engineering proceedings

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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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† Presented at the 1st International Electronic Conference on Processes: Processes System Innovation, 17–31 May 2022; Available online: https://sciforum.net/event/ECP2022.

Abstract: This 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 an 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 in 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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Citation: Sarecka-Hujar, B.; Szulc-Musioł, B. Directional Hemispherical Reflectance in the Analysis of Expired and Unexpired Tablets Containing Nifuroxazide—The Results of a Pilot Study. *Eng. Proc.* **2022**, *19*, 39. https://doi.org/10.3390/ECP2022-12616

Academic Editor: Hoon Kim

Published: 17 May 2022

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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 in 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 abovementioned methods are still not standard procedures in pharmaceutical research.

In the present study, we selected nifuroxazide as a model drug. Nifuroxazide is an oral nitrofuran 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 the anti-cancer activity of nifuroxazide and nitrofuran 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; expiry date November 2019) and unexpired (n = 6; expiry date November 2024) coated 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 for all light that is scattered off 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 taken.

Statistical analysis was 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 Mann–Whitney U test 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 original Viagra® tablets from counterfeit ones [14,15]. The authors demonstrated significant differences in reflectance (maximum difference for 1619.75 nm) for 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 is 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.

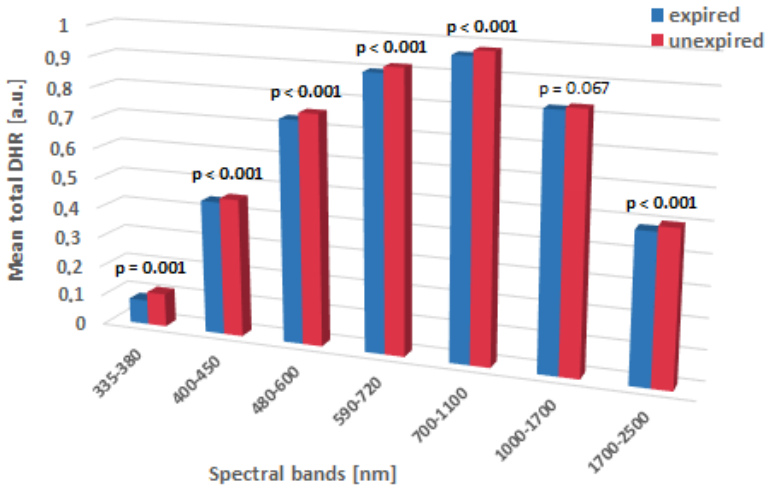

Figure 1. Mean values of total DHR for expired and unexpired tablets containing nifuroxazide. DHR—directional hemispherical reflectance. Significant differences are in bold.

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 could 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.

Author Contributions: Both authors B.S.-H. and B.S.-M. participated equally in conceptualization, methodology, software, formal analysis, investigation, data curation, writing—original draft preparation, writing—review and editing, visualization, and supervision. All authors have read and agreed to the published version of the manuscript.

Funding: The research was funded by the Medical University of Silesia in Katowice, Poland (project number PCN-1-097/N/1/F).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request to the Department of Basic Biomedical Science, School of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia in Katowice, Poland. The data are not publicly available due to privacy restrictions.

