Final Report on the Safety Assessment of Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Oryza Sativa (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 Protein, and Hydrolyzed Rice Protein*

*Note: At the December, 2000 meeting of the CIR Expert Panel, a tentative amended conclusion was reached for the rice oils, fatty acid, and waxes. Were this conclusion made final in 2001, these ingredients would be safe as used.

ABSTRACT

Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Oryza Sativa (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 Protein, and Hydrolyzed Rice Protein are derived from Oryza sativa, rice. These ingredients are further subdivided into oils, fatty acids, and waxes; extracts; brans, starches, and powders; and protein. Their functions in cosmetic formulations vary. Oils, fatty acids, and waxes: The Bran Oil functions in cosmetics as a conditioning agent and solvent in 33 formulations. The Germ Oil functions as a skin-conditioning agent, but was not reported in use. The Bran Acid functions as a surfactant -cleansing agent and was not reported in use. The two Bran Waxes function as binders, conditioning agents, and viscosity increasing agents and were used in 16 formulations. These rice derived ingredients are all comprised of fatty acids commonly used in cosmetic formulations. These members of the rice ingredient group were not toxic in acute studies in animals. A three-generation oral dosing study reported no toxic or teratologic effect in albino rats fed 10% Rice Bran Oil compared to a control group fed Peanut Oil. The undiluted Bran Oil and Hydrogenated Rice Bran Wax were not irritants in animals. The Germ Oil did not produce dermal irritation and the Bran Oil was not a sensitizer. The Bran Oil, Germ Oil, Wax, and Hydrogenated Rice Bran Wax were negative in ocular toxicity assays. A mixture of the Bran Oil and the Germ Oil was not phototoxic in animals. The Bran Oil was negative in an Ames assay, and a component, γ-oryzanol, was negative in bacterial and mammalian mutagenicity assays. The Bran Oil, Wax, and Hydrogenated Rice Bran Wax were not irritants or sensitizers in clinical tests. Data, however, were not available regarding the photosensitization potential of these rice derived ingredients. Extracts: The function of the Rice Bran Extract in cosmetics was not reported, but it was used in six formulations. The Rice Extract was reported to function as a hair conditioning agent and skin-conditioning agent - miscellaneous, but was not in current use. While one study reported that Rice Extract reduced the cytotoxicity of sodium chloride in male rats, overall these ingredients were inadequately characterized and there were inadequate safety test data available. Brans, Starches and Powders: The Bran (an abrasive and bulking agent) was used in one formulation, the Starch (a skin conditioning agent -occlusive) was used in 41 formulations; the Germ Powder (an abrasive) was not reported to FDA to be in use, although one supplier stated it is in use. Oral-dose carcinogenicity studies done on phytic acid and γ-oryzanol (components of the Bran) were negative. In co-carcinogenicity studies, the Bran Oil and Bran-derived hemicellulose and saccharide had significant tumor inhibition; but γ-oryzanol did not inhibit the development of neoplasms. A decrease in cutaneous lesions in atopic dermatitis patients was reported following bathing with a preparation containing the Bran. The Bran was not an irritant in clinical tests. The Starch was considered to be like other plant starches previously considered by the CIR Expert Panel and found to be safe as used. Rice Germ Powder, based on its use as an abrasive in products intended to be rinsed off, was considered to present no significant safety issues. Overall, however, there were insufficient safety test data for the other ingredients in this subgroup. Proteins: Hydrolyzed Bran Protein

and Hydrolyzed Rice Protein function as conditioning agents (hair or skin), although no uses were reported. Isolated cases of allergy to raw rice have been reported, but the relevance to cosmetic use was unclear. Overall these ingredients were inadequately characterized and there were inadequate safety test data available. Based on the available data, however, Oryza Sativa (Rice) Germ Powder and Oryza Sativa (Rice) Starch are safe as used in cosmetic formulations. Currently, the available data are insufficient to support the safety of the other rice-derived ingredients and additional data are needed.

INTRODUCTION

This report is based on a compilation of studies regarding, **Oryza Sativa (Rice) Bran Oil** [CAS Nos. 68553-81-1 and 84696-37-7], **Oryza Sativa (Rice) Germ Oil, Oryza Sativa (Rice) Bran Acid** [CAS No. 93165-33-4], **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**, and **Hydrolyzed Rice Protein**.

All ingredients are derived from rice, *Oryza sativa*. Most of the studies were conducted on Rice Bran Oil or on a mixture of Rice Bran Oil and Rice Germ Oil.

For convenience, the botanical name will be largely omitted from the text, but is included in the headings to remind the reader of the complete names.

CHEMISTRY

Definition

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
Rice Bran Oil is the oil expressed from rice *Oryza sativa* bran (Wenninger et al., 2000).

Oryza Sativa (Rice) Germ Oil
Rice Germ Oil is the oil obtained by the expression of germs of rice, *Oryza sativa* (Wenninger et al., 2000).

Oryza Sativa (Rice) Bran Acid
Rice Bran Acid (CAS No. 93165-33-4) is a mixture of fatty acids derived from Rice Bran Oil (q.v.) (Wenninger et al., 2000).

Oryza Sativa (Rice) Bran Wax and Hydrogenated Rice Bran Wax
Rice Bran Wax is a wax obtained from rice bran, *Oryza sativa* (Wenninger et al., 2000).

Hydrogenated Rice Bran Wax is the end product of controlled hydrogenation of Rice Bran Wax (q.v.) (Wenninger et al., 2000).

Oryza Sativa (Rice) Bran Extract
Rice Bran Extract is an extract of the bran of rice, *Oryza sativa* (Wenninger et al., 2000).

Oryza Sativa (Rice) Extract
Rice Extract is an extract of the grains of rice, *Oryza sativa* (Wenninger et al., 2000).

Bran, Starch and Powder

Oryza Sativa (Rice) Bran

Rice Bran is the broken hulls of rice, *Oryza sativa* (Wenninger et al., 2000). Rice Bran is a by-product of rice milling obtained during polishing of rice. It is the part between the paddy husk and endosperm. Bran consists of 15-20% oil (Rukmini, 1988).

