7340000G – KERACYN™

Version: 24 - 24/APR/2026

1. PRODUCT IDENTIFICATION

Trade Name:	KERACYN™
Manufacturer:	PROVITAL, S.A. P.I. CAN SALVATELLA 08210 BARBERÀ DEL VALLÈS BARCELONA (SPAIN) e-mail: info@weareprovital.com Tf: + 34 -937192350
Kind of Raw Material:	Active Ingredient
Function of the Ingredient (PCPC Inventory):	Skin-Conditioning Agent - Miscellaneous
Function of the Ingredient (UE Inventory):	Skin Conditioning

2. PRODUCT COMPOSITION

Components Breakdown (INCI). Including actives, solvents, preservatives, antioxidants and other additives:

[EU]		CAS	EC
Propanediol	20 - 30 %	504-63-2	207-997-3
Aqua	35 - 45 %	7732-18-5	231-791-2
Glycerin	30 - 40 %	56-81-5	200-289-5
Cynara Scolymus Leaf Extract	2 - 5 %	84012-14-6	281-659-3
Preservatives			
Sodium Benzoate	0,25 - 0,35 %	532-32-1	208-534-8
Additives			
Gluconolactone	1 - 1,2 %	90-80-2	202-016-5
Calcium Gluconate	0,015 - 0,02 %	299-28-5	206-075-8

PCPC [CTFA]		CAS	EC
Propanediol	20 - 30 %	504-63-2	207-997-3
Water	35 - 45 %	7732-18-5	231-791-2
Glycerin	30 - 40 %	56-81-5	200-289-5
Cynara Scolymus (Artichoke) Leaf Extract	2 - 5 %	84012-14-6	281-659-3
Preservatives			
Sodium Benzoate	0,25 - 0,35 %	532-32-1	208-534-8
Additives			
Gluconolactone	1 - 1,2 %	90-80-2	202-016-5
Calcium Gluconate	0,015 - 0,02 %	299-28-5	206-075-8

3. TOXICOLOGICAL INFORMATION

Data obtained in our own toxicological tests and/or bibliographical research

Animal testing:

This product has not been the subject of animal testing or retesting for cosmetic purposes by or on behalf of this company.

General information:

The following herbs have been approved by the German Commission E Monographs: Artichoke leaf (Published July 6, 1988; Revised September 1, 1990)

The following substances are used as Food Additives permitted for human consume by FDA: Artichoke leaves, Cynara scolymus (21CFR172.510)

The following substances have the GRAS status ('Generally Recognized As Safe'): Glycerin (21CFR182.1320)

The CIR Expert Panel concluded that glycerin is safe in the practices of use and concentration described in the Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014, which include the toxicological data.

The Cosmetic Ingredient Review (CIR) Expert Panel concluded that the ingredient Propanediol is safe in the cosmetic practices of use and concentrations as described in the safety assessment. (CIR Final Report, June 13, 2018).

The Cosmetic Ingredient Review (CIR) Expert Panel concluded that the ingredient Sodium Benzoate is safe in the present practices of use and concentration described in this safety assessment. (09/14/2021)

Direct food substances affirmed as generally recognized as safe: Gluconolactone (21CFR184.1318), Calcium gluconate (21CFR184.1199)

Gluconolactone is a permitted food additive in Europe (E575) and in the USA it is considered a safe substance (GRAS) which can be used directly in the food (21CFR184.1318).

Cytotoxicity:

KERACYN (Cod. 73400): Neutral Red Release Assay performed using SIRC cell line. Results: CI50>50%, % of mortality at dilution 50% = 22%. Unimportant cytotoxicity.

Artichoke leaf aqueous dry extract (4.5:1): in primary cultures of rat hepatocytes no cytotoxic effects were observed at concentrations of up to 1 mg/ml (ESCOP 2003, pp122)

Propanediol (RTECS no. TY2010000): IC50 in human-skin cells >2000 µmol/L/48h.

Skin Irritation:

KERACYN (Code 73400): Patch Test on 12 volunteers, occlusive patch for 48 hours. No irritant reactions were registered at 15 minutes and 24 hours after patch removal. Under these conditions, the product KERACYN has a very good skin compatibility.

