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ORIGINAL ARTICLE

Does tomato juice consumption have a positive effect on the physical and psychological states of individuals in the Coronavirus era?

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Abstract

OBJECTIVES: This preliminary study aims to examine the effects of tomato juice, which can be easily consumed regularly, on the physical and psychological states of healthy adults in the Coronavirus era.
DESIGN: Prospective observational study.
MATERIALS AND METHODS: Ten healthy adults (mean age, 39.7±4.2 years) who consumed 180 mL of tomato juice twice daily for 4 weeks were enrolled. Measurements were taken before and after 4 weeks of consumption for the items below. Five salivary stress biomarkers (cortisol, α-amylase, secretory immunoglobulin A, chromogranin A, and oxytocin) were measured using approximately 1ml of passively pooled saliva samples, which were stored at -20°C until measurement. Autonomic nervous system (ANS) activity was evaluated using an acceleration pulse wave meter. Skin moisture content and transepidermal water loss (TEWL) were measured using Multi Display devices® MDD4 with specific probes. Subjective psychological states were assessed using Profile of Mood Status (POMS2®) and a survey on skin condition was conducted.
RESULTS: As for salivary stress biomarkers, tomato juice intake reduced cortisol and significantly increased oxytocin levels (p = 0.0427). No significant changes were observed in ANS activity. POMS2® results showed a significant decrease in confusion and bewilderment (p = 0.0207). Skin moisture content increased significantly (p = 0.0011), whereas TEWL decreased. The skin condition survey revealed significant changes in 10 parameters.
CONCLUSIONS: Tomato juice, which can be easily consumed regularly, may alleviate the stress of healthy adults in the Coronavirus era, supported by positive changes in salivary stress biomarker levels, skin moisture content, TEWL, and POMS2® results of this preliminary study.

Abbreviations:

AH	- Anger-hostility
CB	- Confusion-bewilderment
DD	- Depression-dejection
FI	- Fatigue-inertia
F	- Friendliness
HRV	- Heart rate variability
LF	- Low-frequency power
HF	- High-frequency power
ROS	- Reactive oxygen species
TEWL	- Transepidermal water loss
TA	- Tension-anxiety
TMD	- Total mood disorder
TP	- Total power
VA	- Vigor-activity

INTRODUCTION

The recent sophistication and diversification of the social structure and changes in the social environment have caused individuals to constantly be under stress from numerous physical and psychological stimulations. The situation was further worsened by the outbreak of Coronavirus Disease 2019 in 2020. Under this stressful society's circumstances, food intake containing functional ingredients is considered useful as a voluntary and familiar stress control measure. Notably, vegetables and fruits rich in phytochemicals have recently gained increasing attention in terms of health promotion (Saghafian *et al.* 2018; Aune *et al.* 2017) as foods that may play an important role in functions such as thermoregulation and biological defense.

Among these, tomatoes, consumed globally at an average of 17 kg per person annually (Rothan *et al.* 2017), are crucial for obtaining vitamins, minerals, dietary fibers, and proteins (Ministry of Education, 2020) and serve as key sources of antioxidants, such as carotenoids, lycopene, and polyphenols. A scientific analysis of the health effects of tomatoes and their products (Tilesi *et al.* 2021) has highlighted the extensive research conducted on the health benefits of tomatoes. Studies have proposed that lycopene present in tomatoes may affect blood lipid levels, potentially preventing cardiovascular diseases (Thies *et al.*) and certain types of cancer (Tanaka *et al.* 2012; Chen *et al.* 2015; Applegate *et al.* 2019), particularly relating to oxidative stress. However, comprehensive data on tomato consumption effects beyond the antioxidant ones are limited. To the best of our knowledge, no study has explored the effects of tomato consumption on stress in the Coronavirus era.

Therefore, we conducted a 4-week exploratory study with 10 healthy individuals consuming tomato juice, an easily accessible source of tomato components. Having previously performed a comprehensive evaluation of stress biomarkers through saliva samples as a noninvasive and simple method to assess stress changes (Watanabe *et al.* 2021; Hasebe *et al.* 2023), in this study, we measured the changes in salivary stress biomarker levels, moisture content of the stratum corneum, transepidermal water loss (TEWL), autonomic nervous system activity, mood profiles (Profile of Mood Status second edition, POMS2®), and skin conditions after tomato juice consumption. Overall, we aimed to evaluate stress reduction and physiological changes resulting from tomato juice consumption, gauging the potential practicality of incorporating functional foods such as tomato products into everyday life for stress management of modern society in the Coronavirus era.

