The Efficacy of 7% Palmitoyl Pentapeptide-4 Serum for the Periorbital Wrinkle Reduction

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ABSTRACT

Background: Periorbital wrinkle is a critical assessment point of skin aging which is easily noticeable. The pathogenesis of wrinkle formation is primarily by the reduction and degradation of collagen and elastin fibers which are the major components of dermal extracellular matrix. Derivatized peptide such as Palmitoyl Pentapeptide-4, also known as Pal-KTTKS or Matrixyl, is a collagen stimulator and especially favored for their functional structure, stability and permeability to penetrate the skin. However, there is no study about the safety and efficacy of 7% Palmitoyl Pentapeptide-4 used as the main active ingredient in the skincare for reducing periorbital wrinkles.

Objectives: To study the efficacy of 7% Palmitoyl Pentapeptide-4 serum in periorbital wrinkle reduction.

Method and Materials: Fifteen Asian and Caucasian female subjects age between 35 to 65 years old with periorbital wrinkle (Rao-Goldman scores from 2 to 5 at week 0) and fit all the criteria were enrolled to participate in the study. 7% Palmitoyl Pentapeptide-4 serum and placebo were randomly applied in a split-face design (right and left sides), twice daily in the morning and evening for 8 weeks and were followed-up every 4 weeks. The researcher measured the periorbital wrinkle depth by Visioscan® VC 98, skin viscoelasticity by Cutometer® MPA 580 at week 0, week 4, and week 8 and trans-epidermal water loss (TEWL) by Tewameter® TM 300 at week 0, week 8 of the study. The researcher took photographs of the participants' periorbital wrinkle at week 0 and week 8 which then were assessed by dermatologists for the Rao-Goldman 5-point scoring. Any side effects were recorded throughout the research study and the participants' satisfaction scores were recorded at week 8.

Results: Fifteen participants completed the 8-week period study. All measured scores of treated periorbital wrinkle were statistically significant at the level of 0.05 (Paired t-test). The mean visioscan results have significantly reduced at week 8 with p-value of crow's feet at 0.002 and undereye at 0.001. The mean cutometer and tewameter scores have significantly increased on crow's feet ($p<0.001$) and undereye ($p=0.005$ and $p<0.001$). The participants' satisfaction scores showed higher scores on the treated side compared to placebo ($p<0.001$). No side effects were noted throughout the study from applying both serums.

Conclusion: 7% Palmitoyl Pentapeptide-4 serum was proven to be safe and effective for the periorbital wrinkle reduction by reducing the wrinkle depth, increasing the skin barrier function and skin elasticity on the periorbital area.

Keywords: 7% Palmitoyl Pentapeptide-4, Pal-KTTKS, pro-collagen, periorbital wrinkle, Visioscan

1. Introduction

In this modern era, people are constantly looking for skincare products and treatments to counteract skin aging process especially periorbital wrinkles, a critical assessment point of skin aging that is easy to spot on. (Bae, 2017) As the eyes receive more visual attention than any other part of the face, the periorbital wrinkles will be particularly noticeable relevant to social communication. (Samson, 2010) As a consequence, wrinkle formation creates a common desire to maintain a youthful appearance especially for older individuals who are facing more significant challenges in reducing skin aging signs as they have developed deeper wrinkles and relatively harder to treat because the loss of elasticity and dermal density are more prominent over longer period of time. (Zouboulis, 2019)

The pathogenesis of wrinkle formation is primarily by the reduction and degradation of collagen and elastin fibers which are the major components of dermal extracellular matrix (ECM). (El-Domyati M, 2002) Derivatized peptide such as Palmitoyl Pentapeptide-4 is especially favored for their functional structure, stability and permeability to penetrate the skin. Palmitoyl Pentapeptide-4, also known as Pal-KTTKS, is a fragment of pro-collagen I. This peptide was shown to stimulate dermal matrix production in fibroblast culture and provide additional structural support for the extracellular matrix of our skin. (Gorouhi, 2009) (Robinson, 2005) In other words, Palmitoyl Pentapeptide-4 is a collagen stimulator. It works by triggering a signaling cascade. It is released from the extracellular matrix to increase the proliferation of elastin, proteoglycan, glycosaminoglycan, fibronectin, and collagens (specifically type I, III and IV). As a result, the wrinkles are reduced with the regeneration of the skin matrix cells. This action leads to a visible improvement of skin elasticity, and the skin surface will appear smoother and firmer. (Schagen, 2017)

As an active ingredient in cosmetic and skincare products, 3% Palmitoyl Pentapeptide-4 has been proven as a safe, non-irritating, and non-sensitizing agent. It does not exacerbate acne, well tolerated by oily skin, and it also absorbs into the skin quicker, thus is suitable for anti-wrinkle formula on periorbital area in which the skin is relatively more sensitive and delicate. (Johnson, 2018) Previous studies using 3% of Palmitoyl Pentapeptide-4 have been proven successful in reducing periorbital wrinkles within 6 months.

For all these reasons, the researcher wants to conduct a 3 months clinical trial study of Palmitoyl Pentapeptide-4 efficacy by doubling up the dose to 7% to see if it can result in a significant improvement of periorbital wrinkle reduction within a shorter period of time. Other than that, the researcher also wants to prove the safety of this peptide in the higher, more potent concentration.
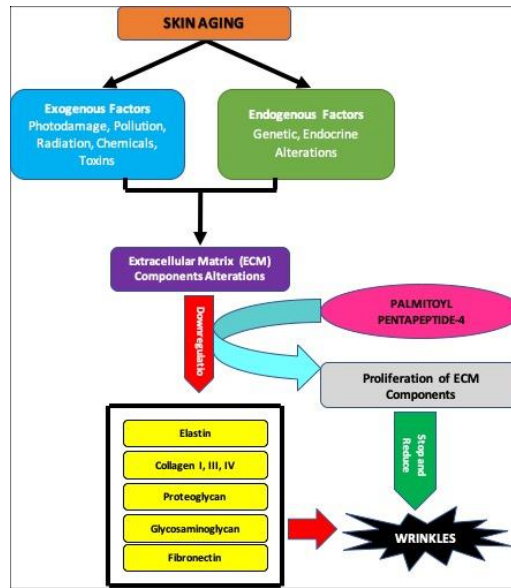
2. Hypotheses and Objectives of the study

2.1. Hypotheses

2.1.1. Palmitoyl Pentapeptide-4 7% serum can effectively reduce periorbital wrinkles by increasing the periorbital skin elasticity and skin barrier function.

