Cosmetic benefit of dietary supplements including astaxanthin and tocotrienol on human skin

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Introduction

Astaxanthin, one of a variety of carotenoids that includes β-carotene, is a frequently consumed natural red color widely and naturally distributed in marine organisms, including Crustacea such as shrimps and crabs and such fish as salmon and sea bream.

Recently astaxanthin has been reported to exhibit strong anti-oxidative action[1,2] 100~1,000 times stronger than vitamin E (alpha-tocopherol), and approximately 40 times stronger than beta-carotene in its anti-oxidative activity. Although used only as a coloring in the past (either as a color food additive[3] or a dye-up agent for cultured fish), astaxanthin has become one of the major materials eagerly anticipated by industries for dietary supplements.

Furthermore its other various specificities have been reported, including anti-inflammatory action[4], anti-atherosclerotic action[5,6], action against diabetes[7,8], retinal protective action against light-induced injury[9], daily rhythm regulating action[10], immunomodulating action[11], anti-stress action[12], muscle function duration improving action[13], semen quality improving action[14] and inhibiting action against bladder cartinogenesis[15]. In terms of dermatological actions, suppression of hyper-pigmentation[16], inhibitions of melanin synthesis and photo-aging[17] have been reported. We have also reported visual wrinkle reduction by topical astaxanthin[18]. These reports, however, are all based on investigations for topical use.

On the other hand, tocotrienol is part of the vitamin E group found in the barley-wheat family, rice bran, palm oil and other grains, and has three double bonds on the side chain of a tocopherol molecule. Like astaxanthin, tocotrienol is a naturally occurring compound that has been frequently consumed and used widely as an anti-oxidant food additive[19].

Tocotrienol also has anti-oxidative action in its physiological activities similar to those of astaxanthin, and its activity has been indicated to be 40~60 times stronger than tocopherol [20].

Among its other properties, blood pressure lowering action[21], cholesterol lowering action[22], improving action against arteriosclerosis[23], and inhibiting action against growth of breast cancer cells[24] have been reported. Most

recently, new specificities not included in tocopherol have been found, such as inhibiting action against angiogenesis[25] and improving the action of whole blood flow[26]. Furthermore, in Europe and America tocotrienol is being widely used topically in cosmetics and other products as a next-generation vitamin E.

Both astaxanthin and tocotrienol have excellent anti-oxidative properties. Astaxanthin, however, possesses properties that act to quench singlet oxygen and to inhibit lipid peroxidation, in contrast to tocotrienol, which possesses the property of scavenging peroxyl radicals[27]. Consequently, these different mode of actions can be expected to produce synergistic action through combination.

Furthermore, the concept of an "Beauty from Within" internal cosmetic has been attracting attention in the dietary supplements field and is an indispensable item for development of new products and improvements to existing products.

Based on the above considerations, we performed a clinical investigation using a dietary supplement containing both astaxanthin and tocotrienol.

1. Method

1-1. Test samples

The dietary supplement containing astaxanthin and tocotrienol (Trade Name: OPENING™ Beauty Foods) was comprised of *Haematococcus plubialis* microalgae extract containing 5% of astaxanthin (Trade Name: ASTAREAL® Oil 50F), palm oil extracts containing 37.5% of tocotrienol (Trade Name: TOCOMIN® 50%) and canola oil as soft gel capsules. Each capsule contains 2 mg of astaxanthin and 40 mg of tocotrienol.

Placebo capsules for control were prepared with only canola oil in soft capsules.

1-2. Subjects

Sixteen (16) healthy women with dry skin, age about forty years old, were used for the study, after obtaining their consent for participation. Taking all subjects' properties into consideration, such as age, physical build, skin-type, and constitution, the subjects were divided into a test group and a placebo control group (each consisted of 8 subjects) by homogeneity of such properties after measuring skin-parameters before beginning the study. **Table 1** shows the subjects' properties.

1-3. Duration and method of study

From January 15, 2002, one capsule of the dietary supplement including astaxanthin and tocotrienol was administered to each subject every evening. Test duration was four weeks. Measurements of each test item were performed at three points, at the beginning of the study, after two weeks and after four weeks. All tests were performed using a double-blind procedure.

1-4. Conditions of measurement

The measurements were performed 15 minutes after administering the capsules to the subjects, who were kept resting in a seated position after washing their faces in an environmental test room conditioned to 20℃-RT and 65%-RH.

