Development of a Generic MEKC Method for the Separation of 15 Antimalarial Drugs by a Design Space Approach

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Malaria is one of the most important parasitic diseases affecting people especially in Africa. As counterfeit is largely present in the African market, it is important to develop a simple method which can control the conformity of medicines used against this disease. The interest of a generic method is to permit the quality control of pharmaceutical formulations whose quantitative and qualitative composition is not well known. For the moment no capillary electrophoresis (CE) method has been developed to analyse simultaneously the major antimalarials but, due to its low consumption of solvent, this technique has an economical advantage for an implementation in Africa.

This project consists in the analysis of 15 antimalarials (artesunate, artemether, amodiaquine, chloroquine, piperaquine, primaquine, quinine, cinchonine, mefloquine, halofantrine, sulfadoxine, sulfalen, atovaquone, proguanil and pyrimethamine). Capillary zone electrophoresis (CZE) was not possible as all these molecules could not be charged at a same pH. Micellar electrokinetic chromatography (MEKC) was then preferred because it also allows separation of neutral compounds.

Preliminary experiments were first realised to select the most crucial factors for antimalarials separation. Several conditions were tested and four parameters as well as their investigation domain were then chosen: pH (5-10), SDS concentration (20-90mM), acetonitrile proportion (10-40%) and temperature (20-35°C). Then, an experimental design methodology using a central composite design (CCD) was carried out. Twenty five experiments were defined by CCD and tested. The experiments performed at low pH could not lead to the detection of all analytes. Therefore, a custom design was performed by the removal of 5 conditions and the addition of 8 conditions at high pH. Migration times (at the beginning, the apex and the end) were extracted for each molecule in each condition.

Mathematical modelling allowed the prediction of the optimal condition in terms of analyte separation. This prediction was verified experimentally and could lead to the separation of 13 compounds in 7 minutes. As the condition did not show a complete separation of the 15 molecules, the buffer concentration and the voltage were modified to enlarge the migration window. Finally all compounds were separated with a higher peak resolution and efficacy in 30 minutes.

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