

SEA SOLUTIONS

BEAUTÉ
BEAUTY

COLLACTIVE™

Marine collagen and elastin peptides

Hydration
Anti-ageing



COLLACTIVE™ is composed of marine collagen and elastin peptides in the same ratio as in the dermis.

COLLACTIVE™ combines the two main constituents of the extracellular matrix and has an anti-wrinkle synergic action: elastin fibres give the dermis suppleness that completes collagen fibres tensile strength.

COLLACTIVE™ polypeptides have a low molecular weight, making it soluble in aqueous phase and fully digestible. COLLACTIVE™ is ideal for nutricosmetics.

- **COLLACTIVE™ REINFORCES SKIN HYDRATION**

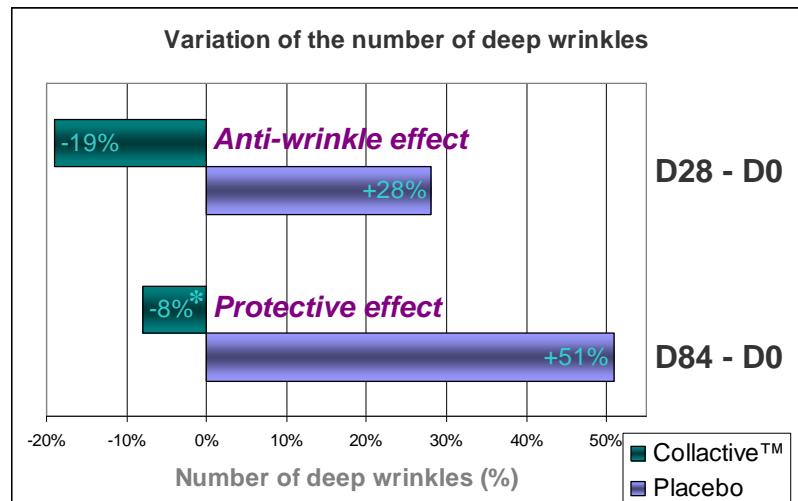
The moisturizing effect of COLLACTIVE™ is supported by a clinical study involving 43 women over 40 years old. The results show an increase of the entire epidermis hydration (+8%) after oral administration of COLLACTIVE™ for 3 months.

- **COLLACTIVE™ HELPS MATURE SKIN BUILD LIFT AND FIRMING CUSHION**

COLLACTIVE™ collagen and elastin polypeptides stimulate the biosynthesis of dermis main constituents to lift and tone slackening areas.

COLLACTIVE™ minimizes apparent lines and wrinkles as per the results of the clinical study (see graph).

On D84, the skin was exposed to cold temperatures, which explain the weaker anti-wrinkle effect at this period. The results highlight the protective effect of COLLACTIVE™ against the harsh conditions in winter.



- **COLLACTIVE™ IS A POTENT ANTIOXIDANT TO FIGHT AGAINST FREE RADICALS**

COPALIS – B.P. 239 – 62203 BOULOGNE/MER Cedex (France)

