL; Functional deep ocean mineral water, FDOM; natural reductive water, NRW; electrolyzed reductive water, ERW; Glycated hemoglobin, HbA1c; 8-hydroxy-2-deoxyguanosine, 8-OH dG; low density lipoprotein, LDL; Deoxyribonucleic acid, DNA; glutamic oxaloacetic acid transaminase, GOT; γ-GTP, γ-glutamyl transpeptidase; functional mineral water, FMW: Functional coherent mineral water, FCMW; power spectral density, PSD; Low frequency, LF; high frequency, HF; very low frequency, VLF; autonomous nervous system, ANS; immunoglobulin A, IgA; body mass index, BMI; Schaumann resonances, SR; heart rate variability, HRV; ultra-low frequencies, ULF; quantum electrodynamic, QED; adenosine triphosphate, ATP; atopic eczema/dermatitis syndrome, AEDS.

Competing Interests:

The author has no financial interests or any other conflicts of interest to disclose.

References

- 1. Shirahata, S, Hamasaki, T, & Teruya, K. (2012). Advanced research on the health benefit of reduced water. *Trends in Food Sci & Technol.*, 23, 124-131.
- 2. Kubomara, K. (1998). Japan redefines functional foods. *Prepared Foods*, 167, 129-32.
- 3. Martirosyan, DM, & Singh J. (2015). A new definition of functional food by FFC: what makes a new definition unique? *Func Food Health Dis.*, *5*(6), 209-223.
- 4. Shirihata, S. (2002). Reduced water for prevention of diseases. In: Shirihata S (Ed.) *Animal Cell Technology: Basic & applied aspects* (12: 25-30). Dordrecht: Kluwer Academic Publishers.
- 5. Shirihata, S. (2004). Reduced water. In:

- Characteristics and application technology Application to the fields of agriculture, foods, and medical therapy (33-45). Tokyo: N.T.S.
- 6) Johansson, B. (2009). Effects of functional water on heart rate, heart rate variability, and salivary immunoglobulin A in healthy humans: A pilot study. *J Alter Compl Med.*, 15(8), 871-877.
- 7) Johansson, B, & Sukhotskaya, S. (2016). Drinking functional coherent mineral water accompanies a strengthening of the very low frequency impact on heart rate variability, and mono and multifractal heart rhythm dynamics in healthy humans. Func Food Health Dis., 6(6), 388-413.
- 8) Del Giudice, E, Pulselli, RM, & Tiezzi, E. (2009). Thermodynamics of irreversible processes and quantum field theory: an interplay for the understanding of ecosystem dynamics. *Ecol Model.*, 220, 1874-1879.
- 9) Brizhik, L, Del Giudice, E, Jörgensen, SE, Marchettini, N, & Tiezzi, E. (2009). The role of electromagnetic potentials in the evolutionary dynamics of ecosystems. *Ecol Model.*, 220, 1865-1869.
- 10) Marchettini, N, Del Giudice, E, Voeikov, V, & Tiezzi, E. (2010). Water: A medium where dissipative structures are produced by coherent dynamics. *J Theor Biol.*, 265, 511-516.
- 11) Hirokawa, N, Tanaka, Y, Okada, Y, & Takeda, S. (2006). Nodal flow and the generation of left-right asymmetry. *Cell*, 125, 33-45.
- 12) Hove, JR, Koster, RV, Forouhar, AS, Acevedo-Bolton, G, Fraser, SE, & Gharib, M. (2003). Intracardic fluid forces are an essential epigenic factor for embryonic cardiogenesis. *Nature*, 421, 172-177.
- 13) Voeikov, VL. (2007). Fundamental role of water in bioenergetics. In Belussov, LV, Voeikov, VL, Martynuk, VS (Eds.)

