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Original Article

Hydrolyzed Collagen Tonic Drink Prevents Worsening of Skin Parameters and Improves Photoaging Classification in Healthy Thai Women: A Randomized Controlled Trial

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ABSTRACT

Background: Skin aging represents a significant public health burden globally, with Southeast Asian populations experiencing accelerated photoaging due to intensive environmental ultraviolet exposure. **Aim:** To evaluate the preventive efficacy of hydrolyzed collagen tonic drink on skin aging parameters in healthy Thai women. **Methods:** A double-blind, randomized controlled trial was conducted with 135 Thai women aged 40-60 years. Participants were randomized to receive either hydrolyzed fish collagen peptides with supportive nutrients (n=67) or active fruit juice control (n=68) daily for 12 weeks. Primary outcomes included skin microtopography parameters measured by Visioscan, skin elasticity assessed by Cutometer, and clinical photoaging classification using Glogau scale. Secondary outcomes examined molecular biomarker changes in procollagen Type I synthesis. **Results:** The collagen group demonstrated significantly attenuated skin surface deterioration compared to placebo. The Wrinkles parameter showed significant between-group differences at week 8 (-100.43 units, p=0.001). Smoothness parameter exhibited protective effects with significant between-group differences at week 8 (-80.08 units, p=0.002). Gross elasticity improved significantly within the collagen group at week 12 (p=0.033). Procollagen Type I synthesis demonstrated superior maintenance in the collagen group versus placebo (between-group percent change difference, p=0.002). Both groups achieved comparable Glogau classification improvements (23.9% versus 20.6%). **Conclusion:** Daily hydrolyzed collagen supplementation with supportive nutrients effectively prevented skin surface parameter deterioration in Thai women, demonstrating meaningful preservation of skin integrity through medium effect sizes for key parameters. These findings support nutritional approaches as complementary strategies for photoaging management in high ultraviolet-exposure populations.

Keywords: Hydrolyzed collagen, Photoaging, Skin elasticity, Dermal aging, Wrinkle

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INTRODUCTION

Skin aging represents a global health challenge with substantial economic implications. Globally, skin and subcutaneous diseases constitute the fourth leading cause of non-fatal disease burden, with disability-adjusted life years reaching 42,883,695.48 in 2019[1]. In the United States, direct medical costs of skin diseases were estimated at $75 billion in 2013, with additional $11 billion in indirect costs[2,3]. Skin aging manifests through two distinct pathways: intrinsic aging, driven by genetic factors and cellular senescence, and extrinsic aging (photoaging), primarily caused by environmental factors such as UV radiation[4,5]. Intrinsic aging is characterized by cellular senescence induced by endogenous oxidative stress, telomere shortening, and accumulation of advanced glycation end products contributing to collagen cross-linking[6,7]. Extrinsic aging involves UV-induced reactive oxygen species production, causing DNA damage and activating matrix metalloproteinases responsible for collagen degradation[4]. These changes result in compromised skin barrier function, increased infection susceptibility, delayed wound healing, and significant psychological impact[8,9]. Asian women exhibit delayed wrinkle formation compared to Caucasian populations due to thicker dermis and higher melanin content, but experience more pronounced gravitational aging[10,11]. Thai women aged 40-60 years present unique challenges, exhibiting the most severe wrinkle levels compared to Japanese and Chinese women, particularly in crow's feet and lower facial regions, attributed to higher UV exposure due to lower latitude and elevated temperatures[12,13]. Crow's feet wrinkles develop later but appear coarser and deeper when they occur[14]. Studies often focus on treatment efficacy rather than prevention, highlighting the need for comprehensive preventive approaches[15,16]. The tropical Southeast Asian environment intensifies aging processes through high levels of UV exposure, high temperatures, and humidity, leading to accelerated photoaging with decreased skin hydration and coarse, deep wrinkles[17-19]. Environmental pollutants further exacerbate skin aging by generating reactive oxygen species[20-22]. Hydrolyzed collagen peptides have demonstrated efficacy in activating the TGF-β/Smad signaling pathway, promoting collagen synthesis and suppressing matrix metalloproteinases. Clinical trials show significant improvements in skin elasticity, moisture, and wrinkle reduction in Asian populations[23]. Supportive ingredients including glutathione provide cellular antioxidant protection, while micronutrients like zinc and selenium support enzymatic processes essential for skin matrix maintenance[24-26]. This study investigated the efficacy of a hydrolyzed collagen tonic drink in preventing skin parameter deterioration and improving photoaging classification in healthy Thai women.

