Oryza

ORYZA OIL & FAT CHEMICAL CO., LTD.

LUTEIN

AMD Prophylaxis
Cataract Prophylaxis
Anti-Oxidative Effect

- **LUTEIN**-P80, -P40
  (Powder, For food)
- **LUTEIN**-L8
  (Liquid, For food)
- **LUTEIN**-PC80, -PC40
  (Powder, For cosmetic)
- **LUTEIN**-LC8
  (Liquid, For cosmtic)

ORYZA OIL & FAT CHEMICAL CO., LTD.

ver. 3.2 YF

L U T E I N

For eye care and anti-oxidant

1. Introduction

IT (Information Technology) is becoming a popular term. In fact, children of school years could not learn without personal computers. They access internet daily via personal computers or cellular phones, and spend more time gazing for illuminated monitors. It is a hard time for eye health.

It is not the case of youngsters. Most people work in offices are obliged to VDT operation for a long time. Gazing for bright monitor is actually heavy stuff for eyes, especially for macula in eyeballs. Macula is a very sensitive part in retina (Figure 1), and works when you look something carefully. Patients with **age-related macular degeneration (AMD)** are growing in number, which may due to environment surrounding with computers or televisions. In European and North American countries, AMD is the most probable cause of vision loss, survey says.

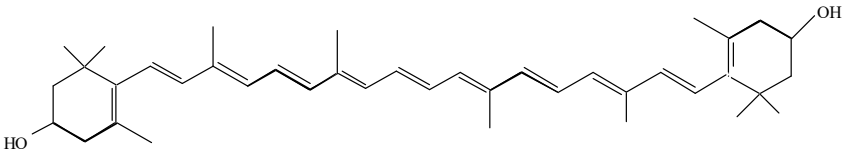
Introduced to you here is a product lineup, rich in lutein and zeaxanthin from marigold flowers, for your healthy life with your eyes.

2. Lutein and Zeaxanthin

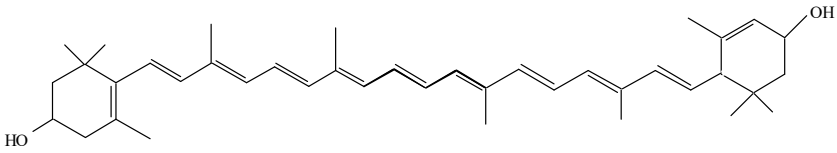
Lutein is a member of xanthophyll, a subgroup of carotenoid, which possesses strong anti-oxidative properties. Zeaxanthin is also a xanthophyll, and always coexists with lutein. Lutein and zeaxanthin are contained in vegetables of dark-green, such as spinach and keel.

3. Structures of Lutein and Zeaxanthin

1) Structures



Lutein



Zeaxanthin

2) Molecular formula

	Molecular formula	Molecular weight	Melting point
Lutein	$C_{40}H_{56}O_2$	568.88	190 ºC
Zeaxanthin	$C_{40}H_{56}O_2$	568.88	207 ºC

4. To Avoid Age-Related Macular Degeneration

Prevention of AMD and cataract

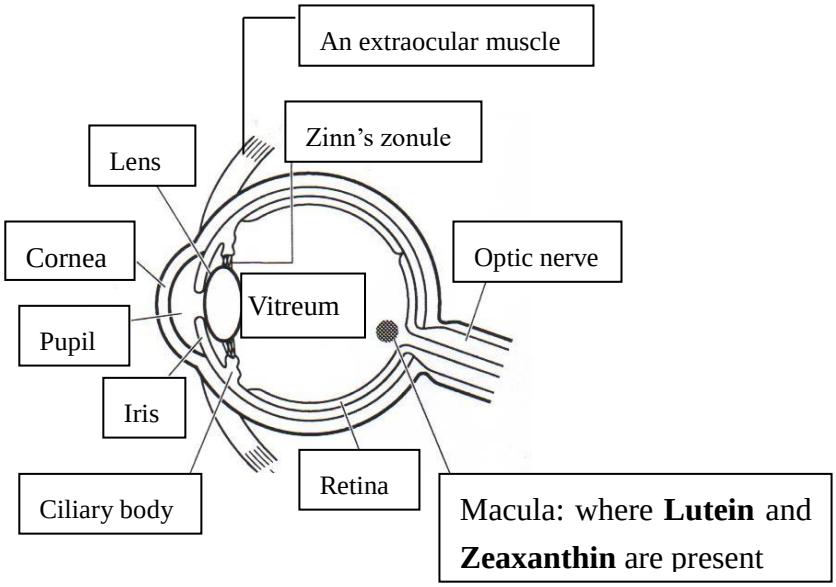


Figure 1. Anatomy of the eye

Cataracts and retinal detachment are disorders of the eye associated with aging, but age-related macular degeneration (AMD) is increasing in recent years.

AMD firstly occurs in one eye. As it gets worse, the center of sight becomes blurring, but it is hardly recognized because it progresses very slowly without pain. Sometimes it leads to blindness. No effective treatment has been established so far, neither surgical nor chemical procedures. Therefore, prevention or delaying progression is recognized as important.

Researches suggest that oxidative degeneration of cells in macula triggers AMD, which increases as lutein decreases in the macular region with aging.

