Oryza

ORYZA OIL & FAT CHEMICAL CO., LTD.

FERULIC ACID

Beauty・Antioxidant・Brain function enhancing effect Food & Cosmetic Material

- FERULIC ACID (Food Grade)
- FERULIC ACID (Cosmetic Grade)

ORYZA OIL & FAT CHEMICAL CO., LTD.

Ver. 1.2 YF

Food & Cosmetic Material

FERULIC ACID

1. Introduction

Rice has been cultivated in large part of Japan for human nutrition and as one of the export resources. In recent years, there are increasing studies focusing on the bioactive components of rice and rice bran. Oryza Oil & Fat Chemical Co., Ltd has been involved in the research and development on the functional benefits of bioactive components of rice bran and rice germ. Rice derived γ-oryzanol, tocotrienols, sterol, squalane and ceramide are now widely used as active ingredient in health food, food additives, pharmaceutical and cosmeceutical products. In this instance, we have successfully developed ferulic acid, 100% extracted and purified from rice germ and rice bran with our technology.

2. What is Ferulic Acid?

Ferulic acid is a derivative of cinnamic acid with molecular formula $C_{10}H_{10}O_4$. In 1886, Hlasiwetz Barth, an Austrian, isolated 3-methoxy-4-hydroxycinnamic acid from the genus Ferula foetida for structure determination. Ferulic acid together with dihydroferulic acid, is a component of lignocelluloses, conferring cell wall rigidity by cross linking lignin and polysaccharides. It is commonly found in seeds of plant such as rice, wheat and oats. Besides, Ferulic Acid exhibited biochemical role in the inhibition of seed germination, inhibition of indole-acetic acid and enzyme, inhibition of decarboxylation activity & other protective effect on micro-organisms and pets.

The syntheis of Ferulic acid was established by Dutt in 1935 when ferulic acid was used as a precursor in the manufacturing of vanillin and malonic acid. There are vast numbers of studies documented on the bio-medical properties of ferulic acid such as antioxidant activity, UV-absorbing capacity & its effect of lignin as precursor in plants metabolic pathway. Ferulic acid, being highly abundant, is indeed difficult to synthesize, Oryza Oil & Fat Chemical has successfully developed an efficient method to extract ferulic acid from rice bran and suitable for applications in the health and beauty arena.

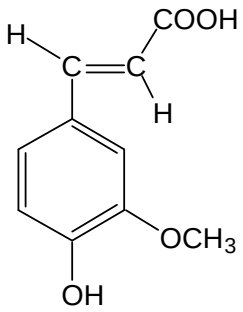

Fig 1. Ferulic acid

3. The functional effect of Ferulic acid

i. Antioxidant Effect

Ferulic Acid, like many phenols exhibits antioxidant effect in response to free radicals by donating hydrogen from its phenolic hydroxyl group. It has been revealed that the antioxidant capacity of phenolic acid is equivalent to lecithin upon comparison with "Ghee", [a class of clarified butter originated from India] on inhibition of time dependent peroxide value.[1)] In addition, the reactive oxygen species scavenging effect of ferulic acid has been reported to be similar to that of superoxide dismutase.[2)]

Reference
1) Gupta S., *et al*., *Milchwissenschaf* , **34**, 205 (1979).
2) Toda S., *et al*., *Plant. Med.* , **57**, 8 (1991).

ii. Prevention of food discoloration

Ferulic Acid is listed as "antioxidant" in the "food additives" list, it has been reported to maintain color tone of Greenpeace, prevent discoloration of Green Tea, and prevent oxidation of banana turning black color, thus reduce bacterial contamination.[3)] In a recent study, the effect of ferulic acid on Red Sea Bream (*Pagrus major*) was examined. Ferulic Acid (0.01, 0.05, 0.1 and 0.5%: Group 2-5) and γ-oryzanol (0.05, 0.1 and 0.5%: Group 6-8) were given to Red Sea Bream for 98 days and color of Red Sea Bream was assessed (Fig. 2) and compared with control (Group 1). Results showed that the color of Red Sea Bream was brighter (Table 1)[4)] in groups fed with ferulic acid and γ-oryzanol, hence, ferulic acid and γ-oryzanol are preventive against photo-oxidation of lutein and astaxanthin in Red Sea Bream.

