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Rapid detection and quantification of falsified Viagra using cloud-based portable NIR technology and machine learning

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ABSTRACT

The prevalence of falsified medications remains a global health challenge, intensified by globalization, internet accessibility, and the high profitability associated with low risks for this type of trafficking. This study demonstrates the innovative integration of portable Near-Infrared (NIR) spectroscopy with a cloud-based advanced data processing and management architecture, offering a rapid, non-destructive, and reliable solution for on-site detection and quantification of falsified Viagra tablets. Leveraging the advantages of portable NIR technology—such as its speed, ease of use, and ability to deliver nearly instantaneous results—this approach not only differentiates authentic from falsified tablets but also accurately determines their absolute sildenafil content. Utilizing data from authentic and seized falsified samples, Principal Component Analysis (PCA), Euclidean distance measurements and Support Vector Machine (SVM) highlight the capability of portable NIR devices to effectively distinguish between these groups. Such models can be seamlessly integrated into an online system paired with a mobile application, enhancing accessibility and efficiency in field settings. Furthermore, machine learning models were developed to quantify sildenafil content in falsified tablets, achieving excellent accuracy compared to a reference chromatographic method. These findings underscore the potential of portable NIR spectroscopy, combined with advanced data treatment, as a transformative tool for field deployment, empowering regulatory bodies and healthcare providers to ensure medication quality and safety with greater speed and precision.

1. Introduction

The issue of falsified medications has been a recognized problem for several decades, first raised at the World Health Assembly in 1998 [1]. Despite numerous efforts, the prevalence of falsified medicines continues to be a significant issue and accurately estimating the scale of this problem remains challenging. Key drivers behind this increase include globalization, widespread internet access, and the high profitability of falsified drug markets, which carry relatively low risks for traffickers. This issue affects nearly every country, though it disproportionately impacts developing regions. In these areas, approximately 10 % of medicines are falsified or substandard, with rates reaching up to 30 % in certain regions [2]. It concerns, in part, countries in Africa and Asia such as Myanmar, Cambodia, Lao PDR, Ghana, Kenya, Tanzania, Uganda, Madagascar, Mali, Mozambique, and Zimbabwe [3]. These falsified drugs often include life-saving medications such as antimalarials and antibiotics, leading to significant health risks, including therapeutic failure and patient deaths [4]. These may, in fact, contain no active pharmaceutical ingredient (API), the incorrect API, or the correct API but in inadequate amounts [5]. Additionally, they may also harbor toxic substances. In a 2023 report, the United Nations Office on Drugs and Crime (UNODC) [6] attributes as many as 267'000 deaths annually in sub-Saharan Africa to falsified antimalarials and up to 169'271 deaths to non-compliant antibiotics, which also exacerbate antimicrobial resistance. In developed countries, falsified medications are less than 1 % of the total market value due to, in part, more effective regulatory bodies, though there is still a significant volume of illegal imports, especially for erectile dysfunction and weight loss tablets [7]. These imported products, primarily from India and China, are not subject to the same quality controls as registered medications, raising concerns of inappropriate use or unsuitable treatment [8]. Efforts to address this issue span multiple fronts, including international treaties like the MEDICRIME Convention,

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initiatives like Interpol's "Pangea" operation, and the European Union's "Falsified Medicines Directive" [9–11].

A key pillar in efforts to mitigate the spread of falsified medicines is the development of simple, rapid, reliable, and decentralized analytical tools designed to: (a) detect falsifications and (b) assess the content (API) or other potentially harmful substances in tested tablets. While highly effective separation techniques, such as High-Performance Liquid Chromatography (HPLC) or Gas Chromatography (GC), are widely used in laboratory settings, there is a critical need for simpler, faster and less expensive methods, including sample preparation, specifically designed for effective use in field applications [12].

In this context, portable techniques based on spectroscopy (Raman, IR, and NIR) have been extensively tested for the detection of falsified drugs [13]. Regarding portable NIR technology, it is generally observed that the devices are highly effective at distinguishing between authentic and falsified tablets. However, for the formal identification and/or quantification of active ingredients, NIR is considered to be less suitable. Indeed, compared to Raman, for instance, NIR spectra result from combinations of harmonic vibrations, making it relatively complex to associate specific peaks (or bands) with compounds (such as an active ingredient) [14].

This study showcases how portable NIR analysis, integrated with a cloud-based architecture for advanced data processing and management, is opening new avenues for decentralized field analysis. A concrete example is presented through the analysis of seized falsified Viagra tablets, showing how differentiation from authentic tablets can be achieved. Furthermore, the potential of this approach to obtain the absolute sildenafil content in falsified Viagra tablets is presented. Ideally, research should focus on medications that address core issues in developing countries, such as antimalarials. However, since the introduction of Viagra for erectile dysfunction in 1998, numerous websites have emerged, allowing people to purchase Viagra tablets easily and anonymously. The drug has been counterfeited multiple times and has been included in the National Specified List of Susceptible Products by the National Association of Boards of Pharmacy in the USA. Products on this list are frequently targeted by counterfeiters, posing a potential risk to public health [15,16].

This initial study on Viagra demonstrates the feasibility of such a methodology, which can subsequently be developed and transposed for other medicines and APIs. It is worth noting that non-approved erectile dysfunction medications are the most illegally imported drugs in Switzerland [17], indicating a potential application for this model, particularly in customs.

