Preliminary hyperspectral analysis of topical application of a concentrated cream to the skin

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Abstract

The skin is a convenient and frequently used route of drug administration in medicine. It provides a protective barrier, preventing harmful external agents from entering the body, while being permeable to selected substances. This makes the skin an interesting research object. The study focused on the effect of concentrated cream application on the optical properties of the skin. The study was conducted on 10 healthy participants (9 women and 1 man, age range 23–50 years; mean age 31.8 years). Measurements were performed using the SPECIM IQ hyperspectral camera (Finland) within the spectral range from 400 to 1030 nm. The study showed that in the key spectral range from 627 nm to 1030 nm, the average reflectance of the skin alone is the highest (0.718) compared to the measurement points after the application of the preparation i.e., time 0 min. (0.694), at time 10 min. (0.711) and at time 20 min. (0.712) ($p < 0.001$). Right after the application of concentrated cream, the average reflectance decreased, while in the next points of 10 min. and 20 min. the reflectance increased. The difference between the max. and min. reflectance (i.e. the value obtained by subtracting the min. from the max.) is the smallest for the skin alone and the highest immediately after the cream is applied, which means the greatest homogeneity of the skin not lubricated with the concentrated cream. In conclusion, the assessment of the quality and correctness of semi-solid preparations as well as the effectiveness of the therapies may be carried out using hyperspectral analysis

Key words:

skin, concentrated cream, homogeneity, hyperspectral analysis, hyperspectral imaging, reflectance

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Introduction

The route of drug administration determines how the drug will be delivered to the body. Drugs are most often administered parenterally and orally. However, a convenient and very well accepted by patients route through which drugs can be delivered to the body is the skin [1]. It is the largest organ, which in an adult has a surface area of 1.6–2 m^2 and a thickness of 0.5–1 mm [2]. Therefore, skin offers wide possibilities for the transport of active substances. The skin consists of three layers: epidermis, dermis, and subcutaneous tissue, with the stratum corneum as the outermost layer of the epidermis being the hardest barrier for active substances to overcome. The skin performs many functions which are necessary for the proper functioning of the entire body, including protection against pathogens and harmful influences of the external environment, such as UV radiation, cold, or heat. In the case of transdermal administration, both the characteristics of the skin and the active substances are of great importance: the condition and properties of the skin, physicochemical parameters of drugs applied to the skin, the presence of sorption promoters, and the quality and properties of drug bases [2–5]. Transdermal penetration also depends on the form of the drug [5].

This study presents a preliminary assessment of skin reflectance during the application of a concentrated cream containing post-biotic plant active ingredients with the use of hyperspectral analysis.

Methods

Model preparation

The model preparation used in the study was a concentrated cream with the following composition: INCI: Avene Thermal Spring Water, Caprylic/Capric Triglyceride, Glycerin, Cetearyl Alcohol, Aquaphillus Dolomite Extract, Arginine, Cetearyl Glucoside, Cetyl Alcohol, Citric Acid, Evening Primrose oil, Palm oil Aminopropanediol Esters, Glyceryl Stearate, Glycine, Oenothera Biennis (Evening Primrose) Oil (Oenothera Biennis Oil), PEG-100 Stearate, Polyacrylate-13, Polyisobutene, Polysorbate 20, Sorbitan Isostearate, Tocopherol, Tocopheryl Acetate, Water (Aqua).

Participants

The study was conducted on 10 healthy participants (9 women and 1 man, age range 23–50 years; mean age 31.8 years). All participants had skin phototype II or III according to the Fitzpatrick classification. The condition for participation was the absence of allergies to cosmetic products and good skin condition. People with a history of anaphylactic shock, people with broken skin, bruises, or skin redness caused by an unknown factor, people who applied cosmetics to the analyzed area on the day of the examination, people with visible bacterial, fungal and viral infections, and people with tattoos were excluded.

Hyperspectral analysis

Hyperspectral imaging is a combination of imaging and spectroscopy, which makes it possible to identify objects in terms of optical and spectral properties. This method is characterized by non-invasiveness. Image acquisition was carried out using a hyperspectral camera, recording radiation of a given energy intensity, in a specific range of spatial coordinates (x, y) and wavelength (λ). In the study, we used the SPECIM IQ hyperspectral camera (SPECIM, Oulu, Finland), which allows for the acquisition of images every 3 nm in the spectral range of 400–1000 nm with a spectral resolution of 5 nm. The image resolution was 512 × 512 pixels, and the dimensions of each pixel were 17.58 × 17.58 μm. The photos were taken using a lens with a focal length of 21 mm, from a distance of approximately 40 cm from the examined object. The images were recorded with a reflectance standard (calibration panel), enabling the determination of the absolute reflectance of the skin in the spectral range of the hyperspectral camera. A detailed analysis of the images taken was performed using the MATLAB 2019 software.

