Researchers at the University of Montreal are Developing New Methods to Monitor Pharmaceutical Compounds in Drinking Water

In response to growing concerns over the presence of residual pharmaceutical products in the city's waste waters and drinking water, a collaboration has been established among the University of Montreal, the Drinking Water Research Chair at the Polytechnic School of Montreal, the City of Montreal and Environment Canada. This group works on the identification and quantification of the pharmaceuticals of most concern. The results of this ambitious study will be used to determine what upgrades might be necessary for the current drinking and waste water treatment systems of Montreal. To conduct this research, the University of Montreal has developed a new online sample preparation method using a customized Thermo Scientific EQuan™ system for solid phase extraction coupled to liquid chromatography and tandem mass spectrometry (SPE-LC-MS/MS) technology. This implementation has resulted in significant cost savings and increased productivity.

Background

Many of the pharmaceutical compounds contained in a drug remain active beyond ingestion of the specific medication either by a person or an animal. Recently, this fact has triggered serious concerns with regards to the possible consequences that these pharmaceutical compounds may have on the environment after excretion by humans or animals. It is not unusual that municipal plants are not engineered to identify or remove all residual pharmaceutical compounds, meaning that they can pass untreated through the sewage system and then be released in the environment. Eventually, these untreated pharmaceutical compounds will be ingested in minor quantities by people, through drinking water.

Driven by these concerns, the Department of Chemistry of the University of Montreal has been trying to develop an efficient method for the precise identification and quantification of the pharmaceutical products of most environmental concern that are present in the St. Lawrence River, a source of drinking water for the City of Montreal. This academic analytical chemistry laboratory employs approximately 20 researchers, mostly graduate and post-doctoral students, and focuses on finding the best analytical method for environmental studies. Around half of the laboratory's research efforts are specifically targeted at pharmaceutical compounds present in the environment.

A research group has been formed, composed of Sébastien Sauvé, associate professor at the University of Montreal, Michèle Prévost, co-holder of the Drinking Water Research Chair at the École Polytechnique de Montréal, Christian Gagnon at Environment Canada and their teams, in order to identify pharmaceutical compounds that the city should be concerned about removing. The end goal is to determine new technology to be used for any possible future upgrades of the drinking water and waste water treatment systems of Montreal.

In 2005, Sébastien Sauvé purchased a customized Thermo Scientific EQuan system to undertake his laboratory's research on the presence of pharmaceuticals in the environment. This system is comprised of the Thermo Scientific Quantum Ultra™ mass spectrometer equipped with the AM (Accurate Mass) option, which Sauvé and his laboratory research team use to identify and accurately measure pharmaceuticals potentially present in the environment. The use of both mass spectrometry (MS) and MS/MS spectra enables accurate mass measurements and thus precise confirmation of the elemental composition of 'known' drugs and their metabolites. Additional chemical information such as the molecular formula of the parent drug or an understanding of the possible metabolic pathways allow for positive identification of the plausible structure of unknown molecules or, at least, narrows down the possibilities to a few close fits.

Sauvé's analytical chemistry laboratory has been using the EQuan system for its continued research on the detection and quantification of the pharmaceutical compounds of most environmental concern that are being released into the St. Lawrence river[1]. *Table 1* and *Figure 1* demonstrate the results of one of these studies, which focused on the extraction, detection and quantification of six of the most common anti-infectives in both untreated and treated sewage.

Compound	Mean mass flow in the St. Lawrence River (g/day)
Sulfamethoxazole	340 ± 30
Trimethroprim	310 ± 20
Ciprofloxacin	320 ± 10
Levofloxacin	118 ± 2
Clarithromycin	830 ± 60
Azithromycin	310 ± 20

Table 1. The average mass flow of the studied anti-infectives at Montreal wastewater treatment plant

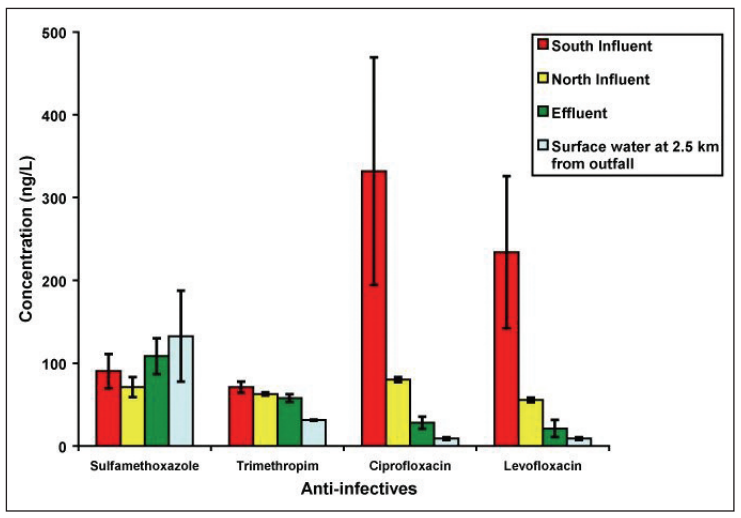

Figure 1.

