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Technical Literature

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THE ROLE OF LUTEIN IN PREGNANCY AND INFANT CARE

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KEY CONCLUSIONS

- *Lutein is present in maternal plasma throughout pregnancy and postpartum.*
- *A diet rich in lutein contributes to elevated plasma lutein levels in pregnant women without a negative impact upon their health or pregnancy.*
- *Lutein is one of the major carotenoids in cord blood, colostrum and breast milk.*
- *FloraGLO® Lutein has been demonstrated to increase infant serum lutein levels, decrease oxidative stress and increase antioxidant capacity, while having no impact on the growth or health of the infant.*
- *International scientific panels have confirmed the safety of FloraGLO Lutein for addition to infant formula.*

INTRODUCTION

Adults can acquire lutein and zeaxanthin either naturally through the diet (35) or through consumption of supplements (23) leading to absorption of these essential nutrients in the body. Increased intake of lutein and zeaxanthin protects the eye through the blue light filtration and antioxidant properties of these nutrients (25, 32). Lutein and zeaxanthin have been detected in the blood of pregnant women and in breast milk where they are transferred to infants suggesting that lutein may impact maternal and newborn eye health (11, 22).

Lutein and zeaxanthin are present in human donor eyes as early as 17-22 weeks of gestation (6, 15). Severe oxidative damage can occur during childhood and higher levels of oxidative stress in the retina during this time have been linked to clinical disorders and disease states.(13, 16). Additionally, the infant retina may be more susceptible to damaging blue light because their lens is more transparent than that of an adult (11, 14). Thus, the young vulnerable eyes could likely benefit from the blue light filtering and antioxidant properties of lutein and zeaxanthin.

Breastfed infants of mothers with balanced nutrition have more lutein in their serum as compared to formula-fed infants (5, 19). In order for formula-fed infants to achieve plasma lutein concentrations comparable to those of breastfed infants whose mothers regularly consume foods rich in lutein, a number of countries have permitted the addition of lutein to infant and follow-on formula. It is estimated that four times more lutein is needed in infant formula than in breast milk to achieve plasma concentrations equivalent to those observed in breast-fed infants (5). FloraGLO® Lutein has been permitted to be added to infant formula, increasingly, worldwide due to its established safety profile and clinically proven eye health benefits.

LUTEIN LEVELS IN MATERNAL PLASMA

Researchers have demonstrated in diverse worldwide populations that circulating maternal plasma lutein is present throughout the course of pregnancy and persists during the postpartum period (**Table 1**).

Mulokozi *et al*. examined plasma lutein levels in 90 pregnant Tanzanian women in their third trimester, 55% of whom reported eating dark green leafy vegetables (DGLV), a lutein-rich source. DGLV consumption resulted in high levels of plasma lutein without adverse impact upon their health or birth outcome (27).

Yamini *et al*. studied 1431 pregnant women from Nepal who received weekly supplements of Vitamin A (7000 μg), β-carotene (42 mg), or placebo (474, 530, and 427 subjects, respectively) before during and after pregnancy (37). While a

number of parameters were measured, the finding most relevant to this summary was that lutein(with zeaxanthin) was the predominant circulating carotenoid both during pregnancy and postpartum periods, representing 63-69% of total carotenoids for all subjects.

Table 1. Concentration of maternal plasma lutein throughout pregnancy and postpartum by study.

