

# CRESSATINE®

## Strengthen hair from the roots

THE HAIR BOOSTER

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#### SUGGESTED MARKETING CLAIMS

- > Promotes hair regrowth
- Strengthens hair's structure and enhances its beauty
- > Encourages hair growth
- > Prolongs the hair growth phase
- > Delays hair shedding

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#### **IN SHORT**

Whether we realize it or not, our hair says a lot about us, reflecting our personality and lifestyle. When it's long and glossy, it can be a powerful tool of seduction, but dull, brittle hair gives the false impression of a person who doesn't take care of himself or herself. So, how do you restore **strength** to tired hair and **keep it growing for longer**?

There's only one solution: target the hair follicle, where hair is produced and grows.

It is essential to have an effect here, where the hair's structure is defined through a **high-sulfur matrix protein called keratin**, which lends the hair its strength and thus its beauty.

By combining **two Super-Leaves** known for their many haircare properties and rich sulfur and mineral content, the Solabia Group has produced a single active ingredient that offers all the properties of both a land-based, sun-loving vine, **Indian cress**, and a fast-growing freshwater plant, **watercress**.



## Indian cress

CRESSATINE<sup>®</sup>, a combination of two leaves to encourage hair to grow stronger from the root and keep growing longer.

## SOLUTION BY SOLABIA

CRESSATINE<sup>®</sup> is an active ingredient obtained as an **aqueous extract of watercress** (*Nasturtium officinale*) **and Indian cress** (*Tropaeolum majus*) leaves and shoots, stabilized with plant glycerin.



Titrated with sulfur, it is designed to facilitate hair growth and strengthen hairs from the root:

- by providing the elements (sulfur and other minerals) needed to produce keratin for solid, well-structured hair.
- by helping initiate hair regrowth via the Wnt pathway.
- by stimulating keratinocyte differentiation via the KGFs (keratinocyte growth factors) released when the Wnt/β-catenin pathway is activated.
- by prolonging the growth phase using the Wnt pathway and KGFs.

With Cressatine<sup>®</sup>, stimulate hair growth, strength, and longevity.

#### TOXICOLOGICAL PROFILE

In vitro ocular irritant potential Het-Cam - product diluted to 10%

In vitro cutaneous irritation OECD 439 - pure product

In vivo cutaneous irritant potential Simple 48h patch-test - pure product

**Sensitizing potential** Marzulli-Maibach - product diluted to 30%

Mutagenicity Ames - product diluted according to the protocol

Phototoxicity OECD 432 – product diluted according to the protocol

#### INCI/CTFA NAME

Glycerin (and) Water (and) Nasturtium officinale extract (and) Tropaeolum majus extract

#### REGULATORY STATUS

Use authorized in the EU, USA, China (China INCI list 2007 and IECIC 2014), Japan, Canada (DSL listed), and Australia

Raw material approved by ECOCERT GREENLIFE, according to COSMOS

#### • APPLICATIONS

Haircare and shampoo: Hair growth Hair loss Strengthening Anti-ageing slightly irritant non irritant non irritant

non irritant, non sensitizing

no mutagenic and pro-mutagenic activity

no phototoxic activity

#### SPECIFICATIONS

#### Appearance

Translucent solution with possibly a slight precipitate

Color

yellow to orange yellow

#### Solubility

Water Butylene glycol Glycerin Ethanol at 20% Mineral/vegetable oils soluble soluble soluble soluble insoluble

#### **Preservative system**

0.1% sorbic acid

2

## **EXPERT RECOMMENDATIONS**

Usage dosestarting at 0.25%Incorporationfor processes at room temperature, incorporate into<br/>the aqueous phase; for hot processes, incorporate<br/>during cooling at a temperature of 45°C or, if the<br/>process requires, directly into the hot mixture at 75°C.Thermostabilitynot temperature-sensitivepH stability3 to 8



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THE SCIENCE

## HAIR, GROWTH and STRENGTH

#### IT'S ALL ABOUT THE HAIR FOLLICLES...

A hair follicle is a dynamic structure that produces hair during tissue remodeling and growth cycles. These cycles are broken into 3 phases:

#### - GROWTH PHASE (anagen)

The dermal papilla cells (fibroblasts) send a signal to the stem cells in the bulge (reservoir) allowing them to proliferate toward the bottom of the follicle. These cells will transform and envelop the dermal papilla to form the hair's sulfur matrix. They divide and differentiate into keratinocytes, the cells responsible for the hair's structure, which is created during the process of **keratinization**.

