Original Article

Serum lutein and its dynamic changes during supplementation with lutein in Chinese subjects

Le Ma MD, Xiao-Ming Lin MD, Xian-Rong Xu MSc, Zhi-Yong Zou MD, Zi-Xin Wang MSc, Yang-Mu Huang MD and Ying Li MSc

Department of Nutrition and Food Hygiene, School of Public Health, Peking University, Beijing, China

Observational epidemiological studies have shown that a high consumption of lutein-containing foods is associated with decreased risk of chronic diseases. However, results are inconsistent, suggesting the possibility that confounders may impact serum lutein concentration after consumption. The present study aimed to determine the factors affecting serum lutein status and to characterize dynamic changes of lutein concentration in serum during lutein supplementation in healthy Chinese subjects. After baseline characteristics were determined, thirty-seven healthy participants were randomized to receive 6 mg lutein/d, 12 mg lutein/d, or placebo for 12 weeks, as well as to be observed for 6 additional weeks after the cessation of supplementation. Serum levels of lutein and β-carotene were measured by HPLC at weeks 0, 1, 3, 6, 9, 12 and 18. Dietary intake was estimated by food-frequency questionnaires. No significant sex differences were found in serum concentration of lutein. Serum lutein level positively correlated with dietary lutein, retinol equivalents, vitamin C, vitamin E, β-carotene and fat intake after adjustment for caloric intake, but not with BMI. After 12-weeks of supplementation, lutein levels increased approximately 1.8-fold and 2.3-fold for the 6-, and 12-mg dose groups respectively, approaching a plateau at week 9, and then decreased to baseline values at week 18. No adverse events or reductions in serum β-carotene were observed throughout the study. Our findings indicate that increasing the consumption of lutein-rich fruit and vegetables can be considered as a long-term, sustainable and safe approach to reach and maintain high serum levels of lutein.

Key Words: lutein, β-carotene, carotenoid, interactions, adults

INTRODUCTION

Lutein, a member of oxygenated carotenoids, has recently received attention for its critical role in preventing chronic and degenerative diseases in humans.[1] A great deal of epidemiological studies suggested that high lutein intake and/or serum levels were associated with a lower risk of developing certain diseases, including specific cancers, cardiovascular and ocular diseases.[2,3] Results from placebo-controlled interventions showed that supplementation with lutein led to an improvement in visual performance.[4]

While the functional improvement is the primary objective in these studies, the assessment of serum lutein level is very useful in terms of establishing lutein status as well as checking efficacy of the intervention. Moreover, information on serum kinetics of lutein is also important in order to establish and adjust effective doses, thresholds for treatment efficacy, timing of the intervention, risk evaluation and prevention of unforeseen additional risks.[5] At present, there is almost a complete lack of information regarding the potential adverse effects attributable to lutein supplements. The metabolism and dynamic changes of lutein in humans remain largely unknown, especially in Asian populations. In groups with different characteristics, at different doses or for a sufficient time, supplementation with lutein may also provoke some unforeseen adverse effects, similar to β-carotene which was observed in cer-

tain groups (smokers, alcohol drinkers, asbestos workers).[6,7] Consequently, evaluating the risks of supplementation with lutein in different population groups should be a preliminary and necessary step for conducting any lutein intervention trials to test its efficacy in relation to prevention and treatment of certain chronic diseases.

Furthermore, it is worth noting that some investigators reported that serum lutein concentrations did not increase after supplementation with lutein, and lutein supplementation even led to a significant reduction in the concentration of serum carotenoids or antioxidant vitamins.[8,9] Such inconsistent results may be explained by the fact that serum lutein and its dynamic changes are affected by multiple factors, including age, gender, BMI, dietary intake, race and probably others.[10,11]

Therefore, the present study aimed to determine factors that affect serum lutein status and to observe the serial changes of serum lutein in healthy Chinese subjects

Corresponding Author: Dr Xiao-Ming Lin, Department of Nutrition and Food Hygiene, School of Public Health, Peking University, 38 Xueyuan Road, Beijing, China, 100191
Tel: +8610-13621368229 or 82805336; Fax: +8610-62015583
Email: linbjmu@bjmu.edu.cn; male@bjmu.edu.cn

with different doses of lutein. In addition, the potential influence of lutein supplementation on serum concentrations of β-carotene was also assessed.

MATERIAL AND METHODS
Subjects
Thirty-seven healthy adults, between 22 and 30 years, volunteered to participate in the present study. The sample size was based on power calculations to detect a 10% change with a power of 0.95. All potential trial participants were interviewed using a questionnaire that sought information about their general health, family history, use of medication or nutritional supplements and smoking status. Individuals were excluded from participation if they met any of the following criteria: smoking, consumption of excessive amounts of alcohol, BMI ≥ 30 kg/m^2, allergies, suffering from a chronic disease and taking dietary supplements (vitamins, carotenoids and minerals) within two month before the start of the study.

