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Amended Final Report on the Safety Assessment of Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Rice Bran Acid, Oryza Sativa (Rice) Bran Wax, Hydrogenated Rice Bran Wax, Oryza Sativa (Rice) Bran Extract, Oryza Sativa (Rice) Extract, Oryza Sativa (Rice) Germ Powder, Oryza Sativa (Rice) Starch, Oryza Sativa (Rice) Bran, Hydrolyzed Rice Bran Extract Hydrolyzed Rice Bran Protein, Hydrolyzed Rice Extract, and Hydrolyzed Rice Protein[1]

This report addresses the safety of cosmetic ingredients derived from rice, Oryza sativa. *Oils, Fatty Acids, and Waxes*: Rice Bran Oil functions in cosmetics as a conditioning agent—occlusive in 39 formulations across a wide range of product types. Rice Germ Oil is a skin-conditioning agent—occlusive in six formulations in only four product categories. Rice Bran Acid is described as a surfactant—cleansing agent, but was not in current use. Rice Bran Wax is a skin-conditioning agent—occlusive in eight formulations in five product categories. Industry did not directly report any use of Rice Bran Wax. Hydrogenated Rice Bran Wax is a binder, skin-conditioning agent—occlusive, and viscosity-increasing agent—nonaqueous in 11 formulations in six product categories. Rice Bran Oil had an oral LD_{50} of >5 g/kg in white rats and Rice Wax had an oral LD_{50} of >24 g/kg in male mice. A three-generation oral dosing study reported no toxic or teratologic effects in albino rats fed 10% Rice Bran Oil compared to a control group fed Peanut Oil. Undiluted Rice Bran Oil, Rice Germ Oil, and Hydrogenated Rice Bran Wax were not irritants in animal skin tests. Rice Bran Oil was not a sensitizer. Rice Bran Oil, Rice Germ Oil, Rice Wax, and Hydrogenated Rice Bran Wax were negative in ocular toxicity assays. A mixture of Rice Bran Oil and Rice Germ Oil had a ultraviolet (UV) absorption maximum at 315 nm, but was not phototoxic in a dermal exposure assay. Rice Bran Oil was negative in an Ames assay, and a component, γ-oryzanol, was negative in bacterial and mammalian mutagenicity assays. Rice oils, fatty acids, and waxes were, at most, mildly irritating in clinical studies. *Extracts*: Rice Bran Extract is used in six formulations in four product categories. Rice Extract is a hair-conditioning agent, but was not in current use. Hydrolyzed Rice Extract is used in four formulations and current concentration of use data were provided for other uses. Hydrolyzed Rice Bran Extract, described as a skin-conditioning agent—miscellaneous, is used in two product categories. Use concentrations are in the 1% to 2% range. Rice Bran Extract is comprised of proteins, lipids, carbohydrates, mineral ash, and water. The content includes palmitic, stearic, oleic, and linoleic acids. Other components include antioxidants such as tocopherols. Rice Extract reduced the cytotoxicity of sodium chloride in male rats. *Bran, Starch and Powder*: Rice Bran (identified as rice hulls) is an abrasive and bulking agent in one formulation. Rice Starch is an absorbent and bulking agent in 51 formulations across a wide range of product categories. Rice Germ Powder is an abrasive and one manufacturer described an exfoliant use, but it was not reported to be used in 2002. Oral carcinogenicity studies done on components of Rice Bran (phytic acid and γ-oryzanol) were negative. Rice Bran did not have an anticarcinogenic effect on 1,2-dimethylhydrazine-induced large bowel tumors. In cocarcinogenicity studies done using 1,2-dimethylhydrazine and other agents, with Rice Bran Oil and Rice Bran-derived hemicellulose and saccharide, tumor inhibition was observed; γ-oryzanol did not inhibit the development of neoplasms. A decrease in cutaneous lesions in atopic dermatitis patients was reported following bathing with a Rice Bran preparation. *Proteins*: Hydrolyzed Rice Bran Protein and Hydrolyzed Rice Protein function as conditioning agents (hair or skin), but only the latter was reported to be used in a few products. An in vitro phototoxicity assay using UVA light found no photochemical toxicity. Rice bran protein hydrolysates are not acutely toxic, are not skin or ocular irritants in animals, are not skin sensitizers in guinea pig maximization tests, and are not irritating or sensitizing in clinical tests. Isolated cases of allergy to raw rice have been reported, but rice, in general, is considered nonallergenic. The Cosmetic Ingredient Review (CIR) Expert Panel considered that safety test data available on certain of these ingredients could be extrapolated to the entire group. Although Rice Bran Extract does contain UV absorbing compounds at low concentrations, clinical experience suggested no phototoxicity would be associated with such materials. Rice derived ingredients generally are considered to be nonallergenic. There were no safety test data available for Hydrolyzed Rice Extract and Hydrolyzed Rice Bran Extract, but their safety may be inferred from that of the extracts from which they are derived. Current levels of polychlorinated biphenyls (PCBs) and heavy metals in rice-derived ingredients used in cosmetics are not a safety concern. The Panel was concerned, however, that contaminants such as pesticides have

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[1]Reviewed by the Cosmetic Ingredient Review Expert Panel. Address correspondence to Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036, USA.

been reported in Rice Bran Oil used for cooking. Pesticides and heavy metals should not exceed currently reported levels for rice-derived cosmetic ingredients. The CIR Expert Panel concluded that these rice-derived ingredients are safe as cosmetic ingredients in the practices of use and concentrations as described in this safety assessment.

INTRODUCTION

This report addresses the safety of cosmetic ingredients derived from rice, *Oryza sativa*, as reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel. Included in this report are data on Oryza Sativa (Rice) Bran Oil (CAS Nos. 68553-81-1 and 84696-37-7), Oryza Sativa (Rice) Germ Oil, Rice Bran Acid (CAS No. 93165-33-40), Oryza Sativa (Rice) Bran Wax (CAS No. 8016-60-2), Hydrogenated Rice Bran Wax, Oryza Sativa (Rice) Extract (CAS No. 90106-37-9), Oryza Sativa (Rice) Bran Extract, Oryza Sativa (Rice) Germ Powder, Oryza Sativa (Rice) Starch (CAS No. 9005-25-8—generic for all starches), Oryza Sativa (Rice) Bran, Hydrolyzed Rice Bran Protein, Hydrolyzed Rice Protein, Hydrolyzed Rice Extract and Hydrolyzed Rice Bran Extract. There are no safety test data available for the last two hydrolysates, but their safety may be inferred from that of the extracts from which they are derived.

To organize the information in this report, these ingredients have been divided into four groups. The oils, fatty acids, and waxes group includes Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Rice Bran Acid, Oryza Sativa (Rice) Bran Wax, and Hydrogenated Rice Bran Wax. The extracts group includes Hydrolyzed Rice Bran Extract, Hydrolyzed Rice Extract, Oryza Sativa (Rice) Extract, and Oryza Sativa (Rice) Bran Extract. The bran, starch, and powder group includes Oryza Sativa (Rice) Bran, Oryza Sativa (Rice) Starch, and Oryza Sativa (Rice) Germ Powder. The protein group includes Hydrolyzed Rice Bran Protein, and Hydrolyzed Rice Protein.

γ-Oryzanol is a phytosterol found in rice-derived ingredients for which safety test data are available and are included under that heading throughout this report.

The CIR Expert Panel also reviewed data from earlier safety assessments of plant oils, acids, and starches, as well as Tocopherol, which is found in rice-derived ingredients. Those earlier findings included:

- Wheat Starch—found safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1980a; Andersen 2003);
- Wheat Germ Oil—found safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1980b, Andersen 2003);
- Cottonseed-derived ingredients—found safe as used in cosmetic products, provided that established limits on gossypol, heavy metals, and pesticide concentrations are not exceeded (Andersen 1998);
- Safflower Oil—found safe in the present practices of use (Elder 1985);
- Avocado Oil—found safe for use as presently incorporated into cosmetic formulations (Elder 1980c; Andersen 2003);
- Sweet Almond Oil—found safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1983)
- Tall Oil Acid—found safe for use in cosmetic products (Elder 1989);
- Tallow and Tallow-derived ingredients—found safe as cosmetic ingredients in the present practices of use (Elder 1990); and
- Tocopherol and Tocopherol-derived ingredients—found safe as used in cosmetic formulations (Andersen 2002).
- The CIR Expert Panel has considered the safety of many fatty acids that are the components of rice-derived ingredients, including:
- Oleic, Lauric, Palmitic, Myristic, and Stearic Acids—found safe in the present practices of use and concentration in cosmetics (Elder 1987); and
- Arachidonic Acid—the available data are insufficient to support the safety in cosmetic products (Andersen 1993).

CHEMISTRY

Definition

Oils, Fatty Acids, and Waxes

As described in the *International Cosmetic Ingredient Dictionary and Handbook* (Pepe et al. 2002), Oryza Sativa (Rice) Bran Oil is the oil expressed from rice *Oryza sativa* bran, Oryza Sativa (Rice) Germ Oil is the oil obtained by the expression of rice germ *Oryza sativa*, Rice Bran Acid (CAS no. 93165-33-4) is a mixture of fatty acids derived from Rice Bran (Oryza Sativa) Oil (q.v.), Oryza Sativa (Rice) Bran Wax is a wax obtained from rice bran, *Oryza sativa*, and Hydrogenated Rice Bran Wax is the end product of controlled hydrogenation of Rice Bran Wax (q.v.).

Extracts

Oryza Sativa (Rice) Bran Extract is an extract of the bran of rice, *Oryza sativa*; Oryza Sativa (Rice) Extract is an extract of the grains of rice, *Oryza sativa*; Hydrolyzed Rice Extract is the hydrolysate of Oryza Sativa (Rice) Extract by acid, enzyme, or other method of hydrolysis; and Hydrolyzed Rice Bran Extract is the hydrolysate of Oryza Sativa (Rice) Bran Extract by acid, enzyme, or other method of hydrolysis (Pepe et al. 2002).

Bran, Starch, and Powder

As described in the *International Cosmetic Ingredient Dictionary and Handbook* (Pepe et al. 2002), Oryza Sativa (Rice) Bran is the broken hulls of rice *Oryza sativa*; Oryza Sativa (Rice)

Starch is a starch obtained from rice, *Oryza sativa*; and Oryza Sativa (Rice) Germ Powder is the powder derived from the rice germ, *Oryza sativa*.

Rukmini (1988) stated that Rice Bran is a by-product of rice milling obtained during polishing of rice. It is the part between the paddy husk and endosperm and consists of 15% to 20% oil.

As reported by Informatics (1974), starches are a GRAS (generally recognized as safe) food ingredient. Plant starches are polymers which consists of monomeric units of D-anhydroglucose. The predominant linkage is 1,4-alpha glucosidic bonds. There are two basic starch polymers, amylose, and amylopectin. They are both composed of anhydroglucose units but differ in the way they are linked and shaped.

Amylose is a linear polymer that contains 1,4-alphaglucose bonds between units. Each unit consists of one primary and two secondary hydroxyl groups except the terminal unit. Amylose has reducing and nonreducing ends that contain varying numbers of hydroxyl units and an aldehydic reducing group.

Amylopectin is a highly branched structure and each branch contains 15–25 anhydroglucose units connected by 1,4-alpha linkages. Branches are connected by linkages attaching carbon 1 of the anhydroglucose unit at the beginning of the branch to carbon 6. Amylopectin is usually larger in size than amylose (Informatics 1974).

Pasapane et al. (1999) reported 17% amylose and 83% amylopectin in Rice Starches. Starches can be physically and/or chemically modified for a specific need. Table 1 identifies the common chemical modifications.

Proteins

As described in the *International Cosmetic Ingredient Dictionary and Handbook* (Pepe et al. 2002), Hydrolyzed Rice Bran Protein is the hydrolysate of rice bran protein derived from acid, enzyme, or other method of hydrolysis and Hydrolyzed Rice Protein is the hydrolysate of rice protein derived similarly.

Chemical Composition

γ-Oryzanol

γ-Oryzanol (CAS No. 11042-64-1) is a phytosterol found in/derived from Rice Bran (Hiraga et al. 1993) or Rice Bran Oil (Kubota and Sekine 1978). Where data are available on γ-Oryzanol, those data will be presented first in each section of this report. Crude rice bran oil contains about 2% or more of γ-Oryzanol, a group of ferulate esters of triterpene alcohols and phytoesters.

An oil registered in Japan as "rice germ oil" is a mixture of Rice Bran Oil and Rice Germ Oil contains 1.0% to 1.5% oryzanol (Ichimaru Pharcos Co. 1998).

Oils, Fatty Acids, and Waxes

Buffa (1976) reported the fatty acid and fatty alcohol composition of two rice-derived waxes given in Table 2. Hydrogenated rice wax is presumed to be Hydrogenated Rice Bran Wax.

Saker et al. (1986) evaluated the chemical components in Rice Germ Oil and found 20.80% fat on dry basis. The fatty acid composition is presented in Table 3.

Rice Germ Oil fatty acids were 27.19% saturated and 71.22% unsaturated. The percentage of unsaponifiable matter, phospholipids, and sterols were 4.51%, 2.43%, and 1.98%, respectively. The carotenoid content of Rice Germ Oil was 0.65 mg/g and the vitamin E content was 0.067%. Vitamins A, D, and K were absent (Saker et al. 1986).

Crude Rice Bran Oil is described as nonedible due to high free fatty acids and unsaponifiables. The unsaponifiable fraction also contains, "appreciable amounts" of waxes (Rukmini 1988).

Rukmini and Raghuram (1991) reported a typical fatty acid composition of finished Rice Bran Oil samples as shown in Table 4.

According to McCaskill and Zhang (1999), among the many sterols present in the unsaponifiable fraction of Rice Bran Oil, oryzanols and tocotrienols have been intensively studied.

TABLE 1
Chemical modifications of Starch (Pasapane et al. 1999)

Specific modification	Description
	Depolymerization
Acid hydrolysis	A strong acid is added to a granular starch slurried in water, and heat is added to degrade the starch
Oxidation	An oxidizing agent is added to a granular starch slurried in water, and heat is added to degrade the starch
Enzymatic action	Enzymes attack and break down the starch molecule at very specific chemical links
Heating	Dried, acidified starch is heated—also know as starch roasting
	Addition of monofunctional substituent groups
Hydrophobic	Hydrophobic moieties are attached to the starch backbone
Cross-linking	The starch is treated to produce chemical cross-links, providing higher, more stable viscosities
Hydroxypropylation	β-hydroxypropyl groups are attached to the starch
Anionic/cationic groups	Anionic and cationic groups can be added for particular functional attributes

TABLE 2
Fatty acid and fatty alcohol composition of Rice Wax and Hydrogenated Rice Wax (Buffa 1976).

