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REVIEW

Criterion-Related Validity of Spectroscopy-Based Skin Carotenoid Measurements as a Proxy for Fruit and Vegetable Intake: A Systematic Review

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ABSTRACT

Carotenoids are a category of health-promoting phytonutrients that are found in a variety of fruits and vegetables and have been used as a biomarker to approximate dietary fruit and vegetable (F/V) intake. Carotenoids are consumed, metabolized, and deposited in blood, skin, and other tissues. Emerging evidence suggests spectroscopy-based skin carotenoid measurement is a noninvasive method to approximate F/V intake. Spectroscopy-based skin carotenoid measurement overcomes bias and error inherent in self-reported dietary recall methods, and the challenges in obtaining, storing, and processing invasive blood samples. The objective of this systematic review was to examine criterion-related validity of spectroscopy-based skin carotenoid measurement as a proxy for F/V intake. The 3 methods examined were resonance Raman spectroscopy (RRS), pressure-mediated reflection spectroscopy (RS), and spectrophotometers. A comprehensive literature search of PubMed, Excerpta Medica Database (Embase), Cumulative Index of Nursing and Allied Health Literature (CINAHL), ProQuest, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials (CENTRAL) was performed in December 2018, yielding 7931 citations. Studies that examined associations between spectroscopy, blood carotenoids, and/or dietary intake were identified and reviewed independently by ≥2 reviewers to determine eligibility for inclusion. Twenty-nine articles met the inclusion criteria and all 29 studies found significant correlations or associations between spectroscopy-based skin carotenoids and plasma or serum carotenoids and/or dietary F/V intake. A majority of the studies evaluated carotenoid concentration in adults; however, 4 studies were conducted in infants and 6 studies evaluated children. Twenty studies specified the racial/ethnic groups from which the samples were drawn, with 6 including ≥20% of the sample from a minority, nonwhite population. The findings of this systematic review support the use of spectroscopy for estimating F/V intake in diverse human populations, although additional validation is needed, particularly among racially/ethnically diverse populations and populations of varying ages. *Adv Nutr* 2020;11:1282–1299.

Keywords: carotenoids, spectroscopy, skin reflectance, fruit and vegetable intake, biomarkers, dietary assessment, resonance Raman spectroscopy, pressure-mediated reflection spectroscopy, spectrophotometers

Introduction

Adequate fruit and vegetable (F/V) intake is associated with positive health outcomes and reduced risk of developing chronic diseases (1). Fruits and vegetables contain a variety of health-promoting bioactive components, such as phytochemicals, vitamins, and minerals (2). Carotenoids are a class of compounds in fruits, vegetables, grains, nuts, legumes, and some animal products that have demonstrated protective properties against macular degeneration, cardiovascular disease, sarcopenia, skin damage from ultraviolet radiation (UV) exposure, and protection against oxidative damage (3, 4).

With >700 identified carotenoids, the most prevalent and highly researched that correlate with F/V intake are α-carotene, β-carotene, lycopene, lutein, zeaxanthin, and β-cryptoxanthin (5). Carotenoids are found in a variety of yellow, red, pink, orange, and green pigmented plant products and some animal products, such as eggs and pink- or red-fleshed seafood (5). Carotenoids are exogenous compounds that must be acquired through dietary sources and cannot be synthesized de novo. Thus, due to the array of foods that contain high amounts of carotenoids, circulating blood carotenoids are considered the gold standard biomarker of F/V intake (6, 7).

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For research, evaluation, and surveillance purposes, F/V intake is objectively assessed using carotenoids measured in serum or plasma samples, or estimated subjectively using dietary recall methods. Serum is derived from coagulated whole blood, and plasma from anticoagulated blood. Both media can be extracted and analyzed for carotenoid concentrations using HPLC or LC-MS (8–11). Although blood biomarkers are a relatively accurate measure and considered the standard for assessing F/V intake, the process of collecting blood samples is mildly invasive and might not reflect long-term dietary intake due to the short half-lives of circulating carotenoids (12, 13). Thus, plasma or serum carotenoids reflect recent dietary intake and are detectable in the blood for ∼2 wk after intake (14, 15).

In addition to serum and plasma carotenoids, F/V intake is also measured using subjective dietary recall methods or dietary observations (16). Commonly used methods include observer-recorded food records, 24-h dietary recall, dietary record, or FFQs. However, all of these dietary recall methods are prone to time burden, subjective biases, and intervention-related biases that can result in inaccurate representation of true dietary intake (17, 18). Because the existing methods for recalling dietary intake contain error and bias, such measures can negatively impact the validity of quantifying F/V intake, demonstrating the need for an objective indicator of dietary intake (19).

Spectroscopy has emerged as a noninvasive, objective approach to measuring dietary intake of fruits and vegetables (20). Spectroscopy measures the absorption and emission of light waves at a specific wavelength to identify the type and density of molecular compounds in the skin (14). Carotenoids are easily identifiable bioactive compounds that can be quantified using optical spectroscopy because they are deposited and primarily visible in the stratum corneum of the skin at a UV range of 400–500 nm (21). To account for intraindividual variability, studies using spectroscopy to determine carotenoid status often assess multiple locations on the human body and use duplicate or triplicate measurements (22–30). The index finger, palm, inner arm, and heel are frequently used as sites for spectroscopy-based carotenoid measurement because the thickness of the skin prevents other skin chromophores, like melanin, from obstructing the detection of carotenoid compounds (21). Additionally, the index finger, palm, inner arm, and heel locations do not experience excessive sun exposure, a major factor in altering the molecular structure of carotenoids, which decreases the amount of identifiable carotenoid molecules (4).

There are various spectroscopy technologies used to identify and quantify carotenoids in the skin, including resonance Raman spectroscopy (RRS), pressure-mediated reflection spectroscopy (RS), and spectrophotometers. RS uses a broadband light source (460–500 nm) to measure the density of skin carotenoids with minimal interference from other compounds (14). Subsequently, the carotenoids are superimposed on a reflection-based absorption spectrum for reference (14). Supradermal pressure is added during the measurement to temporarily limit blood flow to the assessment location to reduce the presence of confounding molecules, specifically oxygenated or deoxygenated hemoglobin (which can interfere with carotenoid absorption), thus minimizing the misidentification of carotenoid compounds (14). RRS utilizes light photons to manipulate the conjugated bonds of the carotenoid molecules to generate excitatory Raman signals (31, 32). The excitatory signals initiate vibrational state changes that alter the bond strength of carotenoids, resulting in a distinct signal on the Raman spectra (31). RRS detects combined concentrations of skin carotenoids with efficiency and precision; however, this method requires expensive instrumentation and analysis software (14). RS and RRS detect the major blood concentrations of carotenoids, but do not detect colorless carotenoids, such as phytoene and phytofluene, due to differences in spectral regions (33). Spectrophotometers are measurement devices that evaluate and analyze the color of dermatological pigments' yellowness and redness, which reflect skin carotenoid concentration (34). Spectrophotometers measure the intensity of light transmitted through a solvent and identify carotenoid compounds due to the absorption or reflection in a specific wavelength within the color spectrum (∼350–500 nm) (34, 35). These advancements in technology have resulted in noninvasive, convenient, and efficient methods of measuring carotenoid status as a proxy for F/V intake (21).

The development and validation of a noninvasive, objective measurement to assess F/V intake has the potential to change the standard for collecting accurate dietary intake data. The aim of this systematic review was to examine criterion-related validity of 3 methods of spectroscopy as a proxy for F/V intake by evaluating studies that examined associations between skin carotenoid status measured via spectroscopy and *1*) serum or plasma carotenoid concentration, or *2*) self-reported dietary intake, or *3*) both serum or plasma carotenoid concentration and self-reported dietary intake.

Methods

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for improved reporting of systematic reviews, the protocol for this systematic review was prospectively registered with PROSPERO (registration number 114,605) (36).