2. Material and methods

2.1. Samples

A total of 30 authentic Viagra tablets (100 mg dosage) from 3 different production batches and 122 falsified Viagra tablets from 23 different seizures were analyzed in this study. All samples were provided by Swissmedic, the Swiss agency for therapeutic products. The seizures of falsified Viagra were initially made by Swiss customs at the Zurich-Mülligen postal center.

2.2. Reference measurements by UHPLC-UV

Of the 122 falsified tablets analyzed with NIR, a sampling of 48 tablets representing 22 different seizures was analyzed using Ultra-High Performance Liquid Chromatography coupled with Ultraviolet detection (UHPLC-UV, Waters, Milford, MA, USA). Once the tablets were weighed, they were placed in an IKA (Staufen, Germany) tube containing two beads. Then, 12.5 ml of a 50:50 (v/v) mixture of water with 0.1 % formic acid and isopropanol was added using an organic solvent dispenser. The tablets were ground for 20 min. The IKA tubes were then placed in an ultrasonic bath for 15 min. The solutions were subsequently diluted by adding water, with the dilution level depending on the amount of sildenafil stated on the tablet. For example, for a tablet stating 100 mg of sildenafil, 25 µL of the solution was taken and 975 µL of water was added to obtain a stock solution with a theoretical sildenafil concentration of 100 ppm. The stock solutions were then centrifuged (Eppendorf, Basel, Switzerland) at 14'500 rpm for 10 min at room temperature. After this step, 700 µL aliquots were placed in analysis vials for UHPLC. It should be noted that the tablets were cut in half and initially only one half was analyzed to preserve part of each tablet. It was eventually decided to analyze both halves of each tablet due to the uncertainty regarding the distribution of sildenafil within the tablets.

Regarding the analysis parameters, mobile phase A was an aqueous phase consisting of water acidified with 0.1 % formic acid (v/v). Mobile phase B was acetonitrile also acidified with 0.1 % formic acid. The pH of the aqueous phase was approximately 2.7, the flow rate was set at 0.5 ml/min, and the injection volume was 1 µL. The column used was an Acquity BEH Shield RP18 1.7 µm, 2.1 × 50 mm (Waters). The column temperature was set to 40°C, and the sample temperature in the injector was 20°C. The analyses were performed in gradient mode for a duration of 4 min with the following distribution percentages for the two mobile phases: 0 min = 85 % A / 15 % B; 2 min = 35 % A / 65 % B; 2.1 min = 0 % A / 100 % B; 3 min = 85 % A / 15 % B; 4 min = 85 % A / 15 % B. Finally, the wavelength selected for UV detection was 293 nm.

2.3. Portable NIR device

The Viavi Solutions Inc. MicroNIR Onsite-W (Scottsdale, AZ, USA) was selected for this study due to its practicality, ease of use, and Bluetooth connectivity. The detector has a linear variable filter (LVF) that is directly coupled to a 128-pixel linear indium-gallium-arsenide (InGaAs) array detector. The detector operates in the NIR spectral range between 950 and 1650 nm. The radiation source consists of two tungsten light bulbs. The system has a 25'000 signal-to-noise ratio, a 10 ms integration time, and a 100 scan capacity per analysis [18]. The device was used with the special attachment for tablet analysis, the "Tablet Probe", which improves the quality of spectral measurements for this type of specimen. In this study, the tablets were placed in the center of an aluminium cup, encased by the Tablet Probe accessory, and 2 spectra were recorded per side of the tablets (cf. Fig. 1). Additionally, for some of the tablets, measurements were done through the plastic "blister" packaging.

2.4. Data treatment

The raw spectra generated by the MicroNIR comprises 125 variables which needed to be pre-processed to be suitable for use in statistical models. A first round of the data processing was carried out using Orange Data Mining (v3.38.1, University of Ljubljana, Slovenia) [19], with the aim to evaluate the capacity to differentiate between authentic and falsified Viagra tablets. Preprocessing steps included the second derivative Savitzky-Golay (polynomial degree 2 and 11 smoothing points) followed by a Standard Normal Variate (SNV). The data were then visualized by performing a Principal Component Analysis (PCA) and plotting the first two principal components (capturing 70 % of total variability).

Using the same pre-processing steps, the distribution of intra-group and inter-group similarity measures was analyzed in Python (v3.10), employing Euclidean distance as the similarity metric. This analysis facilitated the development of a statistical model to establish a decision threshold.

To illustrate another way of classifying tablets as authentic or falsified, a Support Vector Machine (SVM) model was developed using Orange Data Mining (v3.38.1). The preprocessing steps mirrored those used for PCA and Euclidean distance, except that in this case, the average spectrum for each tablet is used rather than the full set of measurements. The dataset was split into a training set (2/3, 101 tablets)

Fig. 1. MicroNIR with Tablet Probe attachment and falsified Viagra pill in aluminium cup.

and a testing set (1/3, 51 tablets). The SVM model was trained with a linear kernel and parameter C = 0.10. Model performance was evaluated using a confusion matrix, with accuracy, precision, recall, and F1-score calculated to assess classification of authentic and falsified Viagra tablets.