This study followed the tenets of the Declaration of Helsinki and was approved by the Medical Ethics Committee of Peking University. Written informed consent was obtained from each subject.

Study design
The study was designed as a randomized, double-blind, placebo-controlled trial. After anthropometric measures, dietary intakes and serum lutein concentration of all subjects were assessed at recruitment, they were randomly assigned to 1 of 3 equal groups on the basis of sex: Group L6, who received 6 mg lutein per day (*n*=12); Group L12, who received 12 mg lutein per day (*n*=13); and a control group, who received a maltodextrin placebo (*n*=12). The treatment preparations were supplied by Beijing Yuguang Bioscience Research Center Co. Ltd. (Beijing, China). To ensure the compliance, the capsules were dispensed to participants per day by professional staff and they were asked to take the capsules on the spot. The volunteers avoided excessive consumption of food items known to contain large amounts of lutein for the entire study and were asked to recorded their habitual diet by food-frequency questionnaires at baseline and at the final study visit.[12] No other dietary or lifestyle changes were required of the participants.

Serum levels of lutein and β-carotene were determined at weeks 0, 1, 3, 6, 9, 12 and 6 weeks after the study (week 18).

Serum lutein concentration
Venous blood samples (5.0 ml) were collected between 07:00 and 08:30 after the subjects had fasted overnight, into Vacutainer™ serum separator tubes with no anticoagulant. Blood specimens were processed at the central laboratory of the School of Public Health, Peking University. Immediately after collection blood samples were placed on ice in the dark, serum was separated from the whole blood within 1 h by centrifugation at 3000 g at 4°C for 10 minutes, and then stored at -70°C until time of analysis (within 5 months). Serum concentrations of carotenoids were shown to be stable under these storage conditions.

Aliquots were prepared following a procedure adapted from the method of Wenzel et al.[13] In brief, serum samples (200 µl) were mixed with 200 µl ethanol to complete the precipitation of proteins. Subsequently, 0.7 ml hexane were added and mixed by vortex for 1 minute followed by centrifuging for 5 minutes (3000×*g*, 4°C). The upper hexane layer was removed and the extraction step was repeated twice. The combined hexane extract was evaporated under a stream of nitrogen, and the residue dissolved in 200 µl of mobile phase (Fisher Scientific, Pittsburgh, PA, USA). An aliquot of 10 µl was removed for analysis with reversed-phase HPLC. All procedures were performed in subdued light.

HPLC was carried out with a Hewlett-Packard/Agilent Technologies 1100 gradient HPLC apparatus with a UV/visible detector at 450 nm and equipped with a C_{18} analytical column (Supelco, Bellefonte, PA, USA) and a Discovery C_{18} pre-column to separate the analytes. The mobile phase was a mixture of acetonitrile and methanol (solvent A, 60:40, v/v; solvent B, 10:90, v/v). The gradient procedure was as follows: from the start of the run to min 5, 100% solvent A was running at a flow rate of 1.2ml/min. Beginning at min 5, the mobile phase transitioned for 5 min to a 15-min run with 100% solvent B at a flow rate of 1.5ml/min.[4,14]

Linearity was evaluated by injection of standard solutions (Sigma-Aldrich, St. Louis, MO, USA) within method range, and the correlation coefficient was >0.998. Recoveries of lutein and β-carotene were 98.3% and 98.4%, respectively. Repeatability was tested by injecting the same sample six times in 24 hours, and RSD was within the range of 1.2-2.7%.

Statistical analyses
For statistical analysis, data were checked for normal distribution with use of the Kolmogorov-Smirnov test. Differences of baseline characteristics between men and women were evaluated with *t* test. Correlation coefficients and those after adjustment for caloric intake were calculated between anthropometric measures, dietary intake, and serum lutein. The multiple linear regression models were used to describe the relationship between various food sources of lutein and serum lutein. To assess the efficiency of randomization, the differences among the groups at baseline were analyzed with chi-square test or analysis of variance. Significant differences during supplementation were measured by using GLM repeated measures analysis. If a significant interaction was found, a subgroup analysis was performed with the Bonferroni test. All statistical calculations were performed with SPSS 10.0 for Windows (SPSS Inc., Chicago, USA), and any differences showing with *p* value of less than 0.05 were considered to be statistically significant.

RESULTS
The results of baseline demographic data and information on nutritional habits before supplementation are summarised in Table 1. There were no significant sex differences in age and dietary nutrient intakes, except for higher energy intake and dietary zinc in men (*p*<0.05). Although the serum lutein concentration was not significantly dif-

ferent between the sexes, the women tended to have a higher lutein concentration than did the men ($p=0.09$).