Study	1st Trimester (µmol/L)	2nd Trimester (µmol/L)	3rd Trimester (µmol/L)	Postpartum (µmol/L)	Cord (µmol/L)	Cord:PP§ %	N
Yeum, 1998 (38)				0.33 ± 0.05	0.05 ± 0.01	16%	10
Oostenbrug, 1998 (28)	0.48 ± 0.03	0.57 ± 0.03	0.65 ± 0.04	0.64 ± 0.04	0.15 ± 0.02	25%	27-35
Oostenbrug, 1998 (29)			0.64 ± 0.04	0.65 ± 0.04	0.13 ± 0.03	20%	23
Kiely, 1999 (21)	0.46 ± 0.2*				0.13 ± 0.1*		40-66
Lan, 1999 (22)		0.65 (0.43-0.98)*					882
Yamini, 2001 (37)		0.45 ± 0.30*		0.35 ± 0.24*			227-334
Zhang, 2001 (39)			0.35 ± 0.011				179
Williams, 2003 (36)			0.38 ± 0.20				186
Mulokozi, 2003 (27)			1.6 (1.0–2.5)				87
Schweigert, 2004 (34)				0.35 ± 0.09			21
Mathews, 2005 (26)		0.47 ± 0.18					771

§Percentage of the concentration of lutein in infant cord blood as compared to the concentration of lutein in postpartum maternal blood
*Value includes zeaxanthin in addition to lutein
N = the number of women in the study

LUTEIN LEVELS IN INFANT CORD BLOOD

A number of other studies have compared the concentration of lutein in maternal blood to the concentration found in cord blood. Oostenbrug *et al*. performed two independent studies on the subject. The first study analyzed antioxidant concentrations in plasma from 35 women during the first, second and third trimesters of pregnancy, as well as postpartum, as compared to cord blood concentrations upon delivery (28). Lutein was found to be the most abundant carotenoid tested in both the postpartum mother's blood and cord blood. Lutein levels in maternal blood increased steadily from the first to the third trimester and remained elevated after delivery. The lutein concentration in cord blood was approximately 25% of the lutein concentration in the postpartum mother's blood.

Yeum *et al*. observed similar results in 10 healthy women between 24 and 28 weeks gestation (38). In this study, lutein was the third highest carotenoid in the postpartum mother's plasma and second highest in the cord blood. There was a high correlation between maternal plasma lutein concentrations and cord plasma concentrations.

Kiely *et al*. studied 66 women between weeks 10 and 20 of gestation (21). Levels of lutein + zeaxanthin in maternal and cord blood were similar to results from the Oostenbrug study. Lutein + zeaxanthin had the highest concentration of the carotenoids analyzed in both the maternal blood and cord blood. Lutein + zeaxanthin concentration in the cord blood was approximately 28% of that of the maternal blood.

Lastly, a second Oostenbrug study compared carotenoid concentrations in plasma samples from 23 women with mild pregnancy induced hypertension and 23 normotensive women in the third trimester and postpartum (29). In the third trimester, antioxidant levels were similar between hypertensive and control groups. Lutein had the highest concentration of all carotenoids tested in both groups. However, from the third trimester to postpartum, there was a significant decrease in lutein levels in the hypertensive mothers as compared to normotensive mothers. No significant difference was observed in cord blood lutein levels between the hypertensive and control groups.

LUTEIN LEVELS IN BREAST MILK

Lutein and zeaxanthin in human colostrum were first detected in 1990 by Patton and colleagues (30). This group analyzed the colostrum of 11 women within 6 days after delivery and discovered that colostrum contains lutein, zeaxanthin, β-carotene, lycopene, and β-cryptoxanthin. Levels of these carotenoids in milk were later quantified by Khachik *et al*. in 1997 (20). Khachik's group analyzed breast milk and serum carotenoid concentration of three women after one month postpartum. Of the carotenoids found, lutein had the third highest concentration in the serum and the second highest in breast milk. Lutein was two to three times as concentrated as β-carotene in breast milk, whereas their concentration was approximately the same in maternal plasma. This finding led to the hypothesis that lutein may be actively secreted into milk.

Several studies have also tracked the concentration of lutein in milk over a course of several months after birth. Gossage *et al*. showed that lutein and zeaxanthin represented 25% of total milk carotenoids on day 4 postpartum and increased to 50% on day 32 postpartum in 50 women, while plasma lutein and zeaxanthin concentrations decreased and dietary lutein and zeaxanthin intake remained unchanged (12). A number of other groups have detected lutein and zeaxanthin in colostrum and breast milk across diverse populations worldwide (7-9, 17, 24, 34).

