

PENTAPHARM

PEPHA[®]-PROTECT

Skin has a new body-guard, PEPHA[®]-PROTECT. This highly purified Water Melon extract protects the DNA in skin cells from damage caused by UV-light induced free radicals.

PRODUCT DESCRIPTION

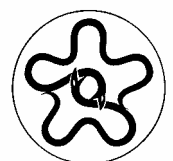
PEPHA[®]-PROTECT is a skin protective active containing naturally occurring vitamins, carbohydrates and amino acids such as Citrulline. Under extreme conditions Watermelon plants develop their own defense system by producing Compatible Solutes. These are water soluble molecules, for example amino acids, which penetrate easily into the skin. Compatible Solutes also can naturally occur in the human body. PEPHA[®]-PROTECT's synergistic composition is very strong in protecting the DNA of the skin's fibroblasts and keratinocytes. PEPHA[®]-PROTECT is a highly concentrated aqueous solution manufactured according to GMP standards.

BACKGROUND

The skin is increasingly exposed to free radicals. This can be partly explained by the decrease of the protective ozone layer and increased pollution due to our modern lifestyle. As a consequence, damage to the DNA, which can be irreversible, causes the appearance of mutations. The natural regeneration of the cells is reduced due to stress, aging and increasing amount levels of free radicals. PEPHA[®]-PROTECT increases the natural defense system of the skin due to the synergistic acting effect of the vitamins, carbohydrates and Citrulline.

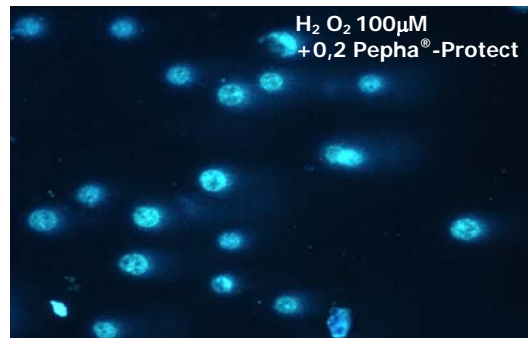
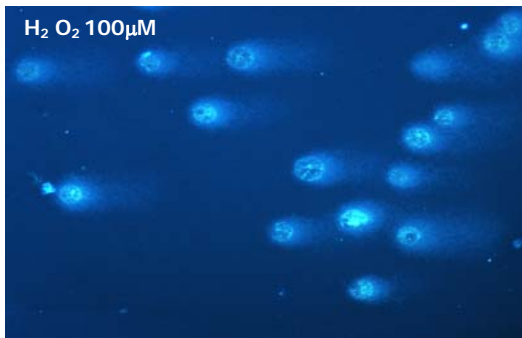
Compatible solutes are able to protect important cell structures such as the DNA from destruction. Such compounds occur in organisms which survive under extreme conditions such as high salt concentration, heat or drought. Watermelon (*Citrullus Lanatus*) grows in the Kalahari Desert and exhibits high drought tolerances. Exposed to such stress the Melon produces its own defense system which Pentapharm then uses for PEPHA[®]-PROTECT. In the Kalahari Desert Watermelon is still used as very important water source. The Melon used for PEPHA[®]-PROTECT is a cultivated plant growing under the same conditions as the wild one. Consequently PENTAPHARM LTD's highly purified Watermelon extract nourishes the skin by its natural water binding habit.

PEPHA[®]-PROTECT is a preventative ingredient of choice to protect the skin against the breakdown of the DNA caused by UV-light and pollution.



EFFICACY

COMET ASSAY

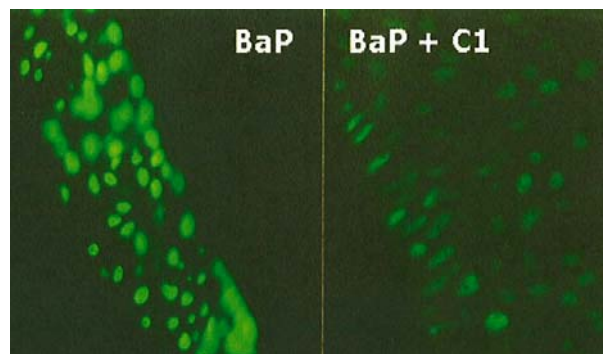


Testing on human epidermal fibroblasts and keratinocytes by the COMET assay has shown excellent DNA protecting capacity. The assay consists of the treatment of cells and then embedding them in an agarose gel on a microscope slide. During electrophoresis, damaged DNA migrates away from the nucleus whereas undamaged DNA does not migrate. The length of the tail corresponds to the amount of fragmented DNA. The protective effect of PEPHA[®]-PROTECT, compared to the stressed cells was increased by 68%.

In Vitro

8 OXO-DG ASSAY

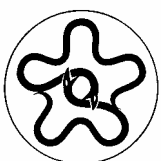
This assay shows the protection activity of PEPHA[®]-PROTECT due to the direct DNA protection. A strong decrease of 8-oxo-dG (oxidized Guanin base) could be observed. Directly damaged DNA showed a very good protection after treatment with different concentrations of PEPHA[®]-PROTECT.