To analyze which factors were directly related to serum lutein concentration, the associations among anthropometric measures, dietary intake and serum lutein were examined. The relationship was particularly apparent when correlational analysis was applied to the adjusted dietary values for caloric intake. As is shown in Table 2 and Table 3, there were significantly positive correlations of serum lutein concentration with dietary intake of lutein,

retinol equivalents, vitamin C, vitamin E (not significant on raw values) and β-carotene were observed. Dietary lutein intake was positively correlated with dietary intake of retinol equivalents, vitamin C (not significant on raw values), and β-carotene. Furthermore, serum lutein concentration was positively correlated with fat intake after adjustment for caloric intake. Because serum lutein was highly correlated with dietary lutein, we next assessed the major food sources of lutein and examined which source of lutein correlated best with serum concentrations of

Table 1. Baseline characteristics of the study participants

Variable	All Subjects	Men (n=19)			Women (n=18)		
		L6	L12	Placebo	L6	L12	Placebo
n	37	6	7	6	6	6	6
Age (y)	24.7±1.7	24.2±1.8	24.0±1.6	26.3±2.1	24.2±1.5	24.5±0.5	25.0±2.0
BMI (kg/m²)	20.2±2.5	20.8±3.4	21.1±1.9	21.8±2.7	18.2±1.2	19.6±1.8	19.6±0.6
Energy intake (MJ/d)*	9.4±0.3	9.4±0.1	9.6±0.2	9.6±0.4	9.3±0.3	9.2±0.2	9.3±0.2
Fat intake (g/d)	63.4±27.8	54.0±31.0	80.7±39.4	65.0±19.4	77.3±24.3	44.5±15.5	55.8±16.3
Dietary intake (mg/d)							
Lutein	2.4±2.0	2.9±2.7	1.6±1.3	1.6±1.1	2.6±1.8	3.3±1.9	2.7±3.0
Retinol equivalents	0.46±0.29	0.42±0.32	0.34±0.20	0.56±0.30	0.46±0.29	0.51±0.45	0.46±0.22
Vitamin C	78.3±59.2	73.9±55.5	59.5±22.7	90.0±51.5	72.9±17.6	102.0±121.7	74.8±48.3
Vitamin E	11.5±5.3	9.1±5.4	13.5±8.7	13.6±4.1	10.0±3.4	10.8±4.7	11.4±3.4
Zinc*	9.6±2.8	10.5±2.6	10.3±1.6	12.0±2.8	8.2±2.4	7.3±1.7	9.3±3.5
β-carotene	3.5±2.5	3.6±2.8	3.5±2.6	3.0±2.6	3.1±2.6	4.1±2.3	3.6±2.7
Serum lutein (μmol/l)	0.34±0.12	0.33±0.12	0.28±0.09	0.33±0.10	0.38±0.12	0.38±0.13	0.37±0.13

Values are mean±SD; * Significant differences between men and women ($p<0.05$).

Table 2. Pearson correlation matrices on raw values

	BMI	Fat intake	Dietary lutein	Dietary retinol equivalents	Dietary vitamin C	Dietary vitamin E	Dietary zinc	Dietary β-carotene	Serum lutein
Age (y)	0.73	0.01	-0.10	0.04	0.09	-0.03	0.17	-0.11	-0.17
BMI (kg/m²)		0.07	0.14	-0.12	-0.10	-0.13	0.23	-0.21	-0.03
Fat intake (g/d)			0.15	-0.08	-0.03	0.40*	0.20	-0.02	0.22
Dietary lutein (mg/d)				0.42*	0.27	0.22	-0.21	0.50**	0.56**
Dietary retinol equivalents (μg/d)					0.81**	0.59**	0.05	0.64**	0.36*
Dietary vitamin C (mg/d)						0.38*	-0.07	0.62**	0.37*
Dietary vitamin E (mg/d)							0.14	0.38*	0.18
Dietary zinc (mg/d)								-0.11	-0.23
Dietary β-carotene (mg/d)									0.42*

Significant correlations: *$p<0.05$, **$p<0.01$.

