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# On-line coupling of achiral Reversed Phase Liquid Chromatography and chiral Supercritical Fluid Chromatography for the analysis of pharmaceutical compounds

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## Highlights:

- A selective comprehensive 2D approach was used for the simultaneous achiral x chiral analysis of pharmaceuticals
- On-line coupling of achiral RPLC and chiral SFC was developed and successfully applied
- A detection limit of around 0.5% for the R form could be achieved with UV detection
- Chemical and enantiomeric purity were evaluated in less than 50 min within a single run

## Abstract

On-line selective comprehensive two-dimensional chromatography combining Reversed Phase Liquid Chromatography and Supercritical Fluid Chromatography (sRPLCxSFC) was investigated for the analysis of chiral pharmaceutical compounds. Preliminary studies were carried out with the aim of overcoming instrumental constraints which are related to such 2D-coupling. The impact of both injection solvent and injection volume on the chiral SFC second separation was assessed with a view to limiting injection effects due to mobile phase compatibility issues between both dimensions. The resulting on-line sRPLCxSFC system was applied to the achiral x chiral analysis of a pharmaceutical sample. Using an Acquity BEH C18 column in the first dimension and a Chiralpak IC column in the second one, both chemical (achiral) and enantiomeric (chiral) purities could be evaluated in less than 50 min within a single run. Under such conditions, a detection limit of about 0.5% for R-enantiomer could be obtained with UV detection. The results obtained in sRPLCxSFC were compared to those obtained in

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