Starch, General

Plant starch is a polymer which consists of monomeric units of D-anhydroglucose. The predominant linkage is 1,4-alphaglucosidic 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 which contains 1,4-alphaglucose bonds between units. Each unit consists of one primary and two secondary hydroxyl groups except the terminal unit. It has reducing and non-reducing ends which 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 types of chemical modifications.

Oryza Sativa (Rice) Starch

Rice Starch is a starch obtained from rice, *Oryza sativa* (Wenninger et al., 2000). Starches are a GRAS (generally recognized as safe) food ingredient (Informatics, 1974).

White rice, resulting from a process of milling called scouring or whitening of brown rice, is the endorsperm of the kernel and is composed primarily of starch (90%) (Mazzo, 1998).

Oryza Sativa (Rice) Germ Powder

Rice Germ Powder is the powder derived from the rice germ, *Oryza sativa* (Wenninger et al., 2000).

Table 1. Chemical Modifications of starch via depolymerization (D) and via addition (A) of monofunctional substituent groups (Pasapane et al., 1999)

Type	Modification	Description of Modification
D	acid-hydrolyzed	a strong acid is added to a granular starch slurred in water, and heat is added to degrade the starch
D	oxidation	an oxidizing agent is added to a granular starch slurred in water, and heat is added to degrade the starch
D	enzyme	enzymes attack and break down the starch molecule at very specific chemical links
D	dextrin	dried, acidified starch is heated - also know as starch roasting
A	hydrophobic	hydrophobic moieties are attached to the starch backbone
A	cross-linking	the starch is treated to produce chemical cross-links, providing higher, more stable viscosities
A	hydroxypropylated	β-hydroxypropyl groups are attached to the starch
A	anionic and cationic	anionic and cationic groups can be added for particular functional attributes

Proteins

Hydrolyzed Rice Bran Protein
It is the hydrolysate of rice bran protein derived from acid, enzyme, or other method of hydrolysis (Wenninger et al., 2000).

Hydrolyzed Rice Protein
Hydrolyzed Rice Protein is the hydrolysate of rice protein derived by acid, enzyme or other method of hydrolysis (Wenninger et al., 2000).

Chemical Composition and Properties

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
Rice Bran Oil contains saponifiable and unsaponifiables, including appreciable amounts of waxes (Rukmini, 1988). Typical finished Rice Bran Oil samples are characterized as a function of fatty acid composition in Table 2 and by mono-, di-, and triglyceride distribution in Table 3.

Table 2. Fatty Acid Composition of Rice Bran Oil (Rukmini and Raghuram, 1991)

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	550 ppm
γ-oryzanol	1.6 %

Among the many sterols present in the unsaponifiable fraction of Rice Bran Oil, oryzanols and tocotrienols have been intensively studied. γ-Oryzanol is further identified below 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.

Table 3. Rice Bran Composition (McCaskill and Zhang, 1999)

Component	%
Triglycerides	68-71
Diglycerides	2-3
Monoglycerides	5-6
Free fatty acids	2-3

Waxes	2-3
Glycolipids	5-7
Phospholipids	3-4
Unsaponifiables	4

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 (McCaskill and Zhang, 1999).

Gamma-oryzanol

γ-oryzanol (CAS No. 11042-64-1) is a phytosterol derived from Rice Bran (Hiraga et al., 1993). Kubota and Sekine (1978) patented an extraction technique from Rice Bran Oil and Rogers et al. (1993) reported an HPLC detection technique.

Crude rice bran oil contains about 2% or more of γ-oryzanol, a group of ferulate esters of triterpene alcohols and phytoesters. 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. Oryzanol has been used to treat nerve imbalance and disorders of menopause. No food additive

Table 4. Physical Properties of Rice Bran Oil and Rice Germ Oil Mixture, Rice Wax, Hydrogenated Rice Bran Wax, and Rice Extract

Property	Rice Bran Oil and Rice Germ Oil mixture [1]	Rice Wax [2]	Hydrogenated Rice Bran Wax [2]	Rice Starch [5]	Rice Extract [3]	Rice Bran Extract [4]
Appearance	light yellow oil	white flakes	light yellow granules		clear, yellowish liquid	
Melting Point		79-83°C	70-77°C			
Specific Gravity	0.913 - 0.923	0.932-0.945	0.912-0.927	0.950		1.02-1.15
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	1.5045	1.465 -1.485	1.3860-1.5000
Density					0.910 - 0.930	
Solubility						soluble in any proportion in water
Heavy Metals	10 ppm max			10 ppm max (Pb)	1 ppm max	
Arsenic	1 ppm max					
pH						4.0-6.5

Maximum Absorption	292 nm

1. Ichimaru Pharcos Co., 1994
2. Buffa, 1976
3. Grau Aromatics GmbH & Co., 1998
4. CTFA, 1999b
5. CTFA, 1999c

determinations have been made by the FDA (McCaskill and Zhang, 1999).

Oryza Sativa (Rice) Germ Oil

An oil registered in Japan as "rice germ oil" is a mixture of Rice Bran Oil and Rice Germ Oil (Ichimaru Pharcos Co., 1998). It contains 1.0 - 1.5% oryzanol. Physical properties of this mixture are cited in Table 4. Studies using this mixture appear under the "rice germ oil" heading in this report.

Rice (Oryza Sativa) Wax and Hydrogenated Rice Bran Wax

Buffa (1976) reported two processing techniques for obtaining the two 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 Rice Bran Wax. In the second technique, the crude wax is hydrogenated and then bleached,

Table 5. Fatty Acid and Alcohol Composition of Rice (Oryza Sativa) Wax and Hydrogenated Rice Bran Wax (Buffa, 1976)

	Carbon No.	Rice Bran Wax (%)	Hydrogenated Rice Bran Wax (%)
Myristic Acid	C_{14}		.32
Palmitic Acid	C_{16}	3.28	18.94
Stearic Acid	C_{18}	.32	60.55
Oleic Acid	$C_{18}F_1$	.32	
Arachidic Acid	C_{20}	.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}	.56	
Behenyl Alcohol	$C_{22}OH$	.38	
Lignoceryl Alcohol	$C_{24}OH$	3.21	.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	$C_{36}OH$	.5	

thereby creating Hydrogenated Rice Bran Wax. Physical properties of the waxes are in Table 4. Buffa (1976) detailed the composition of the Rice Bran Wax and the Hydrogenated Rice Bran Wax (Table 5).

