Nutriceutical Approach to the Metabolic Syndrome

Frank Comhaire

Department of Endocrinology and Metabolic Diseases, Ghent University, Belgium

Corresponding author: Frank Comhaire, Emeritus Professor at Ghent University, University Hospital, Department of Endocrinology and Metabolic Diseases, De Pintelaan, 185, Belgium, Tel: 0032475618555; E-mail: frank@comhaire.com

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Abstract

The metabolic syndrome leads to serious health damage through several pathogenic mechanisms, including insulin resistance, chronic inflammation and oxidative overload. Aside from adaptation of diet and life style, medication is prescribed to the majority of patients. Some patients need bariatric surgery. Complementary and alternative medicine (CAM) offers an opportunity for treatment by using nutriceutical food supplementation. The nutriceutical combination which is proposed here is constituted of Momordica charantia (bitter melon or bitter gourd) extract, together with the antioxidants Astaxanthin and coenzyme Ubiquinone Q10, the anti-inflammatory pantothenic acid in pine bark extract, vitamins B6, B9 and B12, the phyto-adaptogen Lepidium meyenii (Macca), and the amino acid L-acetyl carnitine. The rationale for this combination and its expected therapeutic benefits are highlighted.

Introduction

The metabolic syndrome is probably one of the most important health threatening pathologies in modern society and constitutes a major cardiovascular risk factor. Treatment options include changes of life style and nutrition, as well as medication and bariatric surgery. These mainly aim at reducing insulin resistance, and medication needs to be taken over a very long period of time, with potential toxic side effects.

Nutriceutical food supplements (NFS) which contain herbal extracts, minerals and vitamins in quantities not exceeding the recommended daily intake (RDI) [1], are free of adverse effects [2], and their role and importance have recently been acknowledged by the World Health Organization [3]. The combination of substances with complementary effects is expected to act in synergisms. The NFS generally aims at complementing dietary deficiencies, particularly in elderly persons [4] and patients taking medication [5]. In the metabolic syndrome, a specific NFS focuses on reducing the impact of inflammation and oxidative overload, and on correcting the impaired metabolism.

The present paper describes the rationale for the composition of a specific NFS, and its biological effects in patients with metabolic syndrome/pre-diabetes.

Keywords: Metabolic syndrome; Complementary medicine; CAM; Nutriceutical; Momordica charantia; Prediabetes

Materials and Methods

The composition of the nutriceutical food supplement

The NRF consists of the following products:

Capsules with 350 mg of Momordica charantia (bitter melon or bitter gourd) dry extract 1:4, of which 3 per day.

Pills (called “Improve”, Nutriphyt Ltd. Oostkamp, Belgium) containing: Lepidium meyenii extract (MACA): 250 mg, Pine Bark extract (Pycnogenol®, Horphag, Switzerland) 100 mg, L-acetylcarnitine: 100 mg, Co-enzyme ubiquinone Q10: 25 mg, Astaxanthin (Fuji Health Science, Inc. & AstaReal, Inc., Burlington, NJ, USA): 4 mg, Zincpicolinate: 7.5 mg, Vit B6 (pyridoxine): 3 mg, Vit B9 (folic acid) 0.2 mg, and Vit B12 (cyanocobalamine): 15 µg.

Patients should take 2 pills per day together with twice per day 1 g of fish oil, rich in eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA).

Biological effects of the NFS

Momordica charantia

The extract of the bitter melon has extensively been tested in the treatment of diabetes in rats [6]. It increases sensitivity of the insulin receptor [7], and favourably influences the metabolic syndrome [8] and diabetes [9] in humans.

In the metabolic syndrome, the inhibitory effect of Momordica extract on the 11β-hydroxysteroid dehydrogenase type 1 is particularly relevant [10]. This enzyme favours the hydroxylation of cortisone, that has a primarily mineralocorticoid effect, to cortisol (hydrocortisone) that increases blood sugar by gluconeogenesis (Figure 1). There is evidence for increased activity of this enzyme in adipose cells [11], and that this may be an important aetiological factor in the pathogenesis of obesity-associated diabetes. Inhibitors of 11β-hydroxysteroid dehydrogenase increase energy expenditure and reduce atherosclerosis.

The bitter melon extract increases phosphorylation of acetyl-CoA carboxylase and c-AMP-activated protein kinase (PKA) [12] reducing lipogenesis and increasing thermogenesis and lipolysis [13]. The extract down-regulates the expression of peroxisome proliferator-activated receptor (PPAR)-gamma, nuclear factor kappaB (NF-kB), and interferon-gamma in heart tissue of obese rats, with cardio-protective effect and reduction of inflammation [14].

In addition, the extract has been shown to exert chemo-protective effect against prostate cancer cells [15], human embryonic kidney cells...
and colon cancer cells in vitro [16], and to inhibit Epstein-Barr virus-induced tumour promotion [17].

**Figure 1:** Hydroxylation of Cortisone into Cortisol, and the role of the enzyme 11β-hydroxysteroid dehydrogenase type 1.

**Astaxanthin**

Astaxanthin is contained in the dried biomass of the microscopic algae *Haematococcus pluvialis*. It is a polar carotenoid with potent antioxidant activity. In contrast to Vitamin A (retinol), that inserts longitudinally between the phospholipid layers of the cell membrane, Astaxanthin builds in perpendicularly through the membrane. This explains why Astaxanthin is non-toxic, in contrast to Vit A that has been shown to be toxic and may be teratogenic in higher dose [18-20]. Astaxanthin exerts an antioxidant effect that is many times stronger than that of Vitamin E [21], and it has a documented anti-inflammatory activity [22]. It reduces phospholipid hydroxides, and decreases stress-induced modifications that impair lipid utilization in the mitochondria [23].