A second step of the data processing involved developing a calculation model for sildenafil content in falsified Viagra using reference values obtained through UHPLC-UV analysis. This part was performed on Python (v3.10), using Neural Network model (torch library v2.4.1). The preprocessing methods employed were as follows: 2nd derivative Savitzky-Golay (2nd degree polynomial and smoothing window of 11 points) followed by the removal of the first 5 and last 5 measurement points for repeatability reasons. Finally, an SNV normalization was applied and the average spectrum for each tablet is used. A custom Python script was developed to perform 100 iterations (bootstrapping) on the 48 tablets.

The model architecture consisted of a fully connected feedforward neural network with four layers: an input layer with 115 features (corresponding to the preprocessed NIR spectral variables), followed by three hidden layers with 256, 128, and 64 neurons, respectively, and an output layer with a single neuron to predict sildenafil concentration. LeakyReLU activation functions were applied after each hidden layer to introduce non-linearity. The model was trained using the Adam optimizer with a learning rate of 0.0003 and a weight decay of 1e-5 to prevent overfitting, minimizing the Mean Squared Error (MSE) loss function. Training was conducted over a maximum of 200 epochs with a batch size of 8, incorporating early stopping with a patience of 20 epochs to halt training if the validation loss did not improve, ensuring optimal convergence. For each of the 100 bootstrap iterations, the dataset of 48 tablets was split into a calibration set (32 tablets) and a validation set (16 tablets), with the model retrained and evaluated to compute the Root Mean Square Error of Prediction (RMSEP), the coefficient of determination (R^2) and Relative Prediction Deviation (RPD). This approach provided a statistically representative measure of the model's predictive accuracy in estimating the sildenafil content of the 48 tablets.

3. Results and discussion

This section presents the findings of the study, focusing on the differentiation between authentic and falsified Viagra tablets using portable NIR spectroscopy. The results first highlight the effectiveness of Principal Component Analysis (PCA), Euclidean distance measurements and Support Vector Machine (SVM) in distinguishing between the two groups. Additionally, the ability of machine learning models to estimate sildenafil content in falsified tablets is examined, demonstrating the potential of this approach for rapid field deployment. The following subsections provide a detailed analysis of these aspects.

3.1. Differentiation between authentic and falsified Viagra

Fig. 2 provides a direct comparison of authentic and falsified Viagra tablets, displaying a subset of normalized NIR spectra and photographs of an authentic tablet and a falsified tablet. The spectra exhibit distinct absorbance profiles after only Standard Normal Variate (SNV) normalization, suggesting that differentiation between authentic and falsified Viagra tablets using MicroNIR is highly feasible. This observation is promising, as it indicates that even basic preprocessing can reveal significant spectral differences—a capability further demonstrated across all samples in the subsequent results.

Additionally, the visual comparison between the authentic and falsified tablets reveals clear distinctions, such as variations in color and imprinting. However, while these physical differences are readily apparent, techniques like MicroNIR remain essential for confirming the detection of falsified tablets, particularly in field settings. This is especially critical for non-expert users or in scenarios where a reference tablet is unavailable for direct comparison, ensuring reliable identification without relying solely on visual inspection and user expertise.

When projecting the first two principal components from the PCA analysis of all measurements taken on Viagra tablets (Fig. 3), several key observations emerge. Notably, measurements from authentic samples (in blue) and falsified samples (in red) are fully separated within the PCA space. This means that the two groups can be clearly distinguished based on the NIR signals of the tablets. The observed separation highlights significant differences between the spectra of authentic and falsified tablets, likely related to substantial compositional variations. It is reasonable to assume that falsified tablets rarely replicate the authentic ones in terms of the presence and relative proportions of their components [20]. It is interesting to note that in this case, the vast majority of falsified tablets contain the correct API, sildenafil. Therefore, the spectral differentiation cannot be solely attributed to the absence of the active ingredient.

The significant difference in spectral variability between authentic and falsified Viagra tablets, as evidenced by their spread on the PCA, is particularly noteworthy. The limited spectral variability within authentic tablets underscores their high consistency, reflected in the good repeatability of measurements, likely resulting from stringent manufacturing controls in compliance with Good Manufacturing Practices [21]. This regulatory oversight ensures the stability of composition and spectral properties across different production batches. Conversely, falsified tablets display far greater variability, likely due to inconsistent manufacturing practices and the involvement of multiple unregulated sources. These findings confirm that distinguishing between authentic and falsified Viagra tablets is relatively straightforward using a portable NIR device like the MicroNIR.

Aligned with a classical approach of chemical profiling in forensic science, we adopted a method based on measuring similarities between spectra. The later involves comparing intra-group and inter-group variability to assess the feasibility of implementing a spectral matching model, which could be particularly useful for mobile application deployment. Fig. 4 illustrates all Euclidean distance values obtained by comparing the different spectra. The comparisons between authentic tablets (intra-variability) are shown in blue, while the comparison

