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Dietary fatty acid determines the intestinal absorption of lutein in lutein deficient mice

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ABSTRACT

The present investigation was undertaken to study the influence of dietary lipids [olive (OO), coconut (CNO), groundnut (GNO), soybean (SBO), sunflower (SFO), rice bran (RBO), corn (CO), palm (PO), fish (FO) oils] on the bioavailability and antioxidant property of lutein in lutein deficient (LD) mice. Lutein (200 μM) was dispersed in dietary lipids and administered to LD mice for a period of 15 days. The plasma lutein levels were found to be highest in OO (82%) and CNO (68%), when compared to the control (mixed micelle) group. Further, positive correlation was found between intestinal triacylglycerol lipase and plasma lutein levels, confirming the crucial role of intestinal lipase on lutein micellarization and its intestinal uptake. Results revealed an affirmative correlation between triglycerides, low density lipoproteins and high density lipoprotein levels with plasma and tissue lutein levels, signifying their role in the transportation of newly absorbed lutein to target tissues. Furthermore, lutein accumulation in the liver and the eye was highest in the OO (120% and 117%) and CNO (105% and 109%) fed groups, compared to control. Lutein deficiency resulted in elevated ($p < 0.05$) levels of lipid peroxides, superoxide dismutase, and catalase in plasma and liver microsomes, which have been decreased significantly on feeding lutein. These results may be due to the influence of oleic (dominant in OO) and lauric (dominant in CNO) acids on the activity of intestinal lipase, portal absorption, triglycerides, lipoprotein or cholesterol flux between liver and peripheral tissues, which may modulate the uptake and transport of lutein.

1. Introduction

Lutein and zeaxanthin are gaining tremendous importance in biomedical and nutritional research as they selectively accumulate in the human macula, where they absorb actinic blue light and prevent peroxidation of lipids in the retina (Bernstein, Delori, Richer, van Kuijk, & Wenzel, 2010). Owing to this reason, they have been associated with reduced risk of age-related macular degeneration (AMD) and cataracts (Krinsky, Landrum, & Bone, 2003), which has drove the interest of the scientific community in the health benefits of these xanthophylls and endorsed their inclusion in various nutritional supplements. However, their biological availability is limited due to their lipophilic nature. Hence, to achieve their optimum health benefits, it is vital to increase their absorption and transportation to their target tissues. Intestinal absorption of lutein is ensured through three key limiting steps: (a) release from the food matrix and transfer into the mixed micelles during digestion in the small intestine; (b) uptake by the enterocytes and (c) enterocyte transport and packaging into the chylomicrons for secretion in the bloodstream via lymph (Yonekura & Nagao, 2007). In all these process, dietary lipids play a crucial role in facilitating the intestinal uptake and transport of lutein demonstrating the importance of lipids in lutein absorption. Hence, it is essential to find a suitable lipid source for enhanced absorption and tissue accumulation of lutein.

Specific dietary lipids and nature of fatty acids therein can differently affect intestinal lutein absorption. Monounsaturated fatty acid (MUFA) rich olive and canola oils increase the intestinal uptake of lutein compared to polyunsaturated (PUFA) or saturated fatty acid (SFA) rich fats in healthy rats and humans (Goltz, Campbell, Chitchumroonchokchai, Failla, & Ferruzzi, 2012; Lakshminarayana, Raju, Keshava Prakash, & Baskaran, 2009). On the contrary, butter and coconut oil, rich in SFA lead to higher bioavailability of lutein and tomato carotenoids, when compared to fats rich in MUFA and PUFA in Caco-2 cells/rats and gerbils, respectively (Conlon, King, Moran, & Erdman, 2012; Gleize et al., 2013). These studies clearly infer paucity of information on the use of a wide spectrum of fatty acids or dietary lipids on lutein uptake in lutein deficient animal models. Thus, it is essential to find a suitable dietary lipid as lutein carrier, more importantly, under lutein deficiency, which predisposes the eyes for macular pigment deficiency.

Abbreviations: AcN, acetonitrile; AMD, age-related macular degeneration; CNO, coconut oil; CAT, catalase; CO, corn oil; DCM, dichloromethane; FO, fish oil; GSH, glutathione; GPx, glutathione peroxidase; GST, glutathione-S-transferase; GNO, groundnut oil; HPLC, high performance liquid chromatography; LD, lutein deficient; MDA, malondialdehyde; MeOH, methanol; MUFA, monounsaturated fatty acids; OO, olive oil; PUFA, polyunsaturated fatty acids; PO, palm oil; RBO, rice bran oil; SFA, saturated fatty acids; SBO, soybean oil; SFO, sunflower oil; SOD, superoxide dismutase.