Composition	Carbon no.	Rice Wax (%)	Hydrogenated Rice Wax (%)
Acid			
Myristic Acid	C_{14}	—	0.32
Palmitic Acid	C_{16}	3.28	18.94
Stearic Acid	C_{18}	0.32	60.55
Oleic Acid	$C_{18}F_1$	0.32	—
Arachidic Acid	C_{20}	0.69	1.35
Behenic Acid	C_{22}	16.24	3.64
Lignoceric Acid	C_{24}	42.62	9.26
Cerotic Acid	C_{26}	2.01	0.46
Montanic Acid	C_{28}	1.17	—
Melissic Acid	C_{30}	2.78	—
Lacceroic Acid	C_{32}	1.33	—
Tetratriacontanoic Acid	C_{34}	1.1	—
Hexatriacontanoic Acid	C_{36}	0.56	—
Alcohol			
Behenyl Alcohol	$C_{22}OH$	0.38	
Lignoceryl Alcohol	$C_{24}OH$	3.21	0.92
Ceryl Alcohol	$C_{26}OH$	2.93	1.17
Octacosyl Alcohol	$C_{28}OH$	5.59	1.3
Myricyl Alcohol	$C_{30}OH$	8.35	1.63
Lacceryl Alcohol	$C_{32}OH$	4.64	0.42
Tetratriacontyl Alcohol	$C_{34}OH$	2.22	—
Hexatriacontyl Alcohol	$C_{36}OH$	0.5	—

γ-Oryzanol was identified on the previous page and published studies concerning it are cited throughout this report. Tocotrienols are powerful antioxidants that belong to the vitamin E family. There are at least four forms known and are similar to the tocopherols in chemical structure. Rice Bran Oil is the only readily available oil, other than palm oil, that contains significant levels of tocotrienols (~1000 ppm). A significant portion of the tocotrienols are stripped away with distillate when the oil is deodorized. Tocotrienols may be recovered from the distillate by further fractionation techniques and added back to the oil. These authors reported the rice bran oil fatty acid composition given in Table 5.

TABLE 3
Fatty acid composition of Rice Germ Oil (Saker et al. 1986).

Fatty acids	% in Rice Germ Oil
Myristic	6.92
Palmitic	9.28
Stearic	7.91
Arachidic	3.08
Palmitoleic	4.41
Oleic	17.81
Linoleic	16.22
Linolenic	15.56
Arachidonic	5.48
Arachidotrienoic	5.21

TABLE 4
Fatty acid composition of Rice Bran Oil (Rukmini and Raghuram 1991)

Fatty acid	Percentage
Unsaturated fatty acids	
Oleic acid	38.4%
Linoleic acid	34.4%
Linolenic acid	2.2%
Saturated fatty acids	
Palmitic acid	21.5%
Stearic acid	2.9%
Unsaponifiable fraction (4.2%)	
Tocopherols	81.3 mg%
γ-Oryzanol	1.6%
Squalene	320 mg%

Tsuno Rice, Fine Chemicals Co., Ltd. (2000) provided the composition for Rice Bran Oil and Germ Oil (PRO-15) shown in Table 6.

Extracts

Grau Aromatics GmbH & Co. (1998) provides Oryza Sativa (Rice) Extract containing 10% to 25% extract, >75% sunflower seed oil (solvent used for extraction), and 0.15% DL-α-tocopherol. The ingredient contains proteins, amino acids, peptides, flavonoids, lipids, mineral substances, vitamins, carbohydrates, and starch. It is soluble in oil soluble products, mineral oil, and fatty oils.

Dull (2002) stated that, overall, rice bran extract contains 18% proteins and peptides, 24% lipids, 13% ash, 7% moisture, and

TABLE 5
Rice Bran Oil Fatty Acid Composition (Mccaskill and Zhang 1999)

Fatty acid	Percentage
Myristic	0.25%
Palmitic	21.5%
Stearic	2.9%
Oleic	38.4%
Linoleic	34.4%
Linolenic	2.2%
Arachidic	0.5%
Behenic	0.2%

TABLE 6
Rice Bran Oil and Germ Oil: specifications and composition (Tsuno Rice, Fine Chemicals Co., Ltd. 2000)

Composition	Rice Bran Oil	Rice Germ Oil
Cholesterol	0 g	0 g
Oleic Acid	42 g	42 g
Linoleic Acid	37 g	37 g
Phytosterol	900 mg	1600 mg
Tocopherol	30 mg	30 mg
Tocotrienol	25 mg	25 mg

38% carbohydrates. The fatty acid analysis of rice bran extract is shown in Table 7 (comparable to the fatty acid composition of Rice Bran Oil in Table 4). In addition, other components of rice bran extract were identified and quantified as given in Table 8.

Bran, Starch, and Powder

Oryza Sativa (Rice) Bran contains "a considerable amount of lipids," and some biologically active substances such as inositol, γ-oryzanol, and phytic acid (Fujiwaki and Furusho 1992).

Proteins

The Cosmetic, Toiletry, and Fragrance Association (CTFA 1999a) provided the standard profile of Hydrolyzed Rice Protein components given in Table 9.

Silab (2002) reported that a Hydrolyzed Rice Protein product (Nutriskin®) is an aqueous solution (pH 5.0 to 6.0), transparent, yellow in color, and weak in smell. The components of this product are given in Table 10.

The amino acid composition of Nutriskin® determined after acid hydrolysis (6 N HCl) at 110°C for 24 h is given in Table 11.

TABLE 7
Fatty acid composition of Rice Bran Extract (Dull 2002)

Fatty acid	Percentage
Unsaturated fatty acids	
Oleic acid	44.59%
Linoleic acid	36.49%
Linolenic acid	None
Other unsaturates	None
Total unsaturates	81.08%
Saturated fatty acids	
Palmitic acid	16.89%
Stearic acid	2.03%
Other saturates	None
Total saturates	18.92%

TABLE 8
Level of other components of Rice Bran Extract (Dull 2002).

Component	Concentration (ppm)	Component	Concentration (ppm)
Phosphorus	30000_	Oryzanol	42.0
Inositol	22400	γ-Tocopherol	40.0
Magnesium	14800	Thiamine	40.0
Potassium	9600	Plant sterols	35.0
Sodium	8000	Vitamin B6	25.0
Manganese	520.0	Copper	8.80
Niacin	428.0	β-Tocopherol	3.2
Zinc	176.0	δ-Tocopherol	1.6
Iron	124.0	Folic acid	0.68
Tocotrienols	79.6	Biotin	0.44
α-Tocopherol	53.2	Vitamin B12	0.016

Chemical Composition of Related Ingredients

The CIR Expert Panel has completed a safety assessment (Elder 1987) of the following fatty acids: Oleic Acid (up to 50%), Lauric Acid (up to 25%), Palmitic Acid (up to 25%), Myristic Acid (up to 50%), and Stearic Acid (>50%). In each case, the Panel determined that these ingredients were safe for use in cosmetics at the current concentration of use, which is given in parentheses. The Panel's safety assessment of Arachadonic Acid (Andersen 1993) found the available data insufficient to support the safety of its use in cosmetics, but this fatty acid is not a significant component of rice-derived ingredients; i.e., it was found in one assay of Rice Germ Oil and only at a concentration of around 5%.

The Panel has also completed safety assessments of other ingredients which are themselves comprised of fatty acids. Except for Cottonseed Oil, the conclusion was safe as used. For Cottonseed Oil, a limitation on gossypol, heavy metals, and pesticides was established. Table 12 gives those ingredients, their maximum "as used" concentration, and the approximate fatty acid composition of each. By comparing Table 12 with the previous tables in this section, it can be determined that these ingredients contain fatty acids not dissimilar from those found in rice-derived ingredients.

TABLE 9
Component profile of Hydrolyzed Rice Protein (CTFA 1999a)

Component	Percentage
Protein	Approximately 60% by weight
Carbohydrates	24%
Moisture	<6%
Fat	0.4%
Ash	7%
Sodium	2.4%

TABLE 10
Component profile of Nutriskin® (Silab 2002)

Component	Amount
Dry matter	55–70 g/L
Proteins (Kjeldahl method)	40–55 g/L
Total sugar	7–10 g/L
Mineral ash	6–8 g/L
Total polyphenols	0.30–0.45 g/L
Phenonip (preservative)	5%

Chemical/Physical Properties

Oils, Fatty Acids, and Waxes

Tsuno Rice, Fine Chemicals Co., Ltd. (2000) provided the specifications for Rice Bran Oil and Germ Oil (PRO-15) shown in Table 13. Physical properties of rice bran oil, a rice germ oil mixture, rice bran wax, and hydrogenated rice bran wax are given in Table 14.

Bran, Starch, and Powder

CTFA (1999b) provided the physical properties of rice starch shown in Table 15.

Extracts

The chemical and physical properties of rice extracts are given in Table 16. No data were available for Hydrolyzed Rice Extract or Hydrolyzed Rice Bran Extract.

Method of Manufacture

γ-Oryzanol

Kubota and Sekine (1978) patented an extraction technique to derive γ-Oryzanol from Rice Bran Oil. Rogers et al. (1993) reported high-performance liquid chromatography (HPLC) detection technique for γ-Oryzanol.

General

Mazzo (1998) described three forms of rice: rough, brown, and white. Rough rice is the harvested unshelled rice, whereas brown rice is rice from which the hull has been removed by shelling or hulling. White rice or milled rice, is rice in which all or most of the bran has been removed by some operation of milling called scouring or whitening. Usually the milling is followed by the operation of polishing in which remaining traces of bran are removed from the kernel.

TABLE 11
Amino acid profile of Nutriskin® (Silab 2002)

Amino acid	Percentage	Amino acid	Percentage
Glutamic Acid	18.5	Glycine	4.6
Arginine	10.5	Valine	4.6
Leucine	9.2	Lysine	4.0
Tyrosine	9.1	Threonine	3.3
Phenylalanine	8.1	Histidine	3.0
Aspartic acid	8.0	Isoleucine	2.0
Serine	7.6	Methionine	1.1
Alanine	6.1		

Bran, Starch, and Powder

Mazzo (1998) stated that Rice Bran is extracted for oil and for its protein. Commercial rice bran contains 11.5% to 17.2% protein, 12.8% to 29.6% fat, 6.2% to 31.5% fiber, and 8% to 17.7% ash, depending on processing. The amount of starch in the bran ranges from 10% to 55%, depending on the degree of milling. Phosphorus, primarily in the form of phytates, is the major mineral constituent of rice bran. Potassium, magnesium, and silicon are also present at high levels.

An overview of commercial and theoretical rice bran processing and utilization is shown in Figure 1.

The process of milling abrades the external cell layers (the bran) down to the endosperm, thoroughly mixing the bran material. Native lipase enzymes come in contact with the oil in the aleurone and subaleurone layers, causing rapid hydrolysis of the oil fraction within raw bran; this results in a rapid increase in free fatty acids and glycerol. This enzymatic deterioration, or lipolysis of the oil fraction within the raw bran, is known as hydrolytic degradation.

Heating bran in the presence of moisture permanently denatures lipolytic enzymes and destroys lipolytic microbes. Preserving rice bran from hydrolytic degradation is accomplished by three processes: retained-moisture heating, added-moisture heating, and dry heating at atmospheric pressure. Low levels of trypsin inhibitors and hemagglutinin from the germ are present in raw rice bran and are destroyed under conditions that denature lipolytic enzymes.

The Rice Bran (with germ) fraction contains the majority of the oil in the kernel. The oil content of clean rice bran is 20% to 22%, which is similar to that of soybeans and cottonseed. Once milled, Rice Bran Oil is exposed to lipases in the bran, which results in its rapid breakdown to free fatty acids at an initial rate of 5% to 7% by weight of the oil per day. Due to the rapid increase in free fatty acids, either refining the edible oil or rice bran stabilization by enzyme inactivation must occur as soon as possible after milling to prevent excessive oil refining loss. The yield of refined Rice Bran Oil depends on the age and storage conditions of the rice, milling practices, bran stabilization, conditions used for extraction, and the method of refining the oil. Extraction can occur at high or low temperatures. Many organic solvents can be used for Rice Bran Oil extraction, with the most popular being *n*-hexane. Hexane extraction at about 60°C results in the inclusion of most of the gums and waxes, which yields a greater quantity of crude oil, but only an 80% yield of refined oil. The gums and waxes are then removed. Conversely, low-temperature extraction at about 18°C removes neutral oil, with minimal quantities of gums and waxes, and may yield 98% refined oil (Mazzo 1998).

TABLE 12
Fatty Acids found in other ingredients found safe by the CIR Expert Panel

Ingredient	Maximum concentration of use (%)	Fatty acid composition (%)				
		Palmitic	Stearic	Oleic	Linoleic	Myristic
Avocado Oil (Elder 1980c)	50	20.3	0.4	43.7	22.5	—
Cottonseed Oil (Andersen 1998)*	21	21	—	30	45	2
Sweet Almond Oil (Elder 1983)	50	5.7–7.9	0.5–1.2	66.3–72.4	18.4–22.3	—
Safflower Oil (Elder 1983)	>50	2	—	26	68	—
Tall Oil Acid (Elder 1989)	25	—	—	49	38	—
Tallow (Elder 1990)	>50	24–32	20–25	37–43	2–3	3–6
Wheat Germ Oil (Elder 1980b)	50	11–16	1–6	8–30	44–65	—

*With limits for gossypol, <450 ppm; lead, ≤0.1 mg/kg; arsenic, ≤3 ppm; mercury, ≤1 ppm; PCB/pesticide, ≤3 ppm; and ≤1 ppm for any one residue.

Oils, Fatty Acids, and Waxes

Buffa (1976) reported two processing techniques for obtaining waxes from Rice Bran Oil. In both techniques, Rice Bran Oil is processed (removal of gumming materials, de-acidation, and dewaxed) to obtain a solid oil-and-fat fraction (crude wax). In the first technique, the wax is extracted from this fraction with solvent and then bleached and refined, thereby creating Oryza Sativa (Rice) Bran Wax. In the second technique, the crude wax is hydrogenated and then bleached, thereby creating Hydrogenated Rice Bran Wax.

Mazzo (1998) stated that the two types of refining used with Rice Bran Oil are alkali and physical. Alkali refining works well with oils that contain relatively high amounts of free fatty acids, but results in a greater loss of neutral oil. Physical refining depends on molecular distillation from a thin film, and refining losses can approach the actual free fatty acid content. Physical refining is usually followed by a light alkali refining to remove the last traces of free fatty acids. High levels of residual free fatty acids and wax in refining Rice Bran Oil lead to discoloration of the oil. Timely bran stabilization and careful control of temperatures during extraction and refining can greatly reduce these problems. Refined oil can be bleached with activated bleaching clay just as any other vegetable oil. High-temperature hexane extraction may result in 3% to 4% wax in the crude oil. These waxes can be isolated and purified by crystallizing and precipitating at low temperatures. The waxes may be centrifuged or filtered off and then washed with acetone or ethanol to remove residual oil (Mazzo 1998).

A manufacturer of Rice Waxes (Yokozeki Oil and Fat Industries Co., Ltd. 2000) reported that the waxes from rice are present as an impurity in Rice Oil. The Rice Oil is manufactured from Rice Bran produced at the same stage when the rice grains are milled. The product obtained from Rice Oil by solvent extraction is crude rice wax. This is refined to obtain refined rice wax. The product Ricebran Wax (S-100) is obtained from Rice Bran by the process of extraction and separation. The product R-100 is obtained by hydrogenating S-100 and retaining a suitable concentration of Rice Oil in the Hydrogenated Rice Wax.

