*J. Cosmet. Sci.,* **70,** 277–289 (November/December 2019)

# Assessment of the Effect of Extract Formulation of Date Palm Kernel on Facial Skin Wrinkles: Biophysical Measurements and Digital Profilometry

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*Accepted for publication September 6, 2019.*

**Synopsis**

Previous studies have shown that the date palm kernel contains plenty of phytochemicals of potential rejuvenation benefits to skin. The aim of this study was to investigate a cream form containing date palm kernel extract (DPKE) on facial wrinkle reduction and objective skin parameters in healthy subjects. A cream form containing 5% DPKE was prepared and applied twice daily for 8 weeks on the facial skin of 43 volunteers. Biophysical measurements including skin hydration, elasticity, and pigmentation as well as optical scanning of skin surface were carried out after 4 and 8 weeks. Significant improvement in facial skin hydration, elasticity, and melanin concentration together with reduction in the wrinkle size and depth were observed at the two time points of measurements. In addition, DPKE cream was extremely well tolerated by the facial skin of study participants. The work herein demonstrates and validates the use of cream form containing 5% DPKE over placebo against fine lines and wrinkles, skin pigmentations, skin hydration, and elasticity. This effect may be attributed to synergism of major phytochemicals and phytosterols present in DPKE.

## INTRODUCTION

Skin aging involves several alterations of skin properties such as thinning, reduced elasticity, increased pigmentation, and appearance of wrinkles. These changes are the result of complex internal and external factors. Over the last decade, there has been an interest to use herbal extracts or phytochemicals in cosmetic products to fight the aging process. *Phoenix dactylifera*, commonly known as date palm, is widely cultivated across North Africa and the Middle East for its edible sweet fruit. The date kernel represents 10–15% of the total fruit weight, and studies have indicated that extracts of the date palm kernel contains plenty of biologically active phytochemicals such as carotenoids, polyphenols (e.g., phenolic acids, lignans, flavonoids, and isoflavones), phytosterols, and tannins (1).

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Many of these phytochemicals are considered potential contenders to revive tired aging skin and to have wrinkle-combating properties if used topically for suitable duration. However, a search in the scientific literature on the Internet yields scanty records on the anti–skin aging properties of date palm kernel extracts (DPKE) in human subjects (2,3). Accordingly, additional studies are necessary to boost the available reports and to establish a considerable body of evidence of anti–skin aging function of DPKE.

Assessment of the efficacy of cosmetic preparations on biophysical characteristics of human skin such as texture, roughness, elasticity, thickness, and wrinkle depth can be achieved by variety of techniques; the ideal method should be painless, noninvasive, and provide the specialist with a comprehensive view of skin topography and subsurface structure. Electronic probes with small electronic sensors are now common tools to objectively measure biophysical parameters of skin such as elasticity, hydration, and pigmentation. They can provide clinicians with precise measurements of these parameters in a fast and economic way (4,5). The advancement in digital technology in recent years enabled noncontact measurements of skin relief via optical scanning and digital profilometric analysis (6). The measuring principle uses scanning the surface with light of different wavelengths and at different angles to collect multispectral optical impressions of the skin surface and using these shape illumination 2D images to reconstruct a stereo 3D image of the skin that can be subjected to photometric stereo analysis by specialized software (7). In this study, we used the Antera 3D® camera (Miravex Limited, Dublin, Ireland) as a means for objective measurement of skin surface parameters (8). The purpose of this piece of research, however, was to investigate the antiaging properties of DPKE, formulated in cream form, on the facial skin of 43 healthy volunteers. Assessment of efficacy was based on measurement of skin biophysical parameters and skin profilometric analysis by an Antera 3D® multispectral analyzer.

## SUBJECTS AND METHODS

### SUBJECTS

Forty-three healthy volunteers were enrolled in this study (11 male participants and 32 female participants, age range 39–67 years). Inclusion criteria included the absence of connective tissue or cardiovascular diseases, nonsmokers, and absence of active skin lesions in the region of interest. Participants were instructed not to apply any cosmetic product or medicinal formulation on the skin area of investigation 1 week before and throughout the study. After fulfilling the inclusion criteria, each participant was asked to give informed consent by a research coordinator. The study was conducted in accordance with Al Baha University Faculty of Medicine guidelines and the Declaration of Helsinki.

