ABSTRACT

The submitted thesis is devoted to the quantitative analysis of tyrosine kinase inhibitors, specifically imatinib and nilotinib, by liquid chromatography–mass spectrometry method. The main purpose of developing this new method of analysis at the Department of Clinical Biochemistry and Diagnostics at the University Hospital in Hradec Králové was measuring and monitoring serum or plasma concentration levels of these drugs in patients with chronic myeloid leukemia, less often in patients with gastrointestinal stromal tumour. The main task during the elaboration of the thesis was to fully optimize and validate the method.

Previously, this method for the analysis of tyrosine kinase inhibitors was routinely performed here by high-performance liquid chromatography with spectrophotometric (UV) detection. As part of the modernization of laboratory technology, they started to use high-performance liquid chromatography with mass spectrometry at the workplace. The analytes with their internal standards were obtained by a liquid-liquid extraction process. Then, samples were separated on a C18 reverse phase column using isocratic elution. Subsequently, both analytes were detected by a triple quadrupole tandem mass spectrometer with ESI ion source in a positive mode.

As a part of the method validation was to verify its accuracy and precision. Method's selectivity and sensitivity was also tested. At the same time, the linear dependence and working concentration range in which the new method is fully applicable for the analysis of imatinib and nilotinib were determined. It has been verified that the developed bioanalytical method shows excellent linearity in whole working range, great sensitivity, selectivity, accuracy, precision, trueness and is sufficiently efficient and fast.

This developed method is reliable and fully meets all acceptance criteria issued by the validation guidelines. The optimized and fully validated method was presented at the department of the University Hospital in Hradec Králové.

Keywords:

analysis, tyrosine kinase inhibitors, liquid chromatography, mass spectrometry, chronic myelogenous leukemia