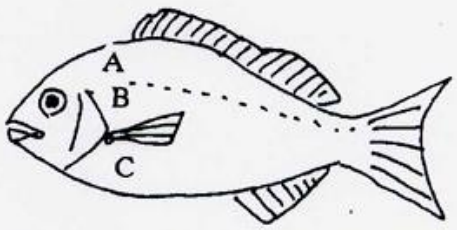

Fig. 2 Measuring Position of Integument Color in Red Sea Bream.
A: head, B: lateral side, C: ventral side.

Table 1 Effect of Supplementation on FA and OZ for Integument Color of Red Sea Bream.

	Group							
	1	2	3	4	5	6	7	8
Head								
L value	32.7 ± 0.8	37.1 ± 1.2**	37.9 ± 1.7*	34.2 ± 1.1	38.7 ± 1.0**	40.9 ± 1.0**	37.1 ± 0.8	38.0 ± 1.4
a value	8.0 ± 0.3	7.9 ± 0.5	8.2 ± 0.4	8.0 ± 0.2	8.1 ± 0.7	8.5 ± 0.2	8.5 ± 0.4	8.0 ± 0.4
b value	10.7 ± 0.7	14.1 ± 0.8**	13.6 ± 1.0*	12.4 ± 0.9	12.7 ± 0.4*	10.5 ± 0.6	12.2 ± 1.0	11.9 ± 0.7
Lateral side								
L value	62.5 ± 1.5	66.7 ± 1.8	66.7 ± 1.2*	68.3 ± 1.3**	64.6 ± 0.9	63.6 ± 1.4	62.5 ± 1.4	62.9 ± 1.2
a value	12.2 ± 0.6	14.3 ± 0.7*	13.7 ± 1.1	13.1 ± 0.5	14.4 ± 1.1	14.3 ± 1.4	15.7 ± 0.6**	14.4 ± 0.9
b value	20.8 ± 1.1	27.7 ± 1.0*	20.9 ± 0.6	20.5 ± 0.9	21.7 ± 1.0	18.2 ± 0.8	21.9 ± 0.7**	18.1 ± 0.8
Ventral side								
L value	82.2 ± 1.2	84.7 ± 0.5	86.1 ± 1.3*	85.3 ± 0.7*	84.0 ± 0.9	84.5 ± 0.7	85.0 ± 0.8	85.0 ± 0.8

Values are expressed as means ± SE of 20 fish par group.
The asterisk indicates significant difference from the control group within the same row (* $p < 0.05$, ** $P < 0.01$).

Reference
3) *Food Chemicals* **8**, 76-79 (1999).
4) Maoka T., Tanimoto F., Sano M., Tsurukawa K., Tsuno T., Tsujiwaki S., Ishimaru K., Takii K. Effects of dietary supplementation of ferulic acid and gamma-oryzanol on integument color and suppression of oxidative stress in cultured red sea bream, Pagrus major. *J. Oleo Sci*. **57**, 133-7, (2008).

iii. Cosmetic Effect (Skin Whitening, Photo-protection)

The structure of Ferulic Acid is similar to tyrosine and is believed to inhibit melanin formation through competitive inhibition with tyrosine [5]. In addition, it has been documented that Ferulic Acid demonstrated strong absorption on harmful UV-wavelength[6]. Recently, it has been reported that Vitamin E Ferulic Acid Ester exhibited inhibitory effect on melanin production [7], it is anticipated to become a potential pigmentation inhibitor.

Besides, comparison results on the effect of ferulic acid, CoQ10, idebenone (an organic compound of quinine family) & kinetin (a type of cytokine) on UV irradiation was documented [8]. In the experiment, mixed solution of (C+E+Ferulic acid) ferulic acid (0.5%), vitamin C (15%) & vitamin E (1%), ubiquinone solution 1%, idebenone solution 1%, idebenone cream 0.5-1%, 0.5%, kinetin solution 0.1% and kinetin cream 1% respectively was applied topically to the skin of pigs for 4 days. The applied area was then irradiated with UVA & UVB at 5 different intensities respectively. Image of irradiated area was taken and cell death area was determined. As illustrated in Fig. 3, skin treated with mixed solution containing ferulic acid showed a UV protective effect compared with control. In comparison with other photo-protective agents, mixed solution containing ferulic acid exhibited most potent protective effect against photo damage and cell death (Fig. 4).