Extracts

CTFA (2003a) provided information from one supplier that Hydrolyzed Rice Bran Extract and Hydrolyzed Rice Extract are obtained by enzyme decomposition of the extract from rice bran and polished rice, respectively. Another supplier indicated that water was added at 4× the volume of polished white rice at an alkaline pH, protease was dissolved in that mixture, and then incubated at 40°C to 50°C for an unspecified time. The mixture was then filtered, neutralized, and heated to 90°C to inactivate

TABLE 13
Rice Bran Oil and Germ Oil: specifications and composition (Tsuno Rice, Fine Chemicals Co., Ltd. 2000)

Specifications	Rice Bran Oil	Rice Germ Oil
Acid value	0.1 max	0.2 max
Unsaponifiable matter	3.5% max	6% max
Peroxide value	2 meq/kg max	5 meq/kg max
Color (Lovibond 133.4 mm)	red 3.5 max; yellow 30 max	red 6.0 max; yellow 40 max
Specific gravity	0.916–0.922	0.913–0.922
γ-Oryzanol	0.4%	1–1.5%

TABLE 14
Physical and chemical properties of Rice Bran Oil and Rice Germ Oil Mixture, Rice Bran Wax, and Hydrogenated Rice Bran Wax

Property	Rice Bran Oil/Germ Oil (Ichimaru Pharcos Co. 1994)	Rice Bran Wax (Buffa 1976)	Hydrogenated Rice Bran Wax (Buffa 1976)
Appearance	Light yellow oil	White flakes	Light yellow granules
Melting point	—	79–83°C	70–77°C
Specific gravity	0.913–0.923	0.932–0.945	0.912–0.927
Saponification value	180–195	75–88	130–160
Iodine value	92–115	5 max	10 max
Refractive index	1.470–1.475	1.478–1.482	1.471–1.474
Heavy metals	10 ppm max	—	—
Arsenic	1 ppm max	—	—

the protease. After another filtration and further purification, parahydroxybenzoate (0.18% by volume) and phenoxyethanol (0.4% by volume) were dissolved in ethanol (3% by volume) and added as preservatives.

Proteins

Hydrolyzed Rice Protein is extracted from rice grains and then is enzymatically digested (CTFA 1999a). Silab (2001b) provided detailed information on the manufacture of Nutriskin®, a Hydrolyzed Rice Protein. Rice seed is the starting material and water is the solvent. After solubilization of rice proteins in water, enzymatic hydrolysis is performed. The soluble and insoluble phases are separated, and the soluble phase further concentrated, followed by sterilization of the membrane.

Contaminants

Oils, Fatty Acids, and Waxes

Rice Bran Oil is used extensively in cooking in Asian countries. The published literature contains numerous articles concerning two incidences of polychlorinated biphenyl (PCB)-contamination in Rice Bran Oil. Exposure was documented in 1968 in western Japan, and in 1979 in central Taiwan (Chen et al. 1984; IARC 1987; Schantz 1996). PCB-intake was estimated at 0.7 to 1.84 g/person (Hsu et al. 1984). The oils also had been contaminated with polychlorinated quaterphenyls (PCQs) and polychlorinated dibenzofurans (PCDs) and some investigators considered PCDs to be the most important etiologic agents for the observed symptoms and signs of poisoning (Kunita et al. 1984; Masuda and Yoshimura 1984).

TABLE 15
Physical and chemical properties of Rice Starch (CTFA 1999b)

Specific gravity	0.950
Refractive index	1.5045
Heavy metals	10 ppm max (as Pb)
Maximum absorption	292 nm
Plant part used	Endosperm

Extracts

Information provided to CTFA (1999d) by suppliers gave the following contaminants and limits for Rice Bran Extract: 1,4-dioxane (<50 ppm); benzene (<50 ppm); chloroform (<25 ppm); methylene chloride (<50 ppm); trichloroethylene (<50 ppm); heavy metals as lead (<20 ppm); arsenic (<3 ppm); iron (<100 ppm); and microbial plate count (<100 organisms/g). Concentrations of other components of the raw material were reported as: 97% to 98.8% solvent (water/propylene glycol, water/butylene glycol, water/glycerin, safflower oil) and 1% preservative. No data were available for the hydrolyzed extracts.

Bran, Starch and Powder

The Food Chemicals Codex limits of impurities on unmodified food starches, including rice starch, are not more than 0.002% heavy metals, not more than 1 mg/kg lead, and not more than 0.005% sulfur dioxide (National Academy of Sciences 1996).

Ultraviolet (UV) Absorption

Several patents for sunscreen formulations describe use of rice bran-derived ingredients. One patent by Loo (1976) reported that Rice Bran Oil applied either undiluted or in a topical formulation was an, "effective sunscreen" against exposure to UV radiation at 295 to 315 nm. The absorption differential (transmittancy of tanning rays 315 to 365 nm/transmittancy of burning rays 295 to 315 nm) was, "many times higher" than that of other oils or sunscreen formulations. It "absorb[ed] UV rays in the burning region to a much greater extent" than other oils or commercial preparations.

Typically, formulations contain 5% or 6% Rice Bran Oil (Loo 1980; Potter and Pugliese 1994; 1995), or 5 parts (by weight) Rice Wax (Yoshida et al. 1990).

A patent by Ishibashi (1994) reported that a skin oil containing 3% γ-oryzanol had a sun protection factor (SPF) of 3.

TABLE 16
Physical and chemical properties of Rice Extract, Rice Bran Extract, and Hydrolyzed Rice Bran Extract

Property	Rice Extract (Grau Aromatics GmbH & Co. 1998)	Rice Bran Extract (CTFA 1999b)	Hydrolyzed Rice Bran Extract (CTFA 2003)	Hydrolyzed Rice Extract (CTFA 2003)
Appearance	Clear, yellowish liquid	—	Light yellow to light brown liquid	Colorless to light yellow to light brown liquid
Specific gravity	—	1.02–1.15		
Refractive index	1.465–1.485	1.3860–1.5000		
Density	0.910–0.930	—		
Solubility	—	Soluble in any proportion in water	Supplied diluted in water	Supplied diluted in water
Heavy metals	1 ppm max	—	Not more than 20 ppm	Not more than 20 ppm
Arsenic	—	—	Not more than 2 ppm	Not more than 2 ppm
pH	—	4.0–6.5	6.0–8.0	6.0–8.0
Plant part used	—	Bran	Bran	Polished rice

Oryzanol had absorption maxima at 231, 291, and 315 nm (Ichimaru Pharcos Co., unknown date). A mixture of Rice Bran Oil and Rice Germ Oil had an absorption maximum at 315 nm (Ichimaru Pharcos Co. 1994). Phototoxicity studies on the oil mixture and oryzanol appear in the Phototoxicity section of this report.

Silab (2001c) reported that Nutraskin®, a Hydrolyzed Rice Protein product, has a UV absorption spectrum with peaks at 219 nm (~3 absorbance units) and 270 nm (~0.7 absorbance units) in the UVC region. The peak at 270 nm falls off to <1 absorbance unit at 300 nm.

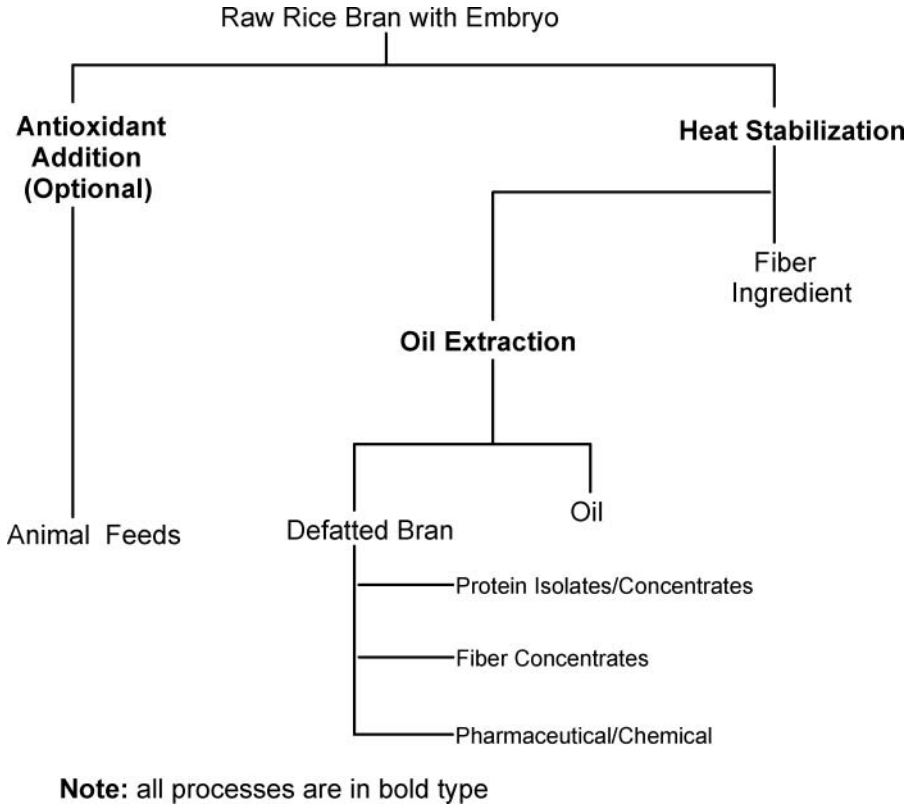

FIGURE 1
Processing and utilization of rice Bran (Mazzo 1998).

Dull (2002) stated that Rice Bran Extract absorbs UV light. The references cited in support of that statement, however, simply identified that UV radiation is absorbed by the components shown in Table 8, such as tocopherol (Ag Center Communications 1997; Young 1986). As the data in Table 8 demonstrate, these UV absorbing compounds are present in Rice Bran Extract only at low levels.

USE

Cosmetic

The functions of the various rice bran-derived ingredients in cosmetic formulations are listed in Table 17. In addition, one manufacturer described an exfolient use for Rice Germ Powder (CTFA 1999c).

As shown in Table 18, industry reports to the U.S. Food and Drug Administration (FDA 2002) listed 39 uses of Rice Bran Oil and 6 uses of Rice Germ Oil. Rice Bran Wax had 8 uses, and Hydrogenated Rice Bran Wax had 11 uses. Rice Bran Extract (and its lipid fraction) was used in 6 formulations, Rice Starch in 51 formulations, Rice Bran (identified as rice hulls) was used in 1 formulation, and Rice Protein was reportedly used in 5 formulations (FDA 2002). Hydrolyzed Rice Extract was used in 4 formulations (FDA 2002) and current concentration of use data (0.02% to 0.3%) were provided by industry (CTFA 2003b).

Hydrolyzed Rice Bran Extract, described as a skin-conditioning agent—miscellaneous, was not reported to FDA by industry to be in use (FDA 2002), but industry did report current concentrations of use (0.0004%) in two product categories (CTFA 2003b). Hydrolyzed Rice Protein was not reported to FDA as being used, but CTFA (2000) did report concentrations of use at 0.5% to 1.0% in skin care products and 0.1% to 2.0% in hair care products (CTFA 2000).

Neither FDA nor CTFA identified current uses or concentrations of Rice Bran Acid, Rice Extract, Hydrolyzed Rice Bran Extract, or Hydrolyzed Rice Bran Protein (FDA 2002; CTFA 2000). Current concentration of use data were not available for Rice Bran Wax, Rice Bran, or Hydrogenated Rice Bran Wax (CTFA 2000). One supplier noted use of Rice Extract at 1% to 10% in cosmetics (Grau Aromatics 1998) and another company used Rice Bran Extract at low (trace) levels (CTFA 1998), but neither identified product type(s).

Dull (2002) described the use of Rice Bran Extract in a moisturizing hand cream (1%), sunscreen (2%), body wash (1%), and a conditioning shampoo (1%). For the hand cream, water (90.95%) and purified methylchloroisothiazolinone/methylisothiazolinone (1%) are combined and the mixture

TABLE 17
Cosmetic functions of Rice Bran–derived ingredients (CTFA 1999a; Pepe et al. 2002)

Ingredient	Chemical class	Function
	Oils, fatty acids, and waxes	
Oryza Sativa (Rice) Bran Oil	Fats and oil	Skin-conditioning agent—occlusive
Oryza Sativa (Rice) Germ Oil	Fats and oils	Skin-conditioning agent—occlusive
Rice Bran Acid	Fatty acids	Surfactant—cleansing agent
Oryza Sativa (Rice) Bran Wax	Waxes	Skin-conditioning agent—occlusive
Hydrogenated Rice Bran Wax	Waxes	Binder Skin-conditioning agent—occlusive Viscosity increasing agent—nonaqueous
	Extracts	
Oryza Sativa (Rice) Bran Extract	Biological products	Not reported
Oryza Sativa (Rice) Extract	Biological products	Hair-conditioning agent Skin-conditioning agent-miscellaneous
Hydrolyzed Rice Extract	Biological products	Not reported
Hydrolyzed Rice Bran Extract	Biological products	Skin-conditioning agent—miscellaneous
	Bran, starch and powder	
Oryza Sativa (Rice) Bran	Biological products	Abrasive; bulking agent
Oryza Sativa (Rice) Starch	Carbohydrates	Absorbent; bulking agent
Oryza Sativa (Rice) Germ Powder	Biological products	Abrasive
	Proteins	
Hydrolyzed Rice Bran Protein	Protein derivatives	Hair conditioning agent Skin-conditioning agent—miscellaneous
Hydrolyzed Rice Protein	Protein derivatives	Hair conditioning agent Skin conditioning agent—miscellaneous

TABLE 18
Frequency and concentration of use of Rice-derived ingredients

Product category (total formulations in category) (FDA 2002)	Formulations in category containing ingredient (FDA 2002)	Concentration of use (%) (CTFA 2000a, 2000b, 2002, 2003b)
	Rice Bran Oil	
Bath oils, tablets, and salts (143)	1	1–39
Other bath preparations (196)	—	1%
Eyebrow pencils (102)	—	0.1%
Eye lotion (25)	—	1%
Mascara (195)	—	0.1%
Other eye makeup preparations (152)	—	0.5%
Hair conditioners (651)	2	0.3%
Tonics, dressings, and other hair-grooming aids (598)	1	—
Other hair preparations (277)	—	—
Foundations (324)	1	0.5%
Lipstick (962)	—	0.1—1%
Makeup bases (141)	—	3%
Other manicuring preparations (55)	2	—
Bath soaps and detergents (421)	—	1%
Other shaving preparation products (63)	—	1%
Skin cleansing (775)	2	0.5–1%
Face and neck skin care (excluding shaving) (310)	5	0.3–3%
Body and hand skin care (excluding shaving) (840)	2	3–4%
Moisturizing creams, lotions, powders, and sprays (905)	14	8%
Night creams (200)	—	0.3%
Paste masks (mud packs) (271)	2	0.2%
Other skin care preparations (725)	5	—
Suntan gels, creams, and liquids (131)	2	3%
Total/range for rice bran oil	39	0.1–39%
	Rice Germ Oil	
Cleansing (733)	1	—
Face and neck (excluding shaving) (304)	2	—
Body and hand skin care (excluding shaving) (796)	2	0.1%
Other skin care preparations (61)	1	—
Total/range for rice germ oil	6	0.1%
	Rice Bran Wax	
Tonics, dressings, and other hair-grooming aids (598)	1	—
Foundations (324)	1	—
Lipstick (962)	2	—
Face and neck skin care (excluding shaving) (304)	3	—
Suntan gels, creams, and liquids (131)	1	—
Total/range for rice bran wax	8	—
	Hydrogenated Rice Bran Wax	
Eyebrow Pencil (102)	3	—
Eyeliner (548)	1	—
Other eye makeup preparations (152)	3	—
Lipstick (962)	1	—
Other makeup preparations (201)	3	—
Total/range for Hydrogenated rice bran wax	11	—