1-5. Measurement parameters

1-5-1. Questionnaire

Skin condition and a skin diary were recorded using a questionnaire based on the FCG (FCG Research Institute, Inc.) model (referred to below as "the FCG model").

1-5-2. Inspection/Palpation by cosmetic specialist

Performed using the FCG model.

1-5-3. Skin moisture content

Corneous moisture content (electrical conduction MS) of the right side outer corners of the eye and cheek was measured using an electrical conductance-type SKICON-200 (IBS).

1-5-4. Sebum content

Sebum content levels of the left side of the brow and cheek were measured using a transmission sebum-meter.

1-5-5. Observation of skin surface

Magnified skin surface photographs of the left side of the outer cantus were recorded using a Medical Nikkol (Nikon) and microscope (x60) (Hirocks).

2. Results

2-1. Skin condition evaluated by subjects' self-assessment

Fig. 1 shows changes of skin condition evaluated by the subjects' self-assessments after two weeks and four weeks compared to the base-line

initial values.

The improved tendency was observed in the test group compared to the control group for all evaluated parameters at both Week 2 and Week 4, in each mean value of the parameters for the eight subjects. “Spots/freckles” evaluated at Week 2 and “acne/pimples” at Week 4 showed statistically significant differences.

2-2. Inspection/Palpation by cosmetic specialist

Fig. 2 shows changes of skin condition evaluated by the specialist’s inspection/palpation at Week 2 and Week 4 compared to the base-line initial values.

In each mean value of the parameters for the eight subjects, the improved tendencies observed in the test group compared to the control group included “dark rings around eyes (significant)”, ”oiliness”, “wrinkles around the forehead or brow” and “flabbiness under eyes” by inspection and “smoothness (significant)”, “moistness” and “elasticity” by palpation at Week 2, and “dark rings around eyes”, “oiliness”, “glossiness”, “acne/pimples”, “grain”, “flabbiness under eyes” and “flabbiness around mouth” by inspection and “smoothness (significant)”, “moistness (significant)” and “elasticity (significant)” by palpation at Week 4.

2-3. Moisture content

Fig. 3 shows changes of moisture content measured at Week 2 and Week 4 compared to the base-line initial values.

Moisture content of the outer corners of the eye measured at Week 4 in the test group increased significantly ($p<0.05$) compared to the initial base-line value. Good moistness of the cheek was also observed but was not statistically significant. On the contrary, in the control group, a slowly decreasing but not statistically significant tendency for the moisture content of both outer corners of the eye and cheek was observed. The values measured at Week 4 showed significant change ($p<0.05$) between the test group and the placebo control group.

2-4. Sebum content

Fig. 4 shows changes of the sebum content measured at Week 2 and Week 4 compared to the base-line initial values.

No change was observed to the sebum content of both the brow and cheek in the test group. For those in the placebo control group, however, the sebum content decreased. Taking the test period into consideration, this may suggest the skin condition in the test group was well maintained compared to

the placebo group.

2-5. Observation of skin surface

Fig. 5 shows magnified skin surface photographs (M4 and M11) in which improvement of wrinkles was observed.

The skin condition in the test group tended to be maintained well compared to the placebo group.

3. Discussion

We studied the effect on the skin of astaxanthin and tocotrienol, which possess strong anti-oxidative action, by oral administration in a double blind clinical test. Consequently, significant improvements were observed in skin moisture content (the outer corners of the eye), the subjects' self-assessment of their skin (spots/freckles, acne/pimples), and the inspection/palpation by cosmetic specialist (dark rings around eyes, smoothness, moistness, elasticity). All of these are important parameters for skin condition. The poor circumstances on the skin during the test period, however, must also be taken into consideration. Furthermore, improvement of skin wrinkles was observed by skin surface observation.

As a result of the above, an excellent cosmetic effect on human skin was observed from concomitant administration of astaxanthin and tocotrienol.

Considering both the cosmetic effect on the skin observed from concomitant oral use of astaxanthin and tocotrienol in this study and the cosmetic effect of topical use of astaxanthin observed in the studies already reported[18], further cosmetic effects on the skin can be anticipated through both oral and topical use.

