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Development and evaluation of a rapid skin taurine measurement device using skin blotting for the early detection of dehydration

Haruka Tsuchiya[1] | **Mari Abe**[1] | **Sanai Tomida**[1] | **Shiho Higashimura**[2] | **Daijiro Haba**[1,3] | **Takeo Minematsu**[4] | **Hiromi Sanada**[4] | **Gojiro Nakagami**[1,3]

[1]Department of Gerontological Nursing/Wound Care Management, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, Japan

[2]Shonan University of Medical Sciences, Yokohama City, Kanagawa, Japan

[3]Global Nursing Research Center, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, Japan

[4]Ishikawa Prefectural Nursing University, Kahoku City, Ishikawa, Japan

Correspondence
Gojiro Nakagami, Department of Gerontological Nursing/Wound Care Management, Graduate School of Medicine, The University of Tokyo, 7-3-1. Hongo, Bunkyo-ku, Tokyo, Japan.
Email: gojiron@g.ecc.u-tokyo.ac.jp

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Abstract

Aim: Skin blotting is a noninvasive method to collect molecules like skin taurine, a dehydration indicator, by applying a membrane to the skin. However, quantifying skin taurine takes an hour due to the long process of staining and measurement. This study aimed to determine optimal staining conditions and assess the reliability and validity of spraying and light transmittance as new methods for skin blotting. Image analysis was used to evaluate the impact of these methods.

Methods: This study consisted of two parts. Study 1 focused on determining taurine staining conditions on the anion exchange membrane. Ethanol concentration for dissolving ninhydrin and spray time were optimized using a standard sample. Light transmittance and image analysis were used to quantify taurine. The relationship between taurine concentration and light transmittance or brightness (from image analysis) was evaluated. Study 2 confirmed the reliability and validity of the new methods using human samples. Reliability was assessed using the intraclass correlation coefficient (ICC), and validity was determined by correlation coefficients between taurine levels quantified by the conventional method with those quantified by light transmittance or image analysis.

Results: The optimal spray time and ethanol concentration were 0.5 s and 90%, respectively, reducing measurement time to 7 min (light transmittance) and 10 min (image analysis). The ICC was 0.48 for light transmittance and 0.81 for image analysis. The correlation coefficients were $r = 0.530$ for light transmittance and $r = 0.609$ for image analysis.

Conclusions: Image analysis, which measures a wider area, showed better reliability and validity in quantifying skin taurine.

KEYWORDS

dehydration, image analysis, noninvasive, older adult, point-of-care testing

1 | INTRODUCTION

Dehydration is defined as a loss of body water (Thomas et al., 2008). Older adults are at a risk of dehydration. Aging-related factors include body water decline, urine concentrating ability (Phillips et al., 1984), cognitive function (Paulis et al., 2018), thirst sensation (Mack et al., 1994; Phillips et al., 1984), medical conditions such as dysphagia (Leibovitz et al., 2007), and intake of diuretics and laxatives (Buaprasert et al., 2021; Lavizzo-Mourey et al., 1988; Wojszel, 2020). The prevalence of dehydration in older adults was reported at 20.0%–38.3%, depending on the population (Buaprasert et al., 2021; Higashimura et al., 2022; Hooper, Bunn, Abdelhamid, et al., 2016; Hooper, Bunn, Downing, et al., 2016; Marra et al., 2016). Dehydration in older adults leads to cognitive decline (Mantantzis et al., 2020), a decrease in daily living activities (Nagae et al., 2023), and frailty (Yoo et al., 2018), which can remarkably decrease their quality of life. Moreover, dehydration increases hospital stay and the mortality rate (Edmonds et al., 2021; El-Sharkawy et al., 2020; Pash et al., 2014). Post-admission dehydration increased the economic burden in the United States (Pash et al., 2014). These negative impacts are caused by the lack of adequate testing methods, leading to delayed detection. Therefore, the method for early detection should be established.

Detection of dehydration is difficult, even for health professionals, as most older adults with dehydration are asymptomatic (Higashimura et al., 2022). Serum osmolality >300 mOsm/L by blood sampling is used as the gold standard for diagnosing dehydration (Thomas et al., 2008). However, blood drawing is painful, and nurses often experience difficulty in blood collection among older adults with dehydration due to a decreased circulating blood volume. Additionally, results from blood sampling do not rapidly occur. As blood sampling is not appropriate for point-of-care testing for early detection and intervention, a noninvasive and rapid method to detect dehydration is required.