Extracts

Oryza Sativa (Rice) Extract
The specifications from one manufacturer identifies Rice Extract as containing 10-25% extract, > 75% sunflower seed oil (solvent used for extraction), and 0.15% of the preservative 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, fatty oils (Grau Aromatics GmbH & Co., 1998). Physical properties are listed in Table 4.

Bran, Starch and Powder

Oryza Sativa (Rice) Bran
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

Hydrolyzed Rice Protein
Hydrolyzed Rice Protein is extracted from rice grains and then is enzymatically digested (CTFA, 1999a). A standard profile of Hydrolyzed Rice Protein components is in Table 6.

Table 6. Component Profile (by weight) of Hydrolyzed Rice Protein (CTFA, 1999a)

Protein	~ 60%
Carbohydrates	24%
Moisture	<6%
Fat	0.4%
Ash	7%
Sodium	2.4%

Contaminants

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
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 0.7-1.84 g/person (Hsu et al., 1984). The oils had also 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).

Extracts

Oryza Sativa (Rice) Bran Extract
Information provided by suppliers gave the following contaminants and limits: 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/gm) (CTFA, 1999b).

Concentrations of other components of the raw material was reported as: 97-98.8% solvent (water/propylene glycol, water/butylene glycol, water/glycerin, safflower oil) and 1% preservative (CTFA, 1999b).

Bran, Starch and Powder

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

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 295-315 nm. The absorption differential (transmittancy of tanning rays 315-365 nm/transmittancy of burning rays 295-315 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 SPF of 3.

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 done on the oil mixture and oryzanol appear in the Phototoxicity section of this report.

Table 7. Cosmetic Functions of Rice Bran-derived Ingredients
(Wenninger et al., 2000)

Ingredient	Chemical Class	Function
	oils, fatty acids, & 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
Oryza Sativa (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

bran, starch & 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, exfolient[1]
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, antistatic agent [2]

[1]Solabia, 1999; [2]CTFA, 1999a

USE

Cosmetic

The functions of the various rice-derived ingredients in cosmetic formulations as described in the *International Cosmetic Ingredient Dictionary and Handbook* (Wenninger et al., 2000) are listed in Table 7. In addition, CTFA (1998) has indicated that Hydrolyzed Rice Protein is used as an antistatic agent and one supplier describes Rice Germ Powder's use as an exfoliant (Solabia, 1999).

As of January 1998, the oil ingredients were used collectively in 49 formulations (Rice Bran Oil had 33 uses, Rice Bran Wax had five uses, and Hydrogenated Rice Bran Wax had 11 uses). Rice Bran Extract (and its lipid fraction) was used in six formulations, Rice Starch in 41 formulations, and Rice Bran (identified as rice hulls) was used in one formulation, (FDA, 1998). The frequency of use data reported to FDA is presented in Table 8.

Table 8. Frequency of Use of Ingredients as Reported to FDA (FDA, 1998)

Product Category	No. Formulations in Category	No. Containing Ingredient
Rice Bran Oil		
Bath Oils, Tablets, and Salts	124	1
Hair Conditioners	636	2
Other Hair Preparations	276	1
Foundations	287	2
Other Manicuring Preparations	61	2
Cleansing	653	2
Face and Neck Skin Care (excl shaving)	263	4
Body and Hand Skin Care (excl shaving)	796	2
Moisturizing	769	10
Paste Masks (mud packs)	255	2
Other Skin Care Preparations	692	5
Suntan Gels, Creams, and Liquids	136	2
1998 total for Rice Bran Oil		**33**
Rice Wax		
Lipstick	790	2

Product Category	No. Formulations in Category	No. Containing Ingredient
Face and Neck skin care (excl. shaving)	263	2
Suntan Gels, Creams, and Liquids	136	1
1998 total for Rice Bran Wax		**5**
Hydrogenated Rice Bran Wax		
Eyebrow Pencil	91	3
Eyeliner	514	1
Other Eye Makeup Preparations	120	3
Lipstick	790	1
Other Makeup Preparations	135	3
1998 Total for Hydrogenated Rice Bran Wax		**11**
Rice Bran Extract		
Tonics, Dressings, and Other Hair Grooming Aids	549	2
Other Hair Preparations	276	1
Moisturizing	769	1
Other Skin Care Preparations	692	1
1998 total for Rice Bran Extract		**5**
Rice Bran Extract, lipid fraction*		
Body and Hand Skin Care (excl shaving)	796	1
1998 total for Rice Bran Extract, lipid fraction		**1**
Rice Starch		
Eye Shadow	506	1
Mascara	167	5
Other Eye Makeup Preparations	120	3
Other Hair Preparations	276	1
Blushers (all types)	238	2
Face Powders	250	4
Foundations	287	1
Bath Soaps and Detergents	385	1
Face and Neck skin care (excl. shaving)	263	2
Body and Hand skin care (excl. shaving)	796	7
Moisturizing	769	1
Paste Masks (mud packs)	255	7
Skin Fresheners	184	1
Other Skin Care Preparations	692	5
1998 total for Rice Starch		**41**
Rice Bran (identified as rice hulls)		
Other Personal Cleanliness Products	291	1

Product Category	No. Formulations in Category	No. Containing Ingredient
1998 total for Rice Bran		**1**

* not recognized as a cosmetic ingredient in the CTFA *International Cosmetic Ingredient Dictionary and Handbook* (Wenninger et al., 2000).

Concentration of use data are no longer reported to FDA (FDA, 1992). Concentration of use data submitted to FDA in 1984 (FDA, 1984) reported 28 of 33 uses of Rice Bran Oil at ≤1%; 2 uses at 1-5%; and 1 use each at 5-10%, 10-25%, and 25-50%; and Rice Wax in lipsticks at 0.1-5%. Current concentration of use data have been provided by the industry (CTFA, 1998a, b and 1999b, e) and Tabulated in Table 9.