#### A closer look at keratinization...

Keratinocytes produce keratin and migrate from the lower follicle toward the skin's surface, losing their nucleus. This causes dead cells to build up in concentric layers (medulla, cortex, cuticle) filled with that oft-mentioned fibrous protein, keratin. Keratin makes up more than 90% of a strand of hair. This scleroprotein is rich in **sulfur-containing amino acids** like cysteine and methionine, minerals, and trace elements like zinc and magnesium. The **structure of the hair is defined by the (strong) disulfide bonds** in the keratin within the follicle.



In order for well-structured hair to form, the keratinocytes must have sulfur-containing proteins, Vitamin B6 and zinc [1]. Other minerals help the hair grow: antioxidant and energizing magnesium, for example, helps activate the B vitamins involved in cellular renewal.

The length of this phase determines how long the hair will grow, and it depends on the proliferation and differentiation of the matrix cells in the lower follicle.

#### - REGRESSION PHASE (catagen)

The matrix dies, meaning that the dermal papilla is no longer in contact with it. There is no longer any exchange between the cells. The follicle and dermal papilla rise toward the epidermis.

#### - RESTING PHASE (telogen)

The cells in the dermal papilla and the bulge are intact and inactive. The hair falls out.

In order for a new hair to develop, the cycle must begin again.



#### IDENTIFYING THE KEY MECHANISMS AND MOLECULES

The development and growth of the hair follicle are influenced by components expressed by the dermal papilla: proteins like Wnt and growth factors like keratinocyte ones (KGFs). These are involved in the intercellular communication pathways and are known to act on the keratinocytes in the follicle. [2-3]

#### → INITIATING HAIR REGROWTH

During the transition from resting to growth phase, the stem cells in the bulge are activated by the Wnt signal, which regulates the expression of their genes. An increase in intracellular  $\beta$ -catenin is detected in the lower bulge. Hair regrowth begins. [4-6]

#### A closer look at Wnt / β-catenin...

Wnt is a family of glycoproteins whose name combines Wg (wingless) and Int (integration site). The Wnt signaling pathway via  $\beta$ -catenin is called the canonical (i.e. preferred) pathway. The Wnt signal activates hair regrowth and contributes to its growth.





Wnt binds to the extracellular receptors, stabilizing the intracellular  $\beta$ -catenin (preventing it from being degraded by the proteasome). It is then able to penetrate the nucleus and serve as a coactivator of transcription factors, stimulating the expression of specific genes involved in hair growth, such as the gene that codes for KGFs. [4]

#### → GROWTH

The hair's development depends on a signaling loop between the keratinocytes and the cells in the dermal papilla. Wnt expression at the keratinocytes level boosts  $\beta$ -catenin in the dermal papilla cells that regulate the signaling pathways, including the growth factors that guide hair morphogenesis. [3]



#### A closer look at KGF or FGF-7...

KGF (Keratinocyte Growth Factor) is an endogenous paracrine mediator that plays an important role in the development, differentiation, and growth of the hair follicle. By binding to a specific receptor on the cells in the hair matrix, KGF helps create a signal that controls the structure of the medulla and gives the hair its shape. [7]

Using the co-culture model (dermal papilla cells/keratinocytes) demonstrates the stimulation of hair regrowth. This *in vitro* allows for interactions between the different culture cells, making it similar to real conditions. The increased rate of  $\beta$ -catenins in the dermal papilla cells and the higher rate of KGF in the growth medium reflects the activation of the Wnt pathway.

