# Screening viagra tablets with near infrared spectroscopy

**Marjo J. Vredenbregt, Dennis Mooibroek, Dries de Kaste and Ronald Hoogerbrugge**

*National Institute for Public Health and the Environment, PO Box 1, 3720 BA Bilthoven, The Netherlands*

## Introduction

Since Pfizer came on the market (1998) with the viagra tablets a large stream of imitations and counterfeits followed.[1] Nowadays, we frequently receive look-alike tablets from all over the world from the Dutch Health Care Inspectorate. The common questions to be answered are:

- Is this an original viagra tablet?
- Does this tablet contain Sildenafil citrate,[2] the active ingredient of viagra?
- Are there any tablets from the same origin?

For identification and for quantification of Sildenafil citrate, the active ingredient of viagra time-consuming chemical analyses are needed. Therefor a near infrared (NIR) screening method was developed to answer these questions quickly. Due to the discriminating power and the speed of analysis NIR might be a powerful tool for screening viagra tablets on authenticity, active ingredients and origin.[3]

## Materials and methods

NIR spectra (12.000–3.000 cm$^{-1}$) were recorded from both sides of seventy original 50-mg viagra tablets (seven batches of ten tablets) produced in Europe and America and supplied by Pfizer, The Netherlands. A library was constructed of the raw spectra (10.000–4.000 cm$^{-1}$) of five tablets from each batch. Wavelength correlation (WC) was applied to the raw spectra of the remaining tablets and after validation the identification criteria were set. A threshold of 0.998 was used for identical tablets.

About 120 different batches of unknown tablets (original tablets, imitations or counterfeits) were received from the Dutch Health Care Inspectorate. All tablets were measured as received on both sides and the raw spectra of each unknown tablet were compared to the library. For identification WC was used with four different thresholds: > 0.998 identical, > 0.99 strongly similar, > 0.98 similar and > 0.95 slightly similar. After identification two or more NIR-spectra of each batch of unknown tablets were added to the library.

To detect any clustering in the tablets principal components analysis (PCA) was applied to all NIR spectra (over 750) without any pre-treatment. The 95 % confidence intervals were calculated around the scores (PC1/PC2) of the original Pfizer viagra tablets and around three groups of imitations of viagra.

Equipment: Spectrum IdentiCheck FT-NIR system PerkinElmer Limited (Beacconsfield Bucks, UK) with IdentiCheck Reflectance Accessory (ICRA) and PbS detector. Software: Spectrum IdentiCheck version 2.00 and Quant+ version 4.10 including WC. WC was always applied using the default filter setting. Background reference Teflon. Spectra were recorded in the diffuse reflection mode, spectral range 12 000–3 000 cm$^{-1}$, optical resolution 16 cm$^{-1}$, 64 scans co-added.

## Results and discussion

In general most imitations and/or counterfeits can easily be distinguished from original viagra tablets because they differ in colour, size and/or shape. Measurement of all kind of different types of look-alike viagra tablets in blue, pink and red and in various shapes and/or sizes resulted in a large amount of different NIR-spectra. Although the imitation viagra tablets sometimes looked very identical to an original Pfizer tablet, the NIR-spectra showed great differences due to the fact that other excipients and/or active ingredients were used (Figure 1).
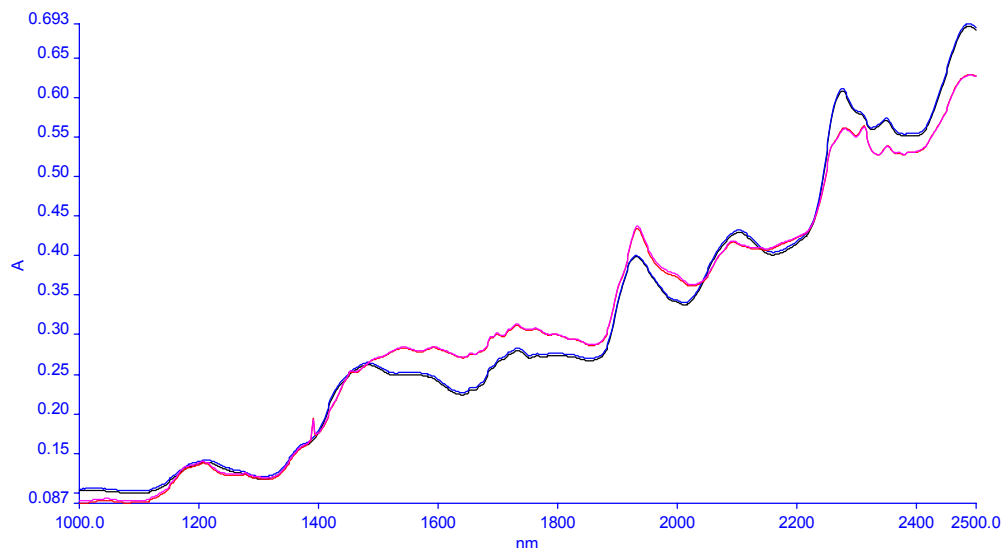


**Figure 1. NIR-spectra (top and bottom) of an original Pfizer viagra tablet (black and blue) and from an imitation tablet (red and pink).**

The NIR spectra of the unknown tablets were correlated to the library of the spectra of original viagra tablets and the spectra of tablets from all other batches measured. According to their highest correlation the NIR-spectra of an unknown tablet could be divided in one of the five ranges of similarity viz. identical, strongly similar, similar, slightly similar and totally different. Most tablets were identified as not originating from Pfizer. Also high correlations were found between the spectra of different batches of imitations and/or counterfeits. The NIR spectra of a counterfeit produced in the Far East and confiscated in the Netherlands and in Switzerland appeared to be identical (WC > 0.998). Criminal investigation confirmed that these tablets originated from the same source indeed.

