



## Comparison of HPLC-MS/MS and Enzyme-multiplied Immunoassay in Tacrolimus Determination and its Application in Therapeutic Drug Monitoring

Wenlong LI #, Guiyan YUAN #, Huanjun LIU, Abdul S. SHAIKH,  
Xianglin KONG, Yanyan WANG & Ruichen GUO \*

*Institute of Clinical Pharmacology, Qilu Hospital of Shandong University;  
Jinan, Shandong Province, China, 250012*

**SUMMARY.** The objective of this study is to compare the correlation of HPLC-MS/MS and enzyme-multiplied immunoassay technique (EMIT), for the determination of tacrolimus (FK506) concentration in human blood and to provide evidence for its rational usage in practice. Blood samples, collected from 346 liver and kidney organ transplant patients in Qilu Hospital of Shandong University, were determined by two methods. The calibration curves were linear within the range of 1.0-30.0 ng/mL for HPLC-MS/MS and 2.5-25 ng/mL for EMIT, respectively. The inter- and intra-day RSDs were less than 15%. The correlation of the two methods was good ( $r^2 = 0.989$ ). Tacrolimus blood concentration, determined by EMIT, was 0.11 ng/mL more than HPLC-MS/MS. The 95% confidence interval was -0.24~0.46 ng/mL. There were no significant statistical differences between the two methods ( $P > 0.05$ ). The HPLC-MS/MS and EMIT methods were suitable for determining tacrolimus blood concentrations. The correlation between the two methods was very good, but tacrolimus blood concentration determined by EMIT was higher than HPLC-MS/MS. Its clinical significance needs to be further evaluated.

**RESUMEN.** El objetivo de este estudio es comparar la correlación entre HPLC-MS/MS y la técnica de inmunoensayo enzimático multiplicado (EMIT) para la determinación la concentración de tacrolimus (FK506) en sangre humana y para proporcionar evidencia de su uso racional en la práctica. Las muestras de sangre, recogidas de 346 pacientes con trasplante de órganos hepáticos y renales en el Hospital de la Universidad de Shandong Qilu, se determinaron mediante ambos métodos. Las curvas de calibración fueron lineales dentro del intervalo de 1,0 a 30,0 ng/mL para HPLC-MS/MS y 2,5-25 ng/mL para EMIT, respectivamente. Los RSDs inter e intra-día fueron < 15%. La correlación de los dos métodos fue buena ( $r^2 = 0,989$ ). La concentración de tacrolimus en sangre, determinada por EMIT, fue de 0,11 ng/mL más que por HPLC-MS/MS. El intervalo de confianza del 95% fue -0,24~0.46 ng/mL. Existen diferencias estadísticas significativas entre los dos métodos ( $P > 0,05$ ). Tanto HPLC-MS/MS como EMIT resultaron métodos adecuados para determinar las concentraciones de tacrolimus en sangre. La correlación entre los dos métodos fue muy buena, pero la concentración de tacrolimus en sangre determinada por EMIT fue superior a la de HPLC-MS/MS. Su importancia clínica necesita aún ser evaluada.

**KEY WORDS:** blood sample, enzyme-multiplied immunoassay technique, FK506, HPLC-MS/MS, tacrolimus.

\* Author to whom correspondence should be addressed. *E-mail:* grc7636@126.com

# These two authors contributed equally to this work.