2.1.2. Palmitoyl Pentapeptide-4 7% serum has minimal side effects and is safe to use as a treatment for deep periorbital wrinkle.

2.1.3. Palmitoyl Pentapeptide-4 7% serum has better satisfactory score in reducing deep periorbital wrinkle compared to placebo.

2.2. Objectives

2.2.1. To study the efficacy of 7% Palmitoyl Pentapeptide-4 serum in reducing periorbital wrinkles.

2.2.2. To study the efficacy of 7% Palmitoyl Pentapeptide-4 serum in increasing the periorbital skin viscoelasticity.

2.2.3. To study the efficacy of 7% Palmitoyl Pentapeptide-4 serum in increasing the periorbital skin barrier function.

2.2.4. To evaluate the participants' satisfaction scores after using 7% Palmitoyl Pentapeptide-4 serum

3. Materials and Methods

The study design of this research project is a comparative controlled split-face, randomized, double-blind clinical trial. The sample size is 15 female volunteers within 35-65 years old with prominent periorbital wrinkles (Rao-Goldman Score from 2 to 5). Prior to study, the researcher gave a thorough explanation before the volunteers signed an informed consent letter to join the research project and comply to all the terms and conditions.

Volunteers medical history and general personal data were collected. Those who were pregnant or breastfeeding, have any history of concomitant skin infection, skin malignancy on the face, chronic skin diseases, connective tissue disorder and/or pre-existing severe systemic diseases, and who recently had cosmetic procedures done on the periorbital area are excluded from the study. A patch test was done to every volunteer before starting the study to observe whether there was any allergy or hypersensitivity reactions to the serum.

An independent physician helped the researcher of this study to divide the volunteers into 2 groups; group left and right through randomization process. The volunteers were then instructed to use the serum twice a day; morning and evening after washing their face, on the periorbital wrinkle area; lateral and inferior, one drop on each landmark (shown in figure 2). One side of the face with 'serum A' and the other side 'serum B' in which one of the serums is a placebo. The duration of the study is 8 weeks with follow-up appointment on week 4.

The volunteers' periorbital wrinkle scores were evaluated according to the Rao-Goldman 5-point visual scoring scale by other dermatologists, and 'before and after' photos were taken at week 0 & 8. The wrinkle depth was measured using Visioscan® VC 98, skin elasticity using Cutometer® MPA 580, and trans-epidermal water loss scores were measured using Tewameter® TM 300 at week 0,4 and 8.
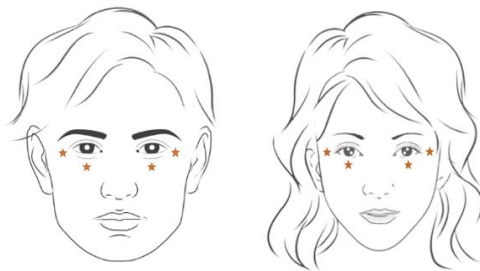

Figure 2. The measurement landmarks are 1.5cm from lateral canthus horizontally outward and 1.5cm downward from lower eyelid at the mid-papillary line

4. Results and Discussion

Demographic of participants general characteristics shows all subjects were female, the mean age of all the subjects was 51.07±8.74 years. There were 11 housewives, 3 employees and 1 government officer. Among the subjects, there was 1 subject with an underlying disease, and 1 with food/drug allergy. There was not any subject with hypersensitivity, personal medication, cosmetic procedures history, pregnancy and lactation. The median of exposure to sunlight duration was 15 minutes. Majority of the subjects had combination skin (33.3%), normal skin (26.7%), dry skin (20.0%) and oily skin (20.0%). 86.7% of the subjects practiced skincare routine in which 26.7% of them include eye wrinkle/serum in the routine.

4.1 Visioscan®VC 98

The crow's feet mean score result on week 0 was 98.05±35.71, week 4 was 89.17±34.09 and week 8 was 74.86±24.15. The differences were statistically significant. They decreased on each visit at the level of 0.05 (p=0.002). As for the placebo, the mean scores did not change significantly on each visit according to the

statistics analysis (p=0.741). The Visioscan scores of crow's feet applied with 7% Palmitoyl Pentapeptide-4 serum are significantly lower than placebo at week 4 and week 8 (p=0.034 and p=0.003).

For the undereye wrinkles, the mean score of Visioscan measurements applied with 7% Palmitoyl Pentapeptide-4 serum on week 0 was 119.96±59.04, week 4 was 100.42±40.47and week 8 was 85.82±37.78. The differences were statistically significant. They decreased on each visit at the level of 0.05 (p=0.001). The mean scores of placebo did not change significantly on each visit according to the statistics analysis (p=0.451).

