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"Assessment of skin physiological changes and efficacy of skincare products in post-menopausal Chinese women"

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1. Introduction

Menopause is defined as the cessation of menstruation for 12 consecutive months. Following menopause, significant changes occur in the body due to neuroendocrine alterations. In the short term, these changes manifest as alterations in body weight, hot flashes, irritability, palpitations, chest tightness, mood swings, insomnia, and atrophy of the vulva. In the long term, the consequences include an increased risk of cardiovascular diseases, cognitive decline, osteoporosis, and cancer [1].

Menopause accelerates skin aging. Specifically, this is manifested as skin thinning, dryness, and reduced elasticity, the formation of wrinkles, sagging, itching, increased sensitivity, impaired wound healing, decreased vascularization, and pigmentation. [2，3，4]

The active ingredients used to improve menopausal skin issues mainly include peptides, isoflavones, polyphenolic phytochemicals, 40-acetoxy resveratrol (4AR), daidzein, leontopodic acid, echinacoside, and asiaticoside, among others [5, 6, 7]. Peptides have been demonstrated to induce collagen synthesis. Isoflavones, which are non-nutritive substances beneficial to health, act as modulators of estrogen receptors. Polyphenolic phytochemicals, also known as phytoestrogens, function as selective estrogen receptor modulators (SERMs), many of which possess agonistic properties for estrogen receptor β (ERβ). 40-Acetoxy resveratrol (4AR).[6, 7, 8]

The investigation of skin changes in menopausal women in China has garnered limited attention in the existing literature.The objective of this study was to investigate skin physiological changes and to evaluate skincare products efficacy for post-menopausal Chinese women.

2. Materials and Methods

2.1 Materials

The skincare products include serum, cream, lotion, and water, the active ingredient is cyclohexapeptide-9.

2.2 Methods

2.2.1 Subjects and Study design

Study 1

The study aims to document changes in skin physiology related to menopause. Sixty (60) healthy Chinese women aged between 40 and 60 years were recruited to participate in the study after providing written informed consent including consent to use photos for the purposes of the study. The subjects were divided into three groups: 20 pre-menopausal women, 20 women who have been post-menopausal for 1–5 years, and 20 women who have been post-menopausal for more than 5 years.

Each subject visited the laboratory once and refrained from using any cosmetics on the day of the visit. Skin physiological parameters including skin hydration, elasticity, firmness, skin color, and wrinkles were assessed.

Study 2

This study aims to test the effect of a skin care regiment in countering the skin-related effects of menopause. In this study 43 healthy post-menopausal Chinese women with no history of cosmetic allergies were recruited. Eligible subjects agreed to avoid sun exposure during the trial period and provided written informed consent including consent to use photos for the purposes of the study.

All subjects were instructed to apply the designated skincare products to their entire face twice daily (morning and evening) for a total duration of 28 days.

Subjects attended follow-up visits at the laboratory at three specific time points: before product use, 14 days and 28 days after product use. Skin physiological parameters, including skin elasticity, firmness, and wrinkles were assessed.

On the day of each follow-up visit, subjects discontinued the use of all cosmetics. Upon arrival at the laboratory, their face was washed with water. Subsequently, subjects rested for 30 minutes in a controlled environment room maintained at a temperature of 22±1°C and a relative humidity of 50%. Thereafter, within the same controlled environment, the skin physiological parameters of the subjects were assessed, and digital facial images were acquired.

2.2.2 Instrumental evaluation

A Corneometer (Courage + Khazaka electronic GmbH, Germany) was used to quantitatively evaluate the moisture content of the stratum corneum, as a measure of hydration of the skin.

A Cutometer (Courage + Khazaka electronic GmbH, Germany) was used to quantitatively evaluate skin elasticity and firmness, by recording the R2 and R7 values.

A Spectrophotometer CM-26dG (KONICA MINOLTA,INC., Japan) was used to quantitatively evaluaty skin color, by recording the L* and ITA° values.

All test sites were randomly allocated to one side of the face.

2.2.3 Photography

A VISIA-CR photo station (Canfield Scientific, USA) was used to take digital images of each subject's face (left, center, and right view) under the following lighting conditions: standard 1 (visible bright).