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The course of concentrated cream application

For each participant, an application region measuring 3 cm × 3 cm was marked on the forearm. The tested concentrated cream was taken from a clean glass dish and applied to designated places. Photos with a hyperspectral camera were recorded for the following time points: 1) before application of the concentrated cream (skin only), 2) immediately after application of the concentrated cream (time 0 min.), 3) 10 minutes after application of the concentrated cream (time 10 min.), 4) after 20 minutes after applying the concentrate (time 20 min. incl.). The application region photos have been appropriately labeled and sorted in the order of registration.

Statistical analysis

Data were analyzed statistically with Statistica 13.0 (TIBCO Software, Palo Alto, California, USA). Quantitative data were presented as mean±SD. The Shapiro-Wilk W test and normality plots were used to assess the variable distribution. Parametric tests were used for variables with a normal distribution (t-student for comparing a variable between two samples, ANOVA for comparing more than two samples) and for variables with distributions deviating from the normal distribution i non-parametric tests (Mann-Whitney U for comparing two samples, Kruskal-Wallis for comparison of more than two attempts). Posthoc analyses were performed in case of statistical results obtained in ANOVA or Kruskal-Wallis tests. Statistically significant results were considered to be those with a p-value <0.05.

Results

Analysis of reflectance

The course of the reflectance curve in the range from 400 to approximately 600 nm was similar for all time measurements. Then, in the infrared spectral ranges, a clear decrease in the reflectance value was visible for the measurement at 0 min. i.e. immediately after applying the concentrate. The curve showing the reflectance of the skin itself stands out on the graph as having the highest reflectance values in the infrared light range. However, the curves for 10 min. and time 20 min. overlap each other (Figure 1).

The analysis of the cumulative average reflectance value for each time measurement of the concentrate application on the skin over the entire spectral range showed a significant difference between the measurements (p=0.008). The average reflectance of the skin itself was significantly higher than the reflectance of the skin immediately after applying the concentrate (p=0.005) (Figure 2). Comparisons of the remaining measurement pairs (i.e. skin alone vs time 10 min., skin alone vs time 20 min., time 10 min. vs time 20 min.) did not reveal any significant differences in the reflectance.

Due to visible differences in the course of hyperspectral curves in the infrared range, an analysis of

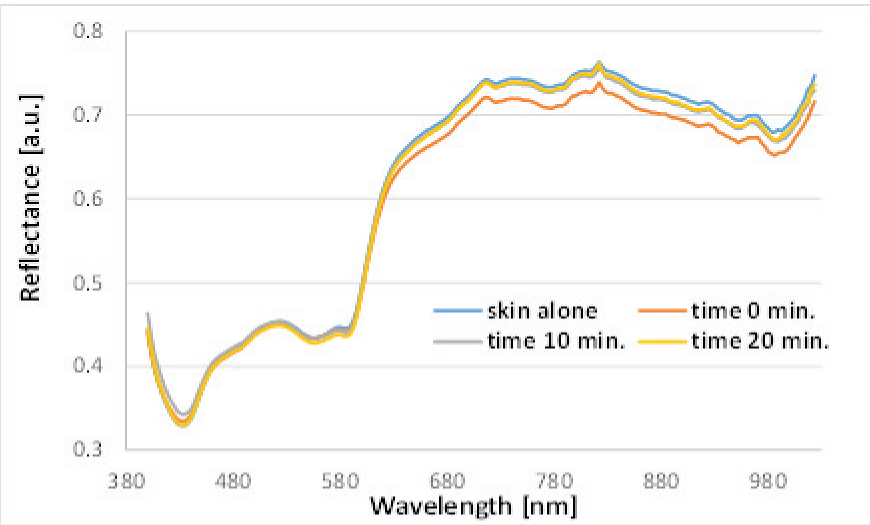

Fig. 1.
Plots of reflectance for subsequent measurements (skin alone, time 0 min., time 10 min., time 20 min.)

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cumulative reflectance was performed in this spectral range (Figure 3). A significant difference was observed in the mean reflectance values between time measurements (p<0.001). In the posthoc analysis, differences were found between individual pairs: skin alone vs. time 0 min., time 0 min. vs time 10 min. and time 0 min. vs time 20 min. (p<0.001 each).

