(36)

The effect of lutein on the total antioxidant status in human blood

Wpływ luteiny na całkowity status antyoksydacyjny we krwi u ludzi

Karolina Jędrzejczak-Pospiech, Jan Błaszczyk

Department of Human Physiology, Medical University of Lodz, Poland
Head of the Department: Professor Jan Błaszczyk, MD, PhD

Abstract: Aim: The aim of the study was to evaluate plasma total antioxidant status after oral lutein supplementation in healthy subjects.
Material and methods: Forty-four healthy subjects aged 20–77 years were enrolled. They were randomized into three groups to receive oral lutein at 8.0, 10.0, or 12.0 mg/day. Baseline plasma total antioxidant status was determined prior to supplementation, and reassessed after three months of oral lutein intake.
Results: An increase in total antioxidant status was observed in all three groups with a significant increase demonstrated in a group receiving a daily lutein dose of 8.0 mg.
Conclusions:
1. Lutein supplementation in healthy subjects caused a dose-dependent total antioxidant status increase.
2. The highest total antioxidant status increase was observed after the intake of the lowest lutein dose.

Key words: reactive oxygen species, age-related macular degeneration, dietary supplements, lutein.

Abstrakt: Cel: ocena całkowitego statusu antyoksydacyjnego osocza po suplementacji luteiną u ludzi zdrowych.
Materiał i metody: do badania przystąpiły 44 zdrowe osoby w wieku od 20 do 77 lat, które zostały przydzielone do 3 grup. Badani z każdej grupy przez 3 miesiące przyjmowali inną dawkę luteiny (8,0 mg, 10,0 mg, 12,0 mg). Przed suplementacją oraz po 3-miesięcznej suplementacji we krwi osób badanych oznaczano całkowity status antyoksydacyjny.
Wyniki: po suplementacji luteiną zaobserwowano wzrost całkowitego statusu antyoksydacyjnego u badanych ze wszystkich trzech grup. Istotny statystycznie wzrost całkowitego statusu antyoksydacyjnego spowodowała dawka 8,0 mg luteiny.
Wnioski:
1. Suplementacja luteiną u ludzi zdrowych powoduje wzrost całkowitego statusu antyoksydacyjnego zależny od zastosowanej dawki.
2. Największy wzrost całkowitego statusu antyoksydacyjnego obserwowano po zastosowaniu najniższej dawki luteiny.

Słowa kluczowe: reaktywne formy tlenu, zwyrodnienie plamki związane z wiekiem, suplementy diety, luteina.

The authors declare no conflict of interest/ Autorzy zgłaszają brak konfliktu interesów w związku z publikowaną pracą

Introduction

Oxygen, an essential element for life, is commonly used in medicine for treatment of carbon oxide poisoning, tissue anoxia (1) and respiratory insufficiency (2). However, it has been also known to exert adverse effect on the body. Its harmful action is associated with the formation of reactive oxygen species (ROS) as a result of energy metabolism. The most well-recognised species include hydroperoxyl radical $HO_2^{\cdot}$, superoxide radical anion $O_2^{\cdot}$, singlet oxygen $^1O_2$, ozone O_3, hydrogen peroxide H_2O_2, nitric oxide $NO^{\cdot}$ and nitric dioxide $NO_2^{\cdot}$ (3–5). Their reactions with all main cell components can damage structures of proteins, lipids and nucleic acids (5).

ROS are metabolic derivative compounds, which are involved in physiological transport (H_2O_2 stimulates glucose transport), regulate blood pressure (HO_2 and $OH^{\cdot}$ affect the synthesis or release of endothelium-derived relaxing factor – EDRF, via inducing vasodilatation effect) and participate in cellular signal transduction. However, their excessive accumulation has a detrimental effect on a human body. The imbalance between the production and neutralization of free radicals causes oxidative stress which damages cell structures, decreases adenosine triphosphate (ATP) levels, increases cell membrane permeability and disrupts the DNA, giving rise to mutations (5). Thus, oxidative stress contributes to aging, cancers and other civilization diseases (e.g. atherosclerosis, hypertension). Furthermore, in ophthalmology, glaucoma, cataract and age-related macular degeneration (AMD) have also been linked to the adverse effects of ROS (3). To control the adverse impact of free radicals, human body has developed a specific protection system consisting of enzymatic and non-enzymatic mechanisms. Glutathione peroxidase, catalase, and superoxide dismutase constitute the enzymatic protective system, whereas vitamins A, C and E, along with manganese, magnesium and zinc ions, as well as a reduced form of coenzyme Q10, flavonoids and carotenoids (lutein and zeaxanthin) belong to the non-enzymatic system (6). The effect of oxidative stress on the human body and an extent

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of protection against its harmful action is quantified using the total antioxidant status (TAS), a plasma-derived parameter, which expresses the capacity of plasma small-molecule antioxidant compounds to destroy free oxygen radicals and eliminate the adverse effects of their activity. Plasma antioxidant activity is mainly expressed by the number of plasma protein thiol groups and by uric acid concentration in serum (7, 8).

