Safety Assessment of Animal- and Plant-Derived Amino Acids as Used in Cosmetics

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ABSTRACT

The Cosmetic Ingredient Review Expert Panel reviewed the safety of animal- and plant-derived amino acids, which function as skin and hair conditioning agents. The safety of α-amino acids as direct food additives has been well established based on extensive research through acute and chronic dietary exposures. The Panel focused its review on dermal irritation and sensitization data relevant to the use of these ingredients in topical cosmetics and relied on its past findings on the safety of α-amino acids. The Panel concluded that these 21 ingredients are safe in the present practices of use and concentration as used in cosmetics.

INTRODUCTION

This safety assessment covers 21 ingredients, which are each mixtures of amino acids derived from specific animal and plant sources. These ingredients function as skin and hair conditioning agents in personal care products. The full list of ingredients in this report is found in Table 1.

A concurrent review of the safety of hydrolyzed proteins from animal and plant sources is being performed by the Cosmetic Ingredient Review (CIR) Expert Panel. The Expert Panel previously has reviewed the safety of α-amino acids and concluded that these ingredients are safe for use in cosmetic ingredients.[1]

CHEMISTRY

The ingredients in this group are related because they each are prepared from proteins by complete hydrolysis to yield amino acid mixtures. The most frequently used method for hydrolyzing proteins to amino acids appears to be heating to at least 110°C with concentrated hydrochloric acid.[2,3] However, some amino acids, including tryptophan, are readily destroyed or are only partially hydrolyzed by hydrochloric acid. For these amino acids, alternate hydrolysis agents, like sulfonic acids, are used in place of hydrochloric acid, or alkaline hydrolysis is performed.[3-5] While these amino acids are produced from proteins, the hydrolysis process commonly racemizes the amino acids and the end product is not primarily in the L- form of the stereoisomers, but is a mixture of L- and D-forms.

The composition of amino acids may be analyzed by chromatographic separation, such as separation with liquid-liquid chromatography ion-exchange columns, and detection, such as detection via mass spectrometry, of the residues after adequate hydrolysis of the substrate.[2,3]

Method of Manufacturing

As noted above, most methods utilized acid hydrolysis at elevated temperatures to hydrolyze proteins to their constituent amino acids. However, one supplier has reported that lycium barbarum (wolfberry) amino acids are derived from the lycium barbarum fruit.[6] The fruit is autolyzed in water to free the cytoplasmic proteins. The proteins are then hydrolyzed with proprietary protease enzymes. The hydrolysis breaks down the fruit proteins into basic amino acid constituents that are water soluble. The product is then purified by filtration and spray-dried to obtain a powdered mixture.

Another supplier reported that amino acids from keratin, lupine, oat, rice, silk, and wheat proteins are manufactured by enzymatic hydrolysis for a specific duration of time and at an elevated temperature (details not provided).[7]

Impurities

Several of the ingredients of this safety assessment, including collagen amino acids and elastin amino acids, may be bovine sourced. These ingredients are highly processed and, as such, FDA does not consider them risk materials for transmission of infectious agents (21 CFR §700.27).

No data were found in the published literature on the impurities of animal- and plant-derived amino acids. A supplier has provided the composition data on amino acids from lycium barbarum and wheat proteins (see Table 2).[6,7] No composition data were discovered for the remaining animal- and plant-derived amino acid ingredients.

USE

Cosmetic

The animal- and plant-derived amino acids in this safety assessment function primarily as hair conditioning and skin conditioning agents in cosmetic formulations.[8] These functions are similar to those of the α-amino acid ingredients.[1]

Table 3a presents the current product formulation data for animal- and plant-derived amino acids. According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP), silk amino acids have the most reported uses in cosmetic and personal care

products, with a total of 328; approximately half of those uses are in non-coloring hair products.[9] Wheat amino acids have the second greatest number of overall uses reported, with a total of 251; again, approximately half of those uses are in non-coloring hair products. The reported product categories of the animal- and plant-derived amino acid ingredients are comparable to those of the α-amino acid ingredients.[1]

In a recent survey of use concentrations by the Personal Care Products Council, silk amino acids had a maximum use concentration range of 8.0 x 10^{-5}% to 0.2%, with the 0.2% reported in shampoos and other personal cleanliness products.[10] Wheat amino acids had a maximum use concentration range of 1.0 x 10^{-4}% to 0.3%, with the 0.3% reported in hair dyes. The use concentrations of the animal- and plant-derived amino acid ingredients are similar, if not lower in some cases, to those of the α-amino acid ingredients.[1]

Those ingredients with no reported uses or use concentrations are listed in Table 3b.

