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The Role of Nutraceutical Food Supplements for a Quality Adjusted Long Life (QALY)

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Abstract

To live long, healthy and happy you must remain physically and intellectually active, avoid stress and anxiety, limit ultra-processed food, have a regular medical check to detect and treat any disease in a curable stage, and take a nutraceutical food supplement. The composition of the example nutraceutical QALY®, consisting of several minerals, plant extracts and vitamins, reduces the cardiovascular mortality by 40%, and decreases the risk of colorectal cancer by 30%. Together with healthy life style, the intake of the nutraceutical may prevent half of the cases of neurodegenerative diseases and dementia.

Keywords: Healthy Ageing; Nutraceutical; Antioxidant; Inflammageing; Food Supplement; QALY; Biological Age

Introduction

In addition to adopting a healthy lifestyle, ageing men can promote their good physical and mental condition by using particular food supplements. The maximum lifespan seems to be genetically determined for each individual person, whereas the quality of life (QALY) of elderly people is probably largely influenced by external factors, amongst others through epigenetic mechanisms.

The prevention and correction of obesity, regular engagement in moderate physical activities, and the early identification and treatment of e.g. hypertension, metabolic syndrome and diabetes, as well as certain forms of cancer or neurodegenerative diseases, are of pivotal importance.

Suppletion in case of hormone deficiencies may be indicated.

In addition, certain nutritional supplements may be used to counter "wear and tear" phenomena by reversing the cellular damage resulting from inflammation (inflammageing), external toxins, and oxidative overload.

To do this, "Nutraceuticals" are used which consist of vitamins, minerals and selected plant extracts. They are taken in quantities that do not exceed the recommended daily dosage, to avoid toxicity. The simultaneous implementation of judiciously selected agents results in synergistic effects.

Life style and regular intake of particular nutraceuticals have been proven to prevent, or delay, the occurrence of metabolic diseases, 30% of colorectal cancers, half of cases of dementia, and 40% of cardio- and cerebrovascular mortality.

Since a large proportion of the population lives in an environment that is highly polluted by agents that accelerate the ageing processes, and since ultra-processed food is becoming an important part of modern nutritional habits, it may be useful to start nutraceutical intake rather early in life (between 40 and 50 years of age).

Mechanisms of Ageing

There are several phenomena that are held responsible for the signs and symptoms of ageing, such as changed neuroendocrine status, impaired immunological processes and "wear and tear", a kind of wearing out of critical cell functions as a result of continuous low-grade inflammation (inflammageing) causing oxidative damage, among other things. The latter is related to the continuous production of free oxygen radicals, which are derivatives of oxygen that can harm the cell membrane, the mitochondria, and the genetic material (DNA).

Reactive oxygen radicals change the composition of the phospholipids of the cell membrane, which becomes less fluid. The enzyme functions, electrolyte pumps and the receptor activities, which are linked to the cell membrane, are impaired. The metabolism leading to the production of adenosine triphosphate (ATP) in the mitochondria becomes less efficient, whereby the energy available for cell survival, activity, and replication is diminished.

Inflammation and redox imbalance are also involved in the impairment of the immune system seen in the elderly [1]. Oxidative damage to DNA causes genetic changes that can be mutagenic and, in some circumstances, promote the occurrence of cancer [2-4].

At the one hand, the average life expectancy of the elderly has increased over the last few decades, at the other hand, all sorts of "diseases of old age" are occurring ever more often – even at relatively young ages – as a result of changed lifestyle, nutrition and of environmental factors. Typical examples are the diseases related to obesity and sedentary lifestyle, such as diabetes, atherosclerosis, and all sorts of cancer and neurodegenerative diseases.

The phenomenal increase of the frequency of cancer and dementia is attributed to continual exposure to ever-larger amounts of numerous chemical agents ("forever chemicals") in the environment and in food.

In addition, the excess consumption of ultra-processed food, which often contains several additives, is found to be harmful.

Food as Medicine

Hippocrates of KOS (460-377 BC) declared: "food should be our medicine, because our medicine is in our food". Foodstuff should not be processed in excess of two manipulations in addition to what is done in normal kitchen cooking, otherwise it is considered "ultra-processed". Nowadays over half of the population uses ultra-processed food as their main source of nutrition. Furthermore, food sold in shops usually has a rel-

atively long capacity of conservation thanks to the addition of several additives, the connection of which to the development of certain pathological processed in the elderly has been proven. Diet remains a key factor in healthy ageing.

