Measurement of the dermal beta-carotene in the context of multimodal optical clearing

Mohammad Ali Ansari, Valery V. Tuchin
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Introduction

Carotenoids are a large water-repelling pigment group of isoprenoid metabolites covering more than 700 compounds [1, 2]. They have essential roles in all photosynthetic organisms due to their important photoprotective and antioxidant properties [3]. Studies have shown that plants, algae, cyanobacteria, some fungi, and nonphotosynthetic bacteria can synthesize carotenoids as well, and many animals rely on food-borne carotenoids as visual pigments, antioxidants, or colorants [3, 4]. The carotenoid molecule is typically a C₄₀ hydrocarbon and forms a chromophore of double bonds in conjugation, which absorbs light in the blue light spectrum. This causes these compounds to be colored ranging from yellow to orange and red [1, 5–8].

In 2018, Widjaja-Adhi et al. investigated the role of carotenoids in the visual procedure. They applied green (532 nm) and blue (405 nm) low-energy lasers to damage the mouse retina and observed that blue laser light treatment triggered the formation of aberrant retinaldehyde isomers in the retina. In addition, they found that zeaxanthin supplementation of mice shielded retinoids from these photochemical modifications. These pigments also reduced the extent of the damage to the retina after the blue laser light insult [6].

Several studies have shown that carotenoids also play a key role in the prevention of many oxidative stress-mediated degenerative diseases such as Alzheimer’s disease (AD). For example, some results have shown that low plasma β-carotene concentrations have been estimated in AD subjects compared with cognitively healthy subjects as presented by Boccardi et al. [9]. They investigated the relation between β-carotene and accelerated cellular aging such as leucocyte telomere length (LTL) and peripheral mononuclear cell (PBMC) telomerase activity in a cohort of old-age subjects. Their results confirmed that lower plasma beta-carotene levels are associated with AD diagnosis independent of multiple covariates [9]. Based on some animal studies (2004–2009), Obulesu et al. emphasized the dietary supplementation of carotenoids to help fight Alzheimer’s, and they recommended further animal studies to understand their mechanism of neuroprotection [10]. Hira et al. applied 50 male mice (3 months old, weighing 30–40 g) categorized into five groups. Groups I, II, and III served as the control group, disease group (streptozotocin 3 mg/kg i.c.v. – intracerebroventricular injection), and standard (piracetam 200 mg/kg, i.p.—intraperitoneally) groups, respectively. Groups IV and V served as treatment groups (beta-carotene at a dose of 1.02 and 2.05 mg/kg, respectively) [11]. Their results showed the administration of beta-carotene reduced streptozotocin-induced cognitive deficit via its antioxidative effects, the inhibition of acetylcholinesterase, and the reduction of amyloid β-protein fragments [11]. Li et al. categorized five studies (2002–2010) to evaluate the effects of dietary intake of vitamin E, vitamin C, and beta-carotene to decrease the relative risk of AD [12], while Dover and her colleagues, during a mean follow-up period of 9.5 years on 5395 participants (55 years and older), statistically studied the consumption of major dietary antioxidants relative to long-term risk of AD and they compared the effects of dietary intake of vitamin E, vitamin C, and beta-carotene on risk of AD [13]. In summary, these results suggest that dietary intakes of vitamin E, vitamin C, and beta-carotene can help lower the risk of AD [11]. Moreover, Muscogiuri et al. reported that beta-carotene can enhance the immune system, since it can increase the
number of T-cell subsets and enhance lymphocyte response to mitogen, increase interleukin-2 production, and potentiate natural killer cell activity, which is vital parameter during ses-

tional influenza or the pandemic of COVID-19 [14, 15].

Carotenoids can be classified into subgroups: carotenes
(having the formula $C_{n}H_{2n}$, such as alpha-, beta-, delta-, and
gamma-carotene and lycopene) and xanthophylls (oxygenated
derivatives of carotenes with formula $C_{n}H_{2n}O_{x}$, such as lutein,
zeaxanthin, and neoxanthin). Some of the carotenoids are
called provitamin A, which yield vitamin A and retinoids such
as alpha- and beta-carotene and beta-cryptoxanthin, while
lycopene, lutein, zeaxanthin, and meso-zeaxanthin are called
non-provitamin A carotenoids [16], and provide significant
protection against the potential damage caused by light strik-
ing this portion of the retina. In the eye, lutein and zeaxanthin
have been shown to filter high-energy wavelengths of visible
light and act as antioxidants to protect against the formation of
reactive oxygen species and subsequent free radicals [16–19].