Table 4.2	7% Palmitoyl Pentapeptide-4	Placebo	Mean difference	p-value (a)
	Mean±SD	Mean±SD		
Crow's feet				
Week 0	98.05±35.71	101.80±36.96	3.75	0.505
Week 4	89.17±34.09	101.64±37.03	12.46	0.034*
Week 8	74.86±24.15	101.25±37.55	26.38	0.003*
p-value (b)	0.002*	0.741		
Under eyes				
Week 0	119.96±59.04	101.94±27.41	18.02	0.196
Week 4	100.42±40.47	101.85±27.02	1.43	0.887
Week 8	85.82±37.78	102.14±25.91	16.32	0.132
p-value (b)	0.001*	0.451		

Table 1: Data were analyzed between group with Paired t-test (a), within group with Repeated measure ANOVA (b)
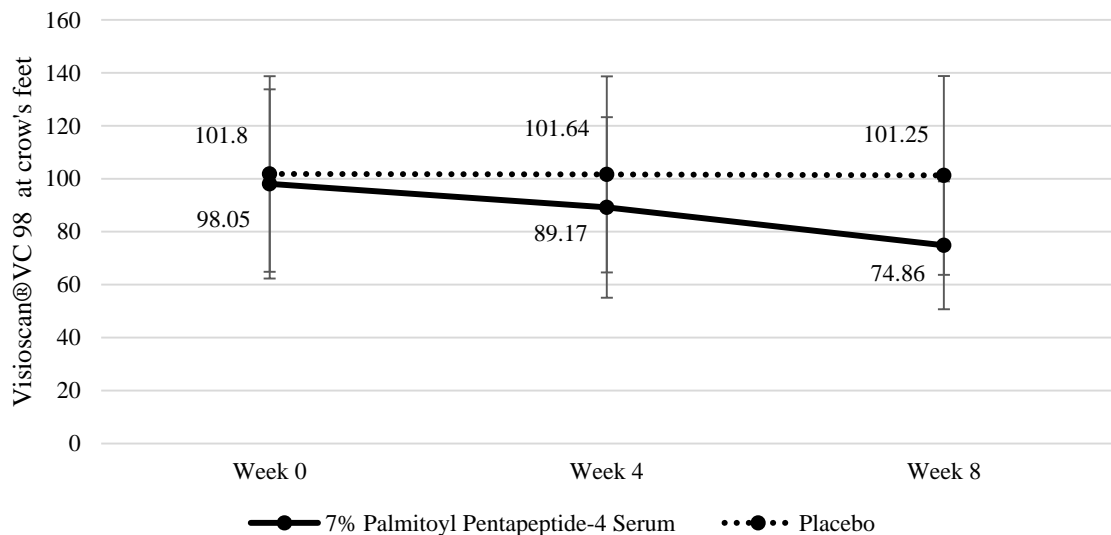

Figure 3: Linear graph shows comparison of Visioscan®VC 98 measurement between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo at crow's feet on week 0, 4, and 8
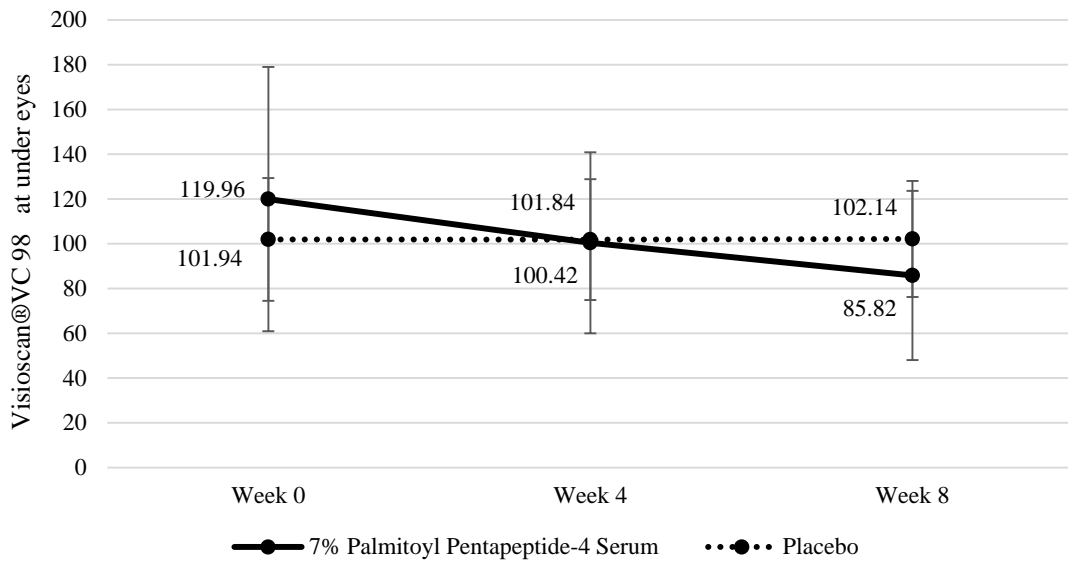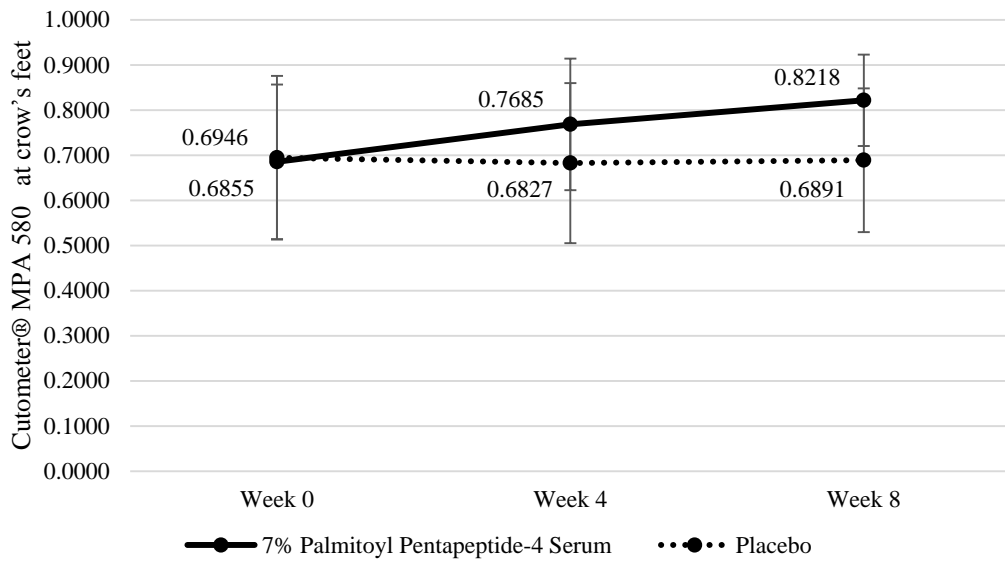
Figure 4: Linear graph shows comparison of Visioscan®VC 98 measurement between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo at undereye on week 0, 4, and 8

