

# Collagen and Ageing

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An innovative liquid nutriscosmeceutical supplement  
to counteract skin and joint ageing

Published by MINERVA Research Labs, makers of  
PURE GOLD COLLAGEN®, GOLD COLLAGEN® FORTE AND ACTIVE GOLD COLLAGEN®







## Introduction

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For thousands of years, women (and many men) have sought to hold back the ravages that time and the environment have wrought on their complexions. Using a bewildering variety of creams, moisturizers, powders and potions we have attempted to make our skins look more youthful, hydrated, taut and toned. In particular we have struggled hard to prevent and then remove the ever increasing web of marks and lines that crease our faces as wrinkles.

Today, this singular focus on external fixes for skin ageing is being challenged. Oral formulations that arrive at the living layer of the skin, the dermis, via the blood stream have become a new and booming category in skin care. In particular those products such as GOLD COLLAGEN®, that contain hydrolysed collagen and antioxidants, are revolutionising the management of fine lines and wrinkles and look set to become an important mainstay in everyone's fight to retain younger skin.

These products are functional foods, not drugs thus they have no side effects. Having said this, there is increasing pressure from

users and regulators for clinical data that support their effects in the body. That's why some companies, such as Minerva Research Labs, the developer and manufacturer of GOLD COLLAGEN® products, are entering into rigorous clinical research programmes, partnering with leading academic institutions in the UK and in Europe, to demonstrate objectively that significant effects are being achieved. This research must be ethically approved, statistically robust and published in scientific peer reviewed journals.

This report looks in detail at what is becoming a step change in managing ageing skin. Importantly, it records the views of internationally renowned researchers and manufacturers who are now at the forefront of this revolution; it also looks ahead to other areas, such as joint care, where these collagen-based 'nutricosmeceuticals' look likely to bring important benefits. This is a comprehensive overview for potential users and healthcare and aesthetic practitioners alike.

**Dr Martin Godfrey MB ChB MRCGP**

*Head of Research and Development at Minerva Research Labs*

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# Collagen: the key to younger, healthier skin

Collagen boosting offers a huge leap forward in the field of management of the ageing process, with a growing number of scientific studies showing exciting evidence that it is possible to rejuvenate ageing or damaged skin, improve function of worn joints and trigger a variety of other body repairs.

Collagen is an essential scaffold protein that gives smoothness and elasticity to skin, and strength and flexibility to muscle and joints, but its production declines with age. Finding a way to halt or even reverse this process is fast emerging as an effective way to transform skin and hair, reduce the pain of joint damage and osteoarthritis, and repair age-related deterioration in other body tissues.

Research projects around the world have already demonstrated it may be possible

not only to improve supplies of collagen in the skin and connective tissues by consuming sophisticated "nutricosmeceutical" collagen supplements, but also to boost natural production of this essential building block that makes up 25% of our dry bodyweight.

Studies have shown that the collagen peptides not only migrate to the extracellular matrix - the spaces between cells - but also improve the function of the fibroblast cells that make not just collagen but also elastin and hyaluronic acid, the other main components of skin. The key question is understanding which of more than two dozen collagen peptides can be most easily and efficiently augmented and how best they can be modified to get into the bloodstream and from there to the sites where they can be used.

Minerva Research Labs based in London, is one of the leading innovators in this new field. Promising research results regarding their collagen supplements have already been published in peer-reviewed journals and have ignited widespread interest from a number of academic research groups.