### PREPARATION OF DPKE CREAM

Four hundred grams of date palm kernels (Sukkary variety) were defatted by *n*-hexane before being ground into a fine powder and extracted three times with 800 ml methanol at 4°C for 24 h. After filtration and centrifugation, the resultant supernatant was concentrated under low pressure at 4°C for 3 h to yield the lyophilized material. A cream formula

containing 5% DPKE was prepared by the method described by Meer et al. (3). In brief, the cream was prepared as an oil-in-water disperse system by heating separately the aqueous phase and the oil phase containing ABIL® EM90 as a nonionic emulsifier (Cetyl PEG/PPG-10/1 Dimethicone, Evonic Industries, Essen, Germany). The methanolic extract of date palm kernels was added in the aqueous phase, and the aqueous phase was added drop by drop to the oil phase at 75°C ± 1.0°C with continued stirring at 2,000 rpm. The emulsion was cooled at room temperature, and the speed of mixer was reduced gradually until the emulsion formed semisolid cream. The same method was used to formulate the base (placebo) cream without adding the DPKE. The composition of the two formulations is presented in Table I.

The stability tests and the physicochemical characteristics of the test and placebo creams were performed at different time points during 8 weeks at 5 ± 0.1°C, 20 ± 0.1°C, 40 ± 0.1°C, 40 ± 0.1°C with 75% relative humidity, and 50 ± 0.1°C (9).

### PATCH TEST

Before beginning the study, a patch test was performed on the skin of 12 volunteers (mean age 46.4 years) to investigate any skin reaction. A 5-cm area was marked on both forearms of each subject, and small amounts of both preparations were applied separately on each forearm; then, the region was covered with surgical dressing. Positive skin reactions were carefully evaluated after 1, 48, and 72–96 h. The reaction was assessed according to the International Contact Dermatitis Research Group standard (10).

### TREATMENT PROTOCOL

The region of interest was the cheek and the temple areas. Both the cream form containing DPKE and the placebo cream were coded and assigned to the right or left side of each volunteer's face according to a computer-generated randomization list. Participants were asked to apply DPKE and placebo formulations separately on each side of the face twice a day for 8 weeks. Follow-up visits took place every 1 week throughout the study.

### CLINICAL ASSESSMENT

Clinical assessment of facial skin was conducted as previously described by using three-point rating scales at baseline and at the end of the study (11). Skin roughness score: 1 = mild, 2 = moderate, and 3 = severe; skin texture homogeneity score: 1 = slightly inhomogeneous, 2 = uneven, and 3 = very uneven; skin melanin pigmentation score: 1 = mild,

**Table I**
Cream Compositions

| Phase | Placebo cream | Cream with DPKE |
|---|---|---|
| Oil phase | Liquid paraffin (17%) ABIL® EM90 (2.5%) | Liquid paraffin (17%) ABIL® EM90 (2.5%) |
| Aqueous phase | Distilled water (q.s 100%) | DPKE (5.0%) Distilled water (q.s 100%) |

2 = moderate, and 3 = severe; skin redness score: 1 = mild, 2 = moderate, and 3 = severe. Assessment was performed to study subjects by two independent dermatologists, and repeat assessments were performed to judge the inter- and intrarater reliability, respectively.

### BIOPHYSICAL MEASUREMENTS

Skin hydration, barrier function, elasticity, pigmentation, and erythema were measured by a multiprobe adapter system (MPA system, Courage and Khazaka electronic GmbH, Koln, Germany). Skin surface hydration was assessed by a Corneometer probe (CM825) (12). The transepidermal water loss (TEWL) was assessed by a Tewameter probe (TM 300), which measures the density gradient of water evaporation from the skin. A microprocessor analyses the values and expresses the evaporation rate in $g/m^2/h$ (13). A Cutometer probe (MPA 850) measures skin elasticity based on the suction method. The settings of measurements were negative pressure 500 Mbar and suction for 3 s followed by 5 s of release. Both skin firmness and elasticity were measured (14). Skin pigmentation and erythema were determined with a Mexameter probe (MX18). Melanin measurement was calculated from the intensity of the absorbed and reflected light at 660 and 880 nm, respectively, whereas erythema was measured at 568 and 660 nm (15). All probes were calibrated daily using standard references, and measurements were taken at baseline, after 4 weeks, and after 8 weeks. Values are displayed as arbitrary units (AU), and each value represents the mean of three measurements obtained from a participant's same area of skin.

### SKIN SURFACE DIGITAL PROFILOMETRY

Skin surface profilometry was performed by an Antera 3D® multispectral analyzer (Miravex Limited) at baseline and after 4 and 8 weeks of treatment. An Antera 3D® camera uses multidirectional illumination light to acquire multiple images and reconstructs a three dimensional image of the facial skin by the aid of computer software (8). After a period of 20 min acclimatization in controlled ambient conditions (24°C ± 1°C with 50 ± 10% relative humidity), the camera was placed directly on the external periorbital region over the crow's feet lines of all subjects and optical scanning images were acquired. After the acquisition of images, several parameters related to skin topography were measured, including wrinkle depth, indentation index of fine lines (marginal size less than 1.5 mm), folds (marginal size less than 2.5 mm), and wrinkles (marginal size less than 5.0 mm). In addition, texture roughness, skin pigmentation (melanin), and redness (hemoglobin) were also assessed. The identical area was digitally identified at each session, and values are presented as the result of triplicate measurements from the same area.

### STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL) Data were represented as the mean ± SD. Multiple comparisons between means were performed as appropriate by using the paired *t*-test or the one-way analysis of variance (ANOVA) followed by Tukey *post hoc* test. In all the tests, a *p*-value of less than 0.05 was considered significant.

## RESULTS

Only 36 subjects of 43 participants completed the study (seven male participants, age range 41–55 years, and 29 female participants, age range 40–65 years). Reasons for dropping out from follow-up visits were given as holiday time, tiredness, and other family issues rather than any problem with the cream preparations. A preliminary patch test revealed no skin reactions observed at 1, 24, and 96 h after removing the test materials in all 12 subjects. The physicochemical characteristics of both the placebo and test creams, kept at different temperatures for 8 weeks, are shown in Table II. The color was pearly white with no changes in homogeneity or phase separation up to 50 ± 0.1°C and up to 40 ± 0.1°C with 75% relative humidity. The presence of the lipophilic emulsifier ABIL® EM 90 stabilized the emulsions at high temperatures.

### CLINICAL ASSESSMENT

Clinical assessment of facial skin appearance was conducted at baseline and after completion of the study (i.e., after 8 weeks). Based on a three-point scale evaluation, there were statistically significant improvements in skin roughness, texture homogeneity, and melanin pigmentation. Skin redness levels were not significantly altered in all subjects (Table III).

### BIOPHYSICAL MEASUREMENTS

Measurements of objective skin parameters with a multiprobe instrument over 8 weeks revealed progressive increases of surface hydration and elasticity together with a progressive decline in both dermal pigmentation and TEWL in DPKE-treated skin compared with placebo cream. Figure 1A illustrates changes of skin hydration at three time points of study. At baseline, the mean values of skin hydration were 41.21 ± 10.32 and 42.10 ± 9.64 AU of placebo and DPKE creams, respectively. After 4 weeks, these values rose to 43.71 ± 11.62 and 52.92 ± 10.25 AU, respectively, and after 8 weeks, the values were 44.21 ± 10.42 and 52.23 ± 11.54, respectively ($p < 0.01$ vs. placebo and $p < 0.001$ vs. baseline for the two time points). Figure 1B illustrates changes of TEWL at three time points of the study. At baseline, the mean readings of TEWL were 12.23 ± 3.11 and 11.76 ± 2.92 g/m$^2$/h of placebo and DPKE creams, respectively. After 4 weeks, these values were 11.72 ± 2.52 and 10.43 ± 2.41 g/m$^2$/h, respectively, and after 8 weeks, the

**Table II**
Physicochemical Characteristics of Placebo and DPKE Creams Kept at Different Temperatures for 8 Weeks

| | Color | Texture | Homogeneity | Phase separation | Immediate skin feel |
|---|---|---|---|---|---|
| 5–40 ± 0.1°C | White | Smooth | Homogeneous | No | Refreshing, cool, no grittiness or greasiness |
| 40 ± 0.1°C with 75% relative humidity | White | Smooth | Homogeneous | No | Refreshing, no grittiness or greasiness |
| 50 ± 0.1°C | White | Smooth | Slight liquefaction | Slight | Refreshing, no grittiness or greasiness |

**Table III**
Clinical Assessment Rated on a Three-Point Scale

| | | After 8 weeks | |
|---|---|---|---|
| | Baseline | Placebo | DPKE |
| Skin roughness score | 2.24 ± 0.81 | 2.17 ± 0.64 | 1.76 ± 0.94**,# |
| Skin texture homogeneity score | 2.18 ± 0.76 | 2.01 ± 0.90 | 1.55 ± 0.66***,# |
| Skin melanin pigmentation score | 2.36 ± 0.95 | 2.28 ± 0.74 | 1.90 ± 0.84*,# |
| Skin redness score | 2.04 ± 0.84 | 2.11 ± 0.72 | 1.93 ± 0.93 |

Data are presented as mean ± SD of 36 subjects. Significance levels: *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$ versus baseline. #$p < 0.05$ versus placebo (ANOVA).

values were 11.53 ± 2.41 and 10.04 ± 2.73 g/m$^2$/h, respectively ($p < 0.05$ vs. both placebo and baseline at the two time points).

