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Maqui and Omega 3: effects on lipid profile, oxidative stress levels and psycho-physical items in human subjects

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ABSTRACT

Aims: to assess short-term efficacy of supplementation with Maqui (*Aristotelia Chilensis* (Mol.Stuntz)), a polyphenol with antioxidant power, and EPA/DHA concerning metabolism, oxidative stress and mental/physical state.

Patients and Methods: a pilot prospective observational clinical/laboratory study was performed on 17 apparently healthy subjects (8 males and 9 females, mean age 47 years). All subjects received for two months: a) Maqui 600 mg per day and b) 360 mg of EPA and 240 mg of DHA (salmon oil) daily. At day 0 and day 60 all subjects underwent nine laboratory tests related to inflammation, metabolism (lipid profile mainly) and oxidative stress parameters. Pre-post treatment weight and BMI was calculated. A few physical and mental parameters were assessed by means of Short-Form 12 questionnaire. Statistical analysis was applied to the resulting data through Wilcoxon test and t-paired test.

Results: laboratory results before and after Maqui + EPA/DHA supplementation were respectively (mean and p-value for the

comparison): total cholesterol 228.8/199.8 mg/dl, p=0.23; low density lipoproteins 127.4/122.1 mg/dl, p=0.13; high density lipoproteins 59.1/57.6 mg/dl, p=0.25; reactive C protein 0.18/0.09 mg/dl, p=0.32; triglycerides 106.1/91.1 mg/dl p=0.09, glycemia 92.9/92.8 mg/dl p= 0.92; total free radicals 338.0/303.6 U.Carr., p=0.002; serum anti-oxidant capacity 2075/2190 umol/l, p=0.04; oxidized lipoproteins 641.8/553.1 uEq/l, p=0.10. SF-12 physical and mental items (mean values and SD) were 51.2 (+/- 6.2) and 41.2 (+/- 3.3) at day 0 and 54.6 (+/- 11.6) and 47.2 (+/- 9.7) at day 60 respectively. One case of transient constipation was recorded.

Conclusions: daily supplementation with Maqui 600 mg + Omega 3 fatty acids (EPA 360 mg + DHA 240 mg) in apparently healthy middle-aged subjects resulted in a statistically significant improvement of oxidative stress parameters. An overall (non statistically significant) improvement of dysmetabolism biomarkers was achieved. Psychological and physical parameters have mildly improved.

keywords: maqui, antioxidants, oxidative stress, omega 3, anthocyanins, lipid profile, delphinidins

INTRODUCTION

The natural process of reactive oxygen species (ROS) production may derange and result in an excessive oxidative stress. In the last thirty-forty years literature data have shown how an imbalance between the ROS generating processes and the antioxidant defence mechanisms may be of relevance in the genesis of multiple diseases, such as cardiovascular diseases, cancer, atherosclerosis, diabetes, neurodegenerative diseases, etc.¹ ROS are continuously eliminated by several intracellular and extracellular antioxidant systems, but an excessive oxidative stress with associated increased ROS production may induce alterations in cellular macromolecules, primarily DNA, lipids and proteins. ROS accumulation results in a series of possible biochemical lesions, with free radicals triggering multiple mutations in the natural cellular bio-architecture; ultimately an alteration of cellular apoptosis mechanisms and the generation

of low grade chronic cellular inflammation (at the basis of the so called “inflammaging”) has been attributed to oxidative stress as well.² Diverse potential fields of interest of natural antioxidants, such as polyphenols, have been highlighted in the prevention or control of different diseases linked to the negative impact of free radicals. Food supplements containing polyphenols, may play a role in a few metabolism alterations, such as dyslipidemias,³ type II diabetes,⁴ amyloid-rich neurodegeneration.⁵ More specifically anti-oxidants may exert a positive effect on a few parameters of oxidative stress and free-radical production, hence they may play a role in the control of cardiovascular degenerative processes,⁶ of inflammaging degeneration and in neurodegenerative diseases.⁷ In the latest years maqui (*Aristotelia Chilensis* (Mol.Stuntz)), an anthocyanin (delphinidin mainly)-rich berry from Chilean Patagonia, has been recognised as one of

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the most powerful antioxidant natural principle in nature.⁸ According to several scientific publications Maqui showed its adjuvant valuable role in several dysmetabolism-related diseases. More specifically maqui administration proved to reduce biomarkers of oxidative stress⁸⁻¹⁰ and to improve lipid and glycemia metabolism.^{8,11,12}