The epidemiological observations very consistently show
that people who consume higher dietary levels of fruits
and vegetables have a lower risk of certain types of cancer;
e.g., in 2003, Chao et al. showed that there is a relationship
between lower risk of breast cancer and increased dietary
intake of beta-carotene [15, 17]. Based on several studies,

It seems that beta-carotene is useful for maintaining nor-
mal redox, immunological, and probably cell-to-cell com-
munication activity in the general population [8–25]. So, the
dermal beta-carotene concentration can be a good indicator
of physical health.

Three methods have been introduced for detection and
measurement of beta-carotene and other carotenoids: (a) mass
spectroscopy and nuclear magnetic resonance (NMR), (b)
high-performance liquid chromatography (HPLC), and (c)
optical methods including Raman spectroscopy and diffuse
reflectance spectroscopy (DRS) or absorption spectroscopy.
Measuring beta-carotene using DRS provides three advan-
tages: (I) low-cost instrumentation, (II) a portable device, and
(III) high discrimination power to distinguish different caro-
tenoids. Here, we overview how one can apply low-cost DRS
to measure dermal beta-carotene. The presence of blood, mel-
a


canopy – were measured to estimate concentration of beta-carotene,
and the beta-carotene contents are measured to be $0.63 \pm 0.05$
and the beta-carotene contents are measured to be $0.57 \pm 0.07$
and $0.22 \pm 0.08$ nmol/g, respectively [31]. Based
on several studies using HPLC and resonance Raman spec-
troscopy, the concentrations of different carotenoids in human
skin are depicted in Table 35.1. It was shown that beta-carotene
in human skin strongly depends on the anatomic site and can
drastically change inter-individually [31, 33].

Results presented in Refs. [28, 34] show that Raman spec-
troscopy is sensitive and reproducible and strongly correlates
with the HPLC analysis of carotenoids, where a single caro-
tenoid is presented. But for skin containing a complex mix-
ture of similar compounds, Raman spectroscopy is not able
to clearly discriminate between the individual carotenoids
[28], or, due to high background autofluorescence in resonance

![FIGURE 35.1 Chemical structures of alpha- and beta-carotene ($C_{n}H_{2n}$) and lycopene ($C_{n}H_{2n}$) based on data depicted in Reference [26].](image-url)
Raman microscopy, this method can underestimate the beta-carotene concentration in skin.

Detection of dermal beta-carotene using multimodal OC

As shown in Figure 35.4(a), the presence of blood, melanin, water, and other chromophores inside skin masks the beta-carotene spectrum (see Figure 35.4(b)). Three OC methods have been applied to detect absorption spectra of beta-carotene: (a) compression, (b) chemical agent, and computational OC methods, which are presented in the following sections.

Compression OC

The optical properties of skin can be changed due to the application of mechanical forces, such as compression and stretching. Compression removes the interstitial water and blood from the area of interest, leading to an increase in optical tissue homogeneity. Due to the interstitial water loss, closer packing of tissue components causes less light scattering (refractive index matching) due to cooperative interference effects and thinner tissue [36–38]. In 2011, Gurjarpadhye et al. showed that changes in the thickness of ex vivo porcine skin during air dehydration results in an increase of refractive index from 1.4 to 1.5 (at a wavelength of 1310 nm) [39]. The optical depth of diffuse reflectance spectroscopy is increased by lowering the scattering and absorption coefficient. In addition, transport of water and blood away from the compressed region helps us to see the absorption spectrum of beta-carotene (in the spectrum of 450–500 nm) as shown in Figure 35.5.

In 2012, Ermakov and Gellermann reported a new reflection-spectroscopy method for the quantitative detection of carotenoid in the living human skin [40]. They used topical pressure in the reflectivity approach presented in Figure 35.6. In this way, blood is squeezed out of the measured tissue volume and the resupply is temporarily blocked. As a consequence, overlapping HbO$_2$ absorptions are effectively removed and any residual HbO$_2$ is converted into Hb, which has about a factor of 2.5 lower absorption strength in the spectral window

![FIGURE 35.2](image-url) Molar extinction coefficient of beta-carotene in ethanol based on data presented in Reference [29].

