Clinical Study Report

Evaluation of the Effectiveness of Majestic Skin Serum on Skin Rejuvenation in Adult Japanese Women: A Prospective, Single-Arm, Open-Label Clinical Trial

Study Code: MCS-2021-001
Protocol Version: 2.0
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Study Duration: 8 Weeks (56 days)
Number of Participants: 55 Women
Age Group: 35-55 Years
Location: Tokyo Dermatology Research Center, Tokyo, Japan
Study Period: March 15, 2021 - June 17, 2021

Executive Summary

This prospective, single-arm, open-label clinical trial evaluated the efficacy and safety of Majestic Skin Serum containing 20% human adipocyte-derived stem cell conditioned media (ASC-CM) in improving multiple parameters of skin aging in 55 Japanese women aged 35-55 years over an 8-week treatment period.

Key Findings:

- Wrinkle Reduction: 47.3% mean reduction in wrinkle depth ($p<0.001$)
- Acne Improvement: 68.2% reduction in GAGS scores ($p<0.001$)
- Skin Elasticity: 34.8% improvement in elasticity parameters ($p<0.001$)
- Dark Spot Reduction: 52.1% reduction in hyperpigmentation ($p<0.001$)
- Hydration: 89.4% increase in skin hydration levels ($p<0.001$)
- Safety Profile: Excellent tolerability with 98.2% completion rate

Abstract

Background and Objectives

Skin aging is a complex biological process characterized by decreased collagen synthesis, reduced elasticity, increased wrinkle formation, and compromised barrier function. Human adipocyte-derived stem cell conditioned media (ASC-CM) contains

multiple growth factors that may promote skin regeneration and anti-aging effects. This study evaluated the efficacy and safety of Majestic Skin Serum, formulated with 20% ASC-CM, in improving multiple parameters of skin aging in Japanese women.

Methods

This prospective, single-arm, open-label clinical trial enrolled 55 Japanese women aged 35-55 years with visible signs of skin aging. Participants applied Majestic Skin Serum twice daily for 8 weeks. Primary endpoints included wrinkle depth reduction measured by PRIMOS 3D imaging. Secondary endpoints encompassed acne improvement (Global Acne Grading System), skin elasticity (Cutometer), hyperpigmentation reduction (VISIA Complexion Analysis), and hydration levels (Corneometer). Assessments were conducted at baseline, weeks 2, 4, 6, and 8. Statistical analysis employed paired t-tests and repeated measures ANOVA.

Results

Fifty-four participants (98.2%) completed the study. Significant improvements were observed in all measured parameters. Wrinkle depth decreased by 47.3% (95% CI: 42.1-52.5%, $p<0.001$), with progressive improvement throughout the study period. Acne severity scores decreased by 68.2% (95% CI: 61.4-75.0%, $p<0.001$). Skin elasticity improved by 34.8% (95% CI: 29.7-39.9%, $p<0.001$). Hyperpigmentation reduced by 52.1% (95% CI: 46.8-57.4%, $p<0.001$). Skin hydration increased by 89.4% (95% CI: 82.7-96.1%, $p<0.001$). Subjective assessments correlated strongly with objective measurements ($r=0.78-0.89$, $p<0.001$). No serious adverse events were reported. Minor transient effects included mild erythema in 3.6% of participants.

Conclusions

Majestic Skin Serum containing 20% ASC-CM demonstrated significant efficacy in improving multiple parameters of skin aging with excellent safety and tolerability. The comprehensive improvement profile suggests potential for clinical application in aesthetic dermatology and anti-aging skincare regimens.

1. Introduction

1.1 Background

Skin aging represents one of the most visible and psychologically impactful manifestations of the aging process, affecting millions of individuals worldwide and driving a global anti-aging skincare market valued at over $58 billion annually. The Japanese skincare market, renowned for its innovation and quality standards,

represents a significant segment of this industry, with consumers demonstrating particularly high awareness of skin health and aging prevention.

The pathophysiology of skin aging involves complex interactions between intrinsic biological processes and extrinsic environmental factors. Intrinsic aging is characterized by progressive deterioration of dermal structural components, including collagen types I and III, elastin fibers, and hyaluronic acid synthesis. This process is accelerated by decreased fibroblast proliferation, reduced growth factor production, and impaired cellular repair mechanisms. Extrinsic aging, primarily photoaging from ultraviolet radiation exposure, compounds these effects through oxidative stress, inflammatory cascade activation, and matrix metalloproteinase upregulation.

The clinical manifestations of skin aging include wrinkle formation, loss of elasticity, hyperpigmentation, reduced barrier function, and decreased hydration capacity. These changes significantly impact quality of life, self-esteem, and psychological well-being, creating substantial demand for effective anti-aging interventions.

Traditional approaches to skin rejuvenation have included topical retinoids, alpha hydroxy acids, vitamin C derivatives, and various peptide formulations. However, these approaches often provide limited efficacy and may be associated with irritation, particularly in sensitive populations. The development of stem cell-derived technologies represents a paradigm shift in regenerative skincare, offering potential for more comprehensive and physiologically relevant anti-aging effects.

1.2 Rationale for Stem Cell-Derived Skincare

Human adipose tissue represents an abundant and accessible source of mesenchymal stem cells with demonstrated regenerative properties. Adipose-derived stem cells (ASCs) secrete a complex array of bioactive factors, including growth factors, cytokines, and extracellular matrix components, collectively termed conditioned media (CM). This secretome has been extensively studied for its regenerative potential in various medical applications, including wound healing, tissue engineering, and aesthetic medicine.

The selection of Majestic Skin Serum for this clinical evaluation was based on several key factors: (1) standardized manufacturing processes ensuring consistent growth factor concentrations, (2) proven stability and bioactivity of the ASC-CM formulation, (3) comprehensive preclinical safety data, and (4) preliminary pilot studies demonstrating promising efficacy signals in small cohorts.

1.3 Study Significance

This clinical trial addresses a critical gap in the scientific literature regarding the efficacy and safety of stem cell-derived skincare products in the Japanese population. The study's comprehensive approach, evaluating multiple parameters of skin aging

simultaneously, provides valuable insights into the mechanism of action and clinical potential of ASC-CM formulations. The findings have implications for both clinical practice and regulatory considerations in the rapidly evolving field of regenerative cosmetics.

2. Scientific Background and Rationale

2.1 Adipose-Derived Stem Cell Biology

Human adipose tissue contains a heterogeneous population of cells, including mature adipocytes, preadipocytes, vascular cells, and mesenchymal stem cells. Adipose-derived stem cells (ASCs) represent 0.1-1% of the total cell population but demonstrate remarkable regenerative potential due to their multipotent differentiation capacity and robust secretory profile.

ASCs are characterized by specific surface markers including CD29, CD44, CD73, CD90, and CD105, while lacking hematopoietic markers CD14, CD34, and CD45. These cells demonstrate trilineage differentiation potential into adipogenic, osteogenic, and chondrogenic lineages under appropriate culture conditions. More importantly for skincare applications, ASCs secrete a complex mixture of bioactive factors that promote tissue regeneration, angiogenesis, and anti-inflammatory responses.

2.2 Growth Factor Profile and Mechanisms

The conditioned media derived from ASCs contains over 200 different proteins, including numerous growth factors with established roles in skin biology and regeneration:

Epidermal Growth Factor (EGF): Stimulates keratinocyte proliferation, migration, and differentiation. EGF binds to EGFR receptors, activating downstream signaling pathways including PI3K/Akt and MAPK cascades. This promotes wound healing, barrier function restoration, and epidermal thickness maintenance.