4.2 Cutometer® MPA 580

The crow's feet mean score results on week 0 was 0.6855±0.1714, week 4 was 0.7685±0.1457 and week 8 was 0.8218±0.1013. The differences were statistically significant. They increased on each visit at the level of 0.05 ($p<0.001$). As for the placebo mean score results, they did not change significantly on each visit according to the statistics analysis ($p=0.614$). The mean score results of crow's feet applied with 7% Palmitoyl Pentapeptide-4 Serum was significantly higher than Placebo at week 4 and week 8 ($p=0.012$ and $p<0.001$).

For the undereye wrinkles, the mean score of Cutometer® MPA 580 measurements applied with 7% Palmitoyl Pentapeptide-4 serum on week 0 was 0.7421±0.1231, week 4 was 0.7615±0.1136 and week 8 was 0.8341±0.1043. The differences were statistically significant. They increased on each visit at the level of 0.05 ($p=0.005$). As for the placebo, the mean scores did not change significantly according to the statistics analysis ($p=0.686$). The mean score results of undereye wrinkles applied with 7% Palmitoyl Pentapeptide-4 serum revealed that the mean scores were significantly higher than placebo at week 0, week 4 and week 8 ($p=0.030$, $p=0.006$ and $p<0.001$).

Table 4.3	7% Palmitoyl Pentapeptide-4 Serum	Placebo	Mean difference	p-value (a)
	Mean±SD	Mean±SD		
Crow's feet				
Week 0	0.6855±0.1714	0.6946±0.1813	0.01	0.754
Week 4	0.7685±0.1457	0.6827±0.1774	0.09	0.012*
Week 8	0.8218±0.1013	0.6891±0.1592	0.13	<0.001*
p-value (b)	<0.001*	0.614		
Under eyes				
Week 0	0.7421±0.1231	0.6545±0.1082	0.09	0.030*
Week 4	0.7615±0.1136	0.6616±0.1248	0.10	0.006*

Table 4.3	7% Palmitoyl Pentapeptide-4 Serum	Placebo	Mean difference	p-value (a)
	Mean±SD	Mean±SD		
Week 8	0.8341±0.1043	0.6501±0.1291	0.18	<0.001*
p-value (b)	0.005*	0.686		

Table 2 Statistical analysis of Cutometer® MPA 580 measurement at crow's feet and undereye applied with 7% Palmitoyl Pentapeptide-4 Serum and Placebo on week 0, 4, and 8.

Data were analyzed between group with Paired t-test (a), within group with Repeated measure ANOVA (b)

Figure 5 Linear graph shows comparison of Cutometer® MPA 580 measurements between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo at crow's feet on week 0, 4, and 8
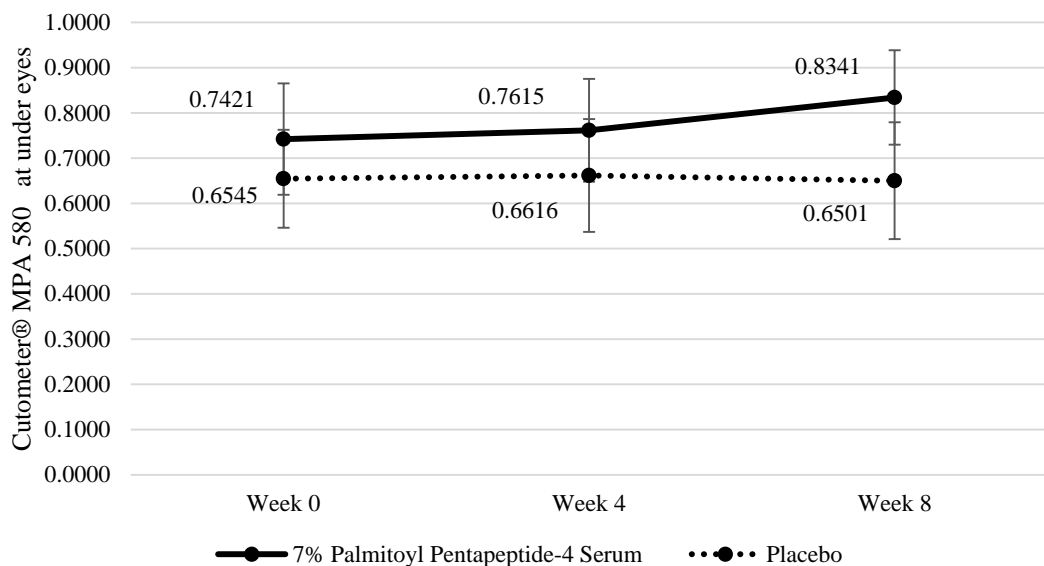

