Hyperspectral analysis as a tool for evaluating the stability of uncoated tablets

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Abstract

In order to assess the stability of a solid drug formulation, imaging methods, including hyperspectral imaging, can be helpful. This technique is categorized as an optical technique used to evaluate the intrinsic quality of the tested products, most commonly foods. However, it may also prove useful in the field of pharmacy responsible for drug control. The aim of the study was to establish whether a noninvasive hyperspectral analysis allows to determine the stability of uncoated tablets containing 250 mg artichoke herb extract. In the study, we used Cynarex tablets with a good expiration date and those with an expired shelf life. All measurements were made using the Specim IQ hyperspectral camera (Finland). The obtained hyperspectral spectra for the two analyzed preparation classes were compared to assess inter alia the homogeneity of the components. The average reflectance assessed together in two spectral bands, i.e. for visible light (400-698 nm) and near-infrared (701-1030 nm), was significantly higher for unexpired tablets. In addition, the analysis homogeneity of ingredient distribution indicated a lower homogeneity of the ingredients in the out-of-date tablets, suggesting a decrease in stability during storage. In conclusion, hyperspectral imaging appears to be a promising, fast and non-destructive method to optimize quality control.

Key words:

hyperspectral analysis, stability, solid dosage forms, uncoated tablets

Introduction

Technologies popular in medicine or other fields of science may also be useful in pharmacy [1,2]. The stability of a drug form determines how long a drug can be stored without compromising its therapeutic effect. This feature plays a key role in the process of approving the finished preparation for use [3]. To assess the stability of a solid drug form, imaging methods can be used, including hyperspectral imaging. It is an optical technique used to assess the internal quality of tested products, including food but also pharmaceuticals. The absorption and reflection of light radiation are specific to each object and are directly related to its chemical composition and physical properties [4]. This technique enables the simultaneous acquisition of spectral and spatial information about the examined objects. The different impact of different wavelengths on the sample allows you to obtain a spectrum that is characteristic of the structure being examined and depends on its composition [5]. However, hyperspectral imaging allows not only the acquisition of the spectrum of a small area of a solid drug form but also the simultaneous imaging of its entire surface. Moreover, it allows for spectral analysis of each pixel of the image separately, enabling, among others, analysis of the uniformity of ingredient distribution, which may be an additional diagnostic criterion in distinguishing stable drugs from those that may have lost their stability due to incorrect storage conditions [6]. This method is characterized by the speed of measurement, ease of sample preparation, and preservation of samples unchanged after measurement.

The disadvantage of this method may be the low penetration depth resulting from the scattering of photons on the object's surface. The average penetration depth depends on the imaging wavelength – the longer the wavelength, the deeper the penetration [4].

The aim of the present study was to establish whether a noninvasive hyperspectral analysis allows to determine the stability of uncoated tablets containing 250 mg artichoke herb extract. Basic and clinical research demonstrated that the extract of artichoke has hepatoprotective and cholesterol-reducing purposes. Cynarin, the main component of the artichoke herb, is a compound with low toxicity.

Material and methods

Analyzed tablets

In the study, two types of the uncoated tablets were analyzed:

1) unexpired *Cynarex* tablets containing 250 mg of dry extract of artichoke herb with a current expiration date (i.e. 2025),

2) expired *Cynarex* tablets with 250 mg of dry extract of artichoke herb and an expiration date set for 2019. Expired tablets were stored at room temperature.

Hyperspectral analysis

Hyperspectral analysis was performed using a Specim IQ hyperspectral camera (Spectral Imaging Ltd., Oulu, Finland) within the wavelength range from 400 nm to 1030 nm (Figure 1).

The hyperspectral profiles of both types of analyzed tablets were compared to evaluate the homogeneity of the ingredients. There is an association between the differences between the curves in the hyperspectral profiles and the homogeneity of the ingredients of the tablets, i.e., the greater the difference between the maximum and minimum reflectance of the hyperspectral profile of the analyzed tablet, the lower the homogeneity.

Fig. 1.
Specim IQ camera (on the left) and the way of placing an example tablet on a reference plate (on the right).

Image analysis, conversion of raw data into a matrix, and extraction of the selected features were performed with the use of MATLAB Version 7.11.0.584 (R2010b) software. The study was funded within the PCN-1-058/K/2/O project funded by the Medical University of Silesia in Katowice (Poland).

