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Development of "Metabarrier" and "Oxibarrier" --- Dietary Supplements Meant for Lifestyle-Related Disease Prevention

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Abstract

We have developed two lifestyle-related disease-prevention supplements, namely "Metabarrier" and "Oxibarrier," for FUJIFILM Corporation to release in October 2007.

"Metabarrier" is a supplement designed for the purpose of reducing internal organ fat. It consists of ingredients that impede sugar and fat absorption, and that promote fat burning. We have confirmed reduction in fat and improvement in enteric areas in our human trial subjects. "Metabarrier" is a mixture of salacia powder, red wine polyphenol, green tea extraction, onion skin extract, and chrome yeast. Among these, the featured element is salacia, an extract from the medicinal plant typically found in Sri Lanka, India and Thailand.

"Oxibarrier" is a strikingly unique blend of water and lipid soluble antioxidants that brings about unparalleled synergetic effects. Featured ingredient is our proprietary dry nano-emulsion of astaxanthin. We have confirmed its characteristic antioxidative effect in our human trial for 8 weeks.

1. Introduction

Until now, FUJIFILM has been on the world's leading edge of the photo imaging field.

Resultant developed technologies are antioxidant technology, nano dispersion and stabilization technology, collagen peptide physicality control technology, and layer constitution technologies that optimize reactivity, reaction rates, diffusion of substances, and interactions of materials; these technologies are cutting-edge enough to apply to healthcare products (e.g., supplements, cosmetics).

With these backgrounds, FUJIFILM went into the healthcare field in September 2006, and has been marketing functional foods and functional cosmetics. Regarding the functional foods, cosmetic foods intended for internal and external care along with cosmetics had initially been developed, but in response to recently growing consumer awareness to measures for lifestyle-related diseases, supplements designed to prevent lifestyle-related diseases, called "Metabarrier" and "Oxibarrier", were developed and in October 2007 launched on the market.

On the development of these functional foods, "Metabarrier" was intended for those who are worried about metabolic syndrome but accidentally often eat excess calories or wish to improve their enteral environment; "Oxibarrier" was intended for those who get tired easily under much stress or wish to live a vigorous life by daily keeping themselves healthy.

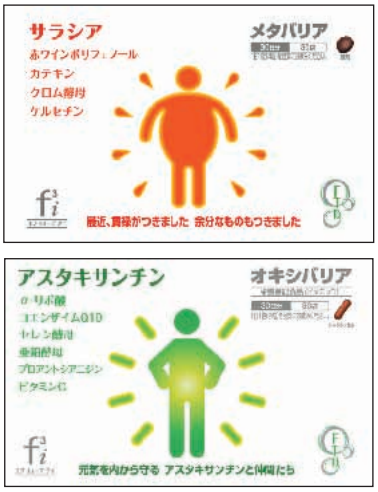

Fig. 1 "Metabarrier" and "Oxibarrier".

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2. Development of "Metabarrier"

For a reason that specific medical checkups and specific health guidance in Japan began in April 2008, people pay increasing attention to metabolic syndrome. According to the 2005 national health and nutrition survey in Japan by the Ministry of Health, Labour and Welfare, about a half (increasing year after year) of those aged 40-74 years old fell into metabolic syndrome or potentially did. Also, women were reported to tend to accumulate fats in internal organs easily as secretion of female hormones is decreased toward menopause.

As illustrated in Fig. 2, the pathophysiology of metabolic syndrome is that accumulation of visceral fat causes abnormality of adipocytokine secretion to impede transportation of glucose by insulin (i.e., to increase insulin resistance), thereby causes a variety of abnormality such as type 2 diabetes, and further triggers arteriosclerosis to develop circulatory system disease such as myocardial infarction and stroke; and removing this visceral fat trigger is the first step to prevention of metabolic syndrome.