A Primos CR system (Canfield Scientific, USA) was used to acquire 3D digital images of each subject's crow's feet wrinkles (left or right view) under 40um capturing windows. The crow's feet wrinkles were analyzed by the Primos CR analysis software.

2.2.4 Statistics analysis

All statistical tests were two-sided, with differences considered statistically significant at $p < 0.05$. Statistical analysis was performed using SPSS software version 28.0 (IBM Corporation, USA). Quantitative data are represented in terms of the mean and standard deviation (SD).

3. Results

3.1 Subject demographic data

Table 1 displays the demographic characteristics of the study populations. In Study 1, a total of 60 Chinese women completed the trial, while in Study 2, 43 Chinese women completed the study. Notably, there were no dropouts in either study. The mean age of subjects in Study 1 was 51 years (±6). Specifically, the mean age of pre-menopausal women was 47 years, that of women who had been post-menopausal for 1–5 years was 51 years, and that of women who had been post-menopausal for more than 5 years was 55 years.

Table 1. Demographic characteristics of subjects for study 1 and study 2

	Study1				Study2
Parameters	All subjects(*N*=60)	pre-menopause(*N*=20)	1-5 years post-menopause(*N*=20)	over 5 years post-menopause(*N*=20)	All subjects(*N*=43)
Age, years [mean±SD]	51±6	47±5	51±5	55±4	55±3
Minimum age	40	40	41	44	47
Maximum age	60	56	58	60	60
Ethnic origin Chinese[*N*(%)]	60(100%)	20(100%)	20(100%)	20(100%)	43(100%)

3.2 Skin physiological changes for post-menopause Chinese women

Table 2 and Table 3 provide detailed information on the physiological skin parameters of post-menopausal Chinese women.

In Study 1, within 5 years after menopause, both R2 and R7 significantly decreased in Chinese women (compared with the pre-menopausal mean values of R2 at 0.64 ± 0.04 and R7 at 0.48 ± 0.06, they decreased by 12.5% and 25%, respectively; Table 2).

Table 2. Changes of skin parameters pre-menopause and 1-5 years post-menopause. *p<0.05

Parameter	Time	Mean±SD
R2	pre-menopause	0.64±0.04
	1-5 years post-menopause	0.56±0.07*
R7	pre-menopause	0.48±0.06
	1-5 years post-menopause	0.36±0.08*

For Chinese women who had been post-menopausal for more than 5 years, both R2 and R7 remained significantly decreased. Specifically, R2 decreased from a pre-menopausal mean value of 0.64 ± 0.04 to 0.60 ± 0.07, and R7 decreased from a pre-menopausal mean value of 0.48 ± 0.06 to 0.41 ± 0.08 (see Table 3). Additionally, it was observed that the skin color of Chinese women who had been post-menopausal for more than 5 years was darker, as

evidenced by significant decreases in both L* and ITA° values ($p < .05$). The mean L* value decreased by 2.9%, from 63.12 ± 2.31 in the pre-menopausal period, while the mean ITA° value decreased by 13.5%, from 38.57 ± 5.78 in the pre-menopausal period (Table 3).
As evidenced by the crow's foot wrinkle images captured by Primos CR and the analyzed wrinkle parameters, the depth of crow's foot wrinkles in Chinese women who had been post-menopausal for more than 5 years significantly increased. Specifically, the mean depth increased from 55.45 ± 14.68 in the pre-menopausal period to 82.00 ± 39.85 (Table 3).

Table 3. Changes of skin parameters pre-menopause and over 5 years post-menopause. *p<0.05

Parameter	Time	Mean±SD
L*	pre-menopause	63.12±2.31
	over 5 years post-menopause	61.26±2.45*
ITA°	pre-menopause	38.57±5.78
	over 5 years post-menopause	33.35±6.64*
R2	pre-menopause	0.64±0.04
	over 5 years post-menopause	0.60±0.07*
R7	pre-menopause	0.48±0.06
	over 5 years post-menopause	0.41±0.08*
Wrinkle depth	pre-menopause	55.45±14.68
	over 5 years post-menopause	82.00±39.85*