5. Bioavailability of Lutein Esters

Fats are digested (hydrolyzed) to fatty acids and glycerol, which are absorbed to blood. It is in the same manner that lutein esters are digested and absorbed. Certain enzymes called *esterases* or *lipases* work for both fat and ester digestion. The enzymatic activity is regulated by fat in stomach and duodenum, so it is reported that bioavailability of lutein esters is enhanced by fat in foods (Berendschot et al. 2000).

Lutein Ester → Free Lutein → Free Lutein in Serum

Bioavailability of lutein esters, in other words, time-course of plasma lutein level when lutein esters are taken, is a major interest of many neutriceutical researchers. Figure 2 shows the lutein assimilation in blood plasma (Berendschot et al. 2000, Granado et al. 1998, Landrum et al. 1997). From these reports, it could say:

1) Lutein level in plasma sheered in a relatively short time (7-10 days).
2) Lutein level in plasma depends on the dose.
3) Lutein remains at its highest level as long as supplementation is continued.
4) Once supplementation stop, basal levels of lutein are reached in a period 15 to 20 days.

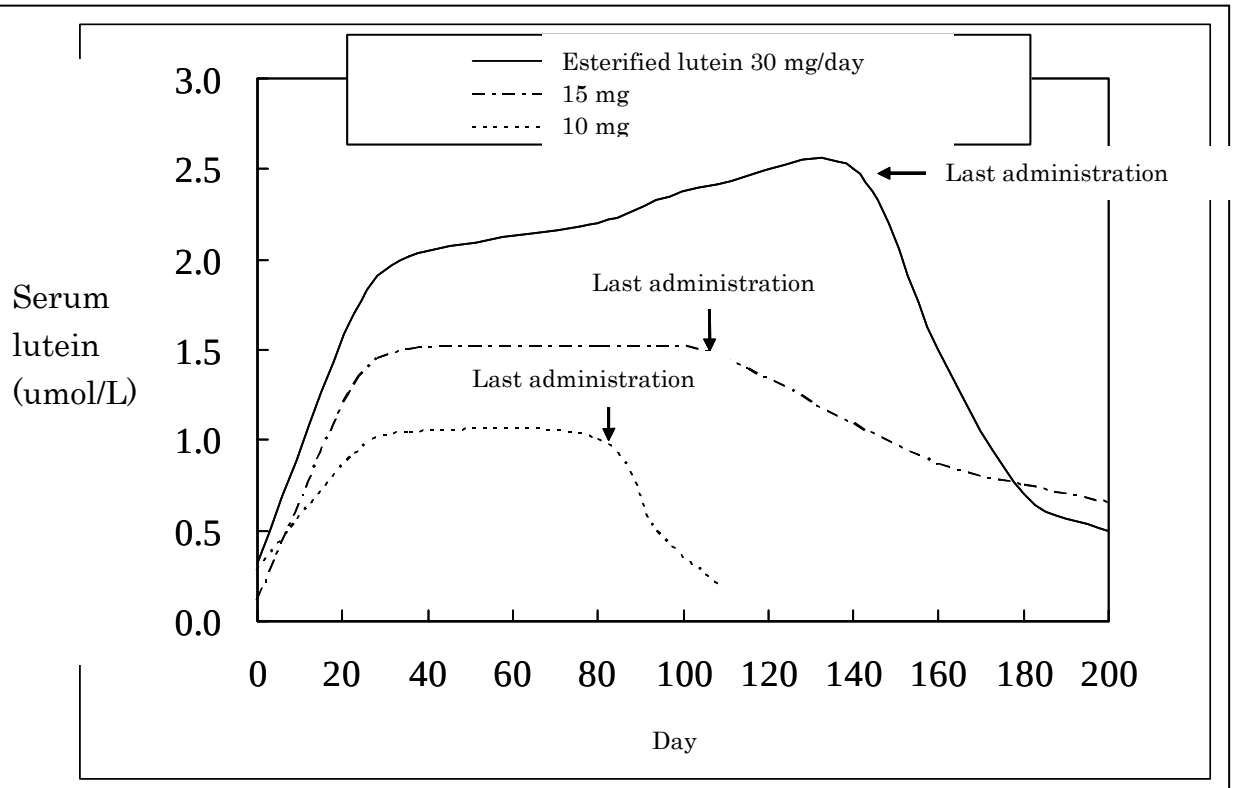


