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Review Article

Wellness Screening for Assessing Benefits of a Rejuvenating Oil

Elena Malmefeldt[1]* and Gundu HR Rao[2]

[1]*Wellness Screening Concept and Health Knowledge AB, Sweden*

[2]*Emeritus Professor, Laboratory Medicine and Pathology, Director, Thrombosis Research, Lillehei Heart Institute, University of Minnesota, Minneapolis, Minnesota, USA*

***Corresponding Author:** Elena Malmefeldt, Wellness Screening Concept and Health Knowledge AB, Sweden.

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Abstract

Metabolic diseases like hypertension, excess weight, obesity, type-2 diabetes, and vascular diseases have increased in prevalence and incidence rapidly, to epidemic proportions worldwide. Studies from several laboratories, have demonstrated altered vascular flow, development of endothelial dysfunction, hardening of the arteries, and subclinical atherosclerosis as the earliest signs of vascular disease. In our efforts to find noninvasive diagnostic tools, to detect metabolic risks we have been testing emerging technologies, including activity trackers like Fitbit, Apple watch, thermal imaging, AGE-Reader (www.diagnoptics.com), as well as several LD-Technology products. We have validated several of their products, for monitoring metabolic risks such as blood pressure, impaired glucose tolerance, lipid abnormalities, insulin resistance, cardiac functions, autonomous risk, sympathetic risk, endothelial dysfunction, and for computing wellness index. In an earlier article we described the use of wellness screening in determining the benefits of structured wellness training on cardiometabolic risks and wellness index. In this study, we have evaluated the effect of transdermal delivery of phytochemical on autonomous nervous system score, vascular function score, and wellness index. Commercially available rejuvenation oil, applied on the skin, showed significant improvement in autonomous nervous score, vascular function score, as well as overall wellness index. We would like to include several other noninvasive technologies for conducting a battery of tests, to improve early diagnosis of metabolic risks, as well as better management of the observed risks, and to follow the progression of these cardiometabolic risks and their regression.

Keywords: Hypertension; Obesity; Type-2 Diabetes; Metabolic Diseases

Introduction

There is a considerable interest and lot of scientific pursuits, to reverse or stop biological aging process. A new study suggests, that scientist may be able to reverse ageing. In this study, volunteers who were given a cocktail of drugs for a year, actually "aged backwards" losing an average of 2.5 years from their biological ages, according to this new study. In this study, participants were given a growth hormone and two diabetes medication. Scientists then monitored the test subject's epigenetic clocks, to understand the effect of how they aged. The study was known as the TRIM (Thymus Regeneration, Immunosuppression, and Insulin Mitigation) trial 2015-2017. The ground-breaking results of this study, was reported by Steve Horvath from the University of Los Angeles to the Nature, which first reported the findings, - "That felt kind of futuristic" [1]. Professor Fahy and associates, have published this futuristic results in the "Aging Cell" (2019) [2]. Determination of epigenetic aging was done my measuring the genomic DNA methylation in previously preserved serum and peripheral blood mononuclear cells (PBMCs) at the Center for Molecular Medicine and Therapeutics, British Columbia. DNA methylation (DNAm) analysis was performed using Illumina Methylation EPICChip. Irrespective of the mechanism that underlies epigenetic age reversal, the four selected epigenetic clocks, including leukocyte telomere length, showed significant regression of epigenetic age.

Life Vantage, a company dedicated to helping people achieve healthy living, launched 'Protandim' the Nrf2 synergizer in Japan. The prevailing view is, that aging is caused by the body's oxidation or oxidative stress. Scientific studies have found, that oxidation is also a precursor to many major diseases. It has been reported, that approximately three billion dollars is being spent to fight oxidation. Protandim has been demonstrated, to decrease oxidation by as much as 60% in humans in just the first 30 days of intake. Lifeline Therapeutics is a publicly held company based in Denver, Colorado. Metabolic disorders by and large, lead to oxidative stress followed

by production of oxygen species (ROS) and injury of cellular and molecular pathways by the action of ROS. The ROS can also damage the β-cells of the pancreas, resulting reduced production of insulin. Furthermore, these mechanisms could affect NF-kB nuclear factor-kB), and protein kinase C (PKC) pathways, and interfere with insulin signaling pathways [3-6]. Inflammation seems to be the major initiator of many processes, that leads to self-healing as well as pathogenesis of major metabolic diseases, including, atherosclerosis, obesity, metabolic syndrome, type-2 diabetes, ischemic heart disease and stroke.