In another paper published by the same research group revealed the UV-protective effect of topical ferulic acid 0.5% on human skin.[9] With these positive finding, ferulic acid has been widely used in cosmetics applications for absorbing the long UV-wavelength as sunscreen or whitening agent. The effect of ferulic acid may be enhanced with systemic application (i.e. oral) of food grade or pharmaceutical grade ingredient.

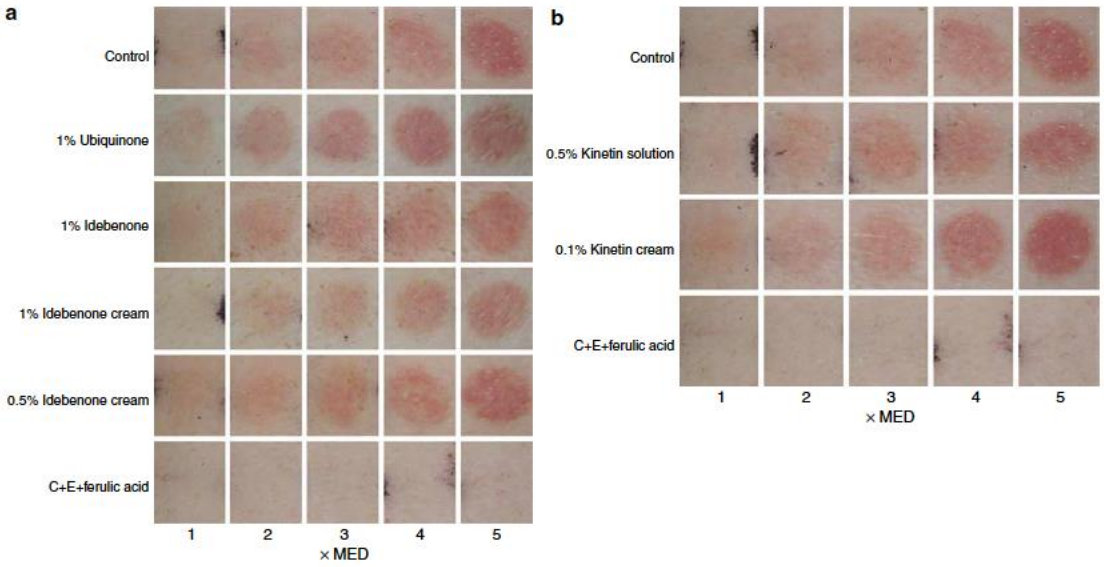

Fig. 3 The photoprotective effect of ferulic acid in pig skin[8)]

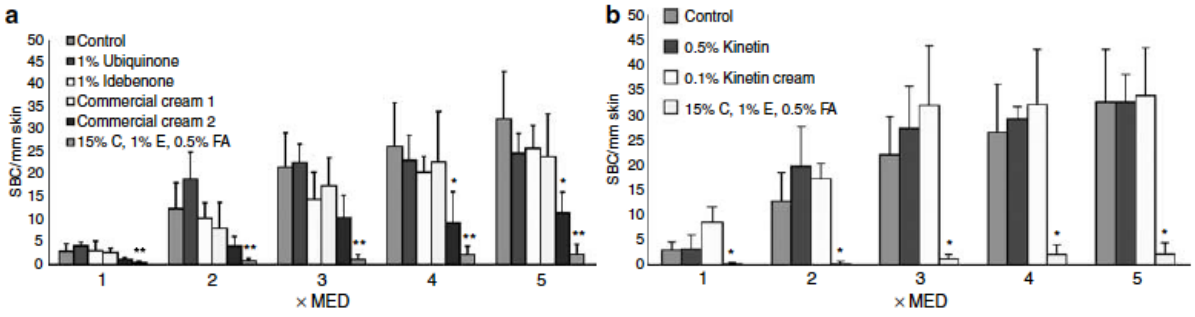

Fig. 4 The inhibitory effect of ferulic acid on pig skin's cell death (a: * P <0.05 vs control, ** P <0.05 vs all samples, b: * P <0.05 vs all samples) [8)]