The PURE "healthy diet score" [5] has been based on the long-term follow-up study of a very large group of individuals from the general population, 35–70 years of age, in 21 low-, middle-, and high-income countries on 5 continents. The consistency of the associations of the score with health events and mortality was examined in independent prospective studies in 70 countries. The healthy diet score was developed based on six foods, each of which has been associated with a significantly lower risk of mortality: fruit, vegetables, nuts, legumes, fish, and dairy (mainly whole-fat). In contrast the negative effect of ultra-processed food on health and disease-free ageing were proven to relate to their unfavourable pro-inflammatory characteristics.

Adaptation of lifestyle, the encouragement of physical movement [6] appropriate nutrition, and the early detection and treatment of "diseases of old age" benefit the quality of life, and extend an individual's life expectancy. Unfortunately, it will be several decades before exposure to harmful environmental factors is substantially reduced. In the meantime, we must strive to limit or counter their deleterious influence, and reduce oxidative and inflammatory cellular damage.

Hormone Replacement Therapy

Late onset hypogonadism (LOH), meaning the excessive age-related decrease of testosterone production in men, causes a syndrome that is defined by a rather complex and non-specific cluster of signs and symptoms. Aside from lack of energy, decreased libido and erectile dysfunction, testosterone concentration, more particularly the total testosterone output, is sub-optimal. Ultimately the diagnose should be confirmed by the disappearance or mitigation of complaints thanks to testosterone substitution therapy.

There is ample evidence that correct testosterone substitution reduces the risk of metabolic syndrome and maintains or increases lean body mass, whilst neither increasing the risk of cardiovascular disease, nor that of prostate cancer. There is also association between hypoandrogenism and shorter life expectancy. The link is confirmed by the observation that testosterone substitution therapy seems to prolong longevity [7].

In women after the menopause, estrogen replacement therapy prevents osteoporosis, maintains skin elasticity, and reduces the risk of Alzheimer disease among genetically predisposed persons. Whereas longevity is only slightly increased, quality of life is substantially improved by low-dose estradiol given transcutaneous. Oral intake of phytoestrogens (such as Naringenin) is allowed in patients treated for breast cancer.

Inflammageing

The role of chronic, continuous low-grade inflammation in the process of ageing is pivotal, and is called inflammageing [8]. This is particularly evident in the case of obesity. Visceral fat tissue is infiltrated by lymphocytes and macrophages that induce inflammation, while adipocytes generate pro-inflammatory cytokines. In addition, increased reactive oxygens (ROS) do suppress mitochondrial activity, affect membrane permeability and function, and alter the production of Adenosine Triphosphate (ATP). As a result, multiple organ dysfunction accelerates biological ageing and increases the risk of disease.

This pathogenic chain of events can be halted by the combination of measures to reduce overweight, such as by "restricted time eating", combined with the regular intake of an appropriate nutraceutical, and appropriate medication or bariatric surgery if indicated.

Components of Nutraceuticals

By way of example, the constituents of a patented anti-ageing nutraceutical, that is available on the market as OTC (over-the-counter) product (QALY®, Jonapharma, Elversele, Belgium) are detailed below (Table1).

Plant Extracts

Pine bark extract

The natural extract of the Mediterranean pine tree is rich in anthocyanidins that exert a strong anti-inflammatory as well as anti-oxidant activity. It also reduces auto-immune reactivity. The prototype Pynogenol® (Horphag, Switserland) is one of the main components of the nutraceutical, and its therapeutic and protective potential has been scientifically documented [9].

It is combined with other anti-oxidants, such as the oxide-re-

ductase Ubiquinol Q 10 and Astaxanthin which is given as the biomass of *Haematococcus pluvialis*.

Table 1: Formulation of the nutraceutical QALY capsules

Ingredient	Amount
Astaxanthin (biomass of *Haematococcus pluvialis*)	2 mg
Oxidoreductase Ubiquinone Q10	25 mg
Pine Bark Extract (*Pinus maritima*)	21 mg
Rose Root Extract (*Rhodiola rosea*)	175 mg
Vitamin B9 (Folic Acid)	0.2 mg
Vitamin B12 (Methylcobalamin)	1.25 µg
Selenomethionine	14 mg
Zinc Bisglycinate	3 mg (Zn content)

Rhodiola rosea extract

The extract of *Rhodiola rosea* is called an "adaptogen". It belongs to the same group as MACA, the extract from *Lepidium Meyenii*. These substances interact with the biological stress response by mitigating the hypothalamo-pituitary-adrenal (HPA) reaction, and by augmenting the concentration of Heat Shock Protein (HSP) that reduces the effects of stress on 3-dimentional protein folding. This strong phytotherapeutical adaptogen reduces the deleterious effects of all levels of stress on both mental and the physical health.

