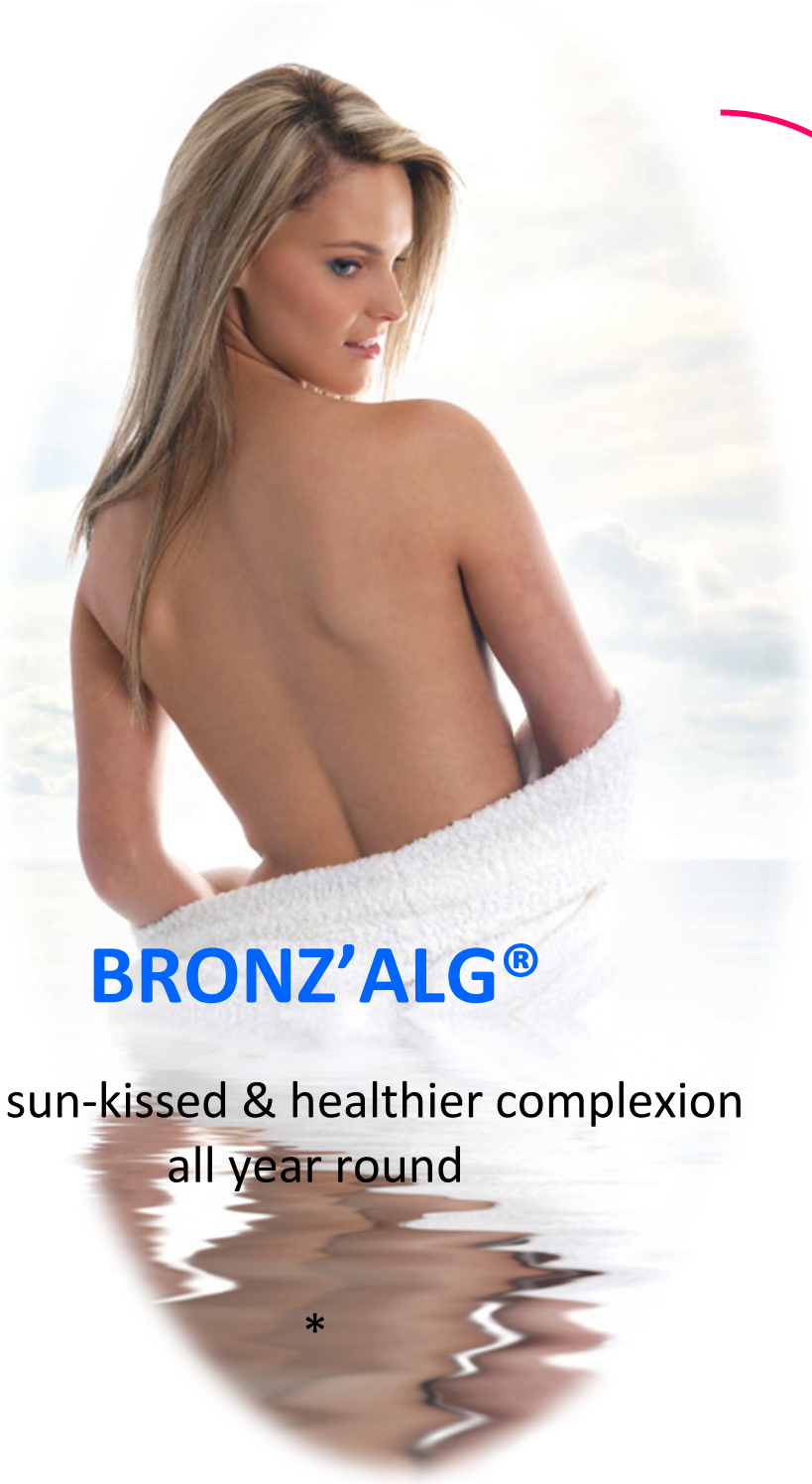


BRONZ'ALG®

For a sun-kissed & healthier complexion
all year round

*

Regulates the major genes of melanogenesis pathways
Provides UVA-UVB protection to skin
Promotes skin pigmentation independent to sun exposure
Accelerates tanning
Revives dull skin for a glowing appearance

Gelyma

An increasing demand in the Cosmetic industry concerns the development of products that may be applied topically to the skin for improving the condition and appearance of skin. Unfornunately sun exposure can damage to the skin.

An alternative to sun tanning is sunless tanning with products providing a pleasant sun tanned look with a potential benefit in terms of photoprotection in order to avoid the risk of UV radiation.

In order to satisfy such criteria, GELYMA offers BRONZ'ALG® that combines a calibrated aqueous extract of the brown seaweed *Bifurcaria bifurcata* with acetyl-tyrosine, the penetration of the algal extract into the skin being enhanced by the presence of acetyl-tyrosine.