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The contents of this publication do not necessarily reflect the views or policies of the USDA or the Agricultural Research Service, nor does mention of trade names, commercial products, or organizations imply endorsement from the US government.
Supplemental Table 1 is available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances.
Address correspondence to RES (e-mail: rescherr@ucdavis.edu).
Abbreviations used: ASA, Automated Self-Administered Dietary Assessment Tool; F/V, fruit and vegetable; RRS, resonance Raman spectroscopy; RS, pressure-mediated reflection spectroscopy.

TABLE 1 Search terms and predefined exclusion criteria applied to article selection process

Search terms	Exclusion criteria
Spectroscopy Primary search terms: spectroscopy, spectrum analysis, Veggie Meter®, skin reflectance Expanded search terms: BioPhotonic scanner, carotenoid sensor(s), optical assessment, optical detection, Raman microscopy, reflectance spectrophotometer, spectroscopic method(s), spectrophotometry Carotenoids Primary search terms: carotenoids, α-carotene, β-carotene Expanded search terms: astacene, β-cryptoxanthin, canthaxanthin, fucoxanthin, lutein, lycopene, zeaxanthin	1. No direct correlation or validation against dietary intake or serum or plasma carotenoids 2. Any dietary intervention using non–whole food supplementation (including fruit or vegetable extracts)—due to differences in dose–response and unrealistic carotenoid concentrations not found in normal dietary amounts 3. Not a peer-reviewed publication, abstract only, review article, or dissertation 4. Nonhuman subjects (including in vitro studies using human cell lines) 5. Nonvalidated methods of recording dietary intake 6. Review articles

Literature search strategy

To identify relevant studies, literature searches of PubMed, Excerpta Medica Database (Embase), Cumulative Index of Nursing and Allied Health Literature (CINAHL), ProQuest Search, Cochrane Database of Systematic Reviews (CDSR), and Cochrane Central Register of Controlled Trials (CENTRAL) were performed in December 2018 to identify studies addressing criterion-related validity of spectroscopy for assessing carotenoid concentrations of human skin as a measure of dietary F/V intake. Primary search terms for spectroscopy included spectrum analysis, Veggie Meter®, and skin reflectance. Primary search terms for carotenoids included carotenoids, α-carotene, and β-carotene. Additional carotenoids, such as lutein and lycopene, were added to expand the search (**Table 1**). Attempts to include human skin and diet as search concepts consistently led to inadequate retrieval of studies, so these concepts were not included in the final search strategies. Exact search terms and the PubMed search strategy are available in **Supplemental Table 1**. All articles identified through literature searching were loaded into Endnote 9.1 (Clarivate Analytics), which was used to identify and remove publications prior to 1990, newspaper articles, and duplicate citations. Remaining items were then loaded into Rayyan (Qatar Computing Research Institute) for the initial review of eligibility criteria (37).

Three authors independently screened titles and abstracts, with disagreements resolved by additional authors. The article abstracts were reviewed using strict inclusion criteria. If the abstract did not report a correlation or validation between spectroscopy and dietary intake and/or serum or plasma carotenoids, the abstract was excluded prior to the full-text review phase. Full-text review was then independently performed by 2 authors to verify eligibility based on study protocol and inclusion criteria. A third author was consulted and assisted with conflict resolution. References from the included articles were hand-searched by 2 authors to ensure no relevant articles were missed in the initial database searches. Seven additional manuscripts eligible for inclusion were identified during this process (22, 29, 30, 38–41).

Inclusion and exclusion criteria

Peer-reviewed publications assessing criterion-related validity of spectroscopy using human skin against dietary intake and/or plasma or serum carotenoids were the focus of this review. Animal models and in vitro studies were excluded. Studies using whole fruits and vegetables with naturally occurring carotenoids were included. Studies using supplementation were excluded due to unrealistic concentrations of carotenoids, which would not be present in whole fruits and vegetables, and limited data regarding the metabolism and bioavailability of dietary supplements and extracts. It should be acknowledged that multiple studies that used high-dose supplementation strategies compared spectroscopy-based skin carotenoid measurements with serum or plasma carotenoids and/or dietary intake at baseline prior to supplementation (42–46). However, due to our previously defined criteria regarding the exclusion of supplementation studies, these studies were not included in the full analysis. Additionally, studies comparing spectroscopy with dermal biopsies were excluded from this review. Although dermal biopsies can confirm the accuracy of spectroscopic measurements, such biopsies would not corroborate a relation between fruit or vegetable intake, and therefore would not support the objective of this review. There were no exclusion criteria for study design, statistical methods/tools, or population characteristics. Explicit eligibility criteria are displayed in Table 1.

Data extraction

Data extraction was performed independently by 2 authors. A third author reviewed the information and compiled the 2 extraction data sets into a single entry to ensure a comprehensive analysis. The following information was extracted: sample characteristics [mean age, race/ethnicity, sex, and BMI (kg/m^2) if provided by the author], study design, type of spectroscopy used, intervention details when

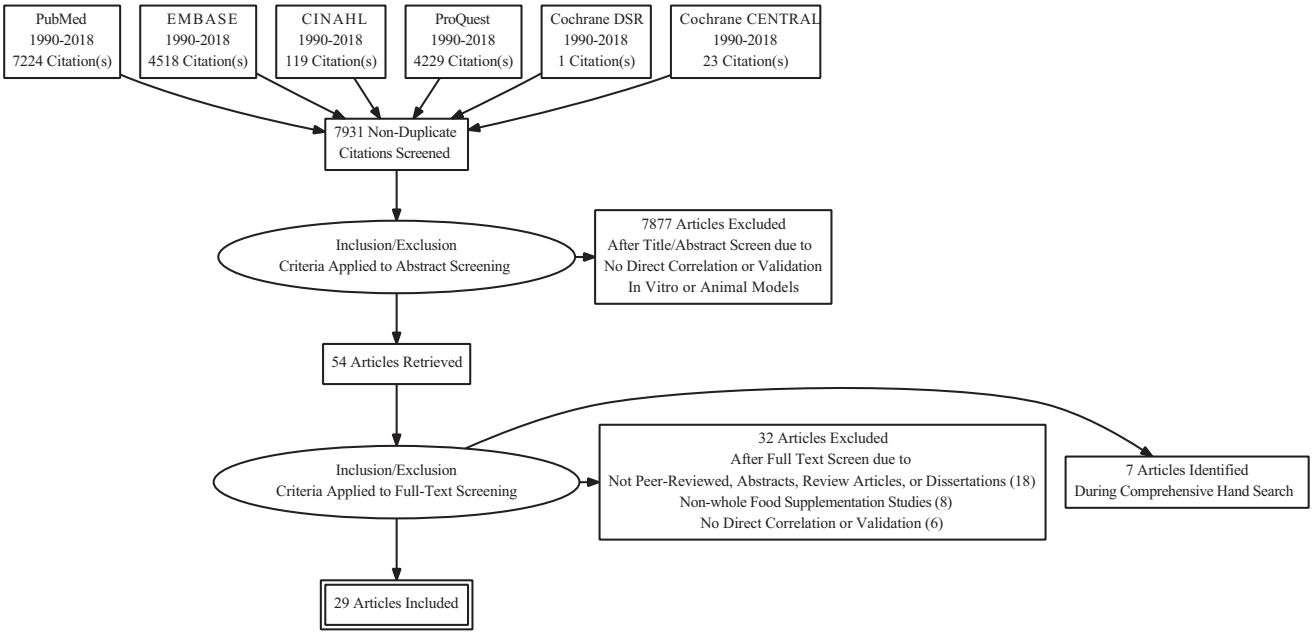

FIGURE 1 PRISMA flow diagram of detailed search strategy and article selection process.

applicable, statistical interpretation of the correlation or validation of spectroscopy against blood and/or dietary intake, and primary findings.