Within the metabolism alterations, triglycerides represent one of the key-factors in the atherogenic process, and more generally of metabolic syndrome. Omega 3 fatty acids have shown a clear positive influence on metabolism and cellular inflammation³ through their two classical components: EPA and DHA. Supplementation with omega 3, which is mostly based on fish oil components, has proved to achieve a decrease of triglycerides level as well.¹⁴

This pilot study has been performed with the aim to assess short-term efficacy of maqui + EPA/DHA supplements on metabolism and oxidative stress of middle-aged apparently healthy subjects, with low-to-mild metabolic dysfunctions. In order to elicit a possible positive effect of the dietary supplements as to above, the following main parameters were investigated: a) biomarkers of oxidative stress and metabolism alterations through laboratory blood testing, b) mental and physical state assessment through a validated score system, c) anthropomorphic basic parameters.

PATIENTS AND METHODS

A pilot prospective observational clinical and laboratory study was performed on 17 middle aged subjects (8 males and 9 females, mean age 47 years, mean BMI 23.9). Inclusion criteria were: subjects in the age 30-55 years, body mass index (BMI) up to 35. Exclusion criteria were: active cancer, cardiac/renal/liver insufficiency, ongoing therapy with steroids, lipid targeting drugs, anti-inflammatory drugs or with hormones, antioxidants, multivitamins.

All subjects signed an informed consent and the study was performed in accordance with the principles of Helsinki Declaration.

The participants of this investigated single group were administered for two months with: a) maqui (*Aristotelia Chilensis* (Mol.Stuntz), maqui, estratto secco titolato KOS srl) two tablets per day, for a total of 600 mg of dry extract 1:10 of maqui berry per day (a dose which is coherent with other literature data,⁹ b) two pearls per day of salmon oil (*Olio di pesce*, KOS srl) (2000 mg daily) corresponding to 360 mg of EPA and 240 mg of DHA per day.

At day 0 all subjects underwent blood examination and the following nine laboratory tests were performed: total cholesterol, low density

lipoproteins (LDL), high density lipoproteins (HDL), reactive C protein (RCP), triglycerides, glycemia, total free radicals, serum anti-oxidant capacity (SAC), oxidized lipoproteins. Blood samples were collected by venipuncture with Vacutainer system; all the metabolites were measured on automatic instrumentation (Architect, Abbott Laboratories). The examined parameters were assessed in plasma fluorure EDTA (glycemia) and on serum (the remaining tests). The following methods were used: esokinase-based spectrophotometry for glycemia; enzymatic method for lipid profile (i.e. total cholesterol, HDL, LDL, triglycerides); immunoturbidimetry for RCP; photometry for free radicals, SAC and oxidized lipoproteins. After 60 days of supplementation all subjects repeated the same blood tests related to cellular inflammation / lipid profile / oxidative stress parameters.

Pre-post/treatment weight and BMI was calculated as well, while blood pressure was measured at day 0, day 30 and day 60. Finally patient-reported outcomes related to a few physical and psychological parameters concerning their daily life were assessed by means of short-form 12 questionnaire (SF-12) at day 0 and day 60.

Any adverse event was recorded throughout the period of the study.

No additional treatment was allowed and a stable life regimen was recommended to all subjects who received a written information on this specific issue.

All data were collected and analysed for statistics by one of the authors (G.M.); statistical analysis was applied to the resulting data by means of PSPP and GraphPad Prism softwares, and p-value was calculated for main variables through t-paired test and through Wilcoxon test. A 0.05 cut-off p-value was considered as statistically significant for all the investigated variables.

RESULTS

An overall improvement of most laboratory parameters was recorded at two months follow-up with a statistically significant difference for oxidative stress biomarkers values.

Pre-post Maqui + EPA/DHA supplementation laboratory results were respectively as follows (mean and p-value for the pre-post/treatment comparison): total cholesterol 228.8/199.8 mg/dl, p=0.23; LDL 127.4/122.1 mg/dl, p=0.13; HDL 59.1/57.6 mg/dl, p=0.25; triglycerides 106.1/91.1 mg/dl p=0.09; oxidized lipoproteins 641.8/553.1 uEq/l, p=0.10; RCP 0.18/0.09 mg/dl, p=0.32; glycemia 92.9/92.8 mg/dl p=0.92; total free radicals 338.0/303.6 U.Carr., p=0.002; SAC