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MATERIALS AND METHODS

Preparation of the Hydrolyzed Collagen Tonic Drink

The active formulation was prepared containing hydrolyzed fish collagen peptides (2,000 g/mol, 90% protein, 5,000 mg), *Chlorella pyrenoidosa* suspension (20 mg, minimum 1% chlorophyll), L-glutathione oxidized hexahydrate (250 mg, 98.0-102.0% purity), *Vitis vinifera* seed extract (60 mg dry equivalent, 50:1 ratio, minimum 95% proanthocyanidins), *Equisetum arvense* extract (10 mg silica, 10:1 ratio, >7.0% silica), zinc gluconate (5 mg zinc, 97-102% purity), and selenium-enriched yeast (50 mcg, 0.10-0.15% selenium). The control formulation comprised erythritol blended with concentrated juices of *Malus domestica*, *Vitis vinifera*, and *Prunus cerasus*, with citric acid for pH stabilization. Both products were manufactured by TCI Co., Ltd. (Taiwan), a GMP-certified facility, and packaged in identical 60-mL amber glass bottles with coded labels to ensure blinding throughout the study.

Study Design and Setting

This double-blind, randomized controlled trial employed a two-arm parallel design with participants allocated to treatment or control groups in a 1:1 ratio. The study received approval from The Human Research Ethics Committee of Thammasat University (Medicine); protocol no: MTU-EC-00-5-112/61), was registered with the Thai Clinical Trial Registry (TCTR20190103002) and conducted according to Good Clinical Practice guidelines and Declaration of Helsinki principles. All participants provided written informed consent.

Participants

The sample size for this double-blind randomized controlled trial was determined using G*Power software version 3.1.7, incorporating alpha 0.05, statistical power (1-β) 0.85, and anticipated effect size (f) 0.3, based on previous studies. Accounting for 37.25% potential attrition resulted in 70 participants per group. Of 140 screened participants, 3 were excluded for not meeting criteria and 1 declined participation, resulting in 136 participants randomized equally into treatment (n=68) and control (n=68) groups. One treatment group participant withdrew due to personal reasons, resulting in final analytical cohorts of 67 treatment and 68 control participants.

Eligible participants were Thai females aged 40-60 years with Glogau photoaging classification types I-III, Fitzpatrick skin phototypes I-IV, Thai language proficiency, capability for protocol compliance, and feasibility for scheduled visit attendance. Exclusions applied to individuals with dermatological conditions at test sites; known allergies to investigational products; gastrointestinal disorders; recent medication use including topical agents within 6 weeks or systemic anti-inflammatory medications, antibiotics, or antihistamines within 4 weeks; hormonal contraception; pregnancy or lactation; clinically significant medical history; immunological or systemic disorders; severe conditions within 6 months including malignancy, cardiovascular disorders, uncontrolled diabetes, or dermatopathology; BMI ≥ 23 kg/m²; substance abuse; concurrent trial participation; and recent intensive solar exposure at test sites.

Interventions

Participants who satisfied the inclusion criteria were randomized into two groups using variable block sizes generated by an independent biostatistician using Microsoft Excel RAND function. Participants were stratified by age and menopausal status before allocation, with randomization codes sealed in opaque envelopes and concealed from investigators. The treatment group received the hydrolyzed collagen tonic drink, while the control group received the placebo formulation. Both groups consumed one bottle daily in the morning on an empty stomach for 12 weeks. A four-week run-in period preceded intervention to optimize treatment effect detection, during which participants avoided UV exposure, sauna use, swimming, and intense physical activity while maintaining consistent lifestyle and dietary habits.

Outcome measurements

To assess the effects of hydrolyzed collagen tonic drink compared to placebo, measurements were collected from participants at baseline (week 0), and at weeks 4, 8, and 12. All assessments followed standardized protocols with participants undergoing facial cleansing with standardized foam, followed by 15-minute acclimatization in controlled conditions (22 ± 2°C, 45 ± 5% humidity). The outcome measures included skin microtopography analysis using Visio scan® VC98 for periorbital skin assessment, measuring skin smoothness (SEsm), skin roughness (SEr), and wrinkles (SEw). Skin elasticity was evaluated using Cutometer® MPA 580 with measurements of gross elasticity (R2), net elasticity (R5), viscoelasticity (R6) and biological elasticity (R7). Photoaging severity was assessed using the Glogau Classification system by a single board-certified dermatologist who remained blinded to treatment allocation. Biochemical analysis included procollagen Type I C-Peptide (PIP) concentrations quantified using enzyme immunoassay from suction blister fluid samples.