#### → GROWTH CESSATION

 $\beta$ -catenin and KGF are present in high concentrations during the anagen phase and then disappear. A loss of expression of the  $\beta$ -catenins blocks the Wnt signal and triggers the transition to the catagen phase. [3; 4; 8]

THE SCIENCE

<sup>[1]</sup> Tenaud I. Zinc, copper and manganese enhanced keratinocyte migration through a functional modulation of keratinocyte integrins. Exp Dermatol. 2000 Dec;9(6):407-16.

<sup>[2]</sup> Danilenko DM. Keratinocyte growth factor is an important endogenous mediator of hair follicle growth, development, and differentiation. Normalization of the nu/nu follicular differentiation defect and amelioration of chemotherapy-induced alopecia. Am J Pathol. 1995 Jul;147(1):145-54.

<sup>[3]</sup> Enshell-Seijffers D. Beta-catenin activity in the dermal papilla regulates morphogenesis and regeneration of hair. Dev Cell. 2010 Apr 20;18(4):633-42.

<sup>[4]</sup> Thompson CC.Hairless is a nuclear receptor corepressor essential for skin function. Nucl Recept Signal. 2009 Dec 31;7:e010.

<sup>[5]</sup> Lien WH. In vivo transcriptional governance of hair follicle stem cells by canonical Wnt regulators. Nat Cell Biol. 2014 Feb;16(2):179-90.

<sup>[6]</sup> Rishikaysh P. Signaling involved in hair follicle morphogenesis and development. Int J Mol Sci. 2014 Jan 22;15(1):1647-70.

<sup>[7]</sup> Schlake T. FGF signals specifically regulate the structure of hair shaft medulla via IGF-binding protein 5. Development. 2005 Jul;132(13):2981-90.

<sup>[8]</sup> Rosenquist TA. Fibroblast growth factor signalling in the hair growth cycle: expression of the fibroblast growth factor receptor and ligand genes in the murine hair follicle. Dev Dyn. 1996 Apr;205(4):379-86.

## **CRESSATINE®:** for hair strength and growth

Meet 2 complementary plants that work together to promote hair strength and growth!



A quick-growing freshwater plant that mirrors the faster hair growth achieved by the added minerals.

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#### → IDENTITY

#### Nasturtium officinale, Brassicaceae family.

*Nasturtium* comes from the Latin name *nasus tortus*, meaning "twisted nose," because of its spicy odor that makes people wrinkle their nose. Its English name is thought to be derived from the Frankish *kresso*, for creeping, or the Latin *crescere*, for grow.

Thanks to its wealth of minerals and vitamins, which give it useful properties as both food and pharmaceutical, watercress was called **healthy body** in Antiquity.

Watercress is not to be confused with other cresses, such as garden cress (*Lepidium sativum*) and land cress (*Barbarea verna*), which grow in dry places.

#### → DEVELOPMENT

This aquatic plant native to Europe forms creeping sprouts under the water and then shoots out of the water. It grows very quickly in water that is shallow, cool, and not stagnant with little sun.

Starting in the 13<sup>th</sup> century, land began to be modified to boost French cress production. True cultivation began in the 18<sup>th</sup> century in Germany and then in France under Napoleon.

#### → PHYTOCHEMISTRY



gluconasturtiin

Sulfur heterosides (glucosinolates like gluconasturtiin), several nitriles, polyphenols, flavonoids, Vitamins C, A and E as well as minerals (calcium, magnesium, iron, zinc, copper).

## Indian cress

## A plant that climbs toward the light, synonymous with the growth of glossy, healthy hair.

#### → IDENTITY

#### Tropaeolum majus, Tropaeolaceae family.

Its Latin name derives from *trophaeum* (trophy), because the shape of the leaves is reminiscent of a shield in Roman Antiquity and the flowers resemble a helmet.

Indian cress received their common French name from "capuce" meaning cowl, because of the form of the flowers which look like monk hood.

The plant's haircare properties have earned it the nickname of plant for hair.