Table 3. Pearson correlation matrices on values adjusted for caloric intake

	BMI	Fat intake	Dietary lutein	Dietary retinol equivalents	Dietary vitamin C	Dietary vitamin E	Dietary zinc	Dietary β-carotene	Serum lutein
Age (y)	0.73	-0.12	-0.13	-0.04	0.01	-0.09	0.03	-0.14	-0.17
BMI (kg/m²)		-0.08	0.02	-0.20	-0.13	-0.26	-0.05	-0.28	-0.03
Fat intake (g/d)			0.27	0.18	0.15	0.42**	-0.09	0.11	0.39*
Dietary lutein (mg/d)				0.45	0.38*	0.30	-0.13	0.61*	0.60**
Dietary retinol equivalents (μg/d)					0.85**	0.68**	0.11	0.65**	0.43**
Dietary vitamin C (mg/d)						0.54*	0.06	0.64**	0.43**
Dietary vitamin E (mg/d)							-0.08	0.49**	0.33*
Dietary zinc (mg/d)								0.04	0.03
Dietary β-carotene (mg/d)									0.49**

Significant correlations: *$p<0.05$, **$p<0.01$.

lutein. Data from our study showed that spinach, peas, lettuce, eggs and peppers were potentially the main contributors of lutein, which accounted for 81% of total lutein intake. When all food sources of lutein were entered together in a regression model, only spinach remained a significant correlate of serum lutein (r =0.38; p=0.04).

The subjects were selected for the study and randomly assigned to three groups on the basis of sex. The baseline characteristics of participants for all groups were comparable (Table 1). No significant differences were seen between the three groups in terms of age, sex, BMI, dietary nutrient intake and serum lutein concentration at baseline.

All members of the study team successfully completed the trial. Total energy and nutrient intakes did not change significantly during the intervention, except for dietary zinc in Group Placebo, decreasing from 10.5mg to 8.7mg over time (p<0.05). No significant adverse events or changes in biochemical or haematological indices were observed throughout the study.

After 12-week intervention, supplementation with 6mg or 12mg of lutein resulted in proportionately increased concentrations of serum lutein, whereas no changes were observed in Group Placebo. The increasing magnitude of serum lutein from baseline significantly correlated with the increase in the dose of lutein. The GLM repeated measures analysis showed statistically significant differences in serum levels of lutein throughout the supplementation period (p<0.001). Serum lutein levels in Group L6 and Group L12 increased approximately 1.8-fold and 2.3-fold, respectively. Serum lutein increased rapidly at the first week (p<0.05), then increased gradually and peaked by week 9. There were no significant changes in terms of lutein concentrations from week 3 to week 12 (p>0.05). Six weeks after discontinuing lutein supplementation, serum lutein concentration had almost decreased to baseline values in both intervention groups (Figure 1). In addition, lutein supplementation did not affect β-carotene level in the serum substantially throughout the study (Figure 2).

The change in terms of lutein values in men was basically consistent with those in women. No statistical sex differences were found in the peak and average maximum change of serum lutein. Age, BMI and dietary lutein intake were not significantly associated with the increase of serum lutein concentrations. To determine the effect of supplement dosage, we examined the plateau lutein concentration in the serum as a linear function of dosage. The linear correlation coefficient r was 0.71 (p<0.001) (Figure
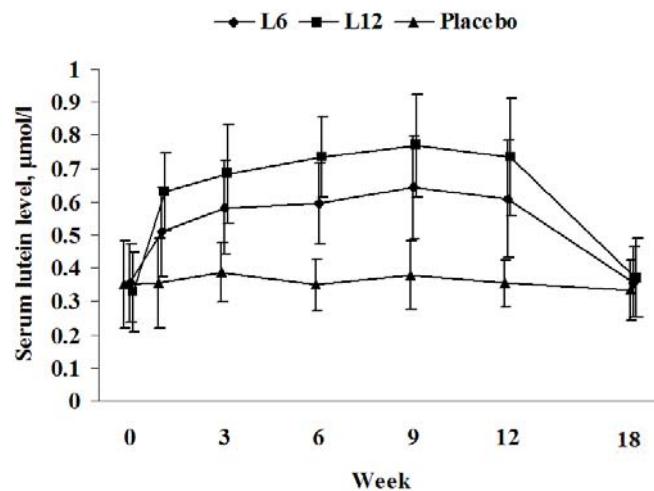

Figure 1. Dynamic changes of lutein concentration in the serum of subjects during lutein supplementation.
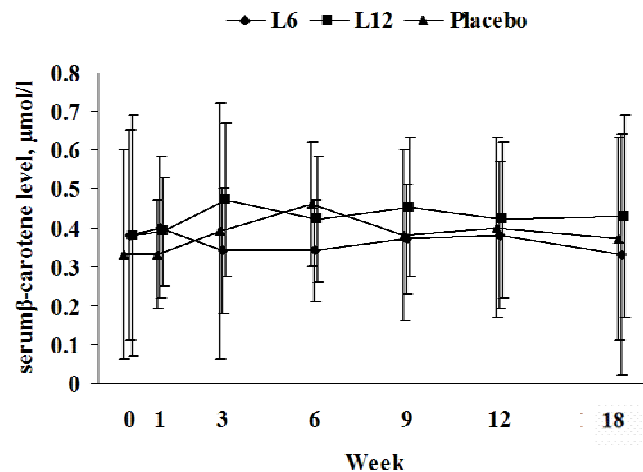

