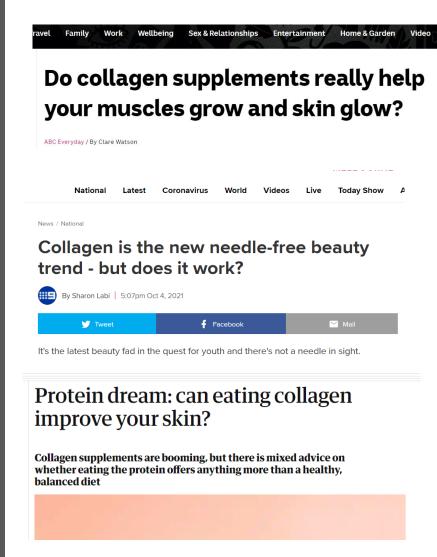
Glow from within

Unlocking the skin health benefits of collagen peptides

Dr Tim Crowe

BSc(Hons), MNutrDiet, PhD







Do collagen supplements work?

Can you really improve your skin, hair, nails and joints simply by popping a pill or eating collagen-enriched foods?

WEBMD HEALTH NEWS

Collagen: 'Fountain of Youth' or Edible Hoax?



Medically Reviewed by Brunilda Nazario, MD on December 12, 2019



Can collagen supplements REALLY reduce the appearance of wrinkles? Reviewers share impressive before and after photos using Proto-col collagen drink sachets - and you can get 30% off with our discount

- The Proto-col Complete Collagen Drink Sachets, which cost £31.95 for a box of 14, are unlike other collagen-boosting collagen drinks on the market
- · They are the first to combine two different collagen peptides in one product
- · MailOnline readers can get 30 per cent off Complete Collagen sachets from Proto-col by applying discount code MAIL30 at checkout

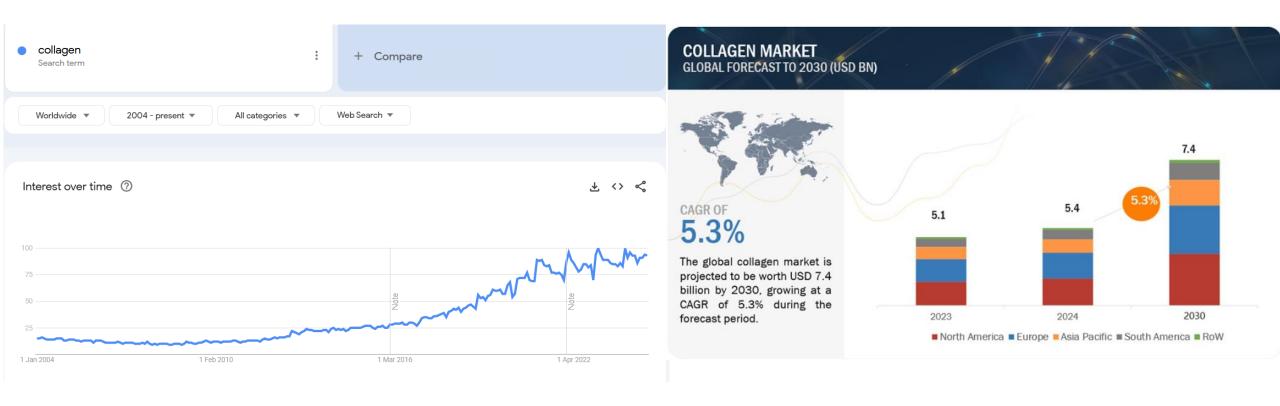
By EMILY KNOTT FOR MAILONLINE PUBLISHED: 23:06 AEDT, 22 October 2021 | UPDATED: 01:33 AEDT, 23 October 2021 The New Hork Times

SCAM OR NOT

Are There Benefits to Collagen Supplements?

Maybe! But get ready for a long-term relationship.

