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Low-cost Portable Raman Instrument, a Tool toward Counterfeit Medication Identification

Jean-Pascal Bourgeois* and Olivier Vorlet

*Correspondence: Prof. J.-P. Bourgeois, Institute of Chemical Technologie (Chemtech), Haute Ecole d'Ingénierie et d'Architechture de Fribourg, HES-SO University of Applied Sciences and Arts Western Switzerland, Boulevard de Pérolles 80, CH-1700 Fribourg, E-mail: jean-pascal.bourgeois@hefr.ch

Abstract: We have successfully built a low-cost (under 500 CHF) portable Raman spectrometer based on scavenged, consumer electronics. The instrument prototype is designed as a tool to help identify counterfeit medication in low-income countries. As a proof of concept, we confirmed the presence of acetaminophen, a type of analgesic, in over-the-counter drugs from around the world.

Keywords: Acetaminophen · Consumer electronics · Counterfeit drugs · Raman spectroscopy · Social networks

Democratization of Analytical Tools

Modern analytical chemistry is expensive. It is based on state-of-the-art scientific instruments, which need to be used in complex facilities by highly trained staff. Therefore, chemical analysis is difficult to access for everyday occupations, and is often reserved for professional use. On the other hand, we are living in a chemically rich environment, and we are exposed to thousands of molecules every day. We can therefore imagine numerous applications where it would be useful to be able to perform chemical analysis with ease. Important questions are, for instance, are there pesticides in my children's food or drink, or additives in my cosmetics, how much sugar or lipids are in a particular food, am I exposed to toxic chemicals in my bedroom? Or is this object full of phthalates…? Many legitimate concerns that could be answered in the future by a democratization of analytical instruments. In this context, the motivation to start this project was to be able to confirm the presence of pharmacologically active substances in medication with an affordable instrument. Our main concern here is the detection of counterfeit drugs missing the key active ingredient.[1,2] For this purpose, a few years ago, our school developed a low-cost capillary electrophoresis instrument.[3] Currently, this instrument is distributed worldwide by the ONG Pharmelp.[4] Taking inspiration from this success story, we wanted to explore other technologies using a similar approach in order to cut down the price and simplify the use of certain analytical instruments.

Raman Spectroscopy

Our first target was Raman spectroscopy,[5] as it showed potential in price optimization. This analytical method allows for qualitative analysis suitable for chemical screening. Raman spectroscopy provides compound-specific spectra that can be compared to a database.[6] With the database as a reference, the spectra can be used to identify a specific molecule allowing for confirmation of presence of known pharmacological compounds in a drug. Additionally, Raman spectroscopy has the advantage that it does not require sample preparation, does not require solvent use, and is non-destructive. In the case of a medical pill, we only need to remove the protective coating on one face of the pill. Finally, the measurement is fast and can be done 'on the go' outside any laboratory facility with an adapted instrumental design. Nevertheless, not all is perfect: Raman scattering is extremely weak, so it needs a high-energy monochromatic illumination and a very sensitive sensor to record it.

Design and Construction

Consumer electronics offer a wide range of affordable access to cutting-edge technologies, like CCD/sensitive surface, diode lasers and wireless connectivity. The design of the instrument takes advantage of all these technologies. Webcams are often used to make do-it-yourself spectrometers, but in the case of a Raman spectrometer, and despite our efforts, the test with webcams ended with no results. The main reason is that the electronic shutter speed in a normal webcam is hardware imposed and cannot extend to long enough values to capture the weak signal. As an alternative, a popular type of device has come to our mind: the 'action camera'. Action cameras have great advantages over a webcams: they run on batteries, do not need a computer, are wireless and most importantly, allow the customer to set the shutter speed manually for up to several seconds. The manipulation of the shutter speed is the key in order to collect enough of the weak Raman scattering signal.

There were two attempts at altering the design of the instrument. The first one was based on a backscattering configuration; thus, it used a dichroic mirror and focused the laser beam on the sample surface. This design is interesting because it does not need a high-energy laser; a few milliwatts is enough. It provided reasonable results, but only for colorless solvent and transparent minerals like artificial diamonds. Unfortunately, no signal could be recorded for powders or opaque chemicals/samples. The position of the sample is critical: non-transparent samples need to be exactly at the focal point. The sensitivity of the setup turns out to be an impossible challenge with the simple design model and low target price. However, this design could be applied in the future to PAT (Process Analytical technology) analysis, specifically with microreactors.

The second design (Fig. 1) is a bit more intuitive: it uses a 90-degree arrangement and does not use a dichroic mirror. It consists of direct illumination of the sample with the laser beam. A small part of the scattered light is then passed through a slit and collected by a collimation lens as it enters the spectrometer. This last design is simple and does not need precise positioning of the sample. Another advantage over the first design is that it illuminates a large spot on the sample, making the measurement more representative as medical pills are often not homogeneous on a micro scale.

