Strategy for developing and optimizing liquid chromatography methods in pharmaceutical development using computer-assisted screening and Plackett–Burman experimental design

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„...connection to the chromatographic apparatus. More sophisticated software utilizes artificial intelligence. An early example is the EluEx, which can suggest initial experimental conditions based on chemical structures [7-9] . The more recently introduced is the..."

Abstract

We describe a three-step method development/optimization strategy for HPLC assay/impurity methods for pharmaceuticals, which include multiple-column/mobile phase screening using a system equipped with a column-switching device, further optimization of separation by using multiple organic modifiers in the mobile phase, and multiple-factor method optimization using Plackett–Burman experimental designs. In the first two steps, commercially available chromatography optimization software, DryLab, was used to perform computer simulations. This allows the method developer to evaluate each condition (one column/mobile phase combination) with retention data from two scouting gradient runs. This approach significantly reduces the number of runs in method development. After a satisfactory separation was obtained, we used a method optimization step with Plackett–Burman experimental designs. The purpose of the 16-injection set experiments was to evaluate nine method factors with regard to method precision, accuracy, sensitivity and specificity. The results provided logical justifications in selecting method parameters such as column temperature, detection wavelength, injection volume, and sample solvent, etc. In data analysis, instead of the traditional mathematical manipulations, we used the graphical methods to examine and present data by creating the so-called main effect plots. Because replicates of design points were not run, the data did not allow the testing of statistical significance. However, it provided visual presentations in a way that is easy to understand for the method developer and end user alike.

Author Keywords: Computer simulation; Plackett–Burman design; Method development; Optimization

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