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# Interest of achiral-achiral tandem columns for impurity profiling of synthetic drugs with supercritical fluid chromatography

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HIGHLIGHTS

- Coupling two columns is an easy way to assemble selectivities in SFC
- Tandem columns improve peak capacity and sensitivity over single columns
- Some column combinations are more effective than others
- The analysis time reduction with tandem columns is currently restricted by system pressure limits

## Abstract

To achieve the most complete impurity profiling of synthetic drugs with a single chromatographic technique, high resolution is required, which may be gained with a combination of high efficiency and versatile selectivity, allowing to separate most similar analytes. Compared to a single-column chromatographic method, coupling complementary stationary phases promises both an increase in efficiency and an increase in selectivity possibilities. With supercritical fluid chromatography (SFC), the use of long columns is facilitated by the low viscosity of the mobile phase. In this paper, we investigate the interest of coupling two achiral stationary phases (Acquity UPC$^2$ HSS C18 SB and Nucleoshell HILIC) that were previously observed to have excellent complementarity in SFC to carry out impurity profiling on 25 individual drug substances containing varied numbers and amounts of impurities. The single-column gradient methods are compared to tandem-column gradient methods with the two possible ordering of columns (C18 phase in first or second position) based on selectivity, peak capacity, sensitivity, UV-estimated purity of the active pharmaceutical ingredient and number of impurities detected with UV-estimated concentration >0.04 %. It appears that it could be more beneficial to have two