With simplicity in mind, we designed the spectrometer module. The optic was made with Google Cardboard lenses. These lenses are polymer-based and can be purchased for less than a dollar. The spectrometer consists of a collimation lens to collect the light, a diffraction grating and a final lens to focus

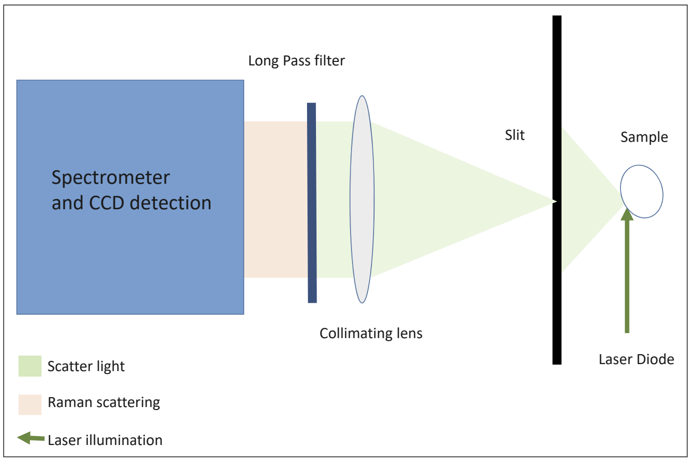

Fig. 1. The schematic 90-degree arrangement design of our low-cost Raman spectrometer.

back the image on the CCD. For the particular target application of our instrument (counterfeit drug detection), we focus on the wavenumber range 800–1500 cm^{-1}. The Raman shifts in this region are specific to the tested chemicals and can be used to find a certain compound in a medical pill.

For both approaches, we used a 532 nm laser diode of cheap manufacture. It turned out that the spectral dispersion of the laser emission was small enough to insure a good resolution of the recorded spectra.

For the construction of the instrument, a laser cutter built the base-structure that can be completed with the different optical modules. The high precision of the laser cutting allows all pieces to be assembled to create a perfect dark room. Absence of light leaking is critical if one wants to use the instrument by daylight.

Proof of Concept

The results presented here are a proof of concept. The experiment was performed on tablets of acetaminophen (paracetamol). This molecule is not the most problematic component on the fraud market, but we selected it because of the ease in obtaining this molecule without a prescription and the large number of generic medicines that exist.

The samples were collected from a few countries around the world. All medical pills were peeled to remove the protection layer, then a 10-second spectrum was collected using our instrument. The results shown in Fig. 2 compare the peeled drug to pure acetaminophen from Sigma-Aldrich as well as an aspirin tablet (acetylsalicylic acid) and Novalgin tablet (metamizole). The pattern of the emission spectra is typical of acetaminophen and is recognizable in comparison with spectra of a chemical reference or a drug containing the active compound. By opposition, the difference with the spectrum of Aspirin and Novalgin is clear and does not need any complex spectrum analysis to figure out this is not acetaminophen. Of course, the interpretation may be more complex as a Raman signal is strongly impacted by fluorescent molecules, by the presence of excipients or by a synergic pharmaceutical compound in the tablet.

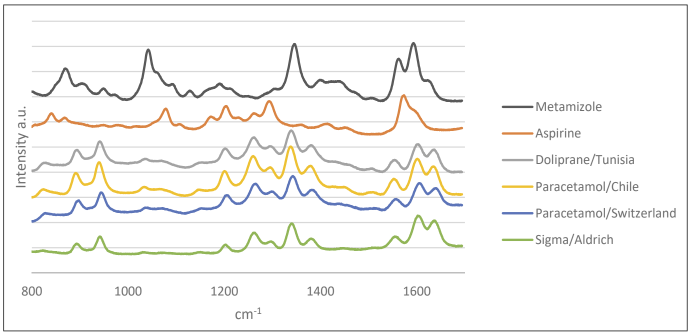

Fig. 2. Raman spectra comparison of several analgesic pills.

Instrumental Chemistry and Social Media

An important contribution that comes with the use of action camera electronics is the wireless connectivity. Despite the fact that you do not have the extra cost of a dedicated computer, everybody can connect the instrument with their smartphone and record the data directly. This comes with a hidden advantage, because with a smartphone, the data can be easily shared worldwide through social networks within an online community. This feature could be useful to identify counterfeit drugs allowing for remote spectrum interpretation, crowdsourcing, data analytics and may help to develop a bigger picture of the problem.

Conclusion

The use of the innovative technology found in consumer electronics together with smartphones for the construction of a low-cost Raman spectrometer is a step towards democratization of instrumental analytical chemistry. Furthermore, the opportunity to take advantage of internet connectivity and social networking to share analytical results is a good tool to help crowdsolve the problems seen in counterfeit medicine.

Acknowledgments

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