
Technical Information

May 2005
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Retinol

Retinol 50 C

Retinol 15 D

Retinol 10 S

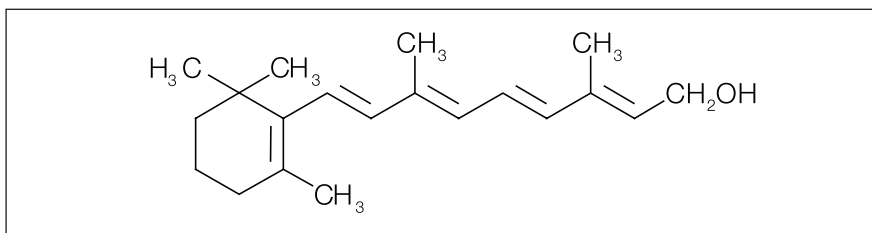
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**Active ingredient for the cosmetics industry. Counteracts skin aging
and improves the appearance of UV-damaged skin.**

cosmetic
SOLUTIONS

- Hair Care
- Skin Care
- Oral Care

 **BASF**
The Chemical Company

Structural formula**Synonyms**

all-trans-Retinol, vitamin A alcohol

Molecular formulaC₂₀H₃₀O**Molar mass**

286.5 g/mol

INCI name

Retinol

CAS-No.

68-26-8 (Retinol)
 Retinol 50 C: 9005-64-5 (Polysorbate 20)
 Retinol 15 D: 65381-09-1, 73398-61-5 (caprylic/capric triglyceride)
 Retinol 10 S: 8001-22-7 (Soybean [Glycine Soya]Oil)

Grades available

	Retinol 15 D	Retinol 10 S	Retinol 50 C
Appearance	Yellow oil that may crystallize at temperatures below 0°C	Yellow oil, with crystals at low temperatures	Yellow oil, with crystals at low temperatures
Solvent	Caprylic/Capric-Triglyceride	Soybean oil	Polysorbate 20
Assay	ca. 15%	ca. 10%	ca. 50%
Stabilizer system	ca. 1% BHT	ca. 1% BHT	ca. 3.5% BHT and ca. 1% BHA

Specification**Retinol 15 D**

Parameter	Requirement	Method
Assay		
- Retinol	500,000-530,000 IU/g 15.0-15.9%	05/0082.00
- BHT	0.9-1.1%	05/0076.00
Purity		
- all-trans-Retinol in total retinol	≥ 95%	05/0079.00
- cis-isomers in total retinol	≤ 5%	05/0079.00
Identity	Passes test	05/0082.00

Retinol 10 S

Parameter	Requirement	Method
Assay		
- Retinol	330,000-370,000 IU/g 9.9-11.1%	USP mod. Meth. 05/0077.00
- BHT	0.9-1.1%	05/0076.00
Purity		
- all-trans-Retinol in total retinol	≥ 95%	05/0079.00
- cis-isomers in total retinol	≤ 5%	05/0079.00
Identity	Passes test	USP 23 Meth.A+B, 05/0078.00 05/0053.00

Retinol 50 C

Assay		
- Retinol	1,425,000-1,650,000 IU/g 42.75-49.50%	05/0077.00
Content		
- BHT	3.15-3.50%	05/0080.00
- BHA	0.90-1.10%	05/0080.00
- Residual solvent, heptane	< 2,000 ppm	05/0081.00
Purity		
- all-trans-Retinol in total retinol	≥ 95%	05/0079.00
- Cis-isomers in total retinol	≤ 5	05/0079.00
Identity		
	Passes test	05/0078.00 05/0053.00

Applications

Retinol is an active ingredient for sophisticated cosmetic skin care products. It is the most effective substance for the care of aging and UV-damaged skin. Most of the signs of aging (wrinkles, lines, and irregular color, lost elasticity) are avoidable. They are almost entirely the result of the way we live and the environment we live in.

Retinol accelerates mitosis, increases enzyme activity, and normalizes keratinisation, which improves and normalizes the cell renewal process. The skin regenerates itself throughout its depth. The epidermis and dermis grow thicker, and the skin becomes more elastic. This reduces wrinkles and lines in number, area, length and width.

