Quantification of human skin diffusivity during *in vivo* optical clearing

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The study is focused on application of optical clearing method with the purpose of improvement of diagnostic and treatment of diseases and pathologies by optical methods. The idea is to predict the development of pathology of internal organs based on measurements taken on external organs. To identify the most suitable optical clearing agent, the effective diffusion coefficient of several agents in human skin *in vivo* was quantified.

MATERIALS AND METHODS

Measurement of diffuse reflectance

Object of study: human skin *in vivo*

Optical clearing agents (OCAs)**:**

Aqueous 40% glucose solution

Aqueous 60% glycerol solution

Aqueous 70% glycerol solution

Aqueous-alcoholic 50% fructose solution

Equipment: USB4000-Vis-NIR spectrometer (Ocean Optics, USA), spectral range 450-950 nm

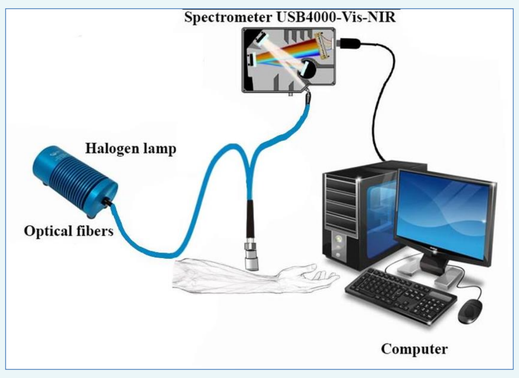

Figure 1. Scheme of the eexperimental setup

Data proccessing

The measured reflectance spectra were used to determine the effective optical density of the skin at each measurement moment *t* of the diffuse reflectance R(t, λ) at certain wavelengths λ [1, 2]:

$$A(t, \lambda) = -\ln[R(t, \lambda)].$$

Then, the expression obtained using the Bouguer-Lambert-Beer law and Fick's second law for the difference between the effective optical density values at the initial $A(t = 0, \lambda)$ and current $A(t, \lambda)$ time moments was used:

$$\Delta A(t, \lambda) = A(t, \lambda) - A(t = 0, \lambda) \sim C_0[1-\exp(-t/\tau)],$$

where

$$\tau = (4z^2/\pi^2)/D,$$

τ is the characteristic diffusion time for the case of one-way diffusion; z is the depth of the studied region, cm; *D* is the effective diffusion coefficient of agent molecules into the skin and water from the skin, cm^2/s; C_0 is the initial concentration of the agent in the skin, mol/L. The depth of the studied region was determined to be 300 μm [3].

To estimate the characteristic diffusion time of the agent in the skin, the time dependence of the optical density of the tissue was approximated by the equation:

$$\Delta A(t, \lambda) = B[1-\exp(-t/\tau)] + y_0.$$

The skin permeability coefficient for OPA was estimated using expression:

$$P = \frac{D}{l}$$

References

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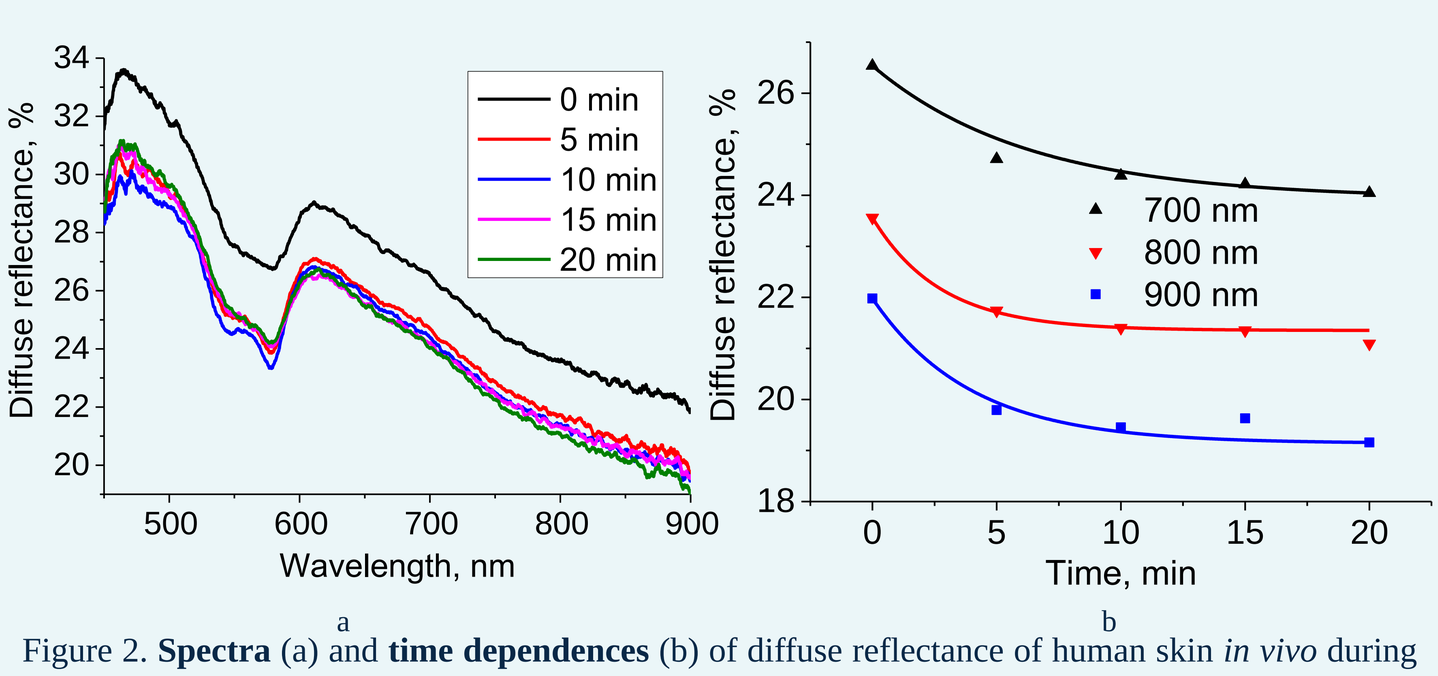
2. A. A. Selifonov, E. I. Selifonova, V. V. Tuchin, "E-cigarette smoking vape impact on optical properties of porcine gingival mucosa measured ex vivo in the range from 200 to 800 nm," SPIE, Optical Technologies for Biology and Medicine, 12192, (2022).
3. V. Colas, W. Blondel, G. Khairallah, C. Daul, and M. Amouroux, “Proposal for a Skin Layer-Wise Decomposition Model of Spatially-Resolved Diffuse Reflectance Spectra Based on Maximum Depth Photon Distributions: A Numerical Study”, Photonics 8(10), 444 (2021).

