

The combination of gas chromatography, mass spectrometry and Raman spectroscopy for identification of legal high products S. Assi¹ and S. J. Preston²



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Objective

The aim of this work was to identify legal high products using gas chromatography, mass spectrometry and Raman spectroscopy with partial least square regression.

Results and Discussion

The molecular weight of the pure substances was correlated with the different variables and the maximum correlation coefficient value obtained was 0.66 and was obtained against a Raman reading (Figure 2). This showed that none of the variables influenced the

Introduction

Legal high products represent a major public health threat due to their unpredicted pharmacological effects/ side effects. This is because they often contain mixtures of drugs/ impurities that do not match their label claim. This complexity in the products stimulates the need for using multiple analytical techniques for their identification.

Experimental

Materials

A total of eight standards of common drugs/ impurities present in legal high products were used (Figure 1). In addition, six legal high products were used.



molecular weight separately.



Figure 2 Correlation map of the different parameters used in the study including (1) molecular weight, (2) retention time, (3 - 8) mass spectral fragments and (9 - 14) maxima Raman peaks. A perfect match (r = 1) is displayed in dark red colour; whereas, a perfect mismatch (r is negative) is displayed in dark blue colour.

PLSR model construction

Figure 1 Raman spectra of (a) 2-aminoindan hydrochloride (2AI), (b) benzocaine (BEN), (c) caffeine (CAF), (d) dextromethorphan hydrobromide (DXM), (e) lidocaine hydrochloride (LID), (f) methyl phenidate (MET), (g) nicotinamide (NIC) and (h) procaine hydrochloride (PRO) measured using the Rigaku First Guard handheld instrument.

Method

The gas chromatograms and mass spectra of the standards products were measured using a Varian GC-MS instrument. In addition, the Raman spectra of the standards and products were measured using a Rigaku First Guard handheld Raman spectrometer with laser excitation wavelength of 1064 nm, thermoelectric cooling and charge coupled device detector.

□The data obtained from both instruments including GC retention times (min), six most abundant EI fragmentation peaks and six highest Raman peaks were used to construct a PLSR model for prediction of the molecular weight of the pure substances.

The PLSR model was constructed with 10 factors using the pure substances parameters including 105 parameters in the calibration set and eight parameters in the validation set.

PLSR model validation

The PLSR loading showed high effect for the molecular ion peak for the compounds. The models showed high accuracy with r^2 values of 0.9981and 0.9991 for the calibration and validation sets respectively (Figure 3). Also, the precision of both the calibration and validation set was within ± 5%.



The accuracy and precision of the model was evaluated using the regression correlation coefficient (r^2) and relative standard errors (RSE) of calibration and prediction values.

Nominal molecular weight (g/ mol) Nominal molecular weight (g/ mol)

Figure 3 Calibration and validation sets of the PLSR model created with the different parameters.

When the model was applied to the products, it showed the ability to predict the molecular weight of the products with accuracy of $\pm 10\%$.

Conclusion

The combination of gas chromatography, mass spectrometry and Raman spectroscopy with PLSR could predict the molecular weight of drugs/ impurities present in legal high products with accuracy of 10%.

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