Several of the amino acids sourced from animals and plants described in this report are used in cosmetic sprays, including aerosol and pump hair and body spray products, and could possibly be inhaled. The maximum concentration of amino acids from animal and plant sources reported to be used in a spray product is 0.02% keratin amino acids in an aerosol hair spray. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 µm, with propellant sprays yielding a greater fraction of droplets/particles <10 µm compared with pump sprays.[11,12] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., able to enter the lungs) to any appreciable amount.[13,14]

The European Commission's Scientific Committee on Consumer Products (SCCP) concluded that the risk of exposure to viruses, such as avian influenza virus or papillomavirus, is negligible through topical application of cosmetic products containing amino acids from the hydrolysis of human hair or chicken feathers.[15]

TOXICOLOGICAL STUDIES

Many of the proteins that serve as the sources of the amino acids that are described in this safety assessment are found in the foods consumed daily. Toxicities from dermal exposure would not be expected to be different from oral exposures and, as such, not concerning to the CIR Expert Panel. Irritation and sensitization are of concern, and the focus in this report. Data from the previous safety assessment on α-amino acids support that these ingredients would not likely be irritants or sensitizers.[1]

IRRITATION AND SENSITIZATION

[From the CIR Safety Assessment of α-amino acids][1]: Cysteine HCl and methionine were used as negative controls in in vitro assays to predict potential skin irritants. In separate efficacy studies, arginine, cysteine, and glycine did not produce any adverse effects in rats, guinea pigs, or mouse skin models. Glutamic acid was used as a negative control in an in vitro study to identify skin sensitizers. Products containing amino acid ingredients at concentrations up to 2.784% were not dermal irritants or sensitizers in HRIPT studies. In several validation studies for in vitro phototoxicity assays, histidine was used as a negative control. Neither magnesium aspartate up to 0.5% nor 1% tyrosine was phototoxic in assays using yeast.

Irritation

Dermal

Non-human in vitro irritation studies are presented in Table 4. In these studies, amino acids derived from keratin, lupine, oat, rice, silk and wheat sources were not dermal irritants.

Ocular

Non-human in vitro ocular irritation studies are presented in Table 5. In these studies, amino acids derived from keratin, lupine, oat, rice, silk and wheat sources were not ocular irritants.

Sensitization

No sensitization studies were available for animal- and plant-derived amino acids.

Phototoxicity

No phototoxicity studies were available for animal- and plant-derived amino acids.

SUMMARY

Amino acids derived from animal and plant sources function primarily as skin and hair conditioning agents in personal care products.

While the expectation is that most animal- and plant-derived amino acids will be produced by acid hydrolysis of proteins from the relevant source, enzymatic cleavage has been reported to be used.

Of the animal- and plant-derived amino acids, amino acids from silk have the most reported uses in cosmetic and personal care products, with a total of 328; the maximum use concentration range was reported to be 8.0×10^{-5}% to 0.2%. The reported functions, product categories, and use concentrations of the animal- and plant-derived amino acid ingredients were comparable to those of the α-amino acid ingredients.

Many of the proteins that serve as the sources of the amino acids that are described in this safety assessment are found in the foods consumed daily. Toxicities from dermal exposure would not be expected to be different from oral exposures and, as such, are not concerning to the CIR Expert Panel. Irritation and sensitization are of concern, and the focus in this report. Data from the previous safety assessment on α-amino acids support that these ingredients would not likely be irritants or sensitizers. Additionally, non-human in vitro dermal and ocular irritation studies determined that amino acids derived from keratin, lupine, oat, rice, silk and wheat sources were not irritants.

DISCUSSION

The Panel acknowledged that the safety of α-amino acids as direct food additives has been well supported based on extensive research through acute and chronic dietary exposures. The Panel determined that this body of research, coupled with the available irritation and sensitization data and use concentrations much lower than those consumed daily in the diet, provide a sufficient basis for determining the safety of amino acids in cosmetic products.