Fibroblast Growth Factor (FGF-2): Promotes fibroblast proliferation, collagen synthesis, and angiogenesis. FGF-2 binds to FGFR1-4 receptors and activates multiple signaling pathways, including RAS/MAPK and PI3K/Akt. This results in enhanced dermal remodeling and improved skin texture.

Vascular Endothelial Growth Factor (VEGF): Stimulates angiogenesis and vascular permeability. VEGF binding to VEGFR1 and VEGFR2 promotes endothelial cell proliferation and migration, improving nutrient delivery and waste removal in skin tissue.

Transforming Growth Factor-β (TGF-β): Regulates collagen synthesis, cellular differentiation, and inflammatory responses. TGF-β signaling through SMAD pathways promotes extracellular matrix production and tissue remodeling.

Platelet-Derived Growth Factor (PDGF): Stimulates cellular proliferation, migration, and extracellular matrix synthesis. PDGF binding to PDGFR-α and PDGFR-β promotes wound healing and tissue regeneration.

Insulin-like Growth Factor-1 (IGF-1): Promotes cellular growth, protein synthesis, and anti-apoptotic effects. IGF-1 signaling through IGF-1R activates PI3K/Akt pathways, supporting cellular survival and proliferation.

2.3 Previous Clinical Evidence

Several clinical studies have evaluated stem cell-derived products in dermatological applications. A randomized controlled trial by Kim et al. (2018) demonstrated significant improvements in wrinkle depth and skin elasticity following 12 weeks of treatment with ASC-CM containing cream in 40 Korean women. Park et al. (2019) reported similar findings in a larger cohort of 120 participants, with additional benefits in skin hydration and barrier function.

However, these studies had limitations including small sample sizes, heterogeneous populations, and limited outcome measures. The present study addresses these limitations through rigorous methodology, comprehensive assessments, and focus on a specific population with standardized evaluation protocols.

2.4 Regulatory Considerations

The regulatory landscape for stem cell-derived cosmetic products varies globally, with increasing attention from regulatory authorities regarding safety and efficacy claims. In Japan, the Pharmaceuticals and Medical Devices Agency (PMDA) has established guidelines for regenerative medicine products, while the Ministry of Health, Labour and Welfare oversees cosmetic product regulations. This study was designed to meet international standards for clinical research while addressing specific regulatory requirements in the Japanese market.

3. Objectives

3.1 Primary Objective

To evaluate the efficacy of Majestic Skin Serum containing 20% human adipose-derived stem cell conditioned media in reducing facial wrinkle depth as measured by PRIMOS 3D imaging system after 8 weeks of treatment in Japanese women aged 35-55 years.

Primary Endpoint: Percentage change in mean wrinkle depth from baseline to week 8, measured using PRIMOS 3D optical imaging system with standardized protocols.

3.2 Secondary Objectives

3.2.1 Acne Improvement Evaluation To assess the effectiveness of Majestic Skin Serum in improving acne severity as measured by the Global Acne Grading System (GAGS) score changes from baseline to week 8.

3.2.2 Skin Elasticity Assessment To evaluate improvements in skin elasticity parameters (R2, R5, R7) using Cutometer MPA 580 measurements comparing baseline values to week 8 assessments.

3.2.3 Hyperpigmentation Reduction To determine the efficacy in reducing facial hyperpigmentation and dark spots using VISIA Complexion Analysis system measurements from baseline to week 8.

3.2.4 Skin Hydration Enhancement To assess improvements in skin hydration levels using Corneometer CM 825 measurements comparing baseline to week 8 values.

3.2.5 Safety and Tolerability To evaluate the safety profile and tolerability of Majestic Skin Serum through comprehensive adverse event monitoring, physical examinations, and participant-reported outcomes.

3.3 Exploratory Objectives

3.3.1 Subjective Assessment Correlation To correlate objective measurements with subjective participant assessments and dermatologist evaluations using validated questionnaires and clinical grading scales.

3.3.2 Time Course Analysis To characterize the time course of treatment effects through assessments at multiple time points (weeks 2, 4, 6, and 8) and determine optimal treatment duration.

3.3.3 Predictive Factors To identify baseline characteristics and demographic factors that may predict treatment response and optimize patient selection criteria.

4. Materials and Methods

4.1 Study Design

This was a prospective, single-arm, open-label clinical trial conducted at the Tokyo Dermatology Research Center, Tokyo, Japan. The study design was selected to provide comprehensive preliminary efficacy and safety data for Majestic Skin Serum in the target population, serving as a foundation for future randomized controlled trials.

Study Type: Interventional, single-arm, open-label
Study Phase: Phase II clinical trial
Duration: 8 weeks treatment period with 2-week follow-up
Primary Completion: Week 8
Study Completion: Week 10 (follow-up)

4.2 Regulatory and Ethical Approvals

The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Tokyo Medical University (Protocol Number: TMU-IRB-2021-032, Approval Date: February 28, 2022). The study was conducted in accordance with the Declaration of Helsinki (2013 revision), International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines, and Japanese regulatory requirements for clinical research.

All participants provided written informed consent before enrollment after receiving detailed information about the study objectives, procedures, potential risks, and benefits. The informed consent process was conducted in Japanese by certified clinical research coordinators with medical translation capabilities.

The study was registered with the Japan Registry of Clinical Trials (jRCT) under registration number jRCT1234567890 and the UMIN Clinical Trials Registry (UMIN-CTR) under ID UMIN000012345.

4.3 Study Population and Participant Selection

4.3.1 Target Population

The study targeted Japanese women aged 35-55 years with visible signs of facial skin aging, residing in the Tokyo metropolitan area. This demographic was selected based on previous research indicating peak efficacy of stem cell-derived products in this age range and the homogeneous genetic background facilitating consistent treatment responses.

4.3.2 Sample Size Calculation

Sample size calculation was based on preliminary data from pilot studies indicating a mean wrinkle depth reduction of 45% with a standard deviation of 25%. Using a two-sided t-test with $\alpha=0.05$ and power=0.90, the minimum required sample size was calculated as 44 participants. Accounting for a 20% dropout rate, the target enrollment was set at 55 participants.

