CROMOIST CM GLUCAN

INCI Name: Sodium Carboxymethyl β-Glucan

CROMOIST CM GLUCAN is a water soluble Glucan derivative isolated from yeast cell walls. It constitutes a powerful biological agent that can increase the skin's resistance to oxidative stress induced by UV-A radiation and protect skin from other environmental hazards. These protective effects are due to the ability of CROMOIST CM GLUCAN to stimulate the skin's own defense mechanisms. With such immunostimulatory activity, CROMOIST CM GLUCAN provides tremendous skin care benefits and offers functionality so exciting that it may revolutionize sun care or skin treatment technology.

By its combined action as a protectant, therapeutic, and film-forming agent, CROMOIST CM GLUCAN provides a natural and non-invasive means of restoring skin to its ideal state and keeping it protected from further environmentally induced trauma. CROMOIST CM GLUCAN offers the following benefits, all of which have been documented by in-vitro and/or in-vivo studies:

- Protects Against UV-A Induced Oxidative Stress
- Stimulates Production of Keratinocyte Cells
- Restores Skin Function
- Promotes Cell Renewal
- Enhances Skin's Self-Protection Mechanism

(Studies available on request.)

Glucan itself is a poly β-(1→3) glucopyranose of high molecular weight. As a polysaccharide, Glucan is a polysaccharide. Polysaccharides have been used for years in personal care as thickening, stabilizing and co-emulsifying agents. Many of these, such as Hyaluronic Acid and Aloe Vera, are bioactive moisturizing agents. As a group, these compounds are very stable, highly tolerant materials that are easy to formulate. Despite its polar character, Glucan is completely water insoluble, and as a result, is cosmetically unacceptable.
Glucan does, however, have pharmaceutical applications and belongs to a class of compounds known as Biological Response Modifiers (BRMs). Glucan has immunostimulatory properties which have been well-documented in the literature. The material is reported to enhance the body's defense mechanisms against bacterial infections and malignant tumors. Glucan is also said to reduce the inflammation of cells and accelerate their re-epithelialization, thereby, promoting wound healing.

**CROMOIST CM GLUCAN** is a carboxymethylated and water soluble derivative of Glucan. **CROMOIST CM GLUCAN** is produced using a technique that involves isolating Glucan from the cell walls of baker's yeast (*Saccharomyces cerevisiae*) and then carboxylating the isolate to obtain the Carboxymethyl Glucan derivative. In this reaction, three out of four glucose units are modified to carboxymethyl glucose (degree of substitution = 0.75). Such a process yields a water soluble, aesthetically pleasing product and ensures the purity and high quality of the material.

**Cromost CM Glucan**
Sodium Carboxymethyl Beta Glucan

\[
\begin{align*}
\text{Glucose and carboxymethylglucose units are linked by } & \beta-(1\rightarrow3) \text{ glycosidic bonds.}
\end{align*}
\]

Characterization of **CROMOIST CM GLUCAN** and its structure has confirmed its chemical identity as Sodium Carboxymethyl β-Glucan. Analysis was carried out using a variety of techniques—namely, \(^{13}\)C-Nuclear Magnetic Resonance (NMR) Spectroscopy, which elucidated the subunit linkage of the polymer and verified carboxylation of the Glucan material; titration/dialysis, which determined the degree of substitution; and Helix→Coil Transition Analysis, which established the presence of a triple helical structure. This particular helical conformation appears to be related to its immunostimulatory activity.

**BENEFITS**

*Protects Against UV-A Induced Oxidative Stress:*
UV-A radiation has been shown to be a strong potentiator of oxidative stress. Oxidative stress is damaging because it reduces the number of anti-oxidant molecules in the epidermis and precipitates phototoxic and photoallergic reactions in and on the skin. One such reaction is the peroxidation of squalene to squalene hydroperoxide. Squalene is one of the main components of the sebum found in the skin and is particularly susceptible to UV-A radiation.
Polysaccharides, including Glucan, are known to be non-specific stimulators in that they enable skin to elicit immune responses to oxidative stress. CROMOIST CM GLUCAN is not an anti-oxidant itself and works differently, providing effects that protect skin against anti-oxidant depletion. This has been confirmed by in-vivo and in-vitro studies, both of which show that CROMOIST CM GLUCAN is highly effective in protecting human skin cells against oxidative stress.