Minerals

Zinc (bisglycinate)

Zinc, together with vitamin B6, plays an important role in the conversion of the essential omega-3 short-chain fatty acids, such as alpha linolenic acid, into long-chain polyunsaturated fatty acids (PUFA), in particular eicosapentaenoic acid (EPA) and docosahexaenoic acid or cervonic acid (DHA). The anti-inflammatory properties of PUFA have been demonstrated in patients with rheumatoid arthritis and similar conditions. Zinc and vitamin B6 are necessary for the elongase and desaturase processes that are active in this conversion.

Zinc is given as bisglycinate, which has high biological availability, is also recommended for DNA stability and protection against mutations. This essential mineral is necessary in many enzymatic processes.

Selenium (Methionine)

Selenium has a strong antioxidant effect that protects against oxidative DNA damage. It is a cofactor of glutathione peroxidase, that is the most potent detoxifying agent. It's antioxidant effect, in combination with the oxidoreductase ubiquinol Q10, reduces cardiovascular mortality by 40% [10], as shown in a prospective randomized, double-blind placebo--controlled trial with 14 years follow-up in elderly Swedish community members.

Selenium deficiency is also linked to poor mental health.

Cereals are the most important food source of selenium. The nutritional intake of this mineral commonly is insufficient since the selenium content of cereals from eastern European countries is low.

Selenomethionine boosts the immune response and it decreases inflammation in response viral infections.

Antioxidants and Vitamins

Oxidative overload can result from tobacco use, from intercurrent inflammatory or infectious conditions, from exposure to toxic environmental factors (including pesticides) and heavy metals, and from hypertension or diabetes. Reactive oxygen species are produced during the Cori- and the Krebs cycles of the anaerobic and the aerobic metabolism of glucose and of fatty acids.

Oxidative overload causes an accelerated conversion of LDL--

cholesterol to oxidized LDL-cholesterol, which is phagocytosed by macrophages in the vascular wall. These macrophages become foam cells, activating inflammation of the vascular endothelium, and promoting the development of atherosclerosis.

Antioxidant treatment may also reduce the risk of neurodegeneration in Alzheimer disease [11].

Oxidative stress induces the conversion of the DNA-nucleotide Guanine into its oxidized teratogenic form 8-hydroxy-2 deoxy guanosine.

Astaxanthin

Astaxanthin is a carotenoid that does not display the toxic and teratogenic side effects of high-dose Vitamin A. It is strong antioxidant which is abundantly present in the biomass of the microscopic *Haematococcus pluvialis*.

Astaxanthin has multiple beneficial effects by stabilizing the fatty acid composition of cell membrane, and protecting the structure of DNA. It prevents oxidation of the lipid composition of the cell membrane. It doubles the time needed for LDL cholesterol to be oxidized to hydroxycholesterol in the vascular wall, hence efficiently protecting the cardiovascular system against atheromatosis [12].

Astaxanthin is preferred over Vit E because the synthetic form of the latter, the d-alfa-tocopherol, which is less efficient than natural Vit E and is given in a much higher dose, may damage the joint junctions between cells, and thus facilitate the migration of e.g. malignant cells.

Ubiquinol Oxidoreductase Q10

The oxidoreductase ubiquinone Q10 plays an important role in mitochondrial function and in the production of adenosine triphosphate (ATP). Q10 promotes muscle function and is necessary for the proper operation of the heart. A deficiency uptake of Q10, or inhibition of its enzymatic functioning can cause heart failure. Statins, given for the reduction of cholesterol in the blood, do inhibit the biosynthesis of Q10 [13].

The supplementary administration of Q10 can compensate for the deficient muscle contractility, and thus combats the occurrence of heart failure among some patients, as well as during statin intake.

Q10 being a specific antioxidant of the mitochondria improves performance, but it also prevents oxidative DNA damage, by which it may reduce the risk of particular types of cancer.

Vitamins B6 (Pyridoxine) B9 (folic acid) and B12 (methylcobalamine)

Vitamin B6 is of particular importance to men since, together with Zinc, it elongates and desaturates short chain unsaturated omega 3, as well as saturated- and omega 6 fatty acids into long chain omega 3 polyunsaturated fatty acids (PUFA). Elevated concentrations of the former were shown to be significantly related to higher prostate cancer grading, and more rapid disease progression.

The Nurses' Health Study, which observationally followed 121 700 medical personnel from 1976 until today, has revealed that supplementary intake of Vit B9 reduces the risk of colorectal cancer by over 30% (RR:0.69) [14].

The combination of vitamins B9 with B12 lowers the concentration of homocysteine in the blood. A high homocysteine level is an independent risk factor not only for atherosclerosis and cardiovascular disease [15], but also for osteoporotic bone fractures. The prevalence of bone fractures is 4 times higher in persons in the highest homocysteine quartile than in those in the lowest quartile, because this amino acid disturbs the protein stability of bone structure.