Conclusion

The cosmetic effect on the skin of dietary supplements containing astaxanthin and tocotrienol was demonstrated in a double blind clinical study. We note, however, that the study was performed during winter, which is a harsh season that creates a particularly dry human skin condition, and also that it is usually very difficult to observe any significant difference to skin condition resulting from the oral administration of dietary supplements. Consequently, it is significant to note that there was achieved a noticeable improvement to skin condition with the oral administration of a dietary supplement containing Ax & T3, despite the harsh environmental condition of winter and the administration limited to oral dietary supplements.

Of course, although dietary supplements containing only astaxanthin and tocotrienol may be preferred, a total inner cosmetic product that combines

ingredients, including skin components such as vitamin C or other water-soluble antioxidants, collagen, hyaluronic acid, and chondroitin sulfate, can be expected to produce a much greater cosmetic effect on the skin.

We anticipate such dietary supplements that are beneficial cosmetically on the skin will be developed and commercialized in the future.

This study was conducted jointly with the Beauty Science Laboratory at FCG Research Institute, Inc.

4. Reference

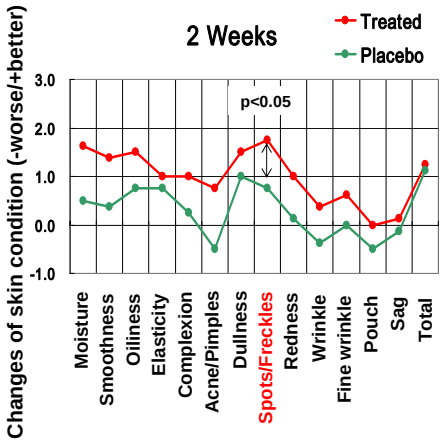
1) Miki, W.: Biological functions and activities of animal carotenoids, *Pure & Apple. Chem.,* **63**, 141-146 (1989).
2) Shimizu, N., Goto, M. and Miki, W.: Carotenoids as singlet oxygen quenchers in marine organisms, *Fisheries Science,* **62**, 134-137 (1996).
3) *Annotation Book for Existing Additives Name List*: The List Annotation, Existing Additives Name Number (403), Japan Food Additive Association, 488 (1999).
4) Kurasige, M., Okazoe, Y., Okimasu, E., Ando, Y., Mori, M., Inui, W., Inoue, M. and Utsumi, K.: Disturbance of biological membrane by free radicals and its protection by astaxanthin, *Cyto-protection & Biology*, **7**, 383-391 (1989).
5) Iwamoto, A., Miki, W. and Itakura, H.: Inhibition of Low-density Lipoprotein Oxidation by Astaxanthin, *J. Atheroscler. Thromb.,* **7**, 216-222 (2000).
6) Iino, T., Ono, K. and Kiso, Y.: Interaction of astaxanthin and lycopene indicating by LDL-oxidized ability, *The 55th Meeting of Japanese Nutrition and Food Society*, Kyoto, 2G-07a (2001).
7) Kenmotsu, N., Jimaima, J., Arai, H. and Nguyen, V. C.: Effects of astaxanthin on the diabetes cataract, *The 51th Meeting of Japanese Nutrition and Food Association,* Tokyo, 170 (1997).
8) Uchiyama, K., Naito, Y., Hasegawa, G., Nakamura, N., Yoshikawa, T. and Takahashi, J.: Effect of astaxanthin against progression/complication in diabetes, *The 15th Carotenoids Symposium,* Toyama, 30 (2001).
9) Tso, Mark O.M. and Lam, T-T.: Method of retarding and ameliorating central nervous system and eye damage. *USPAT*, **5527533** (1996).
10) Nagai, K., Iimori, S., Toyoda, Y., Ono, Y., Kiso, Y. and Tanaka, T.: Effect of astaxanthin on daily rhythm of locomotor activity in rats, *The 74th Annual Meeting of the Japanese Pharmacological Society,* Yokohama, 762 (2001).
11) Jyonouchi, H., Zhang, L. and Tomita, Y.: Studies of immunomodulating actions of carotenoids, II. Astaxanthin enhances in vitro antibody