Analysis of the difference between max.–min. reflectance

In the study, we analyzed the quantity of the difference for the maximum and minimum reflectance values in the entire spectral range (Figure 4). This value determines the degree of homogeneity of the skin. The greater the difference, the less homogeneity.

The max.–min. differences obtained for individual measurement points arranged in the following order: the lowest difference was for skin alone, then for time 20 min., for time 0 min., and the highest difference was for time 10 min. This means that the skin without the concentrated cream had the highest homogeneity, immediately after application of the preparation this homogeneity decreases significantly, and 20 minutes after application it slowly returns to values similar to those of the skin itself.

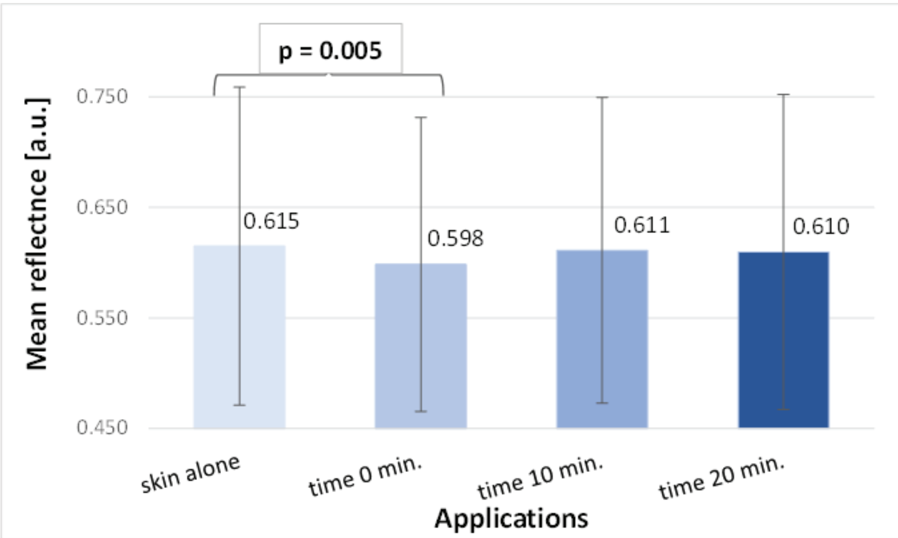

Fig. 2.
Comparison of cumulative average reflectance values for subsequent measurements (skin only, time 0 min., time 10 min., time 20 min.) within the total wavelength range

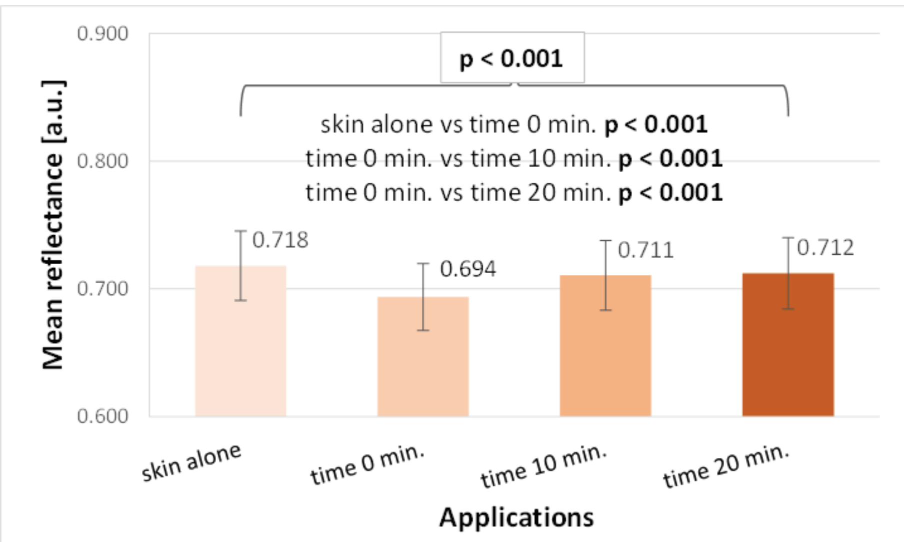

Fig. 3.
Comparison of cumulative average reflectance values for subsequent measurements (skin only, time 0 min., time 10 min., time 20 min.) within the infrared wavelength range (627 nm – 1030 nm).

