Impurity fingerprints for the identification of counterfeit medicines - a feasibility study

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Introduction :

Most of the counterfeit medicines are manufactured in non GMP conditions by uncontrolled or street laboratories. Their chemical composition and purity of raw materials may, therefore, change in the course of time. The public health problem of counterfeit drugs is mostly due to this qualitative and quantitative variability in their formulation and impurity profiles.

During this study, impurity profiles were treated like fingerprints representing the quality of the samples. A total of 73 samples of counterfeit and imitations of Viagra® and 44 samples of counterfeit and imitations of Cialis® were analysed.

The aim of this study was to discriminate illegal samples from genuine ones and to evaluate which of the two applied classification algorithm was the best suited for this purpose.

Experimentals :

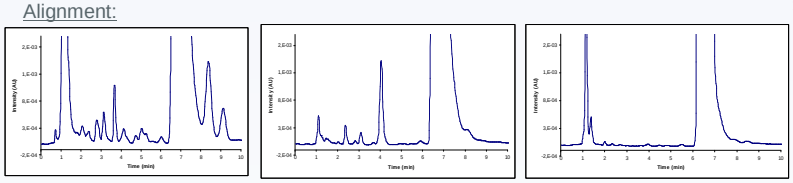
The impurity profiles were obtained on a classical HPLC system with a dual UV detector.
The chromatograms were aligned by linear interpolation adjustment with respect to the highest peak in order to allow a good exploratory analysis.
To reduce the importance of inevitable differences, a common logarithmic transformation of the dataset was performed.

The ability of the method to predict whether a sample is genuine or not has been tested with two different algorithms: k-nearest neighbour (k-NN) and soft independent modelling by class analogy (SIMCA).

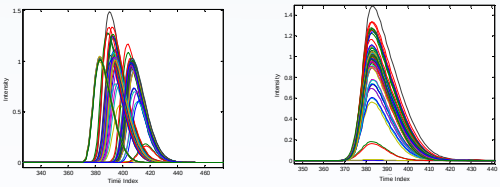
Results :

Viagra®:

Alignment:



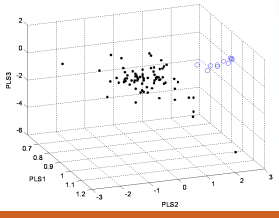
counterfeit imitation genuine



Before alignment After alignment

D-PLS:

A clear discrimination between genuine and illegal samples was achieved. The discrimination is mainly achieved by PLS factor 2 and PLS factor 3.



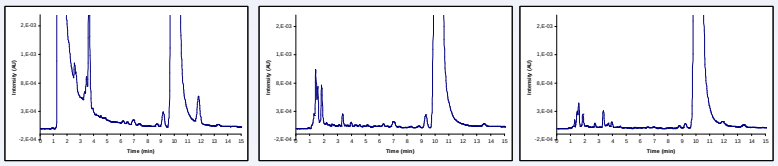
Classification:

The test set size was set at 20 samples among which 2 genuine and the training set was constituted of 55 illegal samples and 8 genuine samples.

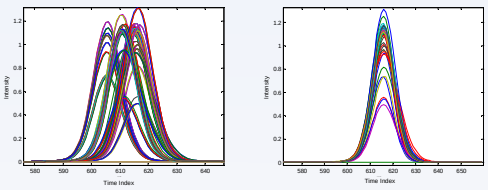
The application of the k-NN algorithm and the SIMCA algorithm returns 100% correct classification rate during both cross-validation and external validation.

Cialis®:

Alignment:



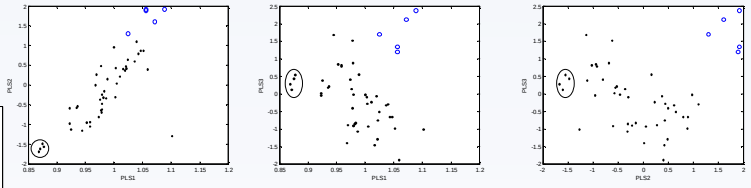
coloured imitation imitation genuine



Before alignment After alignment

D-PLS:

A group of four samples can be distinguished from the other ones (surrounded samples). These tablets are non-coated and their cores are strongly coloured in orange.



Classification:

The test set size was set at ten samples in order to contain two genuine samples. The training set was composed of 36 illegal samples and 3 genuine samples.

The application of the k-nearest neighbour algorithm returned 92,3% correct classification rate (3 illegal samples misclassified, all genuine samples correctly classified) during cross-validation. All samples of the test set were correctly classified during external validation.

For SIMCA, when 3 PCs were used to model the illegal samples, cross validation returned 92,3% correct classification rate (3 illegal samples misclassified, all genuine samples correctly classified) and external validation misclassified 1 sample out of ten, though all genuine samples were classified as genuine.

Conclusions :

After the log transformation of chromatographic fingerprints and using the discriminant PLS approach for exploratory analysis, a clear discrimination between legal and illegal samples was achieved.

From the obtained results, it is concluded that the k-NN algorithm is the best suited.

The obtained results show that this would be interesting to develop a routine method to obtain impurity profiles that could be used to detect counterfeit tablets by a control laboratory. This might be found as a useful approach especially in developing countries with basic analytical equipment.

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