Current available noninvasive methods to detect dehydration include urine test, saliva test, physical assessment, and ultrasound examination (Fortes et al., 2015; Hooper, Bunn, Abdelhamid, et al., 2016; Hooper, Bunn, Downing, et al., 2016; Nagae et al., 2020; Oliver et al., 2008; Yoshihara et al., 2007). Urine tests and physical assessments can be performed quickly; however, the area under the receiver operating characteristic curve (AUC) was 0.42–0.61 for urine tests and 0.43–0.53 for physical assessments, which indicates a lack of accurate dehydration detection (Fortes et al., 2015; Hooper, Bunn, Abdelhamid, et al., 2016; Hooper, Bunn, Downing, et al., 2016). Saliva tests can be performed quickly as well, and their AUC was 0.56–0.76 (Fortes et al., 2015). However, collecting saliva samples is difficult for dehydrated older adults because of the decreased volume of saliva. Additionally, saliva is affected by food and fluid intake time (Ely et al., 2011). Ultrasound examinations use the inferior vena cava diameter as an indicator; however, the inferior vena cava diameter of older adults cannot be correlated with serum osmolality (Nagae et al., 2020).

Our group developed skin blotting to address these challenges. Skin blotting is a method to collect molecules from inside the skin by applying a skin blotting unit made of several types of membrane such as nitrocellulose, polyvinylidene difluoride, nylon, or anion exchange membrane. The anion exchange membrane can collect taurine, which is a negatively charged molecule. Taurine is an amino acid located in the epidermis of the skin (Lobo et al., 2001) and is a major osmolyte that can be an indicator of dehydration (Bedford & Leader, 1993; Nakanishi et al., 1992). Taurine can be quantified after staining the anion exchange membrane with ninhydrin solution (Higashimura, 2020). The correlation with serum osmolality was 0.57, and the sensitivity, specificity, and AUC of the skin blotting method were 77.3%, 81.8%, and 0.789, respectively (Higashimura, 2020), indicating the potential for accurate detection of dehydration. However, skin blotting is difficult to use in clinical practice because the measurement time is over 1 h, as skin blotting requires several processes in an experimental room. To stain the anion exchange membrane, the membrane must be immersed in 2% ninhydrin solution for 20 min and dried for 40 min. The dried anion exchange membrane is set to a 96-well plate filled with distilled water to measure absorbance using a spectrophotometer at 450 nm. These processes are too time-consuming, and the staining and measuring procedures are too complex to use for point-of-care testing.

Our group developed prototype devices for staining and measuring procedures. The staining method was changed to a spray method using an airbrush unit, and the measurement was changed to the handheld spectrometer to measure light transmittance. The airbrush unit can automatically spray in an ordered time. After the sample holder is moved from the airbrush unit to the handheld spectrometer, light transmittance can be measured instantly. This new method can rapidly and easily stain and measure taurine on an anion exchange membrane. However, the conditions for taurine staining and the reliability and validity of the new method were not revealed. Taken together, this study aimed to determine the staining conditions and verify the reliability and validity of the new method to quantify skin taurine concentration. Moreover, to confirm whether the staining and measuring method could affect reliability and

validity, skin taurine on the stained membrane was also quantified by image analysis.

2 | METHODS

2.1 | Study overview

This study consisted of two studies (Table 1).

Study 1: To determine the conditions for taurine staining on anion exchange membranes.

Study 2: To confirm the reliability of the new method and the concurrent validity between the conventional method and the new method to measure skin taurine by skin blotting.

2.2 | Skin blotting methods

The anion exchange membrane (Tokuyama Corporation, Tokyo, Japan) was cut into 10 mm squares, and the nitrocellulose membrane (Bio-Rad Laboratories, Inc., Hercules, CA) was cut into 7 mm squares. The two membranes were applied as skin blotting units (Figure 1) using a surgical tape (Nitto Denko Corporation, Osaka, Japan).

The skin blotting procedure was as follows: (1) The center of the styloid process of the radius and olecranon as the midpoint on the volar forearm was marked to standardize the application position of the skin blotting unit. The volar forearm was selected because it is the most accessible site for measurement in clinical practice. Moreover, the volar side is less susceptible to sun exposure, making it less likely to be affected by ultraviolet radiation. Furthermore, a previous study used the volar forearm for measurement (Higashimura, 2020). (2) The skin surface was wiped with a paper towel prewet by distilled water to remove any proteins that could affect the staining result. (3) Distilled water was applied on the anion exchange membrane and the nitrocellulose membrane. (4) The skin blotting unit was applied for 20 min. (5) A band was wrapped on the skin blotting unit to prevent it from coming off. (6) The skin blotting unit was removed and kept at 4°C until stained and measured.