The skin becomes elastic, fresh and adequately supplied with moisture. It looks clearer and has a healthy color. Blemishes in the skin become less conspicuous.

Efficacy

The effects of topically applied Vitamin A have been confirmed in a large number of studies.

Caldera demonstrated the absorption of Vitamin A through the skin in an in-vivo study. He found a significant increase in blood levels of Vitamin A in his patients after application of an ointment containing Vitamin A (R. Caldera, L. Kersaudy, J. Badoual, G. Olive, The Cutaneous Absorption of Vitamin A, Dev. Pharmacol. Ther. 7, suppl. 1, 213-217 (1984)).

In a survey, Kretz mentions several studies that describe an increased rate of mitosis in rats and mice, a thickening of the epidermis in mice, an increase in the collagen content in the dermis of mice and increased skin elasticity in test persons as a result of the topical application of Vitamin A (A. Kretz; Vitamin A in der Kosmetik; SÖFW-Journal, 119, 21-24 (1993)).

In a clinical study involving 30 test persons, Bertin demonstrated that Retinol applied in a cream increases the biological elasticity of the skin and reduces the depth of wrinkles (C. Bertin et al. Retinol + Melibiose: An Innovative Anti-Aging Association, 20th ISFCC Congress, P 058, 1-7 (1998)).

Safety:

A Safety Data Sheet is available for Retinol. The substance may irritate the skin and was found to have a sensitizing potential in animals.

Retinol was found to be teratogenic when administered to animals at unphysiologically high oral doses. There is some indication for a possible connection between high intake of this substance during pregnancy and birth deformities in humans.

The recommended concentrations given below are based on a risk assessment based on exemplary topical exposure scenarios for cosmetic products as given in the European Union by the recommendations of the Scientific Committee of Cosmetology and Non Food Products (SCCNFP) (Notes of Guidance, 2000). The calculations result in the doses given below with a Margin of Safety of 1000 and higher. This safety factor is suggested for substances, which show severe critical effects such as teratogenicity in animal experiments for the acceptable daily intake according to the WHO risk assessment procedure (1994).

We emphasize that the dermal bioavailability of Retinol and consequently the potential toxicity is dependant on the composition of the formulation of the final product. Thus the dermal absorption rate should be determined with the respective product.

The calculations below can therefore only be considered as examples. The manufacturer of the final cosmetic product has to do in any case an own safety evaluation based on the data of his market formulation.

	Product	Face Cream	Hand Cream	Body Lotion
A	Conc. of Retinol in formulation of the finished product	0.05%	0.05%	0.01%
B	Amount of finished product per application	0.8 g	0.8 g	8 g
C	Number of application(s) per day	2	2	1
D	Exposure of finished product per day (B x C = D)	1.6 g	1.6 g	8 g
E	Exposure of retinol per day (A x D = E)	0.8 mg	0.8 mg	0.8 mg
F	Exposure retinol/kg (50 kg body weight) (E / 50 = F)	16 µg/kg	16 µg/kg	16 µg/kg
G	estimated bioavailability	10%	10%	10%
H	Systemic exposure (SE) (F x G = H)	1.6 µg/kg	1.6 µg/kg	1.6 µg/kg
I	NOAEL (No observed adverse effect level)	2250 µg/kg	2250 µg/kg	2250 µg/kg
K	Margin of Safety (NOAEL/SE) (I / H = K)	1400	1400	1400

NOAEL: No Observed Adverse Effect Level in microgram per kilogram bodyweight from a prenatal toxicity study in monkeys with retinyl palmitate.

Recommended concentrations

	Retinol, %	assumed applications per day
Face cream	0.01-0.05	2
Night cream	0.05-0.1	1
Hand cream	0.01-0.05	2
Body lotion	0.005-0.01	1
After-sun Face cream	0.01-0.05	1
After-sun Body lotion	0.005-0.01	1

Retinol can irritate the skin. Due to the fact that Asian skin is more sensitive, we recommend to stay on the low side of recommended concentrations for products for the Asian market

Solubility

Retinol is miscible with fats and oils.

Technical properties and handling

Retinol is a crystalline solid that is sensitive to oxygen, heat, light and heavy metals. It is therefore dissolved in oils, filled under nitrogen, stabilized with antioxidants and stored in aluminum cans at low temperatures.