Risk of bias and quality evaluation

Quality of the studies was assessed independently by 2 authors using a modified and combined version of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (47) and the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (48). Authors graded the publications based on the quality assessment and risk of bias criteria. If the 2 reviewing authors did not agree on overall quality of the publication, discrepancies were mediated by a third author independently reviewing the discrepancy without prior knowledge of the conflicting ratings. Obvious study limitations such as small sample sizes, population homogeneity, study design, and lack of control group were considered; however, studies were graded holistically.

For the purposes of this article, the data were considered as reported by the author in each study. The correlation strength was also interpreted according to how the authors analyzed the data within the individual articles. However, if the articles did not verbally describe the strength of the correlation coefficients, the following interpretations were used: very strong (0.90–1.0), strong (0.70–0.89), moderate (0.50–0.69), low (0.30–0.49), weak (0.20–0.29), or negligible ($\leq$ 0.19) (49).

Results

Overview of search results

The comprehensive literature search resulted in 16,134 potentially relevant articles based on the initial database literature search. Removal of duplicate articles, publications prior to 1990, and non–peer reviewed publications resulted in 7931 articles. The initial title and abstract screening for eligibility criteria resulted in 54 articles selected for the full-text review. Following the completion of full-text review and hand-search reference screening, 29 studies satisfied the inclusion criteria and were included in the present review. The comprehensive article selection process is depicted in **Figure 1**.

Characteristics of included studies

The included articles varied in study design and comprised cross-sectional studies ($n = 21$), prospective cohort studies ($n = 5$), a randomized crossover trial ($n = 1$), a single-arm experimental trial ($n = 1$), and a randomized controlled trial ($n = 1$). The quality of the studies was classified as very good ($n = 5$), good ($n = 20$), fair ($n = 4$), and poor ($n = 0$).

A majority of the studies involved adult participants; however, 4 studies examined infants (38, 41, 50, 51), and 6 studies evaluated carotenoid status in children (52–57). The number of participants included in the studies ranged from 29 (15, 58) to 497 (59). The race/ethnicity of the participants was variable amongst the studies. Six studies included racially and ethnically diverse populations (53–57, 59), 13 studies focused on predominantly Caucasian subjects (15, 22, 24–30, 38, 60–62), 2 studies only had participants from Thailand (52, 58), and 8 studies did not report the race or ethnicity of the participants (23, 39–41, 50, 51, 63, 64).

Type of spectroscopy used

Three methods of skin carotenoid detection were used in the included articles: RRS, RS, and spectrophotometers. A majority of the studies ($n = 20$) used RRS to measure skin

carotenoids, a technology developed by Werner Gellermann et al. (31, 65). Seven studies used the NuSkin BioPhotonic Scanner (Pharmanex), and 13 studies used unspecified custom-built RRS devices. Seven of the studies used spectrophotometers to measure skin carotenoids; 4 studies (23, 25, 27, 28) used the CM700D spectrophotometer (Konica Minolta), 2 studies (29, 30) used the CM2600D spectrophotometer (Konica Minolta), and 1 study (24) used the Spectro-Guide 450 Gloss 6801 spectrophotometer (BYK-Gardner). Two of the studies used RS to measure skin carotenoids using the Veggie Meter device developed by Igor V Ermakov and Werner Gellermann (59, 62). Information about the types of spectroscopy devices is presented in **Table 2**.

Results of included studies

The included studies can be differentiated by the method of comparison against spectroscopy technique. The efficacy of spectroscopy as an objective biomarker for dietary intake was compared against serum or plasma carotenoid concentrations, self-reported dietary intake data, or both serum or plasma carotenoid concentrations and dietary intake data.

Spectroscopy and plasma or serum carotenoids.

Of the included studies, $n = 11$ articles compared spectroscopy with plasma ($n = 3$) or serum ($n = 8$) carotenoid concentration using HPLC (**Table 3**). Multiple studies correlated spectroscopy to the combined total carotenoids in the blood (39–41, 50, 51, 64) and other studies analyzed both total blood carotenoids in conjunction with individual carotenoid analysis, such as α-carotene, β-carotene, lycopene, lutein, β-cryptoxanthin, and zeaxanthin and correlated spectroscopy data with each specific carotenoid compound (15, 28, 61–63). A majority of the studies analyzing serum or plasma carotenoids used RRS with the exception of 2 studies, 1 study using RS (62) and another using the CM700D spectrophotometer (28).

The correlation coefficients between blood carotenoids and spectroscopy ranged from strong positive correlations to weak positive correlations. Of the studies evaluating blood carotenoids, most studies reported combined total carotenoid concentration when compared with spectroscopy-based skin carotenoids, unless specified. Two of the studies (62, 64) using blood carotenoids as the comparison variable reported very strong correlation coefficients ($r = 0.81$; $P < 0.001$), and 4 of the studies found strong correlation coefficients [$r = 0.78$; $P < 0.001$ (40); $r = 0.72$; $P < 0.001$ (15); $r = 0.72$; $P < 0.01$ (61)] and a linear regression correlation ($R^2 = 0.75$) (51). Three of the studies found moderate correlations for mothers ($r = 0.63$; $P < 0.001$) and a low correlation with infants ($r = 0.39$; $P = 0.02$) (41); $r = 0.47$; $P = 0.001$ (39); $r = 0.44$; $P = 0.01$ (50). In 1 study that specifically examined lycopene, a moderate correlation was observed at pre ($r = 0.450$, $P < 0.0001$) and post ($r = 0.56$; $P < 0.0001$) (63). Only 1 study (28) reported a relatively weak correlation ($r = 0.27$; $P < 0.05$) when comparing the CD700M spectrophotometer with plasma carotenoids. There

TABLE 2 Brief overview of spectroscopy-based skin carotenoid devices[1]

Spectroscopy method	Type of spectroscopy device used	Number of validation studies meeting the eligibility criteria of review	Number of validation studies with multiple racial/ethnic groups included	Number of validation studies with infants and/or children	Number of validation studies using plasma or serum carotenoids	Number of validation studies using dietary intake	Number of validation studies using both plasma or serum carotenoids and dietary intake
Resonance Raman spectroscopy (RRS)	NuSkin BioPhotonic Scanner® (Pharmanex)	7 (52, 55, 56, 58, 60, 63, 64)	2 (55, 56)	3 (52, 55, 56)	2 (63, 64)	3 (52, 55, 58)	2 (56, 60)
	Custom-built scanner	13 (15, 22, 26, 38–41, 50, 51, 53, 54, 57, 61)	4 (38, 54, 57, 61)	6 (38, 41, 51, 53, 54, 57)	7 (15, 39–41, 50, 51, 61)	3 (22, 54, 57)	3 (26, 38, 53)
Pressure-mediated reflection spectroscopy (RS)	Veggie Meter® (Longevity Link Corporation)	2 (59, 62)	1 (59)	0	1 (62)	0	1 (59)
Spectrophotometer	CM700D (Konica Minolta)	4 (23, 25, 27, 28)	0	0	1 (28)	3 (23, 25, 27)	0
	Spectro-Guide 450 Gloss 6801 (BYK-Gardner)	1 (24)	0	0	0	1 (24)	0
	CM2600D (Konica Minolta)	2 (29, 30)	0	0	0	2 (29, 30)	0

[1] Reference citation numbers in parentheses.

