

Preliminary evaluation of the chemical composition of reconstituted cyclophosphamide solutions prepared in a hospital pharmacy

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Background: The impact of reconstitution practices on cyclophosphamide concentration, one of the most frequently prepared antineoplastic drugs, remains poorly explored [1]. Variability in preparation protocols may affect dosing accuracy, reproducibility and physicochemical homogeneity [2]. **Aim:** The aim of this study was to evaluate the cyclophosphamide concentration and the homogeneity of solutions prepared in a hospital setting for administration to oncology patients. **Methods:** Cyclophosphamide reconstituted solutions in hospital settings with an initial concentration of 20 mg/mL were diluted to a final theoretical concentration of 200 µg/mL, according to the range of concentrations of the previously validated HPLC-DAD analytical method (between x and y mg/mL). Five independent samples were analysed for each condition, alongside a blank solution correspondent to the mobile phase, containing water, acetonitrile and methanol. Four conditions were evaluated: diluted solutions after normal reconstitution in hospital setting and withdrawn with a filtered spike (condition A); diluted solutions submitted to mechanical agitation for 5 minutes withdrawn with a filtered spiked (condition B); diluted solutions agitated for 5 minutes and heated (40°C) and withdrawn with filtered spike (condition C); and diluted solutions agitated and heated transferred through a filter-free spike (condition D). **Results:** Samples from condition A showed mean concentrations between 134.86 µg/mL and 369.68 µg/mL and presented the highest standard deviation and coefficient of variation values. Condition B resulted in mean concentrations from 168.24 to 176.36 µg/mL, while Condition C yielded concentrations between 166.74 and 177.11 µg/mL. Condition D showed mean concentrations from, 166.07 to 199.21 mg/mL. Standard deviation and coefficient of variation decreased with agitation and heating. **Conclusions:** Agitation and heating procedures may improve the homogeneity of cyclophosphamide preparations, contributing to greater accuracy of the final concentration, but further analyses are warranted to broaden the findings of this preliminary study.

Keywords: Cyclophosphamide; HPLC-DAD; Concentration variability

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