Collagen is on trend

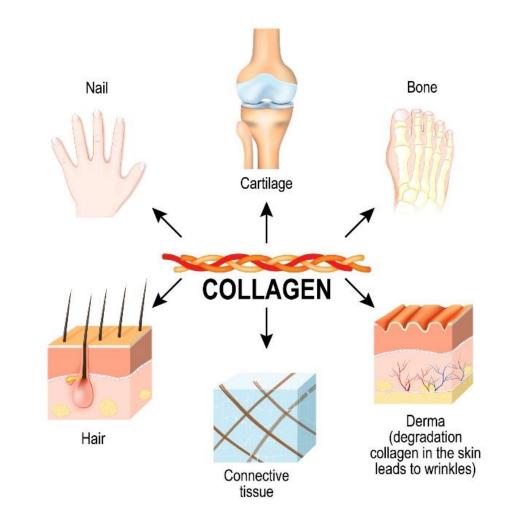


Source: Google Trends

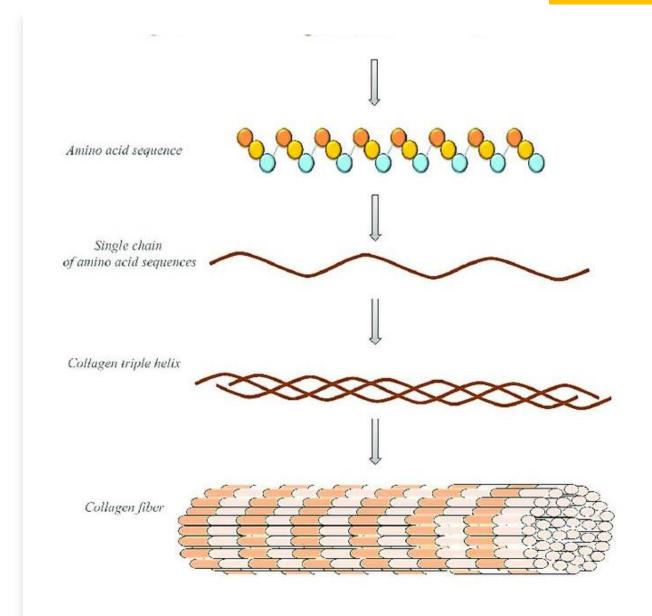
Source: Markets and Markets > Collagen Market www.marketsandmarkets.com/Market-Reports/collagen-market-220005202.html

Collagen is the most abundant protein in our body

30 percent of body protein is collagen Is the main structural component of connective tissue



Collagen is composed of repeating tripeptide units mostly made up of glycine (every third residue), proline and hydroxyproline which make up the bulk of the structure formed into a triple helix chain

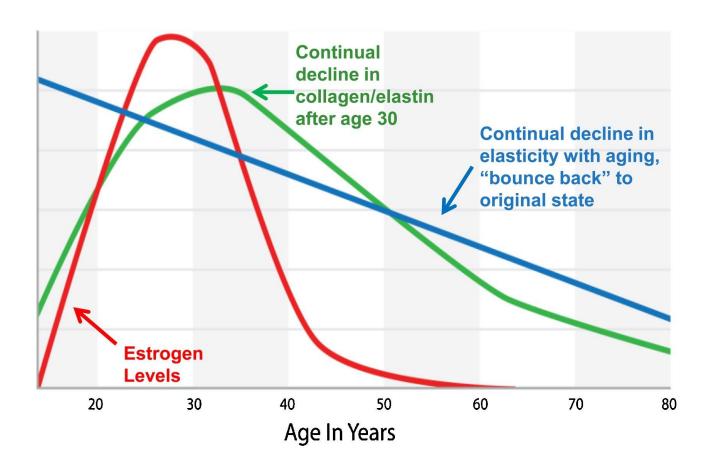


Collagen and elastin with age

Collagen degradation starts in our 20s
Similar falls in elastin and hyaluronic acid

Sunlight, smoking, environmental pollution, alcohol abuse and nutrient deficiencies can all accelerate this loss

All this leads to ↓ volume, ↓ elasticity, ↓ epidermal thickness, ↑ wrinkles and ↓ capacity to retain moisture