Additional details were provided as follows: one manufacturer reported use of Rice Bran Oil at: 0.05% in a shampoo; 0.28% in a night cream; 0.5% in an eye cream; 1.04% in a bath oil, cleansing gel, and facial cleanser; 2.0% in a facial moisturizer; 2.5% in a under makeup moisturizer; 4.0% in a body moisturizer; and 8.0% in a moisturizing skin preparation (CTFA, 1998a). Current data were not found for the other ingredients. In addition, one supplier noted use of Rice Extract at 1-10% in cosmetics (Grau Aromatics, 1998). Another company used Rice Bran Extract at "low (trace) levels" (CTFA, 1998b).

Table 9. Ingredient Concentration of Use Data (CTFA, 1998a, b; 1999b, e)

Ingredient	Product type	Range of Reported Maximum Concentrations
Oryza Sativa (Rice) Bran Oil	Bath oils, tablets, and salts	1-39%
	Other bath preparations	1%
	Eyebrow pencils	0.1%
	Eye lotion	0.5-1%
	Mascara	0.1%
	Other makeup preparations	0.5%
	Hair Conditionsers	0.3%
	Shampoos (non-coloring)	0.05%
	Foundations	0.5%
	Lipstick	0.1-1%
	Makeup bases	3%
	Bath soaps and detergents	1%
	Other shaving preparation products	1%[1]
	Skin cleansing (cold creams, cleansing, lotions, liquids, and pads)	0.5-1%
	Face and neck creams, lotions, powders, and sprays (excluding shaving preparations)	0.3-3%
	Body and hand creams, lotions, powders, and sprays (excluding shaving preparations)	3-4%
	Moisturizing creams, lotions, powders, and sprays	2-8%
	Night creams, lotions, powders, and sprays (excluding shaving preparations)	0.28-0.3%

Ingredient	Product type	Range of Reported Maximum Concentrations
	Paste masks (mud packs)	0.2%
	Suntan gels, creams, and liquids	3%
Oryza Sativa (Rice) Bran Wax	Mascara	8%
	Eyeliner	6%
	Lipstick	4-7%
Oryza Sativa (Rice) Germ Oil	Body and hand creams, lotions, powders, and sprays (excluding shaving preparations)	0.1%
Oryza Sativa (Rice) Starch	Bath Oils, tablets, and salts	97%
	Eyeliner	8%
	Eye shadow	3%
	Powders (dusting and talcum) (excluding shave talc)	6%
	Hair Conditioners	4%
	Blushers (all types)	9%
	Mascara	4%
	Face powders	1%
	Face and neck creams, lotions, powders, and sprays (excluding shaving preparations)	2%
	Moisturizing creams, lotions, powders, and sprays	4%
	Night creams, lotions, powders, and sprays (excluding shaving preparations)	2%

International

Rice Bran Oil, Rice Germ Oil, Rice Wax, Rice Bran Extract, Rice Germ Powder, Rice Starch, and Rice Bran are listed in the Japanese *Comprehensive Licensing Standards of Cosmetics by Category* (CLS). Those which conform to the specifications of the *Japanese Cosmetic Ingredients Codex* (JCIC) [or, in the case of Rice Starch, the *Japanese Standards of Cosmetic Ingredients* (JSCI)] have a precedent for use at unrestricted concentrations in most cosmetic product [or CLS] categories. There has been no precedent regarding use in eyeliners (Rice Germ Oil is permitted for such use). No precedent has been established regarding use of Rice Bran, Rice Bran Extract, Rice Germ Powder in lip or oral preparations (Rempe and Santucci, 1997).

Non-cosmetic - General Food Uses

Rice (Oryza sativa) is the staple food source for half of the world's population. It is non-allergenic, easily digested, 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 compromises about 20% of the rice kernel, the bran and embyro about 8-12%, and the endosperm or milled rice (white rice) about 70-72% (Mazza, 1998).

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% (USA Rice Federation, 1999a).

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
Crude Rice Bran Oil contains high free fatty acids and unsaponifiables and is non-edible - further refining to limit the amount of these two components renders it edible (Rukimi, 1988). 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 self-life of other food products (McCaskill and Zhang, 1999).

Bran, Starch and Powder

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

Oryza Sativa (Rice) Starch
Present only in the endosperm of the grain, Rice Starch makes up 90-93% 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 excipients in pharmaceuticals. Gelantinized 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 desserts 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 (Mazzo, 1998).

Miscellaneous

Oryza Sativa (Rice) Flour
Rice Flour is non-allergenic and is very valuable to persons allergic to gluten and wheat flour products. The flour is extruded to produce rice pasta, chips, and other snacks, as well as cereals (USA Rice Federation, 1999b).

Broken Kernels
Broken Kernels are used to make various products, including rice flour and pet foods (USA Rice Federation, 1999b).

GENERAL BIOLOGY

Absorption

Included in the CIR Wheat Germ Oil Safety Assessment (1980) is information from Valette and Sorbrin (1963), stating that 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.

Blood Effects

Bran, Starch and Powder

Oryza Sativa (Rice) Bran
Takenaka and Itoyama (1993) reported a significant ($p < 0.05$) increase in the number of granular leukocytes and lymphocytes in rats given a 10% Rice Bran fiber diet for two weeks. A significant increase ($p <$

0.01) 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

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
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 ($p < 0.01$) and decreased H^+ concentrations in gastric juices ($p < 0.05$) 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 anti-oxidants such as α-tocopherols that could have exerted a protective effect.

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

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 i.v. or 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.

Bran, Starch and Powder

Oryza Sativa (Rice) Bran
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 ($p < 0.01$) 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

Gamma-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 Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
Purushothama et al, (1995) reported comparatively lower concentrations of cholesterol (TC), triglycerides (TG) 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 ($p < 0.05$) in

high density lipoproteins (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) cholesterol and very low density lipoprotein cholesterol (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 controls 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, a significant reduction ($p < 0.001$) in TC and TG was documented in twelve subjects with high TC, fifteen and thirty 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 (Raghuram et al., 1989).

In reviews of the hypolipidemic action of Rice Bran Oil, it was 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 (Rukmini and Raghuram, 1991; Raghuram and Rukmini, 1995).