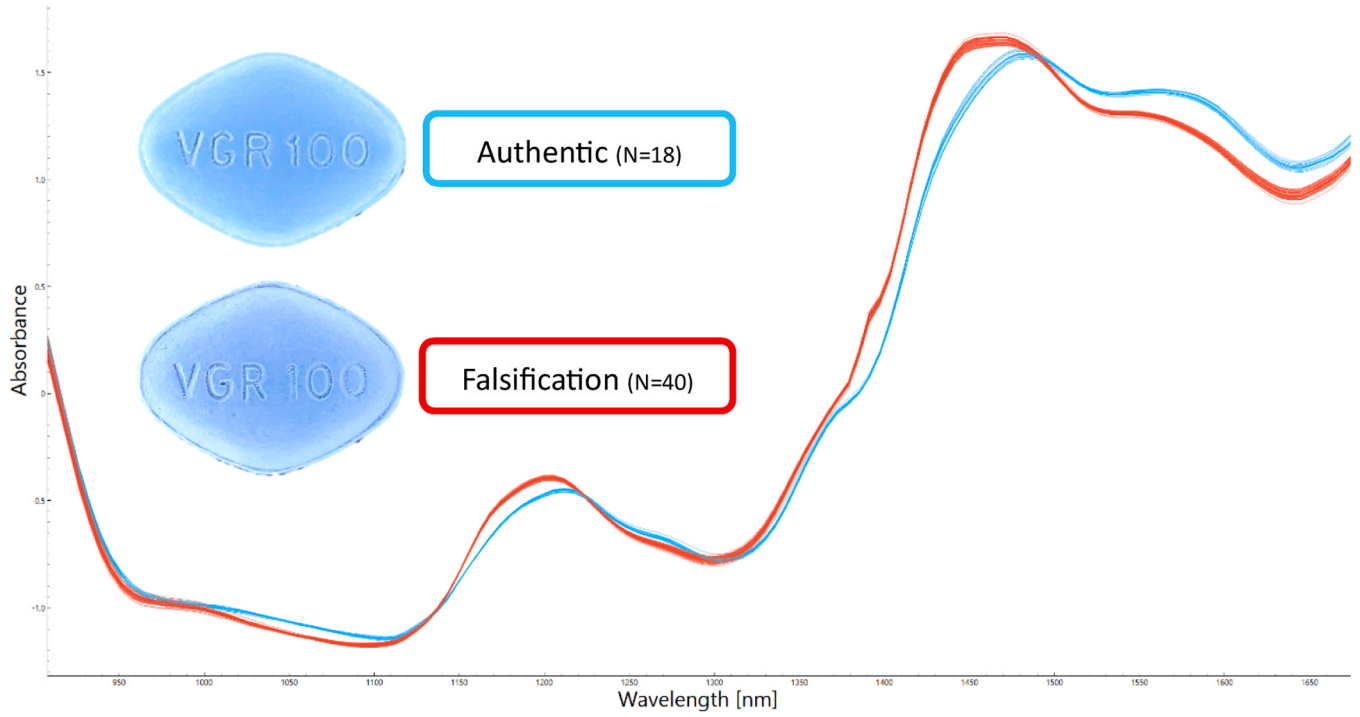

Fig. 2. (A) Subset of MicroNIR spectra after Standard Normal Variate (SNV) normalization, featuring 18 spectra from authentic Viagra tablets (blue) and 40 from falsified tablets (red). (B) Photographs showing an authentic Viagra tablet (top) and a falsified tablet (bottom).

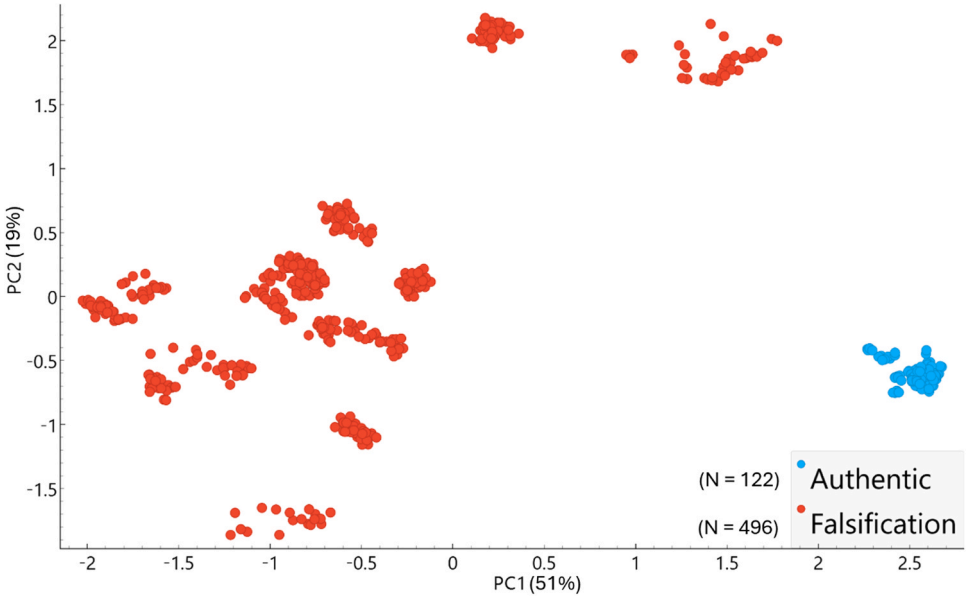

Fig. 3. PCA of the set of measurements on authentic Viagra (in blue, N = 122) and falsified Viagra (in red, N = 496). Preprocessing: 2nd derivative Savitzky-Golay and Standard Normal Variate (SNV).

between authentic and falsified tablets (inter-variability) are shown in red. The distribution of these distances corroborates the observations made with the PCA (Fig. 3), with no overlap between the two distributions, resulting in a classification model with 100 % accuracy. Thus, for new analyses of unknown samples, a simple calculation of the Euclidean distance between NIR spectra of the new tablets and spectra from reference tablets integrated into a database allows a classification as either authentic or falsified.