Figure 2. Metabolism and absorption of esterified lutein

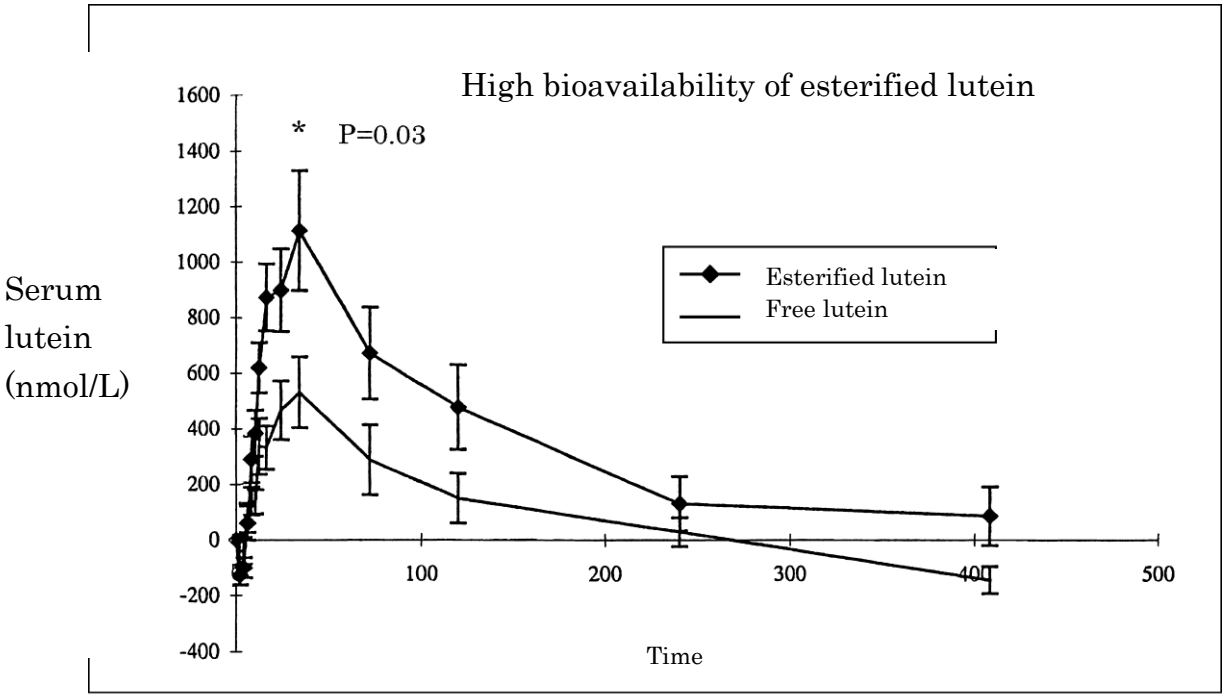
The curve in short broken line corresponds to the results reported by Berendschot where eight subjects took a daily dose of 10 mg of (as lutein esters) for a period of 84 days (Berendschot et al. 2000).The curve in long broken line corresponds to Granado's study where subject supplemented their diets with 15 mg of lutein (in the form of lutein esters) per day for a period of 112 days (Granado et al. 1998)The line curve corresponds to Landrum's study where 2 subjects supplemented their diets with 30 mg of lutein (in the form of lutein esters) per day for a period of 140 days (Landrum et al. 1997)

Literature: Berendschot *et al., LOVS,* **41**, 3322-3326, 2000.
Granado *et al., Br. J. Nutr.,* **80**, 445-449, 1998.
Landrum *et al., Exp. Eye Res.,* **65**, 57-62, 1997.

6. Lutein vs. Lutein Esters in Bioavailability

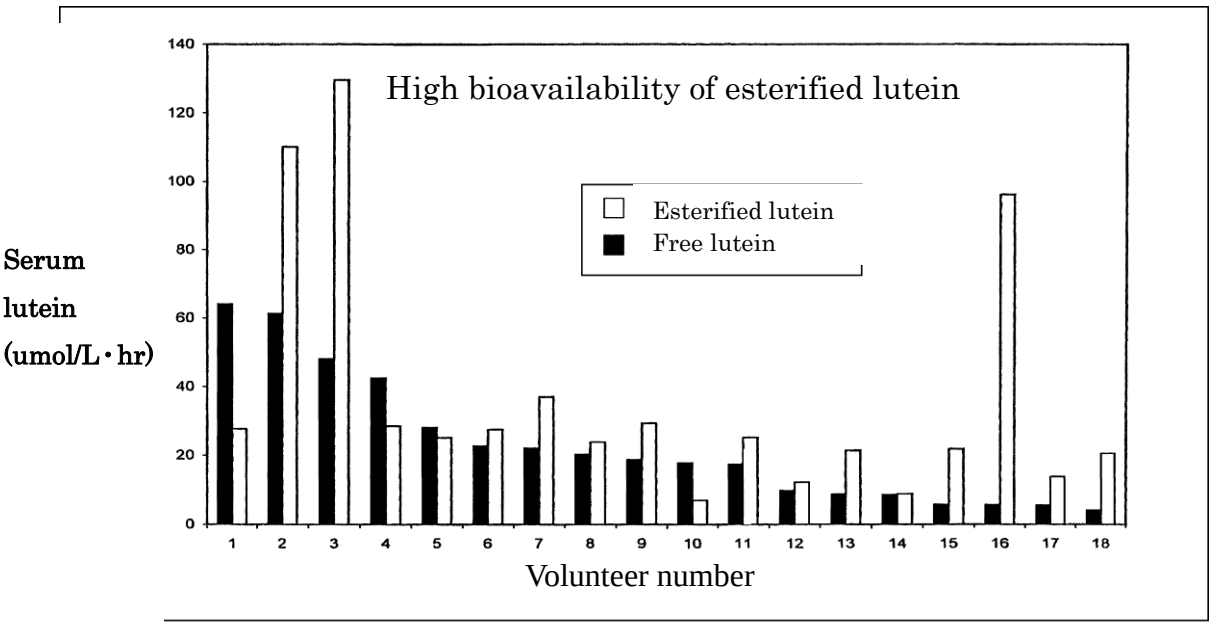
Serum lutein level lutein from the lutein diester formulation appeared in the peripheral circulation more quickly than the free lutein, and attained a higher peak concentration.

