LETTER TO THE EDITOR

Efficacy assessment of a TCA/H2O2 compositum for skin ageing treatment by confocal laser microscopy and optical coherence tomography

Dear Editor,

Skin ageing is a complex phenomenon linked to intrinsic and extrinsic factors, such as ultraviolet exposure, smoking or pollution,[1–4] which involves all skin layers.[5–7] Ageing is characterized by a reduction in collagen synthesis,[4,8,9] a decreased hydration,[5,6] epidermal thickness variations,[7] and an accelerated breakdown and disorganization of collagen fibres[4,8,9] as well as loss of skin elasticity.[10] Chemical peelings can potentially help to reverse these degenerative processes. However, the role of a TCA/H2O2 compositum (PRX-T_{33}®; GPQ SRL, Milan, Italy) containing trichloroacetic acid (33%), hydrogen peroxide and kojic acid (5%) in skin rejuvenation has not been reported so far.

The objective of the current study was to evaluate the efficacy and safety of TCA/H2O2 compositum for skin rejuvenation, through non-invasive skin imaging tools, at baseline and after treatment.

We performed a prospective, single-centre, uncontrolled and open-label post-marketing study on healthy female volunteers, aged 45–60 years, with moderate-severe skin ageing, who were able to comply with all protocol requirements and agree to participate in the study. Exclusion criteria were as follows: laser or chemical peel treatments in the previous six months, allergy to the product, active inflammatory processes or facial infections. The study was conducted according to