Fig. 5 presents the confusion matrix for the testing set (51 tablets, 1/3 of the dataset), illustrating perfect classification performance. The model achieved 100 % accuracy, precision, recall, and F1-score, with all authentic and falsified tablets correctly predicted, as shown by the absence of off-diagonal entries in the matrix. These results demonstrate the SVM's excellent ability to reliably distinguish authentic from falsified Viagra tablets for this dataset, reinforcing the effectiveness of MicroNIR spectroscopy for field-based detection.

Another key aspect is the feasibility of conducting NIR measurements through blister packaging. This approach would allow tablets to remain in their original packaging, ensuring their preservation, which is particularly valuable when the tested medicines are fully compliant.

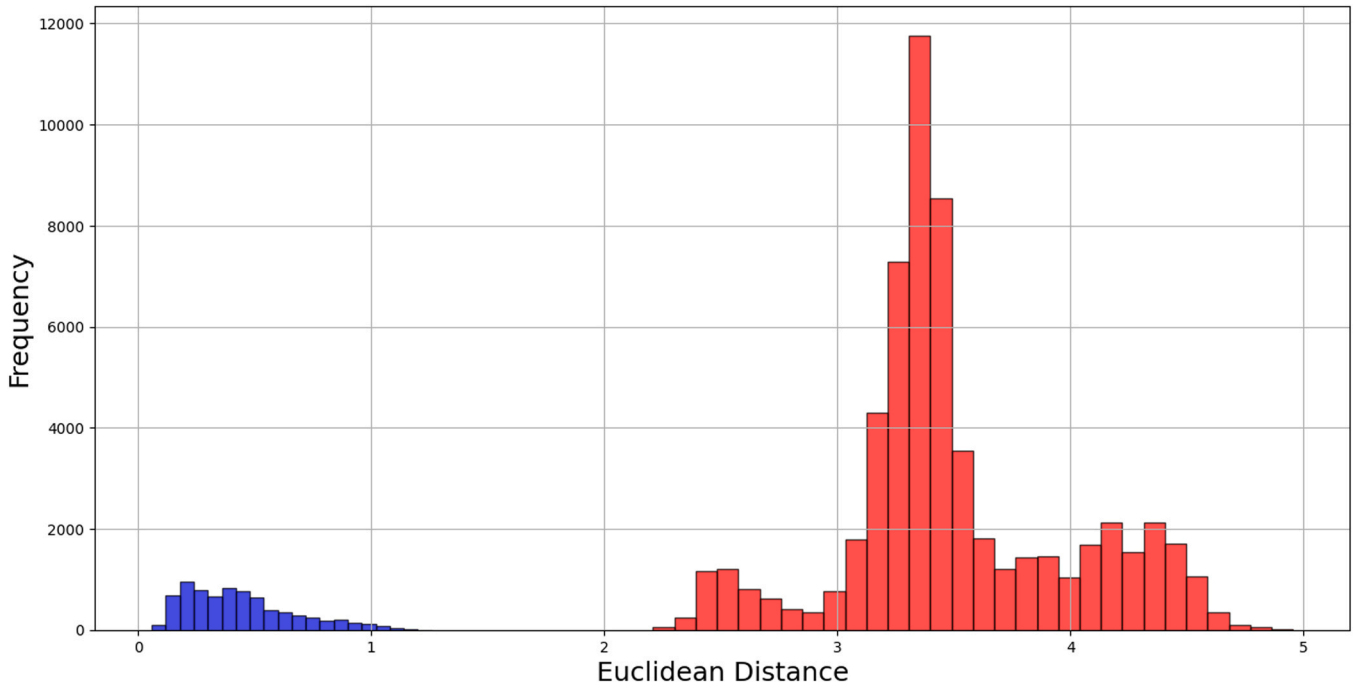

Fig. 4. Distribution of all similarity values (Euclidean distance) for intra-variability (in blue, N = 7'381) and inter-variability (in red, N = 60'512).

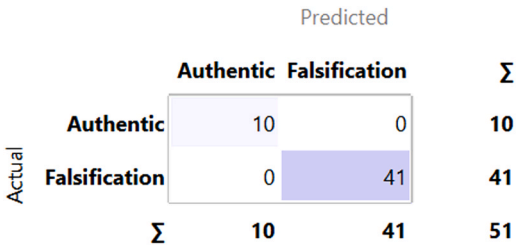

Fig. 5. Confusion matrix for SVM classification of authentic and falsified Viagra tablets.

Moreover, such a method would save time and facilitate the testing of a larger number of samples within a shorter timeframe. Given the properties of NIR radiation, it is expected to penetrate transparent plastic packaging and reach the tablets. However, it is also anticipated that interactions between the NIR radiation and the packaging layer would significantly impact the resulting spectra [22].

Fig. 6 presents the PCA distribution after incorporating measurements taken through blister packaging for both authentic and falsified Viagra tablets. The preprocessing steps included second derivative Savitzky-Golay (polynomial degree 2 and 5 smoothing points) followed by SNV. A total of 89 measurements for authentic tablets and 240 measurements for falsified tablets were added. The PCA results indicate that measurements taken through the blister packaging are clearly distinguishable from those obtained directly from the tablets. This distinction holds true for both authentic and falsified Viagra, highlighting the significant influence of the plastic packaging on the NIR spectra. However, the two categories of Viagra can still be clearly separated despite this additional variability. Based on these results, it can be reasonably concluded that the variability between authentic and falsified Viagra is greater than the variability between direct and through-blister measurements.

