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LC–MS/MS method for simultaneous determination of thalidomide, lenalidomide, cyclophosphamide, bortezomib, dexamethasone and adriamycin in serum of multiple myeloma patients

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Statement of the Problem: Multiple myeloma (MM), a malignant neoplastic serum-cell disorder, has been a serious threat to human health. The determination of 6 commonly used drug concentrations, including thalidomide (THD), lenalidomide (LND), cyclophosphamide (CTX), bortezomib (BTZ), dexamethasone (DXM) and adriamycin (ADM), in MM patients was of great clinical interest. Drug pharmacokinetic monitoring was important to ensure safety and efficacy during chemotherapy, but assays of one or two of these drugs in bio-fluids had been published.

Methodology & Theoretical Orientation: We reported a method for the rapid and simultaneous measurement of the above therapeutics by liquid chromatography-tandem mass spectroscopy (LC–MS/MS) method with solid phase extraction. Analysis was performed on a Waters XBridge^{*}BEH C18 column (2.5 μ m, 2.1 mmx50 mm) with formic acid aqueous solution and acetonitrile as the mobile phase at flow rate 0.3 mL/min.

Findings: All analytes showed good correlation coefficients (r>0.996), and LLOQ of THD, LND, CTX, BTZ, DXM and ADM were 4, 2, 2, 2, 2 and 2 ng/mL, respectively. The inter- and intra-day precisions and stability were expressed as variation coefficients within 15% and relative error less than 15%. Dilution effect, carryover and incurred sample reanalysis were in the acceptable levels.



Fig.3. Serum concentrations of THD, LND, CTX, BTZ, DXM, ADM of 28 MM patients represented with median, lower and upper quartiles (THD and LND were not been showed in the standard style as the others, because there were only 3 cases for THD and 1 case for LND detection).

Conclusion & Significance: Validation method was investigated according to the 2015 edition Chinese Pharmacopoeia guidelines, as US FDA (2013, revision 1) required. The descried method was successfully applied to determine the clinical incurred serum samples from MM patients, and the tested results were also provided to the doctors for consideration. The LC–MS/MS based assay described in this article may improve future clinical studies evaluating common therapeutics for MM treatment.

Biography

Feng Zhang has her research interests in drug safety and efficacy determination. For Traditional Chinese Medicine (TCM), she has suggested a comprehensive strategy to understand the active marker compounds, therapeutic mechanisms and synergistic properties of TCM, by using LC-TOF/MS, LC-MS and LC-UV methods, metabolomics technology, as well as some conventional pharmacological analyses. For chemical drugs, she promotes better standardization of analytical practices in LC-MS based therapeutic drug monitoring analyses in clinical application. It is the key issue that makes the way of LC-MS into clinical routine laboratories.

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