![FIGURE 35.3](image-url) A typical Raman shift spectrum obtained from the human skin with an excitation wavelength at 514.5 nm based on data presented in Reference [32]. The Raman lines at 1005 cm$^{-1}$, 1156 cm$^{-1}$, and 1523 cm$^{-1}$ originate, respectively, from the rocking motions of the methyl groups, and from carbon–carbon single bond and carbon–carbon double-bond stretch vibrations of the conjugated backbone.

### TABLE 35.1

<table>
<thead>
<tr>
<th>Carotenoids composition in human skin (ng per g tissue and based on data presented in references [31, 33])</th>
<th>Mean value (ng/g)</th>
<th>Skin source</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lycopene + Z-isomers</td>
<td>#1</td>
</tr>
<tr>
<td></td>
<td>Beta-carotene</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>Alpha + gamma + delta + zeta carotene</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>Lutein + Zeaxanthin</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Phytoene</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>Phytofluene</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>TOTAL</td>
<td>340</td>
</tr>
<tr>
<td>ND: nondetectable data</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

---

**Reference:** [29]
They applied topical pressure to temporarily squeeze blood out of the illuminated tissue volume.

**Immersion OC**

As mentioned, the optical immersion of tissues in exogenous chemical agents is the most recent technique for controlling the optical properties of biological tissue [36], and the one with the most potential. In 2018, a solution of DMSO 50% with ethanol as the solvent was applied to detect beta-carotene content in a two-layer phantom [8]. The underside layer consisted of Intralipid® 20% (3.3 ml), distilled water (13 ml), agar (0.7 g), and beta-carotene [≥ 97.0% (UV) Sigma-Aldrich] in different concentrations of 0.2, 0.3, 0.4, and 0.6 μM. The upper layer is a mouse ear (2 months old, 20 g) with an average thickness of 250 μm (one-half of its full thickness is composed of two layers – the epidermis and the dermis – and below the skin layers, cartilage forms the structural support for the mouse ear). Ear specimens were immersed in DMSO solution for 15 min, immersion OC [8, 22]. Figure 35.7 shows the schematic of setup and phantom in this study.

In this study, the authors first applied compression OC and studied the variation of diffuse reflectance and absorbance. The results, including error bars, show that the removal of blood dip between 500 and 570 nm depends on the amount of mechanical compression. This is because the transport of blood is a function of the amount of compression and Young’s module of tissue [23]. One can see in Figure 35.8 that, after the application of pressure and when blood is removed, the absorbance decreases due to less blood absorption. Indeed, scattering is also changed a little in this range (scattering by red blood cells and lipids), but, in this wavelength range, blood absorption prevails [8]. Then, the authors simultaneously studied the influence of both compression and a chemical clearing agent on tissue phantoms. Immersion of ears in DMSO leads to a decrease in their optical scattering, so one can see an increase in optical depth (diffusion of DMSO in phantom causes a reduction in the scattering coefficient by refractive index matching) [41]. In addition to DMSO, a combination of 70% glycerol + 30% liquid paraffin as a chemical OC agent (OCA) was also applied to measure dermal beta-carotene as stated in Reference [41].
Measurement of the dermal beta-carotene

In addition to immersion OC, a more sophisticated method based on optical diffusion equation can be applied to detect dermal beta-carotene. Recent studies show that computational OC can be used as a noninvasive method to estimate dermal chromophores [8, 24, 29, 41–45]. In this method, the diffuse reflectance (or absorbance) is used to reconstruct distribution of a particular chromophore of interest that is normally hidden in the background of absorption of hemoglobin, water, and melanin [25, 43]. This method has been demonstrated in application to estimate the concentration of beta-carotene inside a tissue phantom, as depicted in Reference [8].