- Biophotonics and Coherent Systems in Biology (89-104). New York, Springer.
- 14) Montagnier, L, Del Giudice, E, Aissa, J, Lavallee, C, Motschwiller, S, Capolupo, A, Polcari, A, Romano, P, Tedeschi, A, & Vitiello, G. (2015). Transduction of DNA information through water and electromagnetic waves. *Electromagn Biol Med.*, 34(2), 106-112.
- 15) Brizhik, LS, Del Giudice, E, Tedeschi, A, Voeikov, VL. (2011). The role of water in the information exchange between the compartments of an ecosystem. *Ecol Model.*, 222, 2869-2877.
- 16) Shirahata, S, Li, Y, Hamasaki, T, Gadek, Z, Teruya, K, Kabayama, S, Otsubo, K, Morisawa, S, Ishii, Y, & Katakura, Y. (2007). Redox regulation by reduced waters as active hydrogen donors and intracellular ROS scavengers for prevention of type 2 diabetes. In: Smith, R (Ed.), *Cell technology for cell products* (99-101). Dordrecht: Springer.
- 17) Hou, C-W, Tsai, Y-S, Jean, W-H, Chen, C-Y, Ivy, JL, Huang, C-Y, & Kuo, C-H. (2013). Deep ocean mineral water accelerates recovery from physical fatigue. *J Intern Soc Sports Nutr.*, 10(7), 1-7.
- 18) Sugihara, S, Suzuki, C, & Hatanaka, K. (2001). The mechanisms of activation of substances by minimal catalyst water and application in keeping foods fresh. *Water*, *3*, 87-94.
- 19) Ikeda, S, Takata, T, Komoda, M, Hara, M, Kondo, JN, Domen, K, Tanaka, A, Hosono H, & Kawazoe, H. (1999). Mechano-catalysis a novel method for over-all water splitting. *Phys Chem Chem Phys.*, 1, 4485-4491.
- 20) Domrachev, A, Roldigin, GA, Selivanovsky, DA. (1992). Rule of sound and liquid water a dynamically unstable polymeric system in mechanochemically activated processes of oxygen production on earth. *J Phys Chem.*, 66,

- 851-855.
- 21) Johansson, B, & Sukhotskya, S. (2012). Allometric scaling behaviour A quantum dissipative state implies a reduction in thermal infrared emission and fractal ordering in distilled coherent water. *Water*, 3, 100-121.
- 22) Diplock, AT, Aggett, PJ, Ashwell, M, Bornet, F, Fren, EB, & Roberfroid, MB. (1999). Scientific concepts of functional foods in Europe: Consensus document. *Brit J Nutr.*, 81(Suppl. 1), S1-S27.
- 23) Asp, N-G. (2001). Health effects of probiotic and preprobiotic foods. *Scand J Nutr.*, 45, 57.
- 24) Siro, S. (2008). Functional food. Product development, marketing and consumer acceptance A review. *Appetite*, 51(3), 456-467.
- 25) Westmark, CJ. (2014). Definition of functional food. Healthy, functional, and food compounds. Similarities and differences between these categories. Bioactive food compounds. *Introduction to functional food science: Textbook.* 2nd edition. Richardson, TX: Functional food Center.
- 26) FDA Regulation. U.S. Food and Drug Administration. Guidance for Industry: Evidence-based review system for the scientific evaluation of health claims Final.

 http://www.fda.gov/Food/GuidanceRegulation/Guidance

 Documents RegulatoryInformationLabelingNutrition/ucm073332.htm. (Accessed)
- 27) Tashiro, H, Kitahora, T, Fujiyama, Y, & Banba, T. (2000). Clinical evaluation of alkali-ionized water for chronic diarrhea placebo-controlled double-blind study. *Digest Absorp.*, 23, 52-56.

on July 2013).