Mean serum lutein level reached the peak at 32 hours after dose, but had considerable variation among subjects. The peak concentration of lutein diesters is doubled that of free lutein (Figure 3). In addition, AUC (area under curve) comparison of free and ester-form lutein revealed that AUC of ester-form was greater in 14 in 18 subjects (Figure 4). The mean AUC from 0 to 408 hours of lutein diesters was 61.6% greater than that of free lutein. **Data above clearly show that lutein diesters are superior to free lutein in bioavailability.**



Phylips E. Bowen *et al., J. Nutr.* **132**. 3668-3673 (2002)

Figure 3



Phylips E. Bowen *et al., J. Nutr.* **132**. 3668-3673 (2002)

Figure 4

7. Lutein vs. Lutein Esters in Bioavailability
Lutein Esters as Lutein – P80 (Original Data)

7-1. Animal Test (Fasting)

An animal test under fasting condition revealed that serum lutein level reached maximum at four hours after lutein intake, in both cases of free and ester form. The maximum concentration was 82 nmol/L in lutein esters while 43 nmol/L in free lutein, suggesting that **absorption of lutein esters is doubled** that of free lutein. The mean AUC from 0 to 10 hours was 350.5 nmol/L·h in lutein esters while 195.1 nmol/L·h in free lutein, suggesting that **bioavailability of lutein esters is 1.8 times higher**.

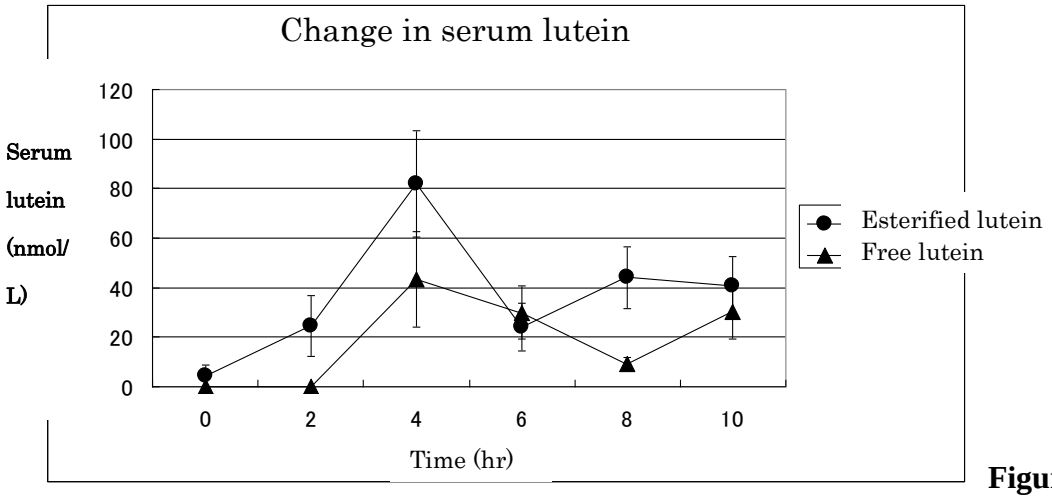


Figure 5

[Method]

Six-week old mice, fasted for 20 hours, were given 10 mL/kg of olive oil containing either 100 mg of lutein – P80 (esters) or 200 mg of 20% emulsified free lutein in 10 mL, equivalent to 40 mg/kg as free lutein.

7-2. Animal Test (Fed)

An animal test under fed condition revealed that serum lutein level reached maximum at two hours after Lutein – P80 intake and six hours after free lutein intake. Compared with absorption under fasting condition, lutein esters were found to be absorbed faster while free lutein slower. The maximum concentration was 57.4 nmol/L in lutein esters while 26.3 nmol/L in free lutein, suggesting that **absorption of lutein esters is more than twice larger** than that of free lutein in the ester case. Comparing the lutein levels at two hours after intake, the lutein level was more than four times larger. The mean AUC from 0 to 10 hours was 350.4 nmol/L·h in lutein esters while 167.4 nmol/L·h in free lutein, suggesting that **bioavailability of lutein esters is also more than twice higher**.

These results clearly showed the effectiveness of taking lutein in ester form in which form lutein exists naturally.