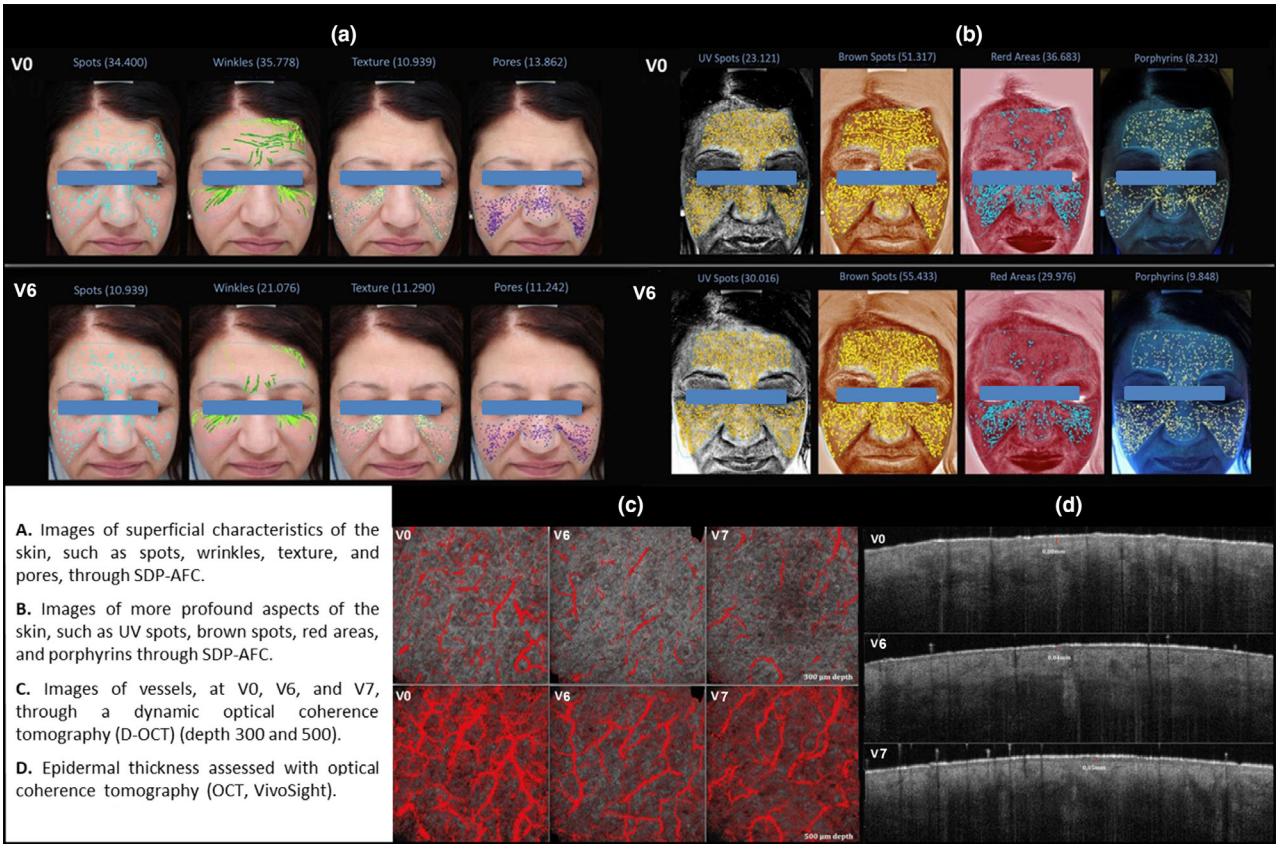

Figure 1 Images of treatment outcomes assessed through non-invasive procedures.

Table 1 Data obtained with coherence tomography (OCT, VivoSight), dynamic OCT (D-OCT), reflectance confocal microscopy (RCM, VivaScope 1500) and standard digital photography with automated features count (SDP-AFC, VISIA®)

N = 15	Score	V0	V6	V7	*P*-value
OCT features					
Epidermal thickness (μm), Mean (SD)		0.052 (0.01)	0.044 (0.006)°	0.042 (0.008)*	0.022° 0.006*
Collagen density, mean (SD)		83.730 (5.148)^	87.747 (7.414)°	74,443 (8.336)*	0.032^ 0.003° 0.001*
Attenuation Index, mean (SD)		0.003305 (0.000403)^	0.003638 (0.000575)	0.00249 (0.001062)*	0.024^ 0.021° 0.007*
D-OCT features					
Pixel density, mean (SD) (depth 300 μm)		10 759.53 (8717.98)	11 486.93 (8341.93)	13 367.86 (6824.81)	0.8171^ 0.3693° 0.5047*
Pixel density, mean (SD) (depth 500 μm)		58 80.13 (22 730.50)	49 544.13 (21 611.83)	49 304.60 (30 129.01)	0.3009^ 0.3755° 0.9802*
Vessel density, *n*, % (depth 300 μm)	0	9 (60%)	6 (40%)	6 (40%)	
	1	5 (33.3%)	8 (53.3%)	8 (53.3%)	
	2	2 (13.3%)	1 (6.7)	1 (6.7)	
	3	0	0	0	
Vessel density, *n*, % (depth 500 μm)	0	3 (20.0%)	2 (13.3%)	2 (13.3%)	
	1	6 (40.0%)	8 (53.3%)	7 (46.7%)	
	2	5 (33.3%)	3 (20.0%)	4 (26.7%)	
	3	1 (6.7%)	2 (13.3%)	2 (13.3%)	
RCM features					
Integrity of collagen fibres, *n*, %	0	0	0	0	
	1	1 (6.7%)	1 (6.7%)	3 (20.0%)	
	2	8 (53.3%)	9 (60.0%)	9 (60.0%)	
	3	6 (40.0%)	3 (20.0%)	3 (20.0%)	
Structures observed through RCM					
Irregular honeycombed pattern, *n*, %	0	0	1 (6.7%)	0	
	1	1 (6.7%)	10 (66.7%)	5 (33.3%)	
	2	5 (33.3%)	1 (6.7%)	6 (40%)	
	3	6 (40%)	3 (20%)	3 (20%)	
	4	3 (20%)	0	1 (6.7%)	
Mottled pigmentation, *n*, %	0	1 (6.7%)	3 (20.0%)	1 (6.7%)	
	1	1 (6.7%)	3 (20.0%)	1 (6.7%)	
	2	4 (26.7%)	5 (33.3%)	2 (13.3%)	
	3	6 (40%)	1 (6.7%)	4 (26.7%)	
	4	0	0	1 (6.7%)	
Polycyclic papillary contours, *n*, %	0	4 (26.7%)	9 (60%)	12 (80%)	
	1	5 (33.3%)	4 (26.7%)	1 (6.7%)	
	2	2 (13.3%)	1 (6.7%)	0	
	3	2 (13.3%)	1 (6.7%)	0	
	4	2 (13.3%)	0	2 (13.3%)	
Thin reticulated collagen, *n*, %	0	14 (93.3%)	12 (80%)	12 (80%)	
	1	0	3 (20.0%)	1 (6.7%)	
	2	1 (6.7%)	0	1 (6.7%)	
	3	0	0	0	
	4	0	0	0	