Types of collagen

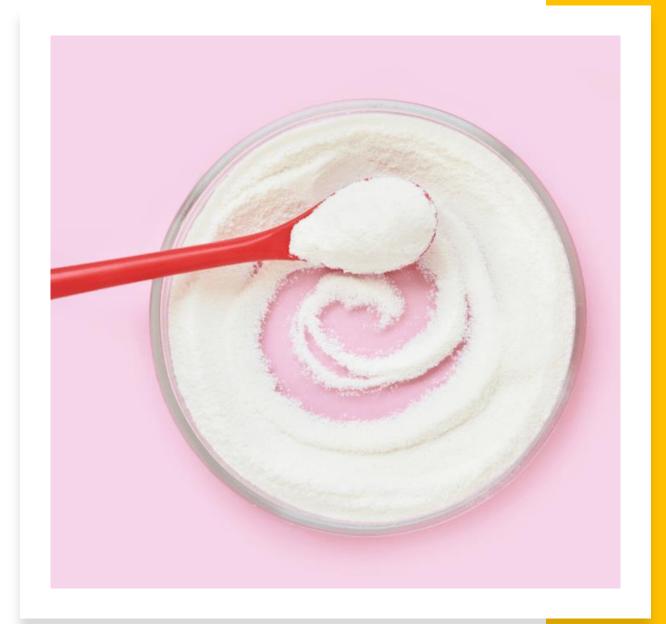
29 distinct types of collagen

Type I found in skin, dentin, corneas, blood vessels, bone and tendons

Type II primarily found in cartilage

Type III found in skin, ligaments, blood vessels and internal organs

Skin is 80% type I and 15% type III



Collagen in our diet

Meat (especially tougher cuts) and meat on the bone with more connective tissue

Organ meats

Chicken skin and chicken wings (joints in the wings provide cartilage)

Pork skin

Eggshell membranes

Fish with skin on, canned fish with bones and whole sardines

Jellyfish



What about bone broth?

Made by simmering bone and connective tissue to extract collagen (in the form of gelatin) as well as additional amino acids, minerals and bone marrow

Not a reliable source of key amino acids (glycine, lysine, proline, leucine, hydroxyproline and hydroxylysine) with a large degree of variability

Poor source of minerals (<50 mg of calcium per cup) and only a good source of micronutrients when vegetables added to it



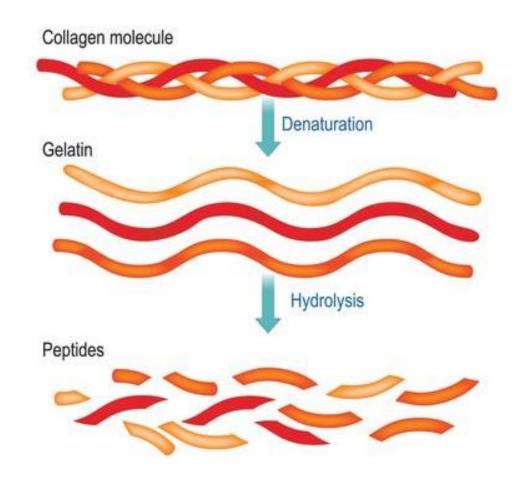
Why hydrolysed collagen?

When you heat collagen, it is denatured to gelatin

Gelatin is large and relatively insoluble

Hydrolysing gelatin breaks it into peptide chains of 30-60 amino acids in length

Hydrolysed collagen has greater water solubility and no gelation at room temperature



But surely it all just becomes single amino acids in the body which are indistinguishable from any other protein source we eat???



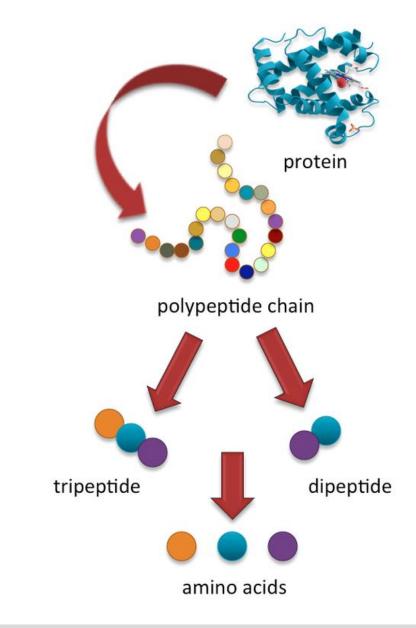
It's all about the peptides

Digested collagen is absorbed as single amino acids and unique di- and tri-peptides

The peptides are most commonly characterised by hydroxyproline-proline and hydroxyproline-glycine sequences

Hydroxyproline-proline also generated by degradation of endogenous collagen in tissue undergoing inflammation and at wound healing sites in the skin

Very few mammalian proteins apart from collagen (and elastin) contain hydroxyproline