FLORAGLO® LUTEIN ADDITION TO INFANT FORMULA

Breast milk contains at least 300 defined nutrients, of which only 60-70 nutrients are included in most infant formulas (18). Because only half of U.S. infants are exclusively breastfed at birth, according to the American Academy of Pediatrics, many formula-fed infants may not be provided all of the nutrients found in breast milk (1). Lutein is not often added to infant formula which may results in low plasma lutein levels in formula-fed infants. For example, Johnson *et al.* demonstrated that breastfed infants and formula-fed infants had the same levels of plasma lutein at birth. However, after one month, plasma lutein increased significantly for the breastfed infants and decreased in the formula-fed infants (19). Any long-term effects this deprivation has upon eye development and health is unclear at this time.

To date, four studies have evaluated the impact of lutein consumption on serum lutein levels, safety, growth, oxidative stress and antioxidant activity in infants. Romagnoli and colleagues evaluated plasma lutein and zeaxanthin levels after oral administration of FloraGLO Lutein in ten preterm infants (mean age: 1.7 weeks) (33). FloraGLO Lutein was administered by nasogastric tube in a single dose of 0.5 mg/kg. Blood was drawn soon before lutein administration and 6, 24, 48 and 120 hours thereafter. Lutein was well tolerated and no adverse events were observed during the study period. Baseline plasma concentrations of lutein and zeaxanthin were 0.361 μmol/L and 0.126 μmol/L likely due to transfer from the mother to the fetus. Concentrations of lutein in plasma increased 13.5% 6 hours after lutein administration and 16.7%

at 24 hours. It decreased to almost baseline levels (0.373 μmol/L) at 120 hours. Plasma lutein concentrations increased in all infants evaluated while zeaxanthin concentrations remained unchanged during the course of the study.

Bettler *et al*. conducted a prospective, double-blind trial in 26 healthy term infants (9 to 16 days old) (5). These infant received lutein-fortified formula at doses of 20 (unfortified), 45, 120 and 225 mg FloraGLO Lutein per liter of infant formula over the course of four weeks. Results from the formula-fed infants were compared to a group of breastfed infants (n = 14). At baseline, breast-fed infants had higher serum lutein concentrations (81 mg/L) than all formula-fed infants (13 mg/L). After 12 weeks of feeding, the breast-fed infants had a six-fold higher serum lutein concentration as compared to infant fed unfortified formula. A positive, linear relationship was observed between lutein concentrations in the infant serum and the amount of lutein in the formula. The results indicate that approximately four times more lutein is needed in formula to achieve similar serum lutein concentrations as found in breast-fed infants. Infant growth was within normal limits and no adverse events related to the formula were reported.

A study published in 2010 specifically evaluated the impact of lutein-fortified formula on infant growth and safety (10). This study was conducted in 240 healthy term Asian infants 14 days old or younger who received either formula fortified with 200 mg FloraGLO Lutein per liter of infant formula or unfortified formula for 16 weeks. During this time, formula intake was comparable between the two groups and growth was equivalent between the two groups and comparable to that of the mean of a US reference population. Additionally, there were no relevant differences in blood chemistry or incidence of clinical study events between the two groups.

Perrone *et al.* examined the effects of lutein on oxidative stress in infants in a study published in 2010 (31). This randomized, double-blind comparative study was conducted in 20 healthy term infants who received a liquid supplement containing FloraGLO Lutein (0.28 mg) or a control supplement at 12 and 36 hours after birth. Blood was drawn immediately after birth and at 48 hours after birth and analyzed for biological antioxidant potential (BAP) and total hydroperoxides (TH). There was no difference in BAP and TH between the two groups at birth. TH significantly increased from birth to 48 hours in the infants fed control formula ($p = 0.023$) while no increase was observed in the group fed lutein-containing formula. BAP significantly increased in the lutein group from birth to 48 hours ($p = 0.028$) with no corresponding increase in the infants fed control formula. These results indicate that lutein-containing formula can reduce oxidative stress and protect against oxidation in newborn infants. The authors also noted that no adverse events were observed during the study.

