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Detecting Falsified Viagra Using Miniaturized Consumer Near-Infrared Spectroscopy

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Abstract

The miniaturized Near-Infrared Spectroscopy (NIRS) enables convenient, non-destructive and real-time testing of medicines that are circulating on the field or throughout the supply chain. We have successfully been able to detect falsified Viagra using a new low-cost, consumer-type NIRS. In like manner, we have distinguished the original Viagra from its generic versions with the same dose. This is a promising way of ensuring medicines authenticity by looking at their chemical 'fingerprints'. Portable screening technologies for medicine quality assurance on the field or throughout the supply chain are currently growing and complementing the current approach for combating the falsified products, i.e., safety features on the packaging and laboratory analysis of suspect samples. In total, 78 spectra of Sildenafil-based tablets were recorded and classified using the K-Nearest Neighbors algorithm that relies on the Euclidean distances between measured values. Accuracy of our model was assessed using cross-validation and bootstrapping techniques. In result, the miniaturized NIRS correctly ordered all tablets according to their manufacturer and indicated the falsified tablets, which spectra not only differed in shape from the authentic versions, but also show high spread in chemo-physical characteristics, which suggest poor manufacturing practices of the falsified products.

Keywords: Near-infrared spectroscopy • Consumer technology • Miniaturization • Falsified and substandard medicine • Viagra • Chemometrics • Artificial intelligence

Introduction

An urgent need of new methods for authentication of medicines has been reported due to growing global spread of Substandard and Falsified (SF) medicinal products that jeopardize patients' health and cause economic losses to healthcare systems, genuine pharmaceuticals manufacturers and patients [1,2]. SF medicines often look identical to their authentic versions, i.e., are packaged in the same way, have same or very similar shape, size and color [3]. However, they contain too little or too much of the active ingredient or are made with toxic substances [4]. According to WHO, SF medicines can be found in all countries, especially when purchased from unlicensed sources and more than 50% of medicines purchased over the Internet, have been found to be counterfeit [5,6]. To date, in EU safety features on the packaging, including unique identifiers and anti-tempering devices, are obligatory for most of prescription medicines and some over-the-counter medicines as per (EU) 2016/161. This is not the case in the regions, which represent the main source of SF medicines, i.e., geographically in Asia and Latin America as well economically middle-income markets [7]. Despite anti-counterfeiting efforts the problem continues to grow as advances in technology make it easier to produce the SF medicines and it is difficult to control the purchases over the Internet [8]. Portable technologies for assuring quality of medicines on the field or throughout the supply chain would complement and extend the current approach for combating the SF products, i.e., placing safety features on the packaging and laboratory analysis of suspect samples. Important works of Dégardin et al. demonstrated both NIR and Raman spectroscopies as reliable techniques for medicine authentication [9,10]. Jung et al. proposed a new approach for automatic classification of falsified Viagra and Cialis tablets using image processing and statistical analysis [11].

Technology

The miniaturized, precise and low-cost Near Infrared Spectroscopy (NIRS) is an emerging consumer technology that looks at medicines chemical 'fingerprints'. NIRS is a major technique, because it allows for fast, non-destructive, direct measurement of materials with little or no sample preparation. Chemometric models or artificial intelligence are used to easily interpret usually complex NIR spectra [12]. To date, the use of NIRS has been mostly limited to professionals in laboratories and manufacturing plants. This is due to high prices >10'000 USD and large sizes of the traditional devices. The new technology has potential to bring NIRS from laboratories onto the field and make it available to consumers. The 2 × 2 × 1 cm^3 black device relies on a novel spectral sensor, supplied by AMS International AG located in Zurich Area, Switzerland and incorporates a complete spectrometer system with light source and tunable Fabry Perrot filter, with resolution of 18 nm and measurement time 400 ms (Figure 1). The device operates in two wavelength ranges of 1350-1650 nm and 1550-1850 nm. This makes it special, in comparison to other miniaturized NIR spectrometers, because this spectral range is more suitable for detecting organic compounds [13]. In consequence, we can generate data with superior quality and achieve high results accuracy.

Materials and Methods

We chose to test Sildenafil-based products (brand name Viagra from Pfizer), because they are among the most often falsified medicines [14]. The falsified sample was sourced in an online pharmacy in EU (Figure 2). Notably, upon delivery, the outer packaging was missing, which contains unique identifiers and anti-counterfeiting marking. This fact would certainly raise attention of regulators and professionals from pharmaceutical industries. However, it would likely be unnoticed by patients. We tested thirty-nine (39) Sildenafil-based tablets including: four (4) lots of authentic 100 mg Viagra, two (2) lots of falsified Viagra, two (2) lots

Figure 1. The miniaturized, precise and low-cost Near Infrared Spectroscopy (NIRS) with mobile connectivity via an app and Bluetooth (white model) that incorporates the miniature NIRS (black).