Figure 2. Dynamic changes of β-carotene concentration in the serum of subjects during lutein supplementation.
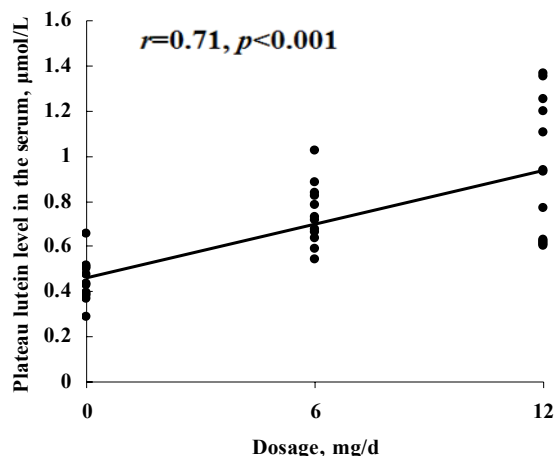
Figure 3. Scatter plot showing the dependency on dose of the elevated plateau concentration of lutein in the serum resulting from lutein supplementation. The regression line represents a linear fit of the data, $r =0.71$; $p<0.001$.
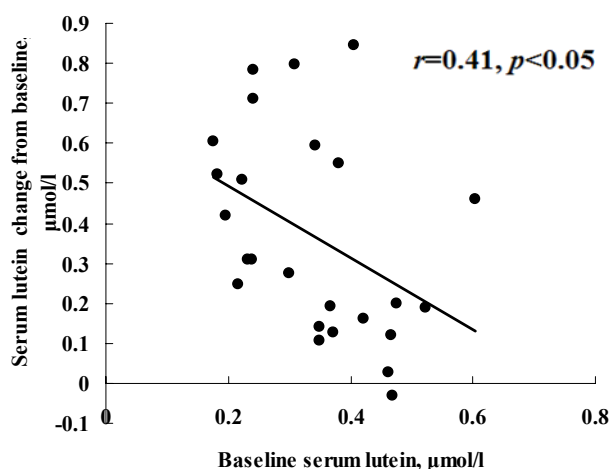

Figure 4. Relation between serum lutein concentration at baseline and the change of lutein concentration in the serum from baseline for the subjects who received lutein supplements. The line represents a linear fit of the data, $r =-0.41$; $p<0.05$.

3). We also examined the hypothesis that the baseline concentration of lutein would be a major factor in determining change of serum concentrations from baseline during supplementation. Figure 4 indicates linear regression analysis with a correlation coefficient of -0.41 that was significant ($p<0.05$) for all 25 subjects who received different supplement dosages.

DISCUSSION
There has been increasing interest in evaluating the effect of lutein on decreasing risk of chronic diseases, especially AMD and cardiovascular diseases. Although supplementation studies have indicated the potential contribution of lutein to the prevention and reversal of certain diseases, considerable controversy exists.[15] Of note, little information is available regarding the safety and serum kinetics of lutein during supplementation with lutein in Asian subjects. Consequently, it is important to evaluate the benefits and risks of lutein supplementation in relation to human health and disease, particularly in Asian populations.

This was the first pilot randomized controlled study to detect serum lutein concentration in Chinese subjects. Our results indicated that serum concentrations of lutein

in Chinese subjects were relatively higher in comparison with those in other studies.[16] Although the reason for this discrepancy was unknown, a plausible explanation was the between-race variation with regard to the bioavailability of lutein, which affected its absorption, breakdown, transport, and storage. Another possible reason was the differences in the major food sources of lutein or other differences in dietary patterns that affect lutein absorption and bioavailability.[17] The results of the present study showed that spinach, with the highest content of lutein, was the most important contributors to lutein intake in the Chinese diet and significantly correlated with serum lutein, which might be able to explain the higher serum lutein in this study compared to other studies. Consistent with the findings of previous studies, we found that women had slightly, and nonsignificantly, higher serum lutein concentration than did men.[18] This slight difference in serum lutein between the sexes might reflect a lower intake of lutein-containing foods in men than in women.