Mechanisms of action

The mechanisms of action of BRONZ'ALG® have been proven by using different methods *e.g*. cosmetogenomic analysis, *in tubo*, *in vitro*, and *in vivo* testing.

BRONZ'ALG ® regulates the major genes of melanogenesis pathways

Genomic analysis on pigmented reconstituted epidermis (phototypes I - II) treated with 3% BRONZ'ALG® for 24h (n=3). Analysis by qRT-PCR on TaqMan cards. Collaboration Strati CELL-Belgium.

Melanogenesis involves transcriptional responses of the pigmentation genes in which a major role is supported by the microphthalmia-associated transcription factor (MITF) regulated by several signaling pathways.

The MITF promoter leads to transcription genes of the melanogenic enzymes tyrosinase (TYR) and tyrosinase-related protein-1 (TYRP-1) that increase melanin synthesis.

BRONZ'ALG® is able significantly to up-regulate the MITF factor and the melanogenic enzymes TYR & TYRP-1 but also to influence different genes of the Wnt/catenin and endothelin/protein kinase signaling pathways implicated in melanin formation, all that makes more compelling the pro-pigmenting capability of BRONZ'ALG®.

In addition, BRONZ'ALG® is capable to facilitate the melanin synthesis in melanocytes (action on SLC24A5) and to improve the interactions melanocytes-keratinocytes (action on E-cadherin).

The table here after summarizes the different implications of BRONZ'ALG® in the melanogenesis pathways.

BRONZ'ALG® is significantly capable to increase the melanin synthesis.

Assay	Gene names	3% BRONZ'ALG®	
		RQ.	*p value*
Involvement in MITF & melanogenic enzymes			
MITF-Hs01117294_m1	Microphthalmia-associated transcription factor	1.7	*0.017*
TYR-Hs00165976_m1	Tyrosinase	1.4	*0.035*
TYRP-1-Hs00167051_m1	Tyrosinase-related protein-1	1.4	*0.035*
Involvement in Wnt/β catenin pathway			
FZD10-Hs00273077_s1	Frizzled family receptor 10	2.0	*0.033*
CALML6-Hs00758338_g1	Calmodulin-like 6	1.6	*0.047*
Involvement in endothelin /protein kinase C pathway			
EDN1-Hs01115919_m1	Endothelin-1	2.1	*0.024*
EDNRB-Hs00240747_m1	Endothelin receptor type B	1.3	*0.037*
PRKCA-Hs00176973_m1	Protein kinase C, alpha	1.2	*0.032*
MAPK14-Hs00176247_m1	Mitogen-activated protein kinase 14	1.4	*0.030*
TNF-Hs00174128_m1	Tumor necrosis factor (TNF superfamily, member 2)	2.0	*0.003*
Involvement in the interactions melanocytes-keratinocytes			
CDH1-Hs01023894_m1	E-cadherin	1.6	*0.047*
Involvement in skin pigmentation			
SLC24A5-Hs01385407_g1	Solute carrier family 24, member 5	1.4	*0.036*

BRONZ'ALG ® protects against free radicals

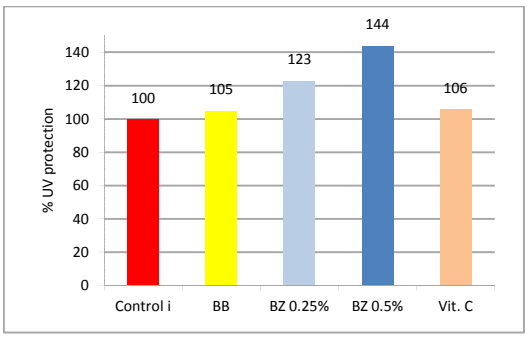
In tubo analysis studies by using DPPH assay.

BRONZ'ALG® offers interesting free radical scavenger properties. Its anti-free radical performance reaches 41% with 2% active. It exists a complementary action between *Bifurcaria bifurcata* extract and the acetyl-tyrosine solution.

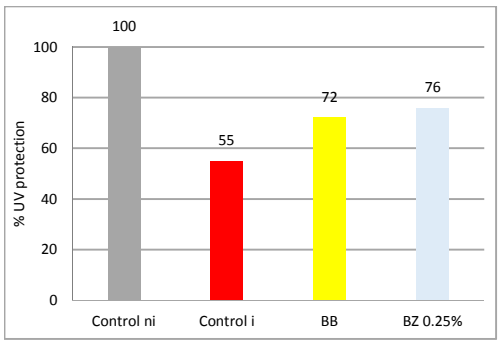
BRONZ'ALG ® protects against UVA / UVB-induced damage

In vitro studies on human keratinocytes submitted to UVA (dose 30 J/cm²) or UVB (15 mJ/cm²) in the presence or absence of different extracts: algal extract (same concentration than in the active), BRONZ'ALG® (BZ 0.25% & BZ 0.5%) vitamin C (dose 5.10^{-5}M). Comparisons with no irradiated and irradiated controls (control ni- control i). Protection evaluated by MTT test 24h after irradiation.