2.3 | Prototype devices

A sample holder (Saraya Co., Ltd., Osaka, Japan) was used to set an anion exchange membrane. Also, the sample holder could be set to the airbrush unit and the handheld spectrometer for staining and measuring taurine on an anion exchange membrane. This has a 7-mm through-hole

TABLE 1 Staining and measuring method of each study.

Study		Study 1	Study 2	
Objective		To determine the conditions for taurine staining and measuring	To confirm reliability	To confirm concurrent validity
Staining method	Immersion method			✓
	Spray method	✓	✓	✓
Measuring method	Absorbance			✓
	Light transmittance	✓	✓	✓
	Image analysis	✓	✓	✓

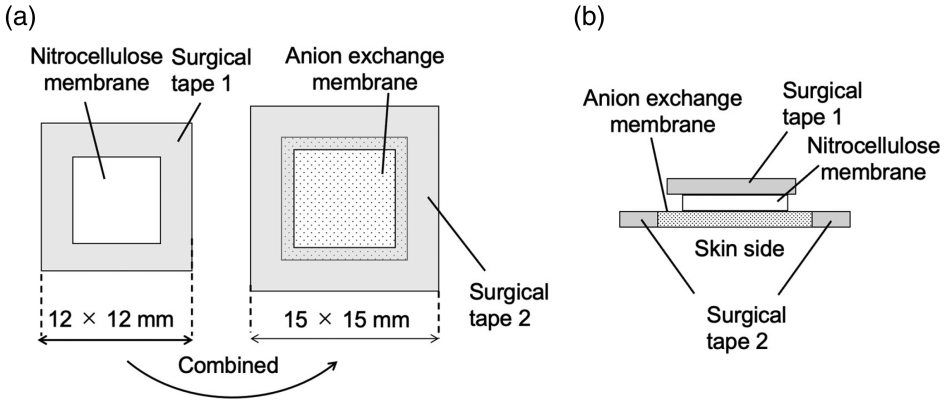

FIGURE 1 Skin blotting unit. (a): Plane view (b): Cross-sectional view.

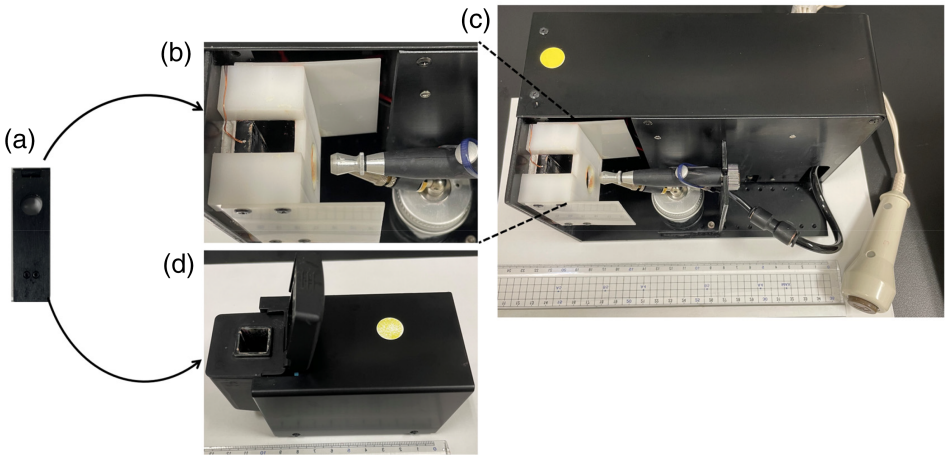

FIGURE 2 Prototype devices. (a): Sample holder. (b): Enlarged image of the airbrush unit. (c): Airbrush unit. (d): Handheld spectrometer. When the skin blotting sample (a) was placed into the airbrush unit (b), staining and drying were performed. Afterward, the light transmittance was measured when the skin blotting sample (a) was set to the handheld spectrometer (d).

for staining and light transmittance measurements. An airbrush unit of 110 × 190 × 130 mm in size (Saraya Co., Ltd.) was used for the spray method to stain and dry the anion exchange membrane. This airbrush could automatically spray ninhydrin solution onto an anion exchange membrane in an ordered time (second). The sample holder was set at a temperature of 40°C to facilitate the drying of the anion exchange membrane after staining with ninhydrin solution. A handheld spectrometer of 120 × 55 × 60 mm in size (Saraya Co., Ltd.) was used to measure light transmittance from 380 to 780 nm (Figure 2).