Multiple factors have the potential to influence availability and metabolism of lutein, including age, gender, BMI, smoking, nutritional status, and genetic factors.[10,11] Thus, we determined the factors affecting serum lutein

status. Because a between-person difference in tissue uptake, as a response to chronic caloric intake, may have implications for dietary intervention studies. We attempted to control for systematic population differences in caloric intake by dividing nutrient values by total caloric intake (nutrient densities).[19] A significant positive correlation was found between dietary lutein intake and serum lutein concentration in this study. Serum levels of lutein may be a good reflection of past lutein intake and, consequently, can be used as a marker of dietary intake. As carotenoids or other antioxidant vitamins are frequently present from similar food items, the results of this trial revealed that serum lutein concentration was also significantly related to dietary intake of retinol equivalents, vitamin C, vitamin E and β-carotene. Additionally, Lutein is circulated through the blood bound to lipoproteins. Consequently, co-consumption of fat may be a potential factor that influence lutein uptake into the serum.[20] In the current study, serum lutein was linearly related to fat intake after the values were adjusted for caloric intake. A direct relation between serum lutein and fat intake suggested that fat-deficient diets might result in decreased intestinal absorption of lutein. An alternative explanation was that the formation of lipid micelles required emulsification of the fat-soluble vitamins stimulated by dietary fat. In addition to dietary intake, competition for carotenoids among body tissues may affect the amount of carotenoids available in the serum.[21] Compared with individuals with low BMI, individuals with high BMI may have a greater number of peripheral binding sites for carotenoids and attenuate serum responses to intervention. Hammond et al. reported that serum levels of lutein were significantly lower in the subjects with high BMI, despite similar overall caloric intake.[22] However, we found no association between serum lutein status and BMI. This inconsistent finding derived in part from the fact that the influence of BMI might only have an effect in subjects whose BMI exceeded 29, while there were no subjects with a BMI over 29 in our study.

Previous studies had investigated the serum response to supplemental lutein in humans.[8,23,24] Landrum et al. supplemented two subjects with lutein esters equivalent to 30 mg of free lutein per day for 140 days.[23] Serum levels of lutein increased by 10-fold within 20 days and returned to baseline concentrations 60 days after supplementation was discontinued. The study conducted by Rosenthal et al. demonstrated that supplementation with 10 mg/d of lutein for 6 months in 15 subjects resulted in a 4-fold increase in plasma lutein concentration.[24] In the present study, serum lutein concentrations in both intervention groups markedly rose with increasing doses of lutein throughout the 12-week period of supplementation, and then decreased to baseline values 6 weeks after lutein supplementation was discontinued, indicating that serum concentration of lutein was responsive to increases and decreases in lutein intake. Approximately 50% of the variance in serum lutein concentration could be attributed to a linear dependency on dose. However, the rate of increase in lutein concentration in this study was smaller than the results from Landrum's and Rosenthal's study.[23,24] Such difference might be due to the relatively high baseline lutein concentration found in subjects of our study. Of note, if pre-supplementation lutein concentrations inversely affected the rate of increase in lutein concentration, we might expect that the changes of lutein concentrations in subjects, whose level was already high, were limited more than changes in those with low levels. This might be attributable to the fact that the accumulation of lutein in serum had almost reached a saturation level in individuals with high levels. In fact, the increase in lutein concentration was significantly negatively related to pre-supplementation concentrations. Thus, our results implied that individuals with low serum level or dietary intake of lutein might benefit more from future lutein interventions. Furthermore, there were no dietary restrictions or changes, and analysis of the dietary records indicated that the subjects maintained their usual nutrient intakes from their self-selected diets throughout the study. Consequently, the improvement in serum lutein was attributed to the supplement.

It was noteworthy that the steady-state (plateau) levels of lutein in serum in both the L6 and L12 groups were between 0.6 and 1.05 mmol/l, which were considered desirable biochemical target for health promotion and disease prevention.[25] Despite the analytical variability and the differences among populations, data from observational studies and intervention trials to support the notion that concentration of lutein in serum above 0.60 mmol/l correlated with a reduced risk for chronic diseases was consistent. On the other hand, serum lutein <1.05 mmol/l seemed to be indicative of safety since they were not related to an unusual serum lutein profile, biochemical or haematological changes or carotenodermia.[26] Therefore, in the present study, daily lutein supplementation at 6 mg or 12 mg for 12 weeks was effective in reaching physiologically significant cut-off points for lutein in serum, which could indirectly correlate with improved health outcomes. The results of this study also agreed with the findings from Seddon et al., who noted that a suggested daily intake of above 6 mg of lutein was associated with a reduced risk for eye diseases, such as cataracts and AMD.[27]

Controlled nutritional studies showed that lutein supplementation lowered β-carotene concentration in human plasma, which indicated that there might be an interaction between carotenoids that one carotenoid inhibited the absorption and/or metabolism of another,[9,28] though comparison of results from available research showed numerous inconsistencies with respect to the nature of this interaction. The results of this trial revealed that there were no significant changes of serum β-carotene concentrations in response to the lutein intervention, suggesting that lutein did not interfere with the absorption of β-carotene. Larger studies needed to be conducted to confirm this observation. Moreover, no adverse events associated with the intervention were reported in participants while they were taking lutein supplements, so our study confirmed that lutein supplementation at 12 mg/day for up to 12 weeks was safe.