Undiluted Propanediol was mildly irritating to rabbit skin in a 24-hour occlusive patch tests; Moreover,undiluted Propanediol in volunteers was non-irritating after a single application of test substance. (CIR Final Report, June 13, 2018).

Glycerin (RTECS no. MA8050000): Draize Test in the skin of rabbit, 500 mg, 24h, mild.

In a study, glycerin (50% in water) was not irritating to subjects with dermatitis (n = 420) when administered for 20 - 24h under occlusion. (IJT 38(Suppl. 3):6-22, 2019)

Skin Sensitization:

KERACYN (Code 73400) Marzulli and Maibach Method: Human Repeated Insult Patch Test. Study in 54 volunteers, product tested at 25%. No irritation, nor sensitisation reaction was registered. Under the test conditions, the product KERACYN has a very good skin compatibility and can be regarded as an hypoallergenic product in this specific context.

Cynara scolymus possesses a medium potential for sensitization through skin contact.Allergic reactions are frequent on-the-job contact with artichokes (PDR FOR HERBAL MEDICINES, 1998, pp 793)

Studies conducted in guinea pigs with an intradermal application of Propanediol at 2.5% and epicutanea at 100% concentration at induction, and an epicutaneous application at 50% and semi oclussive at challenge showed that there was non-sensitizing. In studies with volunteers with Propanediol, the results were not sensitizing, with concentrations of 5% to 75% applied at induction and at challenge. (CIR Final Report, June 13, 2018)

In a sensitization study, natural and synthetic glycerin were not sensitizing to white male guinea pigs (n=12). A moisturizer containing glycerin (65.9%) was not sensitizing in a modified Draize test (n=48). There were no reaction during either the induction or challenge phase. (IJT 38(Suppl. 3):6-22, 2019)

Eye Irritation:

A battery of tests was carried out to determine the ocular irritation potential of KERACYN (Code 73400) at a concentration of 25%: The Hen's Eggs Test on the Chorioallantoic Membrane (HET-CAM), Mean Irritation Index = 2.50. Bovine Cornea Opacity and Permeability Test (BCOP), Irritation Index at 30 min = -0.7, Irritation Index 4 h = 4.4. Study of cytotoxicity in rabbit corneal fibroblasts (SIRC),Neutral Red Release Assay , IC50> 50%,% of mortality at dilution 50% = 22%. All these results show that the produc have a very good ocular compatibility.

Ocular irritation was evaluated in rabbit eyes with undiluted Propanediol, obtaining irritations ranging from

absent to mild that resolved within 48 hours after application.(CIR Final Report, June 13, 2018)
Glycerin (RTECS no. MA8050000): Draize Test eye rabbit = 500 mg/24h, mild.

Mutagenicity:

KERACYN (Cod. 73400): Genic Mutation Bacteria In Vitro Test (Ames Test), using 5 strains of Salmonella typhimurium (TA1535, TA1537, TA98, TA100 and TA102), both in the presence and absence of metabolic activation system (S-9). The product was tested at five dose levels between 3.35 and 53.55 mg/plate. No significant increase in the number of revertants was noted in any of the strains. The trial product can be considered as: No mutagenic.

Cynara scolymus: A study evaluates genotoxic and mutagenic activities of artichoke leaf aqueous extract in mice. Leaf extracts were given by gavage (500 mg/kg, 1000 mg/kg and 2000 mg/kg) for 3 consecutive days. Results revealed leaf aqueous extract shows lack of mutagenicity in vivo, and low genotoxicity and antioxidant activity. (J Food Sci. 2013 Feb;78(2):T367-71).

A mammalian chromosomal aberration test in vitro with Propanediol in V79 cellular line resulted in negative responses with metabolic activation and positives without metabolic activation only whit 2.5 mg/ml dose. In another in vitro study of chromosomal aberration in mammals reported negative results at concentrations up to 5 mg/ml Propanediol. Also, in an in vivo study in rats, fed 500 ppm of Propanediol for 15 weeks negative results were recorded, except at some point in the test, probably for a Propanediol metabolite. Finally, an in vivo study of micronucleus in mouse was negative with a single oral dose of 2150 mg/kg. CIR has evaluated these studies and considers that Propanediol has no mutagenic potential. (CIR Final Report, June 13, 2018).

