

## Recombinant Human Epidermal Growth Factor (rh-EGF)

**INCI Name** : rh-Oligopeptide-1

**CAS No.** : 62253-63-8

**Trade Name** : MC-EGF

### Functions and Uses

	<b>Functions</b>	<b>Uses</b>
<b><i>Skin care</i></b>	<ul style="list-style-type: none"><li>• Rejuvenate skin by stimulating cell proliferation</li><li>• Improves the texture and condition of the skin</li></ul>	<ul style="list-style-type: none"><li>• Anti-aging</li><li>• Anti-wrinkle</li><li>• Minimizing pores</li><li>• Eliminating scars and speckles</li></ul>
<b><i>Hair care</i></b>	Stimulate blood circulation of scalp, improve scalp's nutrient supply	Prevent hair from being dry, yellow and abnormal loss
<b><i>Medicine</i></b>	Stimulate the synthesis of DNA, RNA and hydroxyproline, accelerate the formation of granulation tissue and epithelial cells	Treating burns, wound healing, repairing duodenal ulcer, liver injury and corneas damage  Minimizes the effects of ureteral obstruction, assists the regeneration of nerve tissue and potentiates the effects of anti-cancer drugs

### Description

MC-EGF is produced via biotechnology and purified using proprietary chromatographic techniques (>95% pure). When applied to the skin, epidermal growth factor accelerates healing and increases the rate of skin renewal on aging skin. We have also noticed, the more aged the skin, the more dramatic the response.

- EGF accelerates healing of skin
- EGF increases rate of skin renewal
- EGF will help slow down thinning of aging skin

### Mechanism

Epidermal Growth Factor (EGF) works on the regulation of cell growth and development. This

small protein (only 53 amino acids) has been found to enhance epidermal growth and keratinization. EGF acts directly to stimulate the proliferation of epidermal cells and does not depend on any other systemic or hormonal influences<sup>1</sup>.

Cells that respond to EGF do so because they have receptors on the cell membrane that recognize the factor. Binding of Epidermal Growth Factor to the receptor initiates a cascade of molecular events involving the MAPK/ERK pathway that eventually leads to cell division. EGF only needs to be present at very low concentrations to effect major changes in the cell changes because it is a signal molecule. EGF starts by binding to receptors on the cell surface, is amplified through the MAPK/ERK pathway, and ends with nuclear DNA expressing proteins and producing changes in the cell, e.g. cell division.

EGF has been found to play a role in wound healing by antagonizing reactive nitrogen and reactive oxygen intermediate production by keratinocytes, and reversing the growth inhibitory actions of inflammatory mediators<sup>2</sup>. EGF has also been shown to help with the healing of diabetic ulcers<sup>3</sup>.

EGF acts by binding with high affinity to epidermal growth factor receptor (EGFR) on the cell surface and stimulating the intrinsic protein-tyrosine kinase activity of the receptor. The tyrosine kinase activity, in turn, initiates a signal transduction cascade that results in a variety of biochemical changes within the cell - a rise in intracellular calcium levels, increased glycolysis and protein synthesis, and increases in the expression of certain genes including the gene for EGFR - that ultimately lead to DNA synthesis and cell proliferation.

### Interactions

Alcohol and iodine may probably destroy the characteristic properties of EGF which lead to the decrease of its activity. The skin on which Alcohol or iodine are used should be washed with normal saline prior to apply EGF.

### Specification

<b>Appearance</b>	:	White or yellow-gray loose mass. Quickly dissolve after adding 1ml of distilled water and get a clear solution.
<b>Identification</b>	:	Positive
<b>Purity (SDS-PAGE)</b>	:	≥ 95%
<b>Potency</b>	:	$3.5 \times 10^4 - 1 \times 10^5$ IU (70%—200% of labeled amount $5 \times 10^4$ IU)
<b>pH</b>	:	7.2±0.2
<b>Sterility Test</b>	:	Sterile

### Stability Test

Special activity maintaining technology is applied on MC-EGF. So MC-EGF is more stable than common EGF commercially available.

For example, preparation containing common EGF should be freshly prepared prior to use. If mix common EGF lyophilized powder with injection water, the resulting solution can only be stored for 2 to 3 days in cold temperature. While the activity of MC-EGF will only decrease by 10% over a 60°C water bath for 3 days.

## EGF Formulation Suggestions

### Trace dilution method

Since the amount of EGF added to cosmetics is very small, it is not suitable to directly add frozen dry mass to cosmetics. Trace dilution method is suggested which dissolve EGF frozen dry mass having a known purity in normal saline at a temperature of 5-10°C (or 0.1N acetic acid solution) and dilute with the same solution to have a concentration of 10ppm. The diluted solution may be stored in freezer or under low temperature. The diluted solution should be protected from being contaminated by bacteria since EGF is easily hydrolyzed and loses its activity by enzyme produced by bacteria.

### Temperature

MC-EGF is relatively stable to temperature, and generally, there is no strict temperature limitation when add MC-EGF to cream. The activity of MC-EGF losses very few even at temperature of 60-80°C for 1 hour.

Still, we recommend that MC-EGF is added to the formulation at end of formulation, when product has cooled ( $\leq 45^{\circ}\text{C}$ ).

### pH & alcohol

EGF is very sensitive to pH of cream. Prior to adding diluted EGF solution to cream, the pH value of cream should be adjusted to 5-8. since at pH below 5 and above 8 and temperature 25°C, EGF easily forms polymerid and losses activity. Alcohols are also avoided formulation.

