Rasha Hanafi et al., Insights in Analytical Electrochemistry, 3:2
DOI: 10.21767/2470-9867-C1-002

Determination of capecitabine and its metabolites in plasma of Egyptian colorectal cancer patients

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Colorectal Cancer (CRC) is constantly increasing in incidence both worldwide and at the national level. Chemotherapeutic agents often prescribed in CRC are Capecitabine (CCB) and 5-Fluorouracil (FU). CCB is activated to FU in a three steps reaction giving 5'-deoxy-5-fluorocytidine (DFCR), followed by 5'-deoxy-5-fluorouridine (DFUR) to yield finally FU, the active form, which is later deactivated to 5,6-dihydro-5-fluorouracil (DHFU). Patients exhibited variable responses and adverse events in response to CCB therapy, despite being treated with the same dose. This could be explained by the presence of different possible enzyme SNPs that can occur along the CCB activation and deactivation pathways. This study aims at developing a new method of analysis of CCB and its metabolites using HPLC-UV, to determine the plasma concentrations of CCB and its metabolites DFCR, DFUR, FU, DHFU and 5-Chlorouracil (CLU; the internal standard), followed by a correlation study with the toxicities occurring during therapy, to become a predictive method for toxicity, away from the exhausting genotyping process. A new superior analytical method is presented using computer-assisted method development, which achieved full separation of the six analytes during the least possible gradient time, eluting the compounds at 2.8, 3.2, 4.4, 5.2, 5.8 and 9.9 minutes for DHFU, FU, CLU, DFCR, DFUR and CCB, respectively. The method showed accuracy, precision and robustness upon validation. Clinical results showed a positive correlation between the DFCR concentration and mucositis, as well as, between the DFUR concentration and Hand-Foot Syndrome, confirming that this technique could be used for predicting such toxicities in CRC patients.

Biography

Rasha Hanafi joined the faculty of Pharmacy, Department of Pharmaceutical Chemistry in 2004, where she is currently Associate Professor of Instrumental Analysis and Analytical Chemistry. Dr. Hanafi received her pharmacy bachelor and her master's degree in pharmaceutical analysis from the faculty of Pharmacy, Cairo University in 1996 and 2005, respectively, and her PhD. degree from the faculty of Pharmacy, German University in Cairo in 2009 in biomedical analysis. She was promoted to associate professor in the Supreme Council of Universities in 2016. She is reviewer of international journals, has large number publications in peer reviewed journals and has presented in many conferences around the world. She supervised a large number of PhD and master students in the field of pharmaceutical and biomedical analysis. Dr. Hanafi's research involves analytical method development and validation within the Quality by Design framework, and is is a consultant and trainer for industry and academia.

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