#### → DEVELOPMENT

Native to Peru and Mexico, then introduced in Europe in the 17<sup>th</sup> century, Indian cress can be climbing, tuberous, or dwarf; they grow wild in very sunny mountainous regions.

#### → PHYTOCHEMISTRY

Sulfur heterosides like glucotropaeolin, oxalic acid, Vitamin C, polyphenols and flavonoids.





#### A closer look at ... Sulfur heterosides



Sulfur heterosides are responsible for the plant's fresh and spicy flavor. Leaves that contain this element are eaten in salads or used for seasoning. For example, they are found in mustard, radish, and cauliflower.

## CRESSATINE<sup>®</sup>: BOOST YOUR HAIR'S GROWTH!

Both Indian cress and watercress have been used for centuries for haircare purposes, since their rich sulfur content and other properties make them incredibly beneficial to hair!



#### → HAIRCARE BENEFITS IN COMBINATION

Both plants are known to tone the scalp and thus stimulate the vitality of the bulb. The sulfur they contain helps strengthen hairs from the bulb and prevent shedding.

Indian cress also helps purify the scalp, thus preventing the appearance of dandruff. In addition, it has sebum regulating properties that keep hair from looking oily and anti-inflammatory properties to soothe an irritated scalp.

By combining Indian cress, a sun-loving land-based climber, with quick-growing watercress, Solabia has developed an active ingredient that encourages the growth of strong hair.

## With CRESSATINE®

### grow stronger hair longer,

right from the root!



CRESSATINE<sup>®</sup> is obtained as an aqueous extract of watercress and Indian cress leaves and shoots. The extract is stabilized with plant glycerin and contains 0.1% sorbic acid as a preservative.

Rich in beneficial molecules, CRESSATINE<sup>®</sup> is **titrated with sulfur (≥200mg/kg)** and contains other **minerals** like zinc and magnesium.

#### → HOW CRESSATINE<sup>®</sup> WORKS



#### Strengthens from the root

The added sulfur and minerals help build high-quality keratin, which means stronger hair right from the bulb.



#### **Initiates regeneration** and stimulates growth

A signal transmitted by the dermal papilla involves the Wnt pathway in activating the stem cells in the bulge, which causes them to migrate and form the matrix that will be used to produce a new hair. Activating the Wnt/ $\beta$ -catenin pathway triggers the release of KGF, which stimulates keratinocyte differentiation and thus hair growth while also defining the hair's shape.



**Prolongs the** growth phase

Together, the activated Wnt pathway and presence of KGF slow the hair follicle's transition into the catagen phase.



by

A combination of two sulfurrich leaves to initiate and prolong hair growth strengthening it right from





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the bulb.

## ACTIVATION OF HAIR GROWTH (BIOHC)

#### Purpose:

Conduct an *in vitro* assessment of CRESSATINE®'s effect on hair growth by tracking 2 parameters:

- activation of the Wnt pathway with an increase in intracellular ß-catenin,
- production of KGF resulting from the activation of the Wnt pathway.

**Protocol:** 

#### Study procedure

Follicle dermal papilla cells (FDPC) isolated from normal human scalp were cultured in medium supplemented with growth factors, insulin and fetal calf serum.

Human epidermal keratinocyte (KHN) from newborn foreskin were grown in serum-free medium.

After 4 days, monolayers of KHN in insert are transferred above FDPC. The incubation medium then formed is replaced by a co-culture medium to prepare different experimental conditions:

- Control: no addition to co-culture medium
- $\mbox{CRESSATINE}^{\mbox{\ensuremath{\mathbb{R}}}}$  Group:  $\mbox{CRESSATINE}^{\mbox{\ensuremath{\mathbb{R}}}}$  at 0.25%, 1% ou 2.5% added to the medium

#### Measurement

After 3 days of incubation, tests are performed to carry out different analysis.

FDPC are collected and permeabilized for intracellular β-catenin analysis by ELISA method.

Incubation media is collected for the KGF analysis by ELISA method.