Statistical analysis

Data from this study were analyzed following the per-protocol approach, utilizing IBM SPSS Statistics Version 21.0. Participant characteristics were summarized and reported using frequencies, percentages, and means ± standard error. Baseline characteristics were compared using Student's t-test for continuous variables or chi-square/Fisher's exact test for categorical variables. Between-group comparisons at weeks 4, 8, and 12 used Student's t-test, while within-group changes were evaluated using paired t-tests. Test-retest reliability analysis on 20% of images yielded a reliability coefficient of 0.88, indicating excellent intra-rater consistency for the Glogau Classification assessment. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Baseline Demographic and Characteristics of Participants

The per-protocol analysis included 135 participants who completed the 12-week intervention period, comprising 67 participants in the hydrolyzed collagen group and 68 in the placebo group, representing 99.3% of the originally randomized population. One participant from the treatment group withdrew due to personal reasons unrelated to the intervention, while all placebo group participants completed the study protocol, as illustrated in the Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Figure 1).

Table 1 presents the demographic and clinical characteristics of participants. Baseline characteristics demonstrated balanced distribution between groups across demographic and clinical parameters. Mean age was comparable between the hydrolyzed collagen and placebo groups (49.21 ± 0.69 vs. 48.85 ± 0.63 years, p = 0.704). Statistically significant differences were observed in diastolic blood pressure (73.03 ± 0.56 vs. 68.44 ± 0.25 mmHg, p = 0.023) and pulse rate (75.43 ± 0.13 vs. 72.13 ± 0.14 per min, p = 0.042), though all values remained within normal physiological ranges. The population exhibited balanced distribution across Fitzpatrick skin types, with Type II predominating (47.8% treatment vs. 45.6% placebo), followed by Type III (26.9% vs. 36.8%). Menopausal status was similarly distributed, with approximately 55-57% participants being pre/perimenpausal in both groups.

Table 1. Baseline demographic and clinical characteristics of study participants

Data are presented as Mean ± Standard error (SE) for continuous variables and n (%) for categorical variables. $p < 0.05$, comparing between groups using independent t-test or chi-square test. DBP: diastolic blood pressure; SBP: systolic blood pressure; BMI: body mass index; BA: bachelor's degree.

Variables	Treatment (n = 67)	Placebo (n = 68)	p-value
Age, years	49.21 ± 0.69	48.85 ± 0.63	0.704
Weight, kg	53.48 ± 0.59	52.73 ± 0.64	0.392
Height, cm	157.90 ± 0.63	157.61 ± 0.68	0.758
BMI, kg/m^2	21.43 ± 0.17	21.18 ± 0.17	0.314
SBP, mmHg	119.99 ± 0.63	115.54 ± 0.89	0.077
DBP, mmHg	73.03 ± 0.56	68.44 ± 0.25	0.023
Pulse rate, per min	75.43 ± 0.13	72.13 ± 0.14	0.042
Temperature, °C	36.38 ± 0.24	36.67 ± 0.04	0.215
Fitzpatrick type			
Type I	12 (17.9)	11 (16.2)	0.413
Type II	32 (47.8)	31 (45.6)	
Type III	18 (26.9)	25 (36.8)	
Type IV	4 (6.0)	1 (1.5)	
Type V	1 (1.5)	0 (0)	
Menopausal status			
Pre/perimenopausal	37 (55.2)	39 (57.4)	0.955
Last period ≤ 5 yrs.	19 (28.4)	19 (27.9)	
Last period > 5 yrs.	11 (16.4)	10 (14.7)	
Ethnic Group			
Thai-Central	41 (61.2)	44 (64.7)	0.673
Others	26 (38.8)	24 (35.3)	
Education			
BA and more	54 (80.6)	53 (81)	0.704
Less than BA	13 (19.4)	15 (22.1)	
Occupation			
Indoor	57 (85.1)	55 (80.9)	0.517
Outdoor	10 (14.9)	13 (19.1)	