28) Hayashi, H, & Kawamura, M. (2002). Clinical application of electrolyzed-reduced water. In: Shirahata, S. (Ed.), *Animal cell technology: Basic & applied aspects* (12: 31-36). Dordrecht: Kluwer

- Academic Publishers.
- 29) Gadek, Z, Li, Y, & Shirihata, S. (2006). Influence of natural reduced water on relevant test parameters and reactive oxygen species concentration blood of 320 diabetes patients in the prospective observation procedure. In: Lijima, S, & Nishijima, KI (Eds.), *Animal cell technology: Basic & applied aspects* (14: 377-385). Dordrecht: Springer.
- 30) Osada, K, Li, YP, Hamasaki, T, Abe, M, Nakamichi, N, & Teruya, K. (2010) Anti-diabetes effects of Hita Tenryosui water, a natural reduced water. In: Ikura, K. (Ed.), *Animal cell technology: Basic & applied aspects* (15: 307-313). Dordrecht, Springer.
- 31) Matsubayashi, N, Hisamoto, T, Murao, N, & Hara, T. (2008). About effect of so-called reduced water on diabetes patients. In *The abstract book of the 46th Kyushu Regional Meeting of Japan Diabetes Society*, 42.
- 32) Higashikawa, F, Kuriya, T, Noda, M, & Sugiyama, M. (2009) Verification of improving action of mineral water on lipid metabolism in clinical trials. In: Abstract book of the 7th meeting of the Japanese Society of Preventive Medicine, 20.
- 33) Shirahata, S, Kabayama, S, Nakano, M, Miura, T, Kusumoto, K, & Gotoh, M. (1997) Electrolyzed-reduced water scavenges active oxygen species and protects DNA from oxidative damage. *Biochem Biophys Res Commun.*, 234, 269-274.
- 34) Hamasaki, T, Kashiwagi, T, Imada, T, Komatsu, T, & Li, Y. (2008) Kinetic analysis of superoxide anion radical-scavenging and hydroxyl radical-scavenging activities of platinum nanoparticles. *Langmuir.*, 24, 7354-7367.
- 35) Kajita, M, Hikosaka, K, Litsuka, M, Kanayama, A, Toshima, M, & Miyamoto, Y. (2007). Platinum

- nanoparticles as a useful scavenger of superoxide anion and hydrogen peroxide. *Free Radical Res.*, 41, 615-626.
- 36) Li, Y-P, Nishimura, T, Teruya, K, Maki, T, Komatsu, T, & Hamasaki, T. (2002). Protective mechanism of reduced water against alloxan-induced pancreatic β-cell damage: scavenging effect against reactive oxygen species. *Cytotechnol.*, 40, 139-149.
- 37) Li, Y-P, Teruya, K, Katakura, Y, Kabayama, S, Otsubo, K, Morisawa, S. (2005) Effect of reduced water on the apoptotic cell death triggered by oxidative stress in pancreatic β HIT T15 cell. In: Godia, F, & Fussenegger, M. (Eds.), *Animal cell technology meets genomics* (121-124) Dordrecht: Springer.
- 38) Li, Y-P, Hamasaki, T, Nakamichi, N, Kashiwagi, T, Komatsu, T, & Ye, J. (2011). Suppressive effects of natural reduced waters on alloxan-induced apoptosis and type 1 diabetes mellitus. *Cytotechnol.*, 63(2), 205–210, doi: 10.1007/s10616-011-9343-z.
- 39) Li, Y-P, Hamasaki, T, Teruya, K, Nakamishi, N, Gadek, Z, & Kashiwagi, T. (2010). Suppressive effects of electrolyzed reduced water on alloxaninduced apoptosis and type 1 diabetes mellitus. *Cytotechnol.*, doi:10.1007/s10616-010-9317-6.
- 40) Oda, M, Kusumoto, K, Teruya, K, Hara, T, Maki, S, & Kabayama, S. (1999) Electrolyzed and natural reduced water exhibit insulin-like activity on glucose uptake into muscle cells and adipocytes. In: Bernard, A, Griffiths, WN, & Wurm F. (Eds.), *Animal cell technology: Products from cells, cells as products* (425-427). Dordrecht: Kluwer Academic Publishers.
- 41) Shirahata, S, Nishimura, T, Kabayama, S, Aki, D, Teruya, K, & Otsubo, K. (2001). Anti-oxidative water improves diabetes. In: Linder-Olsson, E. (Ed.), *Animal cell technology: From target to*

