Feasibility of a SERS-based point-of-care for therapeutic drug monitoring: the case of methotrexate

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To date, in spite of their toxicity, the plasmatic concentration of most chemotherapeutic drugs is difficult to monitor in oncological patients, because their quantitative determination is expensive and time consuming. Surface-enhanced Raman spectroscopy (SERS) coupled with multivariate statistical analysis is fast becoming a promising analytical tool for *point-of-care* applications in Therapeutic Drug Monitoring (TDM) [1]. In comparison with standard methods (Gas or Liquid Chromatography coupled with Mass Spectroscopy), it has the remarkable advantages of rapidity, simplicity, low cost, and no need for sample pretreatment.
A recent work by our group reported a first attempt for the direct quantitative determination of a chemotherapeutic drug in human serum samples by means of SERS [2]. In this study, SERS substrates constituted by Au nanoparticles deposited on paper by a simple dipping method have been used for rapid (few minutes) analysis of