MATERIALS AND METHODS

Study design and participants

Ten healthy adults (three males and seven females; mean age, 39.7±4.2 years) residing in urban areas voluntarily participated in this study, demonstrating full understanding of the study objectives and meeting the criteria of no illness or smoking habits for registration (Table 1). A flow chart of this study is shown in Figure 1. Participants consumed 180 mL × 2 bottles/day for 4 weeks (from the 19th/20th of October until 16th/17th of November 2021), due to the fact that skin turnover is approximately 28 days. The time of intake twice a day was left to the discretion of each participant. Measurements were taken before and after this 4-week period. All data were collected between 10:00 and 13:00. Upon arrival in the experimental room, participants rested for 30 min to adjust to the environment. Subsequently, they completed the mood questionnaire and skin condition survey, followed by saliva collection, autonomic nerve activity analysis and measurements of skin moisture content and TEWL. The tomato juice used for this experiment was 100% pure, provided by the Antioxidant Research Institute, Inc. All study protocols were approved by the Review Board and Ethics Committee of Juntendo University Medical School and conformed to the tenets of the Declaration of Helsinki. Informed consent was obtained from all the participants.

Tab. 1. Subjects' characteristics

	Sex	Age
1	Female	26
2	Female	33
3	Female	31
4	Female	43
5	Female	48
6	Male	23
7	Male	31
8	Male	40
9	Female	53
10	Female	64

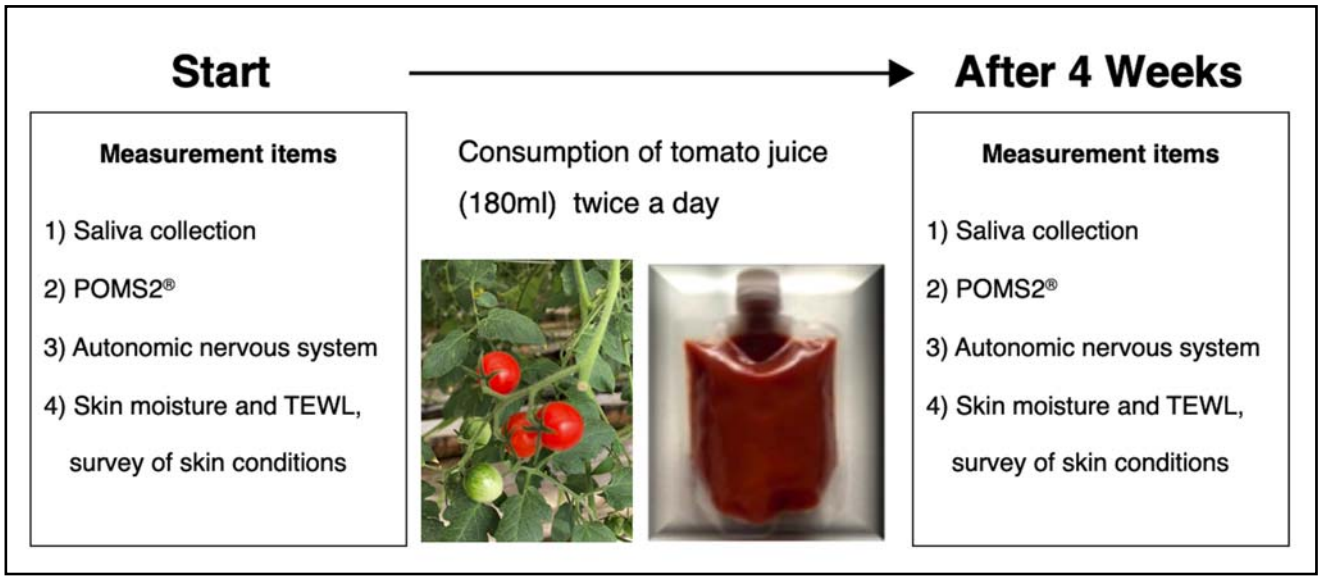

Fig. 1. The study procedure. Saliva samples and autonomic nerve were collected. POMS2® and a survey of skin conditions were administered on the start day of the experiment and after 4 weeks.