- *market* (574-577). Dordrecht: Kluwer Academic Publishers.
- 42) Gadek, Z, & Shirahata, S. (2002). Changes in the relevant test parameters of 101 diabetes patients under the influence of the so called "Nordenauphenomenon". In: Shirahata, S. (Ed.), Animal cell technology: Basic and applied aspects (12: 427-431). Dordrecht: Kluwer Academic Publishers.
- 43) Kim, M-J, & Kim, H-K. (2006). Antidiabetic effects of electrolyzed reduced water in streptozotocin-induced and genetic diabetic mice. *Life Sci.*, 79, 2288-2292.
- 44) Shirahata, S, Murakami, E, Kusumoto, K, Yamashita, M, Oda, M, & Teruya, K. (1999) Telomere shortening in cancer cells by electrolyzed-reduced water. In: Ikura, K (Ed.) *Animal cell technology: Challenges for the 21st century* (355-359). Dordrecht: Kluwer Academic Publishers.
- 45) Ye, J, Hamasaki, Y, Nakamishi, M, Komatsu, T, & Kashawagi, T. (2008). Inhibitory effect of electrolyzed water on tumor angiogenesis. *Biol Pharmaceut Bull.*, 31, 19-26.
- 46) Hamasaki, T, Kashiwagi, T, Aramaki, S, Imada, T, Komatsu, T, Li, Y. (2005). Suppression of ell growth by platinum nanocolloids as scavengers against reactive oxygen species. In: Godia, F, & Fussenegger, M. (Eds.), *Animal cell technology meets genomics* (249-251). Dordrecht, Springer.
- 47) Komatsu, T, Kabayama, S, Hayashida, A, Nogami, H, Teruya, K, & Katakura, Y. (2001). Suppressive effect of electrolyzed reduced water on the growth of cancer cells and microorganisms. In: Linder-Olsson, E. (Ed.), *Animal cell technology: From target to market* (220-223). Dordrecht: Kluwer Academic Publishers.
- 48) Tsai, C-F, Hsu, Y-W, Chen, W-K, Chang, W-H, Yen, C-C, & Ho, Y-C.

- (2009). Hepatoprotective effect of electrolyzed reduced water against carbon-tetrachloride-induced liver damage in mice. *Food Chem Technol.*, 47, 2031-2036.
- 49) Kashiwagi, T, Hamasaki, T, Kabayama, S, Takaki, M, Teruya, K, Katakura, Y. (2005). Suppression of oxidative stress-induced apoptosis of neural cells by electrolyzed reduced water. In: Godia, F, & Fussenegger, M. (Eds.), *Animal cell technology meets genomics* (257-259). Dordrecht, Springer.
- 50) Huang, K-C, Yang, C-C, Lee, K-T, & Chien, C-T. (2003). Reduced hemodialysis-induced oxidative stress in end-stage renal disease patients by electrolyzed reduced water. *Kidney Internat.*, 64, 704-714.
- 51) Huang, K-C, Yang, C-C, Hsu, S-P, Lee, K-T, & Liu, H-W. (2006). Electrolyzed-reduced hemodialysis-induced erythrocyte impairment in end-stage renal disease patients by electrolyzed reduced water. *Kidney Internat.*, 70, 391-398.
- 52) Huang, K-C, Hsu, S-P, Yang, C-C, Ou-Yang, P, Lee, K-T, & Morisawa, S. (2010). Electrolyzed-reduced water improves T-cell damage in end-stage renal disease patients with chronic hemodialysis. *Nephrol Dialys Transplant.*, 25, 2730-2737.
- 53) Nakayama, M, Kabayama, S, Terawaki, H, Nakayama, K, Kato, K, & Sato, T. Less-oxidative (2008).hemodialysis solution rendered by cathode-side electrolyzed application of water. Hemodial Internat. *International* symposium on home hemodialysis, 11, 32-327.
- 54) Nakayama, M, Nakano, H, Hamada, H, Itami, N, Nakasawa, R, & Ito, S. (2010). A novel bioactive hemodialysis system using dissolved dihydrogen (H₂) produced by water electrolysis: a clinical trial. *Nephrol Dialys Transplant.*, 25,