Tel. +33 (0)3 21 10 00 30 – Fax. +33 (0)3 21 10 00 39

info@copalis.fr – www.copalis.fr

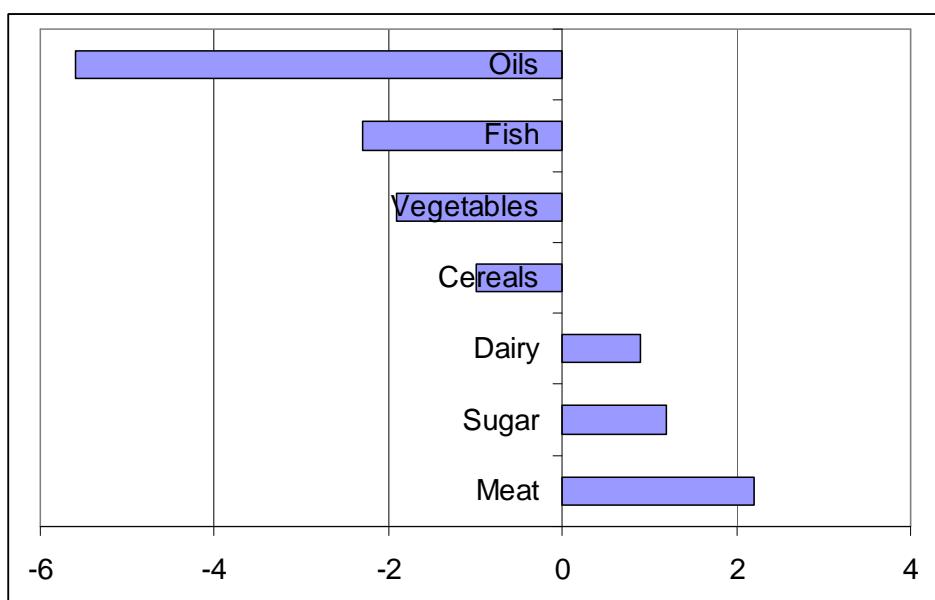
While life is increasingly stressful, time and serenity are becoming a priority among consumers and health, beauty and wellbeing tend to be perceived as a whole. There is an increasing crossover between the idea of inner and outer wellbeing, inner and outer beauty. In such a context, COPALIS has developed a natural oral cosmetic active that meets new market demand for nutricosmetics.

- INTRODUCTION -

Skin characteristics are known to be affected by endogenous and environmental factors, including aging, exposure to sunlight, chemicals, and mechanical damage. To maintain and improve skin condition, a wide variety of skin-care products are on the market. However, many skin problems originate from endogenous sources and food intake is frequently mentioned as influencing skin condition. Part of our knowledge of the relation between nutrients and skin comes from the incidence of skin problems as a result of nutritional deficiencies. But it has also been shown that the **optimization of the diet improve skin condition**^[1, 2, 3].

A study^[2] illustrated that skin wrinkling in a sun-exposed site in older people of various ethnic backgrounds is influenced by the types of foods consumed: 32% of the variance was predicted by food intake. Oils, fish, vegetables and cereals appeared to be protective (collectively explained 20% of the variance) (see figure 1).

Figure 1: Food predictors of skin wrinkling.



Not only food but also dietary supplements are also shown to positively influence skin appearance:

- Being the most abundant protein of the human body, **collagen supplementation has been widely studied**. It has been reported that the oral ingestion of collagen peptides affects various functions of the body. For example, lower bone mineral density in protein malnutrition and joint disease are improved by ingestion of collagen peptides^[4,5]. It has also been reported that hair thickness increased after prolonged ingestion of collagen peptides^[6] and that nail disorders, such as brittle nails, were improved by collagen peptides intake^[7].



- In the dermis collagen peptides supplementation has been widely studied. Matsuda et al.^[8] first showed that the water absorption ability of the skin stratum corneum of 20 volunteers increased after the daily ingestion of 10g of collagen peptides for 60 days. They then showed that collagen peptide supplementation for 62 days induces the increase of fibroblasts density and the increase of collagen fibrils size the density of fibroblasts, and diameter and density of collagen fibrils in the dermis^[9]: the ingestion of collagen peptides improves the mechanical strength of the skin in a collagen-specific manner. Taken together, these results suggest that the daily ingestion of collagen peptide improves the function of both the epidermis and the dermis.
- The effects of the daily ingestion of a collagen hydrolysate mixture (including 5g of type I fish collagen hydrolysate) on the skin properties of 25 women with dry and rough skin were also studied by Matsumoto et al.^[10]. They observed their skin properties before and after 6 weeks of ingestion. The following improvements were noted:
 - o *increase of the moisture of the face cheeks, the forearms and the back of the neck*
 - o *improvement of the viscoelastic properties (pliability and elasticity)*
 - o *skin smoothness, skin wrinkles and skin roughness values improvement (on the cheeks area)*

- CHARACTERISATION OF COLLECTIVE™ MOLECULES -

COLLACTIVE™ is composed of marine collagen and elastin peptides in the same ratio as in the dermis.