Glycerin was not genotoxic in multiple Ames tests using multiple strains of Salmonella typhimurium up to 50 mg/plate. It was not genotoxic in a cytogenetic assay, in a HGPRT assay, sister chromatid exchange assay using CHO cells, unscheduled DNA synthesis assay using rat hepatocytes, or a in vitro chromosome aberration test using CHO cells, up to 1.0 mg/mL was tested in these studies.(IJT 38(Suppl. 3):6-22, 2019)
Moreover in two in vivo chromosome aberration assays, glycerin was not genotoxic when administered orally to rats at 1 mg/kg or by injection into the abdomen at 1000 mg/kg. (IJT 38(Suppl. 3):6-22, 2019)

Acute toxicity:

Cynara leaves extract (19% caffeoylquinic acids): LD50 i.p. rat = 1000 mg/Kg. (Principles and Practice of Phytotherapy, 2000, pp437)

Purified Cynara leaves extract (46% caffeoylquinic acids): LD50 i.p. rat = 265 mg/Kg and LD50 p.o. =2000 mg/kg (Principles and Practice of Phytotherapy, 2000, pp437)

Cynara scolymus Extract (RTECS no. GZ8306000): LD50 i.p. mouse = 1 g/kg.

Cynarin (RTECS no. GD8970000):LD i.p. rat > 800 mg/kg, LD50 i.p. mouse = 1900 mg/kg.

Inulin (RTECS no. NN1099000): LD50 i.p. rat = 128 mg/kg.

Propanediol (RTECS no.TY2010000, Last Updated:200608): LDLo p.o rat = 10g/kg, LDLo i.m. rat = 6 g/kg, LD50 i.p. mice = 4780 mg/kg, LDLo p.o cat = 3 g/kg, LDLo i.v. rabbit = 3 g/kg, LD50 p.o mice = 4500 mg/kg

Propanediol: An approximate lethal dosage of 17 g/kg (70% purity) and > 25 g/kg (99.8% purity) and an LD50 of 14.9 ml/kg were reported in rats by oral route. A LD50 > 20 g/kg was determined in a study in rats by dermal route.Finally, in inhalation studies in rats the animals survived a 4-hour exposure to 2 to 5 g/l. (CIR Final Report, June 13, 2018).

Glycerin (RTECS no. MA8050000): LD50 in rat: p.o. = 12600 mg/kg, i.p. = 4420 mg/kg, s.c. = 100 mg/kg, i.v. = 5566 mg/kg. LDLo in rat i.m. = 10 mg/kg, TDLo in rat i.m. = 5 g/kg, TDLo p.o. en humanos = 1428 mg/kg.

Glycerin (RTECS no. MA8050000): TDLo p.o. in human = 1428 mg/kg.

Glycerin (RTECS no. MA8050000): LD50 p.o. mouse = 4090 mg/kg, LD50 i.p. mouse = 8700 mg/kg, LD50 s.c. mouse = 91 mg/kg, LD50 i.v. mouse = 4250 mg/kg, LD50 p.o. rabbit = 27 g/kg, LD50 i.v. rabbit = 53 g/kg, TDLo i.m. rat = 4 mL/kg, TDLo i.m. rat = 4000 mg/kg.

Subchronic and chronic toxicity:

Artichoke has low toxicity. No toxic effects were observed in rats after oral administration of artichoke leaves extract (10 to 200 mg/kg) for four months or dermal application (1g/kg and 3 g/kg) for 21 days. The dermal LD0 was 6 g/kg in rats. (The Essential Guide to Herbal Safety, Simon Mills and Kerry Bone, Elsevier, Primera edición 2005, pp 438).

Cynarin: Test of 15 days in rat i.p. 50 - 400 mg/kg/day, produced no macroscopic or histological abnormalities or changes in blood parameters (ESCOP 2003, pp122)

In a 40-day study, administration i.p. to rats of Cynarin (50 - 400 mg/kg/day) did not cause macroscopic abnormalities or changes in general appearance, nor did blood parameters change. (ESCOP 2003, pp122)

Cynara scolymus L., leaf, water extract (RTECS No. GZ8326000):TDLo p.o. rat = 2800 mg/kg/7D·I.