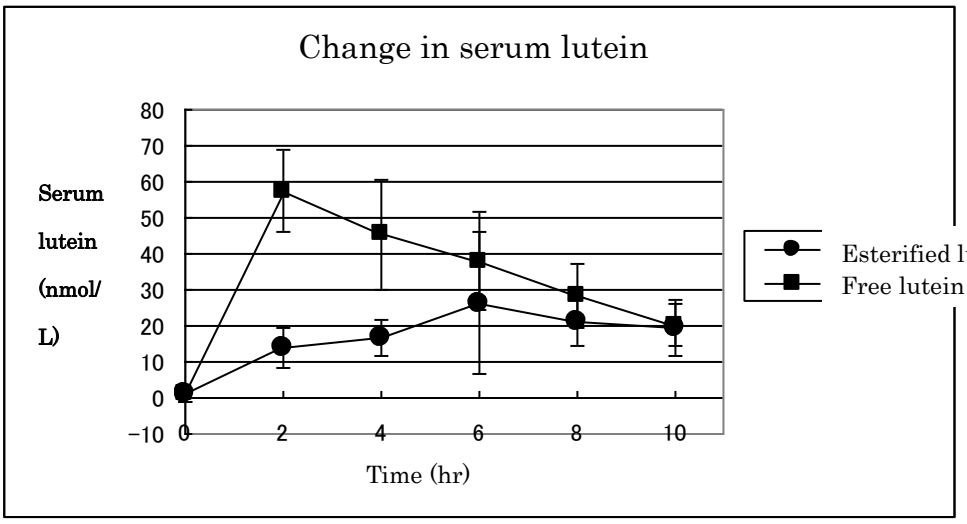


Figure 6

7-3. Human Study

We compared absorptive ability of esterified lutein to free lutein. The serum concentration of lutein given esterified lutein reached to maximum at 24 to32 hr later. On the other hand, the serum concentration of lutein given free were varied and maximu times were 10 to 32 hr later. The average of serum lutein is illustrated in Figure 7. At 32 hr later of consumption of lutein, serum lutein of esterified lutein group was 5.8 times higher than that of free lutein group. The AUC (Area under the concentration) of esterified lutein group was 6 times

larger than that of free lutein group. Hence esterified lutein was found to posses higher bioavailability than free lutein.

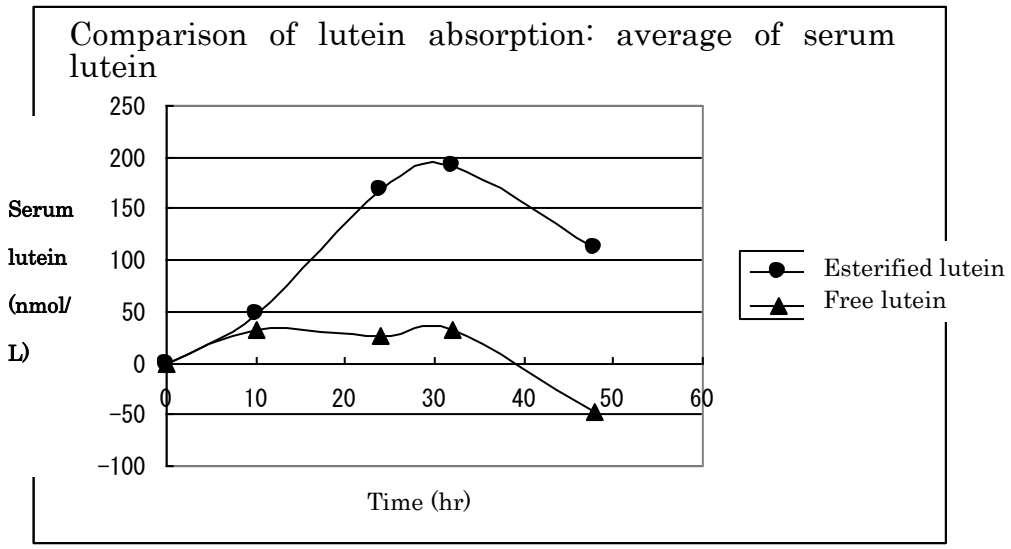


Figure 7

【Method】

① Both lutein (equivalent to 9 mg free lutein) was given with water. LUTEIN-P80 (19.7 mg) was used as esterified lutein and it was packed in a capsule with rice oil (200 mg). 20% Free lutein suspention (45.2 mg) suspendednin 200 mg of rice oil was also packed in a capsule.

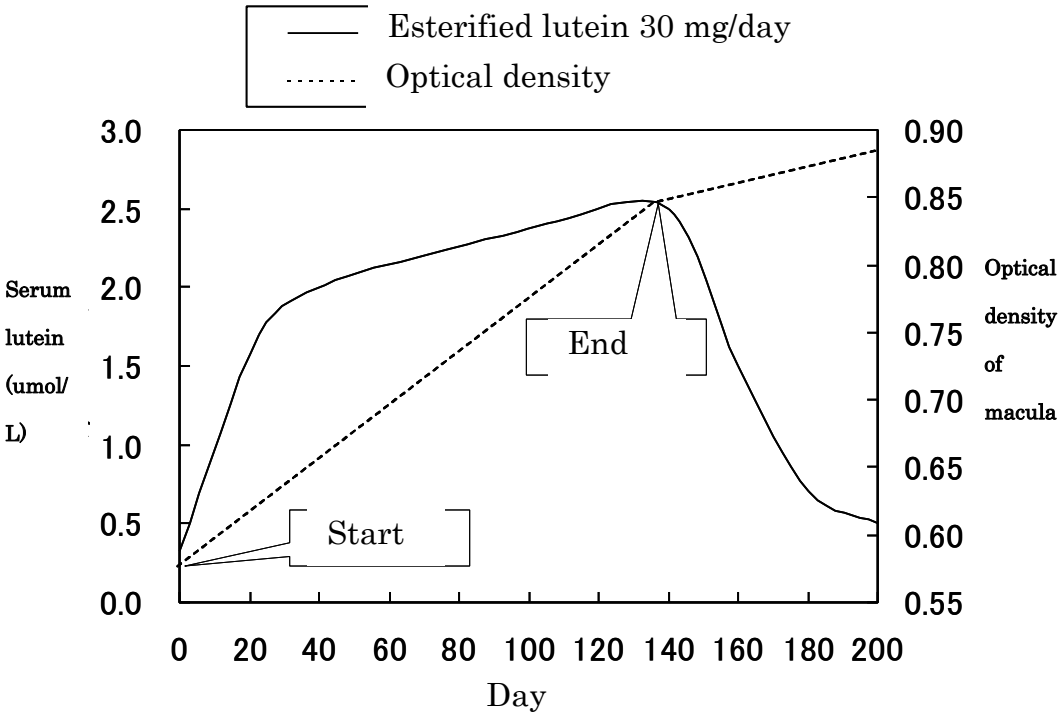
② 5 volunteers participated in the test. We tested esterified lutein first and free lutein was tested 2 weeks later in same volunteers.