Figure 6 Linear graph shows comparison of Cutometer® MPA 580 measurement between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo at undereye on week 0, 4, and 8
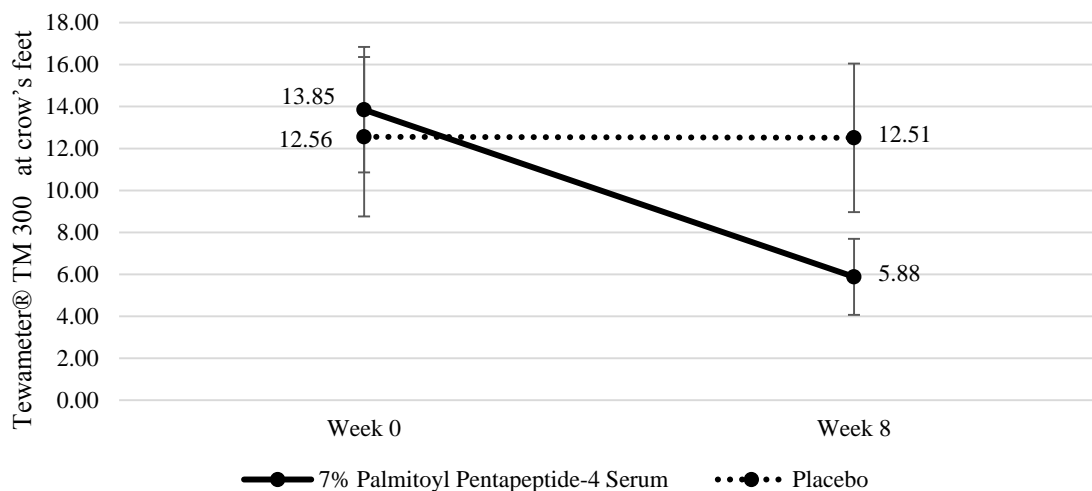
4.3 Tewameter® TM 300

The crow's feet mean score result on week 0 was 13.85±2.99 and week 8 was 5.88±1.81. The difference was statistically significant, decreased from week 0 to week 8 visit at the level of 0.05 (p<0.001) while the placebo side did not change significantly (p=0.741). The tewameter scores of crow's feet applied with 7% Palmitoyl Pentapeptide-4 serum was significantly lower than Placebo at week 8 (p<0.001).

For the undereye wrinkles, the mean score of Tewameter® TM 300 measurements applied with 7% Palmitoyl Pentapeptide-4 serum on week 0 was 14.91±5.82 and week 8 was 6.48±1.92. The difference was statistically significant, decreased from week 0 to week 8 visit at the level of 0.05 (p<0.001). As for the placebo, the results on week 0 was 14.36±6.60 and week 8 was 13.88±6.64. The mean scores did not change significantly between the first and last visit according to the statistics analysis (p=0.107). The tewameter scores of undereye wrinkles applied with 7% Palmitoyl Pentapeptide-4 serum was significantly lower than Placebo at week 8 (p<0.001).

Table 4.4	7% Palmitoyl Pentapeptide-4 Serum	Placebo	Mean difference	p-value (a)
	Mean±SD	Mean±SD		
Crow's feet				
Week 0	13.85±2.99	12.56±3.80	1.29	0.173
Week 8	5.88±1.81	12.51±3.54	6.63	<0.001*
p-value (b)	<0.001*	0.773		
Under eyes				
Week 0	14.91±5.82	14.36±6.60	0.55	0.469
Week 8	6.48±1.92	13.88±6.64	7.39	<0.001*
p-value (b)	<0.001*	0.107		

Table 3 Statistical analysis of Tewameter® TM 300 measurement at crow's feet and undereye applied with 7% Palmitoyl Pentapeptide-4 Serum and Placebo on week 0, 4, and 8. Data were analyzed between group and within group with Paired t-test (a), (b)

Figure 7 Linear graph shows comparison of Tewameter® TM 300 measurements between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo at crow's feet on week 0, 4, and 8
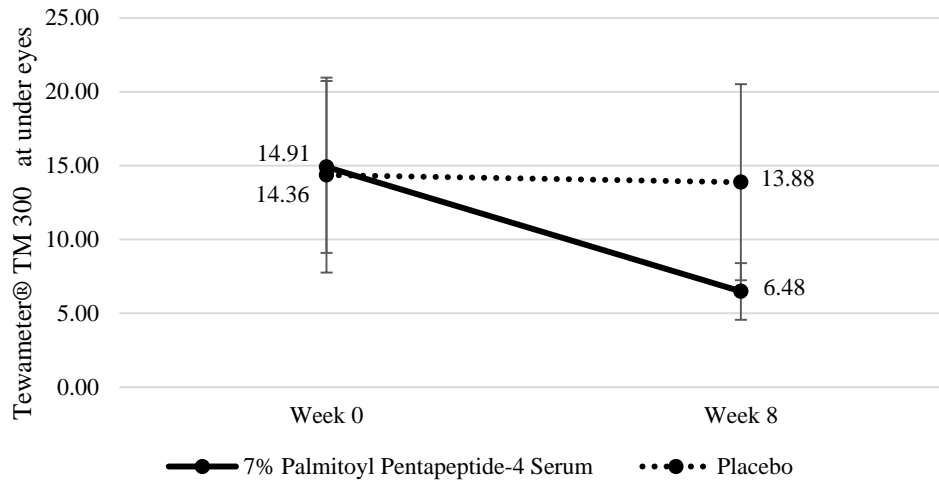
Figure 8 Linear graph shows comparison of Tewameter$^{®}$ TM 300 measurements between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo at undereye on week 0, 4, and 8

4.4 Rao-Goldman 5-Point Wrinkle Scale

The mean scores of at crow's feet applied with 7% Palmitoyl Pentapeptide-4 serum on week 0 was 3.73±1.16 and week 8 was 2.47±0.92. The difference was statistically significant; decreased from week 0 to week 8 visit at the level of 0.05 ($p<0.001$). The mean scores of placebo side did not change significantly between the first and last visit according to the statistics analysis ($p=0.670$). The Rao-Goldman 5-point wrinkle scores for crow's feet applied with 7% Palmitoyl Pentapeptide-4 serum compared to placebo revealed that they were significantly higher than placebo at week 0 ($p<0.001$) but lower than placebo at week 8 ($p=0.001$).