production to T-dependent antigens without facilitating polyclonal B-cell, *Natr. Cancer,* **19**, 269-280 (2993).
12) Yung, S., Asami, S., Toyota, K., Fujii, W., Suwa, Y and Tanaka, R.: Inhibitory effect of astaxanthin against acceleration of metastasis in stress-loading mice, *Japanese J. Nutr. Food*, 50, 423-428 (1997).
13) Lignell, A.: Medicament for improvement of duration of muscle function or treatment of muscle disorder or diseases, *USPAT*, **6245818** (2000).
14) Garem, Y. E., Lignell, A. and Combaire, F.: Supplementation with astaxanthin (AstaCarox®) improves semen quality in infertile men, *The13th Int. Sym. Carotenoids.* Hawaii, 30 (2002).
15) Tanaka, T., Morishita, Y., Suzuki, M., Kojima, T., Okumura, A. and Mori, H.: Chemoprevention of mouse urinary bladder carcinogenesis by the naturally occurring carotenoid astaxanthin, *Carcinogenesis,* **15**, 15-19 (1994).
16) Yamashita, E.: Inhibiting effect of astaxanthin from krill against pigmentation, *Fragrance J.,* **14**, 180-185 (1995).
17) Aragane, K.: Astaxanthin, as an attractive cosmetic material, *The 15th Carotenoids Symposium,* Toyama, 24 (2001).
18) Seki, T., Sueki, H., Kono, H., Suganuma, K and Yamashita, E.: Effect of astaxanthin from *Haematococcus pluvialis* on human skin, *Fragrance J.,* **12**, 98-103 (2001).
19) *Annotation Book for Existing Additives Name List*: The List Annotation, Existing Additives Name Number (291), Japan Food Additive Association, 376 (1991).
20) Serbinova, E., Kagan, V., Han, D. and Packer, L.: Free radical recycling and intermembrance mobility in the antioxidant properties of alpha-tocopherol and alpha-tocotrienol, *Free Radic. Biol. Med.,* **10**, 256-275 (1991).
21) Newaz, M. A. and Nawal, N. N.: Effect of gamma-tocotrienol on blood pressure, lipid peroxidation and total antioxidant status in spontaneously hypertensive rats (SHR), *Clin. Exp. Hypertens.,* **21**, 1297-1313 (1997).
22) Qureshi, A. A., Bradlow, B. A., Brace, L., Maanganello, J., Peterson, D. M., Wright, J. J., Grapor, A. and Elson, C. E.: Response of hypercholesterolemic subjects to administration of tocotrienol, *Lipid,* **30**, 1171-1177 (1995).
23) Temo, A. C., Geller, M., Waotkins, T. R., Gapor, A. and Bierenbaum, M. L.: Antioxidant effect of tocotrienols in patients with hyperlipidemia and carotid stenosis, *Lipids,* **30**, 1179-1183 (1995).
24) Nesaretnam, K., Stephen, R., Dils, R. and Darbre, P.: Tocotrienols inhibit

the growth of human breast cancer cells irrespective of estrogen receptor status, *Lipids,* **33**, 461-469 (1998).
25) Inoguchi H., Hirokane, H., Tsuzuki, T., Miyazawa, H., Nobukawa K. and Igarashi M.: Inhibitory action of tocotrienols against neo-vascularization, *The Meeting of Agricultural Chemistry Association,* Sendai, 253 (2002).
26) Begum, A. N. and Terao, J.: Protective effect of alpha-tocopherol against free radical-induced impairment of erythrocyte deformability, *Biosci. Biotechnol. Biochem.,* **66**, 398-403 (2002).
27) Inui, W.: Biological function of carotenoids and foods – Particularly in relation to active oxygen – *Food Style 21 Seminar*, Tokyo, 3-4 (2000).

FIGURE 1

- Skin condition by individual assessment



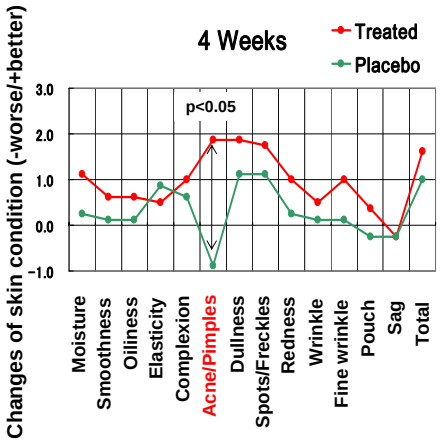
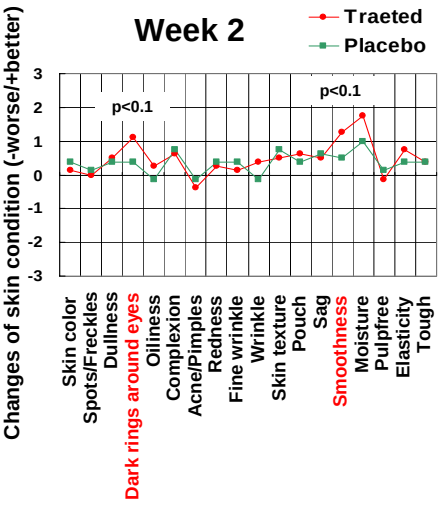