RESULTS



a b

Figure 2. **Spectra** (a) and **time dependences** (b) of diffuse reflectance of human skin *in vivo* during exposure to aqueous-alcoholic 50% fructose solution

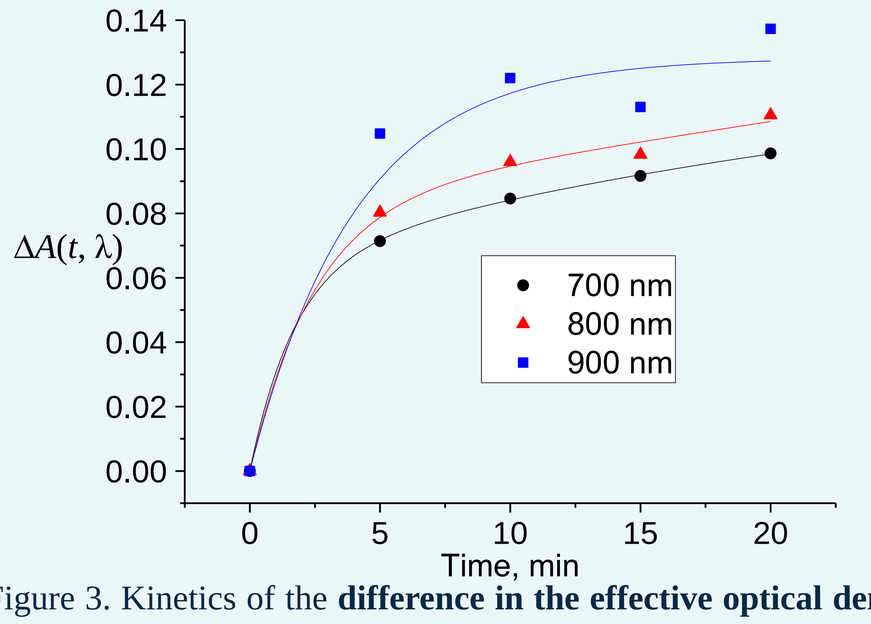


Figure 3. Kinetics of the **difference in the effective optical density values** at the initial and current moments of time ΔA(t, λ) of the skin *in vivo* during the action of aqueous-alcoholic 50% fructose solution

Characteristic diffusion time (*τ*), effective diffusion coefficient (*D*) of OCAs in the skin *in vivo*, effective skin permeability coefficient for OCAs (*P*)

OCAs	*τ*, min	*D*, cm^2/s	*P*, cm/s
Aqueous-alcoholic 50% fructose solution	4.4±1.9	$(1.5\pm0.6)\times10^{-6}$	$(3.2\pm0.1)\times10^{-5}$
Aqueous 60% glycerol solution	4.3±0.3	$(1.4\pm0.1)\times10^{-6}$	$(4.7\pm0.3)\times10^{-5}$
Aqueous 70% glycerol solution	1.9±0.2	$(3.3\pm0.4)\times10^{-6}$	$(10.9\pm1.2)\times10^{-5}$
Aqueous 40% glucose solution	2.1±0.4	$(3.2\pm0.7)\times10^{-6}$	$(10.6\pm2.2)\times10^{-5}$

CONCLUSION

- The decrease of skin diffuse reflectance was observed at application of each OCA in the studied spectral range
- Aqueous **70% glycerol solution** and aqueous **40% glucose solution** showed higher values of skin diffusion coefficient and skin permeability coefficient for agents
- Obtained data can be used to improve optical clearing method in order for diagnostic or treatment disease by optical methods

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