TABLE 3 Summary of studies evaluating the relation between spectroscopy-based skin carotenoid measurements and serum or plasma carotenoids in diverse populations ($n = 11$)[1]

Reference	Study design	Population characteristics (*n*, sex, age)	BMI and race/ethnicity	Type of spectroscopy	Criterion measure	Statistical test	Correlation outcomes	Quality assessment
Bernstein et al. (2012) (39)	Cross-sectional	$n = 53$ 24 M, 29 F 77.4 ± 7.7 y	N/A	RRS—custom-built scanner	Serum; HPLC	Pearson correlations	SCS and total serum carotenoids: $r = 0.47$; $P = 0.001$ SCS and (lutein + zeaxanthin): $r = 0.18$; $P = 0.226$	Good
Chan et al. (2013) (50)	Prospective cohort	$n = 40$ Age range: <33 wk gestation	Birth weight 500–1500 g	RRS—custom-built scanner	Serum; HPLC	Pearson correlations	SCS and total serum carotenoids: $r = 0.44$; $P = 0.01$	Good
Conrady et al. (2017) (61)	Cross-sectional	$n = 88$ 39 M, 49 F 59 ± 17 y	Caucasian ($n = 74$), African ($n = 1$), Asian ($n = 1$), Hispanic ($n = 1$), multinational ($n = 1$), not recorded ($n = 10$)	RRS—custom-built scanner	Serum; HPLC	Linear regression (exact method not stated)	SCS and total serum carotenoids: $r = 0.722$; $P < 0.01$ SCS and serum lutein: $r = 0.655$; $P < 0.01$ SCS and serum zeaxanthin: $r = 0.656$; $P < 0.01$	Good
Ermakov et al. (2013) (51)	Cross-sectional	$n = 32$ Age range: 1 d to 6 y	N/A	RRS—custom-built scanner	Serum; HPLC	Linear fit with correlation coefficient	$R = 0.75$ No P value listed in article	Good
Ermakov et al. (2018) (62)	Cross-sectional	$n = 54$ 24 M, 30 F 54 ± 19 y	Caucasian ($n = 53$), African American ($n = 1$)	RS—Veggie Meter® (Longevity Link Corporation)	Serum; HPLC	Linear regression	SCS and total serum carotenoids: $r = 0.81$; $P < 0.001$	Good
Gellermann et al. (2005) (40)	Cross-sectional	$n = 104$	N/A	RRS—custom-built scanner	Serum; HPLC	Pearson correlations	SCS and total serum carotenoids: $r = 0.78$; $P < 0.001$	Good
Henriksen et al. (2013) (41)	Cross-sectional	$n = 30$ Age range: Newborn (48–72 h)	N/A	RRS—custom-built scanner	Serum; HPLC	Pearson correlations	SCS and infant total serum carotenoids: $r = 0.39$; $P = 0.02$ SCS and maternal total serum carotenoids: $r = 0.63$; $P < 0.001$	Good
Jahns et al. (2014) (15)	Single-arm experimental	$n = 29$ 9 M, 20 F 32.1 ± 2.5 y	BMI = 23.6 ± 0.6 Caucasian ($n = 28$), other ($n = 1$)	RRS—custom-built scanner	Plasma; HPLC	Pearson correlations	SCS and total plasma carotenoids: $r = 0.72$; $P < 0.001$	Good

(*Continued*)

TABLE 3 (*Continued*)

Reference	Study design	Population characteristics (*n*, sex, age)	BMI and race/ethnicity	Type of spectroscopy	Criterion measure	Statistical test	Correlation outcomes	Quality assessment
Perrone et al. (2016) (63)	Prospective cohort	*n* = 71 All F Age range: 38–70 y	BMI = 24.5 ± 3.0	RRS—NuSkin BioPhotonic Scanner® (Pharmanex)	Plasma; HPLC	Pearson correlations	SCS and plasma lycopene: pre ($r = 0.450$; $P < 0.0001$) and post ($r = 0.559$; $P < 0.0001$) 5-y dietary intervention period	Good
Pezdirc et al. (2016) (28)	Randomized crossover trial	*n* = 30 All F 22.0 ± 4.2 y	BMI = 23.4 ± 9.7 Caucasian (*n* = 25), Asian (*n* = 4), other (*n* = 1)	CM700D spectrophotometer (Konica Minolta)	Plasma; HPLC	Spearman correlations	SCS and total plasma carotenoids: $r = 0.27$; $P < 0.05$ SCS and plasma α-carotene: $r = 0.29$; $P < 0.05$ SCS and plasma β-carotene: $r = 0.35$; $P < 0.001$	Very good
Zidichouski et al. (2009) (64)	Cross-sectional	*n* = 372 199 M, 173 F 33.4 ± 10.0 y	N/A	RRS—NuSkin BioPhotonic Scanner® (Pharmanex)	Serum; HPLC	Pearson correlations	SCS and total serum carotenoids: $r = 0.81$; $P < 0.001$)	Very good

[1]BMI measured in kg/m^2. N/A, not available; RRS, resonance Raman spectroscopy; RS, reflection spectroscopy; SCS, skin carotenoid score.

were no discernible differences in correlation coefficient strength between plasma and serum samples.

Spectroscopy and dietary intake.

Of the included studies, $n = 12$ articles correlated spectroscopy with dietary intake data using various subjective dietary collection methods (**Table 4**). FFQs were used in $n = 7$ (22, 24, 29, 30, 52, 54, 57), FFQ in conjunction with the Automated Self-Administered Dietary Assessment Tool (ASA-24) was used in $n = 1$ (55), the Australian Eating Score was used in $n = 2$ (25, 27), the Australian Recommended Food Score, and the Fruit and Vegetable Variety Index were used in $n = 1$ (23), and a USDA resource quantifying F/V servings per day was used in $n = 1$ (58). After recording dietary intake data, carotenoid concentration was estimated using the USDA National Nutrient Database for Standard Reference (24, 52, 55, 58, 66), AusFoods and FoodWorks (25, 27), NutritionQuest (54, 57), the Fred Hutchinson Cancer Research Center for quantification (22), the Australian Guide to Healthy Eating and the Australian Dietary Guidelines (23), the Canadian Nutrient File v2007b (29), or simply by the servings of fruit and vegetables (30).

The correlation coefficients between self-reported dietary intake and spectroscopy were lower than for spectroscopy and serum or plasma carotenoid concentrations. The correlations between spectroscopy and dietary F/V intake were analyzed against multiple variables depending on the study design; dietary intake of fruits and vegetables, total dietary carotenoid intake, or individual dietary carotenoids were used to determine a correlation between spectroscopy-based skin carotenoid measurements and dietary intake as displayed in the "Correlation outcomes" column in Table 4. In terms of the strength of association between the studies comparing spectroscopy-based skin carotenoid measurements with dietary intake, the studies differed in statistical methodologies, and therefore might not be directly comparable. Studies using Pearson correlations found weak to moderate correlation coefficients, with total dietary carotenoids having the strongest correlation [$r = 0.599$; $P < 0.001$ (24) and $r = 0.52$; $P = 0.001$ (54)] and weaker associations with individual carotenoids, such as lutein ($r = 0.197$; $P = 0.01$) and lycopene ($r = 0.287$; $P = 0.01$) (52). Studies using Spearman correlations established weak to low correlations ranging from $\rho = 0.224$ ($P = 0.045$) (30) to $\rho = 0.47$ ($P < 0.001$) (29). Additional methods of linear regression models (β coefficient ± SE) were used to determine the relation between spectroscopy-based skin carotenoid measurements and dietary intake (22, 25, 27, 57). The studies comparing spectroscopy with dietary intake used RRS (22, 52, 54, 55, 57, 58) or spectrophotometers (23–25, 27, 29, 30) to measure skin carotenoid status or skin yellowness/redness.

Spectroscopy and both dietary intake and plasma or serum carotenoids.