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Most of the available studies are performed in healthy or lutein sufficient rodent models. The mechanisms that can explain the effect of dietary lipid on the lutein bioavailability remain to be elucidated in animals previously fed on lutein deficient diet. Previously, we have shown that a single oral dose of lutein fed with olive oil significantly enhanced the plasma and tissue response of lutein in lutein deficient mice (Nidhi, Mamatha, & Baskaran, 2014). However, it is necessary to explicate their intestinal handling, plasma appearance and tissue accumulation after repeated gavages of lutein dispersed in dietary lipids and to investigate the role of intestinal triacylglycerol lipase, which hydrolyzes the lipids in which lutein is entrapped. Hence, the aim of the present study is to evaluate the effect of repeated gavages of lutein dispersed in dietary lipids on (1) plasma response and tissue accumulation of lutein; (2) activity of intestinal triacylglycerol lipase; and (3) plasma and tissue fatty acid and lipid profile and to evaluate the effect of lutein on oxidative stress markers resulting from lutein deficiency. The outcome of this study may have implications in the nutritional and biomedical applications for choosing a suitable dietary lipid for improving lutein bioavailability to protect the eyes from progression of AMD and cataract in the elderly population.

2. Materials and methods6

2.1. Chemicals

Standard lutein (99%), oleic acid, mono-oleyl-glycerol, sodium taurocholate, cholesterol, butylated hydroxyl toluene, glutathione reductase (GR), cytochrome C, xanthine oxidase, β-nicotinamide adenine dinucleotide phosphate monohydrate ($NADPH^+$), dinitro-5-thiobenzoic acid, thiobarbituric acid, 1,1,3,3-tetramethoxypropane (TMP), glutathione (reduced and oxidized), and boron trifluoride–methanol solution and fatty-acid standards were purchased from Sigma-Aldrich (St. Louis, USA). Analytical, high-performance liquid chromatography (HPLC) grade solvents and other chemicals mentioned elsewhere in this study were purchased from Sisco Research Laboratories (Mumbai, India). Materials used for preparing synthetic diet like casein, methionine, cellulose, sucrose, mineral mix, vitamin mix, choline bicarbonate were procured from Himedia (Mumbai, India). Fresh marigold flowers, refined olive (OO), groundnut (GNO), sunflower (SFO), soybean (SBO), rice bran (RBO), corn (CO), coconut (CNO), fish (FO) and palm (PO) oils were obtained from a local market.

2.2. Extraction and purification of lutein

Marigold petals were used to extract and purify lutein (Lakshminarayana, Raju, Krishnakantha, & Baskaran, 2005) and the purity of lutein (97 ± 2%) was ascertained by HPLC (described elsewhere in the text) and used for bioavailability study.

2.3. Animals

An animal experiment was conducted after due clearance from the Institutional Animal Ethical Committee (IAEC; 177/10). Weanling male albino mice [OUTB/Swiss Albino IND–CFT (2c)], weighing 25 ± 2 g, were housed in cages in the institute's animal house facility at room temperature (28 ± 2 °C) and followed a 12 h light–dark cycle. Mice had free access to feed (described elsewhere in the text) and water ad libitum.

2.4. Induction of lutein deficiency and experimental design

Mice (n = 88) were fed semi-synthetic diet (AIN, 1977) devoid of lutein for 10 weeks to deplete the stored lutein, and it was ascertained by plasma lutein concentration (1.3 ± 0.5 pmol/mL) (Nidhi et al., 2014). The composition of semi-synthetic diet (g/kg) used to create lutein deficiency was: casein (200), methionine (3), cellulose (50), sucrose (600), mineral mix (35), vitamin mix (10), choline bicarbonate (2) and peanut oil (100). On confirmation of the lutein deficiency, mice were divided into 11 groups (n = 8 per group). Groups 1 to 10 were gavaged pharmacological dose of lutein (200 μM) dispersed in 200 mg of dietary lipids (OO, GNO, SBO, SFO, CO, RBO, CNO, FO or PO) or mixed micelles (control) with no added dietary lipids for 15 days. Group 11 was considered as the lutein deficient (LD) group that received diet devoid of lutein during the experimental run. Mixed micelles (control) in phosphate buffered saline (200 μL) contained mono-oleoyl-glycerol (2.5 mM), oleic acid (7.5 mM), sodium taurocholate (12 mM), cholesterol (0.5 mM), with lutein (200 μM) (Baskaran, Sugawara, & Nagao, 2003). These dietary lipids were selected on the basis of their distinct fatty acid composition. The fatty acid profile of dietary lipids is outlined in Table 1. CNO is rich in SFA which consisted of lauric (53%), myristic (20%) and palmitic (8%) acids, respectively. Olive oil is rich in MUFA like oleic acid (74% of the total fatty acids). The major fatty acids of palm oil are palmitic acid (42%) and oleic acid (42%). Linoleic acid is the major fatty acid present in SFO, CO and SBO as 67%, 54% and 56%, respectively. RBO and GNO contain both oleic