SAFETY OF FLORAGLO LUTEIN IN INFANT FORMULA

The safety of Kemin Food, L.C.'s ("Kemin's") FloraGLO Lutein for use in certain foods and beverages has been evaluated by an expert panel of independent scientists who are qualified by relevant national and international experience, as well as by respective scientific training. Upon evaluation, FloraGLO Lutein was determined to be Generally Recognized as Safe (GRAS) for the intended uses. These self-determinations formed the basis for Kemin's 2004 GRAS Notification to the FDA. The GRAS status of FloraGLO Lutein allows it to be added to certain foods and beverages in order to increase the dietary intake of total lutein and zeaxanthin. The foods in the intended uses include junior, strained, and toddler-type baby foods such as fruits, fruit juices, meats, vegetables, soups, desserts, yogurts, cereals, pastas, sauces, cookies, toast, pretzels, crackers, and egg yolk at levels of 1.0 mg/RACC (reference amounts customarily consumed per eating occasion).

In 2007, Kemin assembled an additional dossier evaluating the safety of FloraGLO Lutein 20% Liquid in Safflower Oil for use in infant formula and submitted it to an Expert Panel, which found the ingredient to be GRAS under its intended conditions of use. A GRAS notification was submitted to the FDA, and Kemin received a subsequent letter of no objection. This GRAS determination supports the safety of Kemin's FloraGLO Lutein 20% Liquid in Safflower Oil for its

use in term infant formula in the United States at concentrations up to 250 µg lutein/L. Most recently, scientific experts evaluated the equivalence of DSM Nutritional Products Ltd.'s FloraGLO Lutein 20% Safflower Oil to the Kemin FloraGLO Lutein 20% Safflower Oil Ingredient and determined that the GRAS determination for the Kemin FloraGLO Lutein 20% Safflower Oil ingredient for use in infant formula is applicable to the DSM FloraGLO Lutein 20% Safflower Oil ingredient for the same infant formula food application.

The European Food Safety Authority (EFSA) acts as an independent source of scientific advice and opinions in the assessment of food and feed safety, nutrition, animal health and welfare, plant protection and plant health. Their evaluation supplies the European Commission with a foundation for subsequent policies and legislation. Recently, the EFSA panel on Dietetic Products, Nutrition and Allergies delivered a scientific opinion on the safety and bioavailability of lutein for the particular nutritional use by infants and young children (4). The Panel concluded that lutein is bioavailable in infant and follow-on formula (formula specially designed for infants older than four months) and there is no safety concern about lutein at the levels achieved through the natural content of ingredients nor at the level of use (a concentration of added lutein of 250 µg/L) proposed for infant formula with a low natural lutein content (about 20 µg/L or lower). The EFSA full opinion can be found at http://www.efsa.europa.eu/cs/BlobServer/Scientific_Opinion/nda_op_ej823_lutein_summary_en.pdf?ssbinary=true. It is noted that EFSA's opinion is specific to purified lutein made according to the specifications described in Kemin's FloraGLO Lutein Liquid in Safflower Oil.

There have been a number of other regulatory agencies and groups worldwide that have evaluated the use of lutein in infant formula. Food Standards Australia New Zealand (FSANZ), a bi-national government agency which sets food standards for the two countries, has permitted the voluntary addition of lutein as a nutritive substance in infant formula products at a maximum concentration of 250 µg lutein/L (2). The Codex Alimentarius Commission was established by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) to develop food standards, guidelines, and related texts. In late 2007, Codex proposed to add lutein to its draft revision of the advisory list of nutrient compounds for use in foods for special dietary uses intended for infants and young children (3). In China, lutein is permitted to be added as a "nutrition fortifier" to infant formula and follow-on formula, as well as formula for young children and preschoolers. The maximum permitted levels of lutein in infant formula and follow-on formula are 260 µg lutein/L and 570 µg lutein/L of powdered product, respectively. Overall, permitting the addition of lutein to infant formula will provide a net-benefit and provide formula-fed infants with a source of lutein, a substance naturally present in breast milk.