For the undereye wrinkles, the mean score on week 0 was 3.27±1.16 and week 8 was 2.07±0.88. The difference was statistically significant. They decreased on each visit at the level of 0.05 ($p<0.001$). As for the placebo, the mean scores did not change significantly between the first and last visit according to the statistics analysis ($p=1.000$). The mean scores of undereye wrinkle applied with 7% Palmitoyl Pentapeptide-4 serum were significantly higher than Placebo at week 0 ($p<0.001$).

Table 4.5	7% Palmitoyl Pentapeptide-4 Serum	Placebo	Mean difference	p-value (a)
	Mean±SD	Mean±SD		
Crow's feet				
Week 0	3.73±1.16	3.07±0.88	0.67	<0.001*
Week 8	2.47±0.92	3.13±1.06	0.67	0.001*
p-value (b)	<0.001*	0.670		
Under eyes				
Week 0	3.27±1.16	2.33±0.62	0.93	<0.001*
Week 8	2.07±0.88	2.33±0.62	0.27	0.104
p-value (b)	<0.001*	1.000		

Table 4 Statistical analysis of Rao-Goldman 5-point wrinkle score measurement at crow's feet and undereye applied with 7% Palmitoyl Pentapeptide-4 Serum and Placebo on week 0, 4, and 8. Data were analyzed between group and within group with Paired t-test (a), (b),
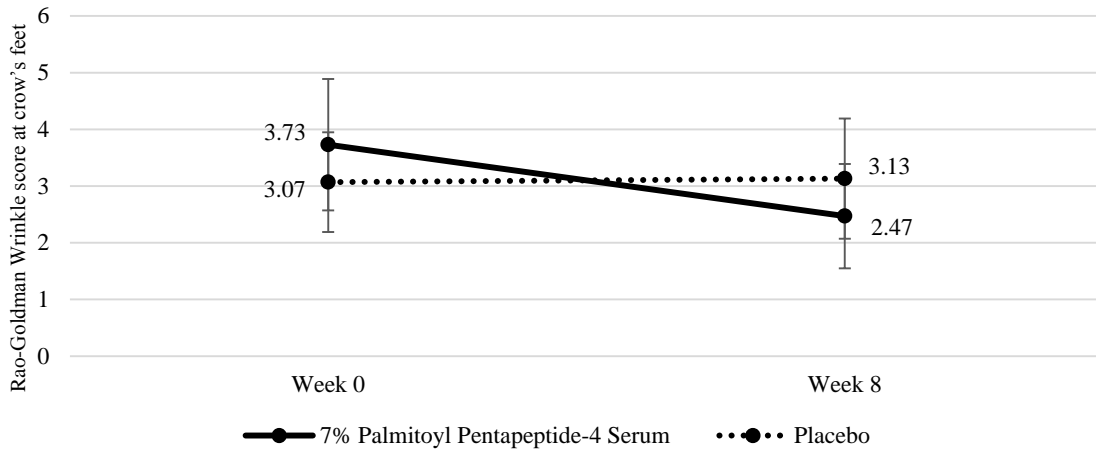
Figure 9 Linear graph show comparison of Rao-Goldman 5-point wrinkle score measurements between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo at crow's feet on week 0, 4, and 8
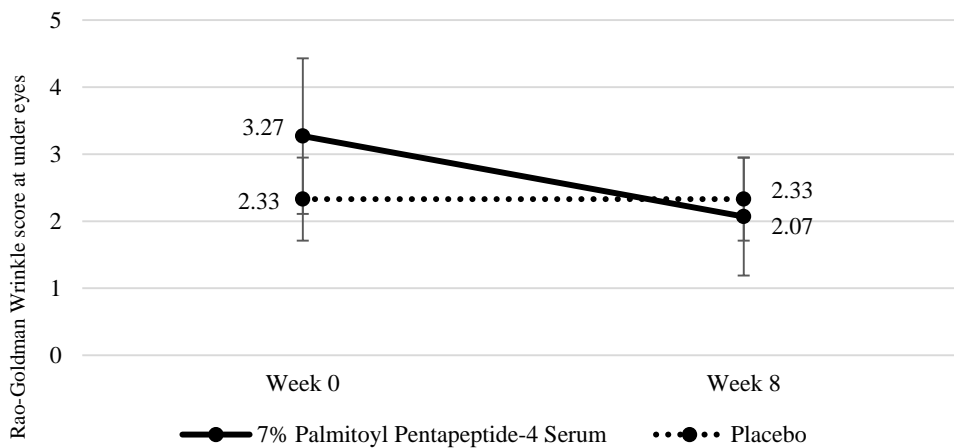

Figure 10 Linear graph show comparison of Rao-Goldman 5-point wrinkle score measurements between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo at undereye on week 0, 4, and 8

4.5 Participant satisfaction scores

The participant satisfaction scores of crow's feet and undereye wrinkles applied with 7% Palmitoyl Pentapeptide-4 serum revealed that the mean scores on week 8 were both significantly higher than placebo (p<0.001 and p<0.001). For crow's feet applied with 7% Palmitoyl Pentapeptide-4 serum, out of 15 participants there were 1 participant scored 2 (average changes & satisfaction), 9 participants scored 3 (good changes & satisfaction), and 5 participants scored 4 (excellent changes & satisfaction). For placebo, there were 2 participants scored 0 (no changes & satisfaction), 11 participants scored 1 (slight changes & satisfaction), and 2 participants scored2 (average changes & satisfaction). For undereye wrinkles applied with 7% Palmitoyl Pentapeptide-4 serum, out of 15 participants there were 3 participants scored 2 (average changes & satisfaction), 7 participants scored 3 (good changes & satisfaction), and 5 participants scored 4 (excellent changes & satisfaction). For

placebo, there were 4 participants scored 0 (no changes & satisfaction), 7 participants scored 1 (slight changes & satisfaction), and 4 participants scored 2 (average changes & satisfaction).