ADDITIONAL INFORMATION

***In vivo* test:** The MED (Minimal Erythema Dose) was measured before treatment and after 28 days of twice-daily application of a cream containing 3% of PEPHA[®]-PROTECT against placebo. A 25% protective effect against UV irradiation was observed. After a one month treatment with a PEPHA[®]-PROTECT -containing emulsion, 79% of the volunteers expressed a desire to buy such a product. For further information see substantiation file

Detection of p53 *In vitro* test: The p53 protein is a key molecule to prevent uncontrolled cell growth. Healthy cells do only contain small amounts of p53. It participates in the regulation of the cell cycle. Phosphorylated p53 is a marker of damaged DNA as it correlates with ongoing DNA damage. After stressing cells by using BaP (Benzoapyren) the amount of phosphorylated p53 was quantified by means of specific fluorescent labelled antibodies. For further information see substantiation file.



CONCLUSION

PEPHA[®]-PROTECT's synergistic composition is very strong in protecting the DNA of the skin's fibroblasts and keratinocytes. Consequently PEPHA[®]-PROTECT decreases erythema after UV irradiation thus protect the skin.

TECHNICAL INFORMATION

PRODUCT SPECIFICATIONS

| | |
|-----------------------------|--|
| Appearance | : clear, yellowish liquid |
| pH | : 4.0 - 5.0 |
| Relative density (20°C) | : 1.00 -1,10 |
| Identity test by: | : corresponds to reference preparation |
| - thin-layer chromatography | |
| Microbial count | : < 100 CFU/ml |
| Specified pathogens | : absent |

PRESERVATION AND MICROBIOLOGY

PEPHA[®]-PROTECT is preserved using 0.3 % sodium benzoate, 0.14 % potassium sorbate and 0.95% Phenoxyethanol. PEPHA[®]-PROTECT is free of specified pathogens. The amount of non-pathogenic microorganisms is less than 100 CFU per ml of PEPHA[®]-PROTECT and meets the CTFA microbiology guidelines. PEPHA[®]-PROTECT fulfills the criteria of the repetitive germ loading test described by Shyam B. Singh-Verma (Parfümerie und Kosmetik 68(7), 414-421, 1987).

SAFETY AND ECOLOGY

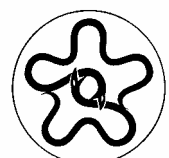
Standard and well-defined safety testing has been performed on PEPHA[®]-PROTECT which has proved the product to be safe for cosmetic use. The data available do not indicate any environmental risks. The manufacturing process is designed to meet the criteria for the assessment of safety, health and protection of people and of the environment set out in the *Responsible Care Program*.

PROCESSING AND DOSAGE

PEPHA[®]-PROTECT can be processed either warm (max.60°C) or cold, and is incorporated into the aqueous phase of a cosmetic formulation. PEPHA[®]-PROTECT is stable over the pH-range of 3 to 6. In formulations, PEPHA[®]-PROTECT is compatible with ethanol at concentrations of up to 50%. For skin care preparations, we recommend the addition of 1 to 3% PEPHA[®]-PROTECT. Basic Guideline Formulations are available upon request.

STORAGE AND SHELF LIFE

PEPHA[®]-PROTECT should be stored in the original sealed containers protected from light in a clean place at a temperature between 2 and 8°C. In order to avoid secondary microbial contamination, following opening, containers should be handled with special care. If stored under the recommended conditions, PEPHA[®]-PROTECT remains stable for at least 3 years.



GENERAL PRODUCT INFORMATION

| | | |
|-------------------|---|--|
| Trade Name | : | PEPHA [®] -PROTECT |
| Product Code | : | 800464 |
| INCI Name (CTFA) | : | Water, Glycerin, Citrullus Lanatus (Watermelon) Fruit Extract |
| EU-Labeling Name | : | Aqua, Glycerol, Citrullus vulgaris, Phenoxyethanol, Sodium benzoate, Potassium sorbate |
| Chemical Name | : | Aqueous solution of a purified extract of Watermelon |
| CAS No | : | 90244-99-8, 56-81-5, 7732-18-5, 532-32-1, 590-00-1, 122-99-6 |
| EINECS/ELINCS No | : | 310-127-6, 200-289-5, 231-791-2, 208-534-8, 246-376-1, 204-589-7 |
| JCID No | : | not listed |
| NICNAS | : | not listed |
| Customs Tariff No | : | 3824.9098 |
| Shelf life | : | 3 years |

COMPOSITION

| A) Ingredient | INCI Name # | Amount* |
|----------------------------------|---|---------|
| As listed in the CTFA Dictionary | Water, Glycerin, Citrullus Lanatus (Watermelon) Fruit Extract | E |

| B) Additives | INCI Name # | Amount* |
|----------------------------------|-------------------|---------|
| Solvent | Water | A |
| | Glycerin | C |
| Preservative | Sodium benzoate | F |
| Preservative | Potassium sorbate | F |
| Preservative | Phenoxyethanol | F |
| Others (antioxidants, colorants) | --- | --- |

CTFA Dictionary

* FDA-Code (A = > 50%, B = 25-50%, C = 10-25%, D = 5-10%, E = 1-5%, F = 0.1-1%, G = < 0.1%)

REMARK

Although these data and information have been prepared with the utmost possible care, we reserve the right to make changes due to product improvement and other considerations.

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