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 U.S. 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.

Gamma-oryzanol

γ-oryzanol is described as a drug used mainly for the treatment of hyperlipidaemia (Tamagawa et al., 1992a). In clinical studies, effects were noted following a typical dose of 300 mg/day p.o. for at least three months (Yoshino et al., 1989; Sasaki et al., 1990).

Bran, Starch and Powder

Oryza Sativa (Rice) Bran

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, apoprotein AI and B concentrations compared to wheat bran in 18 males with normal cholesterol concentrations. A significant decrease ($p < 0.05$) in plasma TG concentration was noted with 15 g/day Rice Bran compared to wheat bran.

ANIMAL TOXICOLOGY

Oral Toxicity

Oils, Fatty Acid, and Waxes

Acute

Oryza Sativa (Rice) Bran Oil

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

Oryza Sativa (Rice) Germ Oil
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 LD50 was > 5 g/kg of body weight and was not considered to be toxic (Celsis, 1999).

Oryza Sativa (Rice) Bran Wax and Hydrogenated Rice Bran Wax
Rice Bran 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).

Chronic

Oryza Sativa (Rice) Bran Oil
Following the food safety evaluation protocol of WHO/FDA/DGHS, a group of 30 albino rats (Wistar strain, 15 each sex) received feed 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 100-120 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 TG. The liver was analyzed for total lipids, TC and TG, 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 Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
Rice Bran Oil (0.5 ml) was applied to an abraded and intact hair-less 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 (Leberco Testing Inc., 1993b).

Undiluted Rice Bran Oil was applied as a single occlusive patch to nine rabbits. Reactions were scored at 2 and 24 h after placement of the occlusive patch. The PII for the group was 0.0; the maximum possible score was 8 (CTFA, 1983).

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).

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 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, a topical booster 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 pre-treated 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 (CTFA, 1984).

Oryza Sativa (Rice) Germ Oil
Following a modified-Draize method, a mixture of Rice Bran Oil and Rice Germ Oil (0.5 ml) was applied 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 (Ichimaru Pharcos Co., 1981b).

A skin contact allergy test was conducted using nine female Hartley guinea pigs. Six guinea pigs were sensitized. These six 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., 1979a).

Primary dermal irritation was assessed 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 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 primary irritation score for this test substance was 0.75 and was not classified as a primary dermal irritant (Celsis, 1999).

Oryza Sativa (Rice) Wax and Hydrogenated Rice Bran Wax
Using the above protocol, Rice Bran Wax (0.5 g) was applied to intact and abraded sites on six white rabbits. Sites were covered with a moistened patch and the trunk of the rabbits was encased with an occlusive wrapping. The Rice Wax had a PII of 0.21 (Leberco Testing Inc., 1991b).

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

Ocular Irritation

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
Rice Bran Oil (0.1 ml) was instilled into 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 ≥ four rabbits had a response in the cornea, iris or conjunctiva; the substance was not an irritant if ≤ one rabbit had a response, and inconclusive if 2-3 rabbits had a response.

Two rabbits had conjunctiva redness scores of 1 (defined as "some vessels definitely injected"; scale 0-3 with scores ≥ 2 considered positive) at the 24 h observation. The condition cleared in one rabbit by 48 h and cleared in the second rabbit by 72 h. The test material was not considered a primary irritant (Leberco Testing Inc., 1993d).

Undiluted Rice Bran Oil was instilled into 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 (CTFA, 1983).

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

Oryza Sativa (Rice) Germ Oil
A mixture of Rice Bran Oil and Rice Germ Oil (0.1 ml) was instilled into the right conjunctival sac of three female albino rabbits. The left eye served as control. Both eyes were rinsed five minutes 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 three rabbits throughout the observation period. One rabbit also had erythema/-edema scores of 1 at the 1 and 4 h observation; the reaction cleared thereafter. The material was not considered an ocular irritant (Ichimaru Pharcos Co., 1981c).

Six albino rabbits had 0.01 ml of Rice Germ Oil instilled into 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 (Celsis, 1999).

Oryza Sativa (Rice) Bran Wax and Hydrogenated Rice Bran Wax
Rice Bran 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 Bran Wax was not considered a primary irritant (Leberco Testing Inc., 1991c).

Hydrogenated Rice Bran Wax was also tested 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 four reading and returning to a score of 1 at the day seven reading. Hydrogenated Rice Bran Wax was not considered a primary ocular irritant (Leberco Testing Inc., 1993e).

Phototoxicity/ Photo Protection

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
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 non-photosensitizing (CIR, 1987); the CIR Tentative Report on tocopherols reported tocopherol acetate not phototoxic in a study of eleven human subjects (CIR, 1999).

Oryza Sativa (Rice) Germ Oil
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 hours, half of the test site was irradiated with the minimum erythemogenic dose (MED) provided by three UV 280-320 nm lamps and three UV 320-400 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 (Ichimaru Pharcos Co., 1979b).

A group of ten guinea pigs (male and female) were used in a study of phototoxicity. 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 310-400 nm. One group of ten animals were prepared as the tested group with doses of 0.1 ml of 100, 75, 50, and 25% of test substance, but not irradiated. Prior to

the irradiation exposures, the minimal erythemal dose of light (MED) and minimal erythemal dosage selection were measured. 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 ten 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 the five animals with very slight erythema and no edema at 24 h (Celsis, 1999).

Gamma-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 (270-320 nm and 320-400 nm). The UV irradiated side was divided into four exposure sections: 1 MED, 2 MED, 3 MED, and 4 MED. 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).

Extracts

Oryza Sativa (Rice) Bran Extract
Safflower Oil was reported as a component of Rice Bran Extract [97-98.8% solvent: water/propylene glycol, water/butylene glycol, water/glycerin, safflower oil (CTFA, 1999b)]. The CIR Final Report of Safflower Oil characterized Safflower Oil as neither a phototoxin nor a photosensitizer based on two clinical studies (CIR, 1985).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Oral

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
The three-generation oral-dose study detailed in the Oral Toxicity-Chronic section of this report, 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).