Environmental Sample Preparation – A Challenging Process

The pharmaceutical compounds that need to be analyzed as part of the research project on the water resources around Montreal are only present at trace levels. As a consequence, sample preparation requires pre-concentration, which typically involves a time-consuming, complicated manual method that is prone to errors. It was therefore necessary for the success of the project that Sauvé and his colleagues at the University of Montreal develop an online pre-concentration method for preparation of water samples both prior to and after treatment by the City's water treatment facility.

"We have to run the sample pre-concentration because, despite the excellent sensitivity of the Thermo Scientific instrument, the quantities of the pharmaceuticals of interest are very low," Sauvé explained. "The greatest challenge of the pre-concentration process is the associated labor since the procedure requires a lot of labor and time to be completed manually. In addition, all of the sample manipulations that occur during the manual pre-concentration increase the potential for errors and reduce the reliability of the results."

Pesticides, antibiotics and veterinary residues pose a significant health threat, thus their presence in drinking water is strictly regulated by U.S., Canadian, Japanese and European Environmental and Water directives. Achieving low limits of detection (LODs) of these substances is of extreme importance in order to comply with the regulatory levels. Traditionally, liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) has been used by the environmental industry for the identification and quantification of these residues. However, this methodology typically requires extensive offline sample preparation, which can be particularly time consuming and expensive.

Benefits Achieved with EQuan

Sauvé worked with Thermo Fisher Scientific to develop methods that use the EQuan system to optimize the pre-concentration of samples online instead of offline, so all the pre-concentration is done through column switching by the system before it feeds directly into the triple quadrupole instrument.

The Thermo Scientific EQuan environmental water monitoring system has been designed to perform reliable and accurate analysis of water samples. The system can provide precise monitoring of trace levels of pesticides, hormones, antibiotics, pharmaceuticals and veterinary products in drinking water. The analytical chemistry laboratory of the University of Montreal has benefited from the implementation of the EQuan system because of its unique ability to significantly reduce sample analysis time, allowing samples to be directly injected and enriched, followed by immediate LC-MS/MS analysis. Furthermore, the use of the EQuan system has considerably improved LODs (up to 100 times) compared to conventional injection techniques.

Detection limits of 10ppt (parts per trillion) are easily achieved by simply injecting filtered and acidified water samples – without further sample preparation.

Apart from the increased reliability and improved LODs, the EQuan solution has also offered another huge benefit to the University of Montreal in the form of greatly reduced personnel costs. "As we evaluate the human resources required to perform the offline analysis in relation to how many resources we can save when implementing an online pre-concentration method, the personnel time savings are very significant," Sauvé commented.

The University of Montreal's EQuan system consists of a Thermo Scientific TSQ Quantum Ultra AM™ mass spectrometer, two Surveyor™ HPLC pumps with a pre-concentration column, an analytical column, a CTC autosampler and an EQuan kit consisting of columns and HPLC accessories. EQuan can use any of the TSQ Quantum series instruments depending on the specific application, including the TSQ Quantum Access™, TSQ Quantum Discovery MAX™ and TSQ Quantum Ultra.

Conclusion

After extensive research, Sauvé and his laboratory staff finalized several online sample preparation methods, each one of them focusing on different pharmaceutical compounds. The team is currently gathering data on the study undertaken in various kinds of water resources around Montreal. The laboratory analyzes 30-40 samples of raw water every day. Samples are gathered from strategic places around the Montreal area, including sites for the intake of water before its treatment and distribution. Using the Thermo Scientific EQuan system has allowed significant reductions of analysis time as well as improving LODs.

References

1 Segura PA, Garcia Ac A, Lajeunesse A, Ghosh D, Gagnon C, Sauvé S. 2007. Determination of six anti-infectives in wastewater using tandem solid phase extraction and LC/MS/MS. Journal of Environmental Monitoring 9:307-313.

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Sampler; for Taking Undisturbed Samples of Sediment

For years, the Beeker Sampler from **Eijkelkamp Agrisearch Equipment** (The Netherlands) has offered the best solution for taking undisturbed underwater sediment samples. When other approaches are used to take samples from underwater sediments it is often the case that the final sample does not truly represent the actual structure of the sediment. This problem is eliminated when the Beeker Sampler is used! The samples are taken in a transparent tube with the original stratification and layer thickness of the sampled material being retained. As a result, a clear description of the profile can be given.

The piston of the Beeker-type sediment core sampler can be operated directly using a rod so that the sample can be pushed out of the device into a sample bucket on site. The rigid steel strips hold the device tightly together.

The Beeker sampler can be used as an independent sampling device. The Beeker-type sediment core sampler is comparable to the Multi sampler and the suction corer, but has a closable head. It is also possible to hammer the device into the soil. The standard kit is suitable for use in water up to a maximum depth of 5 metres. Using extra extension rods, in some cases samples can be taken at an even greater depth.

Due to the compressed air reservoirs and the large hose connections, this corer is very mobile and is suitable for many types of application. The Beeker sampler can sample many types of sediment, which can vary in composition from extremely aqueous and weak to unconsolidated sand, irrespective of the stratification of the bed. Furthermore, the Beeker sampler is light in weight and easy to use, enabling many samples to be taken in a day.

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