2.4 | Calibration curve for taurine quantification

To prepare the anion exchange membrane with standard taurine, a 10-mm square anion exchange membrane and a 20-mm square filter paper were prepared. Taurine solution was prepared with taurine (Nacalai Tesque, Inc., Kyoto, Japan) in distilled water. The filter paper was soaked in the standard taurine solution. After 2 min, the filter paper with taurine solution was placed on the anion exchange membrane for 10 min to infiltrate taurine in the anion exchange membrane. The filter paper was then removed, and the anion exchange membrane was attached to surgical tape with 8-mm square holes. A calibration curve was drawn from the scatter plot using the least-squares method between standard taurine concentration and light transmittance or brightness by image analysis.

2.5 | Measuring and analysis methods

2.5.1 | Measurement by the conventional method (Higashimura, 2020)

(1) The anion exchange membrane that was removed from the skin was cut to a 5.5 mm circle. (2) The anion exchange membrane was then immersed in a 2% ninhydrin solution (Nacalai Tesque, Inc.) diluted with 100% ethanol for 20 min. In the ninhydrin colorimetric method, amino acids undergo hydrolysis and deamination. The primary amines form a purple-colored complex, whereas the secondary amines produce a yellow color. In this case, the anion exchange membrane with taurine exhibited yellow coloration, indicating the presence of secondary amines. (3) The anion exchange membrane was then dried for 40 min. (4) The anion exchange membrane was set in a 96-well plate. (5) Each well was mixed with 0.1 mL of distilled water. (6) An O-ring (MORISEI KAKO Co., Ltd., Tokyo, Japan) was set to prevent the floating of the anion exchange membrane. (7) Absorbance was measured using a spectrophotometer (SpectraMax iD3, Molecular Devices, LLC. San Jose, CA) at 450 nm.

If the concentration of taurine is high, the absorbance will be high. The conventional method takes 1 h to measure the taurine concentration.

2.5.2 | Measurement by the new method

The new method used the spray method and light transmittance. The procedures to measure the skin taurine by the new method were as follows: (1) The anion exchange membrane was attached with a surgical tape that was removed from the skin to the sample holder. (2) The sample holder was set in the airbrush unit and the button was pushed to spray 2% ninhydrin solution. (3) The solution was set to dry for 1 min. (4) Steps 2 and 3 were repeated five times. (5) An additional 1 min was set for drying. (6) The sample holder was moved from the airbrush unit to the handheld spectrometer to measure light transmittance at 460 nm.

A high concentration of taurine is associated with low light transmittance.

2.5.3 | Image analysis

After all the anion exchange membranes were stained and measured by the new method, they were attached to the white paper and scanned. Scanned images were calculated using an image analysis software (ImageJ version 1.53, National Institutes of Health, Bethesda, MD). Image analysis was conducted as follows: (1) The scanned images were imported to the software. (2) Imported images were split into three channels, and then the B channel was selected for analysis based on the measurement wavelength of the conventional and new method. (3) The B channel images were inverted to gray scale. (4) The brightness of a circle 7 mm in diameter at the center of the anion exchange membrane was measured.

If the concentration of taurine was high, the brightness will be high.

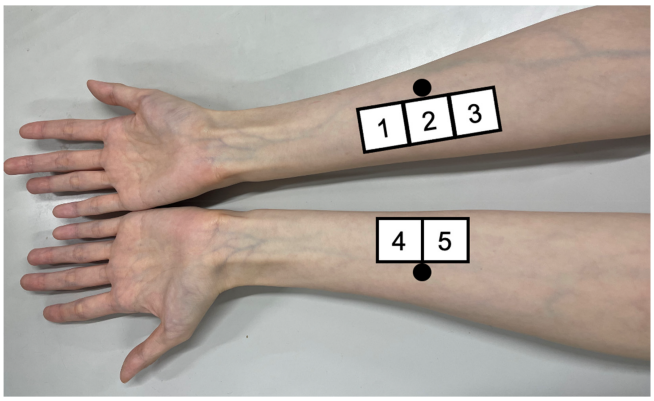

FIGURE 3 Candidate sites for skin blotting unit. Black point shows the marking point: the center of the styloid process of the radius and olecranon. The sites No.1–3 were used for reliability tests in study 2. The sites No. 4 and 5 were used for validity tests in study 2.