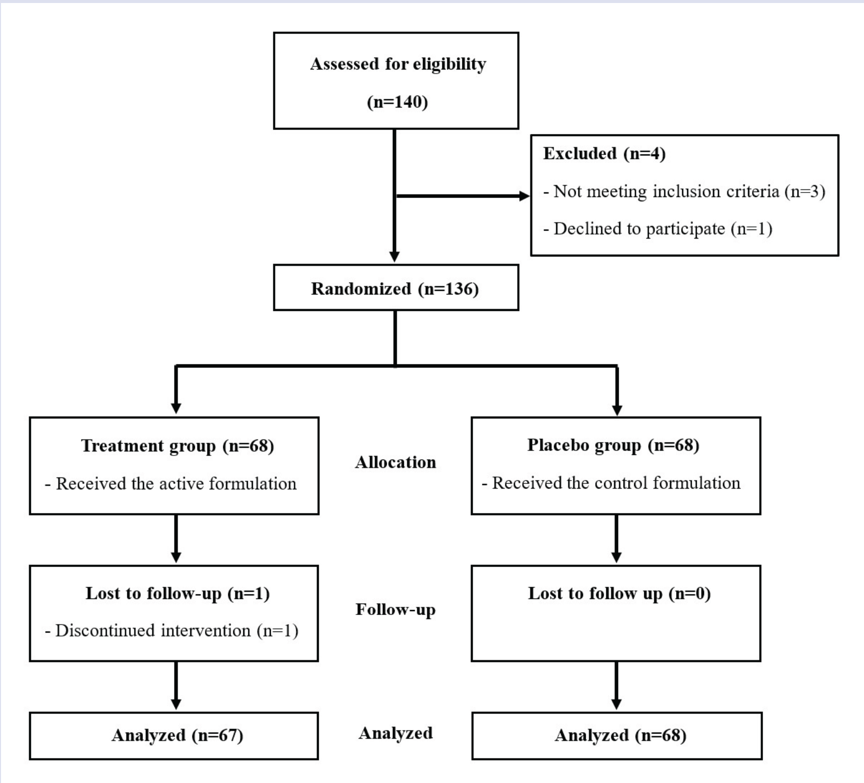

Figure 1. CONSORT flow diagram

Table 2. SELS parameters change between treatment and placebo groups over 12 weeks

Parameter/Times	Treatment (n=67) Mean ± SE	Placebo (n=68) Mean ± SE	Mean Difference Between group (p-value)a	Cohen's d
Wrinkle (SEw), a.u.				
Baseline	344.65 ± 16.33	337.21 ± 17.44	7.44 (0.756)	0.05
Week 4	324.20 ± 16.39	373.88 ± 21.75	-49.68 (0.071)	-0.31
Week 8	333.84 ± 15.85	434.27 ± 25.66	-100.43 (0.001)	-0.57
Week 12	316.42 ± 15.55	338.93 ±17.36	-22.51 (0.342)	-0.17
Mean Difference (p-value)[b]	20.45 (0.288)	-35.66 (0.125)		
Cohen's d (Baseline-week 4)	-0.15	0.23		
Mean Difference (p-value)[c]	10.81 (0.582)	-97.06 (0.001)		
Cohen's d (Baseline-week 8)	-0.08	0.54		
Mean Difference (p-value)[d]	28.23 (0.129)	-1.71 (0.924)		
Cohen's d (Baseline-week 12)	-0.22	0.01		
Smoothness (SEsm), a.u.				
Baseline	381.82 ± 14.63	384.48 ± 14.97	-9.71 (0.634)	-0.02
Week 4	372.43 ± 15.76	415.41 ± 17.62	-42.98 (0.072)	-0.31
Week 8	369.90 ±14.79	449.98 ± 20.24	-80.08 (0.002)	-0.55
Week 12	353.56 ± 12.28	382.79 ± 16.58	-29.23 (0.158)	-0.24
Mean Difference (p-value)[b]	9.39 (0.583)	-30.93 (0.06)		
Cohen's d (Baseline-week 4)	-0.08	0.23		
Mean Difference (p-value)[c]	11.92 (0.491)	-65.51 (0.001)		
Cohen's d (Baseline-week 8)	-0.10	0.45		
Mean Difference (p-value)[d]	28.26 (0.063)	1.69 (0.889)		
Cohen's d (Baseline-week 12)	-0.18	-0.01		
Roughness (SEr), a.u.				
Baseline	3.50 ± 0.20	4.20 ± 0.21	-0.7 (0.018)	-0.42
Week 4	3.58 ± 0.17	3.70 ± 0.17	0.05 (0.874)	-0.09
Week 8	3.47 ± 0.17	3.64 ± 0.19	0.16 (0.674)	-0.12
Week 12	3.47 ± 0.17	3.82 ± 0.20	-0.39 (0.262)	-0.27
Mean Difference (p-value)[b]	0.08 (0.713)	-0.5 (0.029)		
Cohen's d (Baseline-week 4)	0.05	-0.31		
Mean Difference (p-value)[c]	-0.03 (0.892)	-0.56 (0.024)		
Cohen's d (Baseline-week 8)	-0.02	-0.34		
Mean Difference (p-value)[d]	-0.08 (0.789)	-0.37 (0.09)		
Cohen's d (Baseline-week 12)	-0.05	-0.22		

Data are presented as Mean ± Standard Error (SE)

[a] Between-group comparison using Student's t-test. Roughness parameter (baseline imbalance p=0.018) using ANCOVA adjusting for baseline values and assumptions for ANCOVA were tested and met.