#### Mechanism



#### Protocol diagram



#### **RESULTS AND CONCLUSIONS:**

#### 1) ACTIVATION OF WNT/ B-CATENIN SIGNALING PATHWAY



#### CONCLUSION :

The results obtained demonstrate that CRESSATINE<sup>®</sup> significantly actives *vs* control and in a dose-dependent manner Wnt /  $\beta$ -catenin pathway, allowing the regeneration and growth of hair but also prolonging the growth phase.



#### 2) STIMULATION OF KGF PRODUCTION

				**: p <0.01
		CRESSATINE®		®
	Control	0.25%	1%	2.5%
Average concentration of KGF (pg/(µ prot)	0.357	0.441	0.501	0.741
Stimulation of KGF production compared to control	/	+ 23%**	+40%**	+107%**



#### **CONCLUSION:**

The results obtained demonstrate that **CRESSATINE®** significantly KGF production, stimulates vs control and in a dose-dependent manner, which stimulates the causes keratinocytes, wellа structured hair to be produced, and lengthens the anagen phase.

## **EXPERT RECOMMENDATIONS**



Solubility	
Water	$\odot$
Ethanol solution at 20%	$\odot$
Ethanol (95%)	$\overline{\boldsymbol{\varTheta}}$
Glycerin	$\odot$
Butylene glycol	$\odot$
Vegetable oil	$\overline{\mathbf{S}}$
Mineral oil	$\overline{\mathbf{S}}$

)	Gelling agents	
l	Keltone HV (Algin)	$\odot$
)	Keltrol CG-SFT (Xanthan gum)	$(\mathbf{i})$
	Natrosol 250 HHR (Hydroxyethylcellulose)	$(\mathbf{i})$
	Sepigel 305 (Polyacrylamide / C13-14 isoparaffin / Laureth-7)	$\bigcirc$
	Ultrez 10 (Carbomer)	$(\mathfrak{I})$
	Ultrez 20 (Acrylates / C10-30 alkyl acrylate crosspolymer)	
	Cosmedia CTH(E) (Polyquaternium-37 / propylene glycol	
	dicaprylate/dicaprate / PPG-1 trideceth-6)	9

J	Emulsifiers	
8	Emulium delta (Cetyl alcohol / glyceryl stearate / PEG-75 stearate /	$\overline{(\cdot)}$
J	ceteth-20 / steareth-20)	
	Montanov 68 (Cetearyl alcohol / cetearyl glucoside)	$\odot$
	Tego care 450 (Polyglyceryl-3 Methylglucose distearate)	
	Incroquat behenyl TMC (Cetearyl alcohol / Behentrimonium chloride)	$\odot$

Foaming surfactants	
Cocamidopropyl betaine	$\odot$
Decyl glucoside	$\odot$
Sodium laureth sulfate	$\odot$
Polyquaternium-10	$\odot$
Cetrimonium chloride	$\odot$

рΗ

pH stability	
Acidic pH	🙂 ( Up to pH 3)
Neutral pH	$\odot$
Basic pH	😳 ( Up to pH 8)

<b>-</b> 0	
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T° stability	
45°C	$\odot$
75°C	$\odot$



Electrolyte compatibility	
Monovalent salts (e.g.: sodium PCA)	$\odot$
Divalent salts (e.g.: magnesium PCA, zinc PCA)	$\odot$



Compatibility with other substances		
Polysaccharides (Teflose <sup>®</sup> , Fucogel <sup>®</sup> )	$\odot$	
Ceramides and analogs (Rep'Hair <sup>®</sup> )	$\odot$	
Plant extracts	$\odot$	
Zinc pyrithione	$\odot$	
Piroctone olamine	$\odot$	
D-Panthenol (Provitamin B5)	$\odot$	
Vitamin B6 (Pyridoxine)	$\odot$	
Vitamin B3 (PP) (Niacinamide)	$\odot$	
Vitamin H (B7) (Biotin)	$\odot$	

### PROCEDURE:

Incorporate into the aqueous phase for root temperature processes. Incorporate during cooling, from 45°C, for hot processes. If the process requires, directly into the

hot mixture at 75°C.