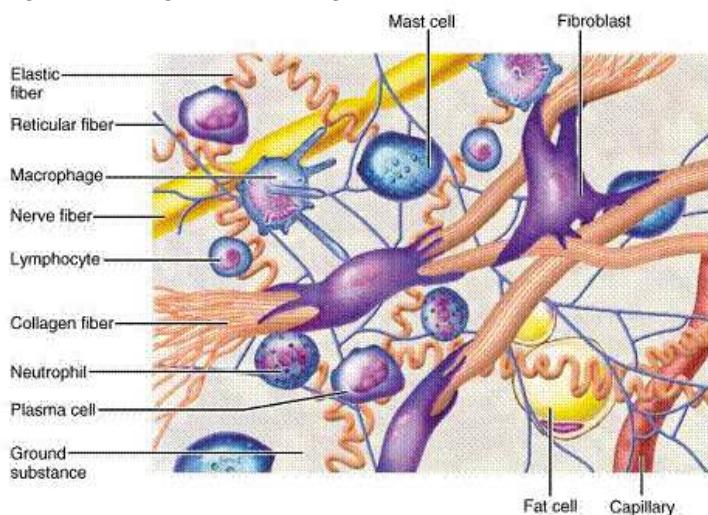
Collagen peptides stem from the hydrolysis of a type 1 collagen, characterised by its triple helix structure with two identical polypeptide chains ($\alpha 1(1)$) and a third that is genetically different ($\alpha 2(1)$). Each of the chains is composed of a sequence of amino acids where the sub-unit Glycine-X-Y is repeated. Glycine therefore represents 35% of all amino acids. Proline and hydroxyproline are also present at levels of respectively 13% and 8% of the total amino acids. COLLACTIVE™ collagen is very similar to human skin collagen. Indeed the dermis predominantly contains type I collagen (85 to 90%).

Elastin is a macropolymeric protein. Highly insoluble and extensively cross-linked, mature elastin is formed from tropoelastin, its soluble precursor. Tropoelastin is an <70-kDa protein consisting of an alternance of hydrophobic regions, responsible for elasticity, and cross-linking domains. Additionally, it ends with a hydrophilic carboxy-terminal sequence containing its only two cysteine residues.

***Collagen and elastin fibers within the skin* (figure 2)**

Collagen and elastin are abundant fibrous proteins in the skin. Many rodlike collagen molecules are cross-linked together in the extracellular space to form collagen fibrils that have the tensile strength of steel. The striping on the collagen fibril is caused by the regular repeating arrangement of the collagen molecules within the fibril. Elastin polypeptide chains are cross-linked together to form rubberlike, elastic fibers. Each elastin molecule uncoils into a more extended conformation when the fibre is stretched and will recoil spontaneously as soon as the stretching force is relaxed. Elastin fibres give the dermis suppleness that completes collagen fibres tensile strength.

Figure 2: diagram of collagen and elastin fibers



In the dermis, collagen fibres form 70% of the total proteins and are the main constituents of the extracellular matrix along with elastin fibres.

Degradation of these two types of fibres is responsible for the appearance of wrinkles and skin ageing.

- HIGH DIGESTIBILITY OF COLLECTIVE™ PEPTIDES -

Hydrolysed collagen and elastin of COLLECTIVE™ can easily be digested due to the peptide nature of these molecules. Published research has shown that collagen, in its hydrolysed form, can be easily absorbed. This property makes COLLECTIVE™ effective and beneficial at low doses in dietary formulas.

Several studies^[11,12] have shown that a substantial increase of collagen specific amino acids in serum is observed after subsequent oral administration of hydrolysed collagen. Iwai et al.^[12] identified a small peptide (Pro-Hyp) in the serum and plasma of healthy human volunteers who ingested collagen hydrolysates.

These results show that the oral administration of COLLECTIVE™ offers a useful source of amino acids for collagen and elastin biosynthesis.

- COLLECTIVE™ PEPTIDES ANTI-AGEING PROPERTIES -

The tolerance, the anti-wrinkle and the moisturizing properties of the daily ingestion of COLLECTIVE™ were assessed through a simple insu and parallel group clinical study.

MATERIAL & METHODS

Tested products

COLLECTIVE™ was put in capsules for its oral administration.

Placebo capsules contained maltodextrin.