[b] Within-group change from baseline to week 4 using paired t-test.

[c] Within-group change from baseline to week 8 using paired t-test.

[d] Within-group change from baseline to week 12 using paired t-test.

Effect of Hydrolyzed Collagen on Skin Surface Parameters

Skin surface evaluation using SELS parameters measured by Visioscan® VC 98 USB revealed differential patterns between groups over the 12-week study period. The wrinkles parameter (SEw) in the treatment group showed non-significant variations from baseline values of 344.65 ± 16.33 arbitrary units through week 4 (324.20 ± 16.39, p = 0.288), week 8 (333.84 ± 15.85, p = 0.582), and week 12 (316.42 ± 15.55, p = 0.129). The placebo group demonstrated progressive changes from baseline (337.21 ± 17.44 units), with significant worsening at week 8 (434.27 ± 25.66 units, within-group change: -97.06 units, p = 0.001, Cohen's d = 0.54), before returning to near-baseline levels at week 12 (338.93 ± 17.36 units, p = 0.924). Between-group analysis revealed significant differences at week 8 (-100.43 units, p = 0.001, Cohen's d = -0.57).

The smoothness parameter (SEsm) in the treatment group remained stable from baseline (381.82 ± 14.63 units) across all assessment points: week 4 (372.43 ± 15.76, p = 0.583), week 8 (369.90 ± 14.79, p = 0.491), and week 12 (353.56 ± 12.28, p = 0.063), with no statistically significant changes at any timepoint. The placebo group showed significant decline from baseline (384.48 ± 14.97 units) to week 8 (449.98 ± 20.24 units, within-group change: -65.51 units, p = 0.001, Cohen's d = 0.45), before recovering to near-baseline levels at week 12 (382.79 ± 16.58 units, p = 0.889). Between-group comparison at week 8 demonstrated significant differences of -80.08 units (p = 0.002, Cohen's d = -0.55) (Table 2).

Effect of Hydrolyzed Collagen on Skin Elasticity Parameters

Cytometer measurements revealed differential patterns across multiple skin elasticity parameters. Gross elasticity (R2) in the treatment group showed significant improvement from baseline (0.641 ± 0.011%) to week 12 (0.672 ± 0.013%, within-group change: -0.031%, p = 0.033, Cohen's d = -0.31). The placebo group maintained stable values throughout the study period, showing no significant changes from baseline (0.641 ± 0.010%) through week 12 (0.644 ± 0.011%, within-group change: -0.002%, p = 0.869). Between-group comparisons revealed no significant differences at any time point.

Net elasticity (R5) demonstrated improvements in both groups. The treatment group showed progressive enhancement from baseline