PRECAUTIONS FOR USE: Do not expose to a temperature greater than 75°C, which would run the risk of denaturing the active ingredients in the product and reducing its effectiveness. Above pH 8, the product color may darken.

#### **FORMULATION EXAMPLE**

Hair Drop Lotion

Hair loss lotion

Hair tidiness shampoo

Anti-dandruff shampoo

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#### HAIR DROP LOTION, REF. : 220301/2



Have a hair-loss problem? Maybe it's time to boost your hair's growth!

This energizing lotion, with a light, non-oily texture, slows hair shedding and encourages hair growth with 2 complementary active ingredients: Cressatine<sup>®</sup>, which stimulates and prolongs hair growth by strengthening it from the root, and Kerastim<sup>®</sup>S, which prevents it from shedding. Apply once a day, ideally in the evening, directly to the entire scalp to get back the dense, vigorous

hair you once had.

	DEMINERALIZED WATER	Aqua	Qsp 100
	Preservatives	/	Qsp
	GLYCERIN	Glycerin	2.00
	ZEMEA (DUPONT)	Propanediol	2.00
А	Ethanol	Alcohol	20.00
	CRESSATINE <sup>®</sup> (SOLABIA GROUP)	Glycerin / aqua / nasturtium officinale extract /	2.50
		tropaeolum majus extract	
	KERASTIM <sup>®</sup> S (SOLABIA GROUP)	Tetrasodium disuccinoyl cystine	2.00
	VITAMIN B3 (ROCHE)	Niacinamide	0.50

В	CITRIC ACID, SOL AT 10%	Citric acid	QSP PH

#### PROTOCOL:

- Prepare phase A at room temperature.

- Homogenise the content.
- Adjust pH with citric acid.

### PHYSICO-CHEMICAL CHARACTERISTICS pH = 5.20 – 5.80 at 20°C

#### HAIR TIDINESS SHAMPOO, REF. : 220302/4



#### Not everyone is affected by dandruff equally!

From the first use, Hair Tidiness Shampoo begins effectively fighting dandruff--without leaving any residue on the hair or scalp.

This formula is enriched with Cressatine<sup>®</sup>, a combination of two Super-Leaves known for their haircare properties. The sulfur contained in Indian cress and watercress renews and strengthens the hair's structure at its root. In addition, Indian cress has purifying and anti-inflammatory properties that help fight dandruff and soothe irritated scalps.

The hair's strength and beauty increases exponentially, while the scalp is lastingly soothed and purified.

A	DEMINERALIZED WATER	Aqua	Qsp 100
	Preservatives	/	QSP
	CARBOPOL AQUA SF 1 (NOVEON)	Acrylates copolymer	8.00
	CRESSATINE <sup>®</sup> (SOLABIA GROUP)	Glycerin / Aqua / Nasturtium officinale extract /	2.50
		Tropaeolum majus extract	

	PLANTAPON 611C (BASF)	Sodium laureth sulfate / Cocamidopropyl betaine / Coco glucoside	25.00
	ABIL SOFT AF 100 (EVONIK)	Methoxy PEG/PPG-7/3 aminopropyl dimethicone	0.50
	LAMESOFT PO 65 (BASF)	Coco glucoside / Glyceryl oleate	1.00
В	ZINC PYRITHIONE (SOQUIBER)	Zinc pyrithione	3.00
	FRAGRANCE TILLEUL 38655-07 (NACTIS)	Perfume	0.30
	CROTHIX LIQUIDE (CRODA)	PEG-150 Pentaerythrityl tetrastearate / Aqua / PEG-6 caprylic /	0.20
		capric glycerides	

#### PROTOCOL:

- Prepare phase A at room temperature Add imgredients of phase B one by one while stirring slowly.

## PHYSICO-CHEMICAL CHARACTERISTICS

pH = 5.30 - 5.90 at 20°C η : 25 000 cps at 20°C, LVT 64, 12 rpm