Figure 1C and D illustrate changes of skin elasticity and firmness at three time points of the study. At baseline, the mean values of skin elasticity were 0.84 ± 0.08 and 0.84 ± 0.09 AU of placebo and DPKE creams, respectively; after 4 weeks, these values were 0.85 ± 0.07 and 0.89 ± 0.06 AU, respectively ($p < 0.05$ vs. placebo and $p < 0.01$ vs. baseline), and after 8 weeks, the values were 0.86 ± 0.09 and 0.94 ± 0.10 AU, respectively ($p < 0.001$ vs. both placebo and baseline). At baseline, the mean firmness in the DPKE test skin was 0.27 ± 0.08 AU, and after 4 and 8 weeks, the firmness had diminished to 0.23 ± 0.06 and 0.21 ± 0.06 AU, respectively ($p < 0.01$ vs. placebo). Figure 1E illustrates changes of skin melanin density at three time points of the study. At baseline, the mean readings of skin melanin were 273.8 ± 27.9 and 265.6 ± 26.4 AU of placebo and DPKE creams, respectively. After 4 weeks, these values were 267.4 ± 30.2 and 260.8 ± 27.5 AU, respectively, and after 8 weeks, the values were 275.2 ± 28.4 and 255.3 ± 26.5 AU, respectively ($p < 0.05$ vs. both placebo and baseline). There were no significant changes in erythema levels for both placebo and DPKE creams over 8 weeks (Figure 1F).

### ANTERA 3D® MULTISPECTRAL ANALYSIS

The significant reduction in the wrinkle depth compared with pretreatment values was confirmed by objective analysis with the Antera 3D® analyzer performed at baseline, and after 4 and 8 weeks of treatment. Several wrinkle measurements showed significant improvements after 4 and 8 weeks compared with both baseline values and placebo cream. With the medium filter, there was a significant decline in the overall size after 4 and 8 weeks by 18.4% and 28.6%, respectively (from 56.4 ± 22.2 to 46.0 ± 21.5 ($p < 0.05$ vs. baseline and placebo), and 40.3 ± 22.1 AU ($p < 0.01$ vs. baseline and placebo, paired *t*-test, Figure 2A). The maximal depth was significantly decreased by 22.5% and 29.6%, respectively (from 0.410 ± 0.19 mm to 0.322 ± 0.18 mm and 0.284 ± 0.23 mm, respectively ($p < 0.05$ vs. baseline and placebo for all, paired *t*-test, Figure 2B). Moreover, significant improvements in the indentation index and skin roughness index were also evident after 4 and 8 weeks; however, the reductions of these parameters were more pronounced after 8 weeks, compared with baseline and placebo levels ($p < 0.01$ and $p < 0.001$, respectively, Figure 2C and D). The overall reduction in the skin color was also