The Panel recognized that there are issues, i.e. MSG symptom complex and phenylketonuria, with sodium glutamate and phenylalanine, respectively, in the diet for certain individuals. However, the Panel concluded that the concentrations of these amino acids in cosmetic products are low, and would not be conducive to significant absorption through dermal application or incidental ingestion, and thus, would not cause systemic reactions in individuals.

While the *International Cosmetic Dictionary and Handbook* does not distinguish among the α-amino acids used in cosmetics that are L-stereoisomers from those that are D-stereoisomers (or are mixtures of L- and D-stereoisomers), the Panel noted that the L-amino acids are Generally Recognized As Safe (GRAS) direct food additives by the FDA (except Methionine which is GRAS as a racemic mixture, and Glycine which is GRAS and has no stereocenter). Amino acids with a mixture of the 2 stereoisomers (DL-) have approved uses as food additives according to the USP Food Chemicals Codex. This safety assessment report addresses D- and L- stereoisomers of the amino acids derived from animal and plant sources. The Panel does not anticipate that there are significant toxicological differences in cosmetic applications among the stereoisomers.

The Panel discussed the issue of incidental inhalation exposure from hair sprays, body and hand sprays, aftershave lotion sprays, and suntan sprays. No inhalation data were available. These ingredients reportedly are used at concentrations up to 0.02% in cosmetic products that may be aerosolized. The Panel noted that 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic toxic effects. The Panel considered other data available to characterize the potential for animal- and plant-derived amino acids to cause systemic toxicity, irritation, sensitization, or other effects. They noted that numerous studies and reviews have been published in the literature regarding the safety of dietary exposure to amino acids, including studies on oral acute and chronic toxicity, carcinogenicity, and genotoxicity, which found no safety concerns for these substances in the amounts at which they are consumed in flavoring agents. Additionally, little or no irritation was observed in multiple tests of dermal and ocular exposure. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at http://www.cir-safety.org/cir-findings.

The Panel expressed concern about the dangers inherent in using animal-derived ingredients, namely the transmission of infectious agents. They stressed that these ingredients must be free of detectible pathogenic viruses or infectious agents (e.g. Bovine Spongiform Encephalopathy (BSE)). These ingredients should be produced according to good manufacturing procedures and should conform to regulations for producing substances from animal-derived materials.

The Panel also expressed concern regarding pesticide residues and heavy metals that may be present in botanical ingredients. Because the plant proteins from which plant-derived amino acids are produced are extensively processed, it is unlikely that these impurities would remain.

The Panel noted the uncertainty regarding method of manufacturing. The Panel considered that vigorous acid hydrolysis would yield amino acids with little or no residual peptides, because such acid hydrolysis attacks all

of the peptide bonds in a protein in a non-preferential manner. The Panel was concerned that enzymatic hydrolysis may fail to completely hydrolyze the source proteins and, thus, may produce di-, tri- or other peptides, as well as amino acids. Such residual peptide impurities may have the potential to cause allergic reactions in sensitive individuals. Further input on the usual methods used to produce amino acids from animal and plant proteins would be useful. If the methodology involves rigorous acid hydrolysis, there is less concern that residual small peptides will be present. In the absence of further clarification, the Panel stated that industry should manufacture animal-and plant-derived amino acids in a way that ensures that no residual peptides remain.

CONCLUSION

The CIR Expert Panel concluded that the animal- and plant-derived amino acids listed are safe in the present practices of use and concentration in cosmetics. The 21 ingredients included in this safety assessment are:

apricot kernel amino acids*
collagen amino acids
corn gluten amino acids*
elastin amino acids*
garcinia mangostana amino acids*
hair keratin amino acids
jojoba amino acids*
keratin amino acids
lupine amino acids
lycium barbarum amino acids*
milk amino acids
oat amino acids
rice amino acids
sesame amino acids*
silk amino acids
soy amino acids
spirulina amino acids*
sweet almond amino acids*
vegetable amino acids
wheat amino acids
yeast amino acids*

*Not reported to be in current use. Were ingredients in this group not reported to be in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

TABLES AND FIGURES

Table 1. Definitions and functions of the ingredients in this safety assessment.[8]