Lutein [C40H56O2; (3R,3'R,6'R)-β-ε-karoten-3,3'-diol] belongs to carotenoids, xanthophyll derivatives, and along with zeaxanthin and mezo-zeaxanthin forms one of the three natural macular pigments in the human eye (9–11). Lutein is distributed throughout the retina, while zeaxanthin and mezo-zeaxanthin are mostly concentrated within the macula. The ratio of these pigments in the retina is 2: 1: 1. In plasma, the level of lutein is three times higher than that of zeaxanthin. The specific lutein structure containing 9 coupled double chains enables its conversion to mezo-zeaxanthin via enzymatic and photochemical transformation (12). Lutein is sourced naturally from fruit and vegetables and requires a small amount of fat, 3.0–5.0 g, in meals to be properly absorbed in the small intestine. Its antioxidant action predominantly involves inactivation of singlet oxygen (13–16) and counteracting lipofuscin photooxidation (13, 15, 16). Lutein also exerts its protective role by absorbing the short wave electromagnetic radiation within the wavelength corresponding to blue colour. Due to its properties, oral lutein intake may play a significant role in preventing age-related retinal diseases such as age-related macular degeneration (AMD) and its complications.

Therefore, lutein is an important compound in controlling the effects of free radicals. This pigment is not produced in the body but exclusively synthesized by plants, thus, a proper diet is very important. The main sources of lutein are green vegetable leaves as well as yellow and orange vegetables. The lutein content in vegetables differs ranging from 0.02 to 40.0 mg/100.0 g. Kale (*Brassica oleracea L*) is known for the highest lutein content (app. 39.0 mg/100.0 g) followed by spinach (app. 11.9 mg/ 100.0 g). The lutein content in fruit is lower, however, it is present in considerable amounts in nectarines, blackberries, gooseberries, avocado, kiwi, raspberries and blackcurrants (17). Pharmaceutical market delivers different types of oral lutein supplements. Proper supplementation contributes to restoring the oxidation-reduction balance, disturbed by the noxious effect of ROS. Crystalline lutein contained in commercially available supplements is better absorbed than the dietary one. Daily intake norms have not been determined to date, therefore, they still remain the subject of research.

The aim of the study

The aim of the study was to evaluate the total antioxidant status (TAS) in plasma of healthy subjects after supplementation with various doses of lutein.

Material and methods

Forty-four healthy subjects aged 20–77 years, who underwent complete ophthalmic examinations, were enrolled in the study. The subjects with severe eye diseases (cataract, glaucoma, diabetic retinopathy), alcohol abuse, smoking or intake of other lutein supplements were excluded. All study participants were randomised into three groups to receive oral lutein supplement (1 tablet daily) containing 8.0, 10.0 or 12.0 mg of lutein. TAS was determined in blood prior to the supplementation and after three months of lutein administration. The TAS kit (Randox no. NX 2332) was used in the study. The study material, i.e. 5.0 ml of venous blood, was collected twice from the basilic vein using a disposable needle and a syringe. The plasma obtained after blood centrifugation was used to determine TAS. The study protocol was approved by the Ethics Committee of the Medical University (no. RNN/483/11/KB).

The statistical analysis and graphical data processing were carried out using Statistica 5.1PL and Office'97 bundles. The Kruskal–Wallis H test (one-way ANOVA on ranks) and the Mann-Whitney U test were used for between-groups comparisons, whereas the Wilcoxon matched pairs test was used for within-groups comparisons. The $p<.05$ was assumed as statistically significant for all comparisons.

Results

The study results are presented in Tables I, II, III and Fig. 1. Oral lutein supplementation led to an increase in TAS observed across all three study groups, with a significant increase demonstrated only in group 1, whose participants received lutein at a dose of 8.0 mg/day (Tab. I).

	Group 1/ Grupa 1.	Group 2/ Grupa 2.	Group 3/ Grupa 3.
Min–max/ Min–max	0.18–1.46	0.85–1.84	0.80–1.50
Median/ Mediana	0.98	1.09	1.06
Arithmetic mean/ Średnia arytmetyczna	0.96	1.13	1.11
Standard deviation/ Odchylenie standardowe	± 0.29	± 0.22	± 0.23
Statistical analysis/ Analiza statystyczna	Kruskal-Wallis ANOVA test H = 2.760, p > .05/ Test ANOVA rang Kruskala-Wallisa H = 2,760, p > ,05 Between-group differences (Mann-Whitney U test)/ Porównania między grupami (test Manna-Whitneya) U (1: 2; 1: 3; 2: 3), p > .05		

Tab. I. The total antioxidant status (TAS) at baseline.
Tab. I. Całkowity status antyoksydacyjny (TAS) przed badaniem.