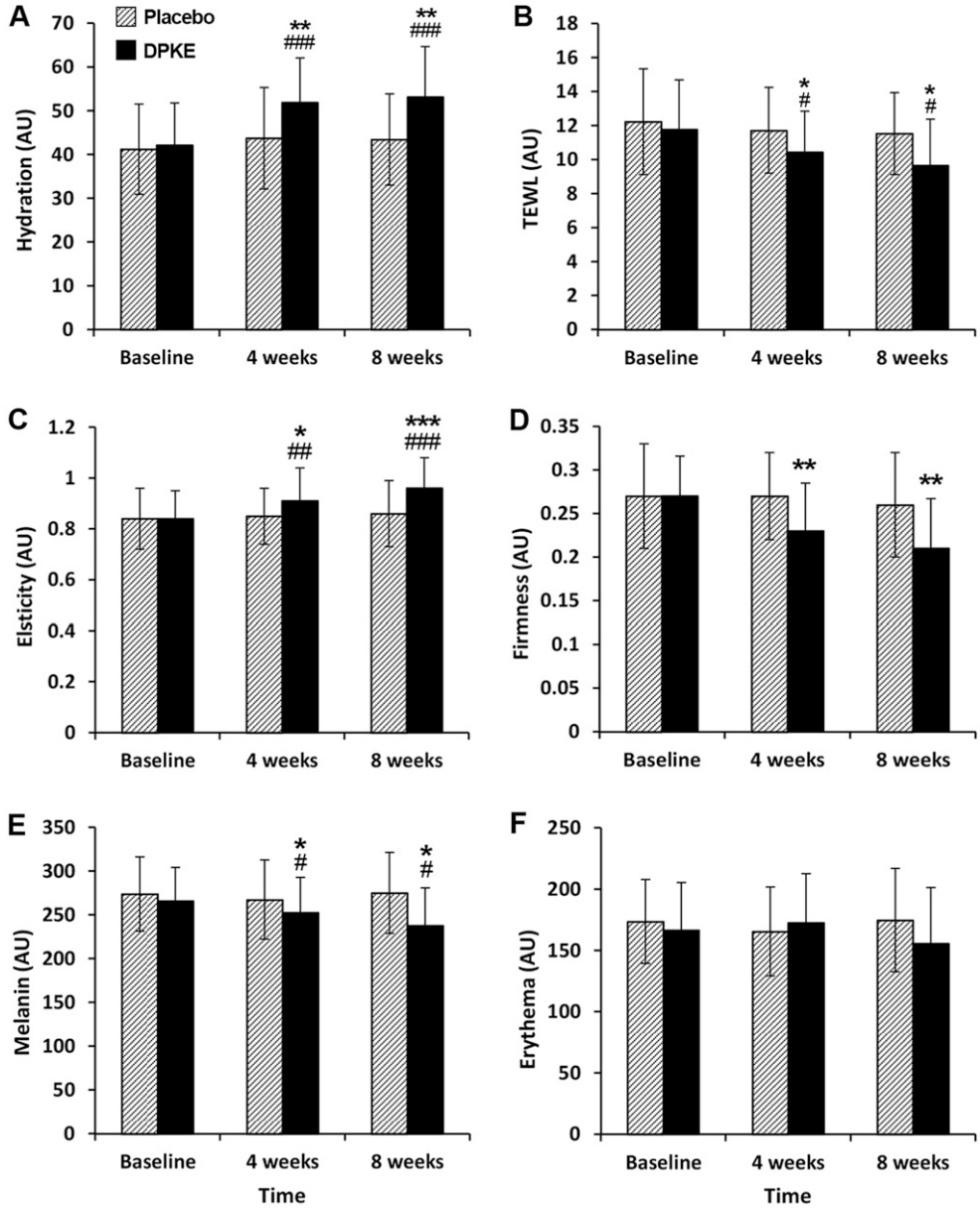


**Figure 1.** Biophysical measurements in 36 subjects at baseline and after 4 and 8 weeks of topical treatment with 5% DPKE cream. (A) Skin hydration, (B) TEWL, (C) skin elasticity, (D) firmness, (E) melanin pigmentation, and (F) erythema. Data are presented in AU as mean ± SD. Significance levels: *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$ versus baseline. #$p < 0.05$, ##$p < 0.01$, and ###$p < 0.001$ versus placebo (ANOVA).

evaluated during the follow-up visits using the Antera 3D. Multispectral analysis of the skin color showed that DPKE cream statistically reduced the average concentrations of skin melanin at the two time points of assessment compared with both the baseline and placebo measurements ($p < 0.05$ for all, Figure 3). The placebo cream had no significant effects on the overall wrinkle size, depth, indentation, and roughness indices or skin