In summary, lutein supplementation for 12 weeks was effective for increasing serum lutein level to physiological concentrations in healthy Chinese subjects, but serum lutein decreased after supplementation discontinued. Thus, increasing the consumption of lutein-rich fruit and vegetables can be considered as a long-term, sustainable and

safe approach to reach and maintain high serum levels of lutein, which is associated epidemiologically with potential health benefits in humans.

REFERENCES
1. Ahmed SS, Lott MG, Marcus DM. The macular xanthophylls. Surv Ophthalmol. 2005;50:183-93.
2. Dwyer JH, Navab M, Dwyer KM, Hassan K, Sun P, Shircore A et al. Oxygenated carotenoid lutein and progression of early atherosclerosis: the Los Angeles atherosclerosis study. Circulation. 2001;103:2922-7.
3. Demmig-Adams B, Adams WW. Antioxidants in photosynthesis and human nutrition. Science. 2002;298:2149-53.
4. Olmedilla B, Granado F, Blanco I, Vaquero M. Lutein, but not alpha-tocopherol, supplementation improves visual function in patients with age-related cataracts: a 2-y double-blind, placebo-controlled pilot study. Nutrition. 2003;19:21-4.
5. Johnson EJ, Hammond BR, Yeum KJ, Qin J, Wang XD, Castaneda C, Snodderly DM, Russell RM. Relation among serum and tissue concentrations of lutein and zeaxanthin and macular pigment density. Am J Clin Nutr. 2000;71: 1555-62.
6. Aliyu OA, Cullen MR, Barnett MJ, Balmes JR, Cartmel B, Redlich CA et al. Evidence for excess colorectal cancer incidence among asbestos-exposed men in the Beta-Carotene and Retinol Efficacy Trial. Am J Epidemiol. 2005;162:868-8.
7. Satia JA, Littman A, Slatore CG, Galanko JA, White E. Long-term use of beta-carotene, retinol, lycopene, and lutein supplements and lung cancer risk: results from the VITamins And Lifestyle (VITAL) study. Am J Epidemiol. 2009;169:815-28.
8. Trieschmann M, Beatty S, Nolan JM, Hense HW, Heimes B, Austermann U, Fobker M, Pauleikhoff D. Changes in macular pigment optical density and serum concentrations of its constituent carotenoids following supplemental lutein and zeaxanthin: the LUNA study. Exp Eye Res. 2007;84:718-28.
9. van den Berg H. Effect of lutein on beta-carotene absorption and cleavage. Int J Vitam Nutr Res. 1998;68:360-5.
10. Broekmans WM, Berendschot TT, Klöpping-Ketelaars IA, de Vries AJ, Goldbohm RA, Tijburg LB, Kardinaal AF, van Poppel G. Macular pigment density in relation to serum and adipose tissue concentrations of lutein and serum concentrations of zeaxanthin. Am J Clin Nutr. 2002;76:595-603.
11. Curran-Celentano J, Hammond BR Jr, Ciulla TA, Cooper DA, Pratt LM, Danis RB. Relation between dietary intake, serum concentrations, and retinal concentrations of lutein and zeaxanthin in adults in a Midwest population. Am J Clin Nutr. 2001;74:796-802.
12. AREDS Research Group. The relationship of dietary carotenoid and Vitamin A, E and C intake with age-related macular degeneration in a case-control study. AREDS Report no. 22. Arch Ophthalmol. 2007;125:1225-32.
13. Wenzel AJ, Gerweck C, Barbato D, Nicolosi RJ, Handelman GJ, Curran-Celentano J. A 12-wk egg intervention increases serum zeaxanthin and macular pigment optical density in women. J Nutr. 2006;136:2568-73.
14. Khachik F, de Moura FF, Chew EY, Douglass LW, Ferris FL 3rd, Kim J, Thompson DJ. The effect of lutein and zeaxanthin supplementation on metabolites of these carotenoids in the serum of persons aged 60 or older. Invest Ophthalmol Vis Sci. 2006;47:5234-42.
15. Cardinault N, Abalain JH, Sairafi B, Coudray C, Grolier P, Rambeau M, Carré JL, Mazur A, Rock E. Lycopene but not lutein nor zeaxanthin decreases in serum and lipoproteins in age-related macular degeneration patients. Clin Chim Acta. 2005;357:34-42.
16. Bone RA, Landrum JT, Guerra LH, Ruiz CA. Lutein and zeaxanthin dietary supplements raise macular pigment density and serum concentrations of these carotenoids in humans. J Nutr. 2003;133:992-8.
17. Molldrem KL, Li J, Simon PW, Tanumihardjo SA. Lutein and beta-carotene from lutein-containing yellow carrots are bioavailable in humans. Am J Clin Nutr. 2004;80:131-6.
18. Hammond BR Jr, Curran-Celentano J, Judd S, Fuld K, Krinsky NI, Wooten BR, Snodderly DM. Sex differences in macular pigment optical density: relation to plasma carotenoid concentrations and dietary patterns. Vision Res. 1996; 36:2001-12.
19. Davies NP, Morland AB. Macular pigments: their characteristics and putative role. Prog Retin Eye Res. 2004;23:533-59.
20. Wang W, Connor SL, Johnson EJ, Klein ML, Hughes S, Connor WE. Effect of dietary lutein and zeaxanthin on plasma carotenoids and their transport in lipoproteins in age-related macular degeneration. Am J Clin Nutr. 2007;85: 762-9.
21. Burke JD, Curran-Celentano J, Wenzel AJ. Diet and serum carotenoid concentrations affect macular pigment optical density in adults 45 years and older. J Nutr. 2005;135:1208-14.
22. Hammond BR Jr, Ciulla TA, Snodderly DM. Macular pigment density is reduced in obese subjects. Invest Ophthalmol Vis Sci. 2002;43:47-50.
23. Landrum JT, Bone RA, Joa H, Kilburn MD, Moore LL, Sprague KE. A one year study of the macular pigment: the effect of 140 days of a lutein supplement. Exp Eye Res. 1997;65:57-62.
24. Rosenthal JM, Kim J, de Monasterio F, Thompson DJ, Bone RA, Landrum JT et al. Dose-ranging study of lutein supplementation in persons aged 60 years or older. Invest Ophthalmol Vis Sci. 2006;47:5227-33.
25. Granado F, Olmedilla B, Blanco I. Nutritional and clinical relevance of lutein in human health. Br J Nutr. 2003;90:487-502.
26. Granado F, Olmedilla B, Gil-Martı´nez E, Blanco I. Lutein ester in serum after lutein supplementation in human subjects. Br J Nutr. 1998;80:445-9.
27. Seddon JM, Ajani UA, Sperduto RD, Hiller R, Blair N, Burton TC et al. Dietary carotenoids, Vitamins A, C, and E, and age-related macular degeneration. Eye Disease Case-Control Study Group. JAMA. 1994;272:1413-20
28. Albanes D, Virtamo J, Taylor PR, Rautalahti M, Pietinen P, Heinonen OP. Effects of supplemental beta-carotene, cigarette smoking, and alcohol consumption on serum carotenoids in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. Am J Clin Nutr. 1997;66:366-72.