2.6 | Study 1

To determine the conditions of staining of taurine on the anion exchange membrane, the ethanol concentration for dissolving ninhydrin and spraying time were considered. Ninhydrin was diluted in 70%, 80%, 90%, or 100% ethanol. Spraying times of 0.5 s or 1 s were considered. In total, eight conditions were considered. The 6400, 3200, 1600, 800, 400, and 200 μM taurine anion exchange membranes with a surgical tape were used. Three samples at each taurine concentration were prepared for each condition. After staining with the airbrush unit and measuring with the handheld spectrometer, the correlation between taurine concentration and light transmittance at 460 nm was calculated for each condition. Pretests have shown that the concentration of skin taurine ranges from 400 to 800 μM. Therefore, the conditions that could measure this range and had the strongest correlation were determined. Also, taurine on the anion exchange membrane stained by the determined condition was quantified by image analysis.

2.7 | Study 2

Study 2 was a cross-sectional study. The inclusion criterion was healthy volunteers who were older than 20 years and the exclusion criterion was participants with forearm injuries. The participant characteristics such as age, sex, and body mass index (BMI) were collected.

For reliability evaluation, skin blotting was performed on adjacent three sites of the forearm. All taurine on the anion exchange membranes was stained by the spray method and measured by light transmittance and image analysis (Figure 3).

For validity evaluation, skin blotting was performed on two adjacent sites of the forearm. One anion exchange membrane was stained by the spray method and measured by light transmittance and image analysis; the other anion exchange membrane was stained and measured by the conventional method (Figure 3).

The left and right arms to which evaluation was conducted, and the position of application were randomized using randomly generated numbers produced by a random function in spreadsheet software (Excel, Microsoft Corporation, Redmond, WA).

Standardized skin taurine was quantified by substituting the absorbance, light transmittance, or brightness into the formula of the calibration curve (400–3200 μM).

To standardize the measurement methods in the conventional method, transmittance method, and image analysis, the same researcher performed the membrane application, staining of obtained samples, and taurine concentration measurements. Moreover, the staining procedure and measurements were conducted in the same laboratory throughout the study.

2.8 | Statistical analysis

Study 1: Pearson's correlation coefficient was used to investigate the relationship between taurine concentration and light transmittance or brightness.

Calibration curve was made by log-transformed taurine concentration.

Study 2: Descriptive statistics were used for participant characteristics. Intraclass correlation coefficients

(1, 1) with 95% confidence intervals (CI) were used to confirm the reliability of the new method. Pearson's correlation coefficient and Bland–Altman analysis were used to reveal the concurrent validity of the new method.

All data were analyzed by the Stata BE17 (Stata Corp, College Station, TX) or the R software system, version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $p < 0.05$.

2.9 | Ethical consideration

All participants were recruited by snowball sampling, given an explanation about the survey, and informed consent was obtained from each participant. Informed consent was obtained in writing from all participants after providing a thorough explanation of the study's purpose, procedures, risks, and benefits. The participants were also informed that the study would be conducted anonymously and that they could withdraw their consent at any time. To ensure their safety, the participant's skin condition was checked before and after skin blotting to prevent any redness or irritation. The participants were also informed that the anion exchange membrane could be removed immediately upon their request if any discomfort occurred during the application. Study 2 was approved by the Research Ethics Committee of the Faculty of Medicine of the University of Tokyo, which was in accordance with the Declaration of Helsinki (No. 2022112NI).

3 | RESULTS

3.1 | Study 1

Among various conditions, the combination of spraying time of 0.5 s and 90% ethanol concentration had a wide measurement range from 400 to 6400 μM taurine concentration with the strongest correlation (Table 2). The higher the taurine concentration, the darker the anion exchange membrane was stained (Figure 4). Pearson's correlation coefficient was −0.982, $p < 0.001$ measured by light transmittance and 0.978, $p < 0.001$ by image analysis (Figure 5). The new method using light transmittance for measurement took less than 7 min to perform, whereas that using image analysis for measurement took less than 10 min to perform.

3.2 | Study 2

Thirty participants were recruited; the median age of the participants was 28.5 years, 22 participants (73.3%) were female, and the median BMI was 20.5 kg/m^2. The BMI, sex, and age of participants did not have a significant impact on the study results. None of the participants experienced redness or itching as a result of anion exchange membrane application.

The intraclass correlation coefficients (1, 1) were 0.48 (95% CI 0.27–0.68) measured by light transmittance, and 0.81 (95% CI 0.69–0.90) by image analysis.

