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Directional Hemispherical Reflectance as a Quick Method for Analysis of Degradation Processes in Commercial Effervescent Tablets †

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Abstract: In the present study we aimed to evaluate the total directional hemispherical reflectance (THR) in expired and unexpired effervescent tablets. Expired tablets were stored under ambient conditions. The THR was measured using SOC-410 Directional Hemispherical Reflectometer (Surface Optics Corporation, San Diego, CA, USA) in seven wavelength bands from ultraviolet, through visible, to near-infrared light. Significantly higher values of THR for the range of 700–1100 nm, and 1700–2500 nm were observed for expired tablets than for unexpired tablets ($p < 0.001$). The measurement of THR may be a rapid method to detect adverse physicochemical changes in effervescent tablets and can be used for a further detailed evaluation of active pharmaceutical ingredients (APIs) and related degradation products.

Keywords: effervescent tablets; solid dosage forms; directional hemispherical reflectance; reflectometer

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1. Introduction

The degradation of active pharmaceutical ingredients (APIs) and the subsequent formation of degradation products affect the pharmaceutical quality of a medicinal product. Therefore, rapid and effective detection of adverse changes occurring in a medicinal product is very important and may be performed with a use of several novel techniques. Among these methods, the analysis of total directional hemispherical reflectance (THR) is of increasing importance. Previously, the THR was used to distinguish falsified pharmaceuticals from the original ones [1]. Analysis of reflectance and transmittance may be useful in the prediction of drug contents in tablets [2]. In addition, some physical aspects of the tablets, i.e., the hardness and porosity may also be evaluated using the near-infrared diffuse reflectance spectroscopy [3].

We assumed that using the method of hemispherical reflectance, adverse physicochemical changes in solid dosage drug forms can be detected.

The aim of the present study was to assess the total directional hemispherical reflectance (THR) of effervescent tablets containing magnesium and vitamin B6 during storage at ambient conditions.

2. Methods

2.1. Analyzed Tablets

The expired (n = 20; expiration date 04.2021) and unexpired (n = 20; expiration 03.2024) effervescent tablets containing magnesium and vitamin B6 (Zdrovit; Natur Produkt Pharma sp. z o. o., Ostrów Mazowiecka, Poland) were analyzed. Both tested types of tablets were evaluated in terms of diameter and thickness (measured using a caliper with an accuracy of 0.1 mm), and in terms of weight.

2.2. Images of the Tablets

The external appearance of the effervescent tablets was also assessed using Olympus Tough camera with a Dermlite attachment (Olympus Europa Se & Co. KG, Hamburg, Germany). Images under visible and UV lights were taken.

2.3. Reflectance Measurements

The measurements of THR were performed with the use of SOC-410 Directional Hemispherical Reflectometer (USA) within seven wavelength bands from ultraviolet to near-infrared, i.e., 335–380 nm, 400–540 nm, 480–600 nm, 590–720 nm, 700–1100 nm, 1000–1700 nm, 1700–2500 nm. The results for total reflectance were obtained for the beam at an angle of 20°. The mirror and diffuse calibration coupons were used to calibrate the reflectometer before the measurement. Each tablet was measured three times.

2.4. Statistical Analyses

Data were analyzed statistically using Statistica 13 software (StatSoft, Tulsa, OK, USA). The values of THR were presented as mean and standard deviation. Due to the preliminary stage of the study, we used a nonparametric test of U Mann-Whitney to compare reflectance values between expired and unexpired effervescent tablets in all spectral bands. The value of $p \leq 0.05$ was considered statistically significant.

3. Results and Discussion

The basic ingredients of effervescent tablets, in addition to the medicinal substance, are a soluble organic acid (usually citric, tartaric, malic, fumaric or adipic acid) and an alkali metal carbonate salt (sodium bicarbonate/carbonate or potassium bicarbonate/carbonate). These substances react in the presence of water to release carbon dioxide, resulting in the rapid release of the active pharmaceutical ingredient [4–6]. Unfortunately, effervescent components are hygroscopic and moisture-labile, and storing tablets at temperatures above 25 °C, accelerates the decomposition of bicarbonate to carbonate. Increasingly, this form provides a source of vitamins and/or minerals or other substances with nutritional or other physiological effects [7,8].

Solid oral dosage forms are commonly manufactured in batches, of which only randomly selected samples are tested by often time-consuming off-line testing. The use of spectroscopic techniques allows for obtaining new spatial information about the sample and additional quality control of samples from a given batch in a non-destructive, non-invasive, fast, and time-saving manner. Moreover, spectroscopic techniques and imaging techniques can be used not only during the entire production process but also during the storage of a pharmaceutical product, making it possible to correlate the data obtained from them with the data obtained using pharmacopoeial stability assessment methods.

3.1. Characteristics of the Analyzed Types of Effervescent Tablets

Both analyzed types of effervescent tablets were cylindrical with flat top and bottom surfaces. The expired effervescent tablets showed some discoloration, impurities, or cracks (Figure 1). Additionally, both types of tablets, expired and unexpired, were characterized by the amount of powder on the surface, which may suggest high friability. The

mean thickness, diameter, and weight of the unexpired tablets were 5.66 mm, 25.20 mm and 4.012 g, respectively. The mean thickness, diameter, and weight of the expired tablets were as follows: 5.73 mm, 25.23 mm and 4.007 g, respectively.