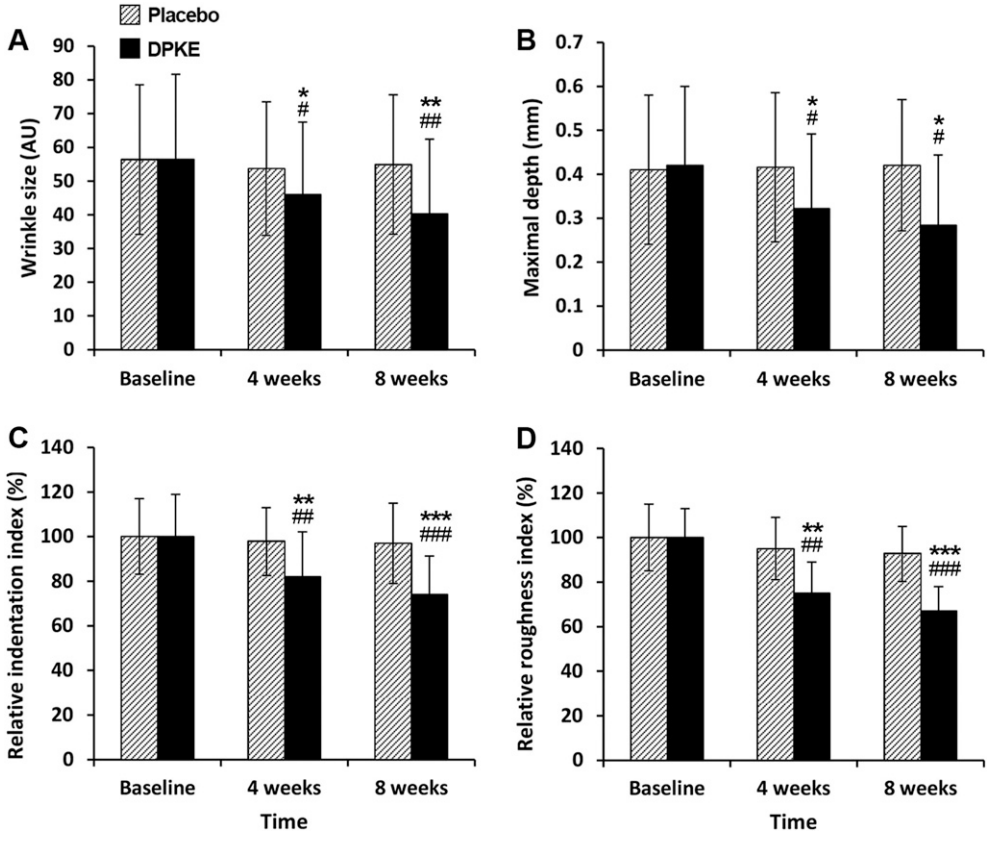


**Figure 2.** Antera 3D® analysis of wrinkle size (A) and maximal depth (B) measured in 36 subjects at baseline and after 4 and 8 weeks of topical treatment with 5%DPKE cream. (C and D) show percentage changes in the relative indentation index and relative roughness index, respectively. Data are presented as mean ± SD in AU for wrinkle size and in millimeters for wrinkle depth. Significance levels: *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$ versus baseline. #$p < 0.05$, ##$p < 0.01$, and ###$p < 0.001$ versus placebo (paired $t$-test).

melanin concentration at the two measured time points. Collective data obtained in both male and female volunteers separately at baseline and after 4 and 8 weeks of treatment with DPKE cream are presented in Table IV.

## DISCUSSION

Aging involves several alterations of skin properties that result in skin thinning along with reduced skin elasticity, increased fragility, pigmentations, and appearance of fine lines and wrinkles. Accordingly, the search for natural and effective skin rejuvenation remedies is an exceptionally large interest for the cosmetics industry. In this study, we investigated the potential of topical DPKE, formulated as cream, in reducing the manifestations of facial skin aging in human volunteers. The work herein demonstrates and validates the use of a cream form containing 5% DPKE over placebo against fine lines and wrinkles, skin pigmentations, hydration, and elasticity. This improvement began to show after 4 weeks of treatment and progressed over 8 weeks. In addition, DPKE cream was

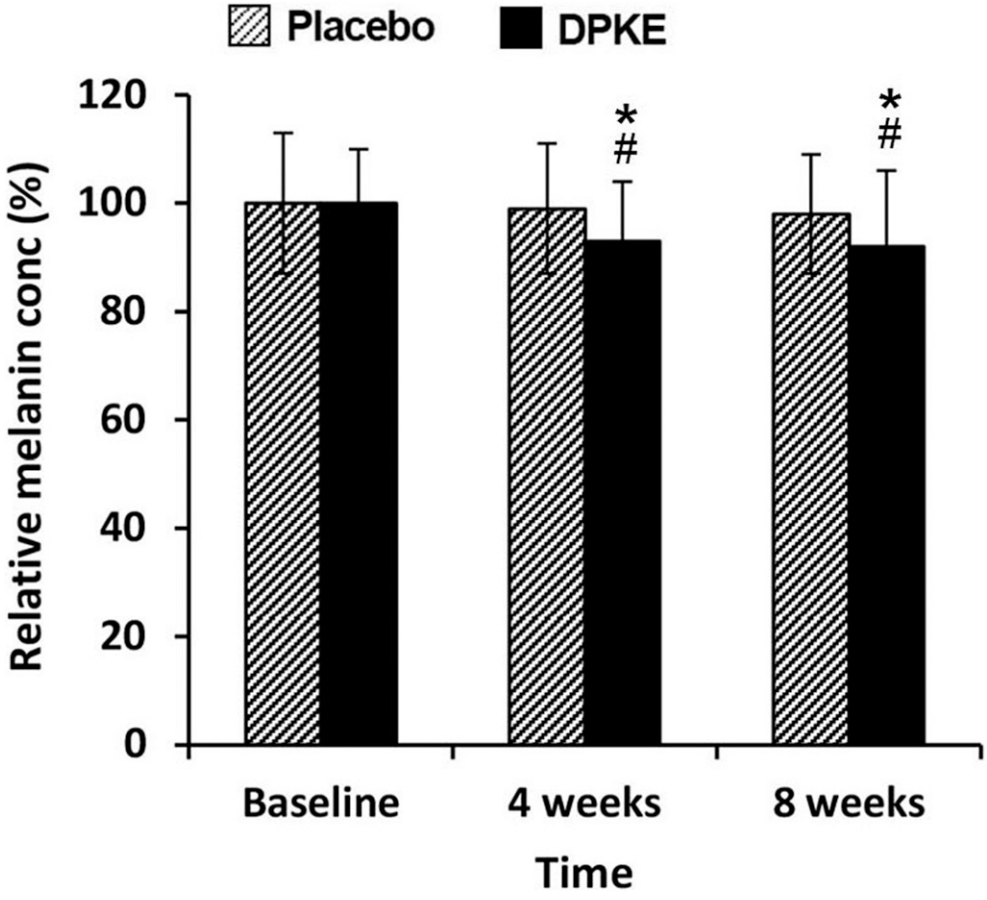


**Figure 3.** Percentage changes in relative melanin concentration after 4 and 8 weeks of treatment. Data are presented as mean ± SD. Significance levels: *$p < 0.05$ versus baseline. #$p < 0.05$ versus placebo (paired $t$-test).