**Oxido-reductase ubiquinone Q10**

Reactive oxygen species (ROS) are generated during the process of energy production during the Krebs cycle in the mitochondria. These ROS must be scavenged since they inhibit the enzymatic reactions of the Krebs cycle, reducing the production of ATP. The anti-oxidant Ubiquinone Q10 improves mitochondrial function [24] and energy production [25], and diminishes lipid peroxidation [26].

**Zinc**

Zinc (zincbi glycinate) is part of many enzymes playing a pivotal role in cell functions. In association with vitamin B6 [27] zinc promotes the conversion of short-chain omega-3 poly-unsaturated fatty acids (such as alfa-linolenic acid) into their long-chain derivatives by acting as co-factors of the elongase and desaturase enzymes [28]. The long-chain polyunsaturated omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) serve as substrates for the energy producing metabolism of the mitochondria.

**L-Acetylcarnitine**

L-Acetylcarnitine is an amino acid that plays a pivotal role in the transportation of the long-chain omega-3 polyunsaturated fatty acids (DHA or Cervonic acid, and EPA) from the cell cytoplasm into the mitochondria, where these are metabolised in the Krebs cycle. L-acetylcarnitine increases the production of energy as ATP [29].

**Vitamins B6, B9 and B12**

The association of vitamins B6 (pyridoxine), B9 (folic acid), and B12 (cyanocobalamine) enhances the metabolism of homocysteine [30], decreasing its concentration and availability in body fluids. Homocysteine concentration is increased in patients with the metabolic syndrome [31], and it is an independent risk factor for vascular disease.

**Lepidium meyenii**

Lepidium meyenii (MACA) belongs to the cruciferous (Brassica) family, and grows in the Peruvian Andes mountains. It is considered a phyto-adaptogen which increases the production of the Heat Shock Protein P 72, thus reduces the negative impact of stress [32,33] on protein conformation and cell death [34].

**Pine bark extract**

The extract of the bark of the (Mediterranean) pine tree (Pycnogenol®, Horphag, Switzerland) is rich in anthocyanidins with anti-oxidant effect, and it reduces inflammatory reaction through the inhibition of the Cyclo-oxygenase (COX) enzymes 1 and 2 [35,36] and of the Nuclear Factor kappa B (NF-kB) [37]. In addition it has a strong anti-oxidant effect and restores the function of the capillary epithelium [38].

**Long-chain poly-unsaturated omega-3 fatty acids**

It is recommended to complement the nutriceutical with the long-chain poly-unsaturated fatty acids of the ω-3 group (DHA and EPA) present in fish oil and krill oil. These fatty acids improve the fluidity and functions of the cell membrane, and they also serve as substrate for the energy metabolism of the mitochondria.

**Clinical experience**

A number of trials have confirmed the effectiveness of the combination of nutriceuticals in correcting, or at least mitigating, the signs and symptoms of the metabolic syndrome. As an example, the laboratory results are listed (Table 1) after 4 weeks of nutriceutical treatment in this first patient treated with the novel approach, being a 72 years old overweight lady.

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<tr>
<th></th>
<th>Before</th>
<th>After</th>
<th>% change</th>
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<tbody>
<tr>
<td>Glycaemia</td>
<td>163</td>
<td>122</td>
<td>-25</td>
</tr>
<tr>
<td>HgbA1c</td>
<td>6.7</td>
<td>6.2</td>
<td>-7.5</td>
</tr>
<tr>
<td>Insulin</td>
<td>81</td>
<td>55</td>
<td>-32</td>
</tr>
<tr>
<td>C-peptide</td>
<td>7.56</td>
<td>7.34</td>
<td>-2.9</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>198</td>
<td>182</td>
<td>-8.1</td>
</tr>
<tr>
<td>Triglycerids</td>
<td>193</td>
<td>159</td>
<td>-17.6</td>
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Table 1: The patient (HJ) was diagnosed with incipient type II diabetes, with postprandial hyperglycaemia, slightly elevated fasting haemoglobin A1c, highly elevated insulin and C-peptide, moderately elevated total cholesterol, triglycerides and C-Reactive Protein (CRP). After 4 weeks of nutriceutical supplementation all biological variables have improved, some returning to normal values.

Table:  | CRP  |
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<td>5.8</td>
<td>5.2</td>
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Conclusion

The metabolic syndrome encompasses a multitude of processes and deregulations of several important cellular functions. Treatment must aim at changing the diet and lifestyle of patients, but this requires the full collaboration and motivation of the person involved. This is often difficult to obtain, and commonly patients relapse into their old habits. Medication can be efficient, as is bariatric surgery, but may carry undesired side effects. The judicious combination of herbal extracts, vitamins, minerals and natural agents in the specific nutriceutical food supplements described above is non-toxic, and does not interfere with the pharmacokinetics of allopathic medication. It may help to restore particular steps of cell metabolism, improving the health of patients. The present paper illustrates the first step (proof of principle) in the process of validation of the nutriceutical supplement by estimating its effects on surrogate markers in an open label setting including a limited number of patients. This should precede possible large scale controlled trials [39].

References