Statistical analysis

The obtained data were statistically analyzed using Statistica 13.0 (StatSoft; Statistica, Tulsa, OK, USA). Data are presented as means ± standard deviations (M±SD). The normality of the distribution of quantitative data was assessed using the Shapiro-Wilk W test. The Student's T-test was used to analyze data showing a normal distribution, while the Mann-Whitney U test was used for data that did not show a normal distribution.

Results

In the hyperspectral image, the average reflectance of unexpired tablets with artichoke extract coincided with the average reflectance of expired tablets within the wavelength range from 400 nm to 500 nm. The spectra for expired and non-expired tablets had absorption peaks in similar ranges. Upward peaks can be observed at 716 nm, 828 nm, and 924 nm (Figure 2).

In the wavelength range above 500 nm, the spectra for both types of tablets begin to diverge and the difference is statistically significant ($p<0.001$). Unexpired tablets with artichoke extract have a higher average reflectance. Higher reflectance means more light is reflected from the tablet surface, thus less light is transmitted into the tablet.

We also analyzed the mean reflectance obtained by hyperspectral analysis evaluated jointly in two spectral ranges, i.e. for visible light (400–698 nm) and near-infrared light (701–1030 nm). Figure 3 shows the average reflectance values in the selected spectral ranges. As expected, the average reflectance value in both visible and near-infrared light is significantly higher for non-expired tablets.

In addition, we analyzed the homogeneity of ingredient distribution for both types of tablets on the basis of the difference between maximum and minimum reflectance. Table 1 shows the results of this analysis.

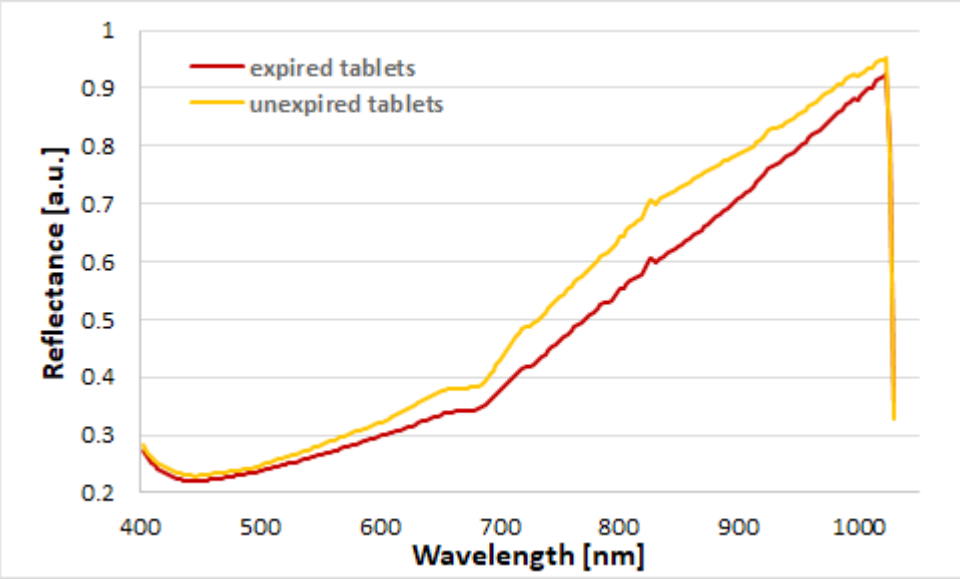

Fig. 2.
Average reflectance charts ranging from 400-1100 nm for expired and unexpired tablets with artichoke extract.