extremely well tolerated when applied daily on facial skin (no irritation, redness, burn, or itching). This is in contrast with other topical treatments containing compounds such as retinoic acid which provides improvements in skin appearance but at the expense of irritating adverse effects such as skin redness and sensitivity (16). In addition to good tolerability, DPKE is easily formulated, chemically stable, and compatible with other formulation constituents, qualifying it to be an ideal agent for use in cosmetic products.

Skin aging is the result of a multifaceted biological phenomenon consisting of two components: intrinsic (chronologic) aging and extrinsic aging. The pathophysiologic elucidation of both components has been well documented in clinical and histologic studies (17). Intrinsic aging is largely a genetic process in which increased production of reactive oxygen species (ROS) alongside with progressive damage to mitochondrial DNA causes cell senescence and impairment of skin repair (18). Extrinsic aging is responsible for most skin deteriorations, and is caused by several factors, of which, exposure to ultraviolet (UV) light (photoaging) is the most crucial, and causes DNA damage in a multiplicity of living tissue (19). Photodamage also involves the generation of ROS that breaks the cellular biosynthesis of collagen and glycosaminoglycans in skin along with decreased keratinocyte

**Table IV**
Collective Data Obtained in Both Male and Female Volunteers at Baseline and after 4 and 8 weeks of Treatment with DPKE Cream

| | Male volunteers ($n = 7$) | | | Female volunteers ($n = 29$) | | |
|---|---|---|---|---|---|---|
| | Baseline | 4 weeks | 8 weeks | Baseline | 4 weeks | 8 weeks |
| Clinical assessment: | | | | | | |
| Roughness score | 2.32 ± 0.83 | — | 1.86 ± 0.87* | 1.72 ± 0.85 | — | 1.14 ± 0.51* |
| Texture homogeneity score | 2.07 ± 0.53 | — | 1.41 ± 0.63* | 2.21 ± 0.75 | — | 1.59 ± 0.62** |
| Pigmentation score | 2.30 ± 0.74 | — | 2.08 ± 1.08 | 2.37 ± 0.99 | — | 1.83 ± 0.80* |
| Redness score | 1.81 ± 0.77 | — | 2.04 ± 0.78 | 2.10 ± 0.85 | — | 1.91 ± 0.96 |
| Biophysical measurements: | | | | | | |
| Skin hydration (AU) | 43.00 ± 10.56 | 49.70 ± 9.83** | 55.23 ± 9.63** | 40.71 ± 9.60 | 53.74 ± 9.66** | 50.93 ± 12.03** |
| TEWL ($g/m^2/h$) | 11.75 ± 3.32 | 10.24 ± 1.57 | 10.12 ± 1.90 | 12.33 ± 3.10 | 10.48 ± 2.54* | 10.02 ± 2.90** |
| Skin elasticity (AU) | 0.844 ± 0.088 | 0.910 ± 0.057 | 0.976 ± 0.113* | 0.836 ± 0.093 | 0.890 ± 0.063* | 0.930 ± 0.094** |
| Skin firmness (AU) | 0.270 ± 0.078 | 0.199 ± 0.047* | 0.171 ± 0.061* | 0.277 ± 0.084 | 0.236 ± 0.057* | 0.218 ± 0.054** |
| Skin melanin density (AU) | 272.9 ± 21.8 | 250.6 ± 20.2 | 264.9 ± 27.3 | 273.5 ± 29.7 | 263.4 ± 28.9 | 254.1 ± 26.3* |
| Erythema (AU) | 176.9 ± 62.8 | 168.6 ± 66.4 | 155.5 ± 74.2 | 167.6 ± 60.3 | 158.9 ± 70.4 | 151.7 ± 68.4 |
| Multispectral analysis: | | | | | | |
| Wrinkle size (AU) | 67.5 ± 19.5 | 44.0 ± 17.6 | 41.8 ± 15.9* | 54.6 ± 22.1 | 46.5 ± 22.5 | 39.2 ± 23.1* |
| Maximal depth (mm) | 0.482 ± 0.117 | 0.315 ± 0.130 | 0.258 ± 0.157* | 0.395 ± 0.194 | 0.323 ± 0.190 | 0.287 ± 0.225* |
| Relative indentation index (%) | 100.0 ± 18.1 | 84.9 ± 16.4 | 78.5 ± 17.5* | 100.0 ± 17.8 | 81.3 ± 16.5** | 80.8 ± 15.4*** |
| Relative roughness index (%) | 100.0 ± 15.5 | 82.5 ± 13.0* | 74.4 ± 12.8** | 100.0 ± 15.2 | 75.1 ± 15.7** | 67.2 ± 13.9*** |
| Relative melanin concentration (%) | 100.0 ± 13.7 | 92.9 ± 14.4 | 86.7 ± 13.5 | 100.0 ± 20.6 | 87.3 ± 20.4* | 85.8 ± 25.4* |