Retinol can crystallize out at low temperatures, but the crystals can be redissolved by heating the can to 50°C. The time needed to redissolve Retinol varies and is dependent on the temperature and time of storage. It is therefore impossible to give exact advice how long it takes to redissolve. Stability tests have shown that the unopened container can be heated to 50°C for up to 5 days without significant loss of Retinol content.

We point out that it is possible to hear remaining crystals inside the aluminum container when rolling it.

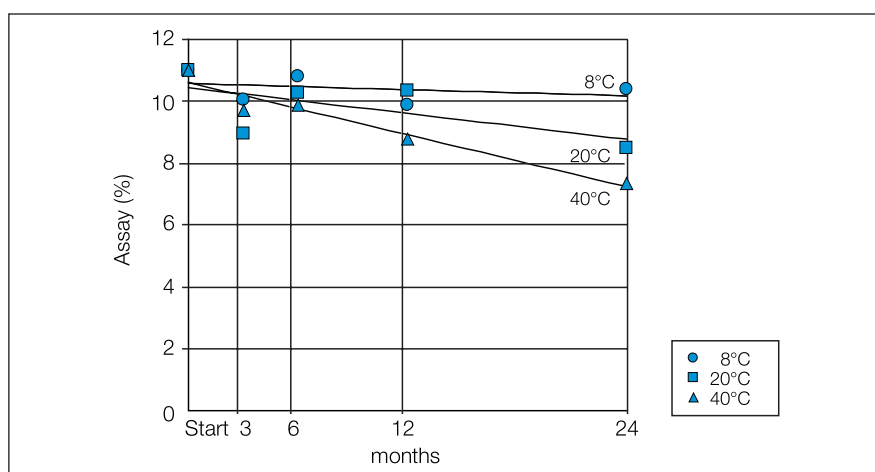
Once a can has been opened, the remaining contents should be kept under an inert gas, and used up quickly. Flushing the container with inert gas (Nitrogen or Argon) requires just spraying inert gas over the Retinol for a few seconds and closing the container tightly.

It is recommended to manufacture retinol formulations under an inert atmosphere and to add the retinol together with chelating agents at a temperature not exceeding 40°C. The finished formulation should be filled under an inert atmosphere into aluminum collapsible tubes which should then be kept below 20°C during storage and transport.

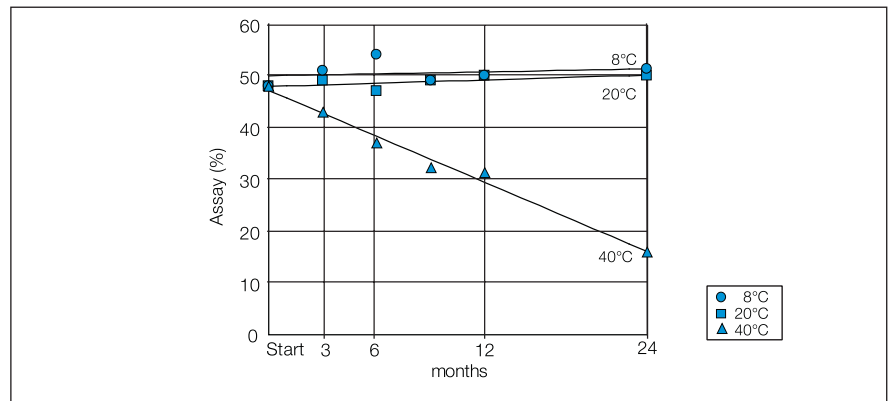
Stability during storage

The stabilities of the different Retinol grades differ, as they contain different antioxidant systems.

Stability of Retinol 10 S during storage at different temperatures:



Stability of Retinol 50 C during storage at different temperatures:



Retinol 50 C is stable for at least 24 months, if stored in the original sealed containers at temperatures below 20°C.