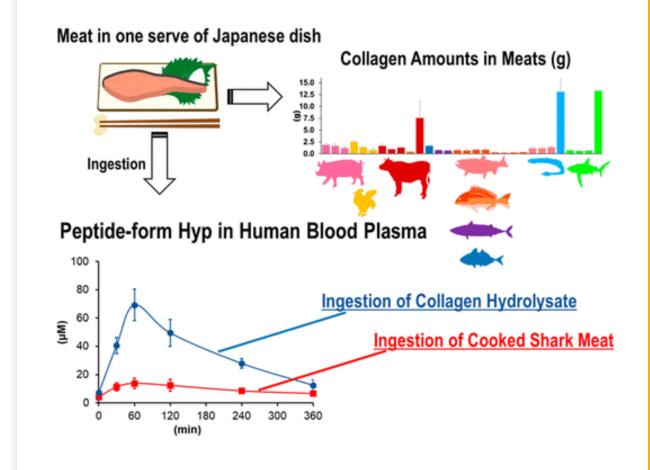


Native collagen vs collagen peptides

Collagen peptides show greater absorption and functional effects than native collagen forms such as gelatin

Native collagen in food also shows poor digestibility and absorption when compared to collagen peptides

Evidence that lower molecular weight peptides have greater antioxidant and improved skin photoageing effects

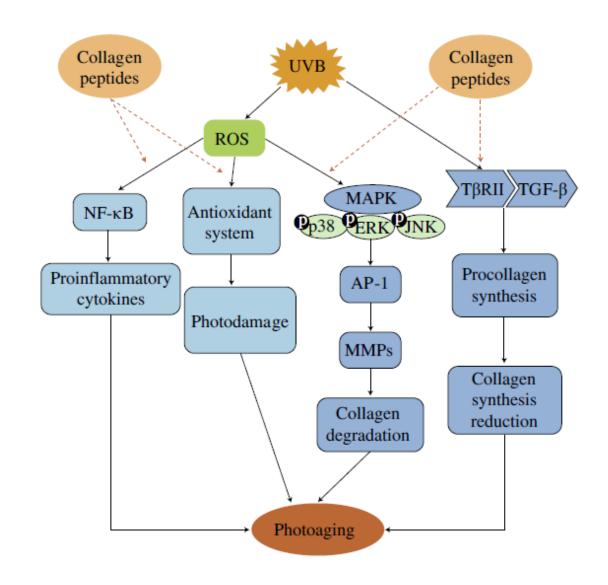


Collagen peptides in the skin

After absorption, collagen peptides are distributed in the body (especially to the skin) where they can remain in place for up to 2 weeks

Act as signalling molecules on fibroblast cell surface receptors to stimulate collagen, elastin and hyaluronic acid production as well as enhance proliferation of these cells

Also enhances the activity of antioxidant defence enzymes and inhibits inflammatory cytokines



But all those newspaper articles say that there is no evidence collagen supplements work. And what evidence there is has been funded by collagen manufacturers???



And then in March 2021, this happened



Review

Effects of hydrolyzed collagen supplementation on skin aging: a systematic review and meta-analysis

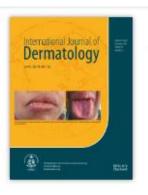
Roseane B. de Miranda MD, Patrícia Weimer MD, Rochele C. Rossi PhD 🔀

First published: 20 March 2021 | https://doi.org/10.1111/ijd.15518 | Citations: 9

Conflict of interest: None. Funding source: None.

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Volume 60, Issue 12 December 2021 Pages 1449-1461





Recommended

Oral collagen supplementation for skin aging: A fad or the future?

Nikita Jhawar BS,

What was studied?

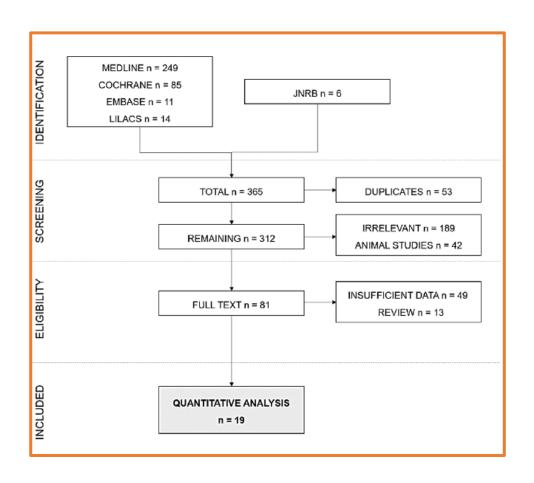
19 placebo-controlled, double-blinded randomised trials

1,125 participants aged 20-70 yrs (95% female) with mean age of 50 yrs

Doses ranged from **0.6 g/d to 12 g/d** for up to 4 months

Used a range of collagen formulations (mostly commercial) with and without additional ingredients (e.g. vitamins, minerals, antioxidants, CoQ10, hyaluronic acid, chondroitin)

Outcomes: Skin hydration, skin elasticity, skin density and wrinkles



What did they find?