In the in-vivo study, a non-invasive technique of determining squalene hydroperoxides was used to evaluate the efficacy of CROMOIST CM GLUCAN in protecting skin from UV-A damage. During testing, treated and untreated skin sites of human volunteers from a 10 member panel were exposed to UV-A radiation and then examined for squalene hydroperoxide, using HPLC Chemiluminescence to detect the presence of this compound. Results (expressed in CL units) show that the level of squalene hydroperoxide in the skin is increased dramatically after UV-A radiation. Untreated skin sites were found to have the highest concentration. As shown below, a significant reduction in the level of squalene hydroperoxide could be detected in skin sites pretreated with the test sample containing CROMOIST CM GLUCAN.

Another study conducted in-vitro measured the concentration of Glutathione (GSH) and Ferritin in cell cultures of human fibroblasts and keratinocytes developed from normal adult skin. Testing consisted of pretreating the cultures with CROMOIST CM GLUCAN at a concentration of 100 µg/ml, exposing them to UV-A radiation (320-450 nm), and then bioassaying for GSH and Ferritin. Because exposure to UV radiation normally affects the levels of these two substances, their intracellular concentrations can be used as endpoints to demonstrate the photoprotective effects of CROMOIST CM GLUCAN against oxidative stress.
While GSH almost immediately drops in concentration on exposure to UV radiation, the GSH levels in human keratinocytes pretreated with CROMOIST CM GLUCAN remained constant upon UV irradiation. Although Ferritin in human fibroblasts tends to increase in concentration on initial exposure, it drops off sharply at higher UV doses. This response is countered by pretreatment with CROMOIST CM GLUCAN. (See graph below.) Traditional treatment with Vitamin E does not appear to produce the same phenomenon.

Fibroblasts treated with CROMOIST CM GLUCAN are strongly protected against depletion of the iron-binding protein Ferritin.

Stimulates Production of Keratinocytes Cells:
CROMOIST CM GLUCAN is able to induce cell proliferation, as shown by a German study, not yet published. The addition of the CM Glucan material to a culture medium of porcine keratinocyte cells resulted in a 30% increase in relative cell count (See graph below). Such evidence suggests that the ability of CROMOIST CM GLUCAN to stimulate the skin's immune response may help regenerate stressed skin cells and restore balance to the skin.

Porcine keratinocytes experience greater cell proliferation with CROMOIST CM GLUCAN.
Restores Skin Function:
The results of in-vivo studies show CROMOIST CM GLUCAN enhances skin function. Skin sites of volunteers were treated with various cosmetic preparations containing CROMOIST CM GLUCAN at different concentrations for 14 days and then immersed in Sodium Dodecyl Sulfate (SDS). Subjecting skin to such a stress can strip the epidermal layer of its lipid content and compromise its barrier function.

Subsequent evaluation of the skin sites in terms of skin humidity, skin roughness and Transepidermal Water Loss (TEWL) showed that the protective effects of CROMOIST CM GLUCAN are positive and appear to be dosage dependent. Pretreatment of skin with the test preparations was found to be highly protective against detergent damage, as reflected by the TEWL scores which are depicted in the bar chart below. The strength of this effect appears to be dependent on the concentration of CROMOIST CM GLUCAN in the various formulations.

CROMOIST CM GLUCAN improves skin function by protecting against TEWL.