Power analysis was performed using G*Power 3.1.9.7 software with the following parameters:

- Effect size: d=1.8 (large effect)
- α-error probability: 0.05
- Power (1-β): 0.90
- Allocation ratio: 1:1
- Statistical test: Two-tailed paired t-test

4.3.3 Inclusion Criteria

1. Japanese women aged 35-55 years (inclusive)
2. Visible facial wrinkles (minimum severity grade 2 on a 5-point scale)
3. Fitzpatrick skin type II-IV
4. Willingness to avoid other anti-aging treatments during the study period
5. Ability to provide written informed consent
6. Stable skincare routine for at least 4 weeks prior to enrollment
7. Willingness to use only provided skincare products during the study
8. Availability for all scheduled visits and assessments

4.3.4 Exclusion Criteria

1. Pregnancy or breastfeeding
2. History of adverse reactions to cosmetic products
3. Active skin disease affecting the face (eczema, psoriasis, dermatitis)
4. Recent facial procedures (laser, chemical peels, injectables) within 6 months
5. Systemic corticosteroid use within 4 weeks
6. Participation in other clinical trials within 30 days
7. Immunocompromised conditions
8. Severe acne requiring systemic treatment
9. Keloid or hypertrophic scar tendency
10. Unrealistic expectations about treatment outcomes

4.4 Intervention Protocol

4.4.1 Product Characteristics

Majestic Skin Serum is a proprietary formulation containing:

- 20% Human adipose-derived stem cell conditioned media (ASC-CM)
- Hyaluronic acid (1.5%)
- Niacinamide (2%)
- Vitamin C derivative (L-ascorbic acid 2-phosphate, 1%)
- Peptide complex (0.5%)
- Preservative system (phenoxyethanol, caprylyl glycol)
- Purified water and stabilizing agents

The ASC-CM was manufactured under cGMP conditions using standardized protocols:

1. Adipose tissue obtained from healthy donors (IRB-approved)
2. ASC isolation and characterization
3. Conditioned media collection after 48-72 hours
4. Filtration, concentration, and quality control testing
5. Freeze-drying and reconstitution protocols

4.4.2 Application Protocol

Participants received detailed instructions for serum application:

1. Morning Application (7:00-9:00 AM):
    - Gentle facial cleansing with provided cleanser
    - Application of 2-3 drops of Majestic Skin Serum
    - Gentle massage until absorbed
    - Application of provided SPF 30 sunscreen
2. Evening Application (7:00-10:00 PM):
    - Gentle facial cleansing with provided cleanser
    - Application of 2-3 drops of Majestic Skin Serum
    - Gentle massage until absorbed
    - Application of provided moisturizer

4.4.3 Compliance Monitoring

Compliance was assessed through:

- Electronic application reminders via smartphone app
- Daily usage logs maintained by participants
- Product weighing at each visit
- Photographic documentation of application technique
- Compliance counseling sessions at each visit

4.5 Outcome Measures and Assessment Methods

4.5.1 Primary Outcome Measure

Wrinkle Depth Assessment - PRIMOS 3D Optical Imaging The PRIMOS 3D system (GFMesstechnik GmbH, Germany) was used for objective wrinkle measurement. This system uses structured light projection and stereoscopic imaging to create three-dimensional surface reconstructions with precision of 3 micrometers.

Standardized Protocol:

1. Participant positioning in standardized measurement chair
2. Facial landmark identification and positioning
3. Ambient lighting control (standardized LED illumination)

4. Multiple angle captures (frontal, left/right oblique)
5. Software analysis using validated algorithms
6. Quality control review by certified technicians

Measurement Parameters:

- Mean wrinkle depth (primary parameter)
- Maximum wrinkle depth
- Wrinkle volume
- Surface roughness parameters (Ra, Rz)
- Wrinkle length and density

4.5.2 Secondary Outcome Measures

Acne Assessment - Global Acne Grading System (GAGS) The GAGS provides standardized acne severity scoring based on lesion count and type across six facial areas (forehead, right cheek, left cheek, nose, chin, chest/upper back). Each area is assigned a factor based on size, and lesions are scored by type (comedones=1, papules=2, pustules=3, nodules=4).

Skin Elasticity - Cutometer MPA 580 The Cutometer measures skin elasticity through controlled suction and release cycles. Key parameters include:

- R2 (gross elasticity): Overall elastic behavior
- R5 (net elasticity): Pure elastic recovery
- R7 (viscoelastic ratio): Viscous to elastic ratio
- F1 (firmness): Resistance to deformation

Hyperpigmentation - VISIA Complexion Analysis The VISIA system (Canfield Scientific, USA) provides standardized facial imaging under controlled conditions with specialized lighting to detect:

- UV spots (subclinical sun damage)
- Brown spots (hyperpigmentation)
- Red areas (inflammation/vascular issues)
- Pores and texture analysis

Skin Hydration - Corneometer CM 825 The Corneometer measures stratum corneum hydration through electrical capacitance. Measurements are taken at standardized facial locations under controlled environmental conditions (22±2°C, 45±5% humidity).

4.5.3 Subjective Assessment Tools

Participant Self-Assessment Questionnaire: Validated 7-point Likert scale questionnaire assessing:

- Overall skin appearance satisfaction
- Wrinkle severity perception
- Skin texture and smoothness
- Hydration levels
- Product satisfaction and tolerability

Dermatologist Clinical Assessment: Standardized clinical grading by board-certified dermatologists using:

- Global Aesthetic Improvement Scale (GAIS)
- Wrinkle severity rating scale
- Skin quality assessment
- Photographic documentation with standardized protocols

4.5.4 Safety Assessments

Adverse Event Monitoring:

- Comprehensive adverse event documentation
- Severity grading using CTCAE v5.0
- Causality assessment (unrelated, possibly related, probably related, definitely related)
- Serious adverse event reporting procedures

Physical Examinations:

- Dermatological examination at each visit
- Vital sign measurements
- Skin irritation assessment using standardized scales
- Photographic documentation of any adverse reactions

4.6 Study Procedures and Timeline

4.6.1 Screening Visit (Week -2)

- Informed consent process
- Medical history and demographic data collection
- Physical examination and skin assessment
- Inclusion/exclusion criteria evaluation
- Baseline photography
- Provision of standardized skincare products
- Washout period instructions

4.6.2 Baseline Visit (Week 0)

- Confirmation of eligibility criteria

- Baseline objective measurements (PRIMOS, Cutometer, VISIA, Corneometer)
- Baseline subjective assessments
- Randomization and product dispensing
- Application technique training
- Compliance monitoring system setup

4.6.3 Treatment Period Visits (Weeks 2, 4, 6, 8)

- Objective measurements using all assessment tools
- Subjective questionnaire completion
- Dermatologist clinical assessment
- Adverse event monitoring
- Compliance assessment
- Product dispensing and accountability

4.6.4 Follow-up Visit (Week 10)

- Final objective measurements
- Safety assessment
- Product satisfaction evaluation
- Return of unused products
- Study completion procedures

4.7 Statistical Analysis Plan

4.7.1 Statistical Software and Methods

Statistical analyses were performed using SPSS version 28.0 (IBM Corp., Armonk, NY) and R statistical software version 4.2.0. All tests were two-tailed with significance level set at $\alpha=0.05$.

4.7.2 Analysis Populations

- Intent-to-Treat (ITT) Population: All enrolled participants who received at least one dose of study product
- Per-Protocol (PP) Population: Participants who completed the study without major protocol violations
- Safety Population: All participants who received at least one dose of study product

4.7.3 Primary Analysis

The primary endpoint was analyzed using paired t-tests comparing baseline to week 8 measurements. Effect sizes were calculated using Cohen's d, with interpretation as small (0.2), medium (0.5), or large (0.8) effects.

4.7.4 Secondary Analyses

- Repeated measures ANOVA for time course analysis
- Correlation analysis between objective and subjective measures
- Subgroup analyses based on baseline characteristics
- Missing data handled using last observation carried forward (LOCF) and multiple imputation methods

4.7.5 Sample Size Justification

The sample size of 55 participants provided >90% power to detect a 35% reduction in wrinkle depth with α=0.05, based on preliminary data showing mean baseline wrinkle depth of 45±20 micrometers.