UVA



UVB

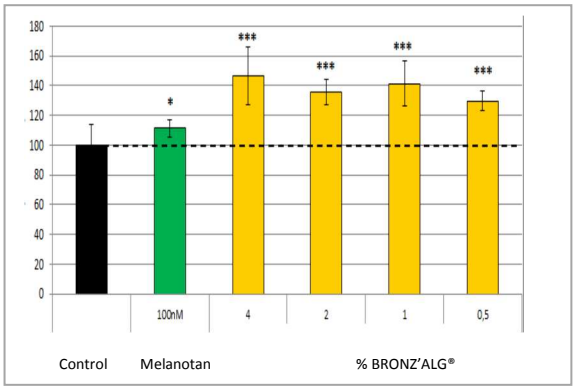


Results validated by two statistical analysis (ANOVA – least significant difference).

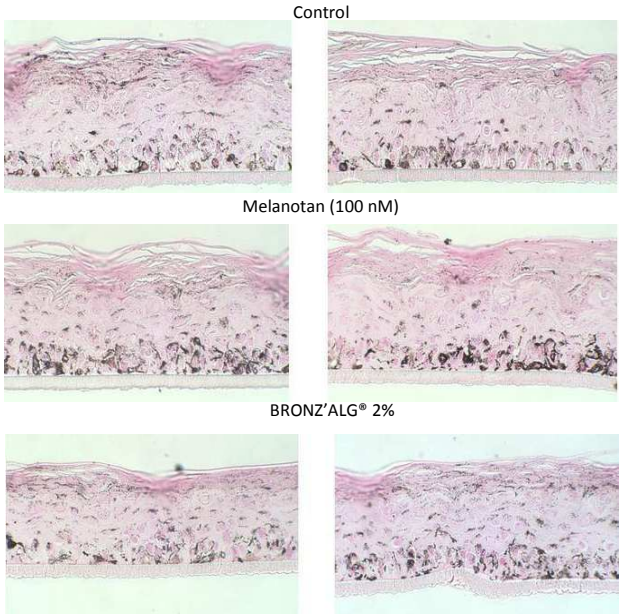
BRONZ'ALG® provides effective protection against both UVA and UVB irradiation.

BRONZ'ALG ® promotes skin pigmentation independent to UV exposure

In vitro studies on reconstituted pigmented epidermis (phototype IV) submitted to different doses of BRONZ'ALG®. Positive control: Melanotan (dose 100 nM). Extraction and quantification of melanin content after 6 days application. Histological staining observations for each experiment by using two staining techniques: Fontana-Masson and HES stains. Collaboration SEPhRA-France.

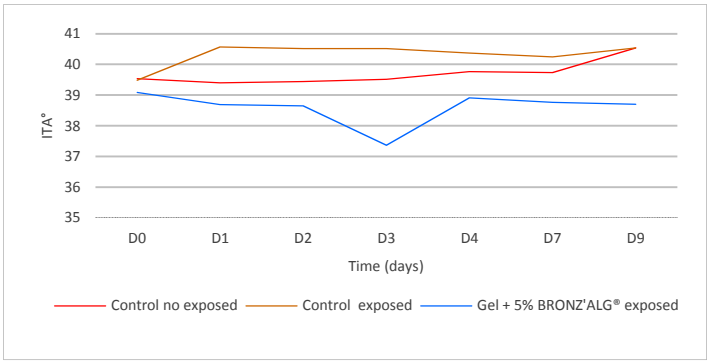


After 6 days application, BRONZ'ALG® highly significantly stimulates the synthesis of melanin by + 30 % with 0.5%
+ 41% with 1%.
compared to the control . Confirmation by histological staining observations.



BRONZ'ALG ® accelerates tanning

In vivo studies on 10 female volunteers, 27-58 years old, phototypes II-III, twice day application of a formulation with 5% BRONZ'ALG for 9 days. Three UVA+UVB exposures performed at Day 0, Day 1 and Day 2.Measurements with a chromameter Minolta CR 400. Evaluation of ITA°.
Collaboration IDEA Clinic-Romania.



The values of ITA° decreases at all times for 9 days. Thereby it exists an acceleration of skin color. Results statistically validated.