Ingredient CAS No.	Definition	Function
Apricot Kernel Amino Acids 65072-01-7 [generic to any amino acids mixture]	Apricot Kernel Amino Acids is a mixture of amino acids derived from the complete hydrolysis of apricot kernels.	Skin-Conditioning Agent-Misc.
Collagen Amino Acids	Collagen Amino Acids is the mixture of amino acids resulting from the complete hydrolysis of collagen. It is characterized by containing a significant level of hydroxyproline.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Corn Gluten Amino Acids 65072-01-7	Corn Gluten Amino Acids is the mixture of amino acids resulting from the complete hydrolysis of corn gluten protein.	Skin-Conditioning Agent-Misc.
Elastin Amino Acids 65072-01-7	Elastin Amino Acids is the mixture of amino acids resulting from the complete hydrolysis of elastin.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Garcinia Mangostana Amino Acids	Garcinia Mangostana Amino Acids are the amino acids obtained by the complete hydrolysis of the protein from the pericarp of Garcinia mangostana.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Hair Keratin Amino Acids 65072-01-7	Hair Keratin Amino Acids are the amino acids obtained by the hydrolysis of human hair.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Jojoba Amino Acids 333338-07-1 65072-01-7	Jojoba Amino Acids is the mixture of amino acids obtained by the complete hydrolysis of jojoba seed protein.	Humectants; Hair Conditioning Agent; Skin-Conditioning Agent-Emollient
Keratin Amino Acids 65072-01-7	Keratin Amino Acids is the mixture of amino acids resulting from the complete hydrolysis of Keratin.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Lupine Amino Acids	Lupine Amino Acids is a mixture of amino acids derived from the complete hydrolysis of lupine protein.	Hair Conditioning Agent; Skin-Conditioning Agent-Humectant
Lycium Barbarum Amino Acids	Lycium Barbarum Amino Acids is a mixture of amino acids derived by the complete hydrolysis of the protein isolated from the whole plant, Lycium barbarum.	Skin-Conditioning Agent-Misc.
Milk Amino Acids 65072-00-6 65072-01-7	Milk Amino Acids is the mixture of amino acids resulting from the complete hydrolysis of Milk Protein.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Oat Amino Acids 65072-01-7	Oat Amino Acids is a mixture of amino acids derived by the complete hydrolysis of oat protein.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Rice Amino Acids 65072-01-7	Rice Amino Acids is the mixture of amino acids derived from the complete hydrolysis of rice protein.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Sesame Amino Acids 65072-01-7	Sesame Amino Acids are the amino acids obtained from the complete hydrolysis of sesame flour.	Skin-Conditioning Agent-Humectant
Silk Amino Acids 65072-01-7	Silk Amino Acids is the mixture of amino acids resulting from the complete hydrolysis of silk.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Soy Amino Acids	Soy Amino Acids is a mixture of amino acids derived from the complete hydrolysis of soy protein.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Spirulina Amino Acids	Spirulina Amino Acids is the mixture of amino acids derived from the complete hydrolysis of the protein obtained from the aquatic plant, Spirulina platensis.	Hair Conditioning Agent; Skin-Conditioning Agent-Humectant
Sweet Almond Amino Acids	Sweet Almond Amino Acids is a mixture of amino acids derived from the complete hydrolysis of Prunus Amygdalus Dulcis (Sweet Almond) Protein.	Skin Protectants; Skin-Conditioning Agent-Humectant
Vegetable Amino Acids 65072-01-7	Vegetable Amino Acids are the amino acids obtained by the complete hydrolysis of Hydrolyzed Vegetable Protein	Skin-Conditioning Agent-Humectant
Wheat Amino Acids 65072-01-7	Wheat Amino Acids is a mixture of amino acids resulting from the complete hydrolysis of wheat protein.	Hair Conditioning Agent; Skin-Conditioning Agent-Misc.
Yeast Amino Acids 65072-01-7	Yeast Amino Acids are the amino acids derived from Yeast.	Skin-Conditioning Agent-Humectant