Measurement of salivary stress biomarker levels

Salivary components were assessed on the experiment day and after 4 weeks. Five salivary stress markers, cortisol, α-amylase, chromogranin A, s-IgA, and oxytocin (Izawa *et al.* 2008; Niimi, 2018), were measured using approximately 1 mL of passively pooled saliva samples collected with a saliva collection aid (Salimetrics LLC; Carlsbad, CA, USA). Samples were immediately frozen at -20°C until analysis. On the day of the assay, they were thawed at room temperature and underwent centrifugation at 1500×g for 15 min. The supernatant was used for measuring cortisol, chromogranin A, s-IgA, and oxytocin levels with a salivary cortisol enzyme immunoassay kit (Salimetrics LLC), human chromogranin A EIA kit (Yanaihara Ins. Inc., Fujinomiya, Shizuoka, Japan), oxytocin ELIZA kit (Enzo Life Sciences, Inc., Farmingdale, NY, USA), and salivary secretion IgA indirect enzyme immunoassay kit (Salimetrics LLC). α-amylase levels were measured using a saliva amylase monitor (Nipro Corporation).

Measurement of autonomic nervous system function

To assess autonomic nervous system function, HRV power spectra were measured using an acceleration pulse wave meter (Paras Analyzer Plus View TAS 9 VIEW, Tokyo, Japan) in a quiet room. A sensor connected to the analyzer was placed on the left index finger of the participant, and all parameters were measured for 2.5 minutes after resting in a sitting position.

The power value obtained from spectral analysis of heart rate variability, integrated by a frequency band of 0.04~0.15Hz, is called LF, Low-frequency which reflects combined sympathetic and parasympathetic nerve function, while HF, High-frequency integrated by a frequency band of 0.15~0.4 Hz, serves as an index of parasympathetic nerve function.

General autonomic nerve activity was assessed using total power (TP). The LF/HF ratio gauges relative sympathetic nerve activity (Russo *et al.* 2017). We applied natural logarithms of LF (LnLF), natural logarithms of HF (LnHF) and natural logarithms of TP (LnTP) for a more normalized distribution.

Evaluation of the psychological status

The psychological status of the participants was analyzed using a 35-item shortened version of the POMS2®, a psychological rating scale assessing transient and distinct mood states (Heuchert & McNair, 2012: Yokoyama & Watanabe, 2015). The POMS2® shortened version, with seven subscales (positive: anger-hostility [AH], confusion-bewilderment [CB], depression-dejection [DD], fatigue-inertia [FI], and tension-anxiety [TA]; negative: vigor-activity [VA], and friendliness [F]), required participants to rate their mood states over the previous 1-week period on a 5-point scale ("not-at-all" [0] to "extremely" [4]). The sum of the scores was calculated for each subscale. The total mood disorder (TMD) score (excluding subscale F) was calculated as follows: TMD = (AH + CB + DD + FI + TA) – VA.

Measurements of stratum corneum skin moisture content and TEWL

Stratum corneum skin moisture content and TEWL of the facial skin under the eyes were measured using Multi Display Devices® MDD4 (MDD4, Integral Corporation, Tokyo, Japan) with the probe Corneometer CM825 for stratum corneum skin moisture content and the probe Tewameter TM HEX for TEWL, respectively.

Evaluation of the skin conditions

The skin condition survey consisted of 20 items (gloss, firmness, texture, transparency, whiteness, make-up,