- 3026-3033.
- 55) Zhu, WJ, Nakayama, M, Mori, T, Nakayama, K, Katoh, J, & Morata, Y. (2011). Intake of water with high levels of dissolved hydrogen (H₂) suppresses ischemia-induced cardio-renal injury in Dahl salt sensitive rats. *Nephrol Dialys Transplant.*, 26, 2112-2118.
- 56) Kitagawa, Y, Liu, C, & Ding, X. (2011). The influence of natural mineral water on aquaporin water permeability and human natural killer cell activity. *Biochem Biophys Res Commun.*, 409, 40-45.
- 57) Jordan, J, Shannon, JR, Grogan, E, Biaggioni, I, & Robertson, D. (1999). A potent pressor response elicited by drinking water. *Lancet*, 353, 723.
- 58) Jordan, J, Shannon, JR, Black, BK, Ali, Y, Farley, M, Costa, F, Diedrish, A, Robertson, RM, Biaggioni, I, & Robertson, D. (2000). The pressor response to water drinking in humans. A sympathetic reflex. *Circulation*, 101, 504-509.
- 59) Cariga, P, & Mathias, CJ. (2001). Haemodynamics of the pressor effect of oral water in human sympathetic denervation due to autonomic failure. *Clin Sci.*, 101, 313-319.
- 60) Routledge, HC, Chowdhary, S, Coote, JH, & Townend, JN. (2002). Cardiac vagal response to water ingestion in normal subjects. *Clin Sci.*, 103, 157-162.
- 61) Schroeder, C, Bush, VE, Norcliffe, LJ, Luft, FC, Tank, J, Jordan J, & Hainsworth, R. (2002). Water drinking acutely improves orthostatic tolerance in healthy subjects. *Circulation*, 106, 2806-2811.
- 62) Boschmann, M, Steiniger, J, Hille, U, Tank, J, Adams, F, Sharma, AM, Klaus, S, Luft, FC, & Jordan, J. (2003). Water-induced thermogenesis. *J Clin Endocrinol Metab.*, 88, 6015-6019.
- 63) Scott, EM, Greenwood, JP, Gilbey, SG, Stoker, JB, & Mary, DA. (2001). Water

- ingestion increases sympathetic vasoconstrictor discharge in normal human subjects. *Clin Sci.*, 100, 335-342.
- 64) Tank, J, Schroeder, C, Stoffels, M, Diedrich, A, Sharma, AM, Luft, FC, & Jordan, J. (2003). Pressor effect of water drinking in tetraplegic patients may be a spinal reflex. *Hypertension*, 41, 1234-1239.
- 65) Tracey, KJ. (2002). The inflammatory reflex. *Nature*, 420, 853-859.
- 66) Ulrich, RS, Simons, RF, Losito, BD, Fiorito, E, Miles, MA, & Zelson, M. (1991). Stress recovery during exposure to natural and urban environments. *J Environ Psychol.*, 11, 201-230.
- 67) Ulrich, RS, & Parsons, R. (1992). Influences of passive experiences with plants on individual well-being and health, In: Relf, D. (Ed), *Human benefits of plants* (93-105). Portland, OR: Timber Press.
- 68) Lohr, VI, Pearson-Mims, CH, & Goodwin, GK. (1996). Interior plants may improve worker productivity and reduce stress in a windowless environment. *J Environ Horticult.*, 14, 97-100.
- 69) Laumann, K, Gärling, T, & Stormark, KT. (2003). Selective attention and heart rate responses to natural and urban environments. *J Environ Psychol.*, 23, 125-134.
- 70) Johansson, B. (2008). Heart rate and heart rate variability response to the transpiration of vortex-water by Begonia Elatior plants to the air in an office during Visual Display Terminal work. *J Altern Compl Med.*, *14*(8), 993-1003.
- 71) Johansson, B. (2009). Effects of functional water on heart rate, heart rate variability, and salivary immunoglobulin A in healthy humans: A pilot study. *J Alter Compl Med.*, 15(8), 871-877.
- 72) Song, L, Schwartz, G, & Russek, L. (1998). Heart-focused attention and heart-brain synchronization: energetic