The transcription factor Nrf2 (nuclear factor erythroid-2-reoated factor-2, Nrf-2) for instance, a master regulator of detoxification, anti-oxidant, anti-inflammatory and other cytoprotective mechanisms, is raised by health promoting factors. This transcription factor activates the transcription of over 500 genes (so called survival genes) in the human genome, most of which have cytoprotective functions. The most healthful diets such as Mediterranean and Okinawa are rich in Nrf2 raising nutrients. Recent studies however, have demonstrated that induction of Nrf2 and Ho-1 expression by Protandim (a mixture of five phytochemicals; Aashaadha, Indian Bacopa, Indian Green Tea, China Milk Thistle and China Turmeric), is associated with a reduction in oxidative stress and fibrosis, preservation of the RV microcirculation, and RV function [8]. Studies by Joe M McCord and associates, on the effect of Protandim on various pathways have shown, significant modulation by Protandim not only of pathways involving antioxidant enzymes, but also those related to Colon Cancer, Cardiovascular disease and Alzheimer's disease [7,8]. On the other hand, Beijing University researchers have reported that an herbal product Berberine, can combat both oxidative stress as well as inflammation and thus ameliorate diabetes [6]. Although the researchers speculate that it works on Nrf2 and AMP kinases, they acknowledge the need for additional studies, to explain the molecular mechanisms involved in the beneficial effects of Berberine.

The company Elysium Health, a startup company founded by Leonard Guarente, an MIT biologist, has developed a product that contains a chemical precursor to nicotinamide adenine dinucleotide or NAD, a compound that cells use to carry out metabolic reactions like releasing energy from glucose. He was with Sirtris Pharmaceuticals and had studied and promoted resveratrol as an antiaging compound. "NAD replacement is one of the most exciting things happening in the biology of aging". Says Nir Baraziali, director of the Institute of Aging Research at the Albert Einstein College of Medicine in New York. The product is called "Basis" and Guarente also says, that he takes Basis every day along with 250 mg of resveratrol. Sinclair, who co-directs Glenn Center for the Biology of aging at Harvard Medical School, says that sirtuins, - 'a group of seven genes', are very important in regulating the aging process. They protect chromosomes, stem cells, and protect cells from senescing. Sirtuins can be activated by a lack of amino acids, or sugars (low calorie diet) or through an increase in NAD.

Some researchers in this area, believe that future breakthroughs in tissue rejuvenation, stem cells, regenerative medicine, molecular repair, gene therapy, pharmaceuticals and organ transplant, will eventually enable humans to have indefinite lifespans. Sale of purported anti-aging products such as supplements and hormone replacements are a very lucrative global industry.

Discussion

Our area of interest is cardiometabolic diseases. Metabolic diseases like hypertension, excess weight, obesity, type-2 diabetes, and vascular diseases have increased to epidemic proportions worldwide [9-12]. Metabolic risk that promote metabolic diseases include, oxidative stress, chronic inflammation, endothelial dysfunction, insulin resistance, hyperglycemia, hardening of the arteries, subclinical atherosclerosis. In our continuing efforts to find noninvasive diagnostic tools for monitoring metabolic risks, we are validating several diagnostic tools and platforms. One such platform is the noninvasive diagnostic platform developed by the LD-technologies of Miami Florida, by Dr Albert Maarek and associates (www.ltdeck.com). We are also using such emerging technologies for monitoring and computing cardiometabolic risks (CMR). At the Institute for Preventive Cardiology (IPC Heartcare, Mumbai), under the leadership of Dr. Pratiksha Gandhi, the Director IPC healthcare, we are using TM Oxi system to monitor cardiometabolic risks. The non-invasive platform uses oximeter, blood pressure monitors and a galvanic skin response monitor to obtain the needed data (Figure 1). A typical print out from this system is presented below (Figure 2). The data on parameters like neuronal activities, lipid markers, blood pressure, IGT markers are algorithm derived and results are expressed as Cardiometabolic risk score (CMRs) and Autonomous Nervous Risk Score (ANRs). For additional details about the use of this technology please refer to the following publications [13,14].