Table 1
Fatty acid profile of dietary lipids used to disperse lutein for repeated gavages to lutein deficient mice.

FA (%)	CNO	OO	PO	SFO	CO	SBO	GNO	RBO	FO
8:0	1.7 ± 0.1^{a}	ND	ND	ND	ND	ND	ND	ND	ND
10:0	6.2 ± 0.2^{a}	ND	ND	ND	ND	ND	ND	ND	ND
12:0	52.7 ± 0.4^{a}	ND	ND	ND	ND	ND	ND	ND	ND
14:0	20.1 ± 0.6^{a}	ND	ND	ND	ND	ND	ND	ND	3.2 ± 0.1^{b}
16:0	7.8 ± 0.3^{a}	13.2 ± 0.3^{ab}	42.1 ± 0.8^{c}	7.2 ± 0.7^{a}	15.4 ± 0.7^{b}	11.5 ± 0.4^{ab}	11.7 ± 0.2^{b}	19.2 ± 0.5^{b}	27.8 ± 0.9^{b}
18:0	1.8 ± 0.2^{a}	4.2 ± 0.1^{b}	4.7 ± 0.2^{b}	2.9 ± 0.1^{a}	1.2 ± 0.2^{a}	3.7 ± 0.1^{ab}	3.2 ± 0.6^{ab}	2.1 ± 0.2^{a}	13.4 ± 0.1^{a}
20:0	ND	0.2 ± 0.0^{a}	0.3 ± 0.0^{a}	ND	0.4 ± 0.0^{a}	0.2 ± 0.0^{a}	2.1 ± 0.2^{b}	1.1 ± 0.1^{b}	ND
22:0	ND	ND	ND	ND	ND	ND	1.9 ± 0.1	ND	ND
SFA	90.3	17.6	47.1	10.1	17	15.4	17	22.4	44.4
18:1	7.4 ± 0.1^{a}	74.4 ± 0.6^{b}	41.7 ± 0.9^{c}	22.8 ± 0.7^{d}	28.5 ± 0.4^{d}	25.6 ± 0.3^{d}	45.5 ± 0.2^{c}	43.4 ± 0.5^{c}	25.1 ± 0.2^{d}
MUFA	7.4	74.4	41.7	22.8	28.5	25.6	45.5	43.4	25.1
18:2	2.3 ± 0.2^{a}	7.3 ± 0.1^{b}	10.8 ± 0.6^{b}	67.1 ± 0.8^{c}	53.7 ± 0.5^{c}	55.9 ± 0.6^{c}	37.5 ± 0.5^{d}	33.8 ± 1.2^{d}	5.6 ± 0.6^{a}
18:3	ND	0.4 ± 0.0^{a}	0.4 ± 0.0^{a}	ND	0.8 ± 0.1^{a}	4.8 ± 0.2^{b}	ND	0.4 ± 0.0^{a}	ND
20:4	ND	ND	ND	ND	ND	ND	ND	ND	1.1 ± 0.1^{a}
20:5	ND	ND	ND	ND	ND	ND	ND	ND	13.0 ± 0.2^{a}
22:6	ND	ND	ND	ND	ND	ND	ND	ND	10.8 ± 0.1^{a}
PUFA	2.3	7.7	11.2	67.1	54.5	60.7	37.5	34.2	30.5

Values are means ± SD (n = 3). Values in rows not sharing a common letter are significantly different ($p < 0.05$) between the groups. ND, not detected; FA, fatty acids. LD, lutein deficient; OO, olive; CNO, coconut; GNO, groundnut; SFO, sunflower; SBO, soybean; RBO, rice bran; CO, corn; PO, palm; FO, fish oils.