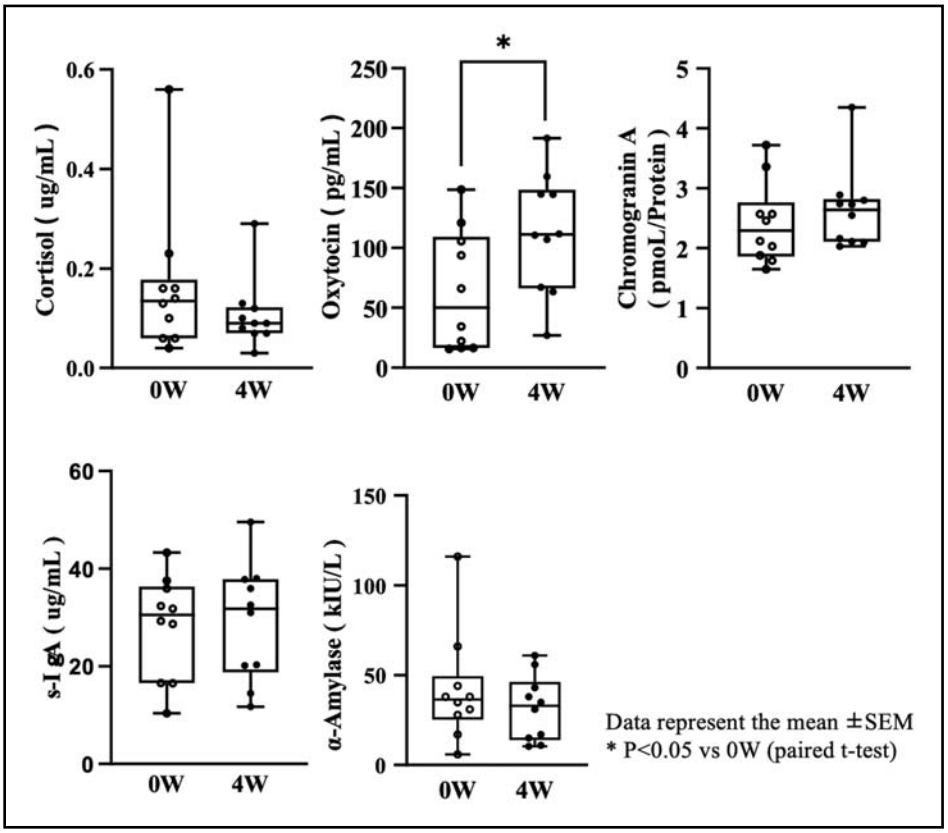

Fig. 2. Changes in salivary stress biomarkers

visible pores, redness, dullness, blotchiness, wrinkles, dryness, swelling, sagging, dark circles, acne, and overall conditions), each of which was rated on a 5-point scale: very good, somewhat good, undecided, somewhat bad, and very bad.

Statistical analysis

All values are represented as the mean ± standard error of the mean. Statistical analyses were performed using a paired t-test. p values (two-tailed) of < 0.05 were considered to indicate statistical significance.

RESULTS

Changes in salivary stress biomarker levels

Figure 2 shows the changes in salivary stress biomarker values before and 4 weeks after tomato juice consumption. Cortisol levels, which tend to increase with the