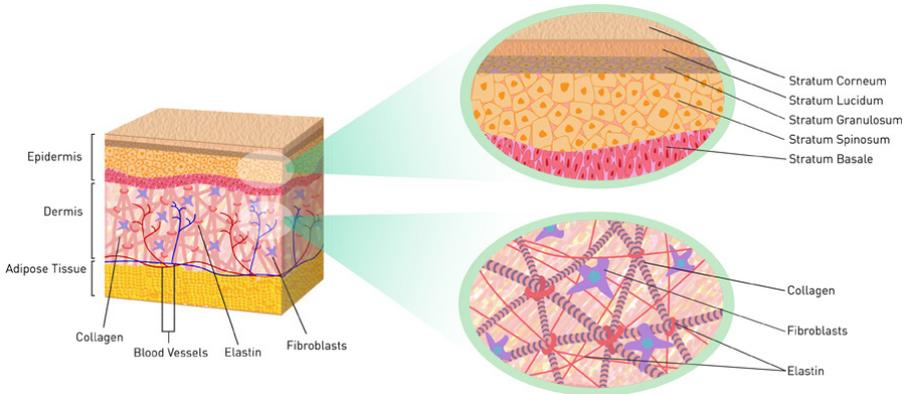


The organisation is now embarking on a £5m investment programme with a number of universities, to build on these preliminary studies. The studies are being funded by the booming sales of Minerva's sophisticated collagen products already on the market. The intention is to push back the frontiers of this new area of knowledge and establish what collagen replacement therapy can achieve. "We are all living longer and working longer. If

collagen supplements can be used to help rising generations maintain fitness, health and physical self-confidence in order to remain productive, we believe this work will have

## What is collagen?

Collagen makes up most connective tissue. It provides the mattress underpinning soft youthful skin and the cushioning to protect joints. Often described as the body's Lego block, it also builds ligaments, tendons, blood vessels, corneas and even dentine in teeth. It occurs in about 28 different forms with type I the variety found in skin, the most common. It is produced by cells called fibroblasts that also produce elastin and hyaluronic acid which maintain the skin's essential moisture and elasticity.



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*The collagen in the skin*

**A significant number of clinical studies have shown combinations of collagen peptides and other active ingredients can stimulate repair mechanisms for skin, muscle, cartilage, hair and nails.**

made a remarkable contribution to society,” Tony Sanguinetti CEO of Minerva. The notion of using oral collagen as a means of boosting body supplies of the anti-ageing compound, is now well established in Japan and elsewhere in Asia. Although growing numbers of informed British consumers are reporting

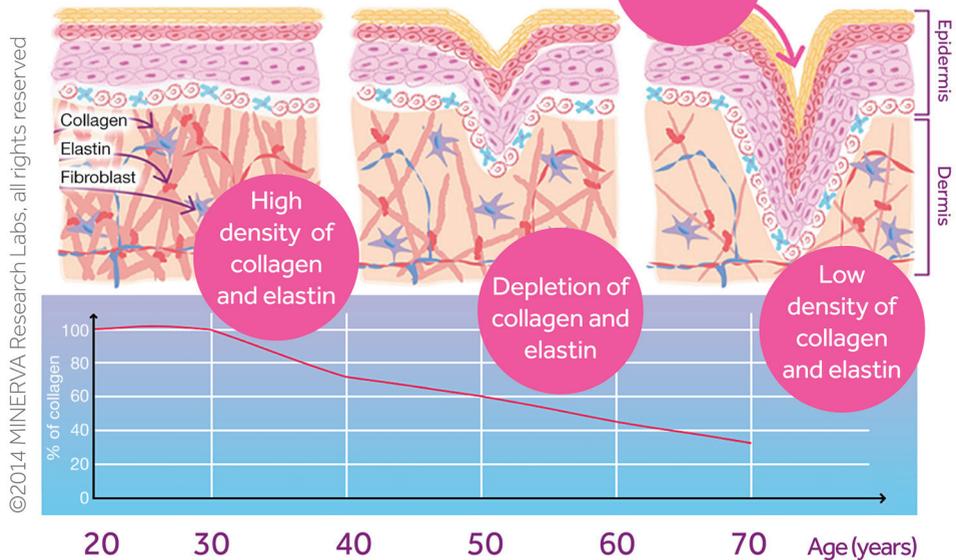
dramatic benefits from oral and particularly liquid collagen, there has until now been little understanding or recognition of the scientific evidence for this approach.

A significant number of clinical studies have shown that a combination of collagen peptides and other active ingredients can stimulate repair mechanisms for skin, muscle, cartilage, hair and nails. The research being funded by Minerva is seeking to understand how these mechanisms work. Their plan is to improve and significantly extend the existing range of products so they are better able to slow down the ageing processes that damage skin and connective tissues, and impact lifestyle.

## Natural ageing process



Pictures for illustrative purpose only



### What is the ageing process in skin?

From early adulthood, fibroblasts become less active and collagen production declines by about 1.5% a year. Ongoing sunlight and pollution exposure and reduced efficiency in eliminating free radical chemicals, add to the damage. However recent studies have shown that if the right

sort of collagen peptides and other active compounds are ingested they will travel to sites in the body where fibroblasts are present. This not only bulks connective tissue but also stimulates fibroblasts to produce more collagen, elastin and hyaluronic acid, rejuvenating skin and other tissues.