Promotes Cell Renewal:
In a separate study, CROMOIST CM GLUCAN was found to have a favorable influence on the rate of cell renewal of skin. (See bar chart on next page.) The extent to which CROMOIST CM GLUCAN enhances cell proliferation was determined by applying Dansyl Chloride to skin sites which had been treated with preparations containing the CM-Glucan material and then measuring the rate at which the induced fluorescence diminishes. This technique is an established method of measuring the rate of cell turnover of the stratum corneum.
The influence of CROMOIST CM GLUCAN on cell renewal enhances skin cell proliferation.

Stimulates the Skin's Self-Protection Mechanism:
CROMOIST CM GLUCAN represents an entirely new approach to skin care. The ability of CROMOIST CM GLUCAN to trigger the skin's own defense mechanisms through the protective effects it provides is the basis of its functionality. CROMOIST CM GLUCAN works by providing protective effects that enhance the environment in which the skin resides. Creating and maintaining such an environment gives skin the resources it needs to protect itself. The result is improved skin function. Better skin function goes hand-in-hand with healthier, firmer skin.

APPLICATIONS
- Sun Care and After-Sun Products
- Treatment Products
- Daily Creams and Lotions
- Foundation Make-up
- AHA Creams and Lotions

CROMOIST CM GLUCAN is expected to have its greatest impact in sun care and skin treatment. CROMOIST CM GLUCAN can be of tremendous value since the benefits it provides in terms of protection against oxidative stress may enhance sunscreen performance. Used in facial creams or foundation make-up, CROMOIST CM GLUCAN can help protect skin against the oxidative stress of day-to-day exposure to the sun. CROMOIST CM GLUCAN can alleviate UV-light related insults and restore balance to the skin—in short, it can actually help prepare the skin for exposure to UV light. As a result, CROMOIST CM GLUCAN may be an excellent protective ingredient in pre-sun type products. Due to its immune stimulatory activity and wound healing properties, CROMOIST CM GLUCAN is effective as a therapeutic agent and can be used in after-sun products to soothe irritated and sunburned skin or in acne preparations to reduce inflammation. Glucan is also known to reduce sun sensitivity. For this reason, CROMOIST CM GLUCAN may be of great interest to formulators working with systems containing α-hydroxy acids.
CROMOIST CM GLUCAN

With frequent use, AHA products tend to make skin overly sensitive to the sun, causing it to burn more quickly and more severely. CROMOIST CM GLUCAN is also capable of lowering the irritation of these AHA-based formulations. Like many other polysaccharides, CROMOIST CM GLUCAN is an excellent film-former and forms a thin cohesive film that creates a perceptibly smooth skin feel. The material also has the capacity to bind water very strongly.

CROMOIST CM GLUCAN is supplied as an aqueous solution containing 2% Sodium Carboxymethyl β-Glucan. Easily formulated, it can be incorporated directly into most systems. It is compatible with other cosmetic ingredients (i.e., nonionic and anionic surfactants, alcohol in concentrations up to 40%) and is tolerant of normal manufacturing conditions (i.e., pH values from 2-10, high salt concentrations, temperatures as high as 80°C). Use Levels: 0.2-4.0%

Safety Profile

Repeat Insult Patch Testing (R.I.P.T.) has shown CROMOIST CM GLUCAN is non-irritating and non-sensitizing. The material has also been found to be nontoxic and noncytotoxic.
PROTECTIVE CREAM WITH CROMOIST CM GLUCAN

Due to the incorporation of **CROMOIST CM GLUCAN**, this cream can protect skin from environmental insult and help it function better. **CROMOIST CM GLUCAN** is a unique protective and therapeutic agent that works by stimulating the skin's own defense mechanisms, resulting in protective effects that enhance skin function and increase the skin's resistance to UVA-induced oxidative stress. **CRODAFOS CES** is a substantive phosphate-based emulsifying system that enhances the delivery of the other ingredients and improves the application properties of the cream.