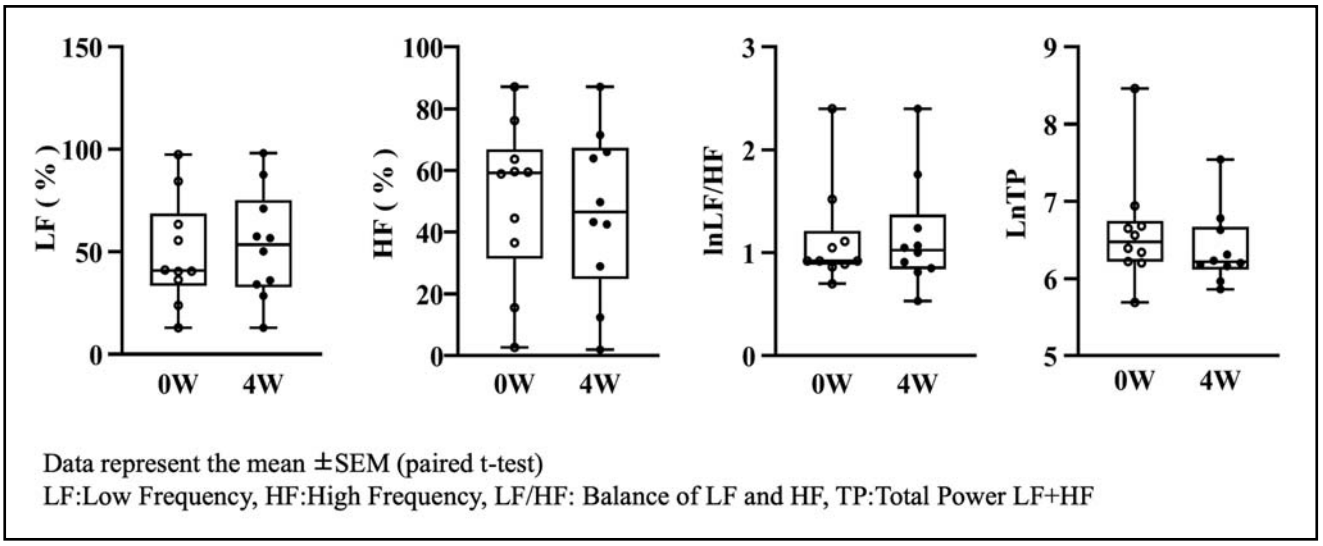

Fig. 3. Changes in the autonomic nervous system

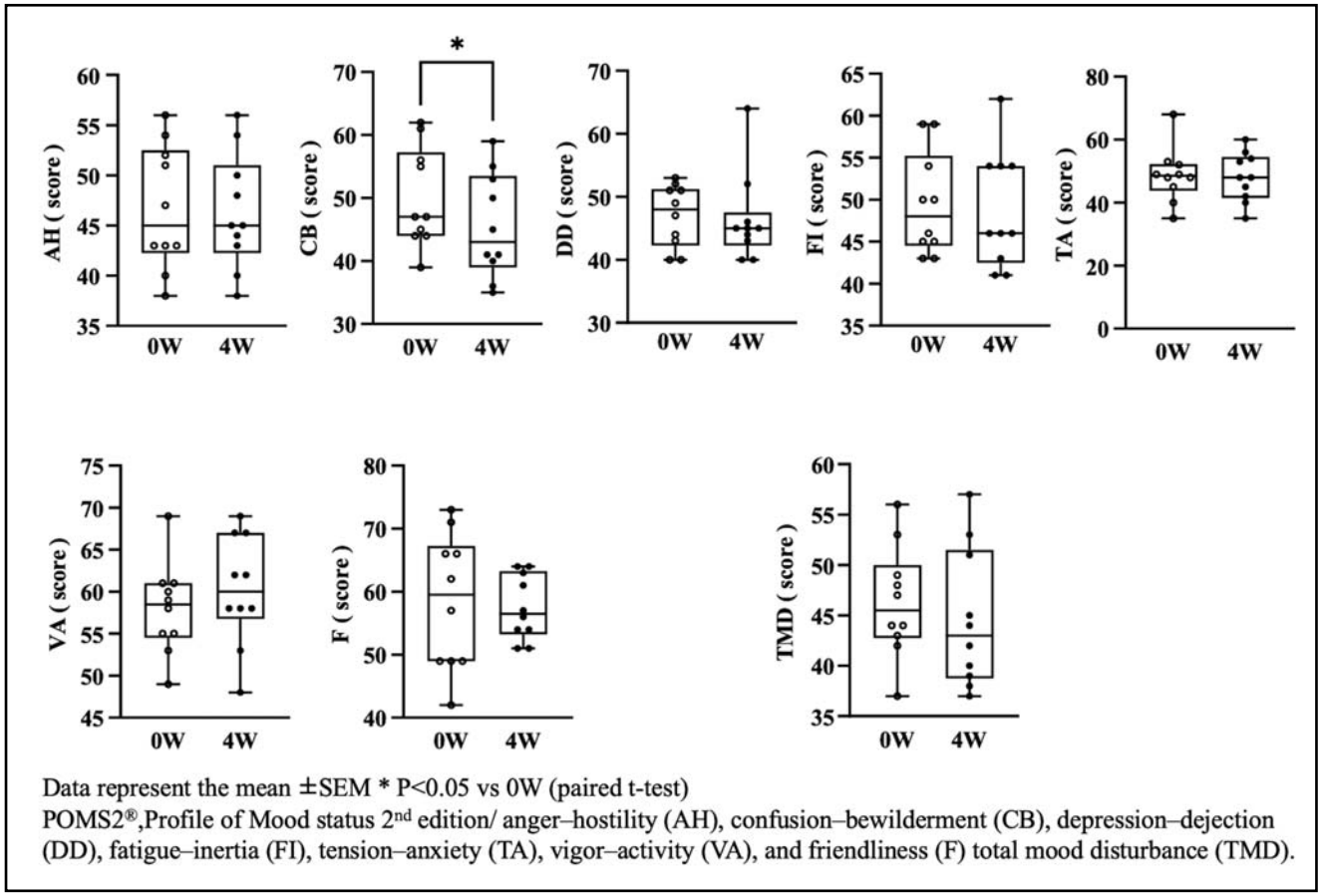

Fig. 4. Changes in psychological status using POMS2®

onset of winter, exhibited a decreasing trend, even though the change was not statistically significant. A significant increase in oxytocin levels was observed ($p = 0.0427$), with no change in s-IgA, chromogranin A, or α-amylase levels.