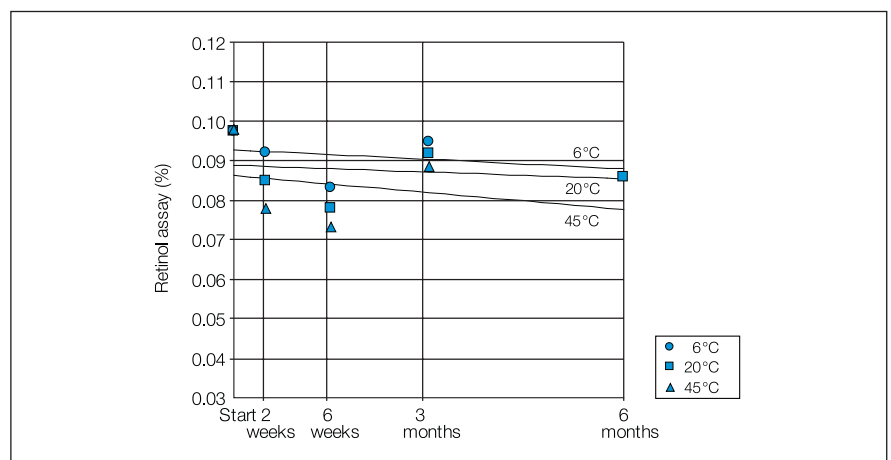
Retinol 15 D and Retinol 10 S are stable for at least 18 months, if stored in the original sealed container at temperatures below 15°C.

Stability in cosmetic formulations

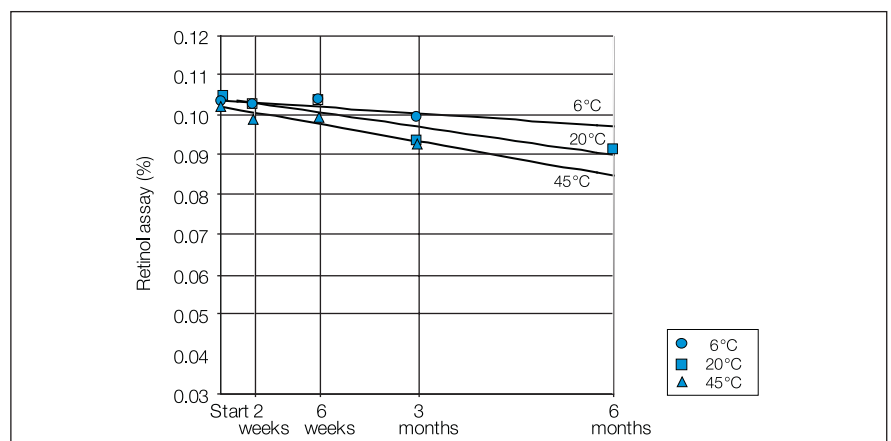
Retinol is stable for at least 6 months in cosmetic formulations that have been manufactured under an inert atmosphere and stored in aluminum tubes at 20°C.

The following examples contain 1% of a 10% solution of Retinol in oil. The resulting concentration in formulation is therefore 0.1%.

Stability of retinol in formulation 62/00076DE (O/W, 1% Retinol 10 S) during storage at different temperatures:



Stability of Retinol in formulation 62/00075DE (W/O, 1% Retinol 10 S) during storage at different temperatures:



Typical formulations

Anti-wrinkle Face Cream, Day, with Vitamin A and E

No. 62/00104

	%	Ingredients	Supplier	INCI name
A	2.00	Cremophor® A 6	(1)	Ceteareth-6, Stearyl Alcohol
	2.00	Cremophor® A 25	(1)	Ceteareth-25
	3.00	Jojoba oil		Jojoba (Buxus Chinesis) Oil
	4.00	Miglyol 812	(11)	Caprylic/Capric Triglyceride
	10.00	Paraffin Oil		Mineral Oil
	3.00	Lanette O	(27)	Cetearyl Alcohol
	5.00	Vaseline		Petrolatum
	0.10	BHT	(20)	BHT
B	5.00	1,2-Propylene Glycol Care	(1)	Propylene Glycol
	0.20	Edeta® BD	(1)	Disodium EDTA
	q.s .	Preservative		
	63.77	Water, dem.		Aqua
C	1.00	Luvigel® EM	(1)	Caprylic/Capric Triglyceride, Sodium Acrylates Crosspolymer
D	0.10	D,L-Alpha-Tocopherol	(1)	Tocopherol
	0.50	Vitamin E Acetate	(1)	Tocopheryl Acetate
	0.33	Retinol 15 D	(1)	Caprylic/Capric Triglyceride, Retinol
	q.s.	Perfume		

Production:

Heat phases A and B separately to 80°C.
Stir phase B into phase A and homogenize.
Stir phase C into phase A+B and homogenize.
Cool to 40°C, add phase D and homogenize again.

