MONITORING OF TYROSINE KINASE INHIBITORS IMATINIB, DASATINIB, AND NILOTINIB IN DRIED CAPILLARY PLASMA MICRO-SAMPLES

Author: Carla Miriane da Silva Augustin[1]; Maitê de Moraes Machado[1]; Bruna Amorin[2]; Mayde Seadi Torriani[2]; Sandrine Comparsi Wagner[2]; Marcella Abreu Meine[3]; Vitória Luiza de Camargo Milczarski[3]
Advisor: Marina Venzon Antunes[1]
Institution: Universidade Feevale - Novo Hamburgo, RS, Brazil[1]; Hospital de Clínicas de Porto Alegre - Porto Alegre, RS, Brazil[2] Universidade Federal de Ciências da Saúde de Porto Alegre[3]

ABSTRACT

INTRODUCTION: Therapeutic drug monitoring of TKIs optimizes efficacy and safety in CML treatment. Miniaturized blood sampling techniques reducing solvent consumption align with green chemistry, enhancing sustainability. These strategies improve logistics, expand clinical applications, and promote a more efficient, environmentally responsible laboratory practice. **OBJECTIVE:** This study proposes the development of an innovative bioanalytical methodology for the quantification of dasatinib, nilotinib, imatinib, and its metabolite in dried capillary plasma micro-samples (DPS) using the HealthID® plasma separation device and UHPLC-MS/MS. **MATERIALS AND METHODS**: The analysis was performed using three 6 mm discs, subjected to a two-step extraction process. In the first step, the discs were incubated with 200 µL of 0.1% albumin at 45°C for 30 minutes, with a 20 µL aliquot separated for chloride analysis. After precipitation with 25% trichloroacetic acid, the discs were extracted with 500 µL methanol containing deuterated internal standards. Analysis was conducted by UHPLC-MS/MS using electrospray ionization in positive mode with a C18 column (2.1×100 mm, 1.7 µm). Elution was performed in a gradient mode with 0.1% formic acid in water and acetonitrile. Multiple reaction monitoring (MRM) transitions were recorded. The method was validated according to FDA guidelines and has been applied to quantify TKIs in plasma samples from nine CML patients treated at Hospital de Clínicas de Porto Alegre. **RESULTS AND CONCLUSION:** The analysis was completed in 6 minutes, with satisfactory linearity ($r > 0.99$) for all analytes. Precision coefficients of variation (CV) were within acceptable limits, ranging from 6.2% to 12.3%, with accuracy between 95.3% and 103.9%. The mean extraction yield of the analytes was 60.5% to 70%, with no significant impact from blood volume variations after chloride-based volume correction (accuracy: 91%–108%). TKI concentrations in DPS samples ranged from 88.2% to 124% of plasma concentrations. Preliminary results indicate the potential of DPS samples for TKI monitoring, with extended stability at room temperature.

Keywords: TKIs; LC-MS/MS; Dried capillary plasma; Therapeutic drug monitoring.

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