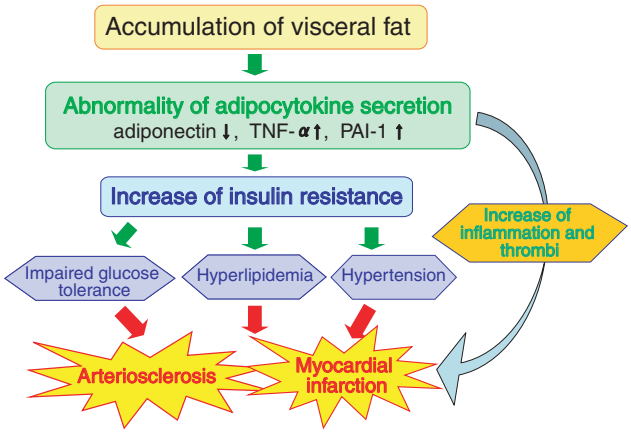

Fig. 2 Mechanisms behind metabolic syndrome.

2.1 Concept and Formulation

An important thing to prevent metabolic syndrome is not to accumulate visceral fat in the body. Increase of visceral fat results from accumulation of excess sugars and fats after excess calories are taken in. Although the best thing to decrease visceral fat may be to reduce the consumption of meals, reduction the total amount of meal consumption leads to reduction of intake of necessary nutrients, often resulting in being tired easily, worsened skin conditions, and unhealthy conditions.

As illustrated in Fig. 3, therefore, compounding of ingredients that impedes absorption of excessively eaten sugars and fats and further promotes burning of them were considered to be efficient for the prevention.

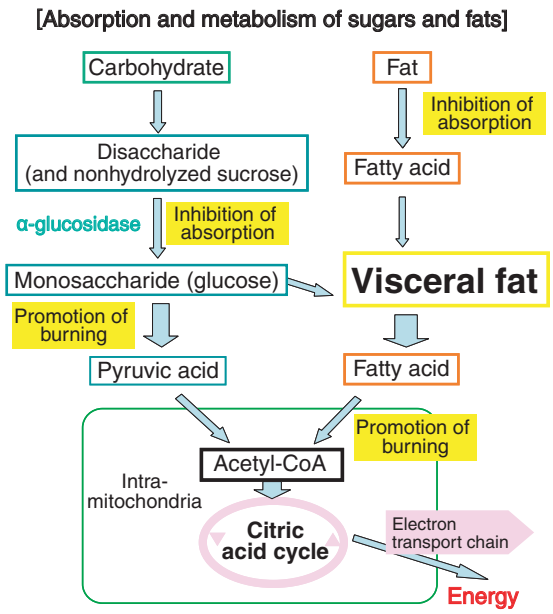

Fig. 3 Absorption and metabolizing route of carbohydrate and fat.

Based on these ideas, "Metabarrier" was formulated by compounding ingredients that slightly differ in effect on the body to select materials that can act on both sugars and fats.

- Ingredients -

Concentrated salacia extracts:

Act on sugars.

Red wine polyphenols:

Act on fats by the red wine effect, also known as the French paradox.

Onion skin extracts:

Contain polyphenols and quercetin which act on fats.

Green tea extracts:

Contain much catechin and act on both sugars and fats.

Chrome:

Is an essential mineral especially for dieting.

2.2 Salacia, the Main Ingredient

Salacia is a vine plant that grows naturally in the South Asian region such as India and Sri Lanka, and especially in Ayurveda, a system of traditional medicine native to India, had been prized as a specific remedy for diabetes mellitus and obesity mainly by royalties and aristocrats. Recently, active ingredients in this plant have been found to be salacinol and kotalanol having α-glucosidase inhibitory activity (Fig. 4) [1), 2)].

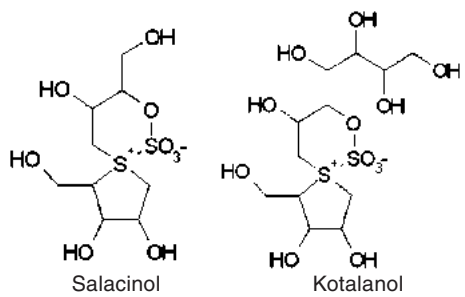

Fig. 4 Main chemical constituents of Salacia.