3.2. Model of Sildenafil content calculation using NIR measurements and machine learning data processing

In order to evaluate the potential of NIR as an absolute quantification method, the sildenafil content in a subset of the tested samples was determined. The reference quantification of sildenafil content was performed using UHPLC-UV. The results were expressed as the mass percentage concentration of sildenafil in the tablets, calculated by dividing the mass of sildenafil in a tablet by the total mass of the tablet. Among the 48 tablets analyzed, sildenafil concentrations ranged from 0.2 % to 16.6 %, with quantities varying from 2 mg to 94 mg. For a detailed list of the results obtained via UHPLC-UV, please refer to Table 1 in Appendix A.

The prediction of the sildenafil content of these tablets using MicroNIR measurement was carried out through a neural network model, trained with a 2/3 calibration set and a 1/3 validation set. After 100 bootstrap iterations, the mean RMSEP value for sildenafil concentration was 0.52 %, the mean R^2 was 0.96 and the mean RPD was 6.73. For falsified tablets with an average weight of 708 mg, this corresponds to an average error of approximately 4 mg in the sildenafil content. In tablets containing an average of 48 mg of sildenafil, the relative error is thus around 8 %. These results underscore the relevance of predictions derived from the NIR measurements, which provide a valuable estimation of the sildenafil content in falsified Viagra tablets through a rapid and non-destructive method, even when dealing with a limited number of samples. Furthermore, the R^2 of 0.96 indicates that 96 % of the variance in sildenafil concentration is explained, while the RPD of 6.73 shows prediction errors are roughly 1/6.7th of the data's variability, collectively demonstrating the model's excellent accuracy and reliability.

Moreover, a similar model, using the same data as this study, is already deployed in a mobile application (Fig. 7). More specifically, the latter is built on the NIRLAB architecture [21]. In essence, it relies on a database of collected spectra, which, in this case, come from falsified Viagra. The system also incorporates data from other techniques, such as HPLC, here focusing on the sildenafil content. Finally, machine learning models (such as Random Forest, Neural Network and K-Nearest Neighbors) are trained to, for example, detect and estimate the content of

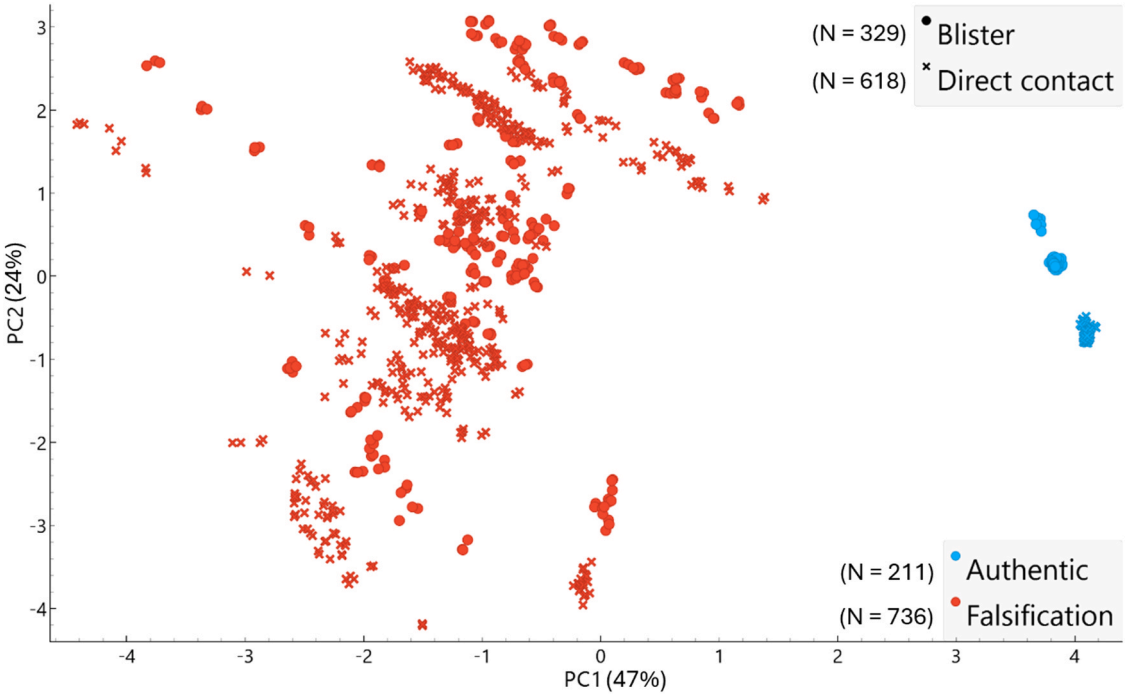

Fig. 6. PCA of the set of measurements on authentic Viagra (in blue, N = 211) and falsified Viagra (in red, N = 736). Measurements through the blister (crosses) and direct contact measurements (circles). Preprocessing: 2nd derivative Savitzky-Golay and SNV.