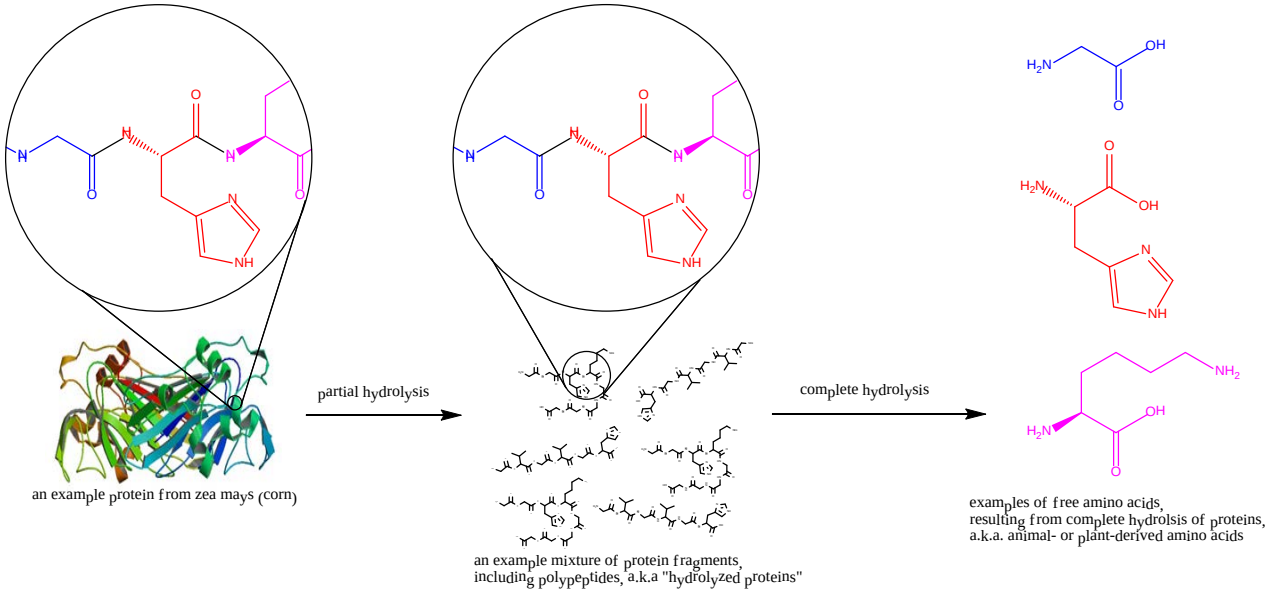

Figure 1. Production of animal- and plant-derived amino acids. [16]

Table 2. Composition of amino acids as reported by suppliers (%).[6,7]

	Lycium barbarum amino acids	Wheat amino acids
Alanine	5	2.7
Arginine	10	3.2
Aspartic acid	17	3.1
Cystine	1	1.8
Glutamic acid	13	36.8
Glycine	4	3.5
Histidine	2	2.2
Isoleucine	3	3.4
Leucine	5	7.3
Lysine	3	1.7
Methionine	1	1.5
Phenylalanine	3	5.4
Proline	12	12.0
Serine	5	5.7
Threonine	4	2.9
Tryptophan	1	NR
Tyrosine	2	2.9
Valine	4	4.1
Ammonia	4	NR

NR = not reported

Table 3a. Frequency and concentration of use for animal- and plant-derived amino acids according to duration and type of exposure.[9,10]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Collagen Amino Acids		**Hair Keratin Amino Acids**		**Keratin Amino Acids**	
Totals*	**38**[a]	0.0003-6	**35**	3	**166**[b]	0.00001-0.5
Duration of Use						
Leave-On	28	0.0003-6	14	3	75	0.00001-0.5
Rinse-Off	10	NR	21	NR	91	0.0005-0.5
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR
Exposure Type						
Eye Area	1	NR	1	NR	2	0.1-0.5
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	4	0.02[c]
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	0.03
Dermal Contact	22	0.0003	2	NR	9	0.0001-0.03
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	10	6	32	3	125	0.00001-0.5
Hair-Coloring	NR	NR	1	NR	21	0.001
Nail	6	0.001	NR	NR	9	0.0005-0.005
Mucous Membrane	1	NR	1	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

	Lupine Amino Acids		**Milk Amino Acids**		**Oat Amino Acids**	
Totals*	**6**	0.0003-0.1	**15**	NR	**7**	0.0002
Duration of Use						
Leave-On	*2*	0.0003-0.1	*1*	NR	*4*	0.0002
Rinse Off	*4*	0.001-0.1	*14*	NR	*3*	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR
Exposure Type						
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	0.0003[d]	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	14	NR	1	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	6	0.0003-0.1	1	NR	6	0.0002
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	13	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