Of the included studies, $n = 6$ analyzed both dietary intake and plasma or serum carotenoids to assess the criterion-related validity of spectroscopy (**Table 5**). Of the studies

TABLE 4 Summary of studies evaluating the relation between spectroscopy-based skin carotenoid measurements and dietary intake in diverse populations ($n = 12$)[1]

Reference	Study design	Population characteristics (*n*, sex, mean age)	BMI and race/ethnicity	Type of spectroscopy	Criterion measure	Statistical test	Correlation outcomes	Quality assessment
Aguilar et al. (2015) (55)	Randomized controlled trial	$n = 58$, 27 M, 31 F 10.8 ± 3.6 y	BMI percentiles: <5th ($n = 4$), 5th to 85th ($n = 41$), >85th ($n = 13$) Caucasian ($n = 46$), Hispanic ($n = 10$), Asian ($n = 1$), Polynesian ($n = 1$)	RRS—NuSkin BioPhotonic Scanner® (Pharmanex)	3 24-h dietary recalls and FFQ	Multivariate linear regression	SCS and FFQ F/V: $R^2 = 0.22$ ($r = 0.47$); $P < 0.01$ SCS and 24HDR F/V: $R^2 = 0.16$ ($r = 0.40$); $P < 0.01$ SCS and 24HDR total carotenoids: $R^2 = 0.17$ ($r = 0.41$); $P < 0.01$ SCS and 24HDR lycopene: $R^2 = 0.16$ ($r = 0.40$); $P < 0.01$ SCS and 24HDR α-carotene: $R^2 = 0.14$ ($r = 0.37$); $P < 0.05$ SCS and 24HDR β-carotene: $R^2 = 0.14$ ($r = 0.37$); $P < 0.01$ SCS and 24HDR (lutein + zeaxanthin): $R^2 = 0.13$ ($r = 0.36$); $P < 0.01$	Very good
Ashton et al. (2018) (23)	Cross-sectional	$n = 148$ 66 M, 82 F 21.7 ± 2.2 y	BMI = 23.9 ± 4.1	CM700D spectrophotometer (Konica Minolta)	ARFS and FAVVA	Spearman correlations	SCS (yellowness) and ARFS total F/V intake: $\rho = 0.30$; $P < 0.001$ SCS (yellowness) and FAVVA total F/V intake: $\rho = 0.39$; $P < 0.001$	Fair
Beccarelli et al. (2017) (54)	Prospective cohort	$n = 30$ 9 M, 21 F 9.9 ± 0.6 y	BMI percentiles: <5th ($n = 0$), 5th to 85th ($n = 13$), 85th to 95th ($n = 12$), >95th ($n = 5$) Non-Hispanic Black ($n = 3$), Asian/Pacific Islander ($n = 11$), Caucasian ($n = 8$), Hispanic/Latino ($n = 1$), other ($n = 3$), multiethnic ($n = 1$), not reported ($n = 3$)	RRS—custom-built scanner	2004 Block Kids FFQ	Pearson correlations	SCS and total dietary carotenoids: pre ($r = 0.46$; $P = 0.001$), post ($r = 0.52$; $P = 0.001$)	Good

(*Continued*)

TABLE 4 (*Continued*)

Reference	Study design	Population characteristics (*n*, sex, mean age)	BMI and race/ethnicity	Type of spectroscopy	Criterion measure	Statistical test	Correlation outcomes	Quality assessment
Bixley et al. (2018) (24)	Cross-sectional	$n = 30$ All M 21.7 ± 2.6 y	BMI = 23.6 ± 3.4 All Caucasian	Spectro-Guide 450 Gloss 6801 spectrometer (BYK Gardner)	FFQ	Pearson correlations	SCS (yellowness) and carotenoid intake: $r = 0.599$; $P < 0.001$ SCS (yellowness) and F/V intake: $r = 0.422$; $P = 0.02$	Fair
Coyle et al. (2018) (25)	Cross-sectional	$n = 118$ All F Median age: 24.7 y	Median BMI = 23.3 All Caucasian	CM700D spectrophotometer (Konica Minolta)	AES 2010	Linear regression (β-coefficient ± SE)	SCS (yellowness) and F/V intake: $\beta = 0.29 \pm 0.03$; $P = 0.0004$	Fair
Pezdirc et al. (2015) (27)	Cross-sectional	$n = 91$ All F Median age: 22.1 y	Median BMI = 22.9 All Caucasian	CM700D spectrophotometer (Konica Minolta)	AES 2010	Linear regression (β-coefficient ± SE)	SCS (yellowness) and F/V intake: $\beta = 0.80 \pm 0.3$; $P = 0.017$	Very good
Rerksuppaphol and Rerksuppaphol (2006) (58)	Cross-sectional	$n = 29$ 2 M, 27 F 31.9 ± 8.3 y	BMI = 21.2 ± 3.2 All born in Thailand	RRS—NuSkin BioPhotonic Scanner® (Pharmanex)	USDA servings per day	Univariate linear regression	SCS and F/V intake ($P = 0.01$)[2]	Fair
Rerksuppaphol and Rerksuppaphol (2012) (52)	Cross-sectional	Asthma: $n = 73$ 40 M, 33 F 9.2 ± 3.4 y No asthma: $n = 350$ 185 M, 165 F 10.3 ± 3.2 y	Asthma: BMI = 17.9 ± 4.0 No asthma: BMI = 18.0 ± 3.9 All children born in Thailand	RRS—NuSkin BioPhotonic Scanner® (Pharmanex)	FFQ	Pearson correlations	SCS and α-carotene: $r = 0.355$; $P = 0.01$ SCS and β-carotene: $r = 0.347$; $P = 0.01$ SCS and β-cryptoxanthin: $r = 0.418$; $P = 0.01$ SCS and lycopene: $r = 0.287$; $P = 0.01$ SCS and lutein: $r = 0.197$; $P = 0.01$	Good
Scarmo et al. (2012) (57)	Cross-sectional	$n = 381$ 193 M, 188 F 3.80 y	BMI percentiles: <5th ($n = 15$), 5th to 85th ($n = 235$), 85th to 95th ($n = 61$), >95th ($n = 51$) Non-Hispanic white ($n = 22$), non-Hispanic black ($n = 98$), Hispanic/Latino ($n = 228$), biracial ($n = 22$), other ($n = 11$)	RRS—custom-built scanner	FFQ	Univariate linear regression	SCS and F/V intake: $\beta = 0.87$; $P = 0.02$	Good

(*Continued*)

TABLE 4 (*Continued*)

Reference	Study design	Population characteristics (*n*, sex, mean age)	BMI and race/ethnicity	Type of spectroscopy	Criterion measure	Statistical test	Correlation outcomes	Quality assessment
Scarmo et al. (2013) (22)	Prospective cohort	$n = 74$ 28 M, 46 F 36.6 y	BMI percentiles: underweight ($n = 4$), healthy ($n = 45$), overweight ($n = 20$), obese ($n = 5$), White ($n = 62$), nonwhite ($n = 12$)	RRS—custom-built scanner	FFQ	Multivariate linear regression	SCS and intake of total carotenoids at baseline: $\beta = 0.28$; $P < 0.01$; over 6 mo: $\beta = 0.23$; $P < 0.01$	Good
Stephen et al. (2011) (29)	Cross-sectional	$n = 82$ 34 M, 48 F Age range: 18–26 y	All Caucasian	CM2600D spectrophotometer (Konica Minolta)	FFQ	Spearman correlation	SCS (yellowness) and F/V intake: $\rho = 0.45$; $P < 0.001$ SCS (yellowness) and β-carotene: $\rho = 0.47$; $P < 0.001$	Good
Whitehead et al. (2012) (30)	Cross-sectional	$n = 35$ 14 M, 21 F 20.74 y, range: 18–25 y	Caucasian ($n = 34$), East Asian ($n = 1$)	CM2600D spectrophotometer (Konica Minolta)	FFQ	Spearman correlation	SCS (redness) and F/V intake: $\rho = 0.224$; $P = 0.045$ SCS (yellowness) and F/V intake: $\rho = 0.251$; $P = 0.038$	Good

[1] BMI measured in kg/m^2. AES, Australian Eating Survey; ARFS, Australian Recommended Food Score; FAVVA, Fruit and Vegetable Variety Index; F/V, fruit and vegetable; RRS, resonance Raman spectroscopy; SCS, skin carotenoid score; 24HDR, 24-h dietary recall.
[2] Correlation value not listed in the manuscript, only *P* value indicating statistical significance. Author did not respond to inquiry.