PCA applied to all NIR spectra showed several clusters in the PC1/PC2 scoreplot (Figure 2). The 95 % confidence intervals around the scores (PC1/PC2) indicated that there might be a relation between some batches. One interesting cluster consisted of six different batches of Chinese viagra tablets containing Sildenafil citrate as active ingredient. Two other clusters of three independent batches each were formed because of the use of other active ingredients viz. Amphetamine and Yohimbine. The identity of both compounds was confirmed by chemical analysis.
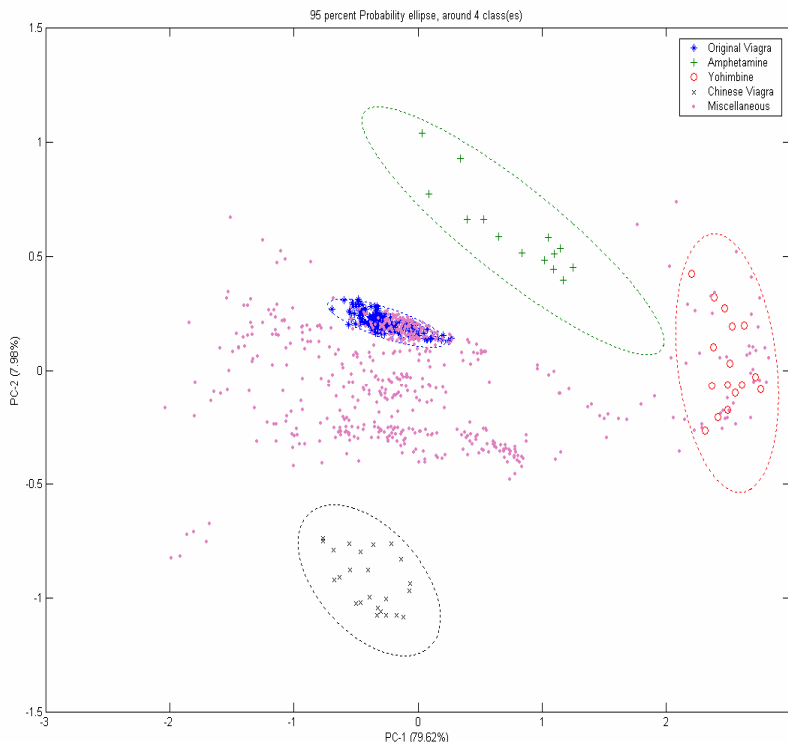
**Figure 2. PCA, scoreplot PC1/PC2 of approx. 750 NIR-spectra (10.000–4.000 cm$^{-1}$) with 95% probability ellipse around the Pfizer viagra tablets and around three groups of imitations of viagra.**

To get more insight in the discriminating power of the technique a closer look was taken to the centre of the PCA plot. After cutting out the data of batches on the edges of the PC1/PC2 plot and recalculating the scores new clusters appeared in the PC1/PC2 plot. These clusters were formed by batches of tablets with the same name (for example, Caverta), tablets with an equal colour and shape, tablets from similar lines of deliverance or by tablets from an Indian manufacture (Androz). After repeating this step five times no more batches could be distinguished from the cluster in the centre of the PCA plot. The scores located in this cluster belong to the library-spectra of original Pfizer viagra tablets, to independent validation-spectra of original viagra tablets and to spectra of unknown tablets. The remaining spectra of twenty unknown tablets could not be differentiated from the original Pfizer viagra tablets. Chemical analysis with HPLC-UV demonstrated that the UV spectrum of unknown tablets showed no peaks that were not detected in an original viagra tablet. Until now it is uncertain whether these tablets are original viagra tablets confiscated in an illegal circuit or that these are just perfect copies.

## Conclusions

NIR spectroscopy has proven to be a powerful tool in screening viagra tablets on authenticity, active ingredients and origin. In addition to the quick answers on the questions above, NIR-spectra also provide a lot of information about the composition, the homogeneity, the quality of a batch and of all kind of unexpected variations of the unknown tablets. This information has proven to be most valuable to guide further chemical and/or forensic analysis.

## References

1. S.H. Frasson Scafi and C. Pasquini, *The Analyst* **126,** 2218 (2001).
2. P.R. Khan, R.D. Jee, R.A. Watt and A.C. Moffat, *Pharmaceutical Sciences* **3,** 447 (1997).
3. D.A. Burns and E.W. Ciurczak, *Handbook of Near-Infrared Analysis, second edition*. Marcel Dekker, Inc. New York, USA (2001).