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of generic 100 mg Eriacta (from Ranbaxy Pharmaceuticals INC in India) and two (2) lots of falsified Kamagra (from Ajanta Pharma in India). In total, we recorded 78 spectra by scanning both sides of each tablet and placing each sample directly on the device. The generic versions of Viagra are very similar to the original – all contain the same Active Pharmaceutical Ingredient (API), but differ in excipient composition and manufacturing source, as indicted by their manufacturer on the labeling. All generated spectra were smoothed and normalized. We classified samples using the K-Nearest Neighbors (K-NN) algorithm and relying on the Euclidean distances between spectra, i.e., between reflectance values recorded at the same wavelength. Principal Component Analysis (PCA) was used for visual presentation of results. We assessed accuracy of the classification model using cross-validation and bootstrapping techniques.

Results and Discussion

Recorded spectra showed distinct differences between authentic Viagra, falsified Viagra, generic Eriacta and falsified Kamagra, inherent to their unlike chemo-physical characteristics (Figure 3). Notably, PCA results for the falsified Viagra and Kamagra did not only differ significantly in spectral 'fingerprints' from the authentic versions, but also showed high spread of measured values, which, for the falsified medicines suggests poor manufacturing practices and lack of quality control in place (Figure 4). We applied the K-Nearest Neighbors (K-NN) algorithm and successfully generated classification rate of 100% correct answers, which means we could recognize all authentic, falsified and generic samples. Miniaturized consumer-type NIRS has been therefore shown as an efficient tool for quick authentication of Sildenafil-based medicines. Accuracy of this calibration model was proven using bootstrapping technique and cross-validation, which were selected as the most suitable for the dataset of 78 spectra.

Conclusion

This article shows miniaturized NIRS in combination with chemometric methods as a new efficient consumer technology for detection of falsified Viagra. We showed 100% accurate classification of thirty-nine (39) Sildenafil-based tablets,

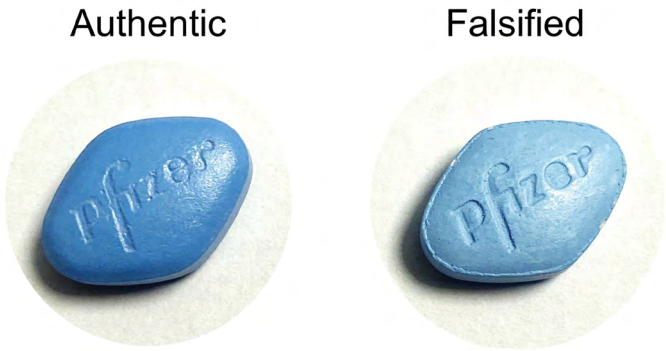

Figure 2. Authentic and falsified Viagra samples.

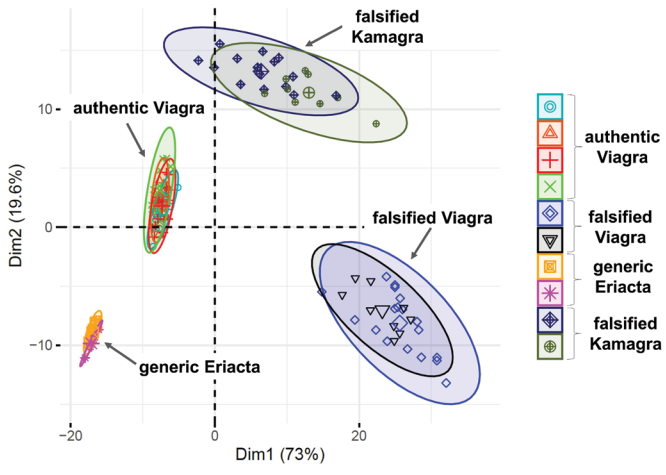

Figure 3. Normalized reflectance spectra of Sildenafil-based medicines.

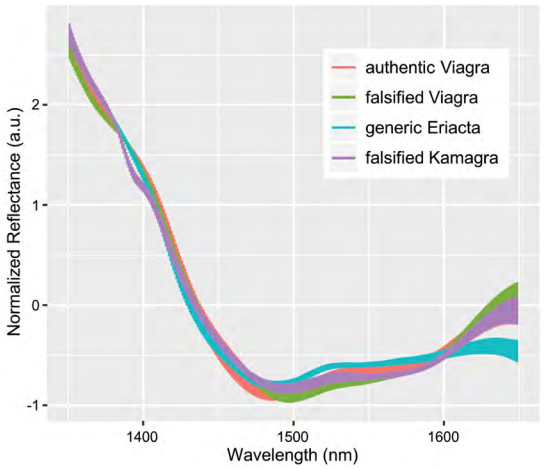

Figure 4. Principal component analysis (PCA) of NIRS spectra recoded for Sildenafil-based medicines.

including authentic Viagra, falsified Viagra and generics. The key advantages of the miniaturized NIRS are low-cost and 'pocket' size, which make it available for many different users e.g. patients, medical professionals or inspectors in middle-income countries. NIRS allows for fast, non-destructive, direct measurement of materials with little or no sample preparation. This is a very promising way of ensuring medicines authenticity on the field and throughout the supply chain that would complement the current approach for combating the falsified products, i.e., safety features on the packaging and laboratory analysis of suspect samples. Miniaturized NIRS can also be used for testing liquids and powders, which should be further investigated.

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