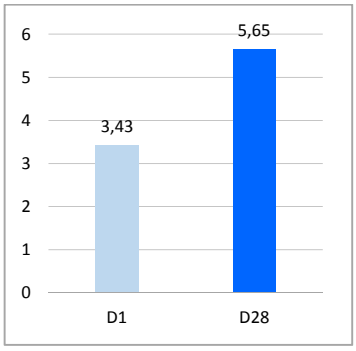
BRONZ'ALG® helps accelerate skin pigmentation induced by UV exposure.

BRONZ'ALG ® revives dull skin for a healthy glowing complexion

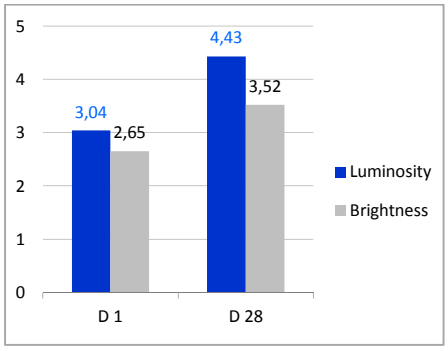
In vivo studies on 23 female volunteers, 38-70 years old, with dull skin. Twice day application of a formulation with 5% BRONZ'ALG for 28 days. Assessments by volunteers and the dermatologist at Day 1 and Day 28. Collaboration IDEA Clinic-France.

Assessment of subjective effectiveness

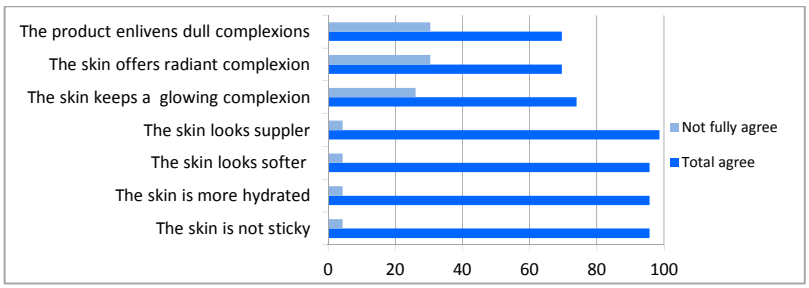
by volunteers

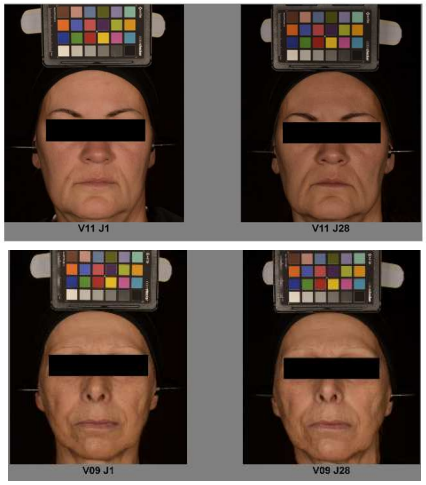


by dermatologist



Assessment of efficacy by volunteers after 28 days of use





BRONZ'ALG® induces healthier look and revives dull skin after 28 days application with a significant improvement in the radiance complexion.

83% of volunteers had a good overall cosmetic opinion of the product.

Cosmetic benefits

BRONZ'ALG® is able significantly to up-regulate the MITF promoter and the melanogenic enzymes tyrosinase –tyrosinase-related protein-1, but also to influence different genes of the Wnt/catenin and endothelin/protein kinase pathways implicated in melanin formation, all that makes more compelling the pro-pigmenting capability of BRONZ'ALG®.

This benefit for increasing melanin synthesis has been confirmed by *in vitro* studies. After 6 days application, with 0.5% BRONZ'ALG®, the synthesis of melanin increases by +30% compared to the control.

Photographs from histological staining observations illustrate

- the increasing of melanin content in cells whatever the tested concentration in active, thereby BRONZ'ALG® increases skin pigmentation independent of exposure to the sun,
- the good preservation of tissues after topical application, that proves the cutaneous acceptability of the product.

The results of the clinical tests on volunteers indicated that BRONZ'ALG® accelerates UV-tanning and revives dull skin for a healthier glowing complexion.

In addition BRONZ'ALG® guarantees efficient skin protection against free radicals and both UVA and UVB radiation, that helps maintain a harmonious tan and improve the skin's own natural UV protection.

Cosmetic applications

Cosmetic products for tan acceleration - Sun care protective products - Daily protection for enhancing glow and radiance.

INCI names: water (and) B*ifurcaria bifurcata* extract (and) acetyl-tyrosine.

Recommended use level: 0.5% - 5%.

GELYMA Parc d'Affaires Marseille Sud (C4) - 1 Boulevard de l'Océan - 13009 Marseille - France
Phone: +33 4 96 14 09 82 - Fax: +33 4 96 14 09 83 - E-mail: gelyma@wanadoo.fr