Supplementation with hydrolysed collagen saw a significant effect on skin hydration, skin elasticity, skin density and wrinkles

Benefit seen by 60 days and maintained for 30 days after end of the study

No adverse events reported in any study

7/19 studies did not involve commercial funding nor were any COI issues reported by the authors

Authors of the review reported no COI and received no funding

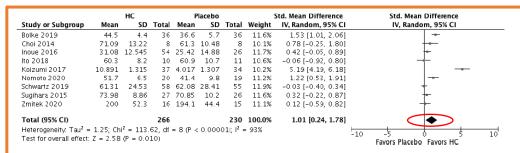
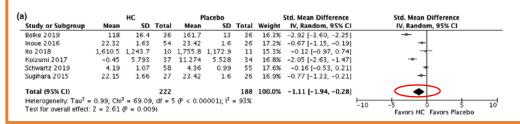


Figure 2 Forest plot for the combined estimate of the included studies evaluating skin hydration in patients supplemented with hydrolyzed collagen (HC) and patients in the placebo group. The horizontal lines represent the effect size \pm confidence interval (95% CI). The summary effect size is represented by the diamond

	HC			P	Placebo			Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Bolke 2019	0.81	0.04	36	0.75	0.06	36	7.3%	1.16 [0.66, 1.67]	+		
Choi 2014	0.786	0.054	8	0.718	0.017	8	6.8%	1.61 [0.44, 2.78]			
Czajka 2018	9.8	0.2	61	7	0.3	59	6.6%	10.95 [9.50, 12.40]			
Genovese 2017	8.07	0.2	60	7.52	0.2	60	7.3%	2.73 [2.23, 3.23]	-		
Inoue 2016	0.758	0.0485	54	0.738	0.045	26	7.3%	0.42 [-0.05, 0.89]	+		
Ito 2018	0.784	0.07	10	0.779	0.06	11	7.1%	0.07 [-0.78, 0.93]	+		
Koizumi 2017	0.938	0.677	37	4.32	0.534	34	7.0%	-5.46 [-6.49, -4.42]			
Nomoto 2020	0.74	0.06	20	0.66	0.07	19	7.2%	1.20 [0.52, 1.89]	-		
Proksch 2014	4.32	0.534	37	0.938	0.677	34	7.0%	5.51 [4.47, 6.56]	-		
Sangsuwan 2020	0.56	0.11	17	0.48	0.08	19	7.2%	0.82 [0.14, 1.51]	-		
Schwartz 2019	5.29	1.04	58	5.32	0.97	55	7.4%	-0.03 [-0.40, 0.34]	+		
Sugihara 2015	0.758	0.109	27	0.697	0.087	26	7.3%	0.61 [0.06, 1.16]	-		
Yoon 2014	0.6097	0.0556	22	0.6446	0.0675	22	7.3%	-0.55 [-1.16, 0.05]	-		
Zmitek 2020	1.38	0.33	16	1.59	0.68	15	7.2%	-0.39 [-1.10, 0.33]	+		
Total (95% CI)			463			424	100.0%	1.27 [0.19, 2.35]			
Heterogeneity, Tau ² = 4.08; Chi ² = 523.55, df = 13 (P < 0.00001); i ² = 98%											
-10 -5 0 5 10									-10 -5 0 5 10 Favors Placebo Favors HC		
									FAVOIS FIACEDO FAVOIS HC		

Figure 3 Forest plot for the combined estimate of the included studies evaluating skin elasticity in patients supplemented with hydrolyzed collagen (HC) and patients in the placebo group. The horizontal lines represent the effect size ± confidence interval (95% CI). The summary effect size is represented by the diamond

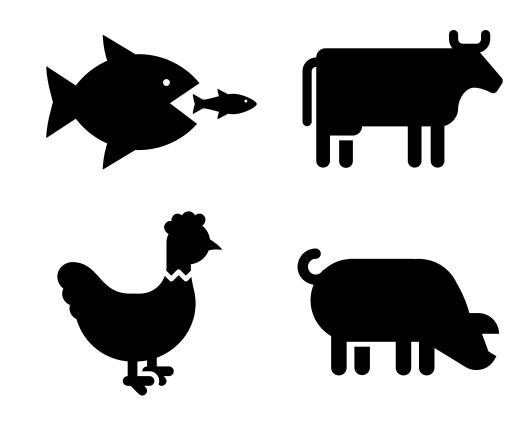


Collagen sources

Marine/fish collagen was the most common source of collagen followed by bovine, porcine and chicken