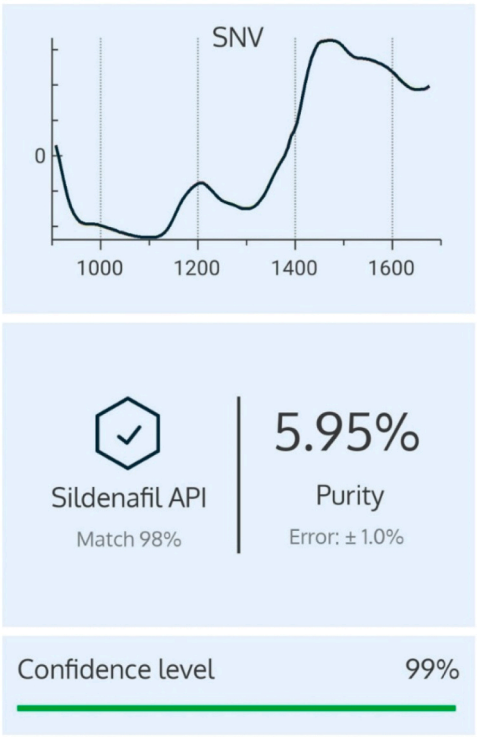

Fig. 7. Screenshot of the mobile application developed by NIRLAB for sildenafil identification and concentration calculation [23].

sildenafil in falsified Viagra pills. These models are securely hosted on a cloud server and used to make predictions for new samples. Thanks to a mobile application that interfaces with both the device and the cloud, the prediction results for a new measurement appear in just a few seconds directly on the phone screen.

Fig. 8 illustrates the complete set of predictions for the validation set samples, after 100 bootstrap iterations on 48 tablets. This represents a total of 1'600 predictions (16 validation samples per iteration across 100 iterations). It can be observed that almost all predictions fall within an error margin of ± 1 % (indicated by dashed lines) for the sildenafil concentration. An exception is observed for tablets with concentrations close to 0 % and 16 %, which represent extreme cases with limited data points. It can be reasonably assumed that increasing the amount of data within these underrepresented concentration ranges would greatly improve the model's precision. It is also generally accepted for this type of machine learning modelling that performance generally improves with larger datasets.

Notably, a tablet with a sildenafil concentration of approximately 9 % exhibits a consistent prediction error greater than 1 %. This may be due to the fact that it is the only tablet at this concentration level and originates from a different seizure, potentially introducing significant variability in its NIR spectra compared to the other tablets.

It should be noted that a sildenafil detection model could not be specifically tested in this case. Since only falsified Viagra tablets containing the correct API were available, it was not possible to investigate differentiation from tablets that do not contain sildenafil as API. While it is conceivable to use simulated tablets – manufactured specifically for the study, some containing the API and others not – the resulting data would likely not be representative or directly applicable in an operational context. This is because NIR spectra measured on simulated tablets would not accurately reflect those of real seized falsified tablets. Ideally, access to real seizures of falsified Viagra tablets that do not contain sildenafil or its analogues would be necessary. Unfortunately, access to such seizures is currently impossible. Nonetheless, it is worth mentioning that a qualification model for detecting the presence or absence of sildenafil could be developed to differentiate the falsified tablets used in this study from unrelated tablets containing other active ingredients. The tablets in question contained one or more of the following API: paracetamol, ibuprofen, aspirin, artesunate, artemether, lumefantrine, dolutegravir, lamivudine, tenofovir disoproxil fumarate, and sofosbuvir.

Despite these limitations, the results obtained so far demonstrate the relevance of this technology as the initial method of analysis for several

