Directional reflectance analysis for identifying counterfeit drugs: Preliminary study

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A B S T R A C T

The WHO estimates that up to 10% of drugs on the market may be counterfeit. In order to prevent intensification of the phenomenon of drug counterfeiting, the methods for distinguishing genuine medicines from fake ones need to be developed.

The aim of this study was to try to develop simple, reproducible and inexpensive method for distinguishing between original and counterfeit medicines based on the measurement of directional reflectance.

The directional reflectance of 6 original Viagra® tablets (Pfizer) and 24 (4 different batches) counterfeit tablets (imitating Viagra®) was examined in six spectral bands: from 0.9 to 1.1 μm, from 1.9 to 2.6 μm, from 3.0 to 4.0 μm, from 3.0 to 5.0 μm, from 4.0 to 5.0 μm, from 8.0 to 12.0 μm, and for two angles of incidence, 20° and 60°. Directional hemispherical reflectometer was applied to measure directional reflectance.

Significant statistical differences between the directional reflectance of the original Viagra® and counterfeit tablets were registered. Any difference in the value of directional reflectance for any spectral band or angle of incidence identifies the drug as a fake one.

The proposed method of directional reflectance analysis enables to differentiate between the real Viagra® and fake tablets. Directional reflectance analysis is a fast (measurement time under 5s), cheap and reproducible method which does not require expensive equipment or specialized laboratory staff.

It also seems to be an effective method, however, the effectiveness will be assessed after the extension of research.

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1. Introduction

In the past 15 years drug counterfeiting has become a global phenomenon that is constantly burgeoning [1–5]. According to the WHO, a counterfeit medicine is defined as: "one which is deliberately and fraudulently mislabeled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without the active pharmaceutical ingredients (APIs), with insufficient active ingredient or with fake packaging." [5]. The WHO estimates that up to 10% of drugs on the market can be falsified [5]. In order to prevent counterfeiting, manufacturers protect themselves by using special

package labelling (e.g. holograms) or product labelling [6,7]. However, despite increasing efforts to eliminate counterfeit products from the pharmaceutical market, this phenomenon keeps on burgeoning [2,8,9]. In many developing countries, especially in Africa, some parts of Asia and Latin America, more than 30% of medicines are counterfeit products [10,11]. The form of the drug which is particularly vulnerable to counterfeiting is a tablet [12].

To prevent intensification of the phenomenon of drug counterfeiting, the methods for distinguishing between genuine and fake medicines need to be developed first. Currently, the advanced methods of chemical analysis, such as Raman spectroscopy [13], chromatography methods [14] or mass spectrometry [15], are mainly applied in this field. The use of these advanced laboratory methods enables to determine the composition of counterfeit products, and on this basis, their possible adverse effects on patients who have taken a counterfeit drug. However, the first step in the fight against drug counterfeiting should be the fastest possi-

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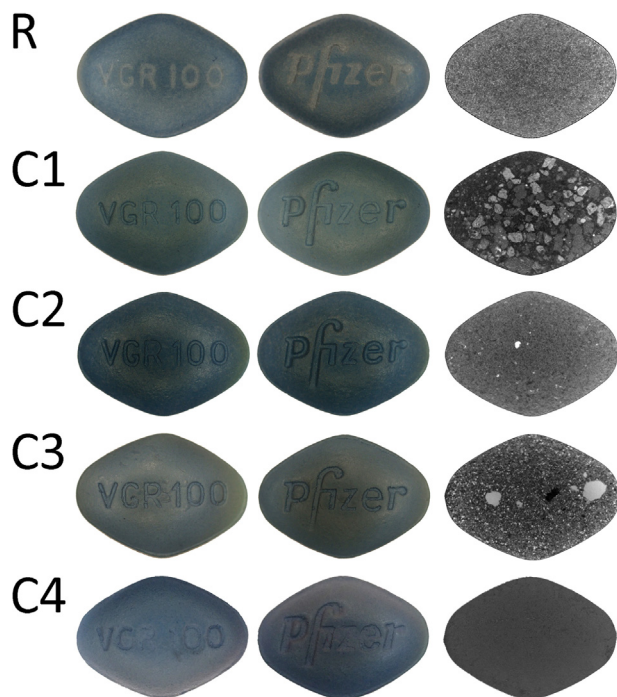 E-mail address: swilczynski@sum.edu.pl (S. Wilczyński).

Fig. 1. Image of the original Viagra® (R) and counterfeit tablets (C1,C2,C3,C4); the first and second column are the tablet obverse and reverse respectively, and the third column represents their microtomographic scans.

ble withdrawal of the falsified drug from the market [3]. For this purpose, it is necessary to develop a reliable and simple tool to distinguish between genuine and counterfeit drugs. The advanced laboratory methods require the possession of laboratory facilities and advanced knowledge and experience of the staff engaged in this type of analysis, which significantly limits their effectiveness in screening analysis of potentially counterfeit medicines.