### Humectant and natural peptides as synergistic agent

EGF, natural peptides and humectants such as sodium hyaluronate in cosmetics produce good synergistic effect. This synergic action is not the sum but the multiplication effect each other.

So natural peptides and sodium hyaluronate are generally recommended to be added to cosmetic formulations containing EGF so as to protect the activity of hEGF, increase its penetration and easy absorption into skin.

### Microbial Attack

EGF is easily decomposed by enzymes produced by microorganisms and loses its activity. So it is extremely important to avoid microbial contamination during processing of products containing EGF as well as storage and transportation.

### Use Level:

**Repairing products** : 2500-5000IU/ml (equivalent to 5-10 $\mu\text{g}/\text{ml}$ )

**Skin care / Serum / Cream** : 1000-2500 IU/ml (equivalent to 2-5 $\mu\text{g}/\text{ml}$ )

**Generally**

<b>Eye creams</b>	: 2000-2500IU/ml (equivalent to 4-5µg/ml)
<b>Day cream</b>	: 1000-1500IU/ml (equivalent to 2-3µg/ml)
<b>Evening cream</b>	: 1500-2000IU/ml (equivalent to 3-4µg/ml)

**BACKGROUND**

Human epidermal growth factor (hEGF) is a single chain peptide with a molecular of 6,200 Dalton. It contains 53 amino acids with three disulfide bonds consisting of asparagine, aspartic acid, cysteine, glutamic acid, histidine, leucine, proline, serine, and tyrosine. It was first isolated from the submaxillary gland of mouse in 1960 by Stanley Cohen, who won the Nobel Prize in Physiology and Medicine for his discovery and research on EGF in 1986. The first isolation of hEGF was from human urine in 1962.

Epidermal growth factor or EGF is a growth factor that plays an important role in the regulation of cell growth, proliferation, and differentiation. It stimulates the synthesis of DNA, RNA, hydroxyproline as well as hyaluronic acid, accelerates cell proliferation and differentiation of various epidermal tissues, such as epidermis of skin, gastrointestinal tract and cornea.

MC-EGF is a highly efficient cell division factor with a variety of biological activity. It can repair epidermis, delay aging, fade speckles, inhibit wrinkles, and moisten skin. The content of EGF in the body determines how old the skin is. So EGF is also called “Beauty Factor” and may be widely used in skin care cosmetics with the following functions:

*Rejuvenate skin:* EGF can promote skin cells to absorb nutrients, speed cell metabolism, accelerate skin cell division and growth, stimulate the synthesis of hyaluronic acid and glycoproteins.

*Accelerate cell regeneration and tissue repair:* EGF can promote the healing of wound surface of skin and mucosa, reduce scar contracture and skin's abnormal proliferation. It produces good effect on scars, especially on keloid after acne.

*Whiten skin:* EGF can promote the growth of new cells which replace injured cells by ultraviolet radiation, reduce the number of melanocytes in the skin.

In the young, the body can produce enough EGF to promote epidermal cell growth, but as age increases (after 25 years old), EGF production decreases gradually, and the renewal of epidermal cells markedly slows down. The deficiency of EGF will result in delayed wound healing, scars, skin aging, and formation of wrinkles, freckles and age pigment. Under these circumstances, prompt supplement of EGF becomes extremely important. While natural EGF is extraordinary expensive and seldom can afford it.

MC-EGF is a recombinant human epidermal growth factor (rh-EGF) obtained by genetic engineering technology. It is identical to EGF in human body so it can be used as an important supplement when body is in dire need of it..

The traditional method to minimize pores and reduce wrinkles is to inject Botox, which has been found to cause severe side effects on the time of reducing wrinkles. Botox can paralyze nerve, and repeated injections cause muscle stiffness and loss of consciousness. Besides, it is extremely expensive for use. rh-EGF, totally identical to natural EGF existing in human body, produced via

bioengineering technology in a economic way, has now become the first choice to eliminate wrinkle while without the adverse reactions of Botox Injection.

rh-EGF is suitable for any ages except younger people who can produce sufficient EGF themselves. EGF is applicable to both men and women, especially for eyes and facial care of women after age 25.

**[Reference]**

<sup>1</sup> Cohen, Stanley (1993). Nobel Lecture 1986. Epidermal Growth Factor. In: Physiology or Medicine 1981-1990: Nobel Lectures, Including Presentation Speeches and Laureates' Biographies, T. Frangmyr and J. Lindsten (eds.) World Scientific Pub Co Inc (May 1993) pp 333-345.

<sup>2</sup> Heck, Diane E.; Laskin, Debra L.; Gardner, Carol R.; Laskin, Jeffrey D. (1992) Epidermal growth factor suppresses nitric oxide and hydrogen peroxide production by keratinocytes. Potential role for nitric oxide in the regulation of wound healing. *J Biol Chem* 267:21277-80.

<sup>3</sup> Tsang, Man Wo; Wong, Wan Keung R.; Hung, Chi Sang; Lai, Kwok-Man; Tang, Wegin; Cheung, Elaine Y. N.; Kam, Grace; Leung, Leo; Chan, Chi Wai; Chu, Chung Min; Lam, Edward K. H. (2003) Human epidermal growth factor enhances healing of diabetic foot ulcers. *Diabetes Care*, 26:1856-1861.