Using such simple methods or devices, that are dedicated (Periscope, Genesis Medical Systems Hyderabad, India, CV-profiler System, Hypertension Diagnostics, Minnesota) one can follow, heart rate variability, endothelial dysfunction and other risks for CMDs. If one can develop a method for monitoring reliable biomarkers, then it is easy to demonstrate the beneficial effects or otherwise of molecules, compounds, supplements, and dietary interventions. We as a part of our bilateral collaboration at the IPC Heartcare, Mumbai, India (www.ipcheartcenter.com), are evaluating, green tea of mulberry leaves as well as green tea from regular tea leaves as supplements to manage postprandial hyperglycemia. A major

Figure 1: Noninvasive Diagnostic Platform for Monitoring Cardiometabolic (CMD) Risks.

Figure 2: Biomarkers for CMDs computed, and calculated as cumulative risk scores.

green tea polyphenol, epigallocatechin-3-gallate, inhibits obesity, metabolic syndrome and fatty liver in high-fat-fed mice model. In addition to the tea mentioned above, we also are evaluating D-ribose, L-arginine, Curcumin, Carnitine, Resveratrol, Anthocyanin-rich blue-berry extract, citrus-derived flavonoid Narangenin, grape seed extract Procyanidon, green tea extract Tegreen, mulberry leaf extract 1-deoxynojirimcin (DNJ), water soluble extract of cinnamon and coffee (Green Coffee), and hibiscus tea. Based on the results of our studies, we plan to screen a variety of phytochemicals, known to lower glycemic load as well as develop a "poly-pill" with indigenous Phyto-chemicals, for the management of postprandial hyperglycemia.

Currently, we are collaborating with a Swedish Wellness Screening company and validating the LD-technology wellness screening platform, - TM-Flow, which monitors autonomic, vascular and cardio-metabolic risk assessments. In our earlier reports we have described the use of this technology to monitor individuals at risk for diabetes's as well as to follow the progress and regression of the clinical complications (Figure 3. Uzomba O, Rao GHR, 2018).

Figure 3: TM-Flow System (LD-Technologies, Miami, Florida. Courtesy: Albert Maarek).

The FOCI -rejuvenation oil (Number 10) is manufactured in Sweden by Intelligent Skin Treatment AB (Company Registratin#556951-6916).

The herbal plants used for the preparation of this oil is listed below:

Helianthus annuus *(Sunflower oil), *Olea Europaea* (Olive) Fruit Oil (olive oil), *Bressica napus Seed* oil (Rapeseed oil), *Sesamum indicum** (Sesame seed oil), *Prunus amygdalus dulcis* (Sweet almond) oil, Argania spinosa kernel oil (Arganolja), *Mauritia Flexuosa* (Buriti oil), *Zingiber officinale* (Ginger Root Oil), Citric acid, *Origanum vulgare* (Organo), *Sambucus Nigra* (Elderberry), *Rosa Canina* (Rose hip) seed oil (Rose hip oil), *Abies Sibirica* oil (Fir needle oil), *Salvia Officinalis* Oil (Sage oil), *Sorbus Aucuparia* (Rowan berry), Potassium sorbate, Calcium carbonate (Calcium), *Picea abies* (leaf oil), *Simmondsia chinensis* (Jojoba seed oil), *Corylus avellana* (Hazel nut oil), *Cocos nucifera* (Coconut oil), *Triticum vulgare* (Wheat germ oil), *Macadamia ternifolia* (seed oil), *Persea gratissima* (Avocado oil), *Rosa mosqueta** (Musk rose seed oil), *Ocimum basilicum* (Basil oil), *Lavandula hybrida** oil, *Foeniculum vulgare* (Fennel oil), *Origanum majorana* (Leaf oil), *Pelargonium graveolens* (Flower oil), *Citrus aurantium dulcis* (Orange peel oil), *Citrus nobilis* (Mandarine orange peel oil), *Lavandula angustifolia** (Lavender oil), *Santalum album* (Sandalwood oil), *Citronellol, Artemisia dracunculus* (Tarragon leaf extract), *Rosa gallica* flower oil – (Rose Oil), *Dipterocarpus turbinatus* (Gurjum balsam oil), Magnesium chloride, Zink oxide, *Hippophae rhamnoides* (Sea buckthorn), *Euterpe Oleracea* Fruit Oil (Acai Berry), Resveratrol, *Murciaria Dubia* fruit extras (Cama camu berry), *Eucalyptos globulus* leaf oil (Eucalyptos oil), Sea Salt, *Mondsia chinensis* seed oil (Jo jo ba oil), copper Gluconate, Ascorbic acid, *Prunus Armeniaca* (Apricot) Kernel oil, Inonotus Obliquus Extract (Chaga), and Gold. All the ingredients are in micro doses, meaning

less than 1%. The ingredients are based on 99% organic substances and 1% natural.

In an earlier study, we demonstrated the beneficial effects of a structured lifestyle training on the wellness score (Figure 4). Both autonomic nervous systems score as well as vascular function scored improved post lifestyle education, and overall wellness score also was significantly improved.

Figure 4: Main Biomarkers Monitored using TM-Flow system.

The individuals that underwent the oil- treatment, were well hydrated and the oil was applied to pulse points, neck and temple. Biomarker tests were done, before the oil treatment and two hours post treatment. Shown in the figure 5 are the results of our screening test before the oil treatment. Overall vascular score was 15%, autonomic nervous system score was 23%, life score 32% and composite wellness index was 70%. Post rejuvenation scores for the same individual was Vascular score 20%, autonomic nervous system score was 29%, lifestyle score was 34% and wellness index was 83%. Several earlier studies have shown, that herbal extracts contain active molecules capable of modulating neuro as well as vascular systems. However, what surprised us in this study was, the rapidity by which such improvements were observed. In our earlier studies using LD-technology systems, we found the effect of l-arginine oral supplements or the mulberry green tea after several days of consumption. This is the first time in our experience, we could see the transdermal effect of biomolecules at such a short span of time.

Figure 5: Pre-rejuvenation oil treatment assessment of metabolic risk and wellness score.

Metabolic risks are assessed under three categories, lifestyle, autonomic nervous system, and vascular function. Under Lifestyle, cardio fitness, diet and emotional parameters are tested.

Under autonomic nervous system, sympathetic response, parasympathetic response and galvanic skin response. Whereas vascular function tests include, blood pressure measurement, and endothelial function tests.

Figure 6: Post rejuvenation oil treatment improvements in wellness score.

Data for post rejuvenation tests are presented in Figure 6. The vascular function score as well as autonomic nervous function scores have dramatically improved. So is the overall wellness index, which has changed from a pretest score of 70 to post treatment score of 83%. Herbal extracts of medicinal plants are known to contain neuroprotective as well as vasoactive molecules. Results of such studies will be discussed later on in the general discussion section.

Figure 7: Post-rejuvenation oil treatment improvements in various metabolic risks (n = 5).

Figure 7 shows the average values for various cardiometabolic biomarkers before and after-oil treatment. Average values for five subjects are presented. Autonomic score (>30), cardiovascular score (>30), endothelial function score (>30)oxidative stress score (>30) and coagulation score (>50). Overall wellness index showed 20% improvement post oil treatment.

