Quantitative Analysis Using New Generation Raman Spectrometers and Chemometrics– Smaller and Faster

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The unique chemical signatures contained in Raman spectra have been used as molecular fingerprints to analyze molecular structures, to identify specific molecules, and to distinguish one material from another. For the past decade, Raman spectroscopy has gained ground in real world applications due to the highly selective nature of Raman signatures, the non-destructive nature when testing, and the convenience of needing no sample preparation. While many Raman applications are based on qualitative analysis, such as raw materials verification and quick identification of unknown chemical compounds, Raman spectroscopy is also suited for quantitative analysis enabled by a high performance instrument and a smart chemometics method. The concentrations of the compounds in a mixture can be predicted by the chemometric model built using calibration samples with known Raman signatures and concentrations.

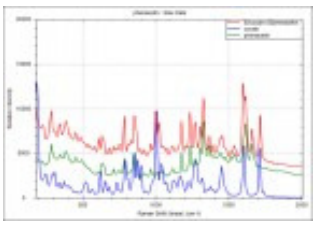
With the technological advancement in opto-electronics and laser components, there has been a rise in handheld and portable Raman instrument for field applications designed for non-technical users while maintaining the performance of a research grade instrument. When combined with powerful chemometric methods, this new generation of Raman analyzers has gradually been established as a new technology platform providing solutions to many real-life problems.

In this article, three real-life Raman quantitative and semi-quantitative analysis applications are discussed. These applications showcase the versatility of Raman spectroscopy and the potential impact that it can make in various industries.

Security – Rapid mixture analysis of suspected powders

Raman technology has been widely used in law enforcement and forensic labs to investigate crime scenes and to identify explosives and illegal drugs. Usually, the substances to be identified are mixtures, whether they are explosive residuals or illicit drugs. Rapid mixture analysis at the crime scene or during drug raids is very critical. Today's Raman technology and software development has progressed to the point that it is possible to equip handheld Raman analyzers with robust mixture analysis capabilities. One good example of such a device is B&W Tek's TacticID™,[1] where the powerful mixture analysis capability is built into a handheld device. The TacticID can identify components in a mixture and produce results in just a few seconds.

Figure 1 shows a report with the mixture analysis that gives the results for a mixture containing two materials: street cocaine and phenacetin. Fig. 2 shows the overlay of the mixture spectrum with the spectra of cocaine and phenacetin. The peaks marked with green dots indicate the peaks from phenacetin and the peaks marked by blue dots are cocaine peaks. The novel algorithm and chemometric analysis is able to identify the different compounds inside the mixture based on the Raman signatures for pure compounds found in the libraries.

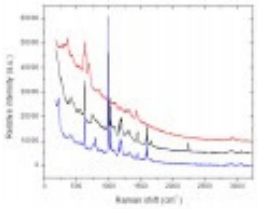


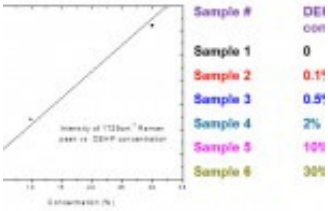
Plastic Toys Safety – Phthalates content analysis in plastic toys

Phthalates are toxic substances that may cause harm to the reproductive organs but are usually added to PVC to make the plastic soft. Even though they can be harmful, some phthalate added-plastics have been found in the manufacturing of toys. Since phthalates and PVC are simply mixed together rather than chemically bonded, the phthalates in PVC will come out when in contact with liquids or they may evaporate over time. In plastic toys, the phthalate concentration levels may reach up to 30% in order for the phthalate to take effect. As small children are more likely to place toys in their mouth, phthalate in the toys is a grave concern. Toys containing phthalates have already been regulated in US and EU[2].

To identify toys laced with phthalates and determine the concentrations, B&W Tek's i-Raman® Plus Portable Raman spectrometer with 785nm laser wavelength was used to develop a quantitative analysis method. The lab grade performance of this instrument in terms of sensitivity and spectral resolution makes it the ideal instrument for this application.