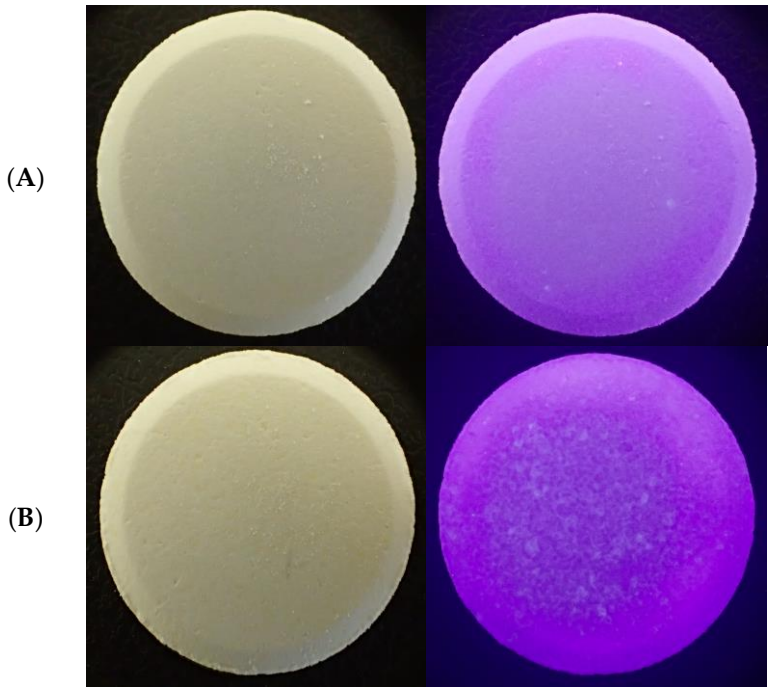

Figure 1. Images of the effervescent tablets (**A**—unexpired; **B**—expired) under visible and UV light.

3.2. Comparison of Expired and Unexpired Tablets in Terms of THR Value

The mean THR was significantly higher within the ranges of 400–540 nm, 480–600, 590–720, and 1000–1700 for the unexpired effervescent tablets compared to expired tablets ($p < 0.001$). In turn, a significantly higher value of THR for the range of 700–1100 nm, and 1700–2500 nm was observed for expired tablets than for unexpired tablets ($p < 0.001$) (Figure 2). Surprisingly, we have observed significant differences in mean THR between the top side and the bottom side of tablets.

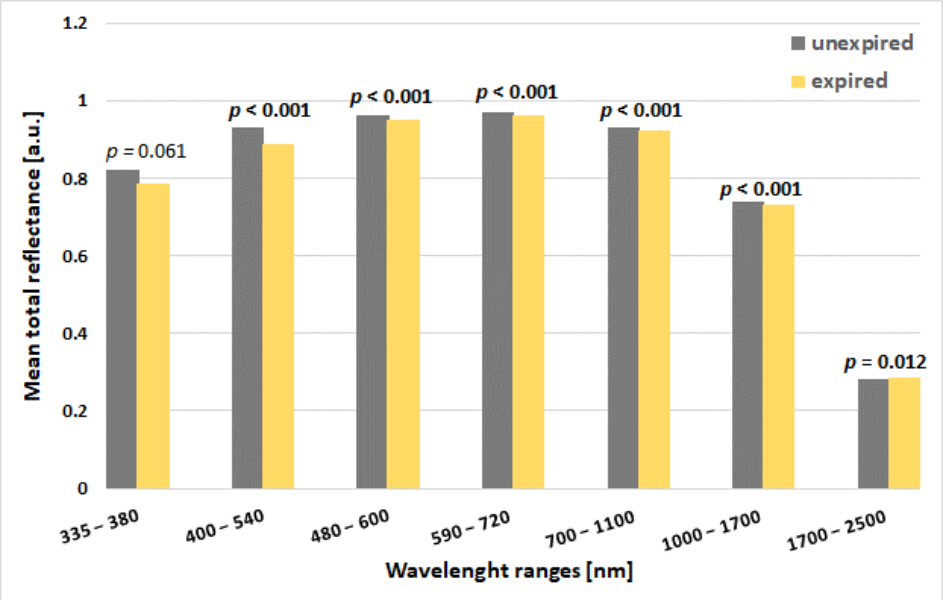

Figure 2. Mean values of total reflectance for expired and unexpired effervescent tablets containing magnesium and vitamin B6. Significant differences are in bold.

4. Conclusions

Lower values of THR for expired effervescent tablets compared to unexpired ones may be explained by the fact that some physicochemical changes occurred during the storage and in this state, the reflectance of the light beam is lower since more light is transmitted inside the tablet.

The measurement of THR may be a rapid test for detecting adverse physicochemical changes in these tablets and can be used for a further detailed evaluation of API and related degradation products.

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Conflicts of Interest: The authors declare no conflict of interest.

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