## What is MINERVA doing?

Minerva is working with a variety of collagen peptides and anti-ageing agents.

There are three different fully tested Minerva oral collagen formulations on the market so far, each incorporating collagen peptides plus vitamins, minerals, oils and antioxidants:

### PURE GOLD COLLAGEN®

first marketed in 2011 with nearly 10 million bottles sold to date



YOUNGER  
LOOKING SKIN



HEALTHY  
HAIR



STRONGER  
NAILS

### ACTIVE GOLD COLLAGEN®

launched in 2013, aimed at people with active lifestyles and those needing support for joints and muscles



YOUNGER  
LOOKING SKIN



JOINT  
COMFORT



MUSCLE  
RECOVERY

### GOLD COLLAGEN FORTE®

launched in 2014, a more sophisticated version, with higher levels of antioxidants, aimed at over 40s



REDUCE  
OXIDATIVE STRESS



REDUCED  
WRINKLES



SKIN  
HYDRATION

Studies have shown all three products have different, but measurable benefits on skin, joints, hair, nails and other types of connective tissues.

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# New research shines a light on anti-ageing solutions

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Minerva's projects are seeking to answer several important questions

## Does Minerva's sophisticated nutraceutical slow down the age related degeneration of natural collagen and elastin from connective tissue?

The answer is that it does seem to. A Minerva funded study led by Janis Shute professor of respiratory pharmacology at Portsmouth University, has investigated how different formulations of collagen peptides and other active ingredients can stimulate skin fibroblast cells to produce more collagen and elastin. Minerva contacted Shute because her laboratory had been working for many years with fibroblasts. Her team has perfected methods of analyzing fibroblasts' response to different stimuli. In this case they used various compounds supplied by Minerva to see what protein production was triggered in the fibroblasts, especially the amount of elastin and collagen produced.

Ageing fibroblasts produce enzymes called matrix metalloproteinases (MMPs) that destroy collagen and elastin in the skin. MMP production is also activated by sunlight

### 1. Digestion

Hydrolysed collagen remains intact through the digestion process in the stomach and small intestine.

### 2. Absorption

Hydrolysed collagen is readily absorbed by the small intestine and passes into the blood stream.

### 3. Distribution

Hydrolysed collagen reaches the skin and joints through the bloodstream activating the fibroblasts in the skin and chondrocytes in the joints.

### 4. Action

The cells are stimulated to produce new collagen, hyaluronic acid and elastin to maintain the health of these tissues.



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## How GOLD COLLAGEN® works

exposure. The objective of the study was to investigate whether a Minerva's collagen formulation could slow this process down. Professor Shute said she agreed to do the project because she had been impressed by very good data from other Minerva clinical trials.

"We are in the process of explaining the mechanism by which hydrolysed collagen and specifically Minerva's products exert their effects on fibroblasts. It will give confidence in the use of this product and its underlying mechanism of action." Her team's results will be published later this year.

**Can sophisticated collagen supplements improve muscle and tendon function to help promote stair-climbing balance in elderly people?**

## Tony Sanguinetti - a collagen pioneer



Tony Sanguinetti, the entrepreneur and nutricosmeceutical pioneer behind Minerva, acknowledges there is a hurdle in convincing women that a collagen drink will actually do a great deal more than any

amount of seductively scented smoothing collagen moisturizer that merely sits on the surface of the skin. But he is himself an advertisement for use of the product. His extraordinarily smooth and unblemished skin belies his 49 years, and is testimony to four years of GOLD COLLAGEN® supplementation.

His interest in the product came about when he was setting up a biotech company in Japan six years ago. "I was observing that lots of Japanese women had remarkably good skin and discovered that oral supplementation with fish collagen was a normal routine for many of them," he says. "I started investigating and discovered a huge amount of research already showing that boosting collagen levels is possible"

"Thousands of food supplements have been launched in the past 30 years, with little innovation, mostly making claims based on old vitamin and mineral research data. We at Minerva are trying to change the market by developing a nutricosmeceutical that really does make a difference and has the research evidence to prove it. We use only top quality natural products formulated and tested with the same rigor as those used in the pharmaceutical industry."