3.3 Evaluate skincare products efficacy for post-menopause Chinese women
In Study 2, among post-menopausal Chinese women, the mean baseline value of R2 was 0.64 ± 0.06. Following the application of the skincare products, R2 exhibited a significant consecutive increase. At Day 14 (D14), it increased by 6.25%, and by Day 28 (D28), it further increased by 14.1%. Similar observations were noted for R5 and R7. For R5, the mean values significantly rose from the baseline of 0.58 ± 0.10 to 0.63 ± 0.12 at D14 and to 0.74 ± 0.14 at D28. For R7, the mean values significantly and consecutively increased from the baseline of 0.40 ± 0.06 to 0.43 ± 0.06 at D14 and to 0.49 ± 0.08 at D28 (Figure 1).

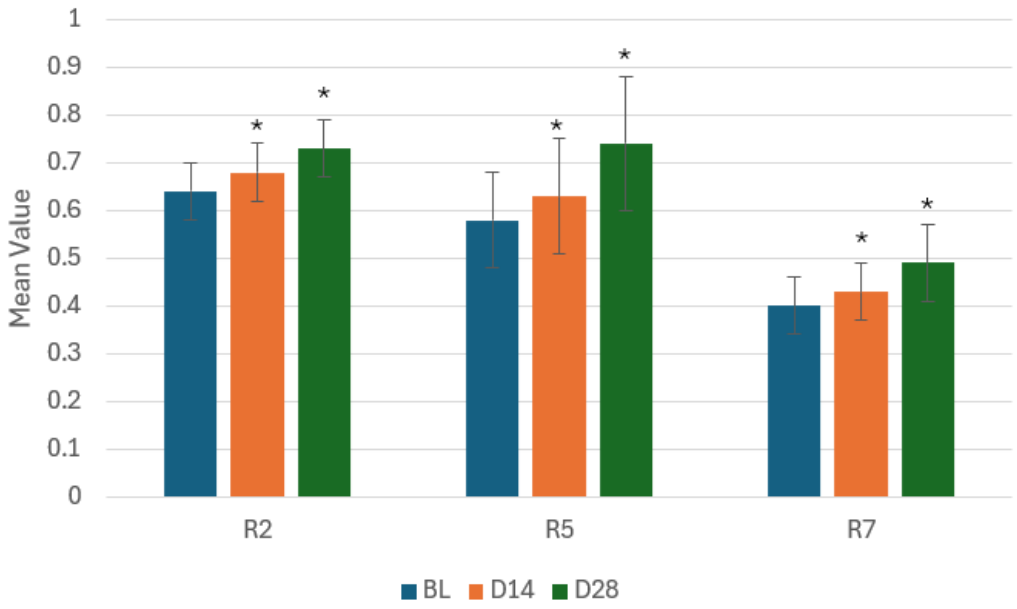

Figure 1. R2, R5 and R7 increased after 14 days and 28 days of applying skin products compared with baseline. * $p < 0.05$

Concurrently, in post-menopausal Chinese women, the F4 level exhibited a significant downward trend after the application of skincare products. At Day 14, compared with the baseline mean value of 6.48±1.51, it decreased by 11.1% (Figure 2).