MUTAGENICITY

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
Rice Bran Oil was tested 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 4-10°C and used in the mutagenicity assay. Rice Bran Oil was not mutagenic (Polasa and Rukmini, 1987).

Gamma-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).

CARCINOGENICITY

Phytic Acid

Because of its application as a natural food additive, phytic acid produced from Rice Bran was studied in a two-year drinking water study. Phytic Acid contains 49.1% acid, 14.7% total phosphate, 0.86% inorganic phosphate, < 0.04% chlorides, < 0.072% sulfates, and 0.0003% arsenic compounds soluble in water. Groups of 120 F344 rats (60 each sex) were provided with water containing 1.25% or 2.5% phytic acid *ad libitum*. The pH of the solutions were 0.90 and 1.15, respectively; control rats received distilled water. A dose-dependent reduction in mean final body weights was observed in dosed rats. Necropsy was done at the end of the study. Necrosis and calcification of the renal papillae were noted in treated rats but not in controls. Specifically, necrosis (and calcification) were noted in one (three) of 57 males and ten (17) of 55 females of the high-dose group, and in one (none) of 59 males and six (six) of 58 females of the low-dose group. Papillomas of renal pelvic epithelium developed in three males and four females of the high-dose group and in three females of the low-dose group. The incidence of neoplasms in other organs were comparable to concurrent and historical controls (Hiasa et al., 1992).

Gamma-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 components in rice (rice bran hemicellulose, rice bran saccharide, and α-glucan fractionated from rice bran saccharide) and γ-oryzanol itself could modify/inhibit the actions of known carcinogens are cited in Table 10.

CO-CARCINOGENICITY & ANTI-CARCINOGENICITY

Extracts

Oryza Sativa (Rice) Extract

Furihata et al. (1996) reported decreased gastric mucosal damage and significantly reduced ($p < 0.01$) replicative DNA synthesis in male F344 rats that had received a concentrated commercial Rice Extract via gastric intubation 3 hours prior to administration of sodium chloride.

Bran, Starch and Powder

Oryza Sativa (Rice) Bran

F344 rats were fed 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 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 (Barnes et al., 1983).

Studies that investigated the anti-carcinogenicity properties of components of Rice Bran and Rice Bran Oil are cited in Table 10. Significant inhibition of carcinogenicity or cytotoxicity of carcinogens was noted with p.o. or i.p. administration of Rice Bran hemicellulose, saccharide, or α-glycan or Rice Extract (Takeshita et al., 1992; Takeo et al., 1988; Furihata et al., 1996). 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).

Table 10: Anti-Carcinogenicity Studies on Components of Rice

Carcinogen/Tumor Administration	Conditions for Rice Administration	Findings	Reference
Rice Bran (or rice bran-derived)			
groups of 25 male F344 rats were given weekly injections of DMH after rice	dosed for 27 weeks with 2 or 4% RBH (5 weeks after DMH)	significant ($p < 0.05$) reduction in colon tumors in 4% RBH group	Aoe et al., 1993
group of 32 male Wistar rats received ENNG dissolved in drinking water for 4 months, followed by 4 months of untreated water	rats received RBS (250 µg/ml) in drinking water for 4 months (started on month 8; total dose was ~ 667 mg/rat)	gastrointestinal tumors noted in 88% of rats from ENNG group and in 46% of rats from ENNG-RBS group ($p < 0.025$). RBS also prevented a reduction in immunocompetence, and prolonged survival in rats with cancer	Takeshita et al., 1992; Nakamura, 1992
groups of ten BALB/C mice were s.c. inoculated with Meth-A	mice received RON on days 1-10	inhibition, significance	Takeo et al., 1988
	p.o. 10 mg/kg	21.0%, ($p < 0.05$)	
	30 mg/kg	45.1%, ($p < 0.01$)	
	100 mg/kg	26.2%, ($p < 0.05$)	
	i.p. 30 mg/kg	50.0%, ($p < 0.01$)	
groups of ten BDF_1 mice were s.c. inoculated with 3LL	mice received RON on days 1-10	inhibition, significance	Takeo et al., 1988
	p.o. 10 mg/kg	29.4%, ($p < 0.05$)	
	30 mg/kg	43.8%, ($p < 0.01$)	
	100 mg/kg	27.5%, ($p < 0.05$)	
	i.p. 30 mg/kg	47.9%, ($p < 0.01$)	
ten BALB/C mice were s.c. inoculated with Meth-A	30 mg/kg RBS p.o. on days 1-10	48.1% inhibition ($p < 0.01$)	Takeo et al., 1988
ten BDF_1 mice were inoculated with 3LL	30 mg/kg RBS p.o. on days 1-10	46.8% inhibition ($p < 0.001$)	
Rice Bran Oil derived (γ-oryzanol)			
wide-spectrum organ carcinogenesis model: rats were initiated with i.p. injections of DHPN, i.g. injections of EHEN, and s.c. injections of DMAB	feed contained 1% γ-oryzanol for 32 weeks	enhancement of lung carcinogenesis noted upon microscopic examination	Hirose et al., 1991
male F344 rats initiated with DMAB	feed containing 2% γ-oryzanol for 40 weeks	no significant difference in prostate lesion incidence	Nakamura et al., 1991
Sprague-Dawley rats received i.g. dose of DMBA	feed contained 1% γ-oryzanol for 35 weeks	final incidence and multiplicities of mammary tumors comparable to controls, but significantly greater number of survivors in γ-oryzanol group	Hirose et al., 1994
TPA was applied to the outer and inner ears of ICR mice then 50 ug of DMBA was applied to the backs of the mice; TPA was then applied twice weekly for 20 weeks; skin tumors were measured every other week	the methanol extract of rice bran and γ-oryzanol were applied to the ear skin were 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

Abbreviations:

RBH: rice bran hemicellulose (extracted from rice bran fiber, consists mainly of arabinose and xylose)
TPA: 12-O-tetradecanoylphorbol-13-acetate
DMH: 1,2-dimethylhydrazine
3LL: Lewis Lung Carcinoma cells (1×10^5 cells/mouse)
RBS: rice bran saccharide (from Rice Bran)
DHPN: 2,2' dihydroxy-di-n-propylnitrosamine
DMAB: 3,2'-dimethyl-4-aminobiphenyl
DMBA: 7,12-dimethylbenz[a]anthracene
RON: α-glucan fractionated from rice bran saccharide

