Quantification of Δ9-Tetrahydrocannabinol and Cannabidiol in Plasma and Decoctions by LC-MS/MS: Application for TDM of Medical Cannabis

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Introduction

Medical cannabis has been increasingly used in several conditions. Monitoring of blood levels of Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD) is necessary for assessing pharmacokinetic parameters in order to optimize drug administration. In this poster we describe the validation of novel UHPLC-MS/MS method for quantifying THC and CBD from plasma and decoctions. The method has been then used on the occasion of the first protected use of medical cannabis on paediatric patients. In validation process particular attention was posed to study potential interferences due to in-source decarboxylation of THC-A and CBD-A in the APCI ion source.

Materials and Methods

100 µL plasma and decoction samples were extracted after the addition of deuterated internal standards with a rapid protein precipitation without any further manipulation. The UHPLC-MS/MS analyses were performed on a TSQ Quantum™ Triple Quadrupole coupled to a Ultimate 3000 UHPLC system using APCI ionization. Quantification was made by choosing a fragmentation transition that gives a very high signal to noise ratio. EMA guidelines were applied in order to validate method performance.

Results and Discussion

The method is linear from 0.16 to 10 ng/mL for both THC and CBD in plasma and from 4.7 to 600 ng/mL in decoctions. Starting from the observation of two additional chromatographic peaks within THC and CBD ion transitions in real sample (Fig 1), we have demonstrated that this interference was due to in-source decarboxylation of THC-A and CBD-A into neutral forms that occurs with APCI but not with HESI. With APCI, THC-A and CBD-A are not able to ionize in their form whereas in HESI they ionize and with their specific transitions they give chromatographic peaks with the same retention times as those found in APCI (Fig 2).

A complete THC-CBD pharmacokinetic profile from young patients treated with decoction was described for the first time (Fig. 3). Data showed a considerable inter-individual variation in plasma concentrations and hence in PK parameters; this is consistent with the intra-subject variability of absorption.

Since the first and main important objective of the different cannabis preparations is to ensure the therapeutic continuity in the treated patients, a strictly standardized preparation and conservation protocol is necessary to guarantee the availability of a homogeneous product.

We believe that the described method is suitable for application in both adults and children for dose optimization purposes or compliance monitoring.