Fig. 5 illustrates a mechanism that absorbs eaten carbohydrates into the body. First, carbohydrates such as starch polysaccharides are hydrolyzed into disaccharides by amylase and then transported to the small intestine. These disaccharides (including originally nonhydrolyzed sucrose), which cannot be absorbed directly as they are, can be absorbed into the body only after hydrolyzed into monosaccharides by the enzyme α-glucosidase present in the epithelium of the small intestine.

Salacinol and kotalanol impede the absorption of disaccharides by inhibiting α-glucosidase present in the small intestine epithelium. Then, unhydrolyzed or unabsorbed disaccharides are transported to the large intestine in an unchanged form to provide an improving effect on the enteral environment by an oligosaccharide-like effect (which improves the enteral environment via activity of good bacteria in the large intestine).

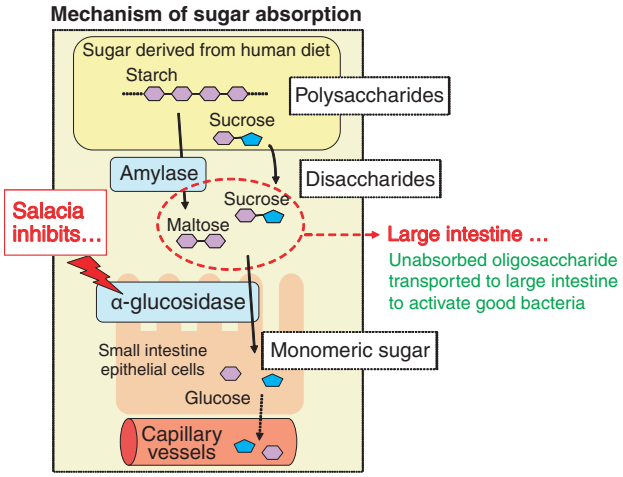

Fig. 5 Absorption mechanism of starch.

Besides Salacia, Guava tea polyphenols, mulberry leaves, and Gymnema leaves are materials that inhibit α-glucosidase or impede absorption of sugars, but Salacia has been reported to have the potent effects [3].

2.3 Evidence on Human Body

After 14 men and women who tended to be obese took in "Metabarrier" for 8 weeks, their body weight, abdominal circumference, and body mass index were measured for change before and after the intake period. Fig. 6 shows the results.

Body weight, abdominal circumference, and BMI before and after intake period

	BW change	AC change	BMI change
Total	-1.7 kg**	-2.0 cm**	-0.6**
Men	-2.7 kg**	-3.4 cm**	-0.9**
Women	-0.9 kg*	-1.2 cm	-0.3*

(expressed as mean)
* $p<0.05$ ** $p<0.01$ BMI = BW/(Height)^2

Fig. 6 Evidence of Metabarrier effectiveness.

As a result of this trial, decreases of body weight, abdominal circumference, and body mass index were observed especially in the men, demonstrating the effectiveness of "Metabarrier". As a general trend, men have more visceral fat and women have more subcutaneous fat, and visceral fat is thought to be metabolized more easily. Because this trial was conducted in a short period, "Metabarrier" was presumed to exert more potent effects on men who metabolize fats more rapidly.

Furthermore, intake of "Metabarrier" was confirmed to change the enteral environment. After 7 healthy men and women took in "Metabarrier" for 7 weeks, their feces were assayed before and after the intake period; as a result, it was found that in the feces, the amount ammonia was decreased and the pH dropped from around 6 to around 5. An intestinal pH of around 5 is thought to help propagation of good bacteria such as lactic bacteria and inhibit inhabitation of bad bacteria such as coliform bacteria -- this is suggested by the decrease of ammonia, a product from bad bacteria.