Independent scientific studies set up by Minerva in partnership with a variety of medical centres of excellence across Europe such as University College London and the University Hospital at Reggio Emilia in Italy, are showing that collagen replacement will:

- Slow skin damage caused by age
- Help repair damage caused by sun exposure
- Help interrupt the process of age-related collagen breakdown
- Help improve joint mobility and reduce arthritic pain in elderly people.

There have already been promising results from numerous other studies.

Now Dr Thomas O'Brien, a senior lecturer in muscular skeletal biomechanics at Liverpool John Moores University, has been recruited by Minerva to test another brand new formulation to see if it is possible to improve quality of life in older people at risk of life-limiting falls. If the trial is successful, the new product will be added to Minerva's portfolio and could also be used to help sportspeople. The four-year study involves a total of 200 people divided into two age groups of young and 65+ year-olds. Each age group will then

be divided again into three groups, with one third to receive ACTIVE GOLD COLLAGEN®, one third to receive the brand new joint specific product and the others receiving placebo. Neither research subjects nor researchers will know who has received the treatment and who has the placebo. The research team will measure improvements in force and strength using high-tech simulated stair-climbing equipment of varied height. They will also use a variety of ultrasound and other scanning techniques to measure changes in bone mineral content, muscle strength and knee tendon properties.

"There have been some related trials suggesting collagen supplements can alleviate osteoarthritis joint stiffness and pain," O'Brien said. "Minerva's *in vitro* experiments have demonstrated positive results and I am optimistic this compound will have an effect."

"We hope to see an improvement in collagen levels in tendons and therefore improved muscle function. We know that exercise is the best solution but most people never do enough. If this new treatment is effective to reduce pain, loss of mobility and falls in elderly people then I am very hopeful we will have done something of benefit to society."

### **Can consumption of GOLD COLLAGEN® FORTE improve collagen quality in the skin of healthy people over 40?**

Research on Minerva's products already on the market, has inspired the team to invest into further studies.

In the past, the only way to examine skin health was by taking a full-depth tissue sample using a hole punch – not a popular option for the face because it would leave a dramatic permanent scar. The latest generation of confocal microscopes gives skin scientists a better way of measuring the efficacy of anti-ageing interventions by lighting up individual microscopic elements in the skin and allowing scientists to study subcellular activity within the dermis.

Dr Caterina Longo, a specialist in the dermatology and skin cancer unit at the University of Reggio Emilia, pioneered the technique for investigating

skin cancer, and has gained a worldwide reputation as an expert in this new field. She has been commissioned by Minerva to conduct a study involving regular comparisons of skin quality in 180 women aged 30 to 60. Half of them will receive Minerva products and the rest will receive an identically packaged and flavoured placebo drink. Longo is hoping to see greater volumes of collagen present in the facial skin of the treatment group at the end of the study. "At the moment, although we can see this product is helping we don't really know the extent of positive effects in the long-term," she said. "It's likely the benefits will be greater in younger women because after the menopause it is harder to make a difference, but we will see. If it does work it would transform the skin, not just in terms of beauty but in terms of health because people would have greater protection against skin cancer."

### **Can GOLD COLLAGEN® prevent and repair the damage caused by sunburn?**

Collagen is destroyed by sun exposure, an effect that can now be measured using latest skin imaging techniques. It is known that antioxidant repair mechanisms to counteract the cell-destroying effects of free radicals, decline with age. Skin scientists in Rome are embarking on a trial to see if the collagen peptides and antioxidant combination in GOLD COLLAGEN® FORTE can stimulate production of new fibroblast cells, and/or increase natural production of collagen and elastin, as well as boosting antioxidant defence mechanisms to

fight skin-ageing. Andrea Corbo, a professor of dermatology who is leading the research, says at least five studies in the past decade



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have suggested high dosage collagen supplementation could be an answer to the skin cancer epidemic which has hit a generation of sun worshippers.

"We will evaluate the benefits of the product in a double blind, placebo-controlled three months trial involving 60 women, 35 to 55 year-olds," he says. "We know collagen-based products do not go through the skin if they are simply applied externally, but there is some evidence that these oral formulations do result in collagen peptides migrating to the skin from the inside."