TABLE 5 Summary of studies evaluating the relation between spectroscopy-based skin carotenoid measurements and both plasma or serum carotenoids and dietary intake in diverse populations ($n = 6$)[1]

Reference	Study design	Population characteristics (*n*, sex, mean age)	BMI and race/ethnicity	Type of spectroscopy	Criterion measure	Statistical test	Correlation outcomes	Quality assessment
Aguilar et al. (2014) (56)	Cross-sectional	$n = 45$ 20 M, 25 F 10.5 y	BMI percentiles: <5th ($n = 4$), 5th to 85th ($n = 34$), >85th ($n = 7$) Caucasian ($n = 34$), Hispanic ($n = 7$), Asian ($n = 3$), Pacific Islander ($n = 1$)	RRS—NuSkin BioPhotonic Scanner® (Pharmanex)	Dietary intake and serum carotenoids; FFQ and ASA-24 and HPLC	Multivariable linear regression	SCS and FFQ dietary intake: $R^2 = 0.32$ ($r = 0.57$); $P < 0.001$ SCS and 24HDR dietary intake: $R^2 = 0.31$ ($r = 0.56$); $P < 0.001$ SCS and total serum carotenoids: $R^2 = 0.62$ ($r = 0.79$); $P < 0.001$	Good
Bernstein et al. (2013) (38)	Cross-sectional	$n = 51$ 24 M, 27 F Age range: 1 d to 7 y	Caucasian ($n = 43$), Hispanic ($n = 4$), multiracial ($n = 4$)	RRS—custom-built scanner	Dietary intake and serum carotenoids; 3-d food diaries and HPLC	Pearson correlations	SCS and total dietary intake: $r = 0.40$; $P = 0.046$ SCS and dietary (lutein + zeaxanthin): $r = 0.57$; $P = 0.0032$ SCS and total serum carotenoids: $r = 0.78$; $P < 0.0001$ SCS and serum (lutein + zeaxanthin): $r = 0.50$; $P = 0.0015$	Good
Van Rensburg and Wenhold (2016) (60)	Cross-sectional	$n = 81$ 19 M, 62 F M: 40.6 ± 12.2 y; F: 42.8 ± 12.0 y	BMI: M = 25 ± 2.2, F = 23.7 ± 2.7 Caucasian ($n = 78$), Indian ($n = 1$), African ($n = 2$)	RRS—NuSkin BioPhotonic Scanner® (Pharmanex)	Dietary intake and serum carotenoids; F/V intake score and HPLC	Pearson correlations	SCS and dietary intake: season 1: $r = 0.38$, $P = 0.016$; season 2: $r = 0.42$, $P < 0.001$ SCS and total serum carotenoids: $r = 0.72$; $P < 0.001$ SCS and serum β-carotene: $r = 0.78$; $P < 0.001$ SCS and serum lycopene: $r = 0.45$; $P < 0.001$ SCS and serum (lutein + zeaxanthin): $r = 0.50$; $P < 0.001$	Good

(*Continued*)

TABLE 5 (*Continued*)

Reference	Study design	Population characteristics (*n*, sex, mean age)	BMI and race/ethnicity	Type of spectroscopy	Criterion measure	Statistical test	Correlation outcomes	Quality assessment
Jilcott Pitts et al. (2018) (59)	Cross-sectional	Part 2: $n = 30$ 32.9 ± 11.8 y	Part 2: BMI 25.1 ± 2.7 African American ($n = 17$), Caucasian ($n = 13$)	RS—Veggie Meter® (Longevity Link Corporation)	Dietary intake and plasma carotenoids; NCI Fruit and Vegetable Screener and FFQ, and LC-MS	Pearson correlations	Part 2: SCS and dietary intake: $r = 0.69$; $P < 0.0001$ SCS and total plasma carotenoids: $r = 0.71$; $P < 0.0001$	Good
Mayne et al. (2010) (26)	Prospective cohort	$n = 74$ 28 M, 46 F 37 y	BMI percentiles: underweight ($n = 4$), healthy ($n = 45$), overweight ($n = 20$), obese ($n = 5$) White ($n = 62$), nonwhite ($n = 12$)	RRS—custom-built scanner	Dietary intake and plasma carotenoids; FFQ and HPLC	Pearson correlations	SCS and dietary intake: $r = 0.52$; $P < 0.001$ SCS and total plasma carotenoids: $r = 0.62$; $P = 0.006$	Very good
Nguyen et al. (2015) (53)	Cross-sectional	RRS and FFQ: $n = 128$ 51 M, 77 F 11.10 ± 0.6 y Blood, RRS, and FFQ: $n = 38$ 11 M, 27 F 11.2 ± 0.5 y	BMI distribution: RRS and FFQ: under ($n = 0$), normal ($n = 65$), over ($n = 33$), obese ($n = 29$), no data ($n = 1$) Blood, RRS, and FFQ: under ($n = 0$), normal ($n = 19$), over ($n = 9$), obese ($n = 10$)	RRS—custom-built scanner	Dietary intake and plasma carotenoids; 2004 Block Kids FFQ and HPLC	Pearson correlations	SCS and dietary intake: $r = 0.40$; $P < 0.0001$ SCS and total plasma carotenoids: $r = 0.62$; $P < 0.001$	Good

[1] BMI measured in kg/m^2. ASA-24, Automated Self-Administered 24-hour Dietary Assessment Tool; F/V, fruit and vegetable; NCI, National Cancer Institute; RRS, resonance Raman spectroscopy; RS, reflection spectroscopy; SCS, skin carotenoid score; 24HDR, 24-h dietary recall.

analyzing blood carotenoids in conjunction with dietary intake, a majority of the studies used RRS with the exception of 1 study using RS (59). Of the 6 studies evaluating both blood carotenoids and dietary intake, 3 studies analyzed plasma carotenoids (26, 53, 59) and 3 studies evaluated serum carotenoids (38, 56, 60). All of the studies analyzing blood samples along with dietary intake used HPLC to quantify the carotenoids in the blood except for 1 study that used the LC-MS extraction method (59). To record dietary intake, a variety of data collection tools were used, including FFQs (26, 53, 59), FFQ in conjunction with ASA-24 (56), multiple-day food recall diaries (38), and Fruit and Vegetable Intake Scores (60). The nutrient analysis of the dietary intake data was performed using the USDA food database (38, 56), the National Cancer Institute standard algorithm, and the Fred Hutchinson Cancer Research Center for quantification (59), NutritionQuest (53), University of Minnesota Nutrition Coding Center Nutrient Data System (26), or the NIH prescribed algorithm for F/V consumption (60).

The correlation pattern mirrored the corresponding studies that evaluated either blood carotenoids or dietary intake, such that the correlation coefficients comparing total serum or plasma carotenoids were all considered moderate to strong correlations and ranged from $r = 0.62$ ($P < 0.006$) (26) to $r = 0.78$ ($P < 0.0001$) (38). Although dietary intake correlation coefficients were lower than blood carotenoids, there were weak to moderate correlations with the skin carotenoids varying from $r = 0.38$ ($P = 0.016$) (60) to $r = 0.69$ ($P < 0.0001$) (59).