Studies using collagen alone were just as effective as those that had additional ingredients in the formulation

Studies using collagen supplements with higher concentrations of Pro-Hyp and Hyp-Gly dipeptides showed skin improvements after 4 weeks and indication of higher degree of efficacy



But wait, there's more



Updated systematic review and meta-analysis of 26 RCTs involving 1,721 people comparing hydrolysed collagen to placebo published in 2023



Supplementation duration was 2 to 12 weeks with doses of 0.6 to 12 g/d with outcomes assessed of skin elasticity and hydration



Significant improvements in skin elasticity and hydration with greatest benefits seen after 8 weeks

	HC			placebo			9	td. Mean Difference	Std. Mean Difference
References	Mean	SD	Total	Mean	S D	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Asserin 2015(fish)	65.28	5.933	11	52.91	6.567	11	3.4%	1.90 [0.86, 2.94]	
Asserin 2015(porcine)	58.13	6.942	11	52.91	6.567	11	4.1%	0.74 [-0.13, 1.61]	
Bolke 2019	44.5	26.4	36	36.6	34.2	36	6.3%	0.26 [-0.21, 0.72]	+-
Choi 2014	71.09	13.22	8	61.3	10.48	8	3.4%	0.78 [-0.25, 1.80]	
Dicerbo 2014	61.98	3.368	15	55.56	3.368	15	4.0%	1.85 [0.98, 2.73]	
Evans 2020	50.24	30.65	17	46.36	34.75	19	5.2%	0.12 [-0.54, 0.77]	
Inoue 2016	31.08	12.545	54	25.42	14.88	26	6.2%	0.42 [-0.05, 0.89]	 -
Ito 2018	60.3	8.2	10	60.9	10.7	11	4.1%	-0.06 [-0.92, 0.80]	
Jung 2021	7.38	8.2	25	2.84	6.5	25	5.7%	0.60 [0.04, 1.17]	-
Kim 2018	61.14	11.31	33	53.02	13.59	31	6.0%	0.64 [0.14, 1.15]	_ -
Koizumi 2017	10.891	8	37	4.017	7.62	34	6.1%	0.87 [0.38, 1.36]	_
Miyanaga 2021	16.181	11	33	6.315	7.405	33	6.0%	1.04 [0.52, 1.56]	_ -
Nomoto 2020	51.7	6.5	20	41.4	9.8	19	5.0%	1.22 [0.53, 1.91]	
Ping 2020	82.5	5.6	25	75.2	7.3	25	5.5%	1.10 [0.51, 1.70]	
Schwartz 2019	61.31	24.53	58	62.08	28.41	55	6.8%	-0.03 [-0.40, 0.34]	+
Sugihara 2015	73.98	8.86	27	70.85	10.2	26	5.8%	0.32 [-0.22, 0.87]	+-
Tak 2021	209	18.7	36	212.1	16	38	6.3%	-0.18 [-0.63, 0.28]	+
Yoon 2014	16.289	2.875	22	12.883	2.094	22	5.2%	1.33 [0.67, 1.99]	
Zmitek 2020	200	52.3	16	194.1	44.4	15	4.9%	0.12 [-0.59, 0.82]	-
Total (95% CI)			494			460	100.0%	0.63 [0.38, 0.88]	•
Heterogeneity: Tau ² = 0.20;	Chi² = 59.63	df = 18 (n)()1): 2 = 1	70%			2.22 (3.00) 0.00)	+ + + + + + + + + + + + + + + + + + + +
Test for overall effect: $Z = 4.94$ (p < 0.00001)									-4 -2 0 2 4
rest for overall effect. Z = 1	1.04 (p < 0.00	001)							placebo HC

Figure 2. Forest plot of the included studies evaluating skin hydration in patients supplemented with HC and patients in the placebo group [26–28,30–35,39,40,43,44,46–50]. (HC: hydrolyzed collagen, CI: confidence intervals, SD: standard deviation, I²: heterogeneity).