Table 4.6	7% Palmitoyl Pentapeptide-4 Serum	Placebo	Mean difference	p-value
Crow's feet	3.27±0.59	1.00±0.54	2.27	<0.001*
Under eyes	3.13±0.74	1.00±0.76	2.13	<0.001*

Table 5 Participant satisfaction scores on week 8Data were analyzed between group with Paired t-test, * $p<0.05$
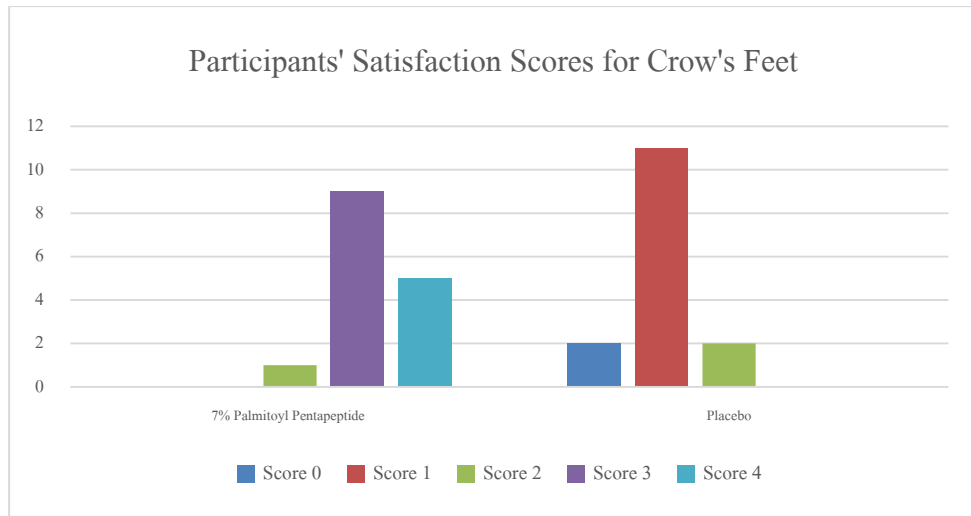

Figure 11 Bar chart reveals the number of participants with each satisfaction score for crow's feet between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo
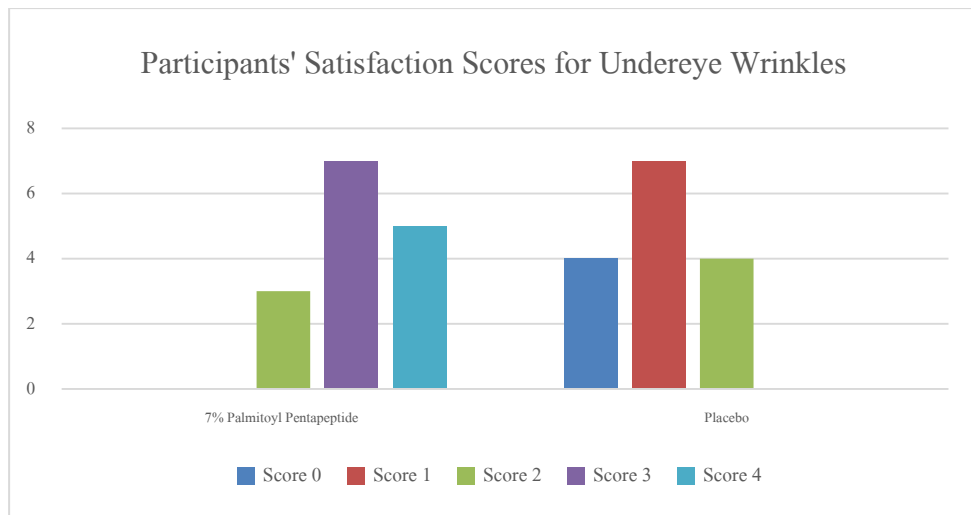

Figure 12 Bar chart reveals the number of participants with each satisfaction score for undereye wrinkles between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo
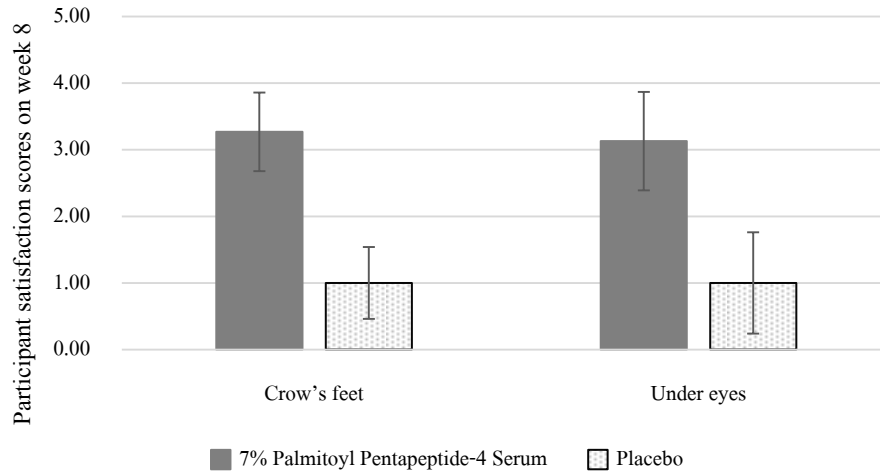
Figure 13 Bar chart reveals the average of all participant's satisfaction scores at crow's feet and under eyes between 7% Palmitoyl Pentapeptide-4 Serum versus Placebo

5. Discussion

5.1. Wrinkles and Palmitoyl Pentapeptide-4

Wrinkles are defined as ridges on skin surface where the cutaneous layer is folded or creased. Wrinkles vary in size and visible texture. Wrinkles which depth and width are less than 1 mm are categorized as fine wrinkles, and those which are more than 1 mm are coarse or deep wrinkles. (Manríquez, 2014) There are multiple findings underlying the formation of wrinkles. Microscopically, the most prominent feature is epidermal atrophy but there are also other changes evident to the histopathology of wrinkles such as flattening of the dermal-epidermal junction, hypodermis atrophy, loss of ECM components, and cutaneous cell telomeres shortening (Baumann, 2009).