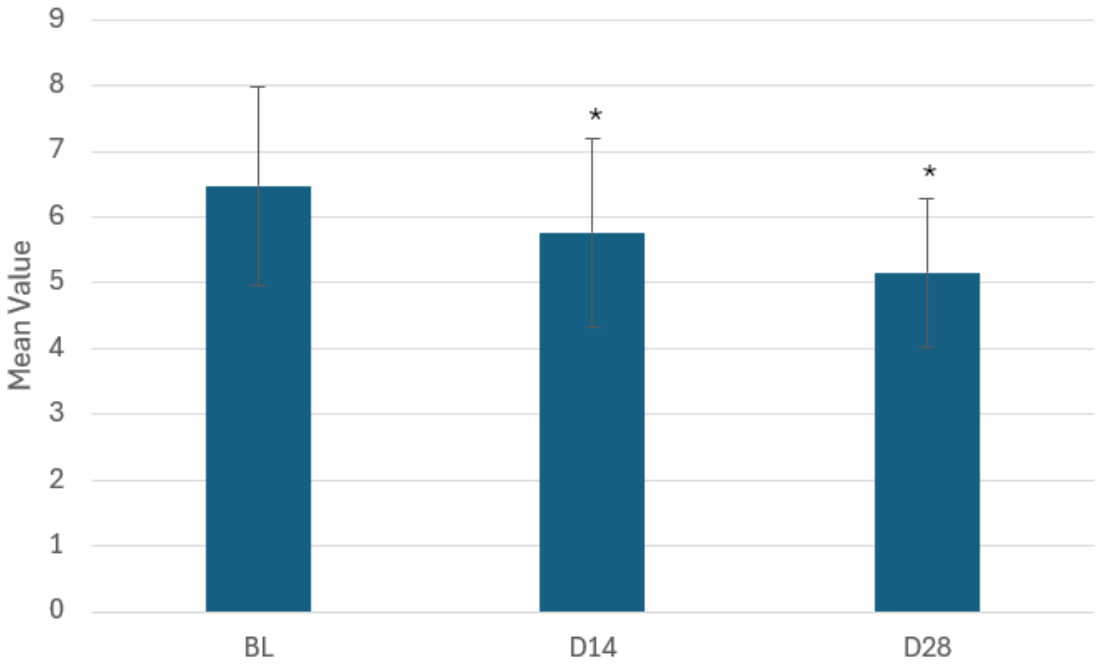

Figure 2. F4 decreased after 14 days and 28 days of applying skin products compared with baseline. * $p < 0.05$

As indicated by the data obtained through image analysis of Primos CR, the depth of crow's feet wrinkles exhibited a significant reduction after the application of skincare products for 28 days, with a decrease of 6.13% from the baseline mean value of 49.28±10.90 (Figure 3). Additionally, the area of crow's feet wrinkles demonstrated a significant consecutive decrease following the use of the products. At Day 14 and Day 28, the mean values decreased from the baseline of 6.46±6.61 to 4.76±3.62 and 4.51±3.81, respectively.

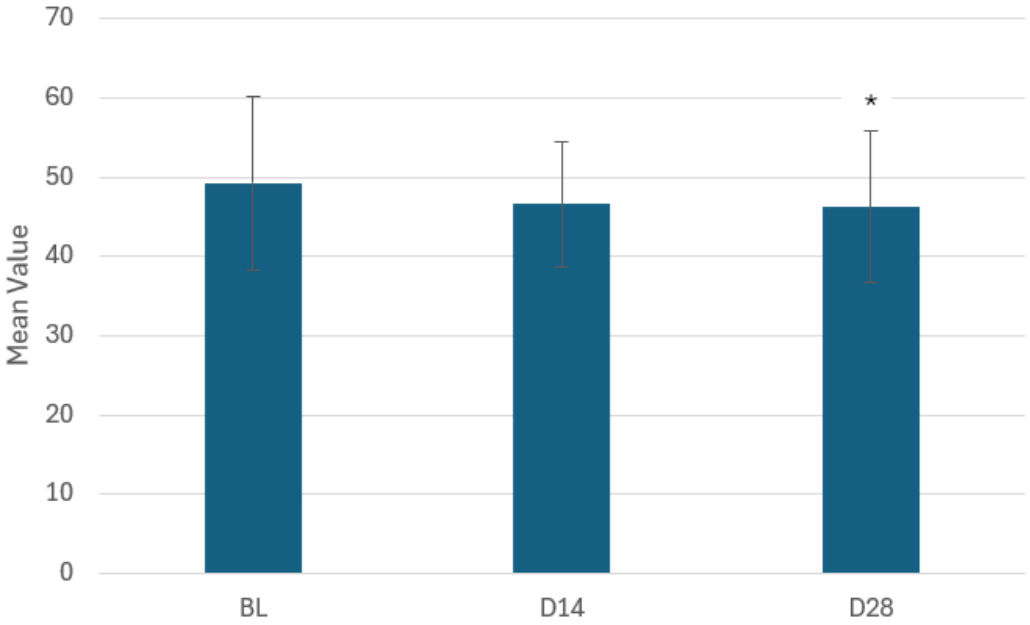

Figure 3. Wrinkle depth decreased after 14 days and 28 days of applying skin products compared with baseline. * $p < 0.05$

Figure 4 presents the images of a typical subject from Study 2. Figure 4a displays the profile image captured by VISIA CR, Figure 4b shows the original image obtained by Primos CR, and Figure 4c illustrates the height image generated after image analysis by Primos CR, where the green areas represent wrinkles. As can be observed from the images, both the depth and area of crow's feet wrinkles were reduced after the application of the skincare products for 14 and 28 days.