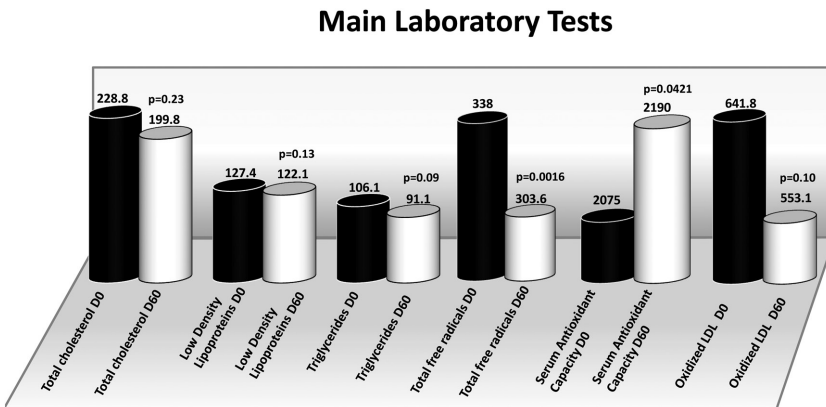


Figure 1 graphic representation of main laboratory parameters

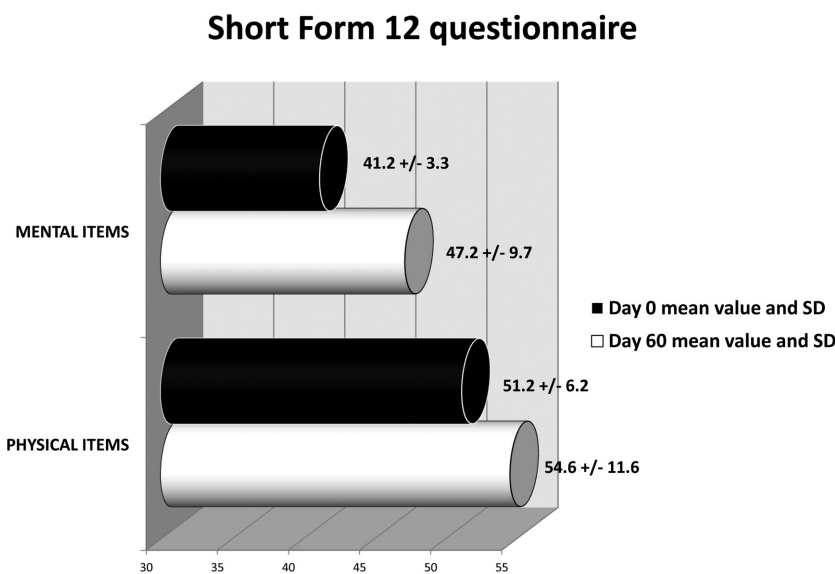


Figure 2 Short-Form 12 data

2075/2190 $\mu\text{mol/l}$, $p=0.04$. Mean weight at day 0 and day 60 was 68.9 Kg and 68.0 Kg respectively ($p=0.19$). Mean values of blood pressure were in the range of normality for all the recruited subjects: the range of systolic/diastolic pressure figures was 130-150 mmHg and 70-85 mmHg respectively) throughout the controls at T0, T30 and T60.

Figure 1 shows the graphic representation of the main laboratory variables analysed and the relative pre-post-supplementation figures.

Mean and standard deviation figures for SF-12 at day 0 for physical and mental items were 51.2 (+/- 6.2) and 41.2 (+/- 3.3) respectively; at day 60 physical and mental figures were 54.6 (+/- 11.6) and 47.2 (+/- 9.7) respectively (Figure 3).

No significant adverse event was reported by the subjects. One case of constipation was recorded and the patient halved the maqui dose to continue the study.

There were no drop-off subjects, hence all data from the 17 included subjects were available for the assessment of the final results.

DISCUSSION

The involvement of oxidative stress as common factor in the pathogenesis of various chronic degenerative diseases has been highlighted in literature.¹ A balance between the production of oxidants/ROS and defensive antioxidants may be essential to a healthy aging. The oxidative stress may be defined as “a state where oxidative force exceeds the antioxidant systems due to loss of the balance between them”.¹⁵

A growing number of studies suggest an association between a polyphenol-rich diet and a positive impact on cardiac¹⁶ and cerebral degenerative diseases.⁷ More generally a positive influence of a few specific anti-oxidant phytochemicals on longevity has been highlighted in recent literature.¹⁷ The beneficial role of maqui on dysmetabolism and against free radicals has been confirmed in different studies,^{8,9} where oxidative stress biomarkers, as well as glycid and lipid metabolism parameters improved.