"We have a variety of imaging techniques to see if collagen is indeed making a difference to the level of damage caused to the skin by sun exposure and if it boosts repair mechanisms. We expect to report some results later this year."

#### **What has research shown so far?**

Dr Sara Sibilla, Minerva's clinical trials manager and senior research scientist, has already published in respected independent peer-reviewed journals four different studies on the benefits of collagen peptides.



"With age collagen, elastin and hyaluronic acid are less produced. Skin dries out and wrinkles form. Our formulations and collagen peptides work in two different ways. They stimulate the production of new collagen and they act as ligands, binding onto receptors on fibroblast membranes and stimulating the fibroblast to produce elastin, as well as the other proteins of the extracellular matrix that skin needs to be healthy. As well as skin benefits, we have also seen improvements

in hair with reduced hair loss, and healthier nails".

#### **What do other scientists think?**

In 2005 the Cochrane Collaboration which assesses research evidence for healthcare procedures, reported on the efficacy of treatments for ageing and sun damaged skin. It said up to 90% of skin damage was the effect of sun exposure and acknowledged that for the first time effective treatments were becoming available that could improve skin, but said at that time the efficacy of oral agents 'largely remains unclear.'

A second review in 2009 discussed collagen damage caused by sun exposure and said injected collagen could produce "visible and microscopic improvement in photo damaged skin but [they] are not without risk and contain no element of prevention."

However, there is growing interest. Professor Des Tobin, director of Bradford University's Centre for Skin Sciences, said "I do think there is something in this. When people are prepared to submit their products to randomized controlled trials, they have to be convinced the trial will show a benefit."

Doris Day a New York dermatologist who has become a prominent media campaigner against facelifts, has pointed to the growing base of clinical results with collagen: "Further independent studies are needed to see if the data holds true, but I think we need to open our minds to more creative approaches," she says.

#### **What about other competing companies?**

Minerva has become one of the major pioneers of sophisticated nutricosmeceuticals along with Shiseido of Japan and Gelita of Germany. Gelita has patented a variety of compounds and its skincare Verisol has been shown to reduce depth of eye wrinkles by 20% after eight weeks use.

Professor Steffen Oesser, a biochemist from Kiel University who now runs Germany's Collagen Research Institute, developed

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Verisol and was the first person to prove by using fluorescent markers, that ingested collagen peptides migrated to skin, connective tissue and joints.

"It would be naïve to say that taking oral collagen can stop you ageing altogether, but it can boost body repair processes, reduce collagen degradation and help with reducing the damage and pain caused by osteoarthritis," he says.

More recently, the American drug giant Pfizer has bought the rights to Imedeen, a once-a-day tablet, which has been shown in published studies to have some benefit in boosting collagen production. A similar tablet product derived from joint research by Nestle and L'Oreal, had been sold across Europe. "There is no question this approach does work" said Patricia Pineau, L'Oreal's director of scientific communications

Meanwhile, L'Oreal has been marketing oral collagen in China through its upmarket Yue Sai brand.

Scientists at Proctor & Gamble, L'Oreal's main rival in global cosmetics, also recognize the benefit of collagen. "There are plenty of studies and publications discussing the benefits of collagen peptides," said Frauke Neuser, a P&G scientific spokesman. "At the cellular level, they have been shown to increase collagen production, which at the macro level leads to significant reduction in fine lines and wrinkles."

### **What do consumers think?**

Modern consumers are now scientifically literate and expect to have access to research evidence for products they buy. This trend has been of huge benefit for PURE GOLD COLLAGEN® which since its launch in 2011 has managed to carve out a phenomenal market with minimal advertising, because women of all ages have been convinced by the science.

A study run by Boots on 17,000 customers taking GOLD COLLAGEN® discovered an evenly spread age range of 18 to 65 year-

olds taking the product. Harrods, London's flagship department store, which was one of the first retailers to stock the product, says 30% of customers are now men.

"Users are people who buy it simply because it improves the appearance of their skin" - Harrods' spokesman said. "There is no particular age group among the men or the women, but there is a growing number of regular customers for it."

There is a growing recognition that quality of life is vastly more important than quantity. As more of us make it to our 80th, 90th birthdays and beyond, we want to ensure we are in a physical condition to enjoy those extra years.

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