③ The capsule containing lutein was given with water (200 mL) to a volunteer. After taking of capsule, a piece of bred, a piece of cream cheese, a cup of low fat yoghurt and a cup of apple juice were given to the volunteer.

④ Blood was collected intravenously at 10, 24, 32 and 48 hr later of lutein taken. Serum lutein was determined by HPLC.

8. Accumulation of Lutein in Macula by Esterified Lutein

Landrum *et al.* in 1997 and Berendschot *et al.* in 2000 individually reported lutein deposition in macula. Landrum used a heterochromatic flicker photometer for measuring optical density of macular pigment directly, and found 50% increase in optical density after 160-day lutein supplementation as shown in Figure 8. Berendschot used scanning laser ophthalmoscopy and reflectance spectral analysis, and obtained similar results by less than 30 mg/day supplementation of lutein esters.



Landrum *et al.*, *Exp. Eye Res.* 65, 57-62 (1997).

Figure 8

9. Blue Ray Absorption

Lutein exists in lens and macula is said to absorb blue ray which injures cell.

10. Lutein Intake

Spinach contains highest level of lutein among vegetables, followed by broccoli, Brussels sprouts, and green beans (Figure 1). Researches recommend 6 mg/day lutein intake (as free lutein) for prevention of AMD. To meet this quantity by spinach alone, you must eat five salad bowls of spinach. Lutein intake by some dietary supplements could be a practical way.

Lutein – P80 of Oryza Oil & Fat Chemical Co., Ltd. has very high lutein content, which is 80% as lutein ester (40% as free lutein). An intake of **15-20 mg/day** is sufficient for prevention of AMD, according to a 6-mg/day recommendation.

11. Stability of Lutein Esters

Lutein esters are stable for months at room temperature in an original packing. Figure 9 shows the stability of Lutein – P80.

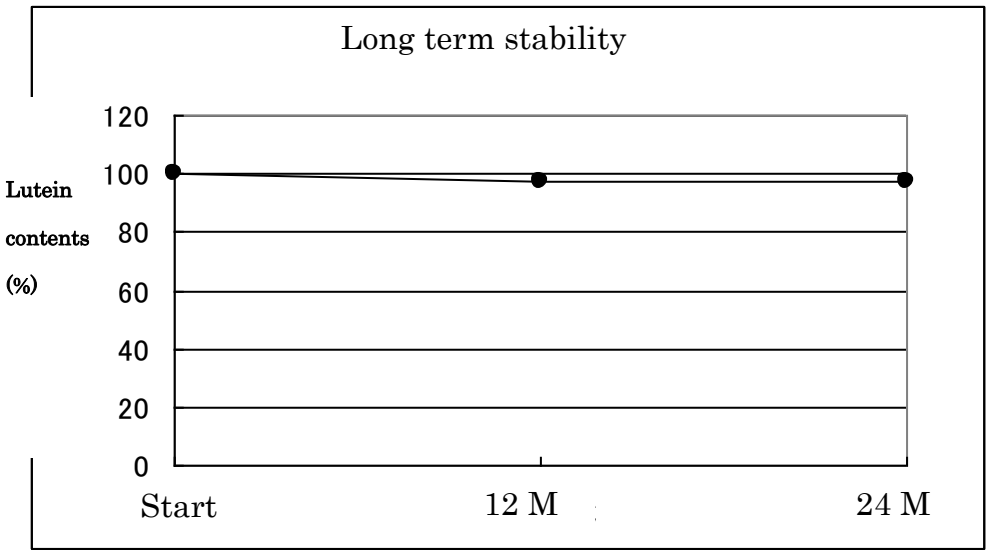


Figure 9

12. Acute Toxicity and Safety

12-1. Residual Agricultural Chemicals

Assayed Items	Results	Detection Limits	Assay Method
BHC	Not Detected	0.02ppm	Gas Chromatography
DDT	Not Detected	0.02ppm	Gas Chromatography
Aldrin	Not Detected	0.01ppm	Gas Chromatography
Dieldrin	Not Detected	0.01ppm	Gas Chromatography
Endrin	Not Detected	0.01ppm	Gas Chromatography
Diazinon	Not Detected	0.05ppm	Gas Chromatography
Parathion	Not Detected	0.05ppm	Gas Chromatography

Test institute: Japan Food Research Center Foundation
Date of report: January 24, 2003.
Issue number: 302120606-001

12-2. Acute Toxicity

Five-week old mice was given orally 5,000 mg/kg of Lutein – P80, and then fed laboratory chow for two weeks. No toxic effect were observed, thus the **LD_{50} (mouse) is > 5000 mg/kg**.