(Continued on next page)

TABLE 18
Frequency and concentration of use of Rice-derived ingredients *(Continued)*

Product category (total formulations in category) (FDA 2002)	Formulations in category containing ingredient (FDA 2002)	Concentration of use (%) (CTFA 2000a, 2000b, 2002, 2003b)
Rice Bran Extract		
Tonics, dressings, and other hair-grooming aids (577)	2	—
Other hair preparations (277)	1	—
Moisturizing (905)	1	—
Other skin care preparations (725)	1	—
Total/range for rice bran extract	5	
Rice Bran Extract, lipid fraction*		
Body and hand skin care (excluding shaving) (840)	1	—
Total/range for rice bran extract, lipid fraction	1	
Rice Starch		
Bath oils, tablets, and salts (143)	—	97%
Eyeliner (548)	—	8%
Eye shadow (576)	1	3%
Fragrance powders (273)	—	6%
Hair conditioners (651)	—	4%
Mascara (195)	5	4%
Other eye makeup preparations (152)	3	—
Fragrance powder (273)	1	—
Other hair preparations (277)	1	—
Blushers (all types) (245)	2	9%
Face powders (305)	5	1%
Foundations (324)	2	—
Bath soaps and detergents (421)	1	—
Face and neck skin care (excluding shaving) (360)	5	2%
Body and hand skin care (excluding shaving) (840)	7	—
Moisturizing (905)	1	4%
Night Creams (200)	1	2%
Paste masks (mud packs) (271)	8	—
Skin fresheners (184)	1	—
Other skin care preparations (725)	7	—
Total/range for rice starch	51	1–97%
Rice Bran (identified as rice hulls)		
Other personal cleanliness products (308)	1	—
Total/range for rice bran	1	—
Hydrolyzed Rice Extract		
Hair conditioners (651)	—	0.03%
Hair sprays—aerosol fixatives (275)	—	0.04%
Shampoos—noncoloring (884)	—	0.03%
Tonics, dressings, and other hair-grooming aids (577)	—	0.05%
Cleansing (775)	1	0.02%
Face and neck skin care (excluding shaving) (360)	—	0.3%
Body and hand skin care (840)	2	—
Other skin care preparations (725)	1	—
Total/range for hydrolyzed rice extract	4	0.02–0.3%
Hydrolyzed Rice Bran Extract		
Face and neck skin care (excluding shaving) (360)	—	0.0004%
Other skin care preparations (725)	—	0.0004%
Total/range for hydrolyzed rice extract	4	—

TABLE 18
Frequency and concentration of use of Rice-derived ingredients *(Continued)*

Product category (total formulations in category) (FDA 2002)	Formulations in category containing ingredient (FDA 2002)	Concentration of use (%) (CTFA 2000a, 2000b, 2002, 2003b)
Hydrolyzed Rice Protein		
Hair conditioners (651)	—	0.1–2.0%
Hair sprays—aerosol fixatives (275)	—	0.1%
Shampoos–noncoloring (884)	—	0.1–0.2%
Tonics, dressings, and other hair grooming aids (577)	—	0.2%
Other hair preparations (277)	—	0.1%
Moisturizing (905)	—	0.1%
Paste masks (mud packs) (271)	—	0.3%
Total/range for hydrolyzed rice protein	—	0.1–2.0%

*Although reported to be used, this ingredient is not identified as a cosmetic ingredient (Pepe et al. 2002).

heated to 50°C. Another mixture of emulsifying wax NF (3%), Rice Bran Extract (1%), and Rice Bran Oil (2%) is made and heated to 50°C. These two mixtures are combined with agitation. Polyacrylamide, C_{13-14} isoparafin, and laureth-7 (total of 2%) are then added with continuing agitation. And finally, cyclomethicone and dimethiconol (total of 1%) are added with continuing agitation.

For the conditioning shampoo, water (52.95%) is combined with TEA (triethanolamine)-lauryl sulfate (20%), sodium laureth sulfate (10%), coco-betaine (8%), and methylchloroisothiazolinone/methylisothiazolinone (0.05%) and heated to 65°C. Another mixture is made of propylene glycol (United States Pharmacopeia) (USP) (4%), soyamidopropyl ethyldimonium ethosulfate (2%), polyethylene glycol (PEG)-150 pentaerythrityl tetrastearate (1%), and Rice Bran Extract (1%) and heated to 65°C. The second mix is added to the first, with agitation.

For the moisturizing sunscreen, water (73.45%) and purified methylchloroisothiazolinone/methylisothiazolinone (0.05%) are combined and the mixture heated to 60°C. Another mixture of emulsifying wax NF (3%), Rice Bran Extract (2%), Rice Bran Oil (3%), octyl methoxycinnamate (7.5%) cococaprylate/caprate (5%), and benzophenone-3 (3%) is made and heated to 55°C. Polyacrylamide, C_{13-14} isoparaffin, and laureth-7 (total of 2%) are added to the first mixture with agitation, followed by the second mixture. With continuing agitation, cyclomethicone and dimethiconol (total of 1%) are added.

For the moisturizing body wash, water (61.65%) and purified methylchloroisothiazolinone/methylisothiazolinone (0.05%) are combined. Guar hydroxypropyltrimonium chloride (0.1%) is added with agitation and this mixture heated to 70°C. While agitating this mix, sodium cocoyl isethionate (3%) is added and the resulting mixture heated to 80°C. Sodium laureth sulfate (3%) and Rice Bran Extract (1%) are combined and added with ongoing agitation. And finally, cocamidopropyl betaine (30%), ammonium sulfate (1%), and mica/titanium dioxide (0.2%) are combined and added, with continuing agitation.

Tables 19a to 19d display the ingredients and percentages for these four product types for comparison purposes (Dull 2002).

The CTFA *International Cosmetic Ingredient Dictionary and Handbook* notes that the ingredients, Oryza Sativa (Rice) Bran, Oryza Sativa (Rice) Bran Extract, Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Extract, Oryza Sativa (Rice) Germ Oil, Oryza Sativa (Rice) Germ Powder, Oryza Sativa (Rice) Starch, and Oryza Sativa (Rice) Wax will all be labeled "Oryza Sativa" in the European Union when regulations for ingredient labeling under the 6th Amendment to the *EC Cosmetics Directive* go into effect (Pepe et al. 2002).

There are no restrictions for the use of any of the Rice ingredients listed in this report in cosmetics in Japan according to the Ministry of Health, Labor, and Welfare (2000).

Noncosmetic

General Food Uses

Mazzo (1998) stated that white rice, resulting from a process of milling called scouring or whitening of brown rice, is the endosperm of the kernel and is composed primarily (90%) of starch. Oryza Sativa (Rice) is the staple food source for half of the world's population. It is nonallergenic, easily digested,

TABLE 19a
Components of a moisturizing hand cream containing Rice Bran Extract (Dull 2002)

Component	Percentage
Water	90.95
Emulsifying wax, NF	3.00
Polyacrylamide + C_{13-14} isoparafin + laureth-7	2.00
Rice Bran Oil	2.00
Cyclomethicone + dinethiconol	1.00
Rice Bran Extract	1.00
Methylchloroisothiazolinone/methylisothiazolinone	0.05

TABLE 19b
Components of a conditioning shampoo containing Rice Bran Extract (Dull 2002)

Component	Percentage
Water	52.95
TEA-lauryl sulfate	20.00
Sodium laureth sulfate	10.00
Coco-betaine	8.00
Propylene glycol USP	4.00
Soyamidopropyl ethyldimonium ethosulfate	2.00
PEG-15 pentaerythrityl tetrastearate	1.00
Rice Bran Extract	1.00
Methylchloroisothiazolinone/methylisothiazolinone	0.05

and provides protein with higher nutritional quality than that in other cereal grains. The rice kernel is composed of a hull, caryopsis or brown rice, and the embryo. The hull comprises about 20% of the rice kernel, the bran and embryo about 8% to 12%, and the endosperm or milled rice (white rice) about 70% to 72%.

According to the USA Rice Federation (1999a) per capita consumption of rice rose to 26.29 pounds in 1999 from 25.38 pounds in 1998. Direct food use (regular-milled, brown, parboiled, and precooked) accounted for 58% of rice sold in the United States. Food processing accounted for 25%, and beer brewing another 17%. All categories had an increase in consumption from 1998 to 1999. Direct food use rose 5%, processed foods went up 10%, and beer use rose 2.5%.

γ-Oryzanol

γ-Oryzanol is described as a drug used for the treatment of hyperlipidemia (Tamagawa et al. 1992a). In clinical studies, a typical dose is 300 mg/day orally (p.o.) for at least 3 months (Yoshino et al. 1989; Sasaki et al. 1990).

TABLE 19c
Components of a moisturizing sunscreen containing Rice Bran Extract (Dull 2002)

Component	Percentage
Water	73.45
Octyl methoxycinnamate	7.50
Coco-caprylate/caprate	5.00
Benzophenone-3	3.00
Emulsifying wax, NF	3.00
Rice Bran Oil	3.00
Polyacrylamide + C_{13-14} isoparafin + laureth-7	2.00
Rice Bran Extract	2.00
Cyclomethicone + dimethiconol	1.00
Methylchloroisothiazolinone/methylisothiazolinone	0.05

TABLE 19d
Components of a moisturizing body wash containing Rice Bran Extract (Dull 2002)

Component	Percentage
Water	61.65
Cocamidopropyl betaine	30.00
Sodium cocoyl isethionate	3.00
Sodium laureth sulfate	3.00
Ammonium sulfate	1.00
Rice Bran Extract	1.00
Mica + titanium dioxide	0.20
Guar hydroxypropyltrimonium chloride	0.10
Methylchloroisothiazolinone/ methylisothiazolinone	0.05

McCaskill and Zhang (1999) stated that the high antioxidant properties of γ-Oryzanol are widely recognized and its ability to reduce plasma cholesterol, reduce cholesterol absorption and decrease early atherosclerosis, inhibit platelet aggregation, and increase fecal bile acid excretion have been studied. γ-Oryzanol has been used to treat nerve imbalance and disorders of menopause, although no food additive determinations have been made by the FDA.

Oils, Fatty Acids, and Waxes

Rice Bran Oil can be used in practically any application to replace other vegetable oils. Some of the uses include frying, margarine component, and coating to extend shelf-life of other food products (McCaskill and Zhang 1999).

Food uses for Rice Wax are mold-release agent, brightener, coatings for chocolates, cakes, and tablets, treatment of vegetables and fruits, and plasticizing material of chewing gum. Industrial uses include polish for cars, floors, and shoes, office ink, textile oiling agent, and resin lubricant (Yokozeki Oil and Fat Industries Co., Ltd. 2000).

Bran, Starch, and Powder

The USA Rice Federation (1999b) described Rice Bran as the outermost layer on brown rice, which gives it its color and nutty flavor. An excellent source of thiamin, niacin, vitamin B-6, iron, phosphorus, magnesium, potassium, and fiber, Rice Bran is an ingredient in cereals, mixes, and vitamin concentrates. The non-food grades are used to feed livestock.

According to Mazzo (1998), Rice Starch is present only in the endosperm of the grain and makes up 90% to 93% of the milled rice dry weight. Native Rice Starch has many applications such as laundry-stiffening agent, paper and photographic paper powder, sugar coating in confectionery, and excipient in pharmaceuticals. Gelatinized Rice Starch is creamy and spreadable, good for custards and puddings. Waxy Rice Starch has excellent freeze-thaw stability and is used as a fat replacer in frozen dessets and gravies. Rice maltodextrins are commercially produced by

hydrolyzing Rice Starch at high temperatures or with enzymes. These products serve as carriers for flavor and provide bulk in products such as frostings, soups, sauces, and salad dressings.

GENERAL BIOLOGY

Skin Absorption

The Cosmetic Ingredient Review safety assessment of wheat germ oil (Elder 1980b) described a report by Valette and Sorbrin (1963) comparing the skin absorption of various oils. The rate of skin absorption was fastest for linseed oil and slowest for rice oil, with wheat germ oil having an intermediate rate of absorption.

Hematologic Effects

Bran, Starch, and Powder

Takenaka and Itoyama (1993) reported a significant ($p < .05$) increase in the number of granular leukocytes and lymphocytes in rats given a 10% Rice Bran fiber diet for 2 weeks. A significant increase ($p < .01$) was also noted in rats that had received 10% hemicellulose (prepared from the fiber); 1% and 2% hemicellulose-diets produced changes comparable to the control diet of unaltered feed. The investigators considered the Rice Bran fiber hemicellulose to be promising in the management of leukopenia.

Protective Effects

γ-Oryzanol

According to Ueda et al. (1976), γ-Oryzanol has a "strong affinity" for the skin; it covers it closely and has a suppressive effect on increases in keratin.

A review by Wheeler and Garleb (1991) disputed the benefits of consuming γ-oryzanol (and other plant sterols) by athletes for anabolic purposes. It was noted that <5% of orally consumed phytosterols are absorbed from the intestinal tract, with the majority being excreted in the feces. The reviewers noted that intraveous (i.v.) or subcutaneous (s.c.) administration of γ-Oryzanol to rats has produced such catabolic events as suppressed release of luteinizing hormone, reduced synthesis and release of growth hormone, and increased release of dopamine and norepinephrine in the brain.

Oils, Fatty Acids, and Waxes

Jayaraj et al (1986, 1987) reported that fresh Rice Bran Oil protects against gastric ulceration in rats, whereas stored oil is ulcerogenic. The protection was restored with the addition of cysteine to the stored oil. Lloris et al. (1991) reported significant reductions in the ulcer index ($p < .01$) and decreased H^+ concentrations in gastric juices ($p < .05$) of rats that had been pretreated with Rice Bran Oil prior to induction of stress ulcers. No changes were noted in the output volume of gastric juices or in gastric concentrations of histamine or pepsin. H^+ concentrations were similarly lower in Rice Bran Oil-treated rats following histamine stimulation, but no significant differences were noted following stimulation with two other stimulators of gastric secretion, betanechol, or pentagastrin. The investigators noted that the oil contains a large percentage of unsaturated fatty acids that can act as precursors in Arachidonic Acid synthesis, which in turn is a precursor of prostaglandins. In addition, Rice Bran Oil contains antioxidants such as α-tocopherols that could have exerted a protective effect.

Extracts

Furihata et al. (1996) reported decreased gastric mucosal damage in male F344 rats that had received a concentrated commercial Rice Extract via gastric intubation 3 h prior to administration of sodium chloride.

Bran, Starch, and Powder

Rice Bran fiber (10% in the feed) reduced bis(tri-n-butyltin)oxide (TBTO)-induced thymus atrophy in rats. A significant difference in relative thymus weights ($p < .01$) was noted in rats that had received rice bran fiber concurrent with TBTO exposure compared to rats that had received TBTO and basal diet. Further investigation established that hemicellulose was responsible for the reduction (Takenaka 1992).