In 2006, Zonios and Dimou presented a simple way to calculate diffuse reflectance, \( R(\lambda) \), from a homogeneous semi-infinite turbid medium. The forward and backscattered light are exponentially attenuated according to the sum of the absorption and reduced scattering coefficients, \( \left\{ \mu_a(\lambda) + \mu_s(\lambda) \right\} \) [43], where \( \mu_a(\lambda) \) is the wavelength-dependent absorption coefficient of tissue. It is well established that exponential solutions of this type constitute an acceptable approximation, especially in one-dimensional geometries [8, 29, 43]. Figure 35.9 depicts the geometry of this problem, e.g., a light with an intensity \( I_0 \) at the top surface of skin (at \( z = 0 \)) is exponentially attenuated as it propagates inside skin, \( I = I_0 e^{-\left(\mu_a(\lambda)+\mu_s(\lambda)\right)z} \). At a given depth \( z \), light is scattered back from a thin layer of thickness \( dz \). The backscattered light is assumed to be proportional to the reduced scattering coefficient \( \mu_s(\lambda) \) and travels back to the surface while being exponentially attenuated by a factor \( e^{-\left(\mu_a(\lambda)+\mu_s(\lambda)\right)dz} \). The total diffuse reflectance is then given by [43]:

\[
R(\lambda) = 2\mu_s(\lambda) \int_0^\infty e^{-\left(\mu_a(\lambda)+\mu_s(\lambda)\right)dz} dz = \frac{\mu_s(\lambda)}{\mu_s(\lambda) + \mu_a(\lambda)} \tag{35.1}
\]

By taking into account of refractive index mismatch, the diffuse reflectance \( R(\lambda) \) from skin can be stated as the following [44]:

\[
R(\lambda) = 2\mu_s(\lambda) \int_0^\infty e^{-\left(\mu_a(\lambda)+\mu_s(\lambda)\right)dz} dz = \frac{\mu_s(\lambda)}{\mu_s(\lambda) + \mu_a(\lambda)} \tag{35.1}
\]
Where \( k_1 \) and \( k_2 \) are the parameters depended on the probe geometry and refractive indices of studied sample; for example, for the setup shown in Figure 38.7(b), they were determined to be 0.025 and 0.075, respectively [8]. The absorption coefficient and reduced scattering of skin can be given as [45]:

\[
\mu_a(\lambda) = C_{mel} \varepsilon_{mel}(\lambda) + C_{beta} \varepsilon_{beta}(\lambda) + C_{bili} \varepsilon_{bili}(\lambda) + C_{water} \varepsilon_{water}(\lambda)
\]

\[
(35.3a)
\]

\[
\mu'_a(\lambda) = (1 - c_1 \frac{\lambda - \lambda_{max}}{\lambda_{max} - \lambda_{min}}) \mu_a(\lambda_{min})
\]

\[
(35.3b)
\]

where \( C_{mel} \), \( C_{beta} \), \( C_{bili} \), and \( C_{water} \) are concentrations of melanin, beta-carotene, blood, bilirubin, and water in the tissue, respectively; and \( \varepsilon_{mel}(\lambda) \), \( \varepsilon_{beta}(\lambda) \), \( \varepsilon_{bili}(\lambda) \), \( \varepsilon_{water}(\lambda) \) are molar extinctions of melanin, beta-carotene, blood, bilirubin, and water, respectively. The parameter \( c_1 \) is a parameter related to effective scatter size, \( \lambda_{min} = 400 \text{ nm} \) and \( \lambda_{max} = 800 \text{ nm} \) [29]. Based on the data presented in Reference [35], the molar extinction coefficients mentioned in the previous relationship can be modeled via the following relations:

\[
\varepsilon_{mel}(\lambda) \approx 1.7 \times 10^{12} \times \lambda^{-3.4}
\]

\[
(35.4a)
\]

\[
\varepsilon_{beta}(\lambda) \approx 1.06 \times 10^{6} \times e^{-\frac{(2228 - \frac{\lambda}{523})^2}{2}} + 1.26 \times 10^{7} \times e^{-\frac{(\lambda - 443)^2}{49}} + 3.84 \times 10^{4} \times e^{-\frac{(\lambda - 443)^2}{1129}}
\]

\[
(35.4b)
\]

\[
\varepsilon_{bili}(\lambda) \approx 0.4 \times \left(4.75 \times 10^{4} \times e^{-\frac{(\lambda - 552)^2}{49}}\right)
\]

\[
+ 0.6 \times \left(3.8 \times 10^{18} \times e^{-\frac{(\lambda - 2089)^2}{447}} + 5.5 \times 10^{7} \times e^{-\frac{(\lambda - 572)^2}{1129}}\right)
\]

\[
+ 5.08 \times 10^{4} \times e^{-\frac{(\lambda - 542)^2}{19}}
\]

\[
(35.4c)
\]

\[
\varepsilon_{water}(\lambda) \approx 2.86 \times 10^{10} \times e^{-\frac{(\lambda - 403)^2}{238}} + 7.65 \times 10^{7} \times e^{-\frac{(\lambda - 502)^2}{3705}}
\]

\[
+ 4.06 \times 10^{4} \times e^{-\frac{(\lambda - 432)^2}{4018}}
\]

\[
(35.4d)
\]