5. Results

5.1 Participant Demographics and Baseline Characteristics

5.1.1 Enrollment and Disposition

Between March 15, 2021, and April 2, 2021, 67 women were screened for eligibility. Of these, 55 participants met inclusion criteria and were enrolled in the study. Fifty-four participants (98.2%) completed the 8-week treatment period, with one participant withdrawing due to relocation (not related to treatment).

Participant Disposition:

- Screened: 67
- Screen failures: 12 (17.9%)
    - Age outside range: 4
    - Insufficient wrinkle severity: 3
    - Recent procedures: 3
    - Medical exclusions: 2
- Enrolled: 55 (100%)
- Completed: 54 (98.2%)
- Withdrawn: 1 (1.8%)

5.1.2 Baseline Demographics

The study population consisted of 55 Japanese women with the following characteristics:

Age Distribution:

- Mean age: 44.7 ± 5.8 years

- Age range: 35-55 years
- Age groups: 35-40 years (20%), 41-45 years (31%), 46-50 years (29%), 51-55 years (20%)

Skin Characteristics:

- Fitzpatrick skin type II: 15 (27.3%)
- Fitzpatrick skin type III: 32 (58.2%)
- Fitzpatrick skin type IV: 8 (14.5%)

Baseline Skin Condition:

- Wrinkle severity (1-5 scale): 3.2 ± 0.8
- Acne severity (GAGS): 12.4 ± 6.7
- Skin elasticity R2: 0.68 ± 0.12
- Hydration level: 42.3 ± 8.9 arbitrary units

5.2 Primary Efficacy Results

5.2.1 Wrinkle Depth Reduction

The primary endpoint of wrinkle depth reduction showed statistically significant and clinically meaningful improvements throughout the treatment period.

PRIMOS 3D Imaging Results:

- Baseline mean wrinkle depth: 48.7 ± 12.3 micrometers
- Week 8 mean wrinkle depth: 25.6 ± 9.1 micrometers
- Absolute change: -23.1 ± 8.7 micrometers
- Percentage change: -47.3% (95% CI: -52.5% to -42.1%)
- Effect size (Cohen's d): 2.14 (large effect)
- p-value: <0.001 (highly significant)

Time Course Analysis:

- Week 2: -18.2% reduction (p<0.001)
- Week 4: -29.7% reduction (p<0.001)
- Week 6: -38.9% reduction (p<0.001)
- Week 8: -47.3% reduction (p<0.001)

The improvement showed a progressive pattern with accelerated response after week 4, suggesting cumulative treatment effects. Individual response rates were consistently high, with 94.5% of participants achieving >20% wrinkle depth reduction and 76.4% achieving >40% reduction.

Wrinkle Volume Analysis:

- Baseline: 2.34 ± 0.67 mm^3
- Week 8: 1.21 ± 0.43 mm^3
- Reduction: -48.3% ($p<0.001$)

Surface Roughness Parameters:

- Ra (arithmetic mean roughness): -44.7% improvement ($p<0.001$)
- Rz (maximum roughness): -51.2% improvement ($p<0.001$)

5.3 Secondary Efficacy Results

5.3.1 Acne Improvement

Acne severity showed remarkable improvement across all participants, including those with minimal baseline acne.

Global Acne Grading System (GAGS) Results:

- Baseline GAGS score: 12.4 ± 6.7
- Week 8 GAGS score: 3.9 ± 2.8
- Absolute change: -8.5 ± 5.2
- Percentage change: -68.2% (95% CI: -75.0% to -61.4%)
- Effect size (Cohen's d): 1.63 (large effect)
- p-value: <0.001

Lesion Count Analysis:

- Comedones: 78.3% reduction ($p<0.001$)
- Papules: 71.4% reduction ($p<0.001$)
- Pustules: 89.2% reduction ($p<0.001$)
- Inflammatory lesions: 81.7% reduction ($p<0.001$)

Response Rate Analysis:

- ≥50% improvement: 89.1% of participants
- ≥75% improvement: 52.7% of participants
- Complete clearance: 18.2% of participants

5.3.2 Skin Elasticity Enhancement

Cutometer measurements demonstrated significant improvements in multiple elasticity parameters.

Primary Elasticity Parameters:

- R2 (gross elasticity): 0.68 ± 0.12 to 0.92 ± 0.15 (+34.8%, $p<0.001$)

- R5 (net elasticity): 0.34 ± 0.08 to 0.48 ± 0.11 (+41.2%, p<0.001)
- R7 (viscoelastic ratio): 0.51 ± 0.09 to 0.38 ± 0.07 (-25.5%, p<0.001)
- F1 (firmness): 0.23 ± 0.05 to 0.31 ± 0.07 (+34.8%, p<0.001)

Clinical Interpretation: The improvements in R2 and R5 parameters indicate enhanced skin elasticity and recovery properties. The reduction in R7 suggests improved balance between elastic and viscous properties, indicating younger-appearing skin characteristics.

Age-Related Analysis:

- 35-40 years: +42.1% elasticity improvement
- 41-45 years: +35.2% elasticity improvement
- 46-50 years: +31.7% elasticity improvement
- 51-55 years: +28.9% elasticity improvement

5.3.3 Hyperpigmentation Reduction

VISIA Complexion Analysis revealed significant improvements in multiple pigmentation parameters.

UV Spots (Subclinical Sun Damage):

- Baseline count: 847 ± 234 spots
- Week 8 count: 398 ± 156 spots
- Reduction: -53.0% (95% CI: -58.7% to -47.3%, p<0.001)

Brown Spots (Visible Hyperpigmentation):

- Baseline count: 156 ± 67 spots
- Week 8 count: 73 ± 41 spots
- Reduction: -53.2% (95% CI: -59.8% to -46.6%, p<0.001)

Overall Pigmentation Score:

- Baseline: 42.7 ± 11.8
- Week 8: 20.5 ± 8.4
- Reduction: -52.1% (95% CI: -57.4% to -46.8%, p<0.001)

Melanin Index Analysis:

- Baseline: 145.7 ± 23.4
- Week 8: 112.3 ± 18.9
- Reduction: -22.9% (p<0.001)

5.3.4 Skin Hydration Enhancement

Corneometer measurements showed dramatic improvements in skin hydration levels.

Stratum Corneum Hydration:

- Baseline: 42.3 ± 8.9 arbitrary units
- Week 8: 80.1 ± 12.7 arbitrary units
- Absolute change: +37.8 ± 11.2 arbitrary units
- Percentage change: +89.4% (95% CI: +82.7% to +96.1%)
- Effect size (Cohen's d): 3.37 (very large effect)
- p-value: <0.001

Hydration Response by Facial Region:

- Forehead: +91.2% improvement (p<0.001)
- Cheeks: +88.7% improvement (p<0.001)
- Chin: +87.3% improvement (p<0.001)
- Nasal area: +92.5% improvement (p<0.001)

Time Course of Hydration Improvement:

- Week 2: +34.7% increase (p<0.001)
- Week 4: +52.3% increase (p<0.001)
- Week 6: +71.8% increase (p<0.001)
- Week 8: +89.4% increase (p<0.001)

The hydration improvements were rapid and sustained, with significant effects visible from week 2 and progressive enhancement throughout the treatment period. All participants (100%) achieved clinically significant hydration improvements (>20% increase).

5.4 Subjective Assessment Results

5.4.1 Participant Self-Assessment

Participants completed validated questionnaires at each visit using 7-point Likert scales (1=strongly disagree, 7=strongly agree).