	Group 1/ Grupa 1.	Group 2/ Grupa 2.	Group 3/ Grupa 3.
Min–max/ Min–max	0.93–1.44	0.88–1.49	0.81–1.55
Median/ Mediana	1.13	1.14	1.16
Arithmetic mean/ Średnia arytmetyczna	1.14	1.17	1.19
Standard deviation/ Odchylenie standardowe	± 0.12	± 0.17	± 0.24
Statistical analysis/ Analiza statystyczna	Kruskal-Wallis ANOVA test H = 0.235, p > .05/ Test Anova rang Kruskala-Wallisa H = 0,235, p > ,05 Between-group comparisons (Mann-Whitney U test)/ Porównania między grupami (test U Manna-Whitneya) U (1: 2; 1: 3; 2: 3), p > .05		

Tab. II. The total antioxidant status (TAS) after 3-month lutein supplementation.
Tab. II. Całkowity status antyoksydacyjny (TAS) po 3-miesięcznej suplementacji luteiną.

Within-group comparisons of baseline and ultimate values/ Porównanie w obrębie grup przed badaniem i po badaniu	Group 1/ Grupa 1.	Group 2/ Grupa 2.	Groupa 3/ Grupa 3.
Test name/ Test	Wilcoxon paired test/ Test kolejności par Wilcoxona	Wilcoxon paired test/ Test kolejności par Wilcoxona	Wilcoxon paired test/ Test kolejności par Wilcoxona
Statistical significance/ Istotność statystyczna	Z = 2.27 p < .05	Z = 1.75 p > .05	Z = 1.60 p > .05

Tab. III. TAS values at baseline and after 3 months of oral lutein intake – within-group comparisons.
Tab. III. Wartości TAS przed badaniem i po 3-miesięcznej suplementacji luteiną – porównania w obrębie grup badanych.

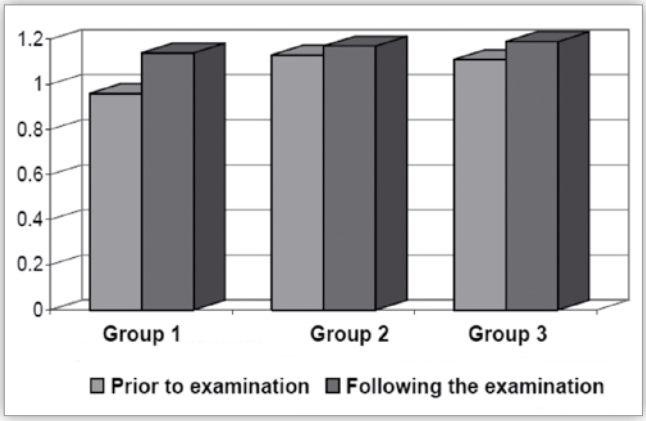

Fig. 1. Mean TAS values in three study groups – at baseline and after 3 months of oral lutein intake.
Ryc. 1. Średnie wartości stężenia TAS u badanych ze wszystkich trzech grup – wartość wyjściowa oraz po 3 miesiącach suplementacji luteiną.

Discussion

The current study assessed the impact of lutein on the total antioxidant status (TAS) in plasma of healthy subjects. TAS is a parameter expressing the bodily ability to neutralise adverse effects of free oxygen radicals, thus inhibiting the development of various diseases including ophthalmic disorders. Lutein intake is recommended for the prevention of eye diseases. The lutein doses of 8.0, 10.0 and 12.0 mg applied in the present study resulted in a considerable improvement in TAS values. The highest statistically significant increase in TAS values after the 3-month supplementation was induced by the lowest lutein dose. It may suggest that 8.0 mg of lutein is sufficient to neutralise the produced free oxygen radicals and inhibit the noxious effect of oxidative stress. Oral lutein intake elevates its plasma concentration, which affects the retina and leads to an increased macular pigment density (16). Lutein administration may minimise the damage to the retina and macula already altered secondarily to AMD. In the USA, the study was performed in 15 patients with AMD symptoms in which a lutein-rich diet (4.0 mg/ daily) caused an increase in the macular pigment content and, more importantly, an improvement in visual acuity (17, 18).

Studies on the effect of dietary supplementation on human body have not, to date, provided the optimal composition of diet and especially the lutein content. According to the research carried out at Harvard University, the intake of 6.0 mg of lutein daily reduces the risk of damage to the macula and retina by 43%. Clinical investigations have proven that daily consumption of 6.0–14.0 mg of lutein halves the risk of AMD (19). However, recent international nutritional studies have demonstrated that the mean lutein intake is 2.2 mg/ d and 1.7 mg/ d in European and North American populations, respectively (20).

The results of the current study indicate that the lowest lutein dose (8.0 mg) resulted in the highest increase in TAS values. The oral intake of 10.0 and 12.0 mg/ d of lutein resulted in a lower and non-significant rise in TAS. Thus, the lutein dose of 8.0 mg daily seems to be sufficient to protect the retina against adverse effects of free oxygen radicals.

Conclusions

1. There is a dose-dependent inverse association between lutein supplementation in healthy subjects and TAS.
2. The highest increase in TAS was observed after the intake of the lowest lutein dose.

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Reprint requests to (Adres do korespondencji):
Karolina Jędrzejczak-Pospiech MD, PhD
Department of Human Physiology, Medical University of Lodz, Poland
Hallera 1st, 90-647 Lodz, Poland,
e-mail: karolina.jedrzejczak-pospiech@umed.lodz.pl