Data are presented as mean ± SD of seven male and 29 female subjects. Significance levels: *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$ versus baseline values (paired $t$-test).

cell turnover, resulting in grave disorganization of the dermal matrix (20). Accordingly, there is plenty of room to explain the essentials of mechanisms underlying the benefits of DPKE observed herein. We suggest that the anti–skin aging effect of DPKE is attributed, at least partially, to preservation of the dermal matrix through prevention of oxidative damage to cellular DNA. This assumption is based on data in the literature documenting the protective role of many antioxidants against the UV-induced oxidative damage to human skin (21). Likewise, researchers have found that date seed extract includes a myriad of polyphenols and tocopherols with robust antioxidant capabilities. Moreover, date kernel oil was reported to have higher oxidative stability than most vegetable oils, including olive oil (1). These observations have led to a series of studies to investigate the notable antioxidant and radical-scavenging properties of date kernel extract on human skin. Dammak et al. (22) have demonstrated that pretreatment with date seed oil significantly ameliorated the expression of p53 in human skin after exposure to UV irradiation by affording free-radical–scavenging properties. Date seed oil was also demonstrated to significantly improve cell viability and reduce depletion of superoxide dismutase, glutathione peroxidase, catalase, and lipid peroxidation in cultured human melanocytes after hydrogen peroxide exposure (23). The experiment was subsequently repeated on human keratinocytes with findings analogous to those of the previous study (24). As both melanocytes and keratinocytes are implicated in the inflammatory process of photoaging, we suggest that these findings may explain some of the rejuvenative properties of DPKE.

Previous studies have shown that date kernel extract contains a high fraction of hydroxytyrosol, one of the most powerful natural antioxidants. This compound has 10 times more antioxidants than green tea and two times more than coenzyme Q10 (25). The extraordinary scavenging activity of hydroxytyrosol has been demonstrated in several studies both *in vivo* and *in vitro* (26,27). In its chemical structure, this compound has an extra hydroxyl group in its benzene ring, granting it greater function as a free radical scavenger and increasing its efficacy under stress conditions (25). In addition, hydroxytyrosol is an amphipathic, water-soluble, and fat-soluble molecule which facilitates its penetration of cellular membranes and makes it a good transporter of substances across skin tissue (28). Studies have also shown that hydroxytyrosol has the ability to inhibit cyclooxygenase and lipoxygenase enzymes of arachidonic acid, reducing the oxidative corrosion characteristic of inflammations, and stimulate the regeneration and repairing of damaged tissue (29).

Alpha ($\alpha$)-tocopherol, a type of vitamin E, is another component present in date kernel extract with significant concentration (1) and is best known for its robust antioxidant function and good penetration into the human skin layers (30). $\alpha$-tocopherol has been used in the treatment of burns, surgical scars, and variety of skin conditions (31). Topical formulations containing $\alpha$-tocopherol have also been found to be effective in reducing infraorbital dark haloes and wrinkles of the lower eyelids (32), although *in vitro* studies revealed that $\alpha$-tocopherol inhibits p53 expression in dermal tissues and protects against the UV irradiation of cultured fibroblasts (33). $\alpha$-tocopherol is, therefore, one of the most shared ingredients in the over-the-counter treatments of skin aging.

Phytosterols and phytoestrogens are additional major phytochemicals found in the lipid soluble fraction of the DPKE. Phytoestrogens are a group of isoflavones that can bind both estrogen receptors ER$\alpha$ and ER$\beta$ (34), and they are considered to be naturally occurring selective estrogen receptor modulators and potential candidates to provide a natural alternative of estrogen replacement in postmenopausal women. Studies have shown that these phytoestrogens have favorable effects on human skin as they can minimize

UV-induced cell damage in cultured keratinocytes, improve skin elasticity, reduce pigmentation and wrinkle depth, and increase the production of type 1 procollagen (35). Moreover, the isoflavone genistein has been reported to provide significant protection against the UV-induced damage in human dermal fibroblasts by significantly boosting the intracellular antioxidant armamentarium in a dose-dependent way (36). Taken together, we suggest that the combination of various ingredients contained in DPKE might provide complementary mechanisms of modulating cellular pathways involved in the process of skin aging, and the effectiveness of these ingredients may be further potentiated by synergism of their individual components.

**FUNDING**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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