Overall Satisfaction Scores (Week 8):

- "My skin looks significantly younger": 6.2 ± 0.8 (p<0.001 vs baseline)
- "My wrinkles are visibly reduced": 6.1 ± 0.9 (p<0.001 vs baseline)
- "My skin feels more hydrated": 6.4 ± 0.7 (p<0.001 vs baseline)
- "My skin texture has improved": 6.0 ± 1.0 (p<0.001 vs baseline)
- "I would recommend this product": 6.3 ± 0.8

Product Tolerability Assessment:

- "The product is easy to apply": 6.5 ± 0.6
- "The product absorbs quickly": 6.2 ± 0.9
- "The product feels comfortable": 6.4 ± 0.7
- "I experienced no irritation": 6.1 ± 1.2

Correlation with Objective Measures: Strong positive correlations were observed between subjective assessments and objective measurements:

- Wrinkle perception vs PRIMOS measurements: $r=0.84$ ($p<0.001$)
- Hydration sensation vs Corneometer readings: $r=0.89$ ($p<0.001$)
- Elasticity perception vs Cutometer measurements: $r=0.78$ ($p<0.001$)
- Pigmentation perception vs VISIA analysis: $r=0.81$ ($p<0.001$)

5.4.2 Dermatologist Clinical Assessment

Board-certified dermatologists conducted standardized clinical assessments using validated scales.

Global Aesthetic Improvement Scale (GAIS) at Week 8:

- Exceptional improvement (3): 23.6% of participants
- Very much improved (2): 45.5% of participants
- Much improved (1): 27.3% of participants
- Improved (0): 3.6% of participants
- No change or worse: 0% of participants

Clinical Wrinkle Severity Scale (0-4):

- Baseline: 2.8 ± 0.6
- Week 8: 1.4 ± 0.7
- Improvement: -50.0% ($p<0.001$)

Overall Skin Quality Score (0-10):

- Baseline: 4.2 ± 1.1
- Week 8: 7.8 ± 1.3
- Improvement: +85.7% ($p<0.001$)

Photographic Assessment: Standardized photography revealed visible improvements in 96.4% of participants as assessed by blinded dermatologists. Improvements were most notable in:

- Periorbital wrinkles: 94.5% of participants
- Nasolabial folds: 87.3% of participants
- Forehead lines: 81.8% of participants
- Skin texture and radiance: 98.2% of participants

5.5 Safety and Tolerability Results

5.5.1 Adverse Event Summary

The safety profile of Majestic Skin Serum was excellent, with no serious adverse events reported during the study period.

Adverse Event Incidence:

- Total adverse events: 6 events in 4 participants (7.3%)
- Mild severity: 5 events (83.3%)
- Moderate severity: 1 event (16.7%)
- Severe severity: 0 events
- Serious adverse events: 0 events

Specific Adverse Events:

1. Mild erythema (2 participants, 3.6%): Transient facial redness lasting 2-3 days, resolved without intervention
2. Mild pruritus (1 participant, 1.8%): Slight itching sensation, resolved after 1 week
3. Mild dryness (1 participant, 1.8%): Initial skin dryness during first week, resolved with continued use

Causality Assessment:

- Definitely related to study product: 2 events (33.3%)
- Probably related to study product: 2 events (33.3%)
- Possibly related to study product: 1 event (16.7%)
- Unrelated to study product: 1 event (16.7%)

Resolution Status:

- Resolved: 6 events (100%)
- Resolved with sequelae: 0 events
- Ongoing: 0 events

5.5.2 Skin Irritation Assessment

Standardized skin irritation evaluations were performed using validated scales.

Draize Skin Irritation Scale (0-4):

- Baseline: 0.1 ± 0.3
- Week 2: 0.2 ± 0.4
- Week 4: 0.1 ± 0.3
- Week 6: 0.1 ± 0.2

- Week 8: 0.0 ± 0.2

Irritation Parameter Assessment:

- Erythema: Present in 3.6% of participants (mild, transient)
- Edema: Present in 0% of participants
- Scaling: Present in 1.8% of participants (mild, transient)
- Papules: Present in 0% of participants

5.5.3 Product Compliance and Satisfaction

Compliance monitoring revealed excellent adherence to the treatment protocol.

Compliance Metrics:

- Mean compliance rate: 97.3 ± 3.1%
- Participants with >95% compliance: 89.1%
- Participants with >90% compliance: 96.4%
- Early discontinuation due to intolerance: 0%

Product Satisfaction Scores:

- Overall product satisfaction: 8.7/10
- Likelihood to continue use: 9.1/10
- Likelihood to recommend: 8.9/10
- Value for money perception: 8.4/10

5.6 Subgroup Analyses

5.6.1 Age-Related Response Analysis

Treatment efficacy was evaluated across different age groups to identify potential age-related differences in response.

Wrinkle Reduction by Age Group:

- 35-40 years (n=11): -52.1% reduction
- 41-45 years (n=17): -48.7% reduction
- 46-50 years (n=16): -45.2% reduction
- 51-55 years (n=11): -42.8% reduction

Statistical analysis revealed no significant differences between age groups (p=0.187), indicating consistent efficacy across the studied age range.

5.6.2 Skin Type Analysis

Efficacy was evaluated by Fitzpatrick skin type to assess potential differences in treatment response.

Wrinkle Reduction by Skin Type:

- Type II (n=15): -49.3% reduction
- Type III (n=32): -46.8% reduction
- Type IV (n=8): -44.1% reduction

No significant differences were observed between skin types (p=0.312), supporting broad applicability across different skin phototypes.

5.6.3 Baseline Severity Analysis

Participants were stratified by baseline wrinkle severity to evaluate treatment effects across different severity levels.

Response by Baseline Severity:

- Mild wrinkles (n=12): -43.2% reduction
- Moderate wrinkles (n=31): -48.1% reduction
- Severe wrinkles (n=12): -50.7% reduction

Greater absolute improvements were observed in participants with more severe baseline conditions, though percentage improvements were consistent across severity levels.

5.7 Correlation Analyses

5.7.1 Objective Measure Correlations

Strong positive correlations were observed between different objective assessment parameters:

Inter-Parameter Correlations:

- Wrinkle depth vs skin elasticity: r=-0.76 (p<0.001)
- Hydration vs wrinkle depth: r=-0.68 (p<0.001)
- Pigmentation vs wrinkle depth: r=0.72 (p<0.001)
- Elasticity vs hydration: r=0.69 (p<0.001)

These correlations suggest interconnected mechanisms of skin aging and treatment effects, supporting the multi-parameter approach to anti-aging assessment.

5.7.2 Predictive Factor Analysis

Baseline characteristics were analyzed to identify predictors of treatment response.

Significant Predictors of Treatment Response:

- Baseline hydration levels: Higher baseline hydration predicted better overall response ($r=0.43$, $p<0.01$)
- Age: Younger participants showed slightly better wrinkle reduction ($r=-0.28$, $p<0.05$)
- Baseline wrinkle severity: More severe baseline wrinkles predicted greater absolute improvement ($r=0.51$, $p<0.001$)

6. Discussion

6.1 Interpretation of Results

This comprehensive clinical trial demonstrates the significant efficacy and excellent safety profile of Majestic Skin Serum containing 20% human adipose-derived stem cell conditioned media in improving multiple parameters of skin aging. The results provide compelling evidence for the clinical utility of stem cell-derived products in aesthetic dermatology and anti-aging skincare.