In 2009, Tseng et al. applied a more sophisticated methodology to measure the absorption coefficient of a blood sample. In this study, the probe has been adjusted into multiple source-detector pairs. The normalized reflectance versus source-detector separation is then fit to a diffusion model by a least-square minimization algorithm to determine the absorption and reduced scattering spectra. The reconstructed absorption spectra are fit linearly with known chromophore absorption spectra to extract chromophore concentrations, and the reduced scattering spectra are fit to a scattering power law to obtain the scattering power [46, 47]. The authors applied the diffusion equation to calculate diffuse reflectance from a two-layer tissue phantom:

\[
R(\lambda, \rho) = \frac{1}{4\pi} \left(1 - R_{\text{fres}}(\theta)\right) \cos \theta L d\Omega
\]

\[
(35.5)
\]

where \( \rho = \sqrt{x^2 + y^2} \), and \( R_{\text{fres}}(\theta) \) is the Fresnel reflection coefficient for a photon with an incident angle \( \theta \) relative to the normal to the boundary. The parameter \( L \) indicates the fluence at the top surface, \( L = \varphi + 3D(\varphi / \varepsilon) \cos \theta \), where
**Measurement of the dermal beta-carotene**

**TABLE 35.2**

Chromophore concentrations of dorsal forearm of 18 subjects reconstructed with two regional fitting (600–1000 nm). Data from Reference [47]

<table>
<thead>
<tr>
<th>Skin Type</th>
<th>Deoxygenated Hemoglobin [µM]</th>
<th>Oxygenated Hemoglobin [µM]</th>
<th>Melanin [%]</th>
<th>Water [%]</th>
<th>Lipid [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-II</td>
<td>0.12 ± 0.51</td>
<td>7.74 ± 3.15</td>
<td>0.87 ± 0.18</td>
<td>21.42 ± 2.56</td>
<td>27.74 ± 5.01</td>
</tr>
<tr>
<td>III-IV</td>
<td>0.08 ± 0.26</td>
<td>9.47 ± 3.41</td>
<td>1.15 ± 0.09</td>
<td>22.46 ± 2.46</td>
<td>26.12 ± 6.04</td>
</tr>
<tr>
<td>V-VI</td>
<td>0.02 ± 0.10</td>
<td>2.72 ± 2.40</td>
<td>1.65 ± 0.23</td>
<td>18.66 ± 3.17</td>
<td>16.56 ± 8.23</td>
</tr>
</tbody>
</table>

As presented in Refs. [8, 35, 44], the simulated absorbance can be applied to measured absorbance for estimating the concentration of beta-carotene (see Figure 35.11). Recently, this method has been applied to measure dermal beta-carotene after a 1-week beta-carotene diet (at least 250 cc/day carrot juice). To do this, one requires a calibrating relation between diffuse reflectance and concentration of beta-carotene inside the tissue phantom. For example, in Reference [41] and similar to Reference [23], a tissue phantom based on the mouse ear alone and together with immersion (70% glycerol + 30% liquid paraffin as a chemical OCA) and compression OC was used. The authors defined delta parameter, \( \Delta = A_{490} - B_{505} \), to clarify the effect of OC on absorption spectrum (\( A_{490} \) is the absorbance at the wavelength of 490 nm and \( B_{505} \) is the absorbance at the wavelength of 505 nm); the parameter \( \Delta \) depends on the beta-carotene content of the tissue and the efficacy of OC. Because the first factor (concentration of beta-carotene) increases the amount of \( \Delta \) parameter and the second one (efficiency of OC) decreases this parameter. Since, the compression OC can displace the blood (and water) and decrease the absorption spectrum around wavelength of 490 nm (absorption peak of beta-carotene) and hence it reduces the amount of parameter of \( \Delta \). The water transport (dehydration) and displacement of blood help us to see the spectra of beta-carotene [35]. Moreover, applying an OC agent such as DMSO or glycerol causes an intrinsic refractive index matching, which may also enhance the efficacy of OC (to decrease absorbance spectra via reduction of light scattering inclusion) [24, 41, 46] and consequently reduce the parameter \( \Delta \). The relation between parameter \( \Delta \) and the concentration of beta-carotene in the tissue phantom was obtained as follows:

\[
\Delta = 17 \times 10^{-4} C + 0.009. \tag{35.7}
\]

Based on the above relation, the value of dermal beta-carotene increases from 0.9 nmol/g to 1.7 nmol/g (after a 1-week beta-carotene diet).