- and physiological mechanisms *Altern Therap.*, *4*, 44-62.
- 73) Raab, F, Schaffer, E, Cornélissen, G, & Fallberg, F. (1993). More on the dentist's role in the prevention of high blood pressure. *Chronobiologia*, 20, 245-50.
- 74) Cornélissen, G, Hallberg, F, Otsuka, K, Singh, RB, & Chen, C-H. (2007). Chronobiology predicts actual and proxy outcomes when dipping fails. *Hypertension*, 49, 237.239.
- 75) Goldberger, GL, Amaral, LAN, Hausdorff, JM, Ivanov, PCh, Peng, CK, & Stanley, HE. (2002). Fractal dynamics in physiology: Alterations with disease and aging. *PNAS.*, 99(19), 2466-2472.
- 76) Malliani, A, Pagani, M, Lombardi, F, Furian, R, Gussetti, S, Cerutti, S. (1991). Spectral analysis to assess increased sympathetic tone in arterial hypertension. *Hypertension*, 17(supplement III), 36-42.
- 77) Borovikova, LV, Ivanova, S, Zhang, M, Yang, H, Botchkina, GI, Watkins, LR, Wang, H, Abumrad, N, Eaton, JW, & Tracey, KJ. (2000). Vagus nerve stimulation attenuates the systematic inflammatory response to endotoxin. *Nature*, 405, 458-462.
- 78) Shannon, JR, Diedrich, A, Biaggioni, I, Tank, J, Robertson, RM, Robertson, D, & Jordan, J. (2002). Water drinking as a treatment for orthostatic syndromes. *Am J Med.*, 112, 355-360.
- 79) Tiller, W, McCraty, R, & Atkinson, M. (1996). Cardiac coherence: a new non-invasive measure of autonomic nervous system order. *Altern Therp.*, 2, 52-65.
- 80) Watterson, JG. (1997). The pressure pixel: unit of life. *BioSystems*, 41, 141-152.
- 81) Porges, SW. (1998). Love: An emergent property of the mammalian autonomic nervous system. *Psychoneuroendocrinol.*, 23, 837-861.
- 82) Slight, P, & Casadei, B. (1995). Relationships between heart rate, respiration and blood pressure

- variability. In: Malik, M, & Camm, AJ. (Eds.), *Heart rate variability* (311-327). New York: Futura Publishing Company.
- 83) Wernet, PH, Nordlund, D, Bergmann, U, Cavalleri, M, Odelius, M, Ogasawara, H, Näslund, LA, Hirsch, TK, Ojamäe, L, Glatzel, P, Pettersson, LG, & Nilsson, A. (2004). The structure of the first coordination shell in liquid water. *Science*, 304, 995-998.
- 84) Huang, C, Wikfeldt, KT, Tukoshima, T, Nordlund, D, Harada, Y, Bergmann, U, Niebuhr, M, Weiss, TM, Horikawa, Y, Leetmaa, M, Ljungberg, MP, Takahashi, O, Lenz, A, Ojamäe, L, Lyubartsev, AP, Shin, S, Pettersson, LG, & Nilsson A. (2009). The inhomogeneous structure of water at ambient conditions. *PNAS.*, 106, 15214-15218.
- 85) Arani, R, Bono, I, Del Giudice, E, & Preparata, G. (1995). QED coherence and the thermodynamics of water. *Int J Modern Phys.*, *B9*, 1813-1841.
- 86) Del Giudice, E, De Ninno, A, Fleischmann, M, Mengoli, G, Milani, M, Talpo, G, & Vitiello, G. (2005). Coherent quantum electrodynamics in living matter. *Electromagn Biol Med.*, 24, 199-219.
- 87) McCraty, R, & Shaffer, F. (2015). Heart rate variability: New perspectives on physiological mechanisms, assessments of self-regulatory capacity, and health risk. Global Adv Health Med., 4(1), 46-61.
- 88) Johansson, B, & Lukacs, A. (2017). Fibonacci optical lattice a resonator of quantum coherent electromagnetic oscillations in nonlinear PET? A promotive waveguide of a coherent water state. *Water J (Accepted)*.
- 89) Gevirtz, R. (2000). Resonant frequency training to restore autonomic homeostasis for treatment of psychological disorders. *Biofeedback*, 27, 7-9.
- 90) Axelrod, S. (1995). Components of heart