Tyrosinase Activity Inhibition

γ-Oryzanol

γ-Oryzanol was tested for its ability to inhibit the tyrosinase-tyrosine relationship in the "skin blackening phenomenon- abnormal melanin deposition." L-Ascorbic acid, a known tyrosinase inhibitor, was used as the reference. A liquid containing 2% agar, 0.2% inhibitor, and 0.1% L-tyrosine was prepared and cooled to solidification. A 0.5% tyrosinase solution was added to the surface and the mixture was incubated. Blackening of the surface of the agar mass was observed. Oryzanol inhibited the formation of melanin (though it was weaker than L-ascorbic acid). The structure of the ferulic acid moiety in oryzanol was considered to resemble tyrosine thereby blocking enzymatic activity (Ichimaru Pharcos, unknown date).

Hypolipidemic Action

Oils, Fatty Acids, and Waxes

Purushothama et al. (1995) reported comparatively lower concentrations of total cholesterol (TC), triglycerides (TGs) and phospholipids in rats that had received either 5% or 20% Rice Bran Oil in the diet compared to control rats that had received similar concentrations of Peanut Oil. A significant increase ($p < .05$) in high-density lipoprotein (HDL) was noted in rats that received 20% Rice Bran Oil compared to controls. Rice Bran Oil-fed rats also had lower low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) compared to controls. The investigators considered that feeding high doses of Rice Bran Oil to rats produced "no deleterious effect on growth or the blood lipid profile."

Similar results were reported earlier by Seetharamaiah and Chandrasekhara (1989). Serum total, free, esterified and (LDL + VLDL)-cholesterol concentrations were significantly lower in rats maintained on 10% Rice Bran Oil compared to control rats that had received Peanut Oil; hepatic lipids were lower in Rice Bran Oil-fed rats. HDL-cholesterol tended to be greater in rats of the Rice Bran Oil group. A further significant decrease in serum total cholesterol (but not in hepatic lipids) was noted when 0.5% oryzanol was added to the Rice Bran Oil diet. Oryzanol and other components of the unsaponifiable matter of Rice Bran Oil was considered responsible for the cholesterol lowering.

In clinical studies by Raghuram et al. (1989), a significant reduction ($p < .001$) in TC and TGs was documented in 12 subjects with high TC, 15 and 30 days after using Rice Bran Oil instead of their usual cooking oil. The response was greater in subjects with greater initial TC and TG values.

In reviews of the hypolipidemic action of Rice Bran Oil, Rukmini and Raghuram (1991) and Raghuram and Rukmini (1995) reported that the fatty acid content of Rice Bran Oil is similar to Peanut Oil. However, the unsaponifiable fraction of Rice Bran Oil contains more phytosterols, triterpene alcohols, tocopherols, and tocotrienols than do other oils. They reported that in animal studies, cycloartenol, a triterpene alcohol present in Rice Bran Oil, effectively lowered cholesterol and TG concentrations when compared to other edible oils. Data suggested that cycloartenol was absorbed and accumulated in the liver. Its structure is similar to cholesterol and the reviewers noted that it could compete for binding sites. Cycloartenol also inhibited cholesterol esterase activity thereby delaying release of cholesterol into the circulation. The reviewers considered that the hypocholesterolemic action of dietary fat depended primarily on the minor components of the unsaponifiable fraction and, to a lesser extent, on the fatty acid content of the oil.

Lichtenstein et al. (1994) reported that consumption of Rice Bran Oil–enriched diet by middle-aged and elderly subjects with moderately elevated concentrations of LDL-cholesterol resulted in plasma lipid and apolipoprotein concentrations and predictive ratios of cardiovascular risks that were similar to those of more commonly used vegetable oils in the United State, such as corn oil and canola oil. A greater than predicted reduction in plasma total cholesterol was noted with Rice Bran Oil treatment and was attributed to the unsaponifiable fraction.

Bran, Starch, and Powder

Sanders and Reddy (1992) reported that Rice Bran (without the fatty acid components of the oil) did not significantly alter body weight or plasma TC, LDL, HDL, and apoprotein AI and B concentrations compared to wheat bran in 18 males with normal cholesterol concentrations. A significant decrease ($p < .05$) in plasma TG concentration was noted with 15 g/day Rice Bran compared to wheat bran.

ANIMAL TOXICOLOGY

Acute Oral Toxicity

Oils, Fatty Acids, and Waxes

Rice Bran Oil had an oral LD_{50} of >5 g/kg in white rats (Leberco Testing Inc. 1993a).

A mixture of Rice Bran Oil and Rice Germ Oil had an LD_{50} of >40 ml/kg in mice (Ichimaru Pharcos Co. 1981a).

A group of 10 Sprague-Dawley rats (5 males, 5 females) were administered by oral intubation a single dose of 5 g/kg of body weight of Rice Germ Oil-K. The animals were observed for 14 days after administration. No clinical abnormalities were noted and no mortalities occurred. The animals were killed and no gross abnormalities were observed at necropsy. The LD_{50} was >5 g/kg. Rice Germ Oil was not considered to be toxic (Celsis Laboratory Group 1999).

Rice Wax suspended in 25% gum arabic solution had an oral LD_{50} of >24 g/kg in male mice (Nippon Bio-Test Laboratories, Inc. 1972).

Hydrogenated Rice Bran Wax (administered 50% in corn oil) had an oral LD_{50} of >5 g/kg in white rats. Rats were killed 14 days after dosing and necropsied; one male rat had a dilated right kidney (Leberco Testing Inc. 1991a).

Consumer Product Testing Co. (1998f) conducted a study in which 10 (5 male and 5 female) albino rats each received a single oral dose of Rice Bran Wax S-100 (Lot No. W90305; a 12.5% suspension heated and cooled in corn oil) at a dose of 5 g/kg body weight (bw). Animals were observed for pharmacological activity and drug toxicity 1, 3, 6, and 24 h after treatment, and daily thereafter for a total of 14 days. At the end of 14 days, the rats were killed and subjected to gross necropsy.

No gross changes were observed in nine of the rats. In one animal, two red nodules attached to fat adjacent to the bladder approximately 3 mm in diameter each and firm to the touch were observed. The LD_{50} was >5 g/kg. The test article was not orally toxic to rats (Consumer Product Testing Co. 1998f).

Proteins

Cosmepar (2000) provided results of an acute oral toxicity test of Hydrolyzed Rice Protein. Male and female Sprague Dawley rats (five each) were individually housed. They were dosed by esophageal tube with 2 g/kg of the liquid material and followed for 14 days. No mortality or other clinical signs, including apathy or weight loss, were reported.

Chronic Oral Toxicity

Oils, Fatty Acids, and Waxes

Following the food safety evaluation protocol of WHO/FDA/(DGHS-Director General of Health Sciences (India)) (World Health Organization/Food and Drug Administration/), Rukmini (1988) fed a group of 30 albino rats (Wistar strain, 15 each sex) a diet containing 10% edible-grade Rice Bran Oil, 20% protein, and adequate amounts of other nutrients. A control group received feed containing 10% Peanut Oil. After 100

to 120 days the rats were mated. Mating, gestation, lactation, and weaning were followed to obtain F_{1a} pups.

A week after weaning, F_0 parents were mated again to obtain mating pups F_{1b}. The procedure was continued until F_{3b} pups were obtained at which time all rats were killed.

Blood samples obtained prior to study termination were analyzed for TC and TGs. The liver was analyzed for total lipids, TC, and TGs, and microscopic examination was done on the heart, lungs, kidneys, ovaries/testes, pancreas, and thymus.

Body weight gain, feed efficiency, fat absorption, nitrogen retention, and organ weights were comparable between Rice Bran Oil–fed rats and control rats. A hypocholesterolemic effect was noted in Rice Bran Oil-fed rats as indicated by the lipid profile (Rukmini 1988).

Dermal Irritation and Sensitization

Oils, Fatty Acids, and Waxes

Ichimaru Pharcos Co. (1979a) conducted a skin contact allergy test using nine female Hartley guinea pigs. Six guinea pigs were injected (in the clipped neck) with an emulsion containing a mixture of Rice Bran Oil and Rice Germ Oil, sodium chloride solution, and Freund's Complete Adjuvant in a 1:1:2 volume. A 0.2-ml dose was divided and injected into four sites. One week later, the neck was again clipped of hair and 0.5 ml of the test material was applied. The site was covered with a polyethylene film for 48 h. Two weeks later, a 24 h patch containing Rice Germ Oil (0.1 ml) was applied to all nine guinea pigs. Sites were evaluated at the time of patch removal, and 24 and 48 h later. No changes were observed.

Ichimaru Pharcos Co. (1981b), following a modified Draize method, applied a mixture of Rice Bran Oil and Rice Germ Oil (0.5 ml) to abraded and intact sites on six female albino rabbits. The sites had been clipped free of hair. The sites were covered for 4 h of exposure and then any remaining test material was removed with ethanol. Sites were evaluated at 24 and 48 h. No reactions were observed.

Undiluted Rice Bran Oil was applied as a single occlusive patch to nine rabbits and reactions were scored at 2 and 24 h after placement of the occlusive patch. The primary irritation index (PII) for the group was 0 on a scale of 0 to 8 (CTFA 1983).

CTFA (1984) reported that Rice Bran Oil was tested in a Magnusson-Kligman maximization test. During induction groups of 10 shaved Dunkin-Hartley guinea pigs received two injections of each of the following: 50% Freund's complete adjuvant (FCA), 5% Rice Bran in propylene glycol, and 5% Rice Bran Oil in FCA (total of six injections). Controls were injected with FCA and propylene glycol. One week later, an additional "booster" of each dose was applied. Because preliminary testing established that 100% Rice Bran Oil did not produce irritation, 5% sodium lauryl sulfate (SLS) in petrolatum was applied 24 h prior to the topical booster. Controls were pretreated with SLS and petrolatum was applied during the booster phase. All guinea pigs were occlusively wrapped for 48 h. Two weeks later, guinea pigs were topically challenged with 24-h occlusive patches of 25% and 50% Rice Bran Oil. Challenge sites were graded 24 and 48 h after patch removal. No reactions were observed.

A moisturizer containing 8.0% Rice Bran Oil applied as a single occlusive exposure to six rabbits had a PII of 1.67 (CTFA 1987a).

Leberco Testing Inc. (1991b) applied Rice Wax (0.5 g) to an abraded and intact hairless site on the back of six New Zealand white rabbits. Sites were covered with a patch and the trunk of each rabbit was encased with an occlusive wrapping for 24 h of exposure. Sites were examined for erythema and edema using the Draize scoring scale at the time of wrapping removal and 48 h later. The Rice Wax had a PII of 0.21 (Leberco Testing Inc. 1991b).

Following the same protocol, Leberco Testing Inc. (1993c) applied Hydrogenated Rice Bran Wax to intact and abraded sites of six white rabbits. The substance had a PII of 0.0.

Leberco Testing Inc. (1993b) applied Rice Bran Oil (0.5 ml) to an abraded and intact hairless site on the back of six New Zealand white rabbits. Sites were covered with a patch and the trunk of each rabbit was encased with an occlusive wrapping for 24 h of exposure. Sites were examined for erythema and edema using the Draize scoring scale at the time of wrapping removal and 48 h later. Scores for the two observation times were averaged to calculate a primary irritation index (PII; scores >5.0 indicated a primary dermal irritant). "Very slight to well-defined" erythema and "very slight" edema were observed, with a PII of 0.88.

Consumer Product Testing Co. (1998a) used 10 (5 male, 5 female) Hartley strain guinea pigs as a test group in a Magnusson and Kligman guinea pig maximization test of Rice Bran Wax S-100, Lot No. W-90305. An additional 10 (5 male, 5 female) Hartley strain guinea pigs were used as a control group. For induction, each animal in the test group received three pairs of subcutaneous injections. The three pairs of injections were made in two rows, one row on each side of the midline as follows: first pair: 0.1 ml of the TM(Titermax)/water emulsion (1:1), without the test article; second pair: 0.1 ml of the test article, at 10% in corn oil; third pair: 0.1 ml of the test article/corn oil, in the TM/water emulsion (0.5% test article/4.5% corn oil/47.5% TM/47.5% distilled water).

Seven days after the injections, an irritating concentration of the test material (25% in petroleum jelly) was topically applied. The suspension (0.5 ml) was spread onto a 2×4-cm piece of filter paper. The filter paper was placed onto the test site and covered with a piece of $1\ ^1/_4$-inch Blenderm tape. Two weeks after the topical induction application, a challenge application was made. A 5×5-cm area on the flank of each guinea pig, in both the test and control groups, was shaved. The test article, 12.5% in petroleum jelly, which was topically screened as the highest non-irritating concentrations, was applied (0.4 ml) to each site with a cotton patch. The animals were wrapped for 24 h after

the dosing. Twenty-one hours after the wraps were removed, any remaining test material was removed with an ethanol wipe. At 48 and 72 h after dosing, each site was observed and scored for erythema and edema. The indices of incidence and severity were calculated for both groups.

Incidence and severity indices at both 48 and 72 h after applications were 0 in test and control groups. The test material was not a sensitizer in guinea pig under the conditions of this test (Consumer Product Testing Co. 1998a).

Consumer Product Testing Co. (1998b) also used 10 (5 male, 5 female) Hartley strain guinea pigs as a test group in a Magnusson and Kligman guinea pig maximization test of Rice Bran Wax B-10, Lot No. M610117 (hydrogenated rice bran wax). An additional 10 (5 male, 5 female) Hartley strain guinea pigs were used as a control group. For induction, each animal in the test group received three pairs of subcutaneous injections. The three pairs of injections were made in two rows, one row on each side of the midline as in the previous study. Seven days later after the injections, an irritating concentration of the test material (25% in petroleum jelly), was topically applied. The suspension (0.5 ml) was spread onto a 2 × 4-cm piece of filter paper. The filter paper was placed onto the test site and covered with a piece of one and 1 $^{1}/_{4}$-inch Blenderm tape.

Two weeks after the topical induction application, a challenge application was made. A 5 × 5 cm area on the flank of each guinea pig, in both the test and control groups, was shaved. The test article, 12.5% in petroleum jelly, which was topically screened as the highest nonirritating concentrations, was applied (0.4 ml) to each site with a cotton patch. The animals were wrapped after the dosing and wraps left in place for 24 h. Twenty-one hours after the wraps were removed, any remaining test material was removed with an ethanol wipe. At 48 and 72 h after dosing, each site was observed and scored for erythema and edema. The indices of incidence and severity were calculated for both groups.

Incidence and severity indices at both 48 and 72 h after applications were 0/0.10 (test/control groups). The test material was not a sensitizer in the guinea pig under the conditions of this test (Consumer Product Testing Co. 1998b).

Consumer Product Testing Co. (1998e) conducted a study in which six New Zealand white rabbits each received a single dermal application of 0.5 g of Rice Bran Wax S-100 (Lot No.W90305) on two test sites, one abraded and one nonabraded. The test sites were occluded for 24 h and were observed individually for erythema, edema, and other effects 24 and 72 h after application. Mean scores from the 24- and 72-h readings were averaged to determine the primary irritation index. The test article was moistened with saline upon dosing. The primary irritation index was 0.05; the test substance was not a primary dermal irritant.

