

Organophosphate nerve agents (OPNAs) are the most toxic warfare agents. They degrade rapidly in nature or in the human body by hydrolysis to give rise to alkyl methyl phosphonic acids (AMPAs). These degradation products can be used as markers of exposure to OPNAs. However, their analysis by liquid chromatography coupled to mass spectrometry (LC-MS) in complex matrices implies the use of effective sample treatment methods. Therefore, Parallel Artificial Liquid Microextraction method (PALME) was developed to extract and concentrate AMPAs. PALME is a microextraction method carried out in a two-plates 96-well system where the aqueous sample and the aqueous acceptor phase are separated by a flat membrane impregnated with organic solvent. This allows the processing of several samples simultaneously. Initially, a plate system as described in the literature was used. Several parameters affecting the extraction of the targeted analytes were studied including, for the first time, new ones such as the effect of ionic strength and temperature on the extraction efficiency.

However, the enrichment factors (EFs) obtained were limited and did not allow to achieve the required sensitivity, despite the exhaustive extraction rates for 3 of the 5 studied compounds. Following this observation, the PALME device was modified by introducing a 96-well donor plate with a donor volume 6 times larger than the classic 96-well plate of 0.5 ml volume. This made possible to reach EFs of 42. The final PALME method developed was then applied for the first time in the environmental field on samples of river water, wastewater and aqueous soil extracts.

In order to meet the 10 principles of green sample preparation, part of this thesis work aimed to make the PALME more "green" by replacing organic solvents, which are harmful to health and the environment, with natural solvents. The octanol used as a solvent in PALME was therefore replaced by a hydrophobic deep eutectic solvent of natural origin (NaHDES) based on thymol and coumarin. This new NaHDES-PALME method associated with LC-MS/MS has been successfully applied to biological samples (urine). It has a sensitivity that meets the OPCW requirements and can therefore be used for medical and/or forensic purposes. It is very simple to implement, conomical, fast, green and high throughput and therefore totally adapted to the emergency context of an intervention on a scene potentially contaminated by OPNAs. Moreover, the optimized operational parameters for the extraction of AMPAs in PALME turned out to be the same as those previously obtained during the optimization of the hollow fiber liquid micro-extraction method (HF-LPME), a similar method of PALME in principle but differing in geometry. This result makes it possible the transfer of many methods already developed in HF-LPME to PALME.