Pearson's correlation coefficient of the standardized skin taurine between the conventional method and spray method with light transmittance measurement was 0.530, $p = 0.003$ (Figure 6a). Pearson's correlation coefficient of the standardized skin taurine between the conventional method and spray method with image analysis was 0.609, $p < 0.001$ (Figure 6b). The bias of Bland–Altman analysis in the conventional method compared to the spray method with light transmittance measurement was 84.2, and the 95% limits of agreement (LOA) were −1102–1270. The bias in the conventional method compared to the spray method with image analysis was −60.9, and 95% LOA, −1235–1113 (Figure 7).

TABLE 2 Conditions of staining of taurine with 2% ninhydrin.

Conditions		Results		
Spraying time (second)	**Ethanol concentration (%)**	**Measuring range of taurine (μM)**	***r***	***p***
0.5	100	400–6400	−0.879	<0.001
0.5	90	400–6400	−0.982	<0.001
0.5	80	1600–6400	−0.975	<0.001
0.5	70	400–6400	−0.947	<0.001
1	100	800–6400	−0.920	<0.001
1	90	800–6400	−0.932	<0.001
1	80	400–6400	−0.976	<0.001
1	70	800–6400	−0.899	<0.001

Note: *r*: Pearson's correlation coefficient.

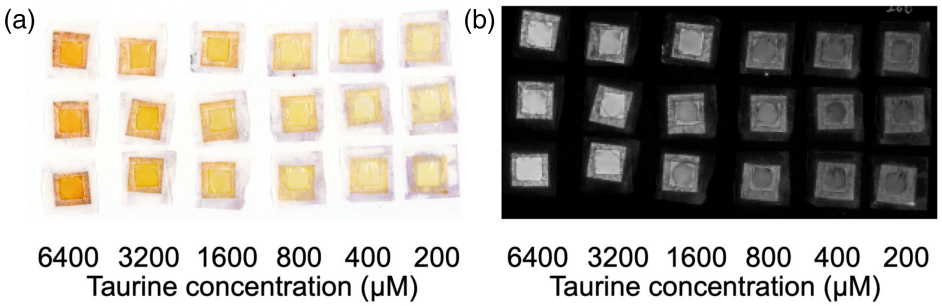

FIGURE 4 The anion exchange membranes after staining with 2% ninhydrin solution. (a): Original scanned images. (b): Inverted B channel images to gray scale.

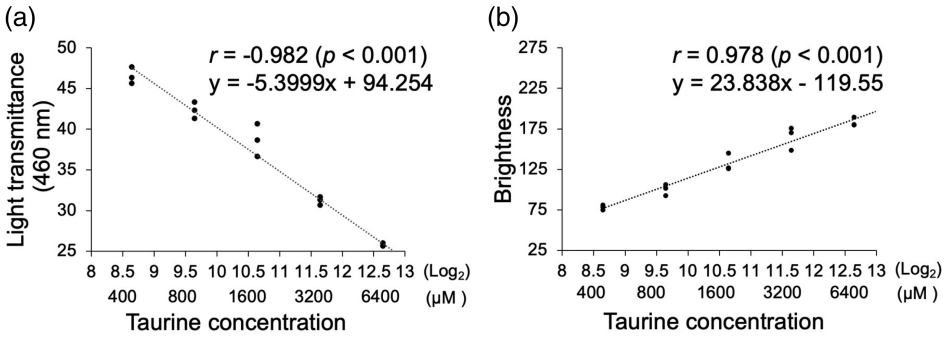

FIGURE 5 Calibration curves for taurine concentration. (a): Taurine concentration and light transmittance. (b): Taurine concentration and brightness. Pearson's correlation coefficient.

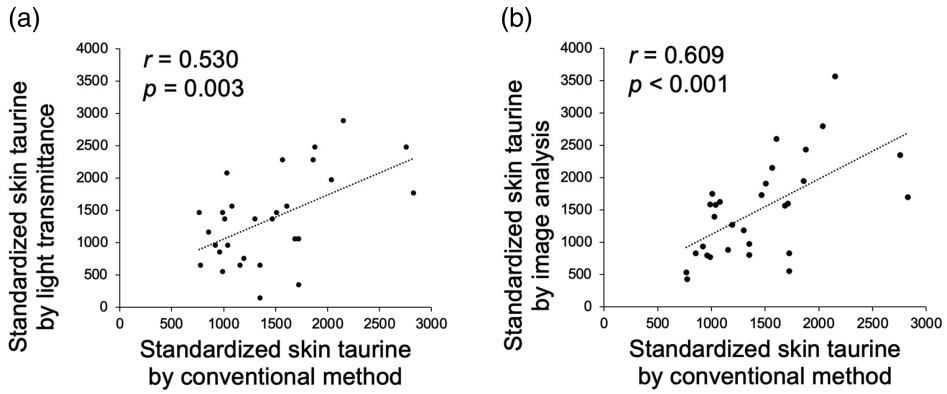

FIGURE 6 Correlation with standardized skin taurine by conventional method and light transmittance or image analysis. (a): Standardized skin taurine by conventional method and light transmittance. (b): Standardized skin taurine by conventional method and image analysis. *r*: Pearson's correlation coefficient.

