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Rapid and sensitive method for simultaneous determination of first-line anti-tuberculosis drugs in human plasma by HPLC-MS/MS: Application to therapeutic drug monitoring

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F irst-line anti-tuberculosis drugs are playing vital roles for curbing rapid spread of tuberculosis. mutidrug therapies are commonly applied in clinical to achieve better treatment outcomes. However, drug resistance and adverse reactions came along with this therapies and therapeutic drug monitoring is a feasible way to precaution side effects. For this reasons, a simple and sensitive method based on LC-MS/MS and single protein precipitation was developed and validated for simultaneously quantifying of pyrazinamide, isoniazid, ethambutol, streptomycin and rifampicin in human plasma. Optimized chromatographic separation was achieved on a ZORBAX SB-C18 column with heptafluorobutyric acid, an ion-pair reagent, in the mobile phase at a flow rate of 0.3mL/min. The mass detection was achieved using electrospray ionization in the positive ion mode with a multiple reaction monitoring scan: m/z 124.1 \rightarrow 79.1 for pyrazinamide, m/z 138.1 \rightarrow 120.9 for isoniazid, m/z 205.3 \rightarrow 116.2 for ethambutol, m/z 582.3 \rightarrow 262.6 for streptomycin, m/z 823.4 \rightarrow 791.2 for rifampicin and m/z 180.1 \rightarrow 110.1 for phenacetin(Internal standard, IS). The LLOQ of pyrazinamide, isoniazid, ethambutol, streptomycin and rifampicin was 200, 80, 0.2, 2000, 200ng/ mL, respectively. The Intra-day and inter-day accuracy and precision were within 15.0%. The method had been successfully applied to simultaneous determination of four first-line Anti-tuberculosis drugs in plasma from tuberculosis patients.

Biography

Shouhong GAO has completed her Master degree of Pharmacy at the age of 27 year in Second Military Medical University. She has served as an associate Professor in Clinical Pharmacy for Drug Safety and Effectiveness since her graduation. For chemical drugs, she promotes better standardization of analytical practices in LC-MS based therapeutic drug monitoring analyses in clinical application. She has published more than 9 SCI papers as (co)first author, and was responsible for five funds as a project leader.

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