ROBUST SFC METHOD OPTIMISATION USING DESIGN SPACE STRATEGY

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Recently, the number of publications about SFC knew an important increase. This phenomenon could be explained by the necessity of rapid, effective and green analytical methods. In order to prove the potential of SFC, the aim of our work was to develop SFC methods for the separation of pharmaceutical compounds using an innovative chemometric approach. Two case studies were investigated in the present project; first, polar compounds were selected as a worst case; secondly, the method development and validation of antibiotic drugs were selected as a more practical case.

Following the context of pharmaceuticals guidelines ICH Q8 R2 and FDA recommendations, the concept of Quality by Design (QbD) was implemented in the pharmaceutical industry environment. As analytical methods could be considered as a part of pharmaceutical development, the QbD concept has to be applied to analytical method development by using Design Space (DS). In the present study, DS could be defined as a subspace of the experimental domain into the chromatographic conditions will ensure the quality of the separation [1].

Firstly, a SFC method to separate 8 pharmaceutical polar compounds was developed [2]. A screening design was performed to select the nature of the stationary and the mobile (modifier and additive) phases. Then, a three factors central composite design was defined to perform the robust method optimisation. The retention time modelling of each compound and the predictive error propagation were used to compute the design space – subspace of the experimental domain wherein the separation between peaks superior than 0 and the total analysis time lower than 15 minutes were guaranteed with a predefined quality level. Then the optimal condition was experimentally tested in order to confirm the prediction. The quality of the separation into the DS was also tested to confirm the method robustness.

The developed method was geometrically transferred to sub 2-µm particles column. The objectives of this transfer were to test the high robustness of the method and to reach better chromatographic performances. Indeed, the analysis time was decreased (six times) and simultaneously the peak capacity was improved [3].

Secondly, the same methodology used for polar compounds was used to optimise a quantitative method of antibiotics in pharmaceutical matrix. This is the first demonstration of the interest of SFC technique for the quality control of medicines. Furthermore, the method was successfully validated according to total error approach and used for the control of medicines form Democratic Republic of Congo.

To conclude, SFC is a really interesting green technique in the field of pharmaceutical analysis. Indeed, recent publications [3-4] showed the interest of SFC for R&D and for QC departments. Furthermore, the robust optimisation interest using DS strategy was successfully demonstrated. The DS strategy should be used for any analytical method development.

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