Table 3. Skin elasticity changes measured by cutometer over 12 weeks

Parameter/Times	Treatment (n=67) Mean ± SE	Placebo (n=68) Mean ± SE	Mean Difference Between group (p-value)a	Cohen's d
Gross elasticity (R2), %				
Baseline	0.641 ± 0.011	0.641 ± 0.010	0 (0.984)	0
Week 4	0.646 ± 0.013	0.621 ±0.011	0.025 (0.143)	0.25
Week 8	0.647 ± 0.013	0.634 ±0.009	0.013 (0.393)	0.14
Week 12	0.672 ± 0.013	0.644 ± 0.011	0.028 (0.098)	0.28
Mean Difference (p-value)[b]	-0.005 (0.701)	0.02 (0.144)		
Cohen's d (Basline-week 4)	-0.10	0.19		
Mean Difference (p-value)[c]	0.006 (0.650)	0.008 (0.475)		
Cohen's d (Basline-week 8)	-0.09	0.11		
Mean Difference (p-value)[d]	-0.031 (0.033)	-0.002 (0.869)		
Cohen's d (Basline-week 12)	-0.31	0		
Net elasticity (R5), %				
Baseline	0.62 ± 0.013	0.614 ± 0.012	0.006 (0.711)	0.09
Week 4	0.636 ± 0.012	0.629 ±0.013	0.007 (0.676)	0.08
Week 8	0.654 ± 0.014	0.646 ±0.015	0.008 (0.706)	0
Week 12	0.675 ± 0.014	0.648 ± 0.013	0.027 (0.174)	0.17
Mean Difference (p-value)[b]	-0.016 (0.183)	0.015 (0.336)		
Cohen's d (Basline-week 4)	-0.16	0.17		
Mean Difference (p-value)[c]	-0.034 (0.031)	-0.032 (0.022)		
Cohen's d (Basline-week 8)	-0.25	-0.34		
Mean Difference (p-value)[d]	-0.054 (0.001)	0.034 (0.029)		
Cohen's d (Basline-week 12)	-0.45	-0.35		
Viscoelasticity (R6), %				
Baseline	0.479 ± 0.023	0.439 ± 0.019	0.039 (0.187)	0.18
Week 4	0.483 ± 0.022	0.515 ± 0.027	-0.032 (0.360)	-0.36
Week 8	0.533 ± 0.025	0.548 ± 0.023	-0.014 (0.673)	-0.67
Week 12	0.547 ± 0.029	0.503 ± 0.023	0.044 (0.239)	0.23
Mean Difference (p-value)[b]	0.003 (0.872)	-.076 (0.014)		
Cohen's d (Basline-week 4)	0	-0.46		
Mean Difference (p-value)[c]	-0.054 (0.056)	-.108 (0.001)		
Cohen's d (Basline-week 8)	-0.27	-0.66		
Mean Difference (p-value)[d]	-0.068 (0.017)	-.063 (0.036)		
Cohen's d (Basline-week 12)	-0.38	-0.38		
Biological elasticity (R7), %				
Baseline	0.424 ± 0.007	0.431 ±0.009	-0.007 (0.528)	0
Week 4	0.435 ± 0.009	0.419 ± 0.008	0.015 (0.224)	0.01
Week 8	0.432 ± 0.009	0.421 ±0.008	0.011 (0.362)	0.01
Week 12	0.444 ± 0.011	0.435 ± 0.008	0.009 (0.492)	0
Mean Difference (p-value)[b]	-0.011 (1)	0.012 (1)		
Cohen's d (Basline-week 4)	0.15	-0.17		
Mean Difference (p-value)[c]	-0.007 (1)	0.011 (1)		
Cohen's d (Basline-week 8)	0.10	-0.15		
Mean Difference (p-value)[d]	0.02 (0.334)	-0.003 (1)		
Cohen's d (Basline-week 12)	0.26	0.05		

Data are presented as Mean ± Standard error (SE).
[a] Between-group comparison using Student's t-test.
[b] Within-group change from baseline to week 4 using paired t-test.
[c] Within-group change from baseline to week 8 using paired t-test.
[d] Within-group change from baseline to week 12 using paired t-test.

Table 4. Changes in Molecular Extracellular Matrix Components from Blister Fluid Analysis

Parameter/Times	Treatment Group (n=20)		Placebo Group (n=25)		Between group	
	Value	p-value[a]	Value	p-value[a]	p-value[b]	Effect size
Procollagen Type I C-Peptide (pg/ml)						
Baseline				-		
Median (IQR)	613.45 (471.10 – 4,170.03)	-	653.20 (573.25 – 3,621.65)		0.664	0.06
Week 12						
Median (IQR)	678.65 (530 – 4,567.15)	-	628.9 (542 – 3,113.15)	-	0.444	0.11
Change from Baseline[c]	67 (-50.68 – 185.7)	0.087	-68.4 (-441.15 – 22.15)	0.156	0.013	0.37
Percent change (%)	6.97 (-6.21 – 24.89)	0.041	-6.54 (-26.94 – 2.69)	0.203	0.002	0.46

All values are presented as median (interquartile range) due to non-normal distribution of biomarker data confirmed by Shapiro-Wilk test ($p < 0.05$ for all parameters).

[a] Within-group p-values from Wilcoxon signed-rank test comparing pre- vs post-treatment values within each group. Not applicable (–) for baseline and follow-up measurements.

[b] Between-group p-values from Mann-Whitney U test. No adjustment for multiple testing was applied as these represent secondary exploratory endpoints.

[c] Change values calculated as Week 12 minus Baseline for each participant.

Table 5. Classification type of Glogau change of the same subjects from week 0 to week 12

Baseline Classification (week 0)	Week 12 Classification			Total at Baseline	p-value[a]
	Type I	Type II	Type III		
Treatment Group (n=67)					
Type I	3	1	1	5	0.006
Type II	3	20	1	24	
Type III	0	13	25	38	
Total at Week 12	6	34	27	67	
Placebo Group (n=68)					
Type I	3	0	0	3	0.023
Type II	3	19	3	25	
Type III	0	11	29	40	
Total at Week 12	6	30	32	68	

[a] p-values were calculated using McNemar-Bowker test for paired nominal data, comparing classification changes within each group from baseline to week 12. Data represent number of subjects in each Glogau classification type at baseline (week 0) and week 12.