		HC		pl	acebo		9	td. Mean Difference	Std. Mean Difference
References	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bolke 2019	0.81	0.24	36	0.75	0.36	36	5.8%	0.19 [-0.27, 0.66]	+-
Campos 2015	0.53	0.04	30	0.456	0.026	30	5.2%	2.17 [1.52, 2.81]	
Choi 2014	0.786	0.054	8	0.718	0.017	8	3.4%	1.61 [0.44, 2.78]	
Czajka 2018	9.8	1.56	61	7	2.3	59	6.0%	1.42 [1.02, 1.82]	-
Dicerbo 2014	25.3	1.369	15	24.7	0.867	15	4.9%	0.51 [-0.22, 1.24]	+-
Evans 2020	50.35	30.38	17	43.26	37.1	19	5.1%	0.20 [-0.45, 0.86]	
Genovese 2017	8.07	1.55	60	7.52	1.55	60	6.1%	0.35 [-0.01, 0.71]	
Inoue 2016	0.758	0.0485	54	0.738	0.045	26	5.7%	0.42 [-0.05, 0.89]	 •
Ito 2018	0.784	0.07	10	0.779	0.06	11	4.4%	0.07 [-0.78, 0.93]	
Kim 2018	0.76	0.06	33	0.73	0.09	31	5.7%	0.39 [-0.11, 0.89]	+-
Koizumi 2017	4.32	3.248	37	0.938	3.948	34	5.7%	0.93 [0.44, 1.42]	
Miyanaga 2021	0.84	0.044	33	0.816	0.044	33	5.7%	0.54 [0.05, 1.03]	-
Nomoto 2020	0.74	0.06	20	0.66	0.07	19	5.0%	1.20 [0.52, 1.89]	
Sangsuwan 2020	0.56	0.11	17	0.48	0.08	19	5.0%	0.82 [0.14, 1.51]	
Schwartz 2019	0.4	80.0	58	0.34	0.15	54	6.0%	0.50 [0.12, 0.88]	-
Sugihara 2015	0.758	0.109	27	0.697	0.087	26	5.5%	0.61 [0.06, 1.16]	-
Tak 2021	0.33	0.1	36	0.36	0.09	38	5.8%	-0.31 [-0.77, 0.15]	
Yoon 2014	0.024	0.016	22	-0.029	0.016	22	4.2%	3.25 [2.33, 4.18]	_
Zmitek 2020	1.38	0.33	16	1.59	0.68	15	4.9%	-0.39 [-1.10, 0.33]	
Total (95% CI)			590			555	100.0%	0.72 [0.40, 1.03]	
Heterogeneity: Tau ² =	0.39; Chi ² =	109.82, c	if = 18 (p < 0.000	01); I ² = 8	84%			
Test for overall effect: Z = 4.49 (p < 0.00001)									-4 -2 0 2 4
	A.								placebo HC

Figure 3. Forest plot of the included studies evaluating skin elasticity in patients supplemented with HC and patients in the placebo group [26–29,31–35,37,39–44,47–49]. (HC: hydrolyzed collagen, CI: confidence intervals, SD: standard deviation, I²: heterogeneity).

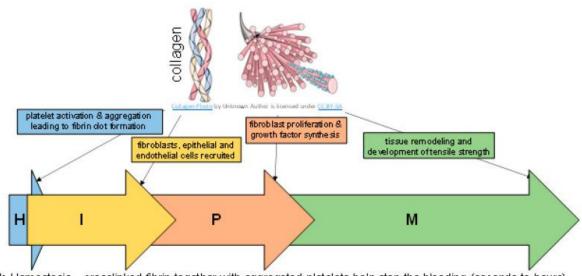
Collagen as an adjunct in wound healing

Chronic wounds are associated with high costs, lower quality of life and significant morbidity and mortality

Develops when progression through the normal phases of wound healing is impaired

Results in \uparrow levels of pro-inflammatory cytokines, \uparrow matrix metalloproteinases (MMPs), destruction of extracellular matrix components and \downarrow activity of growth factors

Besides its function as a scaffold in skin, collagen also plays a pivotal role as a signaling molecule in the regulation of all phases of wound healing



H: Hemostasis – crosslinked fibrin together with aggregated platelets help stop the bleeding (seconds to hours)
I: Inflammation – immune cell activation and recruitment driving the secretion of proinflammatory cytokines that promote recruitment of fibroblasts, epithelial and endothelial cells, infection surveillance and response (hours to days)