- rate variability. Basic studies. In: Malik, M & Camm, AJ (Eds.), *Heart rate variability* (3-19). New York: Armonk Futura Publishing Company.
- 91) Cerutti, S, Bianchi, AM, & Mainardi, LT. (1995). Special analysis of heat rate variability signal. In: Malik, M & Camm, AJ (Eds.), *Heart rate variability* (63-74). New York: Armonk Futura Publishing Company.
- 92) Bernadi, L, Valle, F, Coco, M, Calciati, A, & Sleight, P. (1996). Physical activity influences heart rate variability and very-low-frequency components in Holter electrocardiograms. *Cardiovasc Res.*, 32(2), 234-237.
- 93) Voeikov, VL, Vilenskaya, ND, Minh, HaD, Malyshenko, SI, Buravleva, EV, Yablonskaya, OI, & Timofeev, KN. (2012). The stable state of bicarbonate aqueous systems. *Rus J Phys Chem A.*, 86(9), 1407-1415.
- 94) McCraty, R, Deyhle, A, & Childre, D. (2012). The global coherence initiative: Creating a coherent planetary standing wave. *Glob Adv Health Med.*, *1*(1), 64-76.
- 95) Kleimenova, NG, Kozyreva, OV, Breus, TK, & Raoport, SI. (2007). Pc1 geomagnetic pulsations as a potential hazard of the myocardial infarction. *J Atmosphere Solar-Terrest Phys.*, 69(14), 1759-1764.
- 96) Samsonov, SN, Kleimenova, NG, Kozyreva, OV, & Petrova, PG (2014). The effect of space weather on human heart diseases in subauroral latitudes. *Atmospheric Ocean Phys.*, 59(7), 719-7127.
- 97) Jacobs, JA. (1989). *Geomagnetism*. Dyfed, Academic Press.
- 98) Amaral, LAN, Ivanov, PCH, Aoyagi, N, Hidaka, I, Tomono, S, Goldberger, AL, Stanley, EH, & Yamamoto, Y. (2001). Behavioral-independent features of complex heartbeat dynamics. *Phys Rev Lett.*, 86, 6026-6029.

- 99) Buch, AN, Coote, JH, & Townend, JN. (2002). Mortality, cardiac vagal control and physical training-what's the link? *Experiment Physiol.*, 87(4), 423-435.
- 100) Graziano, G. (1998). On the size dependence of hydrophobic hydration. *J Chem Soc.*, 94, 3345-3352.
- 101) Steel, EA, Merz, KM, Selinger, A, & Castleman, AW. (1995). Mass-spectral and computational free-energy studies of alkali-metal ion-containing water clusters. *J Phys Chem.*, 99, 7829-7836.
- 102) Pecanha, T, Paula-Riberiro, M, Campana-Rezende, E, Bartels, R, Marins, JC, & de Lima, JR. (2014). Water intake accelerates parasympathetic reactivation after high-intensity exercise. *Int J Sport Nutr Exerc Metabol.*, 24, 489-496.
- 103) Brown, CM, Barberini, L, Dulloo, AG, & Montani, JP. (2005). Cardiovascular responses to water drinking: does osmolality play role? Am J Physiol Regul Integr Comp Physiol., 289(6), R1687-1692. Doi:00205.2005.
- 104) Berntson, GG, Norman, GI, Hawkley, LC, & Cacioppo, JT. (2008). Cardiac autonomic balance versus cardiac regulatory capacity. *Psychophysiol.*, 45(4), 643-652.
- 105) Prigogine, I, & Nicolis, G. (1977). Selforganisation in non-equilibrium systems, from dissipative structures to order through fluctuations (90-160). New York: Wiley.
- 106) Chown, M. (2009). Our world may be a giant hologram. *New Scientist*, 2691, 24-27.
- 107) Broecker, WS. (1991). The great ocean conveyor. *Oceanography*, *4*, 79-89.
- 108) Hou, C-W, Tsai, Y-S, Jean, W-H, Chen, C-Y, Ivy, JL, Huang, C-Y, & Kuo, C-H. (2013). Deep ocean mineral water accelerates recovery from physical fatigue. *J Internat Soc Sport Nutr.*, 10(7), 1-7.
- 109) Radhakrishnan, G, Yamamoto, M, &