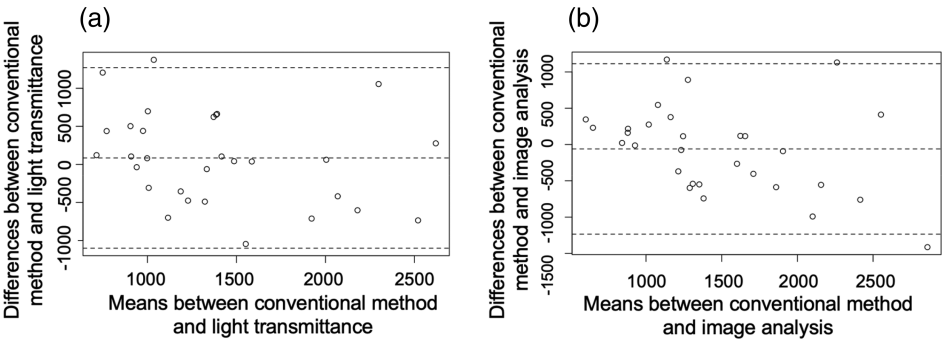

FIGURE 7 Bland–Altman analysis of standardized skin taurine by conventional method and light transmittance or image analysis. (a): Measured by light transmittance. (b): Measured by image analysis. The upper and lower dashed horizontal lines indicate 95% limits of agreement (LOA) and the middle of the dashed line indicates mean difference (bias).

4 | DISCUSSION

This study proposed a new method to measure skin taurine collected by skin blotting for point-of-care dehydration testing. The new method revealed the best condition for taurine staining on the anion exchange membrane. Furthermore, the reliability and concurrent validity of the new method were confirmed, and the relationship between the conventional method and standardized skin taurine was verified. Compared to the conventional method, the new method enabled the measurement of skin taurine concentration in a shorter time and showed

the potential for point-of-care testing of skin taurine. The best condition for taurine staining on the anion exchange membrane was determined in study 1. Other conditions, such as spray distance and ninhydrin concentration, were considered in preliminary experiments before study 1. Spray distance farther than 1 cm and spraying time longer than 1 s resulted in the diffusion of the ninhydrin solution into the surrounding area, and the measurement area was not properly stained. High ninhydrin concentration produced difficulty due to clogging in the nozzle of the airbrush unit and environmental pollution to the surroundings. The shortest drying time was 1 min. Repeatedly spraying and drying five times, an additional 1 min was needed to measure light transmittance dependent on taurine concentration. Therefore, these conditions were fixed (spraying distance, spraying time, ninhydrin concentration, drying time, and the number of repetitions), and the conditions of ethanol concentration and spraying time were examined. In study 1, the strongest correlation between taurine concentration and light transmittance was the condition in which 2% ninhydrin was dissolved in 90% ethanol, sprayed for 0.5 s, and repeated five times. The contact time of ninhydrin adhering to the anion exchange membrane was longer for the 90% ethanol concentration than the 100% ethanol. This is attributed to the volatile nature of the ethanol. In the case of 80% and 70% ethanol, the ninhydrin solution remained in the central part of the anion exchange membrane due to their lower volatility than the 90% ethanol solution; thus, the membranes stained by the condition of 80% and 70% ethanol solution did not dry sufficiently (Gurrala et al., 2019). The imperfect dry status of the ninhydrin solution may have led to a weaker correlation than that in the 90% ethanol solution. If the spraying time is 1 s, the solution spreads over the anion exchange membrane, and the solution is not applied evenly to the center, the measurement area, possibly resulting in uneven staining.

Furthermore, 400–800 μM standardized skin taurine can be measured by the determined condition, which is skin taurine in healthy participants. These results indicate the possibility of using a new method to measure skin taurine concentration. The same strong correlation was observed between 400 and 6400 μM as measured by light transmittance and image analysis.