Palmitoyl pentapeptide-4 is a chain of amino group comprised of five acid residues: Lys-Thr-Thr-Lys-Ser which are linked to a 16-carbon aliphatic chain. This structure allows the molecule to penetrate through the lipid structures of the skin in a stable manner. Palmitoyl pentapeptide-4 is also widely known by other names such as pal-KTTKS and Matrixyl®. This amino acid group is a small, biologically active peptide which has been reported to have the ability in enhancing dermal restructuring and regarded as a signal peptide because the main biomechanism is related to its biosynthetic pathway rather than the transportation or degradation pathways. (Schagen, 2017; Samah, 2011). This peptide is a fragment of type I collagen pro-peptide (procollagen type I) and its main action in dermal restructuring is by triggering cellular responses. An *in vitro* study showed that the optimal result of pal-KTTKS mechanism is more significant in sparse ECM content rather than confluent tissue. Palmitoyl pentapeptide-4 shows less response in a high-density ECM atmosphere. The chain of actions is as listed:

1. The presence of pal-KTTKS as fragment of procollagen type I in the ECM impersonate a condition in which too many collagen chains have been broken down

2. This condition triggers the dermal cells to decrease, eventually stop the process of collagen degradation

3. Once the collagen breakdown is inhibited, a positive feedback of ECM components production is stimulated

4. The stimulatory effect is specifically more significant in increasing the production of collagen type I, III, and IV as well as fibronectin and glycosaminoglycans.

One of the most important contents of Palmitoyl pentapeptide-4 is proline because once it is converted to hydroxyproline, this co-translational process may directly reflect to the collagen synthesis. Hydroxyproline constitutes a relatively high proportion of the total amino acid composition of collagens. Thus, palmitoyl pentapeptide-4 has the ability of enhancing not only collagen type I but also III and IV. However, the specificity to collagen type III and IV instead of other types is yet to be fully understood. (Samah, 2011)

The efficacy of 3% palmitoyl pentapeptide-4 was proven small but significant in a 12-weeks clinical trial study to reduce wrinkles and fine lines on photoaged facial skin. The study conducted by Robinson et al. have concluded that this peptide is a potent compound which can provide an even better result with higher dose. However, the study only used 3ppm in the formulation due to the high cost of the peptide and the budget limitation. As for the skin barrier capacity, the result of the study did not show much changes or improvement using 3% concentration. (Robinson, 2005)

5.2. Skin Elasticity and Skin Barrier

In a healthy tissue, the extracellular matrix (ECM) forms a relaxed interlaced structure of fibers. This network is composed of collagen type I and III, elastin and fibronectin. They are surrounded by and firmly attached to hydrogel of glycosaminoglycan-chain-containing proteoglycans. (Bosman, 2003) Consequently, this relaxed network allows a functionally competent ECM to resist a wide range of tensile stresses as well as compressive stresses because of the binding of the hydrated glycosaminoglycan (GAG) network to the fibrous ECM molecules. (Scott, 2003) An important factor that influences this stable, viscous environment to support the skin elasticity is the condition of the skin barrier. The skin barrier is responsible for preventing water evaporation from the skin, also known as trans-epidermal water loss (TEWL). When the skin barrier function is disrupted, the skin will be dry and scaly which eventually leads to wrinkle formation. The skin barrier also has several other important functions such as preventing allergens and irritants from directly penetrating deep into the skin, and to act as a defender against infections. The defense mechanism is attributed to the corneocytes and the surrounding extracellular function. (Elias, 2005)

From the concept mentioned above, this research study results have shown that the improvement of transepidermal water loss scores from week 0 to 8 are indeed accomodating the skin elasticity scores improvement.

5.3. Safety Assessment

There are many aspects related to the safety assessment of a compound in order for it to be qualified as a safe personal care product. According to (Johnson, 2018), the safe and effective concentration range is from 3% to 7% in topical products and there was neither irritation nor sensitization responses from using this bio-active

ingredient. From this research study, there were not any side effect symptoms reported by the participants throughout 8 weeks of using both 7% Palmitoyl Pentapeptide-4 serum and placebo serum. The result showed that it does not induce redness, dryness, burn, sting, or itch responses. Overall, 7% Palmitoyl Pentapeptide-4 serum was proven to be safe and well tolerated by all participants without inducing any allergy or hypersensitivity reactions.

6. Conclusion

This research study has shown significant improvement of skin elasticity and the reduction of wrinkle depth are significant over 8-weeks period. The measured wrinkle scores have shown significant changes as early as week 0-4. From week 0-8, not only the skin elasticity and wrinkle depth but also TEWL and Rao-Goldman 5-point wrinkle scores have statistically and significantly improved as well. There was neither any side effect nor participant's dissatisfaction complaint in this clinical trial. In conclusion, 7% Palmitoyl Pentapeptide-4 is a safe and effective topical skincare product in reducing moderate to deep periorbital wrinkle.

7. Recommendations

7.1. This study may be useful as a database for further research about skin rejuvenation, anti-aging modalities, topical peptides, skin elasticity, smoothness, and barrier function.

7.2. This research may be used as an alternative of choice for anti-wrinkle topical treatment compared to other topical anti-aging ingredients.

7.3. The efficacy of 7% Palmitoyl Pentapeptide-4 should be tested and compared with other topical peptides.

7.4. The efficacy and safety of 7% Palmitoyl Pentapeptide-4 should also be studied for other skin conditions such as eczema, xerosis, or other conditions related to extracellular matrix disruption and collagen loss.

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