In a inhalation study evaluating exposure to Propanediol, up to 1800 mg/l, 6 h/day for 2 weeks (9 exposures total), reported no remarkable results in rats. A NOEL of 1000 mg/kg/day was reported in rats by oral route. (CIR Final Report, June 13, 2018)

Propanediol. Repeat-Dose Toxicity test after inhalation administration in rat during 9 exposures, NOEL= 1800 mg/m3. (HSDB-Hazardous Substances Databank no. 8263).

Glycerin (RTECS no. MA8050000): TDLo p.o. rat = 96 g/kg/30d-I, TDLo p.o. mouse = 560 g/kg/8w-C, TDLo p.o. mouse = 2800 mg/kg/25w-C.

The NOAEL of glycerin in rats was between 115 and 2300 mg/kg when orally administered in water for 44 days.The NOEL in dogs was 950 when orally administered for 3 days. (IJT 38(Suppl. 3):6-22, 2019)

In repeated dose toxicity studies with humans there were no signs of toxicity or effects on blood or urine production when subjects (n=14) were orally administered glycerin (1.3 - 2.2 g/kg/day) for 50 days.(IJT 38(Suppl. 3):6-22, 2019)

There were no treatment effects when glycerin (100%; 0.5 - 4mL) was administered to 30% of the body surfaces of rabbits for 45 weeks.(IJT 38(Suppl. 3):6-22, 2019)

The inhalation NOAEL was 0.167 for glycerin administered nose only for 5h/day, 5day/week for 13 weeks in rats. (IJT 38(Suppl. 3):6-22, 2019)

Reproductive effects:

Aqueous extract of artichoke (35.7 and 150 mg/kg) administered to sexually mature male rats five times a week for 75 days did not lead to any significant change in the structure of the semen. (The Essential Guide to Herbal Safety, Simon Mills and Kerry Bone, Elsevier, Primera edición 2005, pp 438).

Artichoke leaf: Pregnancy category B2: no increase in frequency of malformation or other harmful effects on the foetus from limited use in women. Animal studies are lacking. Lactation category C: Compatible with breastfeeding. (The Essential Guide to Herbal Safety, Simon Mills and Kerry Bone, Elsevier, First edition 2005, pp 437)

In oral rat studies, no effects on spermatogenesis were observed at values above a dose of 1000 mg/kg/day of propanediol (during 90 days of exposure), nor were effects observed in mothers (doses administered from day 6 to 15 of gestation) or in fetuses. NOAEL 1000 mg/kg/day in mothers and fetuses. (CIR Final Report, June 13, 2018)

Glycerin (RTECS no. MA8050000): TDLo i.t. rat = 280 mg/kg, male 2 day(s) pre-mating ; TDLo p.o. rat = 100 mg/kg, male 1 day(s) pre-mating ; TDLo i.t. rat = 862 mg/kg, male 1 day(s) pre-mating.

In a two-generation reproductive study in rats (n=10/sex), the administration of glycerin (0,20%; 2000 mg/kg/day in drinking water) for 8 weeks before mating until weaning of pups produced no adverse effects on the reproductive efficiency of the parents (F0) or the development of the offspring (F1). (IJT 38(Suppl. 3):6-22, 2019)

When glycerin was administered orally to rats and mice on days 6 through 15 of gestation, there were no adverse effects observed in the dams. The NOAEL for maternal toxicity and teratogenicity was 1310 mg/kg/d for rats and 1280 mg/kg/d for mice. (IJT 38(Suppl. 3):6-22, 2019)

When glycerin was administered orally to rabbits (n=25) on days 6 through 18 of gestation, there were no adverse effects found in the dams. The NOAEL for maternal toxicity and teratogenicity was 1180 mg/kg/d. (IJT 38(Suppl. 3):6-22, 2019)

Other data:

Cynara scolymus has a hepatoprotective action, multiple therapeutic properties and practically no side effects. It is recommended not only in disorders of the liver, but also in the prevention of atherosclerosis and hyperlipidemia or dyspeptic disorders. (Przegl Lek. 2012;69(10):1122-6).

A study aimed to evaluate the effect of Cynara scolymus against diethylnitrosamine (DEN) induced hepatocellular carcinoma in rats. Results pointed that 1 g leaves of artichoke succeeded to protect from hepatocellular carcinoma to a certain degree. In addition, it may be considered as protective food against angiogenesis. (Eur Rev Med Pharmacol Sci. 2011 Dec;15(12):1429-44).