Reference

5) *Fragrance Journal*, No.45, 92 (1980).
6) *Fragrance Journal*, No129,41(1991).
7) *Fragrance Journal*, No9, 19 (1997).
8) Tournas J. A., Lin F. H., Burch J. A., Selim M. A., Monterio-Riviere N. A., Zielinski J. E., Pinnell S. R. Ubiquinone, idebenone, and kinetin provide ineffective photoprotection to skin when compared to a topical antioxidant combination of vitamin C and E with ferulic acid. *J. Invest. Dermatol.* **126**, 1185-7, (2006).
9) Murray J. C., Burch J. A., Streilein R. D., Iannacchione M. A., Hall R. P., Pinnell S. R. A topical antioxidant solution containing vitamins C and E stabilized by ferulic acid provides protection for human skin against damage caused by ultraviolet irradiation. *J. Am. Acad. Dermatol.* **59**, 418-25, (2008).

iv. Growth Enhancing Effect

The structure of Ferulic acid is similar to normetanephrine, the first metabolite of norepinephrine, hence mimicking a stimulatory effect on somatotrophin in pituitary gland.[10)]

Reference

10) Gorewit R. C. Pituitary and thyroid hormone responses of heifers after ferulic acid administration. *J. Dairy Sci.* **66**, 624-9 (1983).

v. Inhibitory Effect of Carcinogenesis of Colorectal Cancer

Ferulic acid inhibited growth of colon cancer cells *in vitro*, [11)] further *in vivo* test confirmed the inhibitory effect on carcinogenesis of colon cancer in rats. [12)]

Reference

11) Mori H., Kawabata K., Yoshimi N., Tanaka T., Murakami T., Okada T., Murai H. Chemopreventive effects of ferulic acid on oral and rice germ on large bowel carcinogenesis. *Anticancer Res*. **19**, 3775-8 (1999).
12) Hudson E. A., Dinh P. A., Kokubun T., Simmonds M. S., Gescher A. C. Characterization of potentially chemopreventive phenols in extracts of brown rice that inhibit the growth of human breast and colon cancer cells. *Cancer Epidemiol Biomarkers Prev.*, **9**, 1163-70 (2000).

vi. Blood Sugar Lowering Effect

It has been documented that ferulic acid may lower blood sugar level of Type 1 & Type 2 diabetic mice [13)] by enhancing insulin secretion.[14)] In a recent study, diabetic mice was given rice derived ferulic acid for 17 days and results showed that plasma insulin level increased while blood sugar level decreased significantly compared to control.[15)] Other findings include increased glycogen synthesis and glucokinase activity in the liver while total cholesterol and LDL-cholesterol were decreased. Therefore, ferulic acid may be beneficial in Type 2 diabetic and for the management of diabetic complications.

Reference

13) Study on synthetic organic chemistry using ferulic acid and its homologous phenols as basic raw materials: Study on the substance conversion of ferulic acid using an organic synthetic method. Ministry of Education, Culture, Sports, Science and Technology (1998-2000).
14) Nomura H., *et al*. Acceleration of ferulic acid and related compounds on insulin secession . Research report of Wakayama industrial technology center, 17-9 (2001).
15) Jung E. H., Kim S. R., Hwang I. K., Ha T. Y. Hypoglycemic effects of a phenolic acid fraction of rice bran and ferulic acid in C57BL/KsJ-db/db mice. *J. Agric. Food Chem*. **55**, 9800-4, (2007).

vii. Blood pressure lowering effect

In a study group by Ardiansyah *et al*., reported that single administration of Ferulic Acid (9.5mg/kg) may lower blood pressure in rats (SHASP).[16] Plasma angiotensin converting enzyme (ACE) was reduced 2 hours after administration of Ferulic Acid, which in turn lower blood pressure. Besides, total cholesterol and triglyceride level was found to be lower which may assist in the regulation of hyperlipidemia.