13. Applications of Lutein

	Applications	Examples
Foods	Eye care, antioxidant	Beverages, hard & soft capsules, tablets, candies, chewing gums, chocolates, wafers, jellies etc
Cosmetics	Antioxidant	Body lotions, body gel etc.

14. Packaging

LUTEIN−P80, P40 (powder, for food) , LUTEIN−PC80, PC40 (powder, for cosmetics)

1 kg Interior packaging：Aluminum bag

Exterior packaging：Cardboard

LUTEIN−L8 (liquid, for food) , LUTEIN−LC8 (liquid, for csmetics)

1kg Interior packaging：Cubic polyethylene container

Exterior packaging：Cardboard

15. Storage

Store in cool, dry an dark place. Use it as soon as possible after open the internal package.

16. Exhibition

＜Food＞

LUTEIN-P80

Ex.：Marigold extract powder or Marigold extract

And

Natural tocopherol

LUTEIN-P40

Ex.：Processed marigold extract powder

OR

Dextrin, Marigold extract and Natural tocopherols

LUTEIN-L8

Ex.：Processed marigold extract liquid

OR

Hydrogenated Glucose Syrup, water, Caprylic/Capric Acid Triglyceride, Glycerin Ester of Fatty Acid, Marigold Extract, Lecithin and Natural tocopherols

＜Cosmetics＞

LUTEIN-PC80

INCI name：Tagetes Erecta Flower Extract (and) Tocopherol

LUTEIN-PC40

INCI name：Dextrin (and) Tagetes Erecta Flower Extract (and) Tocopherol

LUTEIN-LC8

INCI name：Maltose (and) Maltodextrin (and) Water (and) Caprylic/ Capric Triglyceride (and) Tagetes Erecta Flower Extract (and) Glyceryl Myristate (and) Lysolecithin

PRODUCT STANDARD
PRODUCT NAME

LUTEIN-P80

(FOOD)

This product is extracted from flowers of marigold, *Tagetes erecta* (Compositae), and then refined. It contains minimum 80.0% lutein esters.

Appearance: Orange yellow powder with slight unique smell.

Lutein (free)	Min. 40.0 %	(HPLC)
Lutein Esters	Min. 80.0 %	(Lutein (free) × 2)
Total Carotenoid (free)	Min. 42.5 %	(UV-VIS spectrophotometer)
Total Carotenoid Esters	Min. 85.0 %	(Total Carotenoid (free) × 2)
Loss on Drying	Max. 5.0 %	(1 g, 40°C, Reduced Pressure, Posphprus Pentaoxide, 4 h)
Purity Test		
(1) Heavy Metals (as Pb)	Max. 10 ppm	(Sodium Sulfide Colorimetric Method)
(2) Arsenic (as As_2O_3)	Max. 1 ppm	(Standard Methods of Analysis in Food Safety Regulation, The Third Method, Apparatus B)
Standard Plate Counts	Max. 1×10^3 cfu/g	(Analysis for Hygienic Chemists)
Moulds and Yeasts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Coliforms	Negative	(Analysis for Hygienic Chemists)

Composition

Ingredients	Contents
Marigold extract	99.75 %
Natural tocopherols	0.25 %
Total	100.00 %

PRODUCT STANDARD
PRODUCT NAME

LUTEIN-P40

(FOOD)

This product is extracted from flowers of marigold, *Tagetes erecta* (Compositae), and then refined. It contains minimum 40.0 % lutein esters.

Appearance: Orange yellow powder with slight unique smell.

Lutein (free)	Min. 20.0 %	(HPLC)
Lutein Esters	Min. 40.0 %	(Lutein (free) × 2)
Total Carotenoid (free)	Min. 21.0 %	(UV-VIS spectrophotometer)
Total Carotenoid Esters	Min. 42.0 %	(Total Carotenoid (free) × 2)
Loss on Drying	Max. 5.0 %	(1 g, 40°C, Reduced Pressure, Posphprus Pentaoxide, 4 h)
Purity Test		
(1) Heavy Metals (as Pb)	Max. 10 ppm	(Sodium Sulfide Colorimetric Method)
(2) Arsenic (as As_2O_3)	Max. 1 ppm	(Standard Methods of Analysis in Food Safety Regulation, The Third Method, Apparatus B)
Standard Plate Counts	Max. 1×10^3 cfu/g	(Analysis for Hygienic Chemists)
Moulds and Yeasts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Coliforms	Negative	(Analysis for Hygienic Chemists)

Composition

Ingredients	Contents
Dextrin	50.00 %
Marigold extract	49.87 %
Natural tocopherols	0.13 %
Total	100.00 %

PRODUCT STANDARD
PRODUCT NAME

LUTEIN-L8

(FOOD)

This product is extracted from flowers of marigold, *Tagetes erecta* (Compositae), refined, and then emulsified. It contains minimum 8.0 % lutein esters.