Discussion

Summary of results

This systematic review examined current literature that validated spectroscopy against blood measurements, reported dietary intake, or both to investigate whether spectroscopy-based skin carotenoid measurements are an objective, valid biomarker of F/V intake. All 29 included studies found statistically significant correlations between skin carotenoids measured via spectroscopy and plasma or serum carotenoids and/or dietary intake. Although the included studies differed in study design, population size, age, and participant demographics, the evidence provided in all 29 studies supports the use of spectroscopy as a proxy for F/V intake when compared with blood carotenoids and/or self-reported dietary intake. Overall, the strongest correlations existed between spectroscopy and blood carotenoids; however, the data supported statistically significant associations between spectroscopy and blood carotenoids and/or self-reported dietary intake in all of the included studies.

Although the data support the use of spectroscopy as a noninvasive, objective biomarker of dietary F/V intake, additional research is warranted before spectroscopy-based skin carotenoid measurements are considered an equally valid biomarker of F/V intake as plasma or serum carotenoids or validated dietary intake tools. Understanding the metabolism, absorption, and storage of carotenoids among all age groups, and under differing genetic and environmental conditions, is essential to their accurate detection in vivo. Increasing the methodological strength through experimental study designs, such as randomized controlled or crossover trials and dose–response studies, is required to understand the efficacy of spectroscopy-based skin carotenoid measurements as an approximation of F/V intake in individuals or populations. In addition, expanding future research to encompass more diverse populations will improve the generalizability of this technique and the acceptance of spectroscopy-based skin carotenoid measurements as a predictive biomarker of F/V intake.

Differences between spectroscopy devices

The 3 methods of spectroscopy all produced significant correlations between dietary intake and/or blood carotenoids. Of the articles included in this review, a majority used RRS to quantify skin carotenoids. RRS has previously demonstrated increased accuracy and precision in detecting skin carotenoids compared with RS and spectrophotometers; however, RS produced moderate to strong correlations, whereas spectrophotometers produced weak to moderate correlations. Previous research comparing the efficacy of spectroscopy devices found spectrophotometer devices to be more prone to error and chromophore interference than RRS (44); to date, no such research has compared RS with spectrophotometry. However, as reported in Tables 3–5, there were no observable differences in the correlational strength of the relations between method of detection and blood or dietary intake. It is important to continue future research on the sensitivity and specificity of the 3 methods to assess F/V intake.

The 3 spectroscopy devices explored in this review have limitations that could determine which device is most appropriate for specific study purposes. RRS technically has the capacity to detect different carotenoid molecules based on the absorption detection spectrum; however, RRS is unable to produce individualized scores for each carotenoid compound (67). Different wavelengths have varying affinities depending on the carotenoid compound; for example, at 514.5 nm, lycopene exerts an excitation signal 6 times that of β-carotene (68). Therefore, to examine individual carotenoid molecules, the excitation wavelength must be predetermined depending on the length of the conjugated carbon backbone (68). Thus, the individual carotenoid isomers are measured collectively with RRS, to avoid constantly recalibrating the wavelength of the device. RS is dependent on the skin matrix and the potentially confounding chromophores, such as melanin and hemoglobin, that could affect the RS measurement (14). RS is unable to differentiate between the carotenoid isomers due to a more simplified spectral detection methodology, and therefore presents only total dermal carotenoids as the output (14). Spectrophotometers measure skin carotenoids through the dermatological pigmentation of the skin, and therefore are limited by the concentration of skin pigment interference. For accurate evaluation of skin carotenoids using a spectrophotometer, the participants must have a

relatively fair complexion for the device to measure the carotenoid compounds within the color spectrum (69). These limitations should be considered when selecting a device for spectroscopy-based skin carotenoid measurements, acknowledging that many factors, including participant demographics and environmental conditions, can contribute inaccuracies to spectroscopic detection.

Spectroscopy and blood carotenoids

Blood carotenoid concentrations were positively associated with skin carotenoid status measured via spectroscopy. Carotenoids are detectable in plasma or serum for ~2 wk following initial consumption of carotenoid-containing foods (15). In comparison, the deposition of carotenoids into adipose cells increases the longevity of carotenoids in the skin to ~4 wk after dietary intake (15, 53). Carotenoids in the plasma or serum can be analyzed as total combined carotenoids or individual carotenoid compounds, whereas individual carotenoids in the skin cannot be easily detected. As previously confirmed by HPLC analysis of skin tissue biopsies, human skin is relatively enriched in β-carotene and lycopene compared with other carotenoids, and these are found in increased concentrations in the blood, indicating that spectroscopy could be more sensitive to sources of these carotenoids than blood (68, 70). In contrast, carotenoid compounds such as lutein and zeaxanthin are more concentrated in the macula of the eye, and therefore are not often associated with skin carotenoid concentrations (20). Among studies that assessed individual carotenoids in plasma or serum, the reported data confirmed stronger correlations between skin carotenoid scores and blood-derived α-carotene and β-carotene (60). Further research into the relation of plasma or serum carotenoids and skin carotenoids to assess F/V intake and the types of foods that are reflected in the skin is warranted.

Spectroscopy and dietary carotenoids

Studies comparing spectroscopy with dietary intake found positive and statistically significant associations between skin carotenoids and F/V consumption or dietary carotenoids. Among the studies that used self-reporting dietary recalls, reporting bias was a major critique in recall accuracy and was mentioned as a potential limitation in multiple studies (54, 57). The variety of databases used to analyze dietary intake could contribute to inconsistencies in nutrient composition of food items, as does the ability of food composition databases to reflect actual carotenoid content of foods, consequently affecting carotenoid estimation. For instance, processing and storage of fruits and vegetables affects their carotenoid content. Thus, the use of an objective spectroscopy-based skin carotenoid assessment is very appealing due to the decreased likelihood of subjective biases and lack of reliance on nutrient databases. Additional cross-validation studies of skin carotenoids compared with various measures of subjective recall, particularly if skin carotenoid status can be used as a covariate to strengthen dietary intake analysis, would be valuable to the study of dietary intake of fruits and vegetables.

Spectroscopy in diverse populations

Despite the studies in this review generating statistically significant correlations between spectroscopy, blood carotenoids, and/or reported dietary intake, it is imperative to acknowledge potential confounding variables, such as age, sex, BMI, and race/ethnicity (71). The articles analyzed in this review indicated that spectroscopy could be an effective measure of carotenoid status in most ages, including infants, children, and adults. Assessing infant carotenoid status using spectroscopy is challenging due to the thin, delicate skin of newborns and infants, resulting in subdermal laser penetration beyond the epidermis, reducing the accuracy of carotenoid detection. However, RRS scores in infants were strongly correlated with serum carotenoids ($R^2 = 0.75$) in healthy infants, whereas there were relatively weak to moderate correlations in premature infants ($r = 0.44$; $P = 0.01$, and $r = 0.52$; $P = 0.01$), respectively (50, 51). Scarmo et al. (57) detected high skin carotenoid scores along with a positive association between age and skin carotenoid status in a large population of preschool-aged children. The age of participants is also considered as a potential confounding variable due to the lack of knowledge regarding carotenoid metabolism and aging (53, 71, 72). In addition to the limited understanding of carotenoid metabolism, few studies addressed the physiological changes that accompany aging, which could result in difficulties detecting carotenoids using spectroscopy (26, 27). Although only 1 of the studies was conducted primarily in older adults, Bernstein et al. (39) found a positive and significant correlation between serum carotenoid and spectroscopy-based skin carotenoid measurements. Mayne et al. (26) included the lack of older adults as a study limitation and acknowledged the potential differences with skin quality, skin thinning due to collagen loss, and decreased energy intake that can affect the accuracy of spectroscopy in this population. Although the included studies reflected the ages across the lifespan, the sample sizes in some of the studies were relatively small, and therefore might not be generalizable to the broader population in that specific age range.

