A Q&A

Electrochemistry for Detection and Reaction in Pharmaceutical R&D

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Electrochemical detection (ECD) in high-performance liquid chromatography (HPLC) is used in many research areas such as pharmaceutical, clinical, and neuroscience. The detection is based on the measurement of an electric current that results from the oxidation of analytes of interest. Recently, analysts have become interested in using electrochemistry for applications other than detection in HPLC. It is used as reaction technique, thereby the oxidation or reduction of the analytes of interest takes place under controlled conditions in the electrochemical cell and the REDOX products are identified by mass spectrometry (MS). Electrochemistry as a reaction technique is of particular interest to pharmaceutical research and development to mimic drug metabolism, to study drug degradation (stability testing), the fast synthesis of degradants and metabolites as well as to study environmental degradation/persistence of drugs.

The on-line coupling of electrochemistry with mass spectrometry (EC/MS) creates a powerful new platform to investigate various oxidation and reduction processes in life sciences. It is a complementary technique to traditional *in vivo* and *in vitro* methods. To learn more about both electrochemical detection and reactors, *LCGC* recently spoke with Martin Eysberg, director sales and marketing at Antec Scientific.

LGCG: How is Antec Scientific addressing challenges in electrochemistry for detection and reaction in pharmaceutical research and development?

Eysberg: In the field of electrochemical detection, Antec's focus is on application support and development, the concept of "solution and knowledge provider." Over the years, we have used our experience and user feedback to improve our instrumentation to make it robust and easy to use. We also supply complete, turn-key ALEXYS HPLC-ECD Analyzers, ready to use for dedicated applications. Robust methods and dedicated applications are essential criteria for such as for implementing United States Pharmacopoeia (USP) or European Pharmacopoeia (EP) methods.

A few years ago, we stepped into the field of electrochemistry as a pure reaction technique to mimic natures REDOX reactions. After close collaboration with scientists in academia, we introduced the ROXY EC system. The system allows for rapid studying of pharmaceutical degradation, mimicking oxidative metabolomics, fast synthesis of metabolites or degradants, etc. In other words, we bring this additional reaction technique to scientists to help speed up their research and to give them an opportunity to generate more information with substantial cost savings.

LGCG: Why is Antec Scientific a leading provider of electrochemical detectors and reactors?

Eysberg: For over 27 years now, electrochemistry is our daily "Mantra." We do—literally—nothing other than electrochemistry. With such 100% focus and dedication, we have become the Number One provider of electrochemical solutions for detection and reaction.

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In addition, we have a team of scientists, technicians, and qualified distributors around the world with years of experience capable to support our customers and to solve any analytical problem.

LGCG: What are some unique features of the DECADE Elite detector?

Eysberg: The DECADE Elite detector is the fourth generation of Antec's electrochemical detectors. We have built these detectors for 27 years with a focus on sensitivity. In neuroscience, electrochemical detection is mainly used for high-sensitivity trace analysis. Using our DECADE Elite with ADF, and SenCell with AST, we can do neurotransmitters in the brain at femtomole-detection sensitivity. In food and biochemical research, we have our FlexCell with an exchangeable electrode for PAD of carbohydrates. These are just a few features.

In addition, Antec Scientific is the only company in the world that provides a five-year warranty on the glassy carbon flow cells and we are able to recertify these cells.

LGCG: Why should I consider electrochemical detection and not other detection techniques—for example, MS instruments—in some of my application?

Eysberg: You cannot always compare them, as the choice of the detection method is based on different criteria (e.g., need for positive identification, the number of analyses, cost per sample, and requirements for limits of detection, to mention a few). I believe there are two strong pro's for electrochemical detection. The first is cost per analysis. An electrochemical detector is still a lot less expensive than an MS instrument but sensitivity wise it gets close to MS. Second, an electrochemical detector is much easier to use than a MS. By today's standard Electrochemical detectors have become ease in use and Antec has focused on making electrochemical detection simple and robust.

LGCG: Why should I couple the ROXY electrochemical device with mass spectrometer?

Eysberg: The question is not, why should you couple electrochemical reactions with MS? The question is, when and when not?

In the case of electrochemical synthesis, there is no direct need for on-line coupling with MS. The synthesis is usually made in a bulk cell, that operates in DC mode over a period of 30 minutes or longer. It is sufficient to analyse aliquots by MS methods from time to time.

The same applies basically for any other electrochemical reaction that provides stable reaction products, which can be further analyzed by off-line LC/MS techniques.

However, whenever it comes to fast reaction monitoring, or the formation of reactive intermediates, or the formation of short-lived products, the on-line coupling with (LC)/MS offers a new unique advantage that no other technique can offer.

You can get a "fingerprint" of all potential oxidative degradants of a drug compound in only a few minutes, the same applies for generating drug metabolites. In case of S–S-bond reduction in proteins/peptides, the reduction is within a few seconds to allow full integration into top-down as well as bottom-up LC/MS proteomics.

LGCG: Why is it beneficial for scientists to use a ROXY device in pharmaceutical research and development efforts?

Eysberg: ROXY is beneficial for scientists because of the additional information that can be obtained, which is usually impossible with chemical or enzymatic approaches.

For example, classical wet chemistry approaches to synthesize metabolites needed for nuclear magnetic resonance structural identification can take several weeks, Enzymatic can be expensive, does not often work, or does not provide sufficient product conversion in particular if the substrate is hydrophobic. By contrast, electrochemical reactions are much quicker (minutes versus days/weeks) and can work under both hydrophilic and hydrophobic conditions. Another example is disulfide bond reduction in protein therapeutics/antibodies where in many cases, chemical reduction is insufficient, resulting in poor sequence coverage. Electrochemistry has proven to overcome some of these shortcomings, resulting in almost full reduction of highly disulfide stabilized proteins/peptides and consequently significant higher sequence coverage.

LGCG: Who is using the EC/MS in pharma and in which direction will it evolve?

Eysberg: By now, most big pharmaceutical and biotechnology companies as well as academia are using ROXY EC/MS. In almost any enzymatic, aquatic, microbial, or ultraviolet reaction, the underlying principle is REDOX—doesn't matter if it is *in vivo* or *in vitro.*

Electrochemistry "in-electro" allows one to study most of these reactions in real-time and in a well-defined system without external interferences no other technique can offer so far.

For more than 25 years **Antec Scientific** has been a world-leading supplier of analytical instrumentation based on electrochemistry (EC). Antec's line of instruments includes electrochemical detectors (ECD), analyzers built on HPLC-ECD and electrochemical reactors for online coupling with MS (EC-MS).