

Proceeding Paper

Directional Hemispherical Reflectance in the Analysis of Expired and Unexpired Tablets Containing Nifuroxazide—The Results of a Pilot Study [†]

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Abstract: The study aimed to assess the possible usage of total directional hemispherical reflectance (DHR) in terms of the stability of tablets during storage. Expired and unexpired coating tablets containing nifuroxazide were analyzed. Reflectance was determined in seven wavelength bands using SOC-410 Directional Hemispherical Reflectometer (Surface Optics Corporation, USA). Significantly lower ($p < 0.001$) mean total DHR was observed for expired tablets in comparison to unexpired tablets for all the spectral bands apart from one of the infrared range (i.e., 1000–1700 nm). The results indicated that total reflectance lowered during the storage in all spectral bands except infrared.

Keywords: solid dosage forms; drug storage; directional hemispherical reflectance

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1. Introduction

The assessment of physical and chemical stability of a medicinal substance and its drug form is extremely important from a technological point of view. Physical and chemical changes occurring during storage of the drug form may adversely affect its quality, and in turn the safety and efficacy of the treatment. The degradation of the active substance or excipients is caused in particular by sunlight but also by high temperature [1]. The change of physicochemical properties of the drug form is particularly important for uncoated tablets since for the film-coated tablets, the presence of the coating may to some extent offset the adverse effects of storage conditions on the physical stability of the drug.

In the analysis of finished pharmaceutical products, a number of innovative analytical techniques are more and more often used, which allow for the identification of changes occurring in the solid phase [2–5]. These techniques include among others Raman spectroscopy, scanning electron microscopy, computer microtomography, directional hemispherical reflectance analysis and hyperspectral analysis. However, the above mentioned methods are still not standard procedures in pharmaceutical research.

In the present study we selected nifuroxazide as a model drug. Nifuroxazide is an oral nitrofurantoin antibiotic used in bacterial diarrhea [6]. It has been shown to be active against most bacteria causing intestinal infections, both the gram-positive ones (e.g., *Staphylococcus*, *Streptococcus*) and the gram-negative ones (e.g., *Salmonella*, *Shigella*, *Klebsiella*, *Escherichia*, *Citrobacter*, *Enterobacter*, *Yersinia*, as well as *Vibrio cholerae*). Numerous published data have documented anti-cancer activity of nifuroxazide and nitrofurantoin derivatives [7,8]. In addition, the possible use of nifuroxazide in the treatment of some inflammatory diseases was also reported [9–13].

The present study aimed to assess the possible usage of total directional hemispherical reflectance in terms of the stability of tablets during storage.

2. Methods

The expired ($n = 6$; expire date November 2019) and unexpired ($n = 6$; expire date November 2024) coating tablets containing nifuroxazide (HASCO-LEK S.A., Poland) were analyzed. Directional reflectance was determined to assess the total hemispherical reflectance (THR) in seven wavelength bands (i.e., ultraviolet, visible light, near infrared) using SOC-410 Directional Hemispherical Reflectometer (Surface Optics Corporation, USA). THR is the reflectance measured of all light that is scattered off of a test sample at all angles. The measurement of DHR does not discriminate the angle of reflectance; only the total amount of reflected light.

For each tablet 6 measurements within all bands were done.

Statistical analysis were performed with the use of Statistica 13.0 software (STATSOFT; Statistica, Tulsa, OK, USA). Directional reflectance was shown as mean, standard deviation, median, minimum value, maximum value, the 1st and 3rd quartile. Due to the preliminary data we used nonparametric test of U Mann-Whitney to compare reflectance values between expired and unexpired tablets in all spectral bands. The value of $p \leq 0.05$ was considered as statistically significant.

3. Results and Discussion

The reflectance of the solid dosage form is mainly influenced by the quantitative and qualitative composition determining the absorption/scattering of radiation but also by the surface structure. Thus, the analysis of directional reflectance is able to simultaneously determine changes in the composition of the drug as well as changes in its physical structure. So far, no data on the use of hemispherical directional reflectance in the tablet stability are available. Recently, this method was used to distinguish the original Viagra® tablets from the counterfeit ones [14,15]. The authors demonstrated significant differences in reflectance (maximum difference for 1619.75 nm) of the surface of the original Viagra® and counterfeit tablets [15]. The evaluation of reflectance is a fast, time-saving method of high sensitivity and specificity. What more important, no destruction of the drug form is required during the measurement.

Assessment of Directional Reflectance

Mean values of total DHR of the expired and unexpired analyzed tablets within seven spectral bands are shown in Figure 1.

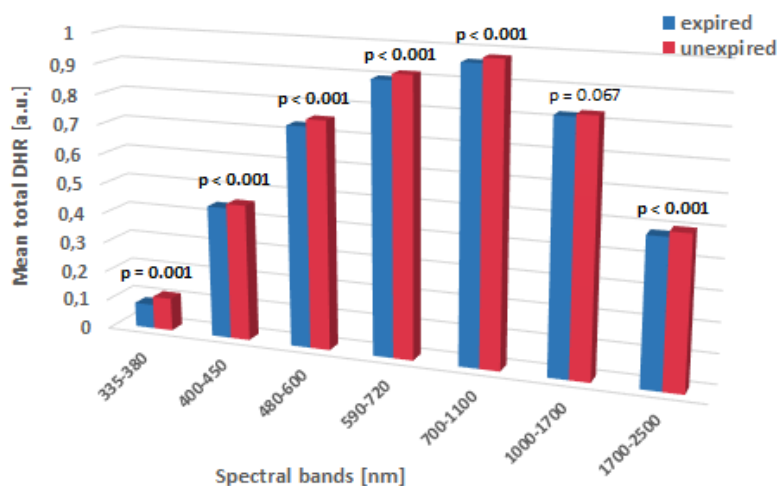


Figure 1. Mean values of total DHR for expired and unexpired tablets containing nifuroxazide. DHR—directional hemispherical reflectance. Significant differences are in bold.

Significantly lower mean DHR was observed for expired tablets in relation to unexpired tablets for all the spectral bands apart from 1000–1700 nm. For both expired and unexpired tablets, the highest total DHR was observed within the spectral band of 700–1100 nm while the lowest for the band of 335–380 nm.

4. Conclusions

The presented method can be a useful tool for monitoring the stability and quality control of solid dosage forms. The results indicated that total reflectance lowered during the storage in all spectral bands except infrared.

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

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