FIGURE 2

- Dermatologist inspection/palpation



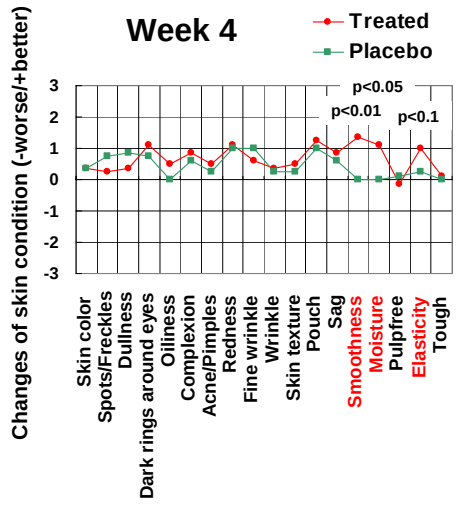


FIGURE 3

- Skin moisture content

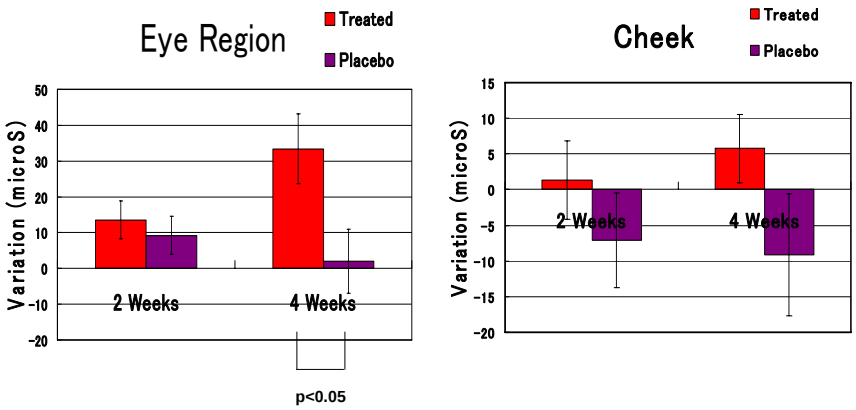


FIGURE 4

- Skin sebum content

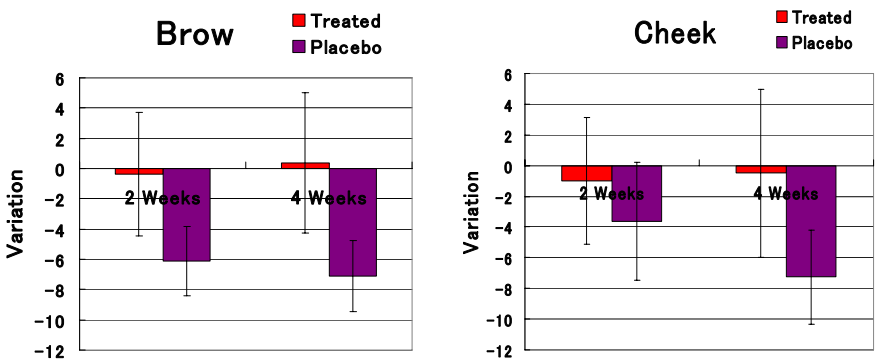
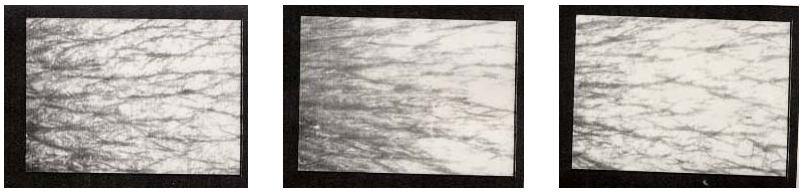


FIGURE 5

- Magnified skin surface inspection

M4



Start ⇨ 2 weeks ⇨ 4 weeks

M11