Topiramate quantitation in human plasma by liquid chromatography-tandem mass spectrometry: Application to therapeutic drug monitoring

Kamal Matar
Kuwait University, Kuwait

Background: Topiramate (TPM) is a new antiepileptic drug (AED) used worldwide in patients with various types of epilepsies and also for prophylaxis of migraine. A rapid, selective, reliable, precise, accurate, and reproducible liquid chromatographic-tandem mass spectrometric (LC-MS/MS) method for quantification of TPM in human plasma using topiramate-d12 as an Internal Standard (IS) has been developed and validated to be used routinely for TDM of TPM.

Methods: The drug and IS were extracted by ether and analyzed on Symmetry® C18 column. Quantitation was achieved using ESI- interface employing MRM mode.

Results: The method was validated over the concentration range of 0.5–30 μg/ml (r>0.99). Intra- and inter-run precisions of TPM assay at three concentrations ranged from 0.7 to 7.8% with accuracy (bias) varied from −10.0 to 2.1% indicating good precision and accuracy. Analytical recoveries of TPM and IS from spiked human plasma were in the range of 84.1 to 90.0% and 90.0 to 111.0%, respectively. Stability of TPM in human plasma samples at different conditions showed that the drug was stable under the studied conditions. Matrix effect study showed a lack of matrix effect on mass ions of TPM and IS.

Conclusions: The described method compared well when assessed by LGC TDM theme program (r>0.99). The suitability of the developed method for TDM was demonstrated by measuring TPM in human plasma samples of epileptic patients treated with TPM. The proposed method is appropriate for routine TDM of TPM.

Biography
Dr. Kamal Matar is an Associate Professor and Chairman of the Department of Pharmacology & Therapeutics. He is also a director of Therapeutic Drug Monitoring & Clinical Toxicology (TDM&CT) Unit, Faculty of Medicine, Kuwait University. He has published over 35 peer-reviewed articles and over 20 abstracts in international conferences. He is serving as a reviewer for some international journals such as: Journal of Chromatography B, Journal of Pharmaceutical & Biomedical Analysis, Chemotherapy, Drugs, Analytical Chemistry Insights and Journal of Antimicrobial Chemotherapy. He is a member of International Association of Therapeutic Drug Monitoring & Clinical Toxicology (IATDMCT), American Association of Clinical Toxicology (AACCT), and European Compliance Academy (ECA). He organized many International Conferences in Kuwait in the area of Population Pharmacokinetics and Clinical Toxicology.

kamal@hsc.edu.kw