	Rice Amino Acids		**Silk Amino Acids**		**Soy Amino Acids**	
Totals*	**1**	0.2	**328**	0.00008-0.2	**22**	0.02-0.2
Duration of Use						
Leave-On	*1*	0.2	*159*	0.00008-0.1	*13*	0.02-0.2
Rinse-Off	NR	NR	*169*	0.001-0.2	*9*	NR
Diluted for (Bath) Use	NR	NR	NR	0.03	NR	NR
Exposure Type						
Eye Area	1	0.2	6	0.002	1	0.2
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	17	0.0001-0.005[e]	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	54	0.002-0.2	5	0.02-0.2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	266	0.00008-0.2	16	NR
Hair-Coloring	NR	NR	2	NR	NR	NR
Nail	NR	NR	3	NR	1	0.02
Mucous Membrane	NR	NR	18	0.03-0.2	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

Table 3a. Frequency and concentration of use for animal- and plant-derived amino acids according to duration and type of exposure.[9,10]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Vegetable Amino Acids		**Wheat Amino Acids**			
Totals	**1**	NR	**251**	0.0001-0.3		
Duration of Use						
Leave-On	NR	NR	*90*	0.0001-0.2		
Rinse Off	*1*	NR	*161*	0.003-0.3		
Diluted for (Bath) Use	NR	NR	*NR*	NR		
Exposure Type						
Eye Area	NR	NR	1	NR		
Incidental Ingestion	NR	NR	NR	NR		
Incidental Inhalation-Spray	NR	NR	6	0.0001-0.01[f]		
Incidental Inhalation-Aerosol	NR	NR	NR	NR		
Dermal Contact	NR	NR	11	0.003-0.05		
Deodorant (underarm)	NR	NR	NR	NR		
Hair - Non-Coloring	1	NR	191	0.0001-0.2		
Hair-Coloring	NR	NR	47	0.02-0.3		
Nail	NR	NR	1	0.02		
Mucous Membrane	NR	NR	5	0.003-0.05		
Baby Products	NR	NR	1	NR		

* Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types my not equal the sum of total uses.

NR – no reported uses

[a]In VCRP, one use reported for ingredient "animal collagen amino acids" in a body and hand product.

[b]In VCRP, one use reported for ingredient "animal keratin amino acids" in a hair conditioner.

[c] In an aerosol hair spray.

[d] In a pump hair spray.

[e] 0.001%-0.003% in an aerosol hair spray; 0.0001%-0.0008% in a pump hair spray; 0.0008%-0.002% in a spray tonic, dressing, other hair grooming aid; 0.003% in a body and hand spray; and 0.005% in an "other" suntan preparation spray.

[f] 0.0001% in an aerosol hair spray, 0.009%-0.01% in a pump hair spray

Table 3b. Ingredients not reported to be in use.[9,10]

Apricot Kernel Amino Acids
Corn Gluten Amino Acids
Elastin Amino Acids
Garcinia Mangostana Amino Acids
Jojoba Amino Acids
Lycium Barbarum Amino Acids
Sesame Amino Acids
Spirulina Amino Acids
Sweet Almond Amino Acids
Yeast Amino Acids

Table 4. Dermal irritation studies.

Ingredient	Concentration	Method	Results	Reference
Non-Human – In Vitro				
Keratin Amino Acids	Not reported	MatTek EpiDerm assay	Non-irritating	[7]
Lupine Amino Acids	Not reported	MatTek EpiDerm assay	Non-irritating	[7]
Oat Amino Acids	Not reported	MatTek EpiDerm assay	Non-irritating	[7]
Rice Amino Acids	Not reported	MatTek EpiDerm assay	Non-irritating	[7]
Silk Amino Acids	Not reported	MatTek EpiDerm assay	Non-irritating	[7]
Wheat Amino Acids	Not reported	MatTek EpiDerm assay	Non-irritating	[7]

Table 5. Ocular irritation studies.

Ingredient	Concentration	Method	Results	Reference
Non-Human – In Vitro				
Keratin Amino Acids	Not reported	MatTek EpiOcular assay	Non-irritating	[7]
Lupine Amino Acids	Not reported	MatTek EpiOcular assay	Non-irritating	[7]
Oat Amino Acids	Not reported	MatTek EpiOcular assay	Non-irritating	[7]
Rice Amino Acids	Not reported	MatTek EpiOcular assay	Non-irritating	[7]
Silk Amino Acids	Not reported	MatTek EpiOcular assay	Non-irritating	[7]
Wheat Amino Acids	Not reported	MatTek EpiOcular assay	Non-irritating	[7]

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