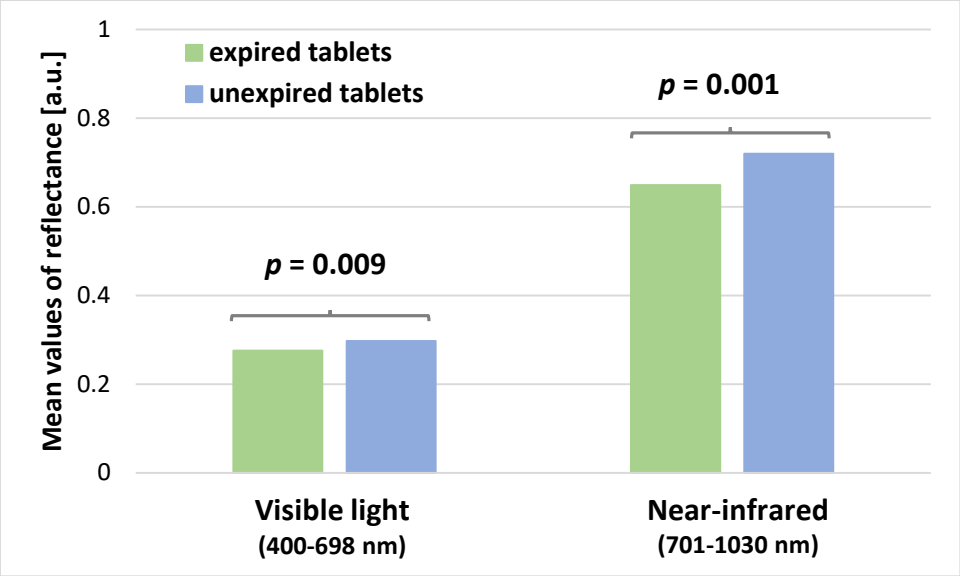

Fig. 3.
Average reflectance obtained in the hyperspectral analysis within the distinguished spectral ranges (i.e. visible light and near-infrared) between expired and unexpired tablets with artichoke extract.

Table 1.
The mean differences between the maximum and minimum reflectance of the analyzed tablets containing artichoke extract

Type of the tablets	M±SD	*p*
Unexpired	0.032±0.036	**<0.001**
Expired	0.312±0.059	

We observed that the difference between the maximum and minimum reflectance varied statistically between the expired and unexpired uncoated tablets with artichoke extract ($p<0.001$). For expired tablets, this difference was significantly higher than in the case of unexpired tablets which means that during the storage the homogeneity of ingredient distribution lowered.

Discussion

Access to good quality, safe, and therapeutically effective medicinal products is regulated by law by controlling them at individual stages of their development [7]. Measuring the reflectance of the tested pharmaceutical preparation may indicate its quality because it allows for estimating the changes occurring inside and on the surface. Consequently, the reflectance value can easily indicate the stability of the drug during storage. During hyperspectral analysis, cameras used for these measurements record a sequence of images, most often in the visible and near-infrared spectral ranges [8]. When the tested object is illuminated, chemical compounds absorb or reflect energy differently at each wavelength (in the case of our research, the measurement took place every 3.1 nm), allowing obtaining information about specific physicochemical changes.

The excipients in the tablets selected for present analysis are microcrystalline cellulose with the addition of colloidal silicon dioxide, crospovidone, magnesium stearate, and talc. These are standard excipients in forming uncoated tablets which makes the identification of hyperspectral parameters easier than in the case of coated tablets due to the greater uniformity of coated tablets [9].

Our study demonstrated that during storage mean values of reflectance when distinguished into visible and near-infrared light were higher in unexpired tablets with artichoke extract compared to expired ones. We also found that unexpired tablets

have greater homogeneity of the ingredients than tablets for which the validity period has passed. In our previous study, the homogeneity of coated tablets with nifuroxazide was analyzed [2]. In addition to expired and unexpired tablets, we also analyzed tablets subjected to thermal stress (40°C for 3 months) and we demonstrated that stressed tablets had the best homogeneity, most likely due to moisture loss.

Similar results were obtained in the study by Pavurala et al [10], in which the use of hyperspectral imaging to assess the uniformity of coating thickness of transdermal drug delivery systems (TDS) was tested. The authors concluded that near-infra-red hyperspectral imaging was successfully validated as a potential non-destructive analytical technique for measuring TDS coating thickness uniformity for dry coatings. The method was also tested by Hossein Vakili et. al. [11] in printed personalized solid dosage forms to quantify the drug content and spatial distribution of the API on the surface of printed solid dosage forms. The authors also concluded this technique as rapid and non-destructive, and more importantly reliable.

Conclusions

Analysis using a hyperspectral camera gives new information on the stability of the uncoated tablets with dry extract of artichoke herb. Unexpired tablets showed higher reflectance within the wavelength ranges from 500 nm to 1030 nm than expired tablets which indicates that more light is reflected from the unexpired tablets. Also, the homogeneity of the tablets assessed on the basis of the difference between max-min reflectance is better for unexpired tablets compared to expired ones.

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