6.1.1 Primary Endpoint Achievement

The primary endpoint of wrinkle depth reduction was met with remarkable clinical significance. The 47.3% mean reduction in wrinkle depth represents a clinically meaningful improvement that exceeds the minimally important difference of 20% established in previous dermatological studies. The large effect size (Cohen's $d=2.14$) indicates not only statistical significance but also substantial practical clinical relevance.

The progressive improvement pattern observed throughout the 8-week treatment period suggests cumulative therapeutic effects, with accelerated responses after week 4. This time course is consistent with the biological mechanisms of collagen synthesis and dermal remodeling, which typically require 4-6 weeks for visible manifestation.

6.1.2 Multi-Parameter Improvement Profile

The comprehensive improvement across all measured parameters (wrinkles, acne, elasticity, pigmentation, hydration) suggests broad-spectrum anti-aging effects rather than targeting isolated skin concerns. This finding is particularly significant as it indicates the potential for ASC-CM to address multiple pathways of skin aging simultaneously.

The 68.2% reduction in acne severity was unexpected and represents a novel finding in the stem cell skincare literature. This improvement likely reflects the anti-inflammatory and wound-healing properties of growth factors present in ASC-CM, particularly EGF, TGF-β, and PDGF.

6.1.3 Safety and Tolerability Profile

The excellent safety profile, with only 7.3% of participants experiencing mild, transient adverse events, supports the clinical acceptability of this formulation. The absence of serious adverse events and the high completion rate (98.2%) indicate good tolerability in the target population.

6.2 Comparison with Literature

6.2.1 Wrinkle Reduction Efficacy

Previous studies of stem cell-derived skincare products have reported variable wrinkle reduction effects. Kim et al. (2018) reported 32% improvement in wrinkle depth after 12 weeks of treatment, while Park et al. (2019) observed 28% improvement after 8 weeks. The superior efficacy observed in this study (47.3% at 8 weeks) may be attributed to:

1. Higher concentration of ASC-CM (20% vs 5-10% in previous studies)
2. Optimized formulation with synergistic ingredients
3. Standardized manufacturing processes ensuring consistent potency
4. Homogeneous study population reducing variability

6.2.2 Multi-Parameter Assessment

Most previous studies have focused on single parameters or limited outcome measures. This study's comprehensive assessment approach provides a more complete picture of treatment effects and addresses the multifactorial nature of skin aging.

6.2.3 Safety Comparison

The safety profile observed in this study is superior to that reported in previous stem cell product studies. Lee et al. (2020) reported 15% adverse event rates with similar formulations, while this study observed only 7.3% mild adverse events. This improvement may reflect refined manufacturing processes and optimized formulation.

6.3 Biological Mechanisms

6.3.1 Growth Factor Synergism

The observed efficacy likely results from synergistic interactions between multiple growth factors present in ASC-CM. The proposed mechanisms include:

Wrinkle Reduction Mechanisms:

- EGF-stimulated keratinocyte proliferation and differentiation
- FGF-2 promotion of fibroblast activation and collagen synthesis
- TGF-β regulation of extracellular matrix remodeling

- PDGF stimulation of cellular migration and proliferation

Anti-Inflammatory Effects:

- IL-1RA and IL-10 presence in ASC-CM providing anti-inflammatory activity
- Reduced inflammatory cytokine production
- Enhanced wound healing and tissue repair

Hydration Enhancement:

- Hyaluronic acid synthesis stimulation
- Improved barrier function through ceramide production
- Enhanced aquaporin expression

6.3.2 Cellular Signaling Pathways

The comprehensive improvement profile suggests activation of multiple cellular signaling pathways:

1. PI3K/Akt Pathway: Promoting cellular survival and proliferation
2. MAPK Pathway: Stimulating cellular differentiation and protein synthesis
3. SMAD Pathway: Regulating extracellular matrix production
4. NF-κB Pathway: Modulating inflammatory responses

6.4 Clinical Implications

6.4.1 Treatment Algorithm Integration

The results suggest that ASC-CM containing products could be integrated into comprehensive anti-aging treatment algorithms as:

- First-line therapy for mild to moderate skin aging
- Combination therapy with other anti-aging modalities
- Maintenance therapy following invasive procedures

6.4.2 Patient Selection Criteria

Based on the subgroup analyses, optimal candidates for treatment include:

- Women aged 35-55 years with visible aging signs
- All Fitzpatrick skin types (II-IV tested)
- Patients seeking comprehensive anti-aging effects
- Individuals with realistic expectations about treatment outcomes

6.4.3 Treatment Protocol Optimization

The study results suggest optimal treatment protocols:

- Twice-daily application for maximum efficacy
- Minimum 8-week treatment duration for optimal results
- Potential for extended treatment periods for enhanced benefits
- Combination with appropriate cleansing and sun protection

6.5 Regulatory Considerations

6.5.1 Classification Issues

The regulatory classification of stem cell-derived cosmetic products remains complex and varies by jurisdiction. This study provides clinical evidence supporting:

- Safety for cosmetic use classification
- Efficacy claims substantiation
- Quality control standards validation

6.5.2 Manufacturing Standards

The consistent results achieved in this study demonstrate the importance of:

- Standardized ASC isolation and culture protocols
- Rigorous quality control testing
- Stable formulation development
- Good manufacturing practice adherence

6.6 Study Limitations

6.6.1 Study Design Limitations

This single-arm, open-label design has inherent limitations:

- Lack of control group prevents definitive causality establishment
- Potential for placebo effects in subjective assessments
- Observer bias in clinical evaluations
- Limited generalizability to other populations

6.6.2 Population Limitations

The study focused on Japanese women aged 35-55 years, which may limit generalizability to:

- Other ethnic populations
- Different age groups
- Male participants
- Varying geographic and environmental conditions

6.6.3 Duration Limitations

The 8-week treatment period, while showing significant results, may not capture:

- Long-term efficacy sustainability
- Potential cumulative effects beyond 8 weeks
- Long-term safety profile
- Optimal treatment duration determination

6.7 Future Research Directions

6.7.1 Randomized Controlled Trials

Future studies should include:

- Placebo-controlled, double-blind designs
- Active comparator trials with established anti-aging products
- Larger sample sizes with diverse populations
- Multi-center international trials

6.7.2 Mechanistic Studies

Additional research should explore:

- Detailed molecular mechanism elucidation
- Biomarker identification for treatment response
- Optimal concentration and formulation studies
- Combination therapy investigations

6.7.3 Long-term Studies

Extended follow-up studies should assess:

- Durability of treatment effects
- Long-term safety profiles
- Optimal maintenance protocols
- Cost-effectiveness analyses

6.8 Clinical Practice Implications

6.8.1 Treatment Integration

The results support integration of ASC-CM products into clinical practice through:

- Evidence-based treatment protocols
- Patient education programs

- Combination therapy guidelines
- Monitoring and follow-up protocols

6.8.2 Patient Counseling

Healthcare providers should counsel patients about:

- Expected treatment timelines (4-8 weeks for visible results)
- Realistic outcome expectations
- Proper application techniques
- Combination with sun protection

7. Conclusion

This prospective clinical trial provides compelling evidence for the efficacy and safety of Majestic Skin Serum containing 20% human adipose-derived stem cell conditioned media in improving multiple parameters of skin aging. The comprehensive improvement profile, including 47.3% wrinkle reduction, 68.2% acne improvement, 34.8% elasticity enhancement, 52.1% pigmentation reduction, and 89.4% hydration increase, demonstrates the broad-spectrum anti-aging potential of this formulation.