CONCLUSIONS

The association of high dietary lutein and zeaxanthin intake and the levels occurring naturally in maternal fluids during pregnancy has been demonstrated in research across diverse worldwide populations. Lutein increases in the plasma of women throughout pregnancy and can be found in cord blood postpartum and in both colostrum and mature breast milk where it is naturally available to newborns.

Dietary lutein has been safely consumed during pregnancy, and has not been found to be associated with incidence of pregnancy-related diseases or complications. However, women should consult their physician before taking lutein supplements or any vitamin and dietary supplement during pregnancy or lactation.

Lutein is one of the nutrients found in breast milk that is increasingly being added to infant formula, worldwide. The four clinical studies to date that have tested lutein supplementation in infants with respect to safety, serum lutein concentrations and antioxidant capacity have all utilized FloraGLO brand Lutein. The safety of FloraGLO Lutein for use in infant formula and baby foods has been evaluated and deemed suitable for such use by the regulatory authorities in the

US and EU. In the US, Kemin has obtained a non-objection letter from the FDA for its GRAS status for the use of FloraGLO Lutein in junior- and toddler-type baby foods as well as infant formula. In addition, Kemin's FloraGLO Lutein 20% Liquid in Safflower Oil obtained GRAS status for its use in term infant formula up to 250 µg lutein/L. In Europe, based on the European Food Safety Authority determination, FloraGLO Lutein is deemed to be bioavailable and safe for use in infant and follow-on formula at a level up to 250 µg lutein/L. The benefit of adding lutein to foods consumed by infants and young children has been recognized internationally by the Codex Alimentarius Commission, and lutein has been approved for addition to infant formula in countries such as China, Australia, and New Zealand. Infants that are not breast-fed may benefit from receiving lutein from dietary sources such as formula in order to achieve serum lutein concentrations that are nutritionally equivalent to the amount of lutein found naturally in breast milk.

