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An UPLC-MS/MS method for the determination of folic acid and its metabolite with MTHER genotype in human plasma

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SUMMARY. **An accurate and validated UPLC-MS/MS method for determination of folic acid and 5-methyltetrahydrofolic acid in human plasma were developed and validated. Plasma samples were prepared by precipitating protein with acetonitrile. The analytes were separated using a reversed-phase BEH C18 column (2.1 × 50 mm, 1.7 µm, Waters, USA) maintained at 40 °C. The mobile phase consisted of acetonitrile and water (containing 0.1% formic acid) with a gradient elution pumped at a flow humane of 0.4 mL/min. The analytes were detected with positive electrospray ionization in multiple reaction monitoring (MRM) mode for target fragment ions m/z 442.11→295.14 for folic acid, m/z 460.26→313.23 for 5-methyltetrahydrofolic acid and m/z 285.1→193.1 for diazepam (IS). Calibration plots were linear throughout the ranges of 1-500 ng/mL for folic acid and 0.25-100 ng/mL for 5-methyltetrahydrofolic acid in human plasma. The mean recoveries of folic acid and 5-methyltetrahydrofolic acid from the plasma exceeded 73.23%. The intra-run and inter-run assay precisions of folic acid and 5-methyltetrahydrofolic acid were both less than 9.77%. The validated method showed the capability of the method to be used as an alternative for plasma analysis in therapeutic drug monitoring.**

RESUMEN. Se desarrolló y validó un método de UPLC-MS/MS preciso para la determinación del ácido fólico y el ácido 5-metiltetrahidrofólico en plasma humano. Las muestras de plasma se prepararon precipitando la proteína con acetonitrilo. Los analitos se separaron utilizando una columna BEH C18 de fase inversa (2.1 × 50 mm, 1.7 µm, Waters, EE. UU.) Mantenida a 40 ° C. La fase móvil consistió en acetonitrilo y agua (que contenía ácido fórmico al 0,1%) con un gradiente de elución bombeado a un flujo humano de 0,4 mL / min. Los analitos se detectaron con ionización por electropulverización positiva en modo de monitoreo de reacción múltiple (MRM) para iones de fragmentos diana m/z 442.11→295.14 para ácido fólico, m/z 460.26→313.23 para ácido 5-metiltetrahidrofólico y m/z 285.1→193.1 para diazepam (ES). Las gráficas de calibración fueron lineales en todos los rangos de 1-500 ng/mL para el ácido fólico y de 0.25-100 ng/mL para el ácido 5-metiltetrahidrofólico en plasma humano. Las recuperaciones medias de ácido fólico y ácido 5-metiltetrahidrofólico del plasma superaron el 73,23%. Las precisiones de ensayo intra-corridas e inter-corridas de ácido fólico y ácido 5-metiltetrahidrofólico fueron ambas menos del 9.77%. El método validado mostró la capacidad del método para ser utilizado como una alternativa para el análisis de plasma en el monitoreo terapéutico de medicamentos.

KEY WORDS: folic acid, 5-methyltetrahydrofolic acid, plasma. therapeutic drug monitoring.

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