Study design

A simple insu / parallel group study was performed on 43 healthy volunteers. Inclusion criteria were:

- Sex: female
- Age: between 40 and 55 years old
- Subjects with wrinkles on crow's-feet



Volunteers were not allowed to use any anti-wrinkle product on the measurement skin area (the use of this kind of product less than a month before the trial starting date was an exclusion criteria as well).

Two grams per day of either COLLECTIVE™ or placebo were ingested with a glass of water for 84 days. The subjects' skin conditions were measured at day 0, day 28 and day 84.

Assessment criteria

Measurements were done on the forearm and the face.

The anti wrinkles effect was evaluated by the measurement of the variation of different parameters of the cutaneous relief with Skin Image Analyser® and with Quantirides® software:

1. furrows of cutaneous microrelief (number and depth)
2. medium wrinkles (number and depth)
3. deep wrinkles (number and depth)

The cutaneous hydration rate was assessed using Hydrascan® and Corneometer®.

The cutaneous tolerance was evaluated through a clinical examination and volunteers were asked to fill a questionnaire to know their subjective evaluation.

RESULTS

			Statistical analysis			% of subjects with the expected effect
Number of deep wrinkles	D28 - D0	COLLECTIVE™	Δ% of the mean	p	significant	
		PLACEBO	28%	0.027	yes	18%
	D84 - D0	COLLECTIVE™	-8%	0.361	no	43%
		PLACEBO	51%	0.007	yes	12%

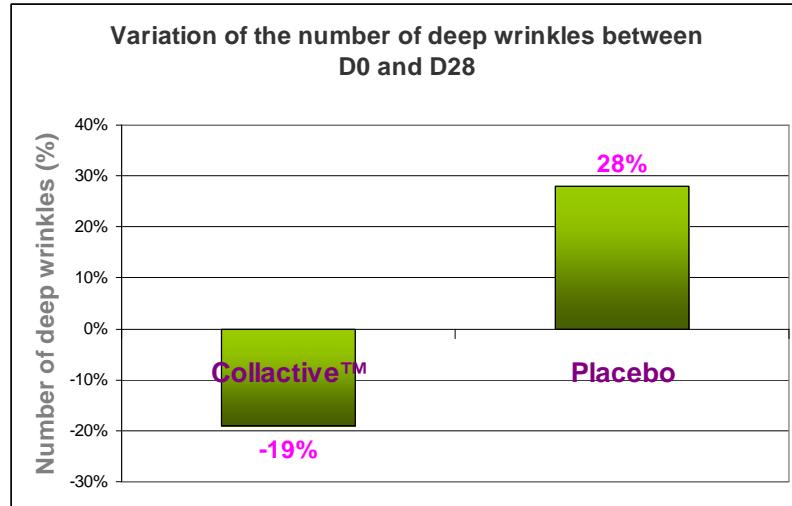
Where Δ is the variation (in percentage) of the number of deep wrinkles between day 0 and the day of measurement.

Under the above conditions, COLLECTIVE™ showed the following cosmetic effects:

- **Smoothing and anti-wrinkle effect after 28 days of treatment:**

In the COLLECTIVE™ group, a significant decrease of the number of deep wrinkles was observed after 28 days for 71% of the subjects. The average deep wrinkles reduction was equal to 19% (see graph 1).

The PLACEBO group showed a deterioration of the cutaneous relief with a significant increase in the number of deep wrinkles of +28% for 82% of the subjects.



