Multi-analyte determination of 26 cytostatics and metabolites by liquid chromatography-electrospray-tandem mass spectrometry: optimization, analytical performance, and study of the stability and optimum storage conditions for their determination in wastewater

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Nowadays, the demand of cytostatics in developed countries has increased. Many of them have been categorized as carcinogenic, mutagenic and teratogenic compounds even at low concentrations [1]. These compounds and their human metabolites are usually directly discharged into the sewage system without any specific control after being administered in the hospitals or by out-patients. Their levels in the environment, though very little investigated, appear relatively low (ng/L to μg/L) [2] as compared to those of other groups of pharmaceuticals; however, due to their highly potent mechanism of action, this specific group of drugs is perceived to be harmful to aquatic organisms and even human health.

The simultaneous multi-analyte determination of cytostatics is rather challenging due to their wide variety of physical-chemical properties and the instability of some of them in aqueous solution. This work describes the development of an analytical method based on liquid chromatography-electrospray-tandem mass spectrometry (LC-ESI-MS/MS) for the determination of up to 26 cytostatics, and investigates the stability of the target compounds in aqueous solution and in wastewater for up to three months under different conditions of pH and temperature. To the authors’ knowledge, apart from some simulating processes using OECD mediums for cyclophosphamide, 5-fluorouracil, cisplatin, gemcitabine, cytarabine and methotrexate [3-5], the long-term stability of cytostatics in sewage or natural waters has not been investigated. The results obtained point out storage at -20 ºC immediately after collection as the best option. On the other hand, acidification of the samples improved the stability of some compounds.

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References