Changes in autonomic nervous system measurements

Figure 3 shows changes in autonomic nervous system activity values before and 4 weeks after tomato juice consumption. Among the average values, LF (sympathetic) exhibited an increasing trend, HF (parasympathetic) showed a decreasing trend, LF/HF (balance between sympathetic and parasympathetic) demonstrated an increasing trend, and TP, indicating overall autonomic nervous system function displayed a decreasing trend. No significant changes were observed in any of the items.

Changes in psychological status using POMS2®

Figure 4 shows the changes in psychological status as measured by the Mood Profile Test (POMS2®) before and 4 weeks after tomato juice consumption. Scores of negative factors, such as CB, decreased significantly ($p = 0.0207$), whereas DD, FI, and TA scores showed a decreasing trend. The score of the positive factor VA showed an increasing trend, although it was not significant. TMD scores, which represent an overall negative mood state, showed a decreasing trend, although it was not significant.

Changes in stratum corneum skin moisture content and TEWL

Figure 5 shows the changes in stratum corneum skin moisture content and TEWL before and 4 weeks after tomato juice consumption. A significant increase in stratum corneum moisture content was observed ($p = 0.0011$). TEWL showed a decreasing trend, although it was not statistically significant.

Changes in skin condition

Table 2 shows changes in the skin condition survey results before and 4 weeks after tomato juice consumption. Significant changes in terms of gloss ($p = 0.0279$), texture ($p = 0.0318$), transparency ($p = 0.0187$), whiteness ($p = 0.0229$), makeup ($p = 0.0239$), visible pores ($p = 0.0248$), blotchiness ($p = 0.0248$), wrinkles ($p = 0.0239$), dark circles ($p = 0.0445$), and overall skin condition ($p = 0.0107$) were observed.

DISCUSSION

In this preliminary study, we examined the biochemical (stress biomarkers), physical (skin condition), and psychological (autonomic nervous system activity

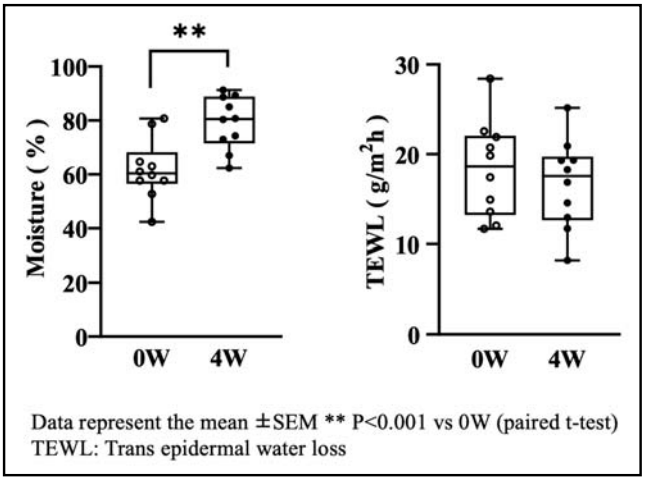

Fig. 5. Changes in stratum corneum skin moisture content and TEWL

and mood) effects of tomato juice consumption on 10 healthy adults.

The sympathetic nervous system dominates under stress and tension, leading to increased heart rate, while relaxation is associated with the dominance of the parasympathetic nervous system and decreased heart rate (Tiwari *et al.* 2021). The LF/HF ratio indicates the balance between sympathetic and parasympathetic nervous system activity, with higher LF/HF values indicating sympathetic dominance and lower values indicating parasympathetic dominance (Russo, 2017), which is a stress indicator. TP, expressed as the sum of LF and HF, serves as an indicator of overall autonomic function.

No significant changes in autonomic nervous system activity values were observed. The occupation and daily routine of the participants in this study were not constant. Thus, their lifestyle on the day before and on the day of participation in the experiment (e.g., sleeping the night before and eating patterns) might have affected the results. LF and HF values vary greatly depending on individual differences and measurement conditions (e.g., room temperature, humidity), and thus, it might be difficult to determine the autonomic nervous system function with only these indices.