Meth-A: Meth-A Fibrosarcoma cells (6 x 10^4 cells/mouse)
ENNG: N-ethyl-N'-nitro-N-nitrosoguanidine EHEN: N-ethyl-N-hydroxynitrosamine

CLINICAL ASSESSMENT OF SAFETY

Allergic Reactions

Investigators have noted that rice commonly was regarded as hypoallergenic and was frequently recommended in diets for allergic patients. However, case reports have documented 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 (van den Hoogen-band and van Ketel, 1983). In another instance, 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 (di Lernia et al., 1992). An atopic housewife also developed similar symptoms after handling rice at a wedding as well as during handling of raw rice for cooking. (Lezaun, 1994). Positive responses to other cereal grains were also observed in these rice-positive women.

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 four 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.

Dermal Irritation

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
In a six-week use study, 30 subjects were instructed to use a moisturizer containing 8.0% Rice Bran Oil for three weeks. Another thirty subjects used a commercially available lotion. After the three week period, all subjects switched to use the "other" lotion for an additional three weeks. Dermatologic exams of the face were conducted at the start and end of the study and at the three-week cross-over. Subjects also answered questionnaires at the end of each three-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 (CTFA, 1987b).

A moisturizer and a body cream each containing 1.04% Rice Bran Oil were tested in the same cumulative irritation study. Ten of an original thirteen participants completed the study (two were dropped due to suspected presensitization; one 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. Both test materials were classified as mild irritants (Hill Top Research, 1989).

Twenty 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 nine days. One woman developed "significant" follicular irritation. The

investigators considered the incidence, "consistent with what has been observed in this assay" (CTFA, 1991).

Oryza Sativa (Rice) Bran Wax and Hydrogenated Rice Bran Wax
Rice Bran Wax and Hydrogenated Rice Bran Wax were patch tested using 27 subjects. Composition was similar to the wax depicted in Table 4. That is, ~ 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 1-72 h after patch removal. 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).

Dermal Sensitization

Oils, Fatty Acid, and Waxes

Oryza Sativa (Rice) Bran Oil
A moisturizer containing 8.0% Rice Bran Oil was tested in a repeat insult patch test (RIPT) using 84 females and 10 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 three-week non-treatment 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 (CTFA, 1987c).

Two formulations each containing 1.04% Rice Bran Oil were tested in RIPTs following the above described protocol. A bath oil was tested as a 10% aqueous dispersion using 87 females and 6 males. 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 (CTFA, 1985a). 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 h and 48 h challenge evaluations (CTFA, 1985b).

A lip balm containing 1.04% Rice Bran Oil was tested in a RIPT using 90 subjects. A total of ten 24 h induction exposures were applied to the same site on the back over a 22 day period. After a two-week non-treatment period subjects were challenged and reactions were scored 48 and 96 h after application. One panelist reacted throughout the induction period and at challenge and re-challenge of this individual with components of the lip balm was recommended. The lip balm was considered negative (Hill Top Research, 1988).

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

A children's shampoo and conditioner containing 0.3% w/w Rice Bran Oil were tested in a 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 semi-occlusive 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 ten applications. Sites were evaluated prior to application of each subsequent patch. Following a two-week

non-treatment 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 subjects 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).

Bran, Starch, and Powder

Oryza Sativa (Rice) Bran
A double-blind, randomized patch study was conducted to investigate whether colloidal grain suspensions induced allergic contact dermatitis in atopic children. Initially, a 15 minute 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 reponse 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 reponse 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 reponse 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).

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 2-5 months. Subjects were evaluated before starting therapy, 2 weeks and 1 month after therapy initiation, and monthly thereafter. In five patients serum IgE concentrations and eosinophil counts (from peripheral blood) were measured prior to and 2-3 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 two 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 four, good in seven, slightly effective in four, and ineffective in one. A non-significant decrease in IgE concentrations and a significant decrease ($p < 0.05$) in eosinophil counts were observed with therapy.

SUMMARY

Prior Safety Assessments

The CIR Expert Panel considered the information from safety assessments done previously on Wheat derived ingredients, Cottonseed derived ingredients, Safflower Oil, Aluminum Starch Octenylsuccinate (because of the starch component), and Tocopherol. These safety assessments are summarized in Table 11.

Rice Ingredients

Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Oryza Sativa (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 Protein, and Hydrolyzed Rice Protein are derived from rice *Oryza sativa*.

Animal and clinical studies have reported that consumption of Rice Bran Oil or Rice Bran had protective effects on blood parameters. Sunscreen patents have described using Rice Bran Oil and Rice Wax. A Rice Bran Oil and Rice Germ Oil mixture had a UV absorption maximum at 315 nm.

Oils, Fatty Acid, and Waxes

Rice Bran Oil functions in cosmetics as a conditioning agent and solvent and was used in 33 formulations in 1998. Rice Germ Oil functions as a skin-conditioning agent and was reported in body and hand creams, lotions, powders, and sprays. Rice Bran Acid functions as a surfactant -cleansing agent and was not reported in use. The two Bran Waxes function as binders, conditioning agents, and viscosity increasing agents and were used in 16 formulations.

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.