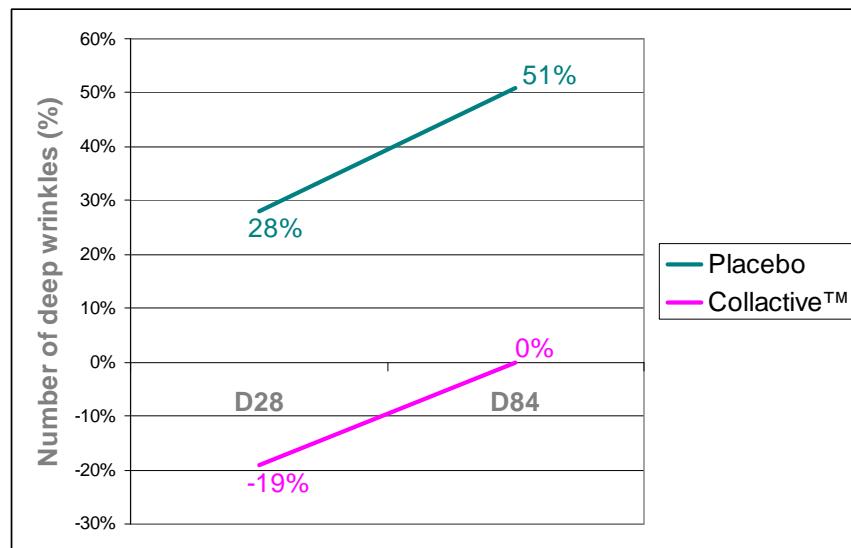
Graph 1: Variation of the number of deep wrinkles on day 28 in the COLLECTIVE™ and Placebo groups

- **A protecting effect after 84 days of treatment:**

Graph 2 above shows:

- o no significant variation in the cutaneous relief parameters in the COLLECTIVE™ group after 84 days
- o in the placebo group, a significant increase in the number of deep wrinkles of +51% on D84 was observed in 88% of the subjects

⇒ These results highlight the protective effect of COLLECTIVE™ against the harsh conditions in winter. Between day 28 and day 84, the skin was exposed to cold temperatures, which explain the weaker anti-wrinkle effect at this period. Indeed, the study was conducted during the winter season and the skin had to fight against harsh conditions. The protective effect of COLLECTIVE™ is confirmed by the observation of the deep wrinkle number variation in the COLLECTIVE™ group versus PLACEBO (see graph 2).



Graph 2: Variation of the deep wrinkles number on day 28 and day 84 - COLLECTIVE™ versus placebo

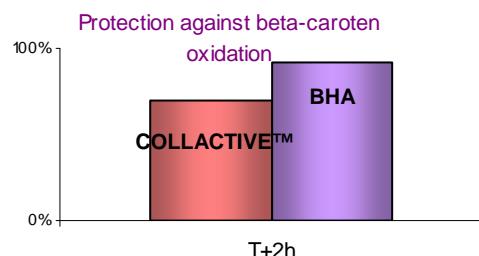
- **A moisturizing effect** on the entire epidermis and on the superior and median layers of epidermis (in average +8%)

DISCUSSION

In the conditions of the study, COLLECTIVE™ showed no side effects.

The results of this study confirmed previous published research^[8,9,10] on collagen peptides. By combining the two main constituents of the extracellular matrix, COLLECTIVE™ has a synergic anti-wrinkle action: elastin fibres give the dermis suppleness that completes collagen fibres tensile strength. When orally administered at 2g/day, COLLECTIVE™ collagen and elastin peptides stimulate the biosynthesis of the dermis main constituents to lift and tone slackening areas. COLLECTIVE™ minimizes apparent lines and wrinkles as per the results of the clinical study.

COLLECTIVE™ has a full anti-ageing action with potent antioxidant properties: the structural constituents of the dermis are thus protected against environmental damage (see graph).



- CONCLUSION -

COLLECTIVE™ is a natural marine bioactive with proven efficacy. It is adapted to nutricosmetics and food with beauty claim in the following formulations:

- anti-ageing
- anti-wrinkle
- eye contour
- moisturizer

Indications: skin ageing prevention

Properties: prevents and diminishes wrinkles – increases the moisture level of dry skin

Recommended use: 2g/day for 1 to 3 months
To be renewed several times a year

- TECHNICAL INFORMATION -

- **ORIGIN**

COLLECTIVE™ is developed in the respect of the environment, and the diversity and availability of the marine world:

- **COLLECTIVE™** stems from the recovery of natural raw materials
- **COLLECTIVE™** is extracted from by-products generated by activities linked to the marine world and therefore represents sustainable use of marine resources

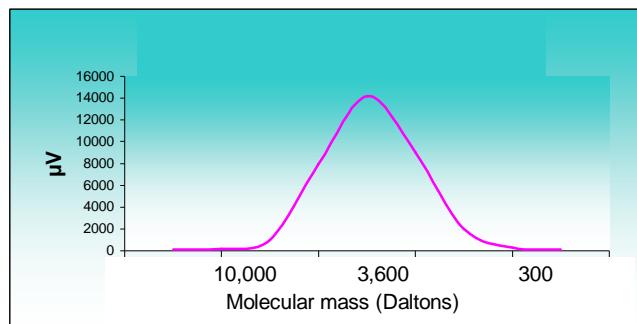
The extraction procedures used during the manufacture of **COLLECTIVE™** call on natural reactions without organic solvents.