Reference

16) Ardiansyah, Ohsaki Y., Shirakawa H., Koseki T., Komai M. Novel effects of a single administration of ferulic acid on the regulation of blood pressure and the hepatic lipid metabolic profile in stroke-prone spontaneously hypertensive. *J. Agric. Food Chem.* **56**, 2825-30, (2008).

viii. Brain function enhancing effect

Cheng *et al*. reported that Ferulic acid (100mg/kg) provides neuroprotection against oxidative stress-related apoptosis after cerebral ischemia/reperfusion injury by inhibiting ICAM-1 mRNA expression in rats.[17] Furthermore, several studies concomitantly reported the protective effect of ferulic acid on amyloid-beta-peptide induced neurotoxicity & oxidative stress. [18-21]

The protective effect of long term administration of ferulic acid against amyloid-beta-peptide induced toxicity *in vivo* was further investigated by Yan *et al.*[22] Results showed that treatment of mice with ferulic acid for 4 weeks attenuated the amyloid-beta-peptide induced memory impairment. Hence, ferulic acid may enhance learning ability and memory function.

Reference

17) Cheng C. Y., Su S.Y., Tang N. Y., Ho T. Y., Chiang S. Y., Hsieh C. L. Ferulic acid provides neuroprotection against oxidative stress-related apoptosis after cerebral ischemia/reperfusion injury by inhibiting ICAM-1 mRNA expression in rats. *Brain Res.* **13**, 136-50, (2008).

18) Mohmmad Abdul H., Butterfield D. A. Protection against amyloid beta-peptide (1-42)-induced loss of phospholipid asymmetry in synaptosomal membranes by tricyclodecan-9-xanthogenate (D609) and ferulic acid ethyl ester: implications for Alzheimer's disease. *Biochim. Biophys. Acta.* **1741**, 140-8, (2005).

19) Cho J. Y., Kim H. S., Kim D. H., Yan J. J., Suh H. W., Song D. K. Inhibitory effects of long-term administration of ferulic acid on astrocyte activation induced by intracerebroventricular injection of beta-amyloid peptide (1-42) in mice. *Prog. Neuropsychopharmacol. Biol. Psychiatry* **29**, 901-7, (2005).

20) Jin Y., Yan E. Z., Fan Y., Zong Z. H., Qi Z. M., Li Z. Sodium ferulate prevents amyloid-beta-induced neurotoxicity through suppression of p38 MAPK and upregulation of ERK-1/2 and Akt/protein kinase B in rat hippocampus. *Acta. Pharmacol. Sin.* **26**, 943-51, (2005).

21) Perluigi M., Joshi G., Sultana R., Calabrese V., De Marco C., Coccia R., Cini C., Butterfield D. A. *In vivo* protective effects of ferulic acid ethyl ester against amyloid-beta peptide 1-42-induced oxidative stress. *J. Neurosci. Res.* **84**, 418-26, (2006).

22) Yan J. J., Cho J. Y., Kim H. S., Kim K. L., Jung J. S., Huh S. O., Suh H. W., Kim Y. H., Song D. K. Protection against beta-amyloid peptide toxicity *in vivo* with long-term administration of ferulic acid. *Br. J. Pharmacol.* **133**, 89-96, (2001).

4. Ferulic Acid – Safety Profile

Acute Toxicity (LD_{50})

LD_{50} conducted using mouse model deduced to be 857mg/kg.

5. Commercial Applications

Application	Example
Food	Soft capsules, tablets, hard capsules, candy, chewing gum, gummy, snacks, cookies, chocolate, wafer, jelly, drink etc.
Cosmetics	Soap, cleanser, shampoo, rinse, toner, lotion, foundation, lip balm, lip sticks etc

6. Packaging

Ferulic Acid (powder, food, cosmetic applications)

5kg	Interior packing:	Double polythene bags, cans
	Exterior packing:	Cardboard Packaging

7. Storage

Store in a cool, dry, dark place.