Panax ginseng (*Araliaceae*), also called Asian, or Korean ginseng, has long been traditionally used in Korea and China, to treat several diseases. Ginsenosides (over thirty of them), are the main active compounds of ginseng. They have displayed a variety of bioactive effects, including anti-oxidation, anti-proliferation, anti-inflammatory, antidiabetic, and vasodilation. The saponins are associated, with many effects on cardiovascular system, including inhibition of platelet aggregation, and the increase of coronary blood flow [15]. It has been shown, that isoquinoline alkaloids, also have the ability to induce vasorelaxation in an endothelium-independent manner, by blocking Ca^{2+} entry into vascular smooth muscle cells. Among non-alkaloid compounds, polyphenols especially flavonoids, seem to be associated with endothelium-dependent relaxation. On the other hand, relaxation induced by sesquiterpenes and phthalide derivatives are endothelium-dependent. Whereas, lignin gomisin A, seems to produce both endothelium-dependent and-independent vasodilation. Several studies have demonstrated, the effect of phytochemicals on vasorelaxation [16-21]. Furthermore, researchers from Iran, have shown that intake of phytochemicals in diet, is associated with decreased risk of mortality from coronary artery disease [22]. Our own studies at the IPCHeartcare, Mumbai, using LD-Technology diagnostic platform, showed that taking l-arginine capsules orally for two weeks, showed improvements in endothelial function and improvements in vascular risk score.

Phytochemicals like curcumin, resveratrol, terpenoids, epigallocatehtin-3 gallate, isothiocyanins, share common properties and play an important role in activating phase 11 detoxifying and antioxidant enzymes like HO-1, GSG-Px, and glutathione -S-transferase and targeting the common transcription factor Nrf2 [23]. As we have mentioned early in our introduction, metabolic risks include, oxidative stress, inflammation, adipose-derived cellular signaling mechanisms, insulin resistance, hyperglycemia, endothelial dysfunction, subclinical atherosclerosis and vascular dysfunction. In a recent article, we have described simple noninvasive techniques, for monitoring vascular dysfunction using thermal imaging [24,25]. We have described in this article, as in our earlier articles, that LD-technology diagnostic platform, monitors dozens of cardiometabolic risks, related to cardiac fitness, autonomic nervous system, and vascular function [26-31]. Development of such noninvasive diagnostic tools, will facilitate screening of indigenous herbal preparations, as well as dietary supplements, that can reduce or reverse these known metabolic risks [26].

Conclusion

In our earlier studies, we have validated the usefulness of LD-Technology's TM-Oxi systems, and TM-Flow Systems. We also have validated Wellness Screening platform, for monitoring the effect of structured lifestyle on wellness score, which is a combined score of lifestyle score, cardiometabolic function score, autonomic nervous system function score and vascular function score. In this study, we have evaluated the effect of a commercial rejuvenation oil, manufactured in Sweden. Of the 14 risks measured, 10 of them showed significant improvement, after the oil treatment. There was considerable improvement in oxidative stress, vascular function, and coagulation profiles. Since the oil contains, the extracts from over fifty herbal medicinal plants, it probably has just about every known molecule (ginenosides, alkaloid and non-alkaloid compounds, curcumin, gastrodin, resveratrol, actoside, echinoside, baicalein, paeoniflorin, tenuigenuin, purarin, protoctechuic acid etc.,) that has been shown to work on detoxifying mechanisms, antioxidant systems, and vasorelaxing and neuroprotective mechanisms. Transdermal drug delivery is a safe and simple method for delivering bioactive molecules. The molecules initially penetrate through stratum corneum without drug accumulation, and then pass to deeper epidermis. When it reaches the dermal layer, it becomes available for systemic absorption via the dermal microcirculation. This route of drug delivery, seems to provide the quickest delivery of active molecules to the sight of action. We would like to continue validating Wellness Screening Platform and develop indigenous complementary therapies for cardiometabolic risks. We would like to include other noninvasive diagnostic tools, like thermal imaging as well as AGE- Readers to the armament, -to better tune, risk assessment, risk management, risk prediction, disease progression and regression.

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