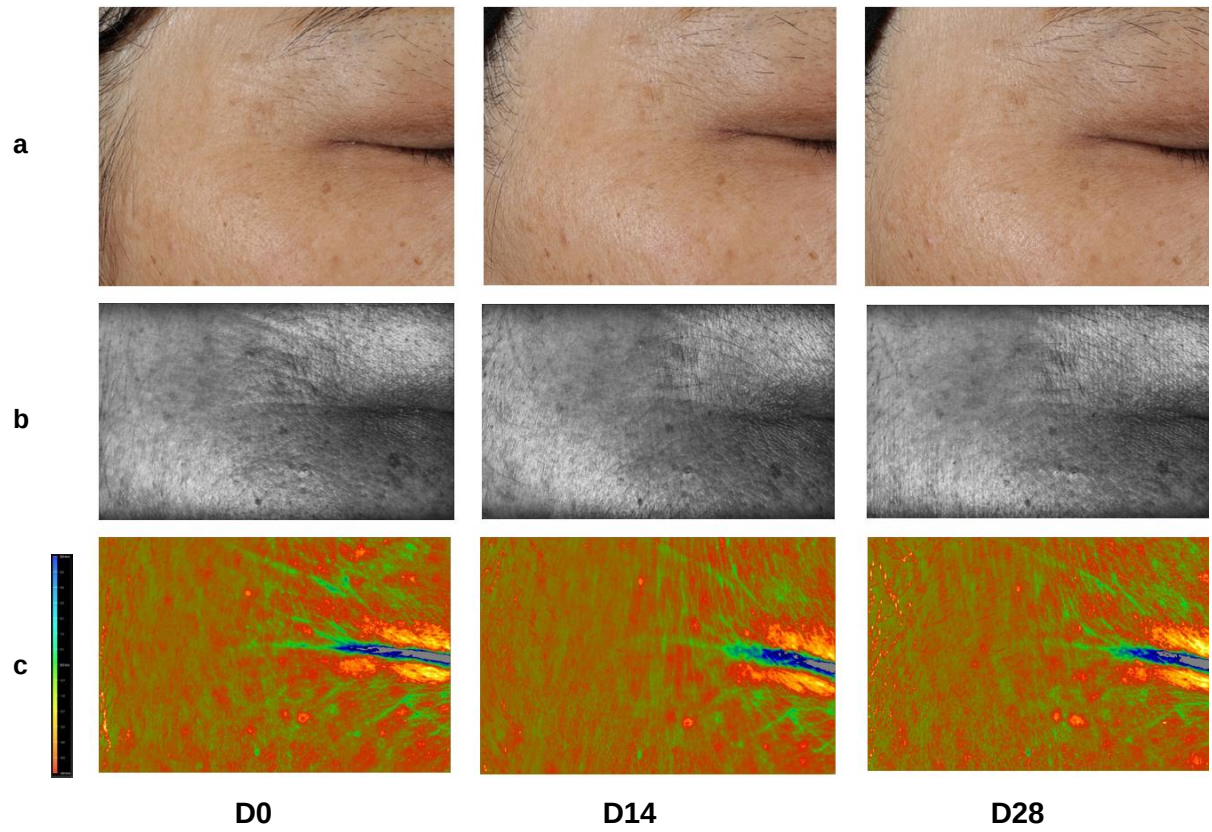

Figure 4. Before and after images of representative subjects: (a) from VISIA CR; (b) from Primos CR; (c) from Primos CR's image analysis(blue: -0.5mm, yellow: 0.5mm).