However, salivary oxytocin levels increased significantly after 4 weeks of tomato juice consumption. Oxytocin was traditionally thought to affect only smooth muscle function in women in terms of reproductive physiology. Nonetheless, recent findings indicate that it not only functions as a neurotransmitter by projecting nerves to a wide range of brain regions but also promotes labor during childbirth, maternal behavior, and trust (Rilling &Young, 2014); improves communication disorders (Meyer-Lindenberg *et al.* 2011); regulates appetite (Maejima *et al.* 2009) and energy expenditure (Kerem et Lawson 2021); It is also called the "happy hormone" and the "strongest brain component." Furthermore, a recent study has reported that oxytocin has anti-aging and dementia-preventive effects (Takahashi *et al.* 2022). The increase in salivary oxytocin levels with tomato juice intake observed in

Tab. 2. Changes of result of skin conditions survey

Subject	0W	4W	*p* Value
Gloss	3.5±0.27	2.9±0.23*	0.0279
Firmness	2.9±0.35	2.7±0.26	0.4433
Texture	3.6±0.34	2.5±0.22*	0.0318
Transparency	3.8±0.33	2.9±0.23*	0.0187
Whiteness	3.7±0.33	2.7±0.30*	0.0229
Makeup	3.2±0.25	2.6±0.16*	0.0239
Visible pores	3.4±0.27	2.7±0.26*	0.0248
Redness	2.7±0.30	2.1±0.31	0.051
Dullness	3.4±0.31	2.9±0.23	0.0522
Blotchiness	3.6±0.27	2.9±0.23*	0.0248
Wrinkles	3.1±0.31	2.5±0.23*	0.0239
Dryness	3.6±0.31	3.2±0.33	0.1039
Swelling	2.7±0.33	2.5±0.22	0.5911
Sagging	2.9±0.41	2.8±0.29	NS
Dark circles	3.4±0.37	2.7±0.30*	0.0445
Acne	2.2±0.44	2.5±0.40	NS
Overall conditions	3.2±0.20	2.4±0.16*	0.0107

Data represent the mean ± SEM. * $p < 0.05$ vs 0W (Paired t-test)

the present study suggests that tomato juice intake may effectively foster a sense of well-being.

In addition, oxytocin secretion has been reported to suppress the secretion of ACTH (adrenocorticotropic hormone), a stress-related hormone (Uvnas-Moberg, 1998). The present results of a significant increase in oxytocin levels and a decrease in cortisol levels, a typical indicator of the hypothalamic-pituitary-adrenal axis stress biomarker after tomato juice consumption, seem to support this report.

A significant increase in moisture content in the stratum corneum was observed after 4 weeks of tomato juice consumption. A previous study has reported that oxytocin decreases cortisol action and reduces skin cell aging (Sasaoka, 2020). Thus, the survey results on physiological skin conditions and subjective symptoms after tomato juice consumption in this study suggest that the improvement was achieved via oxytocin and cortisol levels.

Several reports have been published on the antioxidant benefits of tomato juice. A previous study reported that 100 mL of tomato juice daily for 3 weeks, after extensive physical exercise, reduced elevated levels of oxidative stress-induced reactive oxygen species (ROS) and decreased the production of 8-oxo-dG (Jacob *et al.* 2008), while another study reported that tomato juice rich in natural lycopene and fortified with vitamin C reduced multiple biomarkers of oxidative stress and inflammation (Ali & Siamak, 2020).

Tomato juice consumption may thus have contributed to the improvement in skin conditions of the participants in this study because of its powerful antioxidant effect by scavenging ROS.

Thus, we conducted essential experiments on the biochemical, physical, and psychological effects of tomato juice on its intake. The main findings of this very limited preliminary study included a decrease in cortisol in saliva, a biological stress indicator, and an increase in oxytocin, which suppresses the stress response, as well as an increase in stratum corneum skin moisture content, an effect of oxytocin on skin conditions.

Limitations of this preliminary study and future tasks: this study has the following limitations regarding the experimental setup and execution. This was a preliminary, single-arm study with only ten participants. Therefore, a large sample size with a control group that does not consume tomato juice under the same living conditions is needed to validate our results. The possibility of not reproducing the same results cannot be denied with a different batch of tomato juice even if it is also labeled as 100% pure. The possibility of statistical problem overfitting cannot be denied, since we conducted a broad range of experiments on a limited number of participants. Additional studies are required to measure oxidative stress and antioxidant levels to evaluate the effects of tomato juice consumption on oxidative stress reduction.

In conclusion, the results of this preliminary study suggest that consuming tomato juice may offer stress relief, enhance well-being, and improve skin conditions and mood states in healthy adults. Tomato juice, a food that can be easily consumed regularly, may thus prove useful for stress management of modern life in the Coronavirus era.

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