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

References

1. Bott, R.F.; Oliveira, W.P. Storage conditions for stability testing of pharmaceuticals in hot and humid regions. *Drug Dev. Ind. Pharm.* **2007**, *33*, 393–401. [CrossRef] [PubMed]
2. Han, X.; Cheng, F.J.; Di, B.; Xu, H.; Song, M.; Hang, T.J.; Lu, Y.T. Identification and characterization of new impurities in zopiclone tablets by LC-QTOF-MS. *J. Pharm. Biomed. Anal.* **2021**, *199*, 114056. [CrossRef] [PubMed]
3. Odani, N.; Mohan, S.; Kato, E.; Feng, H.; Li, Y.; Hossain, M.N.; Drennen, J.K.; Anderson, C.A. Determining the effect of photodegradation on film coated nifedipine tablets with terahertz based coating thickness measurements. *Eur. J. Pharm. Biopharm.* **2019**, *145*, 35–41. [CrossRef] [PubMed]
4. Yamashita, S.; Iguchi, K.; Noguchi, Y.; Sakai, C.; Yokoyama, S.; Ino, Y.; Hayashi, H.; Teramachi, H.; Sako, M.; Sugiyama, T. Color change in Perlodel® tablets induced by LED lighting—Photolysis of bromocriptine mesylate. *Pharmazie* **2019**, *74*, 286–289. [PubMed]
5. Thakral, N.K.; Yamada, H.; Stephenson, G.A.; Suryanarayanan, R. Spatial Distribution of Trehalose Dihydrate Crystallization in Tablets by X-ray Diffractometry. *Mol. Pharm.* **2015**, *12*, 3766–3775. [CrossRef] [PubMed]
6. Vanhoof, R.; Hubrechts, J.M.; Roebben, E.; Nyssen, H.J.; Nulens, E.; Leger, J.; De Schepper, N. The comparative activity of pefloxacin, enoxacin, ciprofloxacin and 13 other antimicrobial agents against enteropathogenic microorganisms. *Infection* **1986**, *14*, 294–298. [CrossRef]
7. Bailly, C. Toward a repositioning of the antibacterial drug nifuroxazide for cancer treatment. *Drug Discov. Today* **2019**, *24*, 1930–1936. [CrossRef]
8. El-Sherbiny, M.; El-Sayed, R.M.; Helal, M.A.; Ibrahiem, A.T.; Elmahdi, H.S.; Eladl, M.A.; Bilay, S.E.; Alshahrani, A.M.; Tawfik, M.K.; Hamed, Z.E.; et al. Nifuroxazide Mitigates Angiogenesis in Ehlrich's Solid Carcinoma: Molecular Docking, Bioinformatic and Experimental Studies on Inhibition of Il-6/Jak2/Stat3 Signaling. *Molecules* **2021**, *13*, 6858. [CrossRef] [PubMed]
9. Liu, J.Y.; Zhang, Y.C.; Xie, R.R.; Song, L.N.; Yang, W.L.; Xin, Z.; Cao, X.; Yang, J.K. Nifuroxazide improves insulin secretion and attenuates high glucose-induced inflammation and apoptosis in INS-1 cells. *Eur. J. Pharmacol.* **2021**, *15*, 174042. [CrossRef] [PubMed]
10. Zhu, Y.; Ye, T.; Yu, X.; Lei, Q.; Yang, F.; Xia, Y.; Song, X.; Liu, L.; Deng, H.; Gao, T.; et al. Nifuroxazide exerts potent anti-tumor and anti-metastasis activity in melanoma. *Sci. Rep.* **2016**, *6*, 20253. [CrossRef] [PubMed]
11. Zhao, T.; Jia, H.; Cheng, Q.; Xiao, Y.; Li, M.; Ren, W.; Li, C.; Feng, Y.; Feng, Z.; Wang, H.; et al. Nifuroxazide prompts antitumor immune response of TCL-loaded DC in mice with orthotopically-implanted hepatocarcinoma. *Oncol. Rep.* **2017**, *37*, 3405–3414. [CrossRef] [PubMed]
12. Said, E.; Zaitone, S.A.; Eldosoky, M.; Elsherbiny, N.M. Nifuroxazide, a STAT3 inhibitor, mitigates inflammatory burden and protects against diabetes-induced nephropathy in rats. *Chem. Biol. Interact.* **2018**, *1*, 111–120. [CrossRef] [PubMed]
13. Jia, H.; Zhao, T.; Ji, Y.; Jia, X.; Ren, W.; Li, C.; Li, M.; Xiao, Y.; Wang, H.; Xu, K. Combined nifuroxazide and SAT05f therapy reduces graft-versus-host disease after experimental allogeneic bone marrow transplantation. *Cell Death Dis.* **2016**, *1*, e2507. [CrossRef] [PubMed]

14. Wilczyński, S.; Koprowski, R.; Błońska-Fajfrowska, B. Directional reflectance analysis for identifying counterfeit drugs: Preliminary study. *J. Pharm. Biomed. Anal.* **2016**, *30*, 341–346. [CrossRef] [PubMed]
15. Wilczyński, S.; Koprowski, R.; Marmion, M.; Duda, P.; Błońska-Fajfrowska, B. The use of hyperspectral imaging in the VNIR (400–1000 nm) and SWIR range (1000–2500 nm) for detecting counterfeit drugs with identical API composition. *Talanta* **2016**, *160*, 1–8. [CrossRef] [PubMed]