In addition, artificial neural networks (ANNs) were also used to obtain absorption and scattering coefficients, estimated using diffuse reflectance [48, 49]. Monte Carlo (MC) simulations can be also performed for the sake of possibly obtaining simulated diffuse reflectance to contribute to the ANN as input parameters [48]. They taught ANN using different MC simulation to estimate the absorption coefficient of liquid phantoms (including cholelhe intravenous lipid emulsion (CILE) and Evans Blue (EB) dye into a distilled water). They compared the real value of absorption coefficients with the ANN method as depicted in Figure 35.12.

\[
D = \frac{1}{3}(\mu_r^s + \mu_s^a) \quad \text{and} \quad \varphi \text{ are diffusion coefficient and fluence rate, respectively. In this study, the reflectance curve obtained from the volunteer skin (in a spectrum range of 500–1000 nm) was then fit to Equation 35.5. The “lscurvefit” function in MATLAB (MathWorks, MA, USA) was used to perform the least-squares fittings to recover absorption and reduced scattering coefficients. Table 35.2 shows the mean value of dorsal chromophore concentration within the forearms of 18 volunteers.}

On the other hand, in Equation 35.2 and assuming \( R_0 \) indicates the diffuse reflectance for \( \mu_r(\lambda) = 0 \), so \( \mu_r(\lambda) = k_1 R_0 \). This diffuse reflectance \( R_0 \) can be estimated from the wavelength region 600–900 nm using the scattering power law as mentioned in Reference [8, 45]. Finally, the absorption coefficient is obtained from

\[
\mu_r(\lambda) = \frac{k_1}{k_2} \left[ \frac{R_0}{R(\lambda)} \right]^{-1}. \tag{35.6}
\]

Since, in the visible spectrum, blood and melanin are the main chromophores that affect absorption coefficient of our phantom, while variations in water and lipids do not have significant effects in this spectrum interval. Figure 35.10 shows that analytical OC could extract and quantify the absorption coefficient of each chromophore within a tissue-like optical phantom (as depicted in Figure 35.6) without immersion or mechanical OC methods for detection of beta-carotene.

**FIGURE 35.10** Extracted absorption coefficient of a tissue phantom. The absorption coefficient of skin components inside the tissue phantom are shown based on computational OC. Reprinted with permission from Reference [8].
Some researchers combined spectroscopy and HPLC with ANN methods to reconstruct beta-carotene and lycopene content within fruits and agricultural products [49–51]. For example, Torrecilla et al. applied a neural method to estimate the carotene content in tomato products in standard samples [50]. This method could estimate the beta-carotene content with an error rate of less than 10%. ANN and deep learning have been applied to recover beta-carotene content in food or agricultural products, and it seems that this approach can be used for dermal screening as a new computational OC.

**Summary**
Recent studies show that carotenoids have important role in preventing or decreasing the risk of some diseases such as immunity diseases, neurological disorders, Alzheimer’s disease, photosensitive disorders, and prostate, colon, and oral cancers. Therefore, carotenoid monitoring in skin can be a good indicator of physical health. This chapter aimed to apply low-cost DRS to estimate dermal beta-carotene content. We introduced combinations of compression and immersion OC methods to decrease both light scattering and the effect of blood spectra. The recent presented results depict that the absorption spectrum of beta-carotene can easily be seen after applying experimental OC methods. Then, one can apply computational OC to determine beta-carotene content. We noted that the computational OC can be applied independently or in combination with experimental OC methods. Hence, a combination of experimental OC and computational OC provides a low-cost method to measure dermal beta-carotene in vivo. Finally, it is proposed that a powerful approach to estimate beta-carotene content based on artificial neural networks could open new avenues in this area.

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