In clinical studies of 2 years with extracts of artichoke leaf in 1700 volunteers, only mild adverse effects were reported, mainly gastrointestinal complaints. (ESCOP 2003, pp122)

Treatment with an extract of artichoke leaf was shown to protect the liver and kidney against biochemical and histological alterations and oxidative stress induced by paracetamol. (Hepatoprotective effects of artichoke leaf extract and rosemary extract against Paracetamol induced toxicity in Albino Rats; JPRI 2020)

In a study, Cynara Scolymus (Artichoke) leaf was observed to exert cytotoxic and apoptotic effect on oral squamous carcinoma cell lines. (Anticancer effects induced by artichoke extract in oral squamous carcinoma cell lines; 2020). In another study, artichoke leaf extracts were shown to have cytotoxic activity against colon cancer cells (HT-29 and RKO).(Pro-Apoptotic Activity of Artichoke Leaf Extracts in Human HT-29 and RKO Colon Cancer Cell;IJERPH no. 8; 2021)

4. ECOLOGICAL DATA

Biodegradability:

None test of biodegradability have been performed on this product. However we have been able to conclude that this product can be considered as easily biodegradable due to his composition and the raw material used, considering that ingredients from vegetal origin and the solvents are biodegradable and the raw material from synthetic origin are in a very low concentration.

Glycerin (HSDB no. 492, revision: 20050624): Activated sludge test: 220 mg/l resulted in a COD of 97%; Test in a 5 days: BOD = 82%. Glycerin is considered an easily degradable substance.

Propanediol reached 11 and 16% of its theoretical BOD (Biochemical oxygen demand) using unacclimated and acclimated sewage sludge, respectively, during a 5 day incubation period (Hazardous Substances Databank Number: HSDB-8263)

Aquatic Toxicity:

Glycerin: Multiplication inhibition test in algae (Microcystis aeruginosa) and protozoa (Entosiphon sulcatum): Toxicity threshold = 2900 mg/l and 3200 mg/l (HSDB no. 492, revision: 20050624).

Glycerin (HSDB no. 492, revision: 20050624): LC50 goldfish > 5000 mg/l/24h.

Propanediol: EC50: Daphnia magna age 6-24 hr; Conditions: freshwater. Static, 20 deg C, PH > or= 7.0; Concentration: 8285000 µg/L for 24 hr; EC50: Daphnia magna age 6-24 hr; Conditions: freshwater. Static, 20 degC, PH> or= 7.0; Concentration: 7417000 µg/L for 48 hr; LC50: Carassius auratus weight 3.3 g; Conditions: freshwater, static, 20 deg C, PH 7.0, dissolved oxygen >4.0 mg/L; Concentration >5000000 µg/L for 48 hr (Hazardous Substances Databank Number: HSDB-8263)

Other data:

No data available.

5. CONCLUSION

The European cosmetics legislation (Regulation (EC) No 1223/2009) establishes the need to assess the safety of cosmetic products, taking into account the toxicological profile of the ingredients. To do this, in the case of possible systemic effects, it is necessary to obtain the NOAEL (no observed adverse effects level) for the calculation of MoS (margin of safety). The absence of these considerations shall be duly justified.

The NOAEL value, or else other data used for the same purpose (LOAEL, LD50, etc.), can only be calculated experimentally from toxicological studies that require the use of animals. Since Provital does not perform any animal testing, it has established a system to ensure the safety of its products without the need of NOAEL and the subsequent calculation of MoS. This systematic, in the case of natural complex substances (NCS) has been endorsed by international organisms and renowned toxicologists.

The safety of this ingredient is then established based on the following information: known uses of the active in different fields (medicine, food, cosmetics, etc.), profile of the chemical compounds of the ingredient and bibliographic toxicological information available for the active and its components. The integration and study of all these data allows for a conclusion on the safety of the ingredient.

The components of this product have not registered adverse effects neither in its described uses or in the historical marketing of this company. These data and the available toxicological information lead to the conclusion that the use of this product, under the normal conditions of cosmetic use, involves no risk for consumers.

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