**Ingredients**

**PART A**
- CRODAFOS CES (Cetearyl Alcohol (and) Dicetyl Phosphate (and) Ceteth-10 Phosphate) 4.00
- CRODAMOL GTCC (Caprylic/Capric Triglyceride) 5.00
- CORONA PNL (Modified Lanolin USP) 1.00

**PART B**
- Deionized Water 69.80
- Triethanolamine (98%) 0.20

**PART C**
- Deionized Water 5.00
- HYDROTRITICUM™ WAA (Wheat Amino Acids) 1.00

**PART D**
- Propylene Glycol (and) Diazolidinyl Urea (and) Methylparaben (and) Propylparaben (1) 1.00
- CROMOIST CM-GLUCAN (Sodium Carboxymethyl β-Glucan) 1.00
- INCROMECTANT LAMEA (Acetamide MEA (and) Lactamide MEA) 5.00

**PART E**
- Deionized Water 5.00
- DL Panthenol 2.00

**PROCEDURE**

Combine ingredients of Part A with mixing and heat to 75-80°C. Combine ingredients of Part B with mixing and heat to 75-80°C. Add Part A to B with mixing and cool to 50°C. Add ingredients of Parts C and D with mixing and cool to desired fill temperature.

\[ \text{pH}=4.5\pm0.5 \]
\[ \text{Viscosity}=20,000\text{cps} \pm10\% \text{ (RVT Spindle \#TC @ 10 rpm @ 25°C)} \]

1) Germaben II (ISP/Sutton Labs)

July 19, 1996
PROTECTIVE LOTION WITH CROMOIST CM GLUCAN

This lotion is ideal for every day use due to the protective effects of CROMOIST CM GLUCAN on the skin and is especially beneficial before and after exposure to the sun. By stimulating the skin’s own defense mechanisms, this powerful protectant and therapeutic agent is able to increase the skin’s resistance to UV-A induced oxidative stress and other environmental insults. CRODAFOS CES is a unique conditioning and emulsifying system that enhances the protective and emollient effects of the lotion by promoting better delivery of CROMOIST CM GLUCAN and CRODAMOL PMP, the emollient ester used to reduce the greasiness of the petrolatum.

**Ingredients**

<table>
<thead>
<tr>
<th><strong>W/W%</strong></th>
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<tbody>
<tr>
<td>PART A</td>
</tr>
<tr>
<td>CRODAFOS CES (Cetearyl Alcohol (and) Dicetyl Phosphate (and) Ceteth-10 Phosphate)</td>
</tr>
<tr>
<td>CRODAMOL PMP (PPG-2 Myristyl Ether Propionate)</td>
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<tr>
<td>Petrolatum</td>
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<tr>
<td>PART B</td>
</tr>
<tr>
<td>Deionized Water</td>
</tr>
<tr>
<td>Triethanolamine (98%)</td>
</tr>
<tr>
<td>PART C</td>
</tr>
<tr>
<td>Deionized Water</td>
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<tr>
<td>COLLASOL (Soluble Collagen)</td>
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<tr>
<td>PART D</td>
</tr>
<tr>
<td>Propylene Glycol (and) Diazolidinyl Urea (and) Methylparaben (and) Propylparaben (1)</td>
</tr>
<tr>
<td>CROMOIST CM-GLUCAN (Sodium Carboxymethyl β-Glucan)</td>
</tr>
<tr>
<td>INCROMECTANT LAMEA (Acetamide MEA (and) Lactamide MEA)</td>
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**PROCEDURE**

Combine ingredients of Part A with mixing and heat to 75-80°C. Combine ingredients of Part B with mixing and heat to 75-80°C. Add Part A to B with mixing and cool to 50°C. Add ingredients of Parts C and D with mixing and cool to desired fill temperature.

pH=4.5±0.5; Viscosity=6,000cps ±10% (RVT Spindle # TC @ 10 rpm @ 25°C)

1. Germaben II (ISP/Sutton Labs)

July 16, 1996