Figure 3 shows the Raman spectral overlay of three different toys from three different manufacturers. The common Raman peaks for phthalate at 1040 cm^{-1} and 1729 cm^{-1} are observed in two of the Raman spectra (black and blue), indicating existence of phthalates in these two toys, whereas the phthalate Raman peaks are not apparent in the third Raman spectrum (red), indicating that the toy represented by the red spectrum has little to no phthalate.



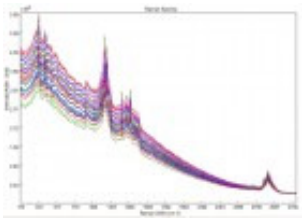


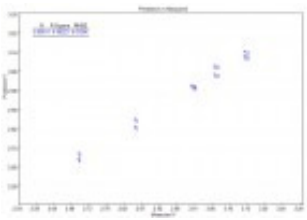
The Raman spectra of six samples with different DEHP (Bis(2-ethylhexyl) phthalate) concentrations ranging from 0% to 30% were used for analysis of phthalate content. After fluorescence background removal, the relationship between Raman peak intensity at 1729cm^{-1} and DEHP concentration within the range of interest is nearly linear (Fig. 4). Based on the results from this sample set, i-Raman Plus Raman system is able to measure DEHP concentration as low as 0.5% or better. Since the concentration of phthalates is usually closer to 30% in order for the phthalate to take effect, it is well within the detection limit of the i-Raman Plus portable Raman spectrometer.

PAT - Pharmaceutical blending process monitoring

Pharmaceutical tablets consist of Active Pharmaceutical Ingredients (APIs) and often multiple excipients, such as fillers, binders, and lubricants. In tablet manufacturing, blending is the process where APIs and excipients are blended together to form a homogenous mixture. Blending process control is very important in deciding final tablet product quality, and yet blending process control can be very challenging when it comes to detection or characterization of the variation in raw materials and final blend homogeneity. The US FDA guidance on pharmaceutical manufacturing process control in regards to API blending processes indicates that each batch should meet established purity specifications; in addition, for dry blended APIs, the validation of blending operations should indicate homogeneity of the blended batch.

Raman spectroscopy in conjunction with chemometric analysis can create a method to quantify the amount of an API in blended powders and in the final tablet. In this example, quantitative analysis of a blending process for tablets with 3mg of an API was conducted using an i-Raman® Plus portable Raman spectrometer with 785nm laser excitation. Eleven powder samples with known API concentrations from 2.40mg to 3.60mg per tablet were used to create the chemometric model (Fig. 5). Chemometric models were developed using B&W TEK's chemometric software, BWIQ™, with API weight per tablet being set as the response. The Partial Least Squares Regression (PLS) was used and performed on the spectral range 800 – 3000 cm^{-1}. The PLS model gives fairly good linear fit to the data with R^2=0.9922 and standard error = 0.01384, as shown in Fig. 6.





Raman spectra from two tablets were then used to predict the amount of API in the tablet. The prediction result is shown in Table 1, which demonstrates that Raman spectroscopy with chemometric analysis is a valuable technology for quantitative analysis of APIs in blend mixtures and in tablets.

Table 1. Prediction result

Prediction Tablet	Predicted API (mg/tablet)
T1-1	2.9668
T1-2	2.9244
T2-1	2.9038
T2-2	2.9296

The new generation of high performance portable and handheld Raman spectrometers combined with advanced chemometric methods has emerged as a new technology for industrial users to develop methods for solving real-world problems. Quantitative and mixture analysis are demonstrated through three applications in different industries, which shows that rapid and non-destructive quantitative analysis have become not only possible but also practical. Compared to the large benchtop lab-grade Raman spectrometers, which cannot be easily placed on-line or at-line for real time analysis, the new generation of portable and handheld Raman spectrometers have shown great potential in industrial applications and will play a major role in the near future.

References

1. TacticID GP datasheet - http://solutions.bwtek.com/acton/ppform/8353/001f/f-005e

2. Thomas Nørbygaard and Rolf W. Berg, Application of FT-Raman spectroscopy for analysis of phthalate esters in PVC plastics, ICORS 2002 Conference Proceedings Abstract. 2002. p. 687-688.