Recommendation: The emulsion must be kept under an inert atmosphere during manufacturing, filling, and storage. It should be filled into aluminum collapsible tubes.

Properties:

Viscosity: approx. 11 800 mPa·s
(Brookfield RVD VII+)
pH value: approx. 6.0

Retinol night care cream**No. 62/00090**

	%	Ingredients	Supplier	INCI name
A	6.00	Cremophor® WO 7	(1)	PEG-7 Hydrogenated Castor Oil
	10.00	Paraffin Oil		Mineral Oil
	3.00	Vaseline		Petrolatum
	5.00	Miglyol 812	(11)	Caprylic/Capric Triglyceride
	5.00	Jjoba Oil		Jjoba (Buxus Chinensis) Oil
	2.00	Elfacos ST 9	(2)	PEG-45/Dodecyl Glycol Copolymer
	1.00	Claytone XL	(148)	Quaternium-18 Bentonite
	0.10	BHT	(20)	BHT
B	3.00	1,2-Propylene Glycol Care	(1)	Propylene Glycol
	0.10	Edeta® BD	(1)	Disodium EDTA
	q.s.	Preservative		
	59.00	Water dem.		Aqua
C	5.00	Water dem.		Aqua
	0.20	Sodium Ascorbyl Phosphate	(1)	Sodium Ascorbyl Phosphate
D	0.50	Retinol 10 S	(1)	Glycine, Soja (Soybean) Oil, Retinol
	0.10	Vitamine E Acetate	(1)	Tocopheryl Acetate
	q.s.	Perfume		

Production:

Heat phases A and B separately to about 80°C.
Stir phase B into phase A and homogenize.
Cool to about 40°C, add phases C and D and homogenize again.

Recommendation:

Do the production of the emulsion and the filling into appropriate containers in the absence of oxygen.

Properties:

Viscosity: 11000 mPa·s Brookfield RVD VII+

Anti-Aging Face Lotion, Day, with Vitamin A and E**No. 62/00103**

	%	Ingredients	Supplier	INCI name
A	0.30	Pemulen TR-1	(6)	Acrylates/C10-30 Alkyl Acrylate Crosspolymer
B	1.00	Luvigel® EM	(1)	Caprylic/Capric Triglyceride, Acrylates Crosspolymer
	5.00	Fitoderm	(133)	Squalane
	5.00	Jojoba oil		Jojoba (Buxus Chinensis) Oil
	5.00	Crodamol PTC	(13)	Pentaerythrithyl Tetracaprylate/Caprates
	1.00	Cremophor® CO 410	(1)	PEG-40 Hydrogenated Castor Oil
	0.50	Vitamin E Acetate	(1)	Tocopheryl Acetate
	0.10	BHT	(20)	BHT
	0.10	D,L-alpha-Tocopherol	(1)	Tocopherol
	0.33	Retinol 15 D	(1)	Caprylic/Capric Triglyceride, Retinol
C	5.00	1,2-Propylene Glycol Care	(1)	Propylene Glycol
	0.20	Edeta® BD	(1)	Disodium EDTA
	q.s.	Preservative		
	76.07	Water, dem.		Aqua
D	0.40	Triethanolamine Care	(1)	Triethanolamine

Production:

Disperse Phase A into phase B.
 Stir phase C into phase A+B and homogenize.
 Neutralize with phase D and homogenize again. Recommendation: The emulsion must be kept under an inert atmosphere during manufacturing, filling, and storage. It should be filled into aluminum collapsible tubes.

Properties:

Viscosity: approx. 7 000 mPa·s
 (Brookfield RVD VII*)
 pH value: approx. 6.0

Suppliers

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3. **Cognis Deutschland GmbH**,
Care Chemicals
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Tel.: 49 211 9740-0
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4. **Noveon Inc.**
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Note

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