Celsis Laboratory Group (1999) assessed the primary dermal irritation of Rice Germ Oil using six New Zealand white rabbits by applying single doses of 0.5 ml Rice Germ Oil-K to two test sites. Both sites were located on each side of the animals vertebral column mid-dorsally. The site on the left was maintained intact and the site on the right was abraded with longitudinal epidermal incisions, sufficiently deep to penetrate the stratum corneum. The sites were then completely encased in an impermeable occlusive wrapping. The wrapping and test article were removed after 24 h following application. Erythema and edema were scored using the Draize skin scoring scale. The test material produced a very-slight to well-defined erythema at the 24 h observation. No edema was noted. The readings were averaged to determine the primary irritation index. The PII for this test substance was 0.75—Rice Germ Oil was not classified as a primary dermal irritant.

Proteins

An aqueous solution of Hydrolyzed Rice Protein was tested for dermal irritation in albino rabbits (Cosmepar 1999a). Undiluted test material (0.5 ml) was applied to the normal shaved skin of the left side of the backs of three male New Zealand albino rabbits (2 to 2.5 kg). The nontreated shaved skin on the left side was the control. Gauze patches were applied over the sites and held in place with adhesive strips (OMNIFIX®), over which was placed a plastic restrictive jacket. After 4 h, the adhesive strip and gauze were removed and the site rinsed with distilled water. Irritation was determined at 1, 24, 48, and 72 h. No signs of erythema, edema, desquamation, or necrosis were seen at any time in any animal.

A guinea pig sensitization test was conducted using this same material (CTFA 2002). In a preliminary test, the dorsolumbar area of three guinea pigs was shaved. Each animal received two of the following concentrations of Hydrolyzed Rice Protein in 0.9% saline: undiluted, 50%, 25%, 12.5%, 6.25%, and 3.125%. Application sites were covered with an occlusive dressing for 24 h, after which time the dressings were removed. The sites were checked 1 h later. No reactions were observed, so the maximum non-irritant concentration was "undiluted" test material.

A maximization approach was used to examine sensitization. Five control animals received intradermal injections (0.1 ml) of Freund's complete adjuvant (50% in saline) at two sites and 0.9% saline at two sites. Ten test animals received intradermal injections (0.1 ml) of Freund's complete adjuvant (50% in saline) at two sites, 50% Hydrolyzed Rice Protein in saline at two sites, and a 50:50 mixture of the Freund's and the test material at two sites. At day 7 the treated areas were painted with a 10% solution of sodium lauryl sulfate. At day 8, control animals received a topical application of 0.5 ml saline and the treatment group received 0.5 ml undiluted Hydrolyzed Rice Protein under occlusive dressing for 48 h.

An untreated area of the back was shaved and 0.25 ml of undiluted Hydrolyzed Rice Protein was applied over a 4-cm^2 area under a semiocclusive dressing for 24 h. No dermal reactions of any kind were observed in control or treated animals. A positive control with a 1% alcohol solution of 1-chloro-2,4-dinitrobenzene produced erythema and desquamation (Cosmepar 1999a).

Ocular Irritation

Oils, Fatty Acids, and Waxes

Ichimaru Pharcos Co. (1981c) instilled a mixture of Rice Bran Oil and Rice Germ Oil (0.1 ml) in the right conjunctival sac of three female albino rabbits. The left eye served as the control. Both eyes were rinsed 5 min after instillation. The cornea, iris, and conjunctiva were examined according to the modified Draize method at 1, 4, and 24 h, and 4 and 7 days after application. Corneal opacity/area of opaque field scores of 1 were observed in the treated eye of all rabbits throughout the observation period. One rabbit also had erythema/edema scores of 1 at the 1- and 4-h observations; the reaction cleared thereafter. The material was not considered an ocular irritant.

CTFA (1983) reported a study in which undiluted Rice Bran Oil was instilled in the conjuctival sac of the eye of six rabbits. Reactions were scored according to the Draize scale (maximum score 110) on days 1, 2, 3, 4, and 7 after instillation. No reactions were noted in the cornea or iris at any observation. One rabbit had a conjunctival score of 2 on days 1 and 2, and another rabbit had a conjunctival score of 2 on days 4 and 7. Rice Bran Oil was considered minimally irritating.

A face lotion containing 8.0% Rice Bran Oil was instilled in the conjunctival sac of three rabbits. No reactions were observed 1 and 2 days after instillation (CTFA 1987a).

Leberco Testing Inc. (1991c) instilled Rice Bran Wax (0.1 ml) in the conjunctival sac of one eye of each of six albino rabbits. The contralateral eye served as the control. Eyes were graded at 24, 48, and 72 h post instillation. The substance was considered a primary ocular irritant if $\geq$4 rabbits had a response in the cornea, iris or conjunctiva; the substance was not an irritant if $\leq$1 rabbit had a response, and inconclusive if 2 to 3 rabbits had a response. Rice wax was tested using the above protocol. Three rabbits had conjunctiva redness scores of 1 at the 24-h observation; the redness cleared in all by the 48-h observation. Rice Wax was not considered a primary irritant.

Leberco Testing Inc. (1993e) also tested Hydrogenated Rice Bran Wax following the same protocol except that additional observations were made at 4 and 7 days post instillation. Four rabbits had conjunctival redness scores of 1 at the 24-h observation; one of these rabbits also had a conjunctival discharge score of 1. The discharge cleared in two rabbits by 48 h, and in a third rabbit by 72 h. It persisted in the fourth rabbit throughout the observation period, increasing to a score of 2 (considered positive) at the day 4 reading and returning to a score of 1 at the day 7 reading. Hydrogenated Rice Bran Wax was not considered a primary ocular irritant.

Leberco Testing Inc. (1993d) tested Rice Bran Oil (0.1 ml) using the same protocol. Two rabbits had conjunctiva redness scores of 1 (defined as "some vessels definitely injected"; scale 0 to 3 with scores $\geq$ 2 considered positive) at the 24 h observation. The condition cleared in 1 rabbit by 48 h and cleared in the second rabbit by 72 h. The test material was not considered a primary irritant.

Celsis Laboratory Group (1999) conducted a study in which six albino rabbits had 0.01 ml of Rice Germ Oil instilled in the conjunctival sac of the test eye. The contralateral eye served as a control. Both eyes were examined and graded at 24, 48, and 72 h post instillation. No ocular lesions or reactions were observed. This material was not considered a primary irritant.

In a study by Consumer Product Testing Co. (1998c), six New Zealand white rabbits, free from visible ocular defects, each received a single intraocular application of 0.1 ml of Rice Bran Wax S-100 (Lot No. L9807091) in one eye. The contralateral eye, remaining untreated, served as a control. The eyes of all animals remained unwashed for 24 h. Observations of corneal opacity, iritis, and conjunctivitis were recorded 24, 48, and 72 h after treatment, and at 4 and 7 days if irritation persisted. The test article was used as a 30% suspension in mineral oil. The average Draize scores at 24, 48, and 72 h were 2.3, 2.0, and 0, respectively. The test article was not an ocular irritant.

Using the same protocol (Consumer Product Testing Co. 1998d), each of six New Zealand white rabbits received a single intraocular application of 0.1 ml of Rice Bran Wax S-100 (Lot No. W90305) in one eye. The test article was used as a 30% suspension in mineral oil. The average Draize scores at 24, 48, and 72 h and 4 and 7 days were 2.0, 1.3, 0.7, 0.7, and 0 respectively. The test article was not an ocular irritant.

Proteins

Three New Zealand albino rabbits were used to test the ocular irritation potential of Hydrolyzed Rice Protein. Hydrolyzed Rice Protein (undiluted aqueous solution) was instilled (0.1 ml) in the conjunctiva of the left eye of each of the rabbits without rinsing. The right eye served as the control. Eye examinations were conducted at 1, 24, 48, 72, and 96 h. No reactions of any sort were found in either eye of each animal (Cosmepar 1999b).

Phototoxicity/Photoprotection

γ-Oryzanol

Ethanol solutions of oryzanol or *p*-aminobenzoic acid (PABA) were applied to the shaved backs of guinea pigs. One half of each back was then irradiated at a distance of 10 cm with three lamps arranged in parallel (270 to 320 nm and 320 to 400 nm). The UV irradiated side was divided into four exposure sections according to minimal erythema dose (MED) levels. At a dose of 3 MED, 100 μg/cm^2 oryzanol had the protection activity of 50 μg/cm^2 PABA (Ichimaru Pharcos, unknown date).

Oils, Fatty Acids, and Waxes

Ichimaru Pharcos Co. (1979b) reported a study in which a 5% emulsion of a mixture of Rice Bran Oil and Rice Germ Oil (0.1 ml) was applied to the clipped back of six female Hartley guinea pigs. After 4 h, half of the test site was irradiated with the MED provided by three UV 280- to 320-nm lamps and three

UV 320- to 400-nm lamps placed in parallel at a distance of 10 cm. The other half of the test site was covered with aluminum foil. Sites were evaluated at 24 and 48 h after irradiation. No phototoxic effects were observed.

According to Rukmini and Raghuram (1991), stearic acid comprises 2.9% and tocopherols comprise a very small fraction of Rice Bran Oil. The CIR Final Report on Oleic Acid, Lauric Acid, Palmitic Acid, Myristic Acid, and Stearic Acid reported a 2.8% formulation of stearic acid in two phototoxicity studies using male guinea pigs to be nonphotosensitizing (Elder 1987) and the CIR final safety assessment of Tocopherol and related ingredients reported that tocopherol acetate was not phototoxic in a study of 11 human subjects (Andersen 2002).

Ichimaru Pharcos Co., Ltd. (1997) studied Oryza Oil S-1 (Rice Bran Oil) in a photo-contact allergy test on 10 female Hartley guinea pigs. The oil was administered undiluted during the sensitization phase, and was used at a 10% concentration adjusted with Vaseline in the challenge phase. The Adjuvant-Strip method was used in this study. Each 0.1 ml of an emulsified mixture of distilled water and Freund's complete adjuvant of the same amount was injected intracutaneously into the corner of a square (2× 4 cm) on the animal's shaved neck. Following the injection, the portion of the neck where the horny layer had been exfoliated by cellophane adhesive tape and 0.1 ml or 0.1 g of the test material had been applied in open condition was irradiated by long wave ultraviolet light (10 J/cm^2) for 5 days once a day.

Three weeks following the photosensitization the test material (0.02 mg or 0.02 g) was applied to an area of 1.5 × 1.5 cm^2 under nonocclusive conditions and was irradiated again at 10 J/cm^2. Again the sheared skin of the neck was used and a control portion of the skin was covered by aluminum foil while being irradiated. Evaluations were made at 24 and 48 h after irradiation. No signs of erythema or edema were observed at either time interval. The test material was considered negative in this study (Ichimaru Pharcos Co., Ltd. 1997).

Celsis Laboratory Group (1999) used a group of 10 guinea pigs (male and female) in a study of phototoxicity of Rice Germ Oil-K. An adhesive backed patch of closed cell foam with pre-cut holes was applied to the shaven backs and 0.1 ml of 100%, 75%, 50%, and 25% of Germ Oil-K was placed into four wells. The solutions were left on for 30 min, after which the test groups were irradiated for 15 min at 310 to 400 nm.

Ten animals in a control group were prepared similarly to the tested group with doses of 0.1 ml of 100%, 75%, 50%, and 25% of test substance, but not irradiated. A positive control group using 0.005% 8-methoxysoralen was also tested. Skin reactions were scored 24 h after irradiation using the Draize scoring table for skin reactions.

Two of 10 animals in the 100% test group had a phototoxic response at 24 h. There was no response at 75%, 50%, or 25% concentrations (in 0.9% sodium chloride) at 24 h. The positive controls produced phototoxic responses in four of five animals with very slight erythema and no edema at 24 h (Celsis Laboratory Group 1999).

Extracts

Safflower Oil was reported as a component of Rice Bran Extract—97% to 98.8% solvent: water/propylene glycol, water/butylene glycol, water/glycerin, safflower oil (CTFA 1999d).

The CIR Final Report of Safflower Oil characterized Safflower Oil as neither a phototoxin nor a photosensitizer based on two clinical studies involving irradiated treatments (Elder 1985).

Proteins

Silab (2001a) reported the results of an evaluation of the phototoxic potential of a Hydrolyzed Rice Protein product, Nutriskin® . Rabbit corneal fibroblasts in culture were treated with Earle's balanced salt solution (EBSS) as the vehicle control or Hydrolyzed Rice Protein (0.1%, 0.25%, 0.5%, 1%, 2.5%, 5%, and 10% in EBSS) in a 96-well plate for 1 h. Two such plates were prepared. One plate was stored in the dark at room temperature and the other was treated with 5 J/cm^2 UVA radiation from a Biosun lamp. Chlorpromazine was used as a positive control and *p*-aminobenzoic acid was the negative control. With cell viability as the end point, these gave the expected results. None of the treatment concentrations reduced cell viability below vehicle control levels. The authors concluded that, at concentrations up to 10%, Hydrolyzed Rice Protein was not phototoxic.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Oils, Fatty Acids, and Waxes

The three-generation oral-dose study detailed in Chronic Oral Toxicity also evaluated the reproductive performance of rats fed on 10% Rice Bran Oil. The percentages of conception, birth weight, litter size, weaning weight, and preweaning mortality were comparable with those of rats fed Peanut Oil in both matings in all three generations. Rice Bran Oil was considered safe for human consumption (Rukmini 1988).

GENOTOXICITY

γ-Oryzanol

γ-Oryzanol was negative in the bacterial DNA repair test, (Rec-assay), the Ames test and the rat bone marrow chromosome aberration test. It was also negative in the metabolic cooperation inhibition test using Chinese hamster V79 cells (Tsushimosto et al. 1991).

Oils, Fatty Acids, and Waxes

Polasa and Rukmini (1987) tested Rice Bran Oil in the Ames test using *Salmonella typhimurium* strains TA98 and TA100 both with and without metabolic activation. Edible grade oil

(200 ml) was shaken continuously with 20 ml dimethyl sulfoxide (DMSO) and then centrifuged. The DMSO layer was separated, stored at 4°C to 10°C and used in the mutagenicity assay. Rice Bran Oil was not mutagenic.

The Environmental Technical Laboratory, Ltd. (1998) examined Rice Wax for mutagenic activity in a histidine-dependent auxotroph of *Salmonella typhimurium* strain TA100. The tests were conducted in the absence and presence of hepatic rat microsomes (S9 mixture) and employed a range of concentrations of Rice Wax up to 5000 μg/ml. Positive and negative controls were also used in this study. No increases in revertant colony numbers over concurrent control counts were obtained following exposure to Rice Wax. It was concluded that Rice Wax did not exhibit any mutagenic activity under the conditions of the test.

Extracts

Furihata et al. (1996) reported significantly reduced ($p < .01$) replicative DNA synthesis in male F344 rats that had received a concentrated commercial Rice Extract via gastric intubation 3 h prior to administration of sodium chloride.

CARCINOGENICITY

γ-Oryzanol

γ-Oryzanol was not carcinogenic to either $B6C3F_1$ mice or F344 rats following chronic oral administration (200, 600, or 2000 mg/kg body weight for at least 2 years). Greater incidences of neoplasms were noted in mice and rats of the highest dose groups, but were not statistically significant compared to corresponding controls (Tamagawa et al. 1992a; 1992b).

The published literature recognizes γ-Oryzanol as a naturally occurring antioxidant (Hirose et al. 1991, 1994; Nakamura et al. 1991). Studies that investigated whether it could modify/inhibit the actions of known carcinogens are cited in Table 20.