4. Discussion

A substantial body of research indicates that following menopause in women, ovarian function declines and follicular depletion occurs, leading to a reduction in estrogen levels. This decline in estrogen is associated with alterations in the stratum corneum lipid profile, which in turn affects skin lipid metabolism. Additionally, there is an increase in cellular degradation. First, the presence of estrogen receptors in skin cells means that when estrogen levels decrease, skin aging is accelerated, and collagen loss is hastened. This manifests as skin thinning, dryness, sagging, and the formation of wrinkles. Second, changes in skin lipid metabolism are reflected in alterations to skin barrier-related parameters, such as moisture content and transepidermal water loss (TEWL). Third, the increase in cellular degradation not only results in dryness and wrinkles but also leads to a diminished capacity for antioxidant defense. [9，10，11，12, 13]

Our investigation into the physiological changes in the skin of Chinese women following menopause revealed that both R2 and R7, indices representing skin elasticity, significantly decreased in individuals who had been post-menopausal for either less than 5 years (include 5 years) or more than 5 years. This decline in skin elasticity is consistent with the loss of collagen, a finding that aligns with the studies reporting collagen depletion in post-menopausal women.[5, 10]

Further stratified observations between the two groups, those who had been post-menopausal for 5 years or less and those for more than 5 years, indicated that the latter group exhibited more pronounced wrinkles, particularly with a significant increase in the wrinkle depth of crow's feet wrinkle. Additionally, skin pigmentation was found to be more intense in the group post-menopausal for over 5 years. This may be that estrogen deficiency results in elevated

tyrosinase activity, which in turn promotes melanogenesis, thereby contributing to skin hyperpigmentation. As a result, the L* and ITA° values, which are indicators related to skin color, were significantly reduced. Lower values of these indices denote darker skin color.

Based on existing literature reports, the use of skincare products plays a positive and effective role in improving skin physiological changes after menopause. A clinical investigation involving Heptapeptide-7 has demonstrated its efficacy in improving skin wrinkles among post-menopausal women. [6] Edwin et al. [7] mentioned in their study that creams, gels, and emulsions containing phytoestrogens, isoflavones, or genistein alone have shown effects in improving skin dryness, thickness, facial wrinkles, fibroblast activity, increasing hyaluronic acid levels, and the production of type I and type III collagen. Topical application of resveratrol analogs has also been shown to improve skin firmness and hydration in individuals with estrogen deficiency.

In our study, 43 post-menopausal Chinese women applied a full set of skincare products containing cyclohexapeptide-9 to their entire face for 4 consecutive weeks. The results indicated that three parameters associated with skin elasticity (R2, R5, and R7) persistently increased after the application of the products. An elevation in these parameters signifies an improvement in elasticity. Meanwhile, the parameter F4, which is related to skin firmness, showed a downward trend after product use, indicating enhanced skin firmness. These findings suggest that skincare products containing cyclohexapeptide-9 can effectively mitigate collagen loss in the skin, thereby increasing its elasticity and firmness.

From the image analysis of crow's feet wrinkles, wrinkle depth and wrinkle area were assessed. Both parameters exhibited a peristent decrease after the application of the skincare products. Moreover, the representative subjects' VISIA CR original images, Primos CR original images, and the height images generated from the Primos CR analysis all demonstrated a marked improvement in crow's feet wrinkle after product use. Thus, these results further validate the efficacy of skincare products containing cyclohexapeptide-9 in improving skin texture.

Although our study has supplemented the data on changes in skin physiological parameters among Chinese menopausal women and demonstrated that skincare products containing cyclohexapeptide-9 can effectively improve the elasticity, firmness, and appearance of wrinkles of post-menopausal women's skin, several limitations should be acknowledged. First, our sample size was relatively small. Second, the study lacked a control group. Future research should aim to address these limitations by conducting more comprehensive and in-depth studies in the aforementioned areas.

5. Conclusion

Skin physiological changes in post-menopausal Chinese women are particularly noticeable. For 1-5 years post-menopause, changes were in skin elasticity. Over 5 years post-menopause, changes were also in skin tone, firmness and wrinkle appearance. After 28 days, skincare products containing cyclohexapeptide-9 significantly enhanced elasticity, firmness and reduced wrinkle appearance in post-menopausal Chinese women.

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