Table 11. Summary Information from Previous Safety Assessments

Ingredients	Pertinent Information	Conclusion	Reference
Wheat Germ Glycerides, Wheat Gluten	5 photosenitization tests: 139 human subjects: 2% Wheat Germ Glycerides: negative photosenitization test: 24 human subjects 2% Wheat Germ Glycerides: negative	Safe	CIR (1979)
Cotton (Gossypium) Seed Oil, Cottonseed Acid, Cottonseed Glyceride, Hydrogenated Cotton Seed Oil, Hydrogenated Cotton Seed Glyceride	PCB/pesticide not more than 3 ppm with not more than 1 ppm for any specific residue arsenic ≤ 3ppm (as Arsenic) gossypol <450 ppm lead ≤ 0.1 mg/kg mercury ≤ 1 ppm (as Hg)	Safe	CIR (1998)
Tocopherol, Tocopheryl Acetate, Tocopheryl Linoleate, Tocopheryl Linoleate/Oleate, Tocopheryl Nicotinate, Tocopheryl Succinate, Dioleyl Tocopheryl Methylsilanol, Potassium Ascorbyl Tocopheryl Phosphate, and Tocophersolan	effects consistent with antioxidant properties	Safe	CIR (1999)
Safflower Oil	2 phototoxicity tests: 25 human subjects/test: 5% Safflower Oil: negative 2 photosensitization tests: 10 human subjects/test: 5% Safflower Oil: negative	Safe	CIR (1985)
Aluminum Starch Octenylsuccinate	the addition of 5% Aluminum Starch Octenylsuccinate can enhance the SPF of titanium dioxide by 40% does not absorb light in the 200-400 nm range not an ocular irritant 25% Aluminum Octenyl Succinate clinical RIPTS: negative	Safe	CIR (1999a)

Ingredients	Pertinent Information	Conclusion	Reference
	3% Aluminum Octenyl Succinate clinical sting, chamber scarification, and closed patch tests: little irritation potential		

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 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

Rice Bran Extract functions as a biological additive and was used in six formulations. Rice Extract functions as a biological additive and was not reported in use.

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

Bran, Starch and Powder

Rice Bran functions as an abrasive and bulking agent and was used in one formulation, Rice Starch functions as a skin conditioning agent -occlusive and was used in 41 formulations; Rice Germ Powder functions as an abrasive and was reported in one use for exfoliating purposes.

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 co-carcinogenicity studies done on Rice Bran Oil and Rice Bran-derived hemicellulose and saccharide, significant 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 Bran Protein and Hydrolyzed Rice Protein function as conditioning agents (hair or skin). No uses were reported.

Isolated cases of allergy to raw rice have been reported.

DISCUSSION

Based upon the available information, the CIR Expert Panel concluded that Oryza Sativa (Rice) Germ Powder and Oryza Sativa (Rice) Starch are safe as used in cosmetic formulations. The Starch was considered to be like other plant starches previously considered by the CIR Expert Panel and found to be safe as used. Rice Germ Powder, based on its use as an abrasive in products intended to be rinsed off,

was considered to present no significant safety issues.

The Expert Panel, however, did not find sufficient information on the other rice derived ingredients. Section 1, paragraph (p) of the CIR Procedures states that "A lack of information about an ingredient shall not be sufficient to justify a determination of safety."

In accordance with Section 30(j)(2)(A) of the Procedures, the Expert Panel informed the public of its decision that the data on Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Oryza Sativa (Rice) Bran Acid, Oryza Sativa (Rice) Bran Wax, Hydrogenated Rice Bran Wax, Oryza Sativa (Rice) Bran Extract, Oryza Sativa (Rice) Extract, Oryza Sativa (Rice) Bran, Hydrolyzed Rice Bran Protein, and Hydrolyzed Rice Protein were not sufficient for determination whether the ingredients, under relevant conditions of use, were either safe or unsafe. The Panel released a Notice of Insufficient Data on September 9-10, 1998 outlining the data needed to assess the safety of the rice ingredients. Comments were received during the 90-day public comment period. But additional concerns remain. Data needed to make a safety assessment are:

For Oryza Sativa (Rice) Bran Oil, Oryza Sativa (Rice) Germ Oil, Oryza Sativa (Rice) Bran Acid, Oryza Sativa (Rice) Bran Wax, and Hydrogenated Rice Bran Wax:

1. dermal photosensitization study

For Oryza Sativa (Rice) Bran Extract and Oryza Sativa (Rice):

1. contaminants*/methods of extraction
2. UV absorption; if there is significant absorption, then a dermal phototoxicity/photosensitization study will be needed
3. two genotoxicity assays one in a mammalian system; if positive, then a 2 year dermal carcinogenicity study using NTP methods may be needed
4. dermal irritation and sensitization at concentration of use
5. 28-day dermal toxicity data
6. reproductive/developmental toxicity
7. ocular irritation, if available

* pending results, additional studies may be needed

For Oryza Sativa (Rice) Bran:

1. concentration of use
2. contaminants*/methods of extraction
3. UV absorption; if there is significant absorption, then a dermal phototoxicity/photosensitization study will be needed
4. two genotoxicity assays one in a mammalian system; if positive, then a 2 year dermal carcinogenicity study using NTP methods may be needed
5. dermal irritation and sensitization at concentration of use
6. 28-day dermal toxicity data
7. ocular irritation, if available

* pending results, additional studies may be needed

For Hydrolyzed Rice Bran Protein, and Hydrolyzed Rice Protein the data needed are:

1. method of extraction
2. UV absorption, if there is significant absorption, then a dermal phototoxicity/photosensitization study will be needed
3. two genotoxicity assays, one in a mammalian system; if positive, then a 2-year dermal carcinogenicity study using NTP methods may be needed
4. dermal irritation and sensitization at concentration of use
5. 28-day dermal toxicity data
6. ocular irritation, if available

***Note:* These rice derived ingredients as used in products should not contain significant levels of**

pesticide residues or heavy metals.

CONCLUSION

The CIR Panel concludes that the available data are sufficient to support the safety of Rice (Oryza Sativa) Germ Powder and Rice (Oryza Sativa) Starch in cosmetic formulations, but that the available data are insufficient to support the safety of Rice (Oryza Sativa) Bran Oil, Rice (Oryza Sativa) Germ Oil, Rice (Oryza Sativa) Bran Acid, Rice (Oryza Sativa) Bran Wax, Hydrogenated Rice Bran Wax, Rice (Oryza Sativa) Bran Extract, Rice (Oryza Sativa) Extract, Rice (Oryza Sativa) Bran, Hydrolyzed Rice Bran Protein, and Hydrolyzed Rice Protein for use in cosmetic products.*

*Note: At the December, 2000 meeting of the CIR Expert Panel, a tentative amended conclusion was reached for the rice oils, fatty acid, and waxes. Were this conclusion made final in 2001, these ingredients would be safe as used.

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