The aim of this study was to try to develop a new, rapid, reproducible, reliable and cheap method for distinguishing original drugs from counterfeit ones under field conditions (mobile laboratories, customs, police). This method should enable to distinguish between the real and fake medicine without special laboratory facilities using an easy-to-use, portable device and provide immediate and repeatable results of analysis. It appears that directional reflectance (DR) analysis may become such a method.

2. Material and methods

2.1. Tablets

The original and counterfeit tablets of one of the most counterfeited drugs − Viagra® produced by Pfizer were compared. The original drug was purchased in a pharmacy in Poland. The study used Viagra® containing 100 mg of sildenafil citrate. The counterfeit drugs was purchased on the black market from a sellers, who advertised it on the Internet. 6 original Viagra® tablets (R) and 6 tablets from 4 different batches of counterfeit drugs (C1, C2, C3 and C4), a total of 32 tablets, were tested. The counterfeit Viagra® came from four independent sources. Fig. 1 shows images of the original and counterfeit tablets and, in the last column, their microtomographic scan. The microtomographic scan demonstrates that the structure of each of the 4 fake tablet batches is different, despite the great similarity of tablets in visible light.

According to the information provided by sellers of counterfeit drugs, they should also contain 100 mg of sildenafil citrate.
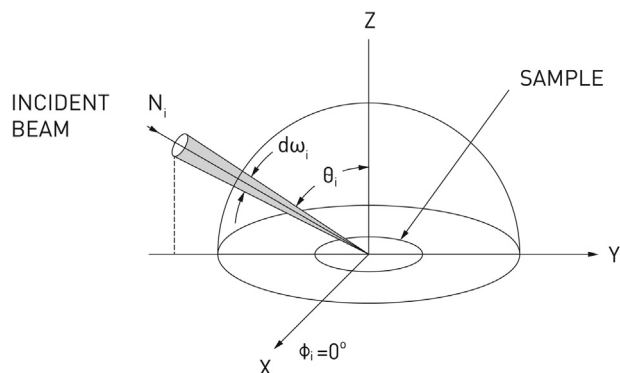

Fig. 2. Diagram illustrating the concept of directional reflectance [16].

The colour, weight and volume of the tested drugs, both counterfeit and real, were very similar: colour of tablets − light blue, the mass of the original and falsified tablets 622 mg ± 17 mg and 651 mg ± 57 mg respectively, the volume of the tablets 443,22 ± 6,31 mm³ and 554,01 ± 61,88 mm³, respectively. The volume of the tablets was determined using the Steinbichler COMET L3D scanner (Steinbichler, Germany). The visual resemblance of the falsified drug to the original one prevents a clear distinction of the medicines.

2.2. Directional reflectance analysis in the near-infrared range

Commercially available SOC-410 Directional Hemispherical Reflectometer (Surface Optics Corporation, San Diego (CA) USA) was applied to determine directional reflectance. The SOC-410 equipped with the DHR (Directional Hemispherical Reflectance) Measurement Head measures the integrated surface reflectance of a surface at two different angles of incidence (20° and 60°) and for six discreet wavelength bands in the 0.9 μm to 12 μm spectral band. The integrating sphere captures the reflected light from the target material (tablet surface), integrating reflections in all directions. Wavelength filtered detectors measure the total light reflected in each wavelength band and converts it to an analog electrical signal.

The directional reflectance (V_d) of a surface is defined as the ratio of the total energy reflected into the subtending hemisphere to the energy incident on the studied surface.

Following the notation of Nicodemus [16], directional reflectance may be expressed in terms of primary quantities as:

$$V_d\left(\theta_i \phi_i\right) = \frac{\int_0^{2\pi} \int_0^{\pi/2} N_r \sin\theta_r \cos\theta_r d\theta_r d\phi_r}{N_i \sin\theta_i \cos\theta_i d\theta_i d\phi_i}$$

where,

V_d − is the reflectance,

θ_i, φ_i − direction of energy incident on the surface (Fig. 2),

N_i − is a radiance function of both position and direction, incident on the surface of an opaque body where some of the radiation is absorbed and the rest is reflected (includes diffuse reflectance or scattering) (Fig. 2),

N_r − is a radiance of the reflected radiation (also a function of position and direction) (Fig. 2).

Directional reflectance (V) was examined for 6 discrete spectral bands for two angles of incidence, 20° and 60° (Table 1). Directional reflectance measurement involves placing the sampling port perpendicular to the surface of the tested tablet. The measurement lasted about 5 s. At this time, the surface of the tablet was sampled three times for 6 spectral bands and for two angles of the incident beam. The measurement was repeated six times for each tested tablet.