3. Development of "Oxibarrier"

Recently, the term "The body rusts" is often heard. Actually, active oxygen in the body is being found to rust the body to induce aging, lifestyle-related diseases, and cancer. Active oxygen is generated naturally in the body (1%-2% of the respired oxygen is thought to be transformed to active oxygen) and is increased by stress, etc. Furthermore, cases often observed recently are that electromagnetic waves radiated from mobile phones are absorbed into the body to generate active oxygen and that external radicals generated from smoking invade into the body. Active oxygen may be divided into several types, typified by superoxide which is formed by oxygen respired into the body; hydrogen peroxide into which superoxide is decomposed by superoxide dismutase (SOD), an antioxidant enzyme in the body; hydroxyl radicals which are formed through reaction of superoxide and hydrogen peroxide with iron ion, etc.; and singlet oxygen which is generated through light excitation of oxygen present in the skin and eyes (Fig. 7). In particular, hydroxyl radicals are the most toxic active oxygen that is suspected to cause cancer development, aging, and many other diseases.

To protect the body from such harms of active oxygen, it is effective to take in highly antioxidant foods daily.

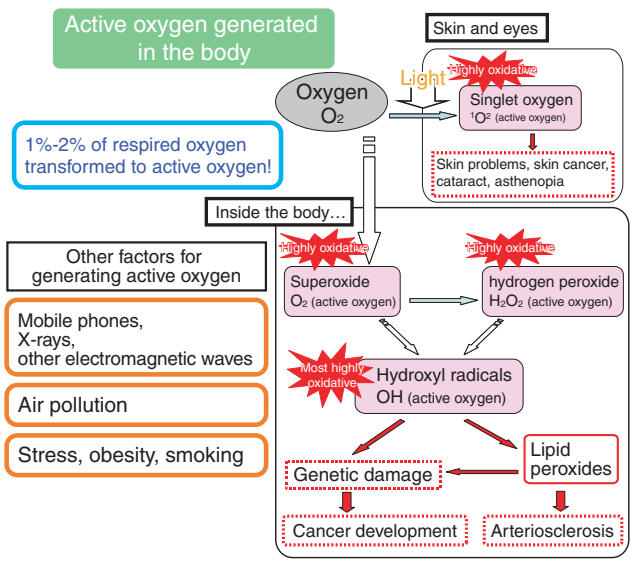

Fig. 7 Species of active oxygen generated inside the body.

3.1 Concept and Formulation

To cope with active oxygen which is generated in various sites of the body, it is effective to take in several gradients having antioxidant effects together. The body may be composed of substances close to water (e.g., blood, cytoplasm) and lipid substances cell (e.g., cell membrane), for each of which more effective ingredients should be selected.

For "Oxibarrier", astaxanthin, coenzyme Q10, α-lipoic acid, proanthocyanidin which is harvested from grape seed as a polypheonl, vitamin C, and vitamin E were selected as active ingredients for hydroxyl radicals. In particular, astaxanthin is also effective for elimination of singlet oxygen, and by our research, has been confirmed to eliminate singlet oxygen at about 90-fold faster rate than vitamin E and at about 1,000-fold faster rate than coenzyme Q10 [4].

To help activity of the internal enzymes SOD and glutathione peroxidase (GPX) which decompose superoxide and hydrogen peroxide, zinc and selenium were additionally compounded for the design as minerals that form these enzymes.

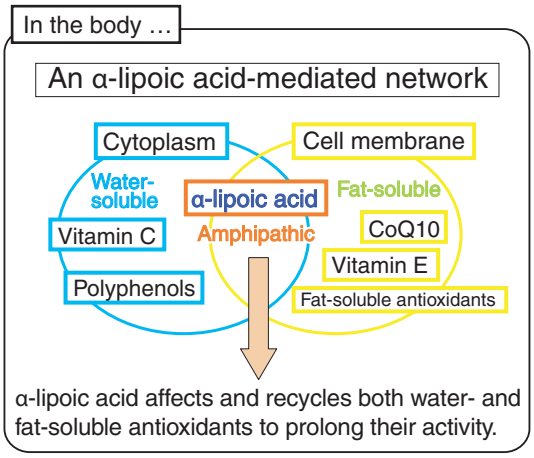

Fig. 8 Antioxidation networks interconnected with α lipoic acid.