- **Standard amino acid distribution* (% on total amino acids)**

Glycine	19.81	Isoleucine	1.06
Proline	11.71	Leucine	2.51
Hydroxyproline	8.74	Tyrosine	1.17
Glutamic acid	9.64	Phenylalanine	1.01
Threonine	2.20	Hydroxylsine	5.15
Aspartic acid	6.04	Lysine	3.51
Alanine	8.76	Histidine	1.12
Valine	1.74	Arginine	8.00
Methionine	1.80	Serine	6.04

*These values may fluctuate depending on the batch

- **Standard molecular distribution**



The molecular weight profile shows that **COLLECTIVE™** has a mean molecular weight of 3600 Da.

- **SOLUBILITY** soluble in water

- **ENERGY VALUE** 360 kcal/100g

- **SPECIFICATIONS**

Appearance	fine powder
Proteins (on crude product)	> 90%
Moisture	< 10%
Ashes	< 7%

NOTE: This scientific document has been drawn up to help users. It has been carefully prepared but the information that it contains is only provided as a guide. Our liability shall not be incurred by it in any way.



- BIBLIOGRAPHY -

1. Boelsma E, Hendriks HFJ, Roza L. Nutritional skin care: health effects of micronutrients and fatty acids. *Am J Clin Nutr* 2001;73:853–64.
2. Purba M, Kouris-Blazos A, Wattanapenpaiboon N, et al. Skin wrinkling: can food make a difference? *J Am Coll Nutr* 2001;20:71–80.
3. Boelsma E et al, 2003. Human skin condition and its associations with nutrient concentrations in serum and diet. *Am J Clin Nutr*, Vol. 77, No. 2, 348-355.
4. Koyama Y., Hirota A., Mori H., et al., 2001. Ingestion of gelatin has differential effect on bone mineral density and body weight in protein undernutrition. *J Nutr Sci Vitaminol* 47:84-86
5. Moskowitz RW, 2000. Role of collagen hydrolysate in bone and joint disease. *Semi Arth Rheum* 30:87-99
6. Scala J., Hollies NRS, Sucher KP., 1976. Effect of daily gelatine ingestion on human scalp hair. *Nutr Rep Int* 13:579-592
7. Tyson TL., 1950. The effect of gelatin on fragile fingernails. *J Invest Dermatol* 14:323-325
8. Sumida E., Hirota A., Kuwaba K., Kusubata M., Koyama Y., Araya T., Irie S., Kasugai S., 2004. The effect of oral ingestion of collagen peptide on skin hydration and biochemical data of blood. *J Nutr Food* 7:45-52
9. Matsuda N., Koyama Y., Hosaka Y., Ueda H., Watanabe T., Araya T., Irie S., Takehana K., 2006. Effects of ingestion of collagen peptide on collagen fibrils and glycosaminoglycans in the dermis. *J Nutr Sci Vitaminol* 52, 211-215, 2006
10. Matsumoto H., Ohara H., Ito K., Nakamura Y., Takahashi S., 2006. Clinical effects of fish type I collagen hydrolysate on skin properties, *New Technologies & Medecine* Vol. 7 No. 4
11. Oesser S., Adam M., Babel W., Seifert J., 1999. Oral administration of (14)C labeled gelatine hydrolysate leads to an accumulation of radioactivity in cartilage mice (C57/BL). *J. Nutr.*, 129(10), 1891-1895.
12. Iwai K., Hasegawa T., Taguchi Y., Morimatsu F., Sato K., Nakamura Y., Higashi A., Kido Y., Nakabo Y., Ohtsuki K., 2005. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatine hydrolysates. *J Agric Food Chem* 53:6531-6536