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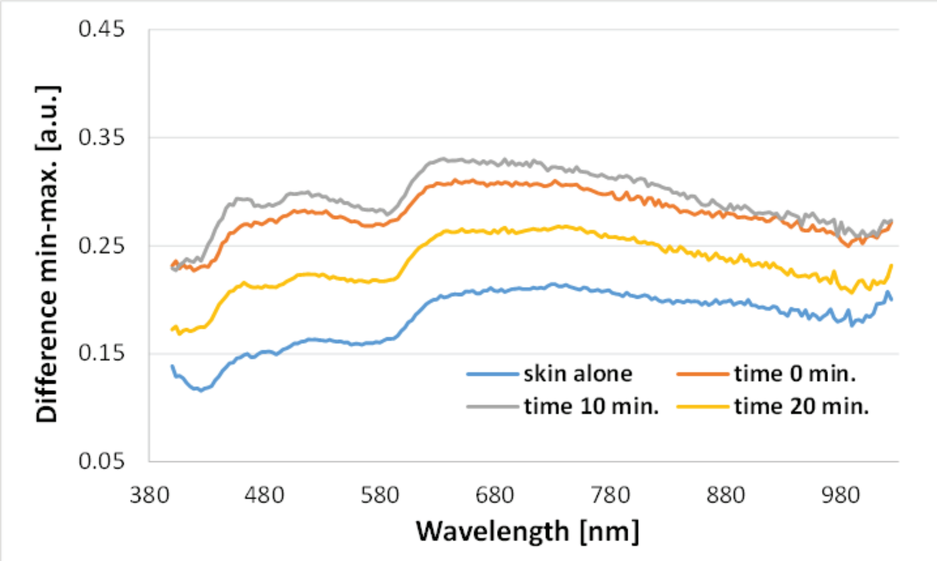

Fig. 4.
Max.–min. reflectance difference plots for each application.

Discussion

The above analysis shows that hyperspectral imaging is a simple, non-invasive, and precise tool for assessing the homogeneity of the application of semi-solid concentrated formulations to the skin and observing the optical properties of the skin.

Homogeneity of application is an important issue due to the effectiveness of ongoing therapies. Uneven application of a therapeutic preparation on the skin results in different effects on the lubricated region – the lack of effect of the drug in one area and its overdose in another place. Hyperspectral imaging also makes it possible to check the correctness of the effect of a given preparation by comparing the obtained reflectance values with those of the same, but properly acting preparation.

The application of a concentrated cream with a UV filter changes the optical properties of the skin, causing increased reflection of incident light, which protects the skin from the harmful effects of ultraviolet radiation.

The analysis showed that the course of the average reflectance curves is similar for all time points in the range from 400 to about 627 nm. Differences in the course of reflectance curves become apparent at wavelengths corresponding to visible red light and infrared (from 627 nm to 1030 nm in the present case). Hydration of the skin, induced by the application of a moisturizer, at this spectral range, causes reduced scattering and thus increased penetration of light into the deeper layers of the skin and results in a decrease in reflectance [6]. Therefore, the average reflectance of the skin without the applied product in the red and infrared light range is the highest, while immediately after the application of concentrated cream, its value decreases. At time points of 10 and 20 minutes after application, the value of the average reflectance approaches that of the skin itself.

We observed that in the spectral range of visible light from 400 nm to 626 nm, the reflectance had a lower value than in the red light and infrared range. This is due to the chromophores present in the skin, including melanin and hemoglobin, whose reflectance curves increase with wavelength and determine (without taking into account many other factors) the appearance of the reflectance curve of human skin [7,8].

The homogeneity of the application is evaluated based on the results of differences in the maximum and minimum values of the average reflectance. If there is a small scatter of reflectance values on the lubricated skin area, then homogeneity is high. Skin alone (i.e., without an applied product) has the highest homogeneity, which decreases immediately after the application of concentrated cream.

After 10 min. of application, the homogeneity continues to decrease slightly, however after 20 min., when the preparation has already started to absorb and "disappear" from the skin surface, the homogeneity begins to increase.

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Conclusions

The average reflectance of the skin not covered with the cream was statistically significantly higher than the average reflectance of the skin immediately after the application of the concentrate in the entire analyzed spectral range. In the range of visible red and infrared light, the same regularity was demonstrated, and additionally the average reflectance of the skin immediately after the application of the concentrate was statistically significantly lower than the average reflectance of the skin 10 and 20 min. after the application of the preparation.

From the analysis, it can be concluded that the presence of chromophores in the skin determines the specific course of the reflectance curve of human skin, where the highest reflectance occurs in the red visible light and infrared range. The highest homogeneity is characterized by the skin itself. After the application of the concentrated cream, there is a decrease in homogeneity. As the product is absorbed into the skin, the parameter increases.

Hyperspectral imaging can be successfully used to assess the quality and efficacy of preparations applied to the skin by analyzing the optical properties of the skin that change after application and to evaluate the effectiveness of therapies that use the skin as a drug delivery route.

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