Appearance: Orange yellow vicious liquid with slight unique smell

Lutein (free)	Min. 4.0 %	(HPLC)
Lutein Esters	Min. 8.0 %	(Lutein (free) × 2)

Purity Test

(1) Heavy Metals (as Pb)	Max. 10 ppm	(Sodium Sulfide Colorimetric Method)
(2) Arsenic (as As_2O_3)	Max. 1 ppm	(Standard Methods of Analysis in Food Safety Regulation, The Third Method, Apparatus B)
Standard Plate Counts	Max. 1×10^3 cfu/g	(Analysis for Hygienic Chemists)
Moulds and Yeasts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Coliforms	Negative	(Analysis for Hygienic Chemists)

Composition

Ingredients	Contents
Glutinous starch Syrup	40.0 %
Water	28.0 %
Caprylic/capric Acid triglyceride	12.4 %
Marigold extract	9.975 %
Glycerin ester of fatty acid	8.0 %
Lecithin	1.6 %
Natural tocopherols	0.025%
Total	100.0 %

PRODUCT STANDARD
PRODUCT NAME

LUTEIN-PC80

(COSMETIC)

This product is extracted from flowers of marigold, *Tagetes erecta* (*Compositae*), and then refined. It contains minimum 80.0% lutein esters.

Appearance: Orange yellow powder with slight unique smell.

Lutein (free)	Min. 40.0 %	(HPLC)
Lutein Esters	Min. 80.0 %	(Lutein (free) × 2)
Total Carotenoid (free)	Min. 42.5 %	(UV-VIS spectrophotometer)
Total Carotenoid Esters	Min. 85.0 %	(Total Carotenoid (free) × 2)
Loss on Drying	Max. 5.0 %	(1 g, 40°C, Reduced Pressure, Posphprus Pentaoxide, 4 h)
Purity Test		
(1) Heavy Metals (as Pb)	Max. 10 ppm	(The Second Method of The Japanese Standards of Quasi-Drug Ingredients)
(2) Arsenic (as As_2O_3)	Max. 1 ppm	(The Third Method of The Japanese Standards of Quasi-Drug Ingredients)
Standard Plate Counts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Moulds and Yeasts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Coliforms	Negative	(Analysis for Hygienic Chemists)

Composition

Ingredients	Contents
Tagetes erecta flower extract	99.75 %
Tocopherol	0.25 %
Total	100.00 %

PRODUCT STANDARD
PRODUCT NAME

LUTEIN-PC40

(COSMETIC)

This product is extracted from flowers of marigold, *Tagetes erecta* (*Compositae*), and then refined. It contains minimum 40.0 % lutein esters.

Appearance: Orange yellow powder with slight unique smell.

Lutein (free)	Min. 20.0 %	(HPLC)
Lutein Esters	Min. 40.0 %	(Lutein (free) × 2)
Total Carotenoid (free)	Min. 21.0 %	(UV-VIS spectrophotometer)
Total Carotenoid Esters	Min. 42.0 %	(Total Carotenoid (free) × 2)
Loss on Drying	Max. 5.0 %	(1 g, 40°C, Reduced Pressure, Posphprus Pentaoxide, 4 h)
Purity Test		
(1) Heavy Metals (as Pb)	Max. 10 ppm	(The Second Method of The Japanese Standards of Quasi-Drug Ingredients)
(2) Arsenic (as As_2O_3)	Max. 1 ppm	(The Third Method of The Japanese Standards of Quasi-Drug Ingredients)
Standard Plate Counts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Moulds and Yeasts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Coliforms	Negative	(Analysis for Hygienic Chemists)

Composition

Ingredients	Contents
Dextrin	50.00 %
Tagetes erecta flower extract	49.87 %
Tocopherol	0.13 %
Total	100.00 %

PRODUCT STANDARD
PRODUCT NAME

LUTEIN-LC8

(COSMETIC)

This product is extracted from flowers of marigold, *Tagetes erecta* (Compositae), refined, and then emulsified. It contains minimum 8.0 % lutein esters.

Appearance: Orange yellow vicious liquid with slight unique smell

Lutein (free)	Min. 4.0 %	(HPLC)
Lutein Esters	Min. 8.0 %	(Lutein (free) × 2)

Purity Test

(1) Heavy Metals (as Pb)	Max. 10 ppm	(The Second Method of The Japanese Standards of Quasi-Drug Ingredients)
(2) Arsenic (as As_2O_3)	Max. 1 ppm	(The Third Method of The Japanese Standards of Quasi-Drug Ingredients)
Standard Plate Counts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Moulds and Yeasts	Max. 1×10^2 cfu/g	(Analysis for Hygienic Chemists)
Coliforms	Negative	(Analysis for Hygienic Chemists)

Composition

Ingredients	Contents
Hydrogenated starch hydrolysate	40.0 %
Water	28.0 %
Caprylic/capric triglyceride	12.4 %
Tagetes erecta flower extract	10.0 %
Glyceryl myristate	8.0 %
Lysolecithin	1.6 %
Total	100.0 %

ORYZA OIL & FAT CHEMICAL CO., LTD. striving for the development of the new functional food materials to promote health and general well-being.

From product planning to OEM - For any additional information or assistance, please contact :

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ORYZA OIL & FAT CHEMICAL CO., LTD.