- Maeda, H. (2009). Intake of dissolved organic matter from deep seawater inhibits atherosclerosis progression. *Biochem Biophys Res Commun.*, 387, 25-30.
- 110) Fu, Z-Y, Yang, FL, Hsu, H-W, & Lu, Y-F. (2012). Drinking deep seawater decreases serum total low-density lipoprotein-cholesterol in hypercholesterolemic subjects. *J Med Food.*, 15(6), 535-541.
- 111) Yazici, Z, Kaya, Y, & Baltaci, AK. (2008). The effects of boron administration on plasma leptin and lactate levels in ovarietomiced rats which had acute swimming exercise. *Neuro Endocrinol Lett.*, 29, 173-177.
- 112) Nielsen, FH. (1994). Biochemical and physiologic consequences of boron deprivation in humans. *Environ Health Perspect.*, 102, 59-63.
- 113) Santos, DA, Matias, CN, & Monteiro, CP. (2011). Magnesium intake is associated with strength performance in elite basketball, hand ball and volleyball players. *Magnes Res.*, 24, 215-219.
- 114) Manuel, Y, Keenoy, B, Moorkens, G, & Vertommen J. (2000). Magnesium status and parameters of the oxidant-antioxidant balance in patients with chronic fatigue: effects of supplementation with magnesium. *J Am Coll Nutr.*, 19, 374-382.
- 115) Rock, E, Astier, C, & Lab, C. (1995). Dietary magnesium deficiency in rats enhances free radical production in skeletal muscle. *J Nutr.*, 125, 1205-1210.
- 116) Garcia, LA, DeJong, SC, & Martin, SM. (1998). Magnesium reduces free radicals in an in vivo coronary occlusion-reperfusion model. *J Am Coll Cardiol.*, 32, 536-539.
- 117) Markiewicz-Gorka, I, Zawadzki, M, & Januszewska, L. (2011). Influence of selenium and/or magnesium alleviation on alcohol induced oxidative stress in rats, normalization function of liver and

- changes in serum lipid parameters. *Hum Exp Toxicol.*, 30, 1811-1827.
- 118) Adipudi, V, & Reddy, VK. (1994). Effect of chronic lithium chloride on membrane adensosine triphosphatases in certain postural muscles of rats. *Eur J Pharmacol.*, 259, 7-13.
- 119) Sheldon, JH, & Ramage, H. (1931). A spectrographic analysis of human tissues. *Biochem J.*, 25, 1608-1627.
- 120) Burch, GE, Threefoot, SA, & Ray, CT. (1955). The rate of disappearance of rb86 from the plasma, the biologic decay rates of rb86, and the applicability of

- rb86 as a tracer of potassium in man with and without chronic congestive heart failure. *J Lab Clin Med.*, 45, 371-394.
- 121) Yokoi, K, Kimura, M, & Itokawa Y. (1996). Effect of low dietary rubidium on plasma biochemical parameters and mineral levels in rats. *Biol Trace Elem Res.*, *51*, 199-208.
- 122) Hataguchi, Y, Tai, H, Nakajima, H, & Kimata H. (2005). Drinking deep-sea water restores mineral imbalance in atopic eczema/dermatitis syndrome. *Eur J Clin Nutr.*, 59, 1093-1096.