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A novel method for the quantification of Lamotrigine in human plasma using UPLC with tandem mass spectrometry

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Introduction: Lamotrigine is an anticonvulsant drug used in the treatment of epilepsy and bipolar disorder. A novel high performance liquid chromatography positive ion electrospray ionization tandem mass spectrometry method was developed and validated for the quantification of Lamotrigine in human plasma.

Method: The plasma sample was precipitated using acid and subsequently extracted using liquid-liquid extraction. The analyte was separated using an isocratic mobile phase on a reverse phase UPLC column to meet the demands of the clinical laboratory for speed of analysis and chromatographic resolution. Detection was carried out by MS/MS in the multiple reaction monitoring mode using the respective (M+H)+ ions, m/z 255.9 → 255.9 and m/z 261.9 →261.9 for the internal standard. The parent ion was monitored in the MRM mode with negligible collision energy as the product ions were not sensitive enough for detection. The developed method was validated as per the US FDA guidelines for bioanalytical method validation (May2001).

Results: The assay exhibited a linear dynamic range of 4-2000 ng/ml for Lamotrigine in human plasma. The lower limit of quantification was 4 ng/ml with a relative standard deviation of less than 9.2 %. No interference by endogenous substances or matrix effect was observed. The intra-day and inter-day accuracy and precision (%CV) values were in the range of 98.1-105.7% and 1.44-14.6% respectively. The spiked plasma samples were found to be stable at ambient temperature for 5 hrs, after long-term storage at -80°C for 93 days, and after 3 freeze-thaw cycles. The processed plasma samples were found to be stable in autosampler for 48hrs at 5°C. A very short run time (2min) for each sample made it a high throughput method for estimation of clinical samples. Thus the developed and validated method for estimation of Lamotrigine in human plasma could be successfully used to evaluate plasma concentration profiles in human subjects.

In silico design of novel, high-affinity neuraminidase inhibitors for influenza A/H1N1/2009 virus

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Since March 2009, an outbreak of H1N1 influenza in Mexico has led to hundreds of confirmed cases and a number of deaths. Neuraminidase is one of the major surface glycoproteins of the influenza virus. This viral enzyme cleaves the terminal sialic acid from the cellular receptor, to which newly formed virions are attached. This cleavage releases the progeny virions from the infected cell, enabling them to infect other cells. By blocking this releasing mechanism, the virus completes replication only once, preventing further infection. Therefore, neuraminidase has been considered a suitable target for designing anti-influenza drugs, and structure-based design of neuraminidase inhibitors has become an important area of research that could potentially yield promising drug candidates. The neuraminidase of the influenza virus is the target of antiviral drugs oseltamivir and zanamivir. Clinical practices have shown that zanamivir and oseltamivir are effective in treating the Influenza A/H1N1/2009 virus. However, drug resistance strains are also emerging. The complex structure of Influenza A/H1N1/2009 neuraminidase and these antiviral drugs is not available yet. In the present study, we have built the Influenza A/H1N1/2009 structure model by homology modeling. 523,366 compounds from ZINC database have been screened by docking study. Finally by using molecular dynamics simulation we aimed to figure out potent candidates for Influenza A/H1N1/2009 flu virus.