In study 2, the result of the reliability evaluation revealed that measuring a wide area by image analysis can be better for measuring skin taurine in humans. Intraclass correlation coefficients measured by light transmittance were lower than those measured by image analysis. The difference in intraclass correlation coefficients may be attributed to the uneven taurine adhesion in samples collected from human skin compared to prepared samples. The skin blotting method could collect taurine through tight junctions (Minematsu et al., 2014). Therefore, individual skin status may affect the uniformity of taurine collection by skin blotting (Dąbrowska et al., 2018). The handheld spectrometer emitted a single beam and measured only one central point of the anion exchange membrane, while image analysis used a wider area for measurement. Measurement at only one point using the handheld spectrometer resulted in a large variation in the measured values from human samples. It is expected that measuring a wide area using image analysis will obtain more reliable skin taurine values as an indicator of dehydration. Furthermore, the light transmittance method requires a device that can generate light and measure transmittance. However, if the measurement is conducted through image analysis over a 7-mm area, a device that can read image brightness would suffice. This simplification of the functionality would bring us closer to the goal of enabling a more straightforward detection of dehydration.

From the result of the validity evaluation, the correlation was moderate between the conventional method and light transmittance or image analysis. The ranges of taurine concentration may have been narrow due to the recruitment of solely healthy volunteers. This may have resulted in a weak correlation and narrow range of LOA of Bland–Altman analysis. Validity could be more appropriately examined if the study were conducted on a population with a wider range of taurine.

This study had some limitations. In study 2, hospitalized older adults could not be recruited because of the coronavirus 2019 pandemic. The study participants were young and were at lower risk for dehydration. Therefore, the validity of the new method could not be properly examined. Dehydrated individuals may have taurine concentrations greater than 400–800 μM.

In the future, it is necessary to increase the sample size and include a wider range of participants, such as older adults and people with dehydration. Skin blotting is a noninvasive method that has already been used in older individuals with fragile skin (Koyano et al., 2018), and it is a simple procedure, as the automated staining process and the required time to obtain the taurine value is less than 7 (by light transmittance)–10 (image analysis) min. Also, the result of the reliability evaluation revealed that measuring by image analysis can be better than measuring by light transmittance for measuring skin taurine in humans. Therefore, the test can be performed at any time and location if the post-staining images are captured and evaluated with a mobile camera, such as a smartphone equipped with an application. Currently, all procedures, including the preparation of ninhydrin using ethanol, were performed in the laboratory, making it difficult to develop a portable device with the current method.

However, if ampules containing the adjusted ninhydrin solution can be made, then a portable device can be developed. For example, visiting nurses bring the devices to the older adults' homes and detect dehydration at once. Therefore, visiting nurses can intervene at the older adults' homes and prevent the adverse effect of dehydration. A device has already been developed that uses smartphones to analyze images for point-of-care testing (Schary et al., 2022). Thus, skin taurine collection, rapid staining, and image analysis will lead to point-of-care testing in the future.

In conclusion, in this study, the best conditions for taurine staining on the anion exchange membrane were considered, and 90% ethanol for the dilution of ninhydrin and 0.5 s of spraying time were revealed to be the optimal conditions. Moreover, this study revealed the reliability and validity of the new method, with image analysis exhibiting better results than measurement by light transmittance. The taurine measurement method using image analysis enables a wide range of taurine concentrations to be measured, and the high intraclass correlation coefficient suggests that it could serve as a potential method for the early detection of dehydration.

AUTHOR CONTRIBUTIONS

Haruka Tsuchiya: Protocol, Experiment, Data collection, Data analysis, Manuscript writing. Mari Abe: Protocol, Data collection, Data analysis, Manuscript writing. Sanai Tomida: Protocol, Experiment. Shiho Higashimura: Project development, Protocol, Data analysis. Daijiro Haba: Project development, Protocol. Takeo Minematsu: Project development, Protocol, Data analysis. Hiromi Sanada: Project development, Project Management. Gojiro Nakagami: Project development, Protocol, Data collection, Data analysis, Manuscript writing, Project Management.

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CONFLICT OF INTEREST STATEMENT

All authors declare no conflicts of interest related to this study.

ORCID

Haruka Tsuchiya https://orcid.org/0009-0009-6647-6267
Mari Abe https://orcid.org/0000-0003-0903-3637
Daijiro Haba https://orcid.org/0000-0001-8820-0952
Takeo Minematsu https://orcid.org/0000-0001-5859-7290
Hiromi Sanada https://orcid.org/0000-0003-1912-1251
Gojiro Nakagami https://orcid.org/0000-0002-9650-2464

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