Type I = mild photoaging (age 20-30s); Type II = moderate photoaging (age 30-40s);

Type III = advanced photoaging (age 50s and older).

(0.62 ± 0.013%) at week 8 (0.654 ± 0.014%, within-group change: -0.034%, p = 0.031, Cohen's d = -0.25) and week 12 (within-group change: -0.054%, p = 0.001, Cohen's d = -0.45). The placebo group also exhibited significant improvements at week 8 (0.614 ± 0.012% to 0.646 ± 0.015%, within-group change: -0.032%, p = 0.022, Cohen's d = -0.34) and week 12 (within-group change: -0.034%, p = 0.029, Cohen's d = -0.35). No significant between-group differences were observed at any time point (Table 3).

Effect of Hydrolyzed Collagen on Molecular Biomarkers

Molecular biomarker analysis from suction blister fluid revealed differential patterns in procollagen Type I concentrations between groups. A subset of participants from the treatment group (n=20) and placebo group (n=25) provided blister fluid samples for biomarker analysis. Baseline median concentrations were comparable between treatment (613.45 pg/ml, IQR: 471.10-4,170.03) and placebo groups (653.20 pg/ml, IQR: 573.25-3,621.65), with no significant between-group difference (p = 0.664).

After 12 weeks, the treatment group demonstrated a median increase of 67 pg/ml (IQR: -50.68 to 185.7), representing a 6.97% improvement from baseline (IQR: -6.21% to 24.89%, p = 0.041). The placebo group showed a median decrease of -68.40 pg/ml (IQR: -441.15 to 22.15), representing a -6.54% decline from baseline (IQR: -26.94% to 2.69%, p = 0.203). Between-group analysis revealed significant differences in both absolute change (p = 0.013) and percent change (p = 0.002), with medium effect sizes (r = 0.46 for percent change, r = 0.37 for absolute change) (Table 4).

Effect of Hydrolyzed Collagen on Glogau Photoaging Classification

Clinical photoaging assessment using Glogau classification demonstrated improvements in both groups over the 12-week study period. In the treatment group, 23.9% of participants (16/67) advanced to better classification categories, This included 13 participants progressing from Type III to Type II and 3 participants improving from Type II to Type I. At study completion, 6 participants achieved Type I classification, 34 were classified as Type II, and 27 remained in Type III category. These improvements were statistically significant (McNemar-Bowker test, p = 0.006).

The placebo group demonstrated a 20.6% improvement rate (14/68), with 11 participants progressing from Type III to Type II and 3 participants improving from Type II to Type I. At week 12, 6 participants achieved Type I classification, 30 were classified as Type II, and 32 remained in Type III. Changes were statistically significant (McNemar-Bowker test, p = 0.023). The Number Needed to Treat was calculated as 30 (95% CI: 15-120) (Table 5).

Safety Evaluation

The safety evaluation of participants, conducted through detailed medical histories and physical examinations at each follow-up throughout the study, revealed no adverse effects in both the hydrolyzed collagen group and the placebo group. A total of 135 participants were found to be free of any side effects, and the majority expressed satisfaction with the interventions they received. This sentiment was particularly pronounced in the treatment group, where participants reported improvements in overall skin appearance and texture following the hydrolyzed collagen tonic drink intervention.

DISCUSSION

This randomized controlled trial demonstrates that oral supplementation with hydrolyzed fish collagen combined with supportive nutrients effectively attenuates age-related skin deterioration in Thai women aged 40-60 years. The intervention achieved meaningful preservation of skin integrity through convergent pathways, with surface topography parameters demonstrating medium effect sizes for wrinkles and smoothness at week 8. Biomechanical assessment revealed preservation of critical viscoelastic properties, while enhanced procollagen Type I synthesis validated the structural benefits at the molecular level. Clinical Glogau assessment demonstrated comparable improvement rates between groups, suggesting that while both formulations enhanced overall appearance, the treatment group achieved superior structural preservation as evidenced by objective measurements.

The selective improvement in collagen-dependent parameters without affecting elastic fiber properties indicates targeted dermal remodeling consistent with the established 8-week efficacy timeline. This stabilizing effect against age-related skin deterioration likely results from synergistic action of hydrolyzed fish collagen peptides with selected supporting nutrients through multiple complementary pathways. At the molecular level, collagen hydrolysate ingestion enhances TGF-β and Smad3 expression while suppressing Smad7, consequently stimulating collagen synthesis and reinforcing extracellular matrix integrity[27-31]. Bioavailable peptides influence TGF-β/Smad-mediated upregulation of structural matrix genes, activation of PI3K/AKT/mTOR pathways for cellular proliferation, and regulation of matrix metalloproteinases to maintain homeostasis[32-34].

Supportive phytonutrients such as Chlorella extract provide complementary benefits through inhibition of advanced glycation end products[35], antioxidant activity against reactive oxygen species[36], suppression of inflammatory mediators including TNF-α and IL-6[37], and protection against UV-induced damage[38]. L-Glutathione contributes through neutralization of cellular oxidants[39,40], while grape seed proanthocyanidins prevent photoaging through dual mechanistic pathways involving immunomodulatory effects and direct dermal protection[41-44]. This multi-targeted approach addresses both synthetic and degradative aspects of collagen homeostasis, potentially explaining the comprehensive improvement observed in dermal parameters.

Our findings are consistent with Lee et al.[45], who investigated liquid collagen in Korean women using placebo controls. While both studies demonstrate oral collagen efficacy in Asian populations, our active control design provides unique clinical insights. The observed elasticity improvements in both groups reflect fruit-derived antioxidant benefits, demonstrating effective isolation of collagen-specific effects beyond general nutritional support. Both investigations support complementary therapeutic strategies with consistent 6-8-week efficacy timelines. Lee et al. demonstrated therapeutic improvements for existing photoaging, while our study reveals collagen's preventive potential against age-related deterioration. The antioxidant properties in our control formulation likely contributed through oxidative stress reduction[46,47]. These complementary findings indicate that oral collagen supplementation offers distinct clinical applications.

Our results align with Lu et al.[48], who conducted a randomized trial of fish collagen tripeptide in women of similar demographics. However, Lu et al. reported greater magnitude improvements in skin parameters compared to our study. The superior efficacy likely reflects formulation advantages, including bonito elastin peptides that provided direct precursors for elastic fiber synthesis[34,49-51]. When elastin peptides are combined with collagen peptides, they exhibit synergistic effects that enhance skin elasticity through upregulation of hyaluronic acid and hydroxyproline[52]. Lu et al. utilized specialized tripeptides with molecular weights below 500 Da, demonstrating superior bioavailability compared to standard hydrolyzed peptides[53,54]. Their structural protein strategy with salmon nasal cartilage compounds directly supplemented dermal matrix components[55,56], contrasting with our antioxidant-protective approach. These mechanistic differences suggest that combination formulations targeting both structural supplementation and protective pathways may optimize clinical outcomes.

Clinically, these findings have important implications for women with mild to moderate photoaging seeking preventive interventions. The number needed to treat of 30 indicates that collagen supplementation with supportive nutrition offers a modest but meaningful complementary approach to conventional photoaging management. The intervention appears most beneficial for individuals demonstrating early signs of elasticity loss and surface textural changes, making it particularly suitable for preventive dermatological care in Asian populations where maintaining skin quality is prioritized. Our protective stabilization approach demonstrates complementary efficacy, preventing natural deterioration progression.

The limitations of this study include the relatively short intervention period of 12 weeks, which may not fully capture the long-term effects of sustained collagen supplementation. Additionally, the study population was limited to Thai women aged 40-60 years, potentially limiting the generalizability of findings to other ethnic groups or age ranges. The study design did not include biochemical assessment of oxidative stress markers or inflammatory cytokines, which could provide additional mechanistic insights. Furthermore, dietary intake assessment was not systematically controlled, which may have influenced outcomes through variations in baseline nutritional status.

While significant prevention of wrinkle progression and maintenance of skin smoothness were observed, the modest effect size suggests this intervention is best positioned as a complementary approach rather than primary treatment. Future investigations should explore optimal formulation combinations, dose-dependent effects, and potential synergies with conventional treatments to maximize clinical benefits in diverse populations. Long-term studies assessing sustained supplementation over 6-12 months would provide valuable insights into the durability of observed effects and optimal treatment protocols for preventive skin aging management.

CONCLUSION

Daily consumption of the hydrolyzed collagen tonic drink provides a significant protective effect against the deterioration of key skin surface parameters in Thai women with photoaging. The findings support the use of this nutritional supplementation as a viable complementary strategy for the preventive management of early-stage skin aging.

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