Cocarcinogenicity and Anticarcinogenicity

Bran, Starch, and Powder

Barnes et al. (1983) fed F344 rats a 20% bran diet (rice, wheat, corn, or soybean) diet for life. Control rats were fed a no-fiber-added diet. All rats were injected with the carcinogen 1,2-dimethylhydrazine (DMH) at weeks 8 and 10 of age. All surviving rats were killed nine months after the first DMH dose. Survival was increased in all rats receiving bran diets. The incidence of large bowel neoplasms was 86% in rats fed Rice Bran and 95% in control rats. The difference was not significant.

Studies that investigated the anti-carcinogenicity properties of specific components of Rice Bran and Rice Bran Oil are cited in Table 20.

Inhibition of carcinogenicity or cytotoxicity of carcinogens was noted with administration of Rice Bran hemicellulose, saccharide, or α-glycan (Takeshita et al. 1992; Takeo et al. 1988). In contrast, γ-oryzanol administered orally to rats did not significantly reduce the incidence of neoplasms (Nakamura et al. 1991; Hirose et al. 1994), and in one study, enhanced the incidence of lung carcinogenesis (Hirose et al. 1991).

CLINICAL ASSESSMENT OF SAFETY

Allergic Reactions

It is commonly understood that rice is regarded as hypoallergenic and that rice is frequently recommended in diets for allergic patients. However, van den Hoogenband and van Ketel (1983) did report a case of contact urticaria in response to raw rice. A 25-year-old female had recurrent attacks of Quincke's edema following ingestion of cereal; intracutaneous testing revealed positive results for some brands of raw rice.

Ikezawa et al. (1992) reported the creation of a hypoallergenic rice by enzymatic decomposition of the proteins considered to be the major allergens of rice. Forty-four panelists with recalcitrant atopic dermatitis with suspected rice allergy eliminated both rice and wheat-based foods from their diets and ate this new rice for 4 weeks. The extent of overall skin lesions was expressed by using the atopic dermatitis affected area and severity index (ADASI). A significant decrease in ADASI was observed at observations made during weeks 2 and 4 and at the end of the study. "Moderate" to "remarkable" improvement was observed in 77% of the panelists, and "moderate" to "remarkable" reduction in steroid ointment use was noted. Exacerbation of symptoms was observed in four cases, indicating the new rice still contained some allergens.

di Lernia et al. (1992) reported that a 17-year-old female who threw raw rice at a wedding developed acute erythema of the hands, edema of the eyelids, dyspnea, and cough—prick tests, open scratch and handling tests, and radioallergosorbent (RAST) tests were positive for rice. Lezaun (1994) reported a case of an atopic housewife who developed similar symptoms after handling rice at a wedding as well as during handling of raw rice for cooking. Positive responses to other cereal grains were also observed in these rice-positive women.

Dermal Irritation

Oils, Fatty Acids, and Waxes

Nakayama (1976) patch tested 27 subjects with Rice Wax and Hydrogenated Rice Bran Wax. Approximately 73% of the tested Rice Wax was comprised of behenic acid, lignoceric acid, octacosyl alcohol, and myricyl alcohol. The composition of the tested Hydrogenated Rice Bran Wax was not reported. Patches containing 3%, 5%, and 10% of both waxes (in a lanolin base) were applied to two sites on the back of each panelist. Patches from one site were removed after 24 h of contact and patches on the other site were removed after 48 h of contact. Sites were evaluated for 1 to 72 h after patch removal.

TABLE 20
Anticarcinogenicity studies on components of Rice

Carcinogen/tumor cell administration	Conditions for Rice administration	Results compared to controls (carcinogen and/or tumor but were fed basal diet)	Reference
		Rice Bran derived	
Groups of 25 male F344 rats; weekly injections of 1,2-dimethylhydrazine at day 35	27 weeks with 2% or 4% rice bran hemicellulose (extracted from rice bran fiber, consists mainly of arabinose and xylose) beginning day 0	Significant ($p < .05$) reduction in colon tumors in 4% rice bran hemicellulose group	Aoe et al. 1993
Group of 32 male Wistar rats received *N*-ethyl-*N*′-nitro-*N*-nitrosoguanidine in drinking water for 4 months, followed by 4 months of untreated water	Rats received rice bran saccharide (derived from rice bran) at 250 μg/ml in drinking water for 4 months beginning at month 8	Gastrointestinal tumors noted in 88% of rats from carcinogen only group and in 46% of rats from carcinogen/rice bran saccharide group ($p < .025$). rice bran saccharide prevented a reduction in immunocompetence, and prolonged survival in rats with cancer	Takeshita et al. 1992; Nakamura 1992
Groups of 10 BALB/C mice received subcutaneous inoculations of Meth-A fibrosarcoma cells (6×10^4 cells/mouse)	α-Glucan fractionated from rice bran saccharide days 1–10	Oral 10 mg/kg: 21.0% inhibition ($p < .05$) 30 mg/kg: 45.1% inhibition ($p < .01$) 100 mg/kg: 26.2% inhibition ($p < .05$) Intraperitoneal 30 mg/kg: 5.0% inhibition ($p < .01$)	Takeo et al. 1988
Groups of 10 BDF_1 mice received subcutaneous inoculation of Lewis lung carcinoma cells (10^5 cells/mouse)	α-Glucan fractionated from rice bran saccharide on days 1–10	Oral 10 mg/kg: 29.4% inhibition ($p < .05$) 30 mg/kg: 43.8% inhibition ($p < .001$) 100 mg/kg: Intraperitoneal 27.5% inhibition ($p < .05$) Intraperitoneal 30 mg/kg: 47.9% inhibition ($p < .001$)	Takeo et al. 1988
10 BALB/C mice received subcutaneous inoculation of Meth-A fibrosarcoma cells (6×10^4 cells/mouse)	30 mg/kg rice bran saccharide (derived from rice bran) p.o. on days 1–10	48.1% inhibition ($p < .01$)	Takeo et al. 1988
10 BDF_1 mice received subcutaneous inoculation of Lewis lung carcinoma cells (1×10^5 cells/mouse)	30 mg/kg rice bran saccharide (derived from rice bran) p.o. on days 1–10	46.8% inhibition ($p < .001$)	Takeo et al. 1988
		γ-Oryzanol	
Rats were initiated with intraperitoneal injections of 2,2′ dihydroxy-di-*n*-propylnitrosamine; intragastric injections of *N*-ethyl-*N*-hydroxynitrosamine; and subcuteneous injections of 3,2′-dimethyl-4-aminobiphenyl	Rats received feed containing 1% γ-oryzanol for 32 weeks	Enhancement of lung carcinogenesis by all initiators noted with microscopic examination	Hirose et al. 1991

(Continued on next page)

TABLE 20
Anticarcinogenicity studies on components of Rice *(Continued)*

Carcinogen/tumor cell administration	Conditions for Rice administration	Results compared to controls (carcinogen and/or tumor but were fed basal diet)	Reference
Male F344 rats initiated with 3,2′-dimethyl-4-aminobiphenyl	Rats received feed containing 2% γ-oryzanol for 40 weeks	No significant difference in prostate lesion incidence	Nakamura et al. 1991
Sprague-Dawley rats received intragastric dose of DMBA	Rats received feed containing 1% γ-oryzanol for 35 weeks	Incidence and multiplicities of mammary tumors comparable to controls; significantly greater survivaf in γ-oryzanol group	Hirose et al. 1994
12-*O*-tetradecanoylphorbol-13-acetate applied to the outer and inner ears of ICR mice twice weekly for 20 weeks, then 50 μg of 7,12-dimethylbenz [a]anthracene was applied to the backs of the mice	The methanol extract of rice bran and γ-oryzanol were applied to the ear skin where the TPA was applied	The 50% inhibitory dose of compounds contained in the rice bran oil and γ-oryzanol was 0.2–0.3 mg/ear	Yasukawa et al. 1998

Weak positive reactions were noted but were similar to those noted for the lint byssus control, and were not dose dependent. The investigator considered the results to indicate, "almost no acute primary irritation" (Nakayama 1976).

CTFA (1987b) reported a use study in which 30 subjects were instructed to use a moisturizer containing 8.0% Rice Bran Oil for 3 weeks. Another thirty subjects used a commercially available lotion. After the 3-week period, all subjects switched to use the "other" lotion for an additional 3 weeks. Dermatologic examinations of the face were conducted at the start and end of the study and at the 3-week cross-over. Subjects also answered questionnaires at the end of each 3-week use period. The test lotion produced an acceptably low incidence of "skin reactions." However, it produced an unacceptable level of perceived discomfort and/or irritation. Follow-up testing traced the subjective discomfort to silicone fluid contained in the test lotion. The same lotion (containing 8.0% Rice Bran Oil) without the silicone fluid when tested on those with ocular area reactions to the original lotion did not evoke discomfort. The re-formulated lotion was recommended for consumer use.

Hill Top Research (1989) tested a moisturizer and a body cream each containing 1.04% Rice Bran Oil in a cumulative irritation study. 10 of an original 13 participants completed the study (2 were dropped due to suspected presensitization; 1 was dropped for reasons unrelated to testing). Each test material (0.2 ml) was applied to a separate area on the back for 23 h of contact. Subjects were instructed to remove the patch, shower, and then report for site evaluation and patch reapplication. Each material was applied to the same site a total of 21 consecutive times.

The moisturizer had a total score of 26 and the body cream had a score of 31; the maximum score was 630. Each test material was classified as a mild irritant (Hill Top Research 1989).

In another test reported by CTFA (1991), 20 females were instructed to apply a body lotion containing 1.04% Rice Bran Oil to the upper chest and neck area twice a day for 9 days. One woman developed "significant" follicular irritation. The investigators considered the incidence, "consistent with what has been observed in this assay."

Proteins

Hydrolyzed Rice Protein (Nutriskin®) was used in a cutaneous tolerance test using 10 volunteers (Cosmepar 1999c). The mean age of the nine women and one man was 46 years; their skin was described as nonsensitive. The test material was applied (0.02 ml) using Finn chambers attached to the forearm and back. Finn chambers with no test material were simultaneously applied. After 48 h, the Finn chambers were removed and the sites observed 1 h later. Two of the individuals had slight erythema, but no edema. None of the others had erythema or edema. At 48 h after removal of the Finn chambers, no reactions were seen in any individual.

Dermal Sensitization and Photosensitization

Oils, Fatty Acids, and Waxes

CTFA (1985a, 1985b) reported results of testing two formulations each containing 1.04% Rice Bran Oil in repeated-insult patch tests (RIPTs). A bath oil was tested as a 10% aqueous dispersion using 87 females and 6 males. Nine induction patches were applied to the same site during a three week period. Subjects were instructed to remove the patches after 24 h of exposure. Sites were evaluated prior to application of successive patches. After a 3-week nontreatment period, subjects were challenged with a single 24-h patch applied to a previously unexposed area. Reactions were scored 24 and 48 h after patch removal. Seventeen subjects had instances of "barely perceptible"

or "mild" reactions during the induction period. One panelist had a "barely perceptible" reaction at the 24-h challenge evaluation. The bath oil had no allergic sensitization potential. A body cleanser was tested as a 0.5% aqueous solution on 85 females and 9 males. Ten subjects had instances of "barely perceptible" or "mild" reactions during the induction period. One panelist had a "barely perceptible" reaction at the 24- and 48-h challenge evaluations.

CTFA (1987c) also reported that a moisturizer containing 8.0% Rice Bran Oil was tested in RIPTs using 84 females and 10 males. Nine induction patches were applied to the same site during a 3-week period. Subjects were instructed to remove the patches after 24 h of exposure. Sites were evaluated prior to application of successive patches. After a 3-week nontreatment period, subjects were challenged with a single 24-h patch applied to a previously unexposed area. Reactions were scored 24 and 48 h after patch removal. Twenty-seven subjects had "barely perceptible" or "mild" reactions during induction; in fourteen of these subjects a reaction was noted only at one observation. No reactions were observed at challenge.

Hill Top Research (1988) tested a lip balm containing 1.04% Rice Bran Oil in an RIPT using 90 subjects. A total of 10 24-h induction exposures were applied to the same site on the back over a 22-day period. After a 2-week nontreatment period, subjects were challenged and reactions were scored 48 and 96 h after application. One panelist reacted throughout the induction period and at challenge. The lip balm was considered negative by the authors.

AMA Laboratories (1989) tested a face/body cream containing 1.04% Rice Bran Oil in a RIPT; 100 subjects completed the protocol. A total of nine 24-h induction patches were applied to the back within a 3-week period. Following a 2-week nontreatment period subjects were challenged. No reactions were noted during induction or at challenge.

Ivy Laboratories (1996) tested 25 healthy, Caucasian adult volunteers ranging in age from 18 to 57 years in a photocontact allergenicity test. None of the subjects had a medical or dermatological illness and none were sensitive to sunlight or to topical preparations and/or cosmetics. The test sample used in this study contained 1.04% Rice Bran Oil in a lip balm.

The MED of each subject was determined by exposing one side of the midback to a series of exposures (1 cm diameter in circular areas) in 25% increments from the xenon arc solar simulator. The subject's MED is the time of exposure that produces a minimally visible erythema at 20 to 24 h post exposure.

The test material (80 mg) was applied to a designated skin site measuring 2 × 2 cm over the lower back using plastic 1-cc disposable tuberculin syringes. The sites were then covered by squares (2 × 2 cm) of nonabsorbing cotton cloth and the patches fastened to the skin with overlapping strips of occlusive tape. The patches were left in place for 24 h. At the end of the period, the patches were removed and the sites wiped off with dry gauze and then exposed to 3 MEDs from the xenon arc solar simulator.

The sites were then left open for a 48-h period and then the patches were reapplied to the same designated test site under an occlusive dressing. Twenty-four hours later, the patches were again removed and the sites reexposed to another dose of 3 MEDs of solar simulated radiation. This sequence was repeated for the same test sites twice weekly for a total of 3 weeks. Ten to 14 days following the last induction exposure, the subjects returned to the testing facility for a single challenge exposure.

The test materials were then applied as previously specified (80 mg) in duplicate to new designated skin sites measuring 2×2 cm on the opposite side of the lower back, under an occlusive dressing for a period of approximately 24 h. One set of patches was then removed and any excess material wiped off with dry gauze. Each site was then irradiated with 4 J/cm^2 of UVA. The duplicate set of patches remained unirradiated and served as control unexposed treated sites. All test sites were examined for reactions at 48 and 72 h following exposure of the sites to UVA radiation.

No reactions were seen during the induction phase, except for some mild erythema, desquamation and tanning which are to be expected following repeated exposures to 3 MEDs. No untoward or abnormal reactions of any kind were seen following the challenge in any of the 25 panelists. Under the presently described test conditions, the above test material was not found to possess a photocontact sensitizing potential in human skin (Ivy Laboratories 1996).

Consumer Product Testing Co. (1997) tested a children's shampoo and conditioner containing 0.3% *w*/*w* Rice Bran Oil in an RIPT using 111 subjects (90 females, 21 males). The shampoo was prepared as a 10% dilution using distilled water. The test materials (∼2 ml) were applied in semiocclusive patches to the upper back. Subjects were instructed to remove patches after 24 h. Patching was done three times per week for a total of 10 applications. Sites were evaluated prior to application of each subsequent patch. Following a 2-week nontreatment period, subjects were challenged at both the induction patch application site and at an unexposed site on the volar forearm. Sites were evaluated at 24 and 48 h after application.