P: Proliferation – Fibroblast proliferation and collagen deposition, angiogenesis, granulation tissue formation, new epithelium formation (days to weeks)

M: Maturation – Remodeling of ECM and increase in tensile strength of wound (weeks-months/years)

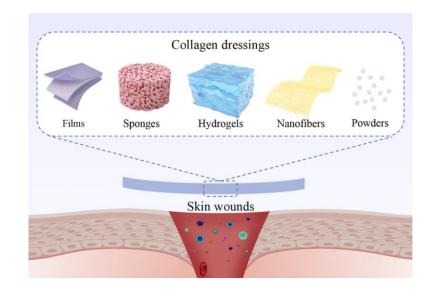
Collagen dressings and wound healing

Systematic review of 11 RCTs involving 961 patients with chronic wounds (pressure ulcers, diabetic foot ulcers and venous leg ulcers)

Use of collagen dressing compared to SOC had a higher rate of wound healing as defined as complete healing (53% vs 34%) and a faster healing velocity

Collagen dressings are costly in the short term, but the cost can be offset by improved wound healing rate and accelerated wound healing





Hydrolysed collagen and burns: RCT

34 adults with 20-30% of body surface area burns

Randomly assigned to an oral collagen-based supplement (36 g hydrolysed collagen, 1,000 kcal) or isocaloric placebo (35 g soy protein) plus usual meals (both groups) for 4 weeks

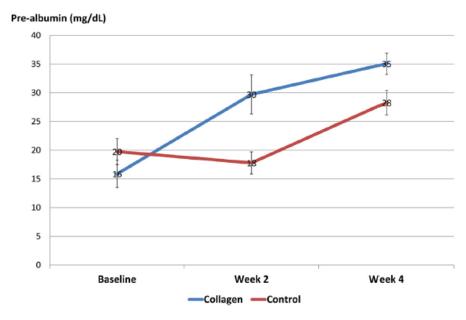
Serum pre-albumin higher at weeks 2 and 4 in collagen group

Week 2: Complete wound healing (defined as absence of a burn ulcerand the presence of a new layer of epithelium) in 8 (50%) patients in the collagen group at week 2 vs 1 (6.7%) in placebo group

Week 4: Full healing of wounds in all patients in collagen group vs 6 (40%) patients in the placebo group

Length of hospital stay in collagen group 9.4 days vs 13.5 for placebo group (p=0.063)

No differences in energy and protein intakes between groups



Hydrolysed collagen and pressure ulcers: RCT

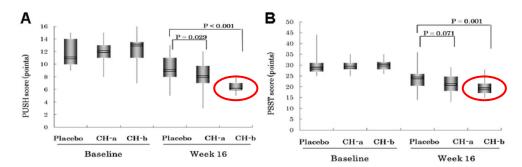
122 adults with stage II or III pressure ulcers

Randomly assigned to an oral collagen supplement at low (CH-a) and high (CH-b) levels of di-peptides (Hyp-Gly and Pro-Hyp) at 10 g/day or placebo for 16 weeks

PU healing assessed by PUSH and PSST scores (assessor blinded)

PUSH, PSST and wound area of high collagen di-peptide group (CH-b) significantly lower than placebo group at week 16

PUSH score of low collagen di-peptide group (CH-a) significantly lower than placebo group at week 16



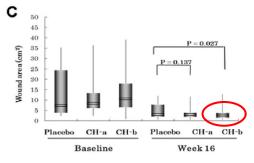


Figure 2. Comparisons of the primary treatment efficacy parameters (the Pressure Ulcer Scale for Healing (PUSH) score (A), Pressure Sore Status Tool (PSST) score (B), and wound area (C)) between the baseline and week 16. Data are expressed as mean values (N=38,35, and 39 for the CH-a, CH-b and placebo groups, respectively). The PUSH and PSST scores and the pressure ulcer surface area of the CH-b group were significantly lower than those of the placebo group at week 16 (PUSH score, P<0.01; PSST score, P=0.01; wound area, P=0.027). The PUSH score of the CH-a group was significantly lower than that of the placebo group at week 16 (P=0.029).





Most of the criticisms made about collagen in the popular press are way off the mark and not reflective of the scientific evidence





There is very good evidence that a range of hydrolysed collagen forms can improve various aspects of skin health including skin hydration, skin elasticity and wrinkles



Greatest benefits of collagen supplementation for skin health can be seen by 8 weeks and with doses ranging from a few grams up to 12 grams per day



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