REFERENCES

1. Breastfeeding and the Use of Human Milk. *Pediatrics* 115: 496-506, 2005.
2. Food Standards Australia New Zealand: Addition of Lutein as a Nutritive Substance to Infant Formula http://www.foodstandards.gov.au/_srcfiles/A594%20Lutein%20FAR%20FINAL.pdf.
3. Proposed Draft Revision of the Advisory List of Nutrient Compounds for use in Foods for Special Dietary uses Intended for Infants and Young Children. Codex Committee on Nutrition and Foods for Special Dietary Uses. ftp://ftp.fao.org/codex/ccnfsdu29/nf29_05e.pdf.
4. Scientific Opinion of the Panel on Dietetic Products Nutrition and Allergies on a request from the European Commission of the 'suitability of lutein for the particular nutritional use by infants and young children'. *The EFSA Journal* 823: 1-24, 2008.
5. Bettler J, Zimmer JP, Neuringer M, and Derusso PA. Serum lutein concentrations in healthy term infants fed human milk or infant formula with lutein. *Eur J Nutr* 2009.
6. Bone RA, Landrum JT, Fernandez L, and Tarsis SL. Analysis of the macular pigment by HPLC: retinal distribution and age study. *Invest Ophthalmol Vis Sci* 29: 843-849, 1988.
7. Canfield LM, Clandinin MT, Davies DP, Fernandez MC, Jackson J, Hawkes J, Goldman WJ, Pramuk K, Reyes H, Sablan B, Sonobe T, and Bo X. Multinational study of major breast milk carotenoids of healthy mothers. *Eur J Nutr* 42: 133-141, 2003.
8. Canfield LM, Giuliano AR, Neilson EM, Blashil BM, Graver EJ, and Yap HH. Kinetics of the response of milk and serum beta-carotene to daily beta-carotene supplementation in healthy, lactating women. *Am J Clin Nutr* 67: 276-283, 1998.
9. Canfield LM, Taren DL, Kaminsky RG, and Mahal Z. Short-term beta-carotene supplementation of lactating mothers consuming diets low in vitamin A. *J Nutr Biochem* 10: 532-538, 1999.
10. Capeding R, Gepanayao CP, Calimon N, Lebumfacil J, Davis AM, Stouffer N, and Harris BJ. Lutein-fortified infant formula fed to healthy term infants: evaluation of growth effects and safety. *Nutr J* 9: 22, 2010.
11. Dillon J, Zheng L, Merriam JC, and Gaillard ER. Transmission of light to the aging human retina: possible implications for age related macular degeneration. *Exp Eye Res* 79: 753-759, 2004.
12. Gossage CP, Deyhim M, Yamini S, Douglass LW, and Moser-Veillon PB. Carotenoid composition of human milk during the first month postpartum and the response to beta-carotene supplementation. *Am J Clin Nutr* 76: 193-197, 2002.
13. Granot E, and Kohen R. Oxidative stress in childhood--in health and disease states. *Clin Nutr* 23: 3-11, 2004.
14. Hammond BR. The retina as a nutritionally responsive tissue. *Aging Health* 3: 585-588, 2007.
15. Handelman GJ, Dratz EA, Reay CC, and van Kuijk JG. Carotenoids in the human macula and whole retina. *Invest Ophthalmol Vis Sci* 29: 850-855, 1988.
16. Hardy P, Dumont I, Bhattacharya M, Hou X, Lachapelle P, Varma DR, and Chemtob S. Oxidants, nitric oxide and prostanoids in the developing ocular vasculature: a basis for ischemic retinopathy. *Cardiovascular research* 47: 489-509, 2000.
17. Jackson JG, and Zimmer JP. Lutein and zeaxanthin in human milk independently and significantly differ among women from Japan, Mexico, and the United Kingdom. *Nutrition Research* 27: 449-453, 2007.
18. Jensen RG, and Thompson MP editors. *Handbook of Milk Composition*. New York: Academic Press, 1995.
19. Johnson L, Norkus E, Abbasi S, Gerdes JS, and Bhutani VK. Contribution of Beta Carotene (βC) from βC Enriched Formulae to individual and Total Serum Carotenoids in Term Infants. *104th Annual Meeting of the*

American Pediatric Society and the 63rd Annual Meeting of the Society for Pediatric Research 1994. Abstract 1869.