Table 1 *Continued*

N = 15	Score	V0	V6	V7	*P*-value
Coarse collagen, *n*, %	0	1 (6.7%)	2 (13.3%)	1 (6.7%)	
	1	2 (13.3%)	1 (67%)	2 (13.3%)	
	2	3 (20%)	0	2 (13.3%)	
	3	2 (13.3%)	5 (33.3%)	5 (33.3%)	
	4	7 (46.7%)	7 (46.7%)	5 (33.3%)	
Huddle collagen, *n*, %	0	10 (66.7%)	11 (73.3%)	11 (73.3%)	
	1	3 (20.0%)	2 (13.3%)	3 (20%)	
	2	2 (13.3%)	2 (13.3%)	1 (6.7%)	
	3	0	0	0	
	4	0	0	0	
Curled bright structure, *n*, %	0	10 (66.7%)	11 (73.3%)	8 (53.3%)	
	1	2 (13.3%)	1 (6.7%)	4 (26.7%)	
	2	2 (13.3%)	3 (20%)	2 (13.3%)	
	3	1 (6.7%)	0	1 (6.7%)	
	4	0	0	0	

SDP-AFC features

	V0		V6		V7	
Mean (SD)	**Absolute scores**	**Features counts**	**Absolute scores**	**Features counts**	**Absolute scores**	**Features counts**
Spots	30.17 (5.734)	158.66 (35.29)	33.91 (8.87)	160.26 (44.59)	33.32 (7.43)	174.07 (45.12)
Wrinkles	39.33 (14.48)	225.06 (78.47)	42.41 (15.24)	231.00 (92.93)	42.04 (13.31)	244.84 (89.03)
Texture	15.60 (5.14)	900.46 (322.03)	15.69 (6.50)	895.73 (361.89)	18.29 (7.31)	1040.23 (405.90)
Pores	15.31 (6.79)	649.53 (288.76)	15.51 (5.85)	664.80 (244.22)	16.06 (7.66)	667.61 (349.37)
UV spots	33.51 (7.46)	529.66 (62.11)	35.07 (7.91)	522.60 (64.11)	29.91 (11.36)	513.76 (65.80)
Brown spots	54.96 (9.47)	585.40 (89.25)	55.78 (9.98)	576.93 (93.07)	53.35 (10.76)	568.15 (82.92)
Red areas	31.63 (6.71)	376.80 (106.08)	29.73 (5.47)	352.66 (77.61)	29.53 (6.33)	379.23 (122.43)
Porphyrins	14.94 (8.37)	1940.60 (1043.53)	12.79 (8.10)	1705.00 (1092.66)	15.08 (10.32)	2081.00 (1418.42)

D-OCT Score: 0 (absent); 1 (few vessels); 2 (moderate vessels); 3 (many vessels). RCM Score: 0 (absent); 1 (few fragmented collagen fibres); 2 (moderate fragmented collagen fibres); 3 (many fragmented collagen fibres). Score of the structures observed through RCM: 0 (absent); 1 (<25%); 2 (25–50%); 3 (50–75%); 4 (75–100%).
V0, Baseline; V6, visit at one week after the last treatment; V7, visit at 12 weeks after the last treatment.
^T0 vs. T1. °T0 vs. T2. *T1 vs T2.

the principles of the Declaration of Helsinki. All patients signed informed consent.

All participants received a total of five treatments with the TCA/H2O2 compositum, one per week, as per standard product protocol, and were followed up for 12 weeks. Treatment results were assessed through non-invasive procedures. These procedures included standard digital photography with automated features count (SDP-AFC), reflectance confocal microscopy (RCM) (Vivascope-1500; MAVIG GmbH, Munich, Germany), optical coherence tomography (OCT) and dynamic-OCT (D-OCT) (VivoSight; Michelson Diagnostics Ltd., Kent, UK). Images were acquired at baseline (V0), six weeks (V6) and 12 weeks (V7) after treatment and assessed according to recently standardized protocols.[7,8] Additionally, a patient satisfaction questionnaire (from 0 'not satisfied' to 3 'very satisfied') was administered to patients. All adverse events after the procedure were recorded. Statistical analysis was performed using IBM SPSS 26.0 (IBM Corp, Armonk, NY, USA).