Studies controlling for individual variability resulted in differences in carotenoid status based on BMI classification (25, 27, 53–59, 63). Nguyen et al. (53) found incongruencies between reported dietary intake, skin carotenoids, and plasma carotenoids and attributed this to the increased BMI within a subgroup of participants due to the storage of circulating carotenoids into adipose cells. To limit the effect of BMI potentially altering skin carotenoid status, some studies controlled for weight by only including nonobese, adult participants with a BMI <30 (15, 24, 60). Additional methods of stratifying analyses by weight or BMI percentile were used to minimize the potential effect of adiposity on skin carotenoid detection (51, 53, 55–57). It should be noted that studies using BMI percentiles for stratifying data analyses were conducted in study populations primarily

consisting of child participants, and therefore extrapolating these results to adult populations could result in inaccurate assumptions.

Race and ethnicity can impact skin carotenoid measurements due to the interference of confounding compounds, such as melanin (14, 23, 24, 51). Melanin is detected within a similar absorption spectrum as carotenoids, that is, 360–560 nm (73). To minimize the effect of skin pigmentation, many studies used the palm or the heel to measure skin carotenoids, because there is minimal melanin interference and an increased thickness of the stratum corneum to prevent the laser from penetrating beyond the storage location of carotenoids (26, 51, 53, 57, 62). RS accounts for the potential melanin obstruction through an automatic deconvolution algorithm to correct for residual melanin and other biochrome compounds that can interfere in the tissue site (74). Therefore, RS has a lower specificity for the exclusive detection of carotenoid molecules due to the potential error of this algorithmic computation (14). To the authors' knowledge, there have been no studies evaluating the algorithmic correction in individuals with high melanin concentrations, although it can be assumed that a larger margin of error is associated with a higher concentration of skin chromophores. With regards to RRS, it has been observed that melanin interference can be easily corrected by spectrophotometrically measuring the melanin content of the skin and correcting for individual differences in skin pigmentation; however, these methods of correcting for melanin interference cause RRS to underestimate skin carotenoids whereas RS overestimates skin carotenoid status (14, 62, 75, 76). Ermakov et al. (62) investigated the effects of melanin interference in carotenoid detection using both RS and RRS and found that both methods had very low correlation coefficients when compared with melanin indices, indicating no significant association between melanin and RS or RRS. Spectrophotometers specifically measure the melanin in the skin and provide a melanin index, which can be used to adjust for differences in melanin concentration (62, 77). However, all 7 of the studies that used spectrophotometers included in this review adjusted for potential melanin interference by selecting predominantly homogeneous Caucasian sample populations (23–25, 27–30).

Genetic factors can also influence carotenoid metabolism and detection via spectroscopy (78). Jilcott Pitts et al. (59) attempted to determine the effectiveness of spectroscopy to measure skin carotenoids in a diverse population and found that the association between self-reported total F/V intake and RS-assessed skin carotenoids was nonsignificant among African-American participants, although the association was significant in a Caucasian subsample within the same study. As discussed above, melanin might not be a significant confounder, suggesting a potential genetic difference between races/ethnicities (59, 78). There are many regulatory proteins involved in the uptake, transport, and cleavage of carotenoids that could be susceptible to genetic modifications resulting in alterations to protein transcription (78). These modifications, including single nucleotide polymorphisms, can affect the use or storage of carotenoids, thus resulting in inaccurate reflection of dietary intake of fruits and vegetables (78, 79). It has been demonstrated through genome sequencing that different ethnic groups display varying efficiencies of carotenoid metabolism, and that ethnic origin should be considered as a covariate when assessing skin carotenoids using spectroscopy (79).

Spectroscopy and seasonality

Seasonality can affect skin carotenoid concentrations by either reflecting differences in dietary intake of carotenoid-rich foods or skin carotenoid oxidation by UV exposure (22). Dietary data collected by Beccarelli et al. (54) showed seasonal variations due to increased consumption of carotenoid-rich autumn vegetables, such as sweet potatoes, compared with springtime vegetables lower in carotenoids, such as cucumbers. Other researchers have controlled for potential seasonal effects of sun exposure on skin carotenoid status by conducting studies during only 1 season (56). Mayne et al. (26) evaluated skin carotenoid scores over a 6-mo period in a climate with notable seasonal differences and found no differences by season, with intraclass correlation coefficients over the 6 time points that ranged from 0.85 to 0.89. In agreement with Mayne et al., a 1-y study by Jahns et al. (80) found no differences in skin carotenoid scores based on season; however, blood carotenoids were lower in the summer, lending credence to the potential of seasonality to affect skin carotenoid scores. Additional studies are warranted to determine the effect of seasonality on skin carotenoid status, and researchers should collect data on season of measurement to test as a potential confounder in statistical models.

Spectroscopy in nonclinical settings

A subordinate aim of multiple studies was to determine the feasibility of using spectroscopy in atypical, nonclinical settings. Community environments, such as daycare centers (62), elementary schools (53, 54), small food (corner) stores (59), and outdoor community parks (62) were all locations assessed for field feasibility in both child and adult participants. Jilcott Pitts et al. (59) and Scarmo et al. (57) reported the average time it took to complete triplicate measurements and found, respectively, that on average it took ~94 s per participant to record triplicate measures using RS, or 30 s per measurement using RRS.

Conclusions

The reviewed literature suggests that all 3 spectroscopy methods are valid tools for quantifying skin carotenoids as an approximation of F/V intake. The data collected from spectroscopy-based skin carotenoid measurements were positively and significantly correlated with blood carotenoids and/or reported dietary intake, supporting the use of spectroscopy as a valid biomarker of dietary intake of F/V intake.

Application of the findings

The data provided in this review support the use of spectroscopy as a reflective measure of F/V intake in diverse ages and racial/ethnic groups; however, more research is required for these results to be extrapolated to the general population. Many of the studies included in this review conducted on-site data collection in various community settings because spectroscopy provides a rapid and painless measure of dietary intake in a matter of seconds. This technology has the potential to enhance the health field by providing information on dietary patterns and tracking dietary behaviors to support preventive health services (26, 51, 61, 63). The consistent monitoring of carotenoid status can increase early detection or track the progression of various chronic diseases (51, 52, 61, 63, 81); however, current methods of spectroscopy are unable to diagnose acute or chronic diseases exclusively based on carotenoid status.

As a result of the successful implementation of spectroscopy techniques in the community setting, this method could be used to assess the outcomes of nutrition intervention programs in large, diverse populations (82). Spectroscopy can provide an objective reflection of F/V intake in children in the school setting (53, 54). This rapid and quantitative assessment of skin carotenoids can be an impactful method for evaluating nutrition-based interventions because effective strategies to support obesity and chronic disease prevention in both children and adults are public health priorities (82).

Limitations of the review

It is imperative to acknowledge that the current review presents several limitations. Although the findings were established in diverse populations in different ages and ethnic groups, a majority of the studies were cross-sectional, or prospective cohort study designs, and therefore do not provide the degree of evidence to prove causation that results from randomized controlled trials. In addition, non–whole food supplementation was an exclusion criterion to complete the objective of this review—that spectroscopy is a valid biomarker of F/V intake. High-dose supplementation likely results in substantial increases in both spectroscopy-based skin carotenoid measurements and plasma or serum carotenoids; however, this is not indicative of normal dietary intake as would be seen in nutrition surveillance or intervention evaluation studies. Thus, we limited our review to articles that did not include high-dose supplementation, to investigate the sensitivity of the spectroscopy-based skin measurement devices to detect changes in carotenoid concentrations that are found naturally in fruits and vegetables. Additionally, the use of dietary supplements was also excluded due to potential differences in bioavailability and gastrointestinal absorption compared to dietary consumption of fruits and vegetables (83). However, due to this exclusion criterion, it was noted that multiple studies were excluded that used natural food concentrates, such as kale extract or high-carotenoid additives. Nonetheless, the elevated concentration of carotenoids likely exceeded the typical daily intake and therefore studies using any type of non–whole food supplementation were excluded from the review. Finally, it should also be recognized that due to the high volume of potential articles retrieved during the comprehensive literature search, only articles published in English were considered for this review.

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