Nine subjects (seven females, two males) dropped out of the study for reasons unrelated to the test material. Mild erythema in response to the conditioner was observed in one subject at the fourth and fifth induction observation. No reactions were observed at challenge. The shampoo and conditioner, "did not indicate a potential for dermal irritation and/or sensitization" (Consumer Product Testing Co. 1997).

Ivy Laboratories (2000) conducted a photocontact allergenicity potential assay in 25 healthy Caucasian subjects (17 males and 9 females) ranging in age from 18 to 49 years. All subjects had skin types ranging from I to III (burns easily; never tans to burns moderately, tans gradually). The test sample contained 1.5% Rice Bran Oil in a lotion. None of the subjects had a medical or dermatological illness and none were sensitive to sunlight or to topical preparations and/or cosmetics.

The test patches were applied to the lower back of each subject. In the pretesting phase, the MED of each subject was determined by exposing one side of the midback to a series of exposures (1 cm diameter circular areas) in 25% increments from a xenon arc solar simulator. Approximately 40 mg of the test material was applied to 2 × 2-cm skin sites over the lower back and covered with nonwoven cotton cloth. The patches were fastened to the skin with occlusive tape and left in place for 24 h. At the end of this period, the patches were removed and the sites were wiped off with dry gauze and exposed to 3 MEDs from the xenon arc solar simulator. The sites were then left open for a 48-h period, after which the patches were reapplied to the same designated test site under an occlusive dressing. Twenty-four hours later, the patches were removed and the sites reexposed to 3 MEDs of solar simulated radiation. This sequence was repeated to the same test sites twice weekly for a total of 6 weeks (total of six exposures).

Twelve days following the last induction dose, the subjects returned for a single challenge exposure. The test material was applied as previously specified (40 mg) in duplicate to new designated skin sites measuring 2×3 cm on the opposite side of the lower back, under occlusive dressings for a period of approximately 24 h. One set of patches was then removed and any excess test material was wiped off with gauze. The sites were then exposed to 4 J/cm^2 of UVA light (spectrum between 320 and 420 nm). The duplicate patches remained unirradiated and served as controls. All test sites were examined for reactions at 48 and 72 h following exposure of the site to the UVA radiation.

No side effects or unexpected reactions of any kind were observed. No reactions suggestive of a photocontact allergy was seen in any panelist at either 48 or 72 h post exposure. Under the present conditions described, the test materials in the lotion did not possess a detectable photocontact-sensitizing potential in human skin (Ivy Laboratories 2000).

Bran, Starch, and Powder

Pigatto et al. (1997) conducted a double-blind, randomized patch study to investigate whether colloidal grain suspensions induced allergic contact dermatitis in atopic children. Initially, a 15-min open patch of a colloidal rice flour solution was applied to the back of 65 children aged 6 months to 2 years (43 were atopic and 22 were normal). As no urticarial response was observed, occlusive patches containing 0.007% and 0.7% colloidal rice flour were applied. If no positive response was observed at 24 h, the contralateral patch remained in place for another 24 h. Sites were evaluated at the time of patch removal and also at 72 and 96 h.

One atopic child had a mild irritant response to the 0.007% rice solution at 48 h, but no allergic reactions were observed in any of the children. RAST tests were done on 55 children. Eight had a positive response to one of the test substances (details not given); these eight were atopics. The investigators considered that topical colloidal grains did not induce sensitization (Pigatto et al. 1997).

Proteins

Consumer Product Testing Co. (2002) conducted a repeated insult patch test of Hydrolyzed Rice Protein. Of the 112 subjects (74 women, 38 men) who qualified, 108 (71 women, 37 men) completed the study. Subjects ranged in age from 16 to 78 years with no visible skin disease. According to the authors, the 4 drop-outs were unrelated to the application of test material.

Undiluted Hydrolyzed Rice Protein (∼0.2 ml) was applied to an absorbant pad of a clear adhesive dressing and this was applied to an area on the upper back to form a semiocclusive patch. The initial patches were removed at 24 h at the clinic. All subsequent patches were removed by the subjects at 24 h, per instructions. Each site was evaluated prior to reapplication. Patches were applied three times per week for a total of nine applications.

Subjects were untreated for 2 weeks, at which time a challenge patch was applied to a virgin test site adjacent to the original induction site. The patch was removed at the clinic after 24 h and the site observed. A final observation was made at 72 h.

One subject developed moderate erythema with possible mild edema at the seventh induction application. Induction was continued at an adjacent site with no erythema or edema. No other subjects developed any skin reaction during induction. None of the subjects had any reactions to the challenge at either 24 or 72 h. The authors concluded that the test material was not irritating or sensitizing (Consumer Product Testing Co. 2002).

Therapeutic Use

Fujiwaki and Furusho (1992) investigated the therapeutic value of Rice Bran broth-bathing in treating atopic dermatitis. Broth was prepared by boiling rice bran with water and then cooling and filtering the mixture. Seventeen subjects with mild to severe atopic dermatitis were instructed to mix 1 L of the broth with bath water, once a day, followed by a shower with fresh water. The therapy continued for 2 to 5 months. Subjects were evaluated before starting therapy, 2 weeks and 1 month after therapy initiation, and monthly thereafter. In five patients serum immunoglobulin (IgE) concentrations and eosinophil counts (from peripheral blood) were measured prior to and 2 to 3 months after therapy initiation.

One subject developed redness and itching just after bathing and discontinued therapy. None of the remaining 16 subjects had adverse effects. A significant decrease in the dermatitis score was noted after 2 weeks of therapy and no subject had a recurrence of his/her initial disease. One subject's dermatitis improved such that steroid ointment treatment was no longer needed. In another two subjects the dosage and grade of steroid treatment was reduced, and another three had a reduction in either dosage or grade of ointment. Of the 16 subjects who completed the protocol, therapy was considered to be excellent in 4, good in 7, slightly effective in 4, and ineffective in 1. A nonsignificant decrease in IgE concentrations and a significant decrease ($p < .05$) in eosinophil counts were observed with therapy (Fujiwaki and Furusho 1992).

SUMMARY

Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Rice Bran Acid, Oryza Sativa (Rice) BranWax, Hydrogenated Rice Bran Wax, Oryza Sativa (Rice) Extract, Oryza Sativa (Rice) Bran Extract, Oryza Sativa (Rice) Germ Powder, Oryza Sativa (Rice) Starch, Oryza Sativa (Rice) Bran, Hydrolyzed Rice Extract, Hydrolyzed Rice Bran Extract, Hydrolyzed Rice Bran Protein, and Hydrolyzed Rice Protein are cosmetic ingredients derived from rice, *Oryza sativa*.

Oils, Fatty Acids, and Waxes

Rice Bran Oil functions in cosmetics as a conditioning agent-occlusive and was reported to FDA by industry to be used in 39 formulations in 12 product categories in 2002. Industry directly reported use in 19 product categories.

Rice Germ Oil functions as a skin-conditioning agent—occlusive and was reported to FDA by industry to be used in six formulations in four product categories in 2002. Industry directly reported use in only one product category. Rice Bran Acid is described as a surfactant—cleansing agent, but was not in use in 2002. Rice Bran Wax functions as a skin-conditioning agent—occlusive and was reported to FDA by industry to be used in eight formulations in five product categories in 2002. Industry did not directly report any use of Rice Bran Wax.

Hydrogenated Rice Bran Wax functions as a binder, skin-conditioning agent—occlusive, and viscosity-increasing agent—nonaqueous and was reported to FDA by industry to be used in 11 formulations in six product categories in 2002. Industry did not directly report any use of Rice Bran Wax.

Rice Bran Oil had an oral LD_{50} of >5 g/kg in white rats and Rice Wax had an oral LD_{50} of >24 g/kg in male mice. A three-generation oral dosing study reported no toxic or teratologic effects in albino rats fed 10% Rice Bran Oil compared to a control group fed Peanut Oil. In primary dermal irritation studies, undiluted Rice Bran Oil had a PII of 0.00 and 0.88, Rice Wax had a PII of 0.21, and Hydrogenated Rice Bran Wax had a PII of 0.0 (scores >5.0 were considered irritants). Rice Germ Oil did not produce dermal irritation and Rice Bran Oil was not a sensitizer. Rice Bran Oil, Rice Germ Oil, Rice Wax, and Hydrogenated Rice Bran Wax were negative in ocular toxicity assays. A mixture of Rice Bran Oil and Rice Germ Oil had a UV absorption maximum at 315 nm, but was not phototoxic in a dermal exposure assay.

Rice Bran Oil was negative in an Ames assay, and a component, γ-oryzanol, was negative in bacterial and mammalian mutagenicity assays.

Formulations containing 1.04% or 8.0% Rice Bran were at most mildly irritating in clinical studies. Rice Bran Oil was negative in six RIPTs (maximum concentration tested was 8.0%). Rice Wax and Hydrogenated Rice Bran Wax were patch tested and produced "almost no acute primary irritation" in 27 subjects.

Extracts

The function of Rice Bran Extract in cosmetics was not reported, but this ingredient was reported to FDA by industry to be used in six formulations in four product categories in 2002. Industry did not directly report any use of Rice Bran Extract.

Rice Extract is described as a hair-conditioning agent, but was not in use in 2002.

Hydrolyzed Rice Extract has no reported function in cosmetics, but industry reported to FDA in 2002 that it is used in four formulations and current concentration of use data were provided for other uses.

Hydrolyzed Rice Bran Extract, described as a skin-conditioning agent—miscellaneous, was not reported to FDA by industry to be in use in 2002, but industry did report current concentrations of use in two product categories.

The recommended concentration of use of Rice Bran Extract in a moisturizing hand cream, conditioning shampoo, and moisturizing body wash was 1%, and in a moisturizing sunscreen, 2%.

Rice Bran Extract is comprised of proteins, lipids, carbohydrates, mineral ash, and water. The fatty acid content includes palmitic, stearic, oleic, and linoleic acids. Other components include antioxidants such as tocopherols.

Rice Extract reduced the cytotoxicity of sodium chloride in male rats.

Bran, Starch, and Powder

Rice Bran (identified as rice hulls) functions as an abrasive and bulking agent and was reported to FDA by industry to be used in one formulation in 2002. Industry did not directly report any use.

Rice Starch functions as an absorbent and bulking agent and was used in 51 formulations in 16 product categories in 2002. Industry directly reported uses in 11 product categories, some different from those reported to FDA. Rice Germ Powder functions as an abrasive and one manufacturer described an exfoliant use, but no uses were reported to FDA by industry in 2002, nor did industry directly report any use.

Oral-dose carcinogenicity studies done on components of Rice Bran, phytic acid and γ-oryzanol were negative. Rice Bran did not have an anti-carcinogenic effect on DMH-induced large bowel tumors. In cocarcinogenicity studies done using the carcinogen 1,2-dimethylhydrazine and other agents, with Rice Bran Oil and Rice Bran–derived hemicellulose and saccharide, tumor inhibition was observed; γ-oryzanol did not inhibit the development of neoplasms.

A decrease in cutaneous lesions in atopic dermatitis patients was reported following bathing with a Rice Bran preparation.

Proteins

Hydrolyzed Rice Bran Protein and Hydrolyzed Rice Protein function as conditioning agents (hair or skin). No uses of either ingredient were reported to FDA by industry in 2002, but industry directly reported uses of Hydrolyzed Rice Protein in seven product categories.

The UV absorption spectrum of Hydrolyzed Rice Bran Protein shows peaks in the UVC region of the spectrum and an

in vitro phototoxicity assay using UVA light found no photochemical toxicity, as would be expected. Rice bran protein hydrolysates are not acutely toxic, are not skin or ocular irritants in animals, are not skin sensitizers in guinea pig maximization tests, and are not irritating or sensitizing in clinical tests. Isolated cases of allergy to raw rice have been reported, but rice, in general, is considered nonallergenic.

DISCUSSION

The Panel expects that the protein and starch composition of Oryza Sativa (Rice) Germ Powder and Oryza Sativa (Rice) Starch will not be significantly different from other rice-derived ingredients for which data are available; i.e., data on hydrolyzed rice protein in this report and on Wheat Starch in a previous report suggest that Oryza Sativa (Rice) Germ Powder and Oryza Sativa (Rice) Starch are safe for use in cosmetics.

The available data on the Oils, Fatty Acids, and Waxes demonstrated that the fatty acid composition of these ingredients includes fatty acids previously determined safe by the CIR Expert Panel. Animal and human toxicity data of the rice-derived Oils, Fatty Acids, and Waxes did not suggest any toxicity. Based on their consideration of all the available information, the CIR Expert Panel concluded that Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Rice Bran Acid, Oryza Sativa (Rice) Wax, and Hydrogenated Rice Bran Wax are safe as used in cosmetic formulations.

In a similar fashion, the Panel considered the composition of rice bran and bran extracts. The carbohydrate component raised no safety issues and the fatty acids that were present were those previously determined by the Panel to be safe. An analysis of other components did not identify heavy metals that would be of concern. Antioxidant components were present, but did not present safety concerns.

Rice Bran Extract does contain UV absorbing compounds, but at low concentrations, and clinical experience suggested no phototoxicity would be associated with such materials.

Plant protein and peptides were found in the extract. Peptides from rice protein are not sensitizers as seen in studies using Hydrolyzed Rice Protein. Rice was generally considered to be non-allergenic. In addition, the levels of use that are likely for extracts are in the range of 2% to 3%, further reducing the possibility that any component would result in a safety concern.

There were no safety test data available for Hydrolyzed Rice Extract and Hydrolyzed Rice Bran Extract, but their safety may be inferred from that of the extracts from which they are derived.

The available safety test data support the safety of Hydrolyzed Rice Bran Protein in cosmetic formulations and the components identified in Hydrolyzed Rice Protein were not significantly different.

The Panel also recognized that there are no currently available concentration of use data for Rice Bran Acid and Hydrolyzed Rice Bran Protein. Were these ingredients to be used in the future, the Panel expects that their future use would be at concentrations no greater than currently reported for similar ingredients; i.e., Rice Bran Acid would be used at concentrations no greater than Rice Bran Oil (from which it is derived) and Hydrolyzed Rice Bran Protein would be used at concentrations no greater than Hydrolyzed Rice Protein.

Current levels of PCBs and heavy metals in rice-derived ingredients used in cosmetics are not a safety concern. The Panel was concerned, however, that contaminants such as pesticides have been reported in Rice Bran Oil used for cooking. Pesticides and heavy metals should not exceed currently reported levels for rice-derived cosmetic ingredients.

CONCLUSION

The CIR Expert Panel concluded that Oryza Sativa (Rice) Bran, Oryza Sativa (Rice) Bran Extract, Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Oryza Sativa (Rice) Germ Powder, Oryza Sativa (Rice) Extract, Oryza Sativa (Rice) Starch, Oryza Sativa (Rice) Wax, Hydrogenated Rice Bran Wax, Hydrolyzed Rice Bran Extract, Hydrolyzed Rice Bran Protein, Hydrolyzed Rice Extract, Hydrolyzed Rice Protein, and Rice Bran Acid are safe as cosmetic ingredients in the current practices of use and concentrations as reflected in this safety assessment.

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