Of these ingredients against hydroxyl radicals, α-lipoic acid was employed for the formulation of "Oxibarrier" because its amphipathic property has been reported to affect both water- and fat-soluble substances to prolong their activity.

3.2 Development of Dry Nano Emulsion Composed of Astaxanthin

Astaxanthin, a carotenoid contained in Haematococcus algae, recently attracts much attention regarding its high antioxidant potency. Astaxanthin eliminates singlet oxygen at about 90-fold faster rate than vitamin E and at about 1,000-fold faster rate than coenzyme Q10, so is expected to prevent oxidation of bad cholesterol (low density lipoprotein-cholesterol or LDL cholesterol) and arteriosclerosis of which active oxygen in the body is a cause and to improve damage to the skin caused by ultraviolet rays.

Astaxanthin is a fat-soluble substance that is more likely to be absorbed when dispersed finely and is difficult to handle in an oil form because needing to be mixed with minerals containing water-soluble or –insoluble ingredients, so for the design of "Oxibarrier", a dry nano emulsion of astaxanthin was developed newly. This dry emulsion was confirmed to have 1.6-fold higher absorbability than a conventional product by a rat experiment (Fig. 9).

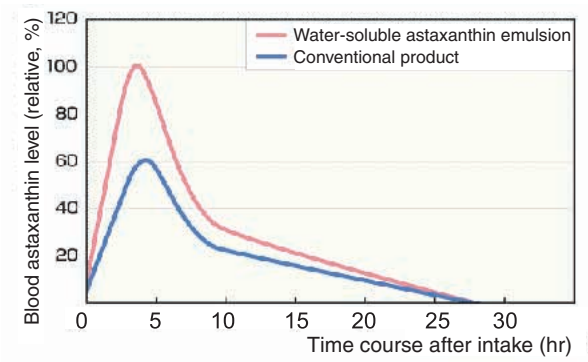

Fig. 9 Effect of emulsion size on the absorbability of astaxanthin.

3.3 Evidence on Human Body

After 14 men and women who tended to be obese took in "Oxibarrier" for 8 weeks, their serum total antioxidant status (STAS) and lipid peroxide (LPO) were measured for change before and after the intake period.

STAS represents the total capability of serum to protect from harms of active oxygen, so higher value is desirable; LPO is the amount of blood lipid peroxidized by active oxygen, so higher value represents an undesirable condition of more oxidative stress. By measuring the two indices, oxidative stress imposed on the body can be estimated.

Fig. 10 shows the results.

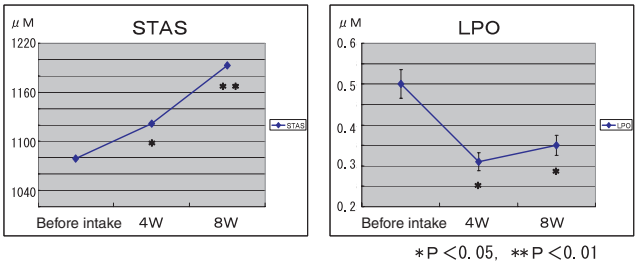

Fig. 10 Evidence for Oxibarrier effectiveness.

It was confirmed that intake of "Oxibarrier" elevated the STAS and lowered the LPO to decrease the oxidative stress remarkably.

4. Conclusion

We developed the supplement that takes advantage of the characteristics of the functional food material Salacia known also in Ayurveda and the supplement that takes advantage of the characteristics of astaxanthin, a carotenoid occurring naturally, having very high antioxidant potency.

We will continue to make efforts to contribute extensively to improvement in quality of life (QOL) of people in society through the development of functional foods.

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