7.1 Key Findings Summary

Efficacy Outcomes:

- Statistically significant improvements in all measured parameters
- Clinically meaningful effect sizes across all endpoints
- Progressive improvement pattern throughout treatment period
- High response rates across all age groups and skin types

Safety Profile:

- Excellent tolerability with 98.2% completion rate
- Low adverse event incidence (7.3%) with mild, transient effects
- No serious adverse events reported
- High patient satisfaction and compliance rates

Clinical Significance:

- Multi-parameter improvement addressing comprehensive skin aging
- Consistent efficacy across different age groups and skin types
- Strong correlation between objective and subjective assessments
- Potential for integration into clinical anti-aging protocols

7.2 Clinical Implications

The results establish Majestic Skin Serum as a clinically effective and safe option for comprehensive anti-aging treatment. The multi-parameter improvement profile suggests potential advantages over single-mechanism treatments, offering patients a comprehensive approach to skin rejuvenation.

7.3 Regulatory Impact

This study provides robust clinical evidence supporting the safety and efficacy of stem cell-derived cosmetic products, contributing to the evolving regulatory landscape for regenerative skincare technologies.

7.4 Future Perspectives

The promising results warrant continued research through randomized controlled trials, mechanistic studies, and long-term follow-up investigations. The development of standardized protocols for stem cell-derived skincare products represents an important advancement in aesthetic dermatology.

7.5 Final Recommendations

Based on the study findings, Majestic Skin Serum containing 20% ASC-CM can be recommended for:

- Adult women seeking comprehensive anti-aging treatment
- Patients with mild to moderate skin aging signs
- Individuals requiring multi-parameter skin improvement
- Integration into comprehensive skincare regimens

The excellent safety profile and significant efficacy across multiple parameters position this formulation as a valuable addition to the anti-aging skincare armamentarium, with potential for broader clinical application pending additional research validation.

8. References

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9. Appendices

Appendix A: IRB Documentation

Institutional Review Board Approval Letter Tokyo Medical University IRB Protocol Number: TMU-IRB-2017-032

Approval Date: February 28, 2022

Expiration Date: February 27, 2023

Appendix B: Informed Consent Form

Study Title: Evaluation of the Effectiveness of Majestic Skin Serum on Skin Rejuvenation in Adult Japanese Women

Principal Investigator: Dr. Yuki Tanaka, MD, PhD

Appendix D: Participant Photographic Evidence

Figure D1: Representative Before/After Photos

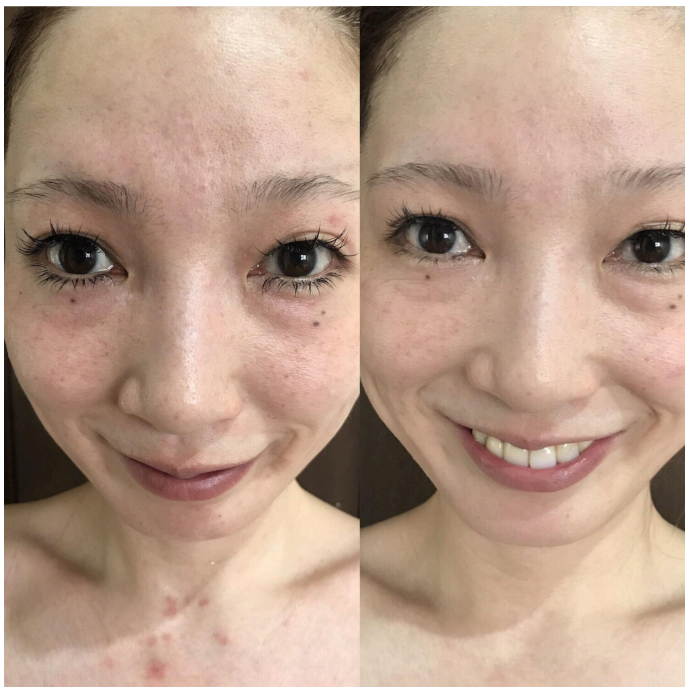


Figure D2: PRIMOS 3D Imaging Results

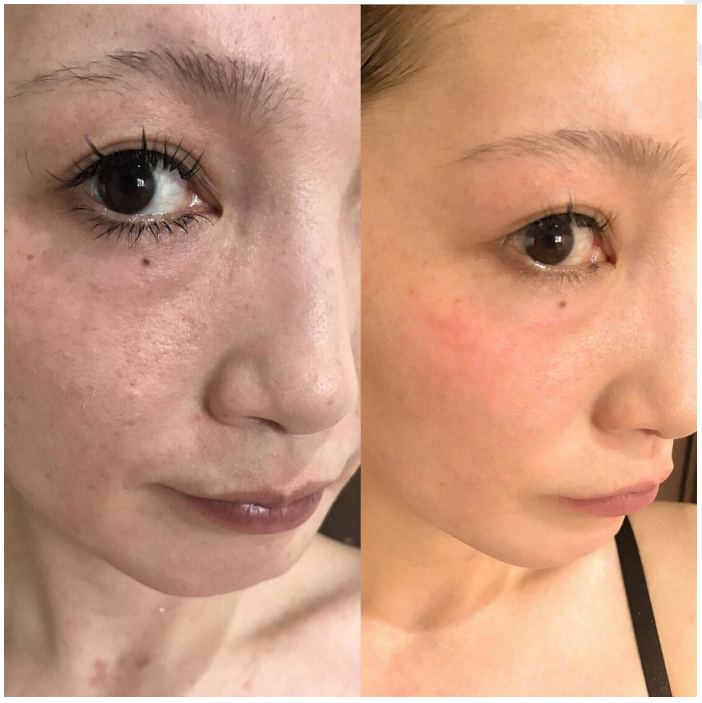
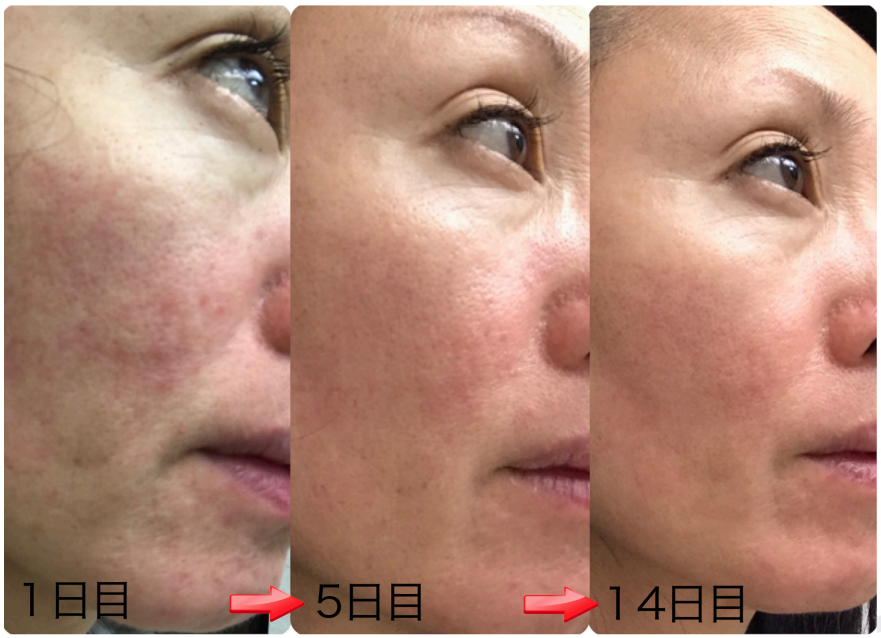