8. Ferulic Acid –Expression

Ferulic Acid (Food grade)
Expression: Ferulic Acid
Rice Bran Extract

Ferulic Acid (Cosmetic grade)
INCI: Ferulic Acid

*Please refer to your nation's standard.

PRODUCT STANDARD

PRODUCT NAME

FERULIC ACID

(FOOD)

This product is extracted and refined from the rice bran of *Oryza sativa* Linne (Gramineae). Dried product contains minimum of 98.0 % ferulic acid ($C_{10}H_{10}O_4$).

Appearance — White or light yellowish brown crystalline powder. It has no smell or light unique smell.

Certification Test

(1) This product has maximum values of absorption spectrum at wavelength 236 nm. and 322 nm respectively under the measurement of extinction spectra of ethanol solution. (1-100000)

(2) When 0.01 g of this product is dissolved in 10 ml of potassium hydroxide ethanol solution, solution turns to yellow colour.

(3) 0.01 g of this product is dissolved in 2 ml of acetone and 0.1 ml solution of ferric chloride ethanol(1-50), solution turns to reddish brown colour.

Content of Ferulic Acid — Min. 98.0 %

(QUANTITATIVE ANALYSIS)

Dry this product with P_2O_5 under reduced pressure for 4 hours at 40℃. Dissolve 0.02g in ethanol in a 50 ml volumetoric flask, add ethanol to volume. (solution A) On the other hand, dissolve 0.02 g of standard Ferulic Acid in ethanol in a 50 ml volumetric flask, and add ethanol to volume. (solution B). Analysis is performed by High Performance Liquid Chromatography (HPLC) as follows using 5 μl of solution A and B. Measure the area of solution A & solution B respectively.

Column	:	capcellpak C18 (4.6 mm φ × 250 mm)
Column Temperature	:	35℃
Mobile phase	:	Methanol/0.1% phosphoric acid=50/50
Flow rate	:	1.0 ml/min
Detection	:	UV(322 nm)

$$\text{Quantity of Ferulic Acid (\%)} = \frac{WS(g)\times PS(\%)}{WT(g)\times 100} \times \frac{AT}{AS} \times 100$$

WT： Weight of sample (g)
WS： Weight of standard (g)
AT： Area of solution A
AS： Area of solution B
PS： Purity of standard

Loss on Drying	Max. 0.5 %	(Analysis for Hygienic Chemists,1g,105℃,3h)
Ignition Residue	Max. 0.1 %	(The Japanese Standards for Food Additives)
Melting Point	171 ～ 174℃	(The Japanese Standards for Food Additives)
Purity Test		
（1） Heavy Metals	Max. 10 ppm	(The Japanese Standards for Food Additives)
（2） Arsenic	Max. 1 ppm	(Standard Methods of Analysis in Food Safety Regulation)
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

Ingredient	Content
Ferulic Acid	100 %

PRODUCT STANDARD

PRODUCT NAME

FERULIC ACID

(COSMETIC)

This product is extracted and refined from the rice bran of *Oryza sativa* Linne (Gramineae). Dried product contains minimum of 98.0 % ferulic acid ($C_{10}H_{10}O_4$).

Appearance — White or light yellowish brown crystalline powder. It has no smell or lightly unique smell.

Certification Test

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Column Temperature	:	35℃
Mobile phase	:	Methanol/0.1% phosphoric acid=50/50
Flow rate	:	1.0 ml/min
Detection	:	UV(322 nm)

$$\text{Quantity of Ferulic Acid (\%)} = \frac{WS(g)\times PS(\%)}{WT(g)\times 100} \times \frac{AT}{AS} \times 100$$

WT： Weight of sample (g)
WS： Weight of standard (g)
AT： Area of solution A
AS： Area of solution B
PS： Purity of standard

Loss on Drying	Max. 0.5 %	(1g,105℃,3h)
Ignition Residue	Max. 0.1 %	(The First Method, 5 g)
Melting Point	171 ～ 174℃	
Purity Test		
（1）Heavy Metals	Max. 10 ppm	(The Second Method)
（2）Arsenic	Max. 1 ppm	(The Third Method)
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

Ingredient	Content
Ferulic Acid	100 %

Ref: The Japanese Standards of Quasi-Drug Ingredients.

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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