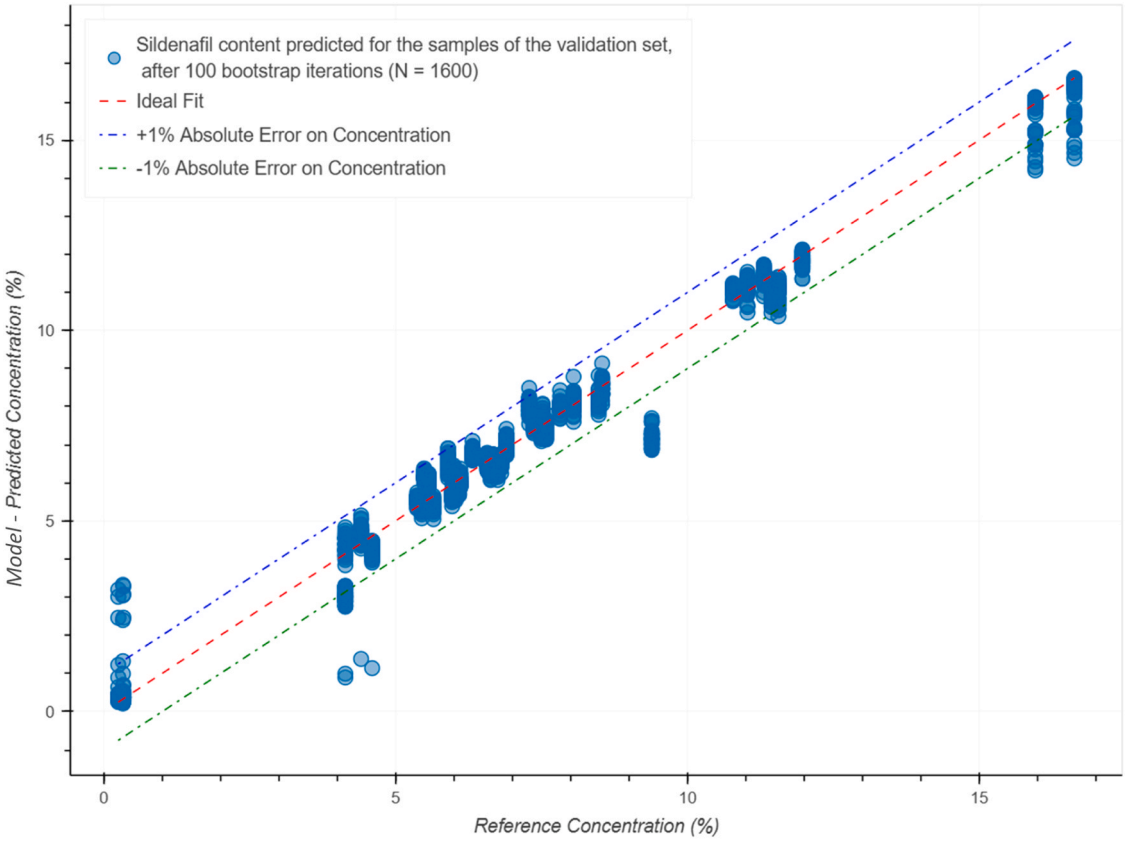

Fig. 8. Sildenafil content prediction for the samples of the validation set, after 100 bootstrap iterations (N = 1600).

applications. One of the most appropriate uses appears to be the deployment of these NIR portable devices on the field, particularly at points of sale and transit where potentially falsified medications are prevalent. Their use can be envisioned at customs checkpoints, in drugstores such as local pharmacies, and also in markets, where it has been evidenced that these kinds of falsified products are proposed.

With this technology, a significant number of suspected medications can be analyzed in a rapid and non-destructive manner. The results are directly interpretable, facilitating on-site decision-making and triaging regarding which samples should undergo further testing. As demonstrated by the results on falsified Viagra, the authenticity of tablets can be rapidly and reliably assessed. Similarly, the presence or absence of the expected API and their quantities can be estimated, although additional tests are required for APIs other than sildenafil. If doubts persist regarding analyzed specimens, complementary field-based approaches, such as portable Raman spectroscopy [14,22,24] or the Global Pharma Health Fund (GPHF)-Minilab (Giessen, Germany) [25,26], can be employed. These techniques can confirm or refine the results obtained from NIR measurements, while also providing additional information about the tested tablets. Ultimately, if needed, specimens can always be sent to the laboratory for analysis with a reference method, such as HPLC-UV or LC-MS, to obtain definitive and more comprehensive results.

Integrating a portable measurement device, such as the MicroNIR, into a cloud-based architecture offers the advantage of enabling advanced data processing models, such as those developed in this study, to be deployed and easily accessed for field measurements. This has been successfully implemented in this study through the NIRLAB ecosystem. Such an architecture offers another key capability: since both the reference database and the data processing models are stored on a cloud server and accessible via an online platform, updates are highly efficient. Specifically, when new samples are analyzed with NIR measurement and sufficient confidence is achieved through complementary techniques, they can be swiftly and easily integrated into the database and model. This integration improves the model's accuracy and ensures it remains representative of real-world conditions. For instance, if the composition of authentic Viagra were to change, updating the authentication model would require only a few reference spectra and a relatively short amount time. This updated model would then be immediately available across all deployed devices utilizing it.

The results of this study suggest that detecting falsified tablets is currently feasible when measurements are performed through transparent packaging. However, additional analyses on authentic tablets, particularly using various types of packaging, are necessary to better understand the resulting variability.

Additionally, the development of a model for sildenafil concentration calculation through blister packaging should be explored. Given the impact of packaging on the spectra, a decrease in model performance can be anticipated. Therefore, direct measurements on tablets placed in an aluminium cup should remain the recommended approach. A potential workflow could involve performing an initial measurement through the packaging to gain preliminary information about the tablet's authenticity. If the result does not confirm the authenticity of the medicine, the tablet can be removed from the packaging for direct measurement in an aluminium cup.

4. Conclusion

The integration of portable NIR technology with a cloud-based ecosystem integrating machine learning models offers a transformative solution for addressing medicine falsification. This approach enables the rapid and non-destructive testing of pharmaceutical products while supporting nearly real-time updates of reference databases. Such flexibility ensures that the detection model remains adaptable and relevant amid evolving falsification methods. This approach empowers healthcare providers, regulatory authorities, and customs officials with

immediate and actionable data, enhancing the efficiency and reliability of field-based medicine screening, fostering safer pharmaceutical practice, particularly in vulnerable regions. Future research should focus on expanding the model to cover a broader range of medications and further optimizing its capabilities to detect and quantify APIs across diverse packaging and environmental conditions.

CRediT authorship contribution statement

Esseiva Pierre: Writing – review & editing, Supervision, Resources, Project administration, Methodology, Data curation, Conceptualization. **Rais Hervé:** Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Schelling Cédric:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Formal analysis, Data curation. **Delémont Olivier:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Data curation, Conceptualization. **Rudaz Serge:** Writing – review & editing, Visualization, Validation, Supervision, Project administration, Methodology, Conceptualization. **Stanojevic Stefan:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Coppey Florentin:** Writing – review & editing, Validation, Software, Methodology, Data curation.

Declaration of generative AI and AI-assisted technologies in the writing process

Parts of the manuscript were proofread using ChatGPT 3.5 and 4.0. The authors subsequently reviewed and revised the content as needed, and they assume full responsibility for the accuracy and integrity of the final publication.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpba.2025.116940.

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