Omega 3 fatty acids have been shown to improve lipid profile and reduce chronic-low-grade cellular inflammation.^{13,14,18}

The combination of these two active ingredients was recognised as beneficial in longevity medicine and seems to play a role in the control of the inflammaging process.¹⁹ The present study aimed to assess the short-term efficacy of the administration of maqui tablets (600 mg per day) and omega 3 pearls (corresponding to 360 mg of EPA and 240 mg of DHA per day) through the monitoring of a few parameters related to metabolism, oxidative stress and psychological/physical state in middle-aged subjects, having apparently no relevant diseases.

The results of this preliminary study confirm the statistically significant improvement of the two main biomarkers of oxidative stress (total free radicals and SAC), which is mostly attributable to the delphinidins of maqui. In fact anthocyanins in maqui berry are mostly represented by delphinidins, which were shown to exhibit a significant bioavailability and efficacy on different targets in the so called “healthy aging” process.^{8,9,20} Conversely no other statistically significant difference was found in the lipid profile after the combined administration of the two food supplements.

In fact triglycerides, LDL, total cholesterol and oxidized LDL presented an overall improvement in the vast majority of the subjects, but the difference was not statistically significant within the investigated cohort.

Interestingly, subjects with altered lipid profile showed better results, whereas no specific changes were highlighted in the glycemia (which basically

resulted in the range of normality pre-post-dietary supplements administration), HDL and RCP figures. It is possible to speculate that the investigated nutraceuticals could have shown a more pronounced action in patients with pathologic lipid profile, type II diabetes and in older age.

A larger group of subjects would have been needed to validate these preliminary outcomes, possibly through a comparison with a placebo-group. Higher doses of maqui and especially of omega 3 could have been used, eventually aiming at a more intense anti-oxidant and anti-inflammaging effect. Scapagnini and coll.⁹ showed similar results on oxidative stress biomarkers, whereas little changes in the lipid profile were achieved in their randomized controlled study as well.

We acknowledge that SF-12 is a very generic questionnaire, based on a scoring system which responds more to life style modifications than to nutrition/nutraceutical influence on the daily mental and physical changes. Additionally the placebo-effect on the achieved improvement of the SF-12 questionnaire cannot be excluded. Somehow supplementation with maqui dry extract under the form of tablets, in combination with omega 3 pearls, has slightly improved the overall SF-12 scores. Some previously reported positive influence of maqui and delphinidins on AMP-kinase^{19,21} may corroborate the positive influence especially on the physical items changes.

Of interest, also omega 3 fatty acids have shown a positive influence on depressive mood,²² which may partially explain the relatively higher scoring in the mental items after the two months of supplementation with fish oil.

No relevant changes were noted in the weight and BMI figures at the end of the study, as well as blood pressure remained basically stable during the study duration in the investigated subjects. No relevant side effect was reported by the investigated subjects, though no specific test was performed to assess any change of liver/renal function. However literature data do not report any specific safety issue for the two phytonutrients administered in this study.

The two main limitations of this study are the limited number of the investigated individuals and the lack of a control group, which may jeopardise the final results. Anyway this trial was intended as a pilot and preliminary investigation on the possible positive properties of maqui and of omega 3 fatty acids in subjects with limited metabolic alterations and oxidative stress. Our pilot study includes results which are linked to both nutrients, hence it is not possible to extrapolate the effects of each substance. Further studies are definitely needed to possibly confirm the data of our observational study on a small group of patients.

CONCLUSIONS

Daily supplementation with maqui 600 mg + omega 3 fatty acids (EPA 360 mg + DHA 240 mg) in middle-aged subjects, with mild metabolic alterations and oxidative stress level, resulted in a statistically significant reduction of free radicals and in an improvement of the anti-oxidant defence mechanisms. An overall (non statistically significant) improvement of dysmetabolism biomarkers was achieved as well. A mild improvement of psychological and physical parameters has been recorded in the investigated cohort of subjects. No relevant side effects were reported and no significant alteration of blood pressure or of body weight was recorded during the study.

A larger trial, eventually with higher doses and anyway with a control group, is to be considered to possibly corroborate these preliminary results.

AUTHOR CONTRIBUTIONS

Attilio Cavezzi conceived the study and coordinated the protocol management and data collection; Giovanni Mosti was in charge of the statistical analysis; Roberto Corsi and Elena Fioroni performed the laboratory test; The rest of the authors contributed to the data collection. The authors have no potential conflict of interest which pertains to this manuscript. No funding has been provided by any company for this study. This manuscript has never been published elsewhere.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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