EXTRACTIVE-LIQUID ELECTRON IONIZATION-MASS SPECTROMETRY (E-LEI-MS): A SYSTEM FOR COMBINING AMBIENT SAMPLING AND ELECTRON IONIZATION IN TARGETED AND UNTARGETED ANALYSIS

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Real-time analytical techniques aim to reduce and simplify analysis time/steps providing rapid results. The direct analysis also allows for reducing the use of toxic components therefore the impact on the environment. In this regard, several ambient mass spectrometry (AMS) techniques have been recently developed. AMS is defined as the "desorption of molecules and formation of ions outside the mass spectrometer directly from samples in their native environment with no or minimal sample preparation" [1]. Inspired by this principle, Extractive-Liquid Electron Ionization-Mass Spectrometry (E-LEI-MS) has been developed [2]. E-LEI-MS is a new real-time approach that combines ambient sampling with electron ionization (EI). The advantages of E-LEI-MS are the elimination or at least the simplification of the sample preparation and the identification of compounds based on comparison with the National Institute of Standards and Technology (NIST) library spectra. The E-LEI-MS system introduces the liquid phase containing analytes directly into the EI similar to the Direct-EI (DEI) interface [3] previously developed in this laboratory. Therefore, the vaporization and ionization of the analytes occurs inside the mass spectrometer, rather than affected by ambient conditions. This feature makes E-LEI-MS very different from other AMS techniques that are mainly based on electrospray ionization (ESI). The E-LEI-MS system uses a solvent release mechanism that allows the formation of a droplet on the sample surface and the dissolution of analytes. The system is suitable for the use of different solvents that are selected based on the target molecules. The solution formed on the sample surface containing the analytes is aspirated by the MS vacuum via a sampling tip; this mechanism makes E-LEI-MS suitable for the analysis of solid and liquid samples. Currently, the system can provide qualitative results, so its use should be considered mainly for screening purposes. The matrices investigated so far using the E-LEI-MS system were chosen based on experimental evidence demonstrating the validity of other real-time techniques in various application fields. For example, there are various AMS food applications. These include food safety testing, in particular, the rapid determination of pesticide residues in food [4]. Pesticides are key compounds in the food market but their presence represents a risk to human and animal health and for the environment. The analysis of chlorpyrifos, a pesticide used in citrus crops, was proposed as the first E-LEI-MS/MS application. Switching from a single quadrupole mass spectrometer to a triple quadrupole (QqQ) mass spectrometer allowed us to perform tandem MS, increasing the system selectivity and sensitivity for determining components contained at trace level. E-LEI-MS can operate in scan, selected ion monitoring (SIM), and multiple reaction monitoring (MRM) modes, depending on the application goals and requirements.

The E-LEI-MS system is a prototype still in continuous optimization. The current configuration (**Fig. 1**) includes many of the components described by A. Arigò *et al.* [2], adapted for coupling the sampling components to an Agilent Technologies 7010 triple quadrupole mass spectrometer (Agilent Technologies, Santa Clara, CA, USA) equipped with an EI source. Two fused silica capillaries (40 μm I.D.; 375 μm O.D.; Polymicro Technologies, Phoenix, USA and 30 μm I.D.; 375 μm O.D. Polymicro Technologies, Phoenix, USA) connect the sample surface to the mass spectrometer through an MV201 manual microfluid 3-port valve (LabSmith, Livermore, CA, USA). The first capillary is different from the one used in the previous configuration. This change was necessary to regulate the aspiration strength of the vacuum, which proved to be less powerful in the QqQ compared to the vacuum generated by the single quadrupole. The solvent-release device consists of a KD Scientific syringe pump (KD Scientific Inc., Holliston, MA, USA) equipped with a 1-mL syringe (Hamilton, Bonaduz, Switzerland). The solvent flows through a Teflon tube resulting in a tee connection crossed by the sampling tip. The sampling tip is the E-LEI-MS core and consists of two coaxial tubings. The inner tubing (orange) connects the sample surface to the on–off valve and the outer tubing (yellow, peek tube; 450 μm I.D.; 660 μm O.D.; Postnova Analytics GmbH; Landsberg, Germany) allows the solvent delivery.

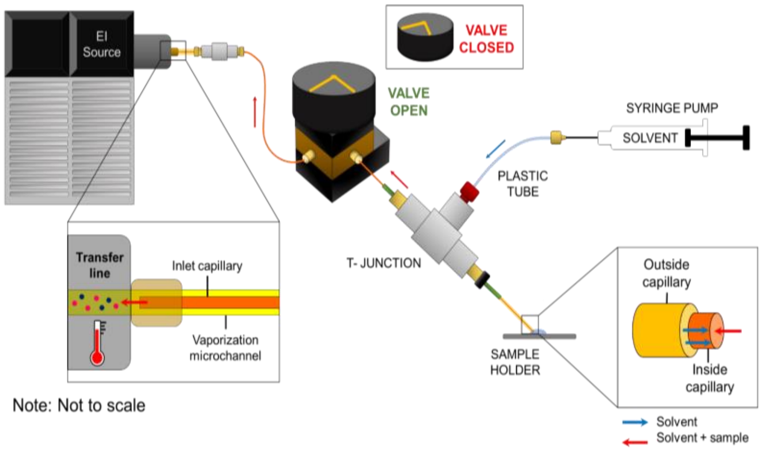

Figure 1: E-LEI-MS configuration.

The instrumental prototype can be further optimized. Inspired by the structure of the LEI (Liquid Electron Ionization) interface [5], the introduction of a capillary as a vaporization microchannel would allow the high temperature of the transfer line to vaporize the analytes before entering the ion source (IS); this allows the analytes to be easily aspirated by the high vacuum. In addition, the transfer line reaches a higher temperature than the source, helping to evaporate high boiling point compounds. Improving the system configuration means increasing the E-LEI-MS system efficiency, but also working toward making it a portable device [6]. Performing analysis *in situ* is an interesting goal and also an important environmental aspect because it avoids sample transport and storage. Coupling E-LEI-MS with a high-resolution mass spectrometer, which would increase the system identification power, is another potential possibility. E-LEI-MS has been already successfully used for a wide range of applications including the detection of illegal drugs on banknotes, the detection of active ingredients in tablets, and the identification of unknown compounds in paintings [2]. The results obtained with the E-LEI-MS demonstrate its versatility, both for the type of molecules that can be analyzed and the different application fields. Inspired by other AMS scientific evidence [7], new applications can be explored. An example of future E-LEI-MS/MS application is the detection of markers for bacterial identification in biological samples. Moreover, the high specificity of the MRM acquisition mode makes the system suitable for determining substances subject to regulation, such as allergens, which are used as fragrances in cleaners and cosmetic products. Allergens residue on cleaned surface can be investigated by E-LEI-MS. More generally, as a screening technique, E-LEI-MS could be used for quality control analysis in forensic, food, pharmaceutical, and cosmetic areas. In addition, the potential of E-LEI-MS in untargeted analyses of complex matrices, such as food, will be also explored.

Some green aspects of this technique have already been mentioned. The lack of sample preparation and the low solvent volume used make E-LEI-MS an environmentally friendly technique. AGREE green assessment tool [8] was used to evaluate the E-LEI-MS obtaining good results [2]. However, some aspects still need to be improved; for example, avoid the use of toxic solvents preferring water or less polluting solvents.

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