Vitamin B intake has proven to prevent brain shrinkage in persons with elevated homocysteine concentration. Lowering of homocysteine concentration by vitamin B was also found to protect the coronary arteries against atherosclerosis [16].

Patients taking Metformin for the treatment of type II diabetes are at high risk of homocysteine excess, since this drug inhibits Vitamin B12 absorption from food. Elderly persons living in retirement homes commonly experience Vitamins B9 and B12 deficiency, because of the lack of fresh food ingredients and vegetables.

Krill oil

Krill oil is produced from a small maritime crustacea called *Euphasia superba*, which constitutes the zooplankton. It contains

a high amount of the phosphate esters of the poly unsaturated fatty acids (PUFA) ei-cosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The absorption after oral administration of these PU-FA-esters is optimal.

The beneficial effect of moderate dose of supplementary PUFA has been documented for the prevention of atherosclerosis in cardiovascular disease, and the preservation of cognitive accuracy in ageing. Their effectiveness is mainly by improving the fluidity of the cell membrane, especially in the presence of the antioxidant astaxanthin.

Additional Substances

The substances enumerated below are not included in the "basic formulation" of QALY®. They are examples of non-pharmaceutical products that may be given to prevent functional deficiencies among the elderly and to promote their health and wellbeing.

Sodium Dichloroacetate

Sodium dichloroacetate occurs naturally in the red algae of the *Asparagospis genus*, and is available in pure form by synthesis (DCA-lab, Vilnius, Lithuania). It activates the pyruvate dehydrogenase in the cell mitochondria, by blocking the inhibiting effect of pyruvate dehydrogenase kinase. Low dose treatment of no more than 12.5 mg/kg bodyweight is not toxic, and it enhances cellular metabolism and energy production. It is indicated in case of (chronic) fatigue and general weakness of the elderly.

Hericium erinaceus

Hericium is extracted from the *Lion 's mane* mushroom. It is used since several centuries in Yajurveda's medicine to treat and prevent degenerative diseases of the brain. Its mode of action has largely been unravel, and its clinical effectiveness in cases of early dementia has been documented [17].

Momordica charantia (bitter melon)

Momordica extract works exactly through the same biological mechanisms as the pharmaceutical Metformin, but its long-term use does not cause renal damage. It lowers glycemia and hemoglobin A1c by improving the insulin receptor sensitivity.

The increasing concentration of HgA1c with age is associated with tissue ageing because of its oxidation into AGE's (Advanced Glycated End Products), that are highly toxic. Therefore, the continuous intake of *Momordica charantia* extract is indicated in both patients with type II diabetes, and in every person with metabolic syndrome or obesity.

Carnitine

L-Carnitine has an essential role in the transportation of fatty acids into the mitochondria, where these are aerobically metabolized in the Krebs cycle, generating the energy carrier Adenosine Triphosphate (ATP). It is of pivotal importance in all muscles, the heart in particular. In food L-carnitine mainly originates from meat. The production in the human body takes place in the liver and kidneys. Since the function of these organs may decay during ageing, and the uptake from nutrition may decrease, the supplementary substitution with L--carnitine may be recommended to sustain muscular and cardiac function in the elderly.

L-Carnitine can also be added to the formulation as it reduces the risk of frailty.

Discussion

A "healthy lifestyle" with sufficient physical movement, a balanced diet, a controlled caloric intake to combat obesity, and the early detection and treatment of "diseases of the elderly" are the cornerstones of a strategy that can improve the well-being and the quality of life (QALY) of ageing people. Living in a strongly polluted environment, humans are continuously exposed to numerous agents, many of which are carcinogenic and/or disturb the hormone balance, and which may deregulate the proper function of cells and organs. This takes its toll on health at an advanced age. There is strong epidemiologic evidence that the use of certain nutritional supplements can counteract the deleterious influence of chronic exposure to environmental toxins and of modern lifestyle (nurses' health study) [18].

It is, however, important the intake of e.g. multivitamins should not exceed the recommended daily dose. This reinforces the statement by Paracelsus (1493-1541): "All things are poisons, for there is nothing without poisonous qualities. It is only the dose which makes a thing poison". Except for rare cases of gastrointestinal intolerance, the food supplement

described is free of side effects. Some interactions with the enzymatic metabolism of particular medications may need adaptation of the dose of these in exceptional cases.

Conclusion

The combination of judiciously selected ingredients in the particular nutraceutical described here (QALY®), enhances the potential of each individual constituent by synergism. Irrefutable scientific research has revealed that complementing the diet with a balanced supplement delays, and can reverse biological ageing. It can help to prevent certain diseases such as metabolic syndrome and diabetes, cardiovascular atherosclerosis, dementia, or colorectal cancer.

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