A total of 15 females with a mean age of 54.93 years (SD ± 4.94) were included. Interestingly, OCT showed a significant reduction in epidermal thickness (at V6 $P = 0.022$ and V7 $P = 0.006$, respectively, as compared to V0) and a significant increase in the attenuation coefficient, expressed as an improvement in collagen fibres, and an increase in collagen density at V6, as compared to V0 ($P = 0.024$ and $P = 0.032$, respectively). Both parameters were found to be decreased at V7. Furthermore, UV spots and brown spots, estimated through SDP-AFC, showed differences after treatment, despite not statistically significant. Additionally, a trend in terms of keratinocyte structure improvement as well as a reduction in mottled pigmentation and polycyclic contours were observed at V6 with RCM, as compared to V0 (Table 1 and Fig. 1). In accordance with skin imaging results, 80% of patients ($N = 12$) were very satisfied, reporting an improved skin texture, a plumped appearance in the major part of cases (73.3%) and a brighter face, which made it unnecessary to apply routine make-up. The treatment did not

cause pain or side-effects, except for mild erythema in three patients, with spontaneous resolution.

In conclusion, despite the low number of patients enrolled, the TCA/H2O2 compositum was proven to be an effective and safe skin rejuvenation treatment, as assessed through non-invasive skin imaging tools, enabling the evaluation not only of the epidermis but also of dermal variations after treatment. However, studies including a larger number of patients and a long-term follow-up might be necessary to confirm these results.

Acknowledgement

The authors would like to thank all their collaborators and the i2e3 Biomedical Research Institute team. The patients in this manuscript have given written informed consent to publication of their images or case details.

Conflicts of interest

The authors have no conflicts of interest to disclose. This study was supported by GPQ srl with a research grant to the University of Modena and Reggio Emilia.

F. Peccerillo,[1,*] G. Odorici,[2] S. Ciardo,[3] M. Greco,[3] S. Guida,[3] F. Farnetani,[3] G. Pellacani[3]

[1]Dermatology Unit, Arcispedale Santa Maria Nuova, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy, [2]Department of Dermatology, University of Ferrara, Ferrara, Italy, [3]Department of Dermatology, University of Modena and Reggio Emilia, Modena, Italy

*Correspondence: F. Peccerillo. E-mail: francescapeccerillo@gmail.com

References

1 Addor FAS. Beyond photoaging: additional factors involved in the process of skin aging. *Clin Cosmet Investig Dermatol* 2018; **11**: 437–443.
2 Puri P, Nandar SK, Kathuria S, Ramesh V. Effects of air pollution on the skin: a review. *Indian J Dermatol Venereol Leprol* 2017; **83**: 415–423.
3 Flament F, Bazin R, Laquieze S, Rubert V, Simonpietri E, Piot B. Effect of the sun on visible clinical signs of aging in Caucasian skin. *Clin Cosmet Investig Dermatol* 2013; **6**: 221–232.
4 Guida S, Pellacani G, Ciardo S, Longo C. Reflectance confocal microscopy of aging skin and skin cancer. *Dermatol Pract Concept* 2021; **11**: e2021068.
5 Guzmán-alonso M, Cortazár TM, Guzmàn-alonso M, Cortazar TM. Water content at different skin depths and the influence of moisturizing formulations. *Househ Pers Care Today* 2016; **11**: 35–40.
6 Waller JM, Maibach HI. Age and skin structure and function, a quantitative approach (I): Blood flow, pH, thickness, and ultrasound echogenicity. *Ski Res Technol* 2005; **11**: 221–235.
7 Ciardo S, Pezzini C, Guida S *et al*. A plea for standardization of confocal microscopy and optical coherence tomography parameters to evaluate physiological and para-physiological skin conditions in cosmetic science. *Exp Dermatol* 2021; **30**: 911–922
8 Guida S, Ciardo S, De Pace B *et al*. The influence of MC1R on dermal morphological features of photo-exposed skin in women revealed by reflectance confocal microscopy and optical coherence tomography. *Exp Dermatol* 2019; **28**: 1321–1327.
9 Shin JW, Kwon SH, Choi JY *et al*. Molecular mechanisms of dermal aging and antiaging approaches. *Int J Mol Sci* 2019; **20**: 2126.
10 Sellheyer K. Pathogenesis of solar elastosis: synthesis or degradation? *J Cutan Pathol* 2003; **30**: 123–127.

DOI: 10.1111/jdv.17596