Original Article

Serum lutein and its dynamic changes during supplementation with lutein in Chinese subjects

Le Ma MD, Xiao-Ming Lin MD, Xian-Rong Xu MSc, Zhi-Yong Zou MD, Zi-Xin Wang MSc, Yang-Mu Huang MD and Ying Li MSc

Department of Nutrition and Food Hygiene, School of Public Health, Peking University, Beijing, China

中国人群血清叶黄素水平及叶黄素干预过程中的动态变化趋势

观察性研究结果显示摄取含叶黄素的食品与慢性疾病的患病危险性呈负相关。但是许多研究的结果并不一致，这可能归因于各种混杂因素影响血清叶黄素浓度。本研究目的在于确定影响中国健康人群叶黄素水平的因素，并观察叶黄素干预过程中血清叶黄素的变化趋势。在基线调查后，37名健康受试者被随机分配到6 mg叶黄素组、12 mg叶黄素组或安慰剂组，进行12周的干预试验，并在干预停止后继续观察6周。分别在干预0、1、3、6、9、12和18周采用HPLC法测量血清叶黄素和β-胡萝卜素浓度。采用膳食频率表评价膳食摄入情况。性别之间血清叶黄素浓度未见显著性差异。能量调整后，血清叶黄素浓度与膳食叶黄素、维生素A、维生素C、维生素E、β-胡萝卜素和脂肪的摄入量呈正相关，而与BMI无关。在干预过程中，血清叶黄素浓度在9周达到峰值，在18周返回到基线水平。6 mg叶黄素组和12 mg叶黄素组血清叶黄素浓度分别增长为干预前的1.8倍和2.3倍。干预中未见不良反应及血清β-胡萝卜素的降低。本研究结果显示长期摄取含叶黄素的蔬菜和水果可安全有效地将血清叶黄素浓度维持在较高水平。

关键词：叶黄素、β-胡萝卜素、类胡萝卜素、相互作用、成年人