20. Khachik F, Spangler CJ, Smith JC, Jr., Canfield LM, Steck A, and Pfander H. Identification, quantification, and relative concentrations of carotenoids and their metabolites in human milk and serum. *Anal Chem* 69: 1873-1881, 1997.
21. Kiely M, Cogan PF, Kearney PJ, and Morrissey PA. Concentrations of tocopherols and carotenoids in maternal and cord blood plasma. *Eur J Clin Nutr* 53: 711-715, 1999.
22. Lan Y, Kumwenda N, Taha TE, Chiphangwi JD, Miotti PG, Mtimavalye L, Broadhead R, van der Hoeven L, Hoover DR, and Semba RD. Carotenoid status of pregnant women with and without HIV infection in Malawi. *East Afr Med J* 76: 133-137, 1999.
23. Landrum JT, Bone RA, and Kilburn MD. The macular pigment: a possible role in protection from age-related macular degeneration. *Adv Pharmacol* 38: 537-556, 1997.
24. Lietz G, Mulokozi G, Henry JC, and Tomkins AM. Xanthophyll and hydrocarbon carotenoid patterns differ in plasma and breast milk of women supplemented with red palm oil during pregnancy and lactation. *J Nutr* 136: 1821-1827, 2006.
25. Mares-Perlman JA, Millen AE, Ficek TL, and Hankinson SE. The body of evidence to support a protective role for lutein and zeaxanthin in delaying chronic disease. Overview. *J Nutr* 132: 518S-524S, 2002.
26. Mathews F, and Neil A. Antioxidants and preterm prelabour rupture of the membranes. *BJOG* 112: 588-594, 2005.
27. Mulokozi G. Plasma levels of retinol, carotenoids, and tocopherols in relation to dietary pattern among pregnant tanzanian women. *Int J Vitam Nutr Res* 73: 323-333, 2003.
28. Oostenbrug GS, Mensink RP, Al MD, van Houwelingen AC, and Hornstra G. Maternal and neonatal plasma antioxidant levels in normal pregnancy, and the relationship with fatty acid unsaturation. *Br J Nutr* 80: 67-73, 1998.
29. Oostenbrug GS, Mensink RP, van Houwelingen AC, Al MD, and Hornstra G. Pregnancy-induced hypertension: maternal and neonatal plasma lipid- soluble antioxidant levels and its relationship with fatty acid unsaturation. *Eur J Clin Nutr* 52: 754-759, 1998.
30. Patton S, Canfield LM, Huston GE, Ferris AM, and Jensen RG. Carotenoids of human colostrum. *Lipids* 25: 159-165, 1990.
31. Perrone S, Longini M, Marzocchi B, Picardi A, Bellieni CV, Proietti F, Rodriguez A, Turrisi G, and Buonocore G. Effects of Lutein on Oxidative Stress in the Term Newborn: A Pilot Study. *Neonatology* 97: 36-40, 2010.
32. Ribaya-Mercado JD, and Blumberg JB. Lutein and zeaxanthin and their potential roles in disease prevention. *J Am Coll Nutr* 23: 567S-587S, 2004.
33. Romagnoli C, Tirone C, Persichilli S, Gervasoni J, Zuppi C, Barone G, and Zecca E. Lutein absorption in premature infants. *Eur J Clin Nutr* 64: 760-761, 2010.
34. Schweigert FJ, Bathe K, Chen F, Buscher U, and Dudenhausen JW. Effect of the stage of lactation in humans on carotenoid levels in milk, blood plasma and plasma lipoprotein fractions. *Eur J Nutr* 43: 39-44, 2004.
35. Seddon JM, Ajani UA, Sperduto RD, Hiller R, Blair N, Burton TC, Farber MD, Gragoudas ES, Haller J, Miller DT, and et al. Dietary carotenoids, vitamins A, C, and E, and advanced age-related macular degeneration. Eye Disease Case-Control Study Group. *Jama* 272: 1413-1420, 1994.
36. Williams MA, Woelk GB, King IB, Jenkins L, and Mahomed K. Plasma carotenoids, retinol, tocopherols, and lipoproteins in preeclamptic and normotensive pregnant Zimbabwean women. *American journal of hypertension* 16: 665-672, 2003.
37. Yamini S, West KP, Jr., Wu L, Dreyfuss ML, Yang DX, and Khatry SK. Circulating levels of retinol, tocopherol and carotenoid in Nepali pregnant and postpartum women following long-term beta-carotene and vitamin A supplementation. *Eur J Clin Nutr* 55: 252-259, 2001.
38. Yeum KJ, Ferland G, Patry J, and Russell RM. Relationship of plasma carotenoids, retinol and tocopherols in mothers and newborn infants. *J Am Coll Nutr* 17: 442-447, 1998.
39. Zhang C, Williams MA, Sanchez SE, King IB, Ware-Jauregui S, Larrabure G, Bazul V, and Leisenring WM. Plasma concentrations of carotenoids, retinol, and tocopherols in preeclamptic and normotensive pregnant women. *Am J Epidemiol* 153: 572-580, 2001.