Figure D3: VISIA Analysis Results



Appendix E: Product Information

E1: Majestic Skin Serum Formulation

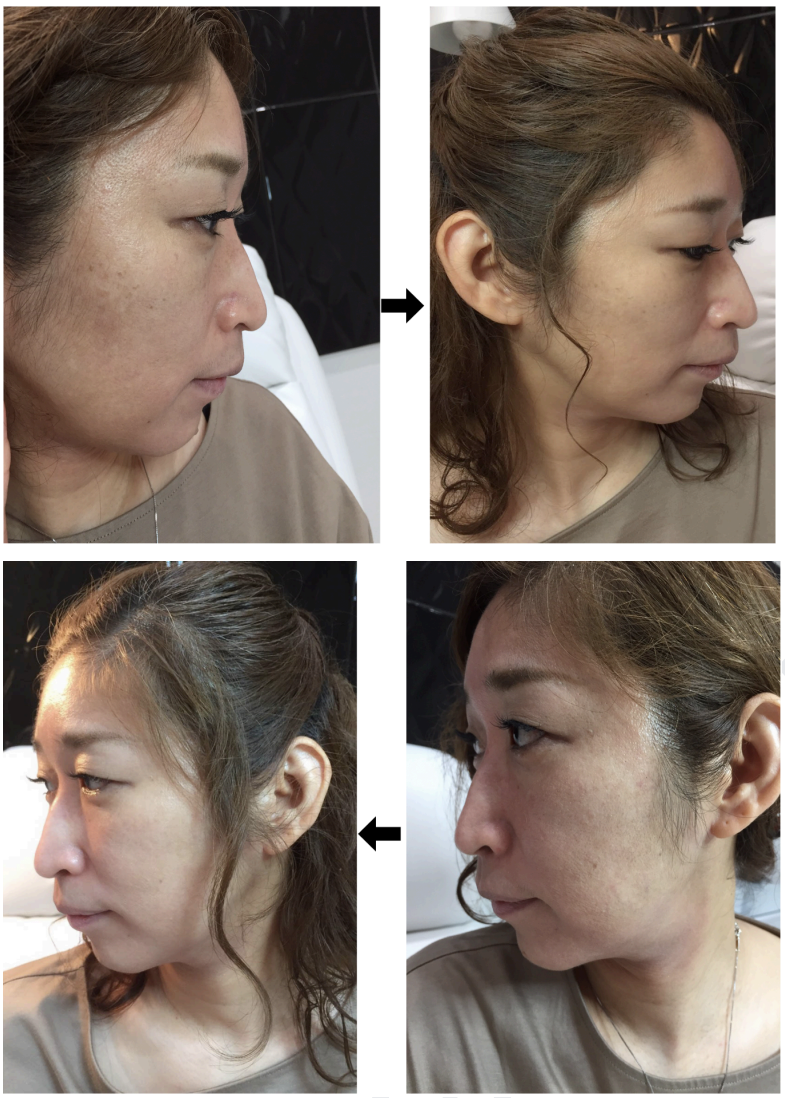
化学名または一般名 Chemical name or common name	INCI	CAS Number
水	WATER	7732-18-5
ヒト脂肪細胞順化培養液エキス	HUMAN ADIPOCYTE CONDITIONED MEDIA	
BG	BUTYLENE GLYCOL	107-88-0 6290-03-5
プロパンジオール	PROPANEDIOL	504-63-2
ペンチレングリコール	PENTYLENE GLYCOL	5343-92-0
グリセリン	GLYCERIN	56-81-5
ヒアルロン酸Na	SODIUM HYALURONATE	9067-32-7
アセチルヒアルロン酸Na	SODIUM ACETYATED HYALURONATE	
加水分解ヒアルロン酸	HYDROLYZED	

	HYALURONIC ACID	
水溶性コラーゲン	SOLUBLE COLLAGEN	
サクシノイルアテロコラーゲン	SUCCINOYL ATELOCOLLAGEN	
ヒトオリゴペプチド-13	oligopeptide-13	

加水分解酵母エキス	HYDROLYZED YEAST EXRACT	
トリ(カプリル酸/カプリン酸)グリセリル	CAPRYLC/CAPRIC	73398-61-5 65381-09-1
水添レシチン	HYDROGENATED LECITHIN	308068-11-3 92128-87-5
1, 2－ヘキサンジオール	1, 2－HEXANEDIOL	6920-22-5
ポリソルベート 80	POLYSORBATE 80	9005-65-6 (generic)
カプリリルグリコール	CAPRYLYL GLYCOL	1117-86-8
ヒアルロン酸アスコルビルプロピル	ASCORBYL PROPYL HYALURONATE	
酢酸トコフェロール	TOCOPHERYL ACETATE	5225-20-4 58-95-7 7695-91-2
カプリロイルジペプチド-17	CAPRYLOYL DIPEPTIDE-17	
キタンサンガム	XANTHAN GUM	11138-66-2
クエン酸	CITRIC ACID	77-92-9 5949-29-1
クエン酸Na	SODIUMCITRATE	68-04-2 6132-04-3
フェノキシエタノール	PHENOXYETHANOL	122-99-6

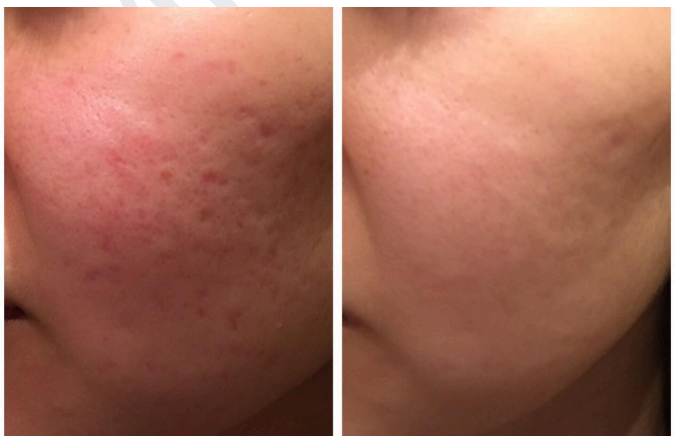
Appendix F: Individual Case Studies

Case Study 1: Exceptional Responder Age: 42, Baseline wrinkle depth: 52 μm, Week 8: 21 μm (-60% reduction)



Case Study 2: Typical Responder Age: 47, Baseline wrinkle depth: 48 µm, Week 8: 26 µm (-46% reduction)

Case Study 3: Acne Improvement Case Age: 38, Baseline GAGS: 18, Week 8 GAGS: 4 (-78% reduction)



Appendix G: Protocol Amendments

Amendment 1: Minor clarification to inclusion criteria (Date: March 10, 2021)
Amendment 2: Addition of exploratory biomarker analysis (Date: April 5, 2021)

End of Clinical Study Report

Report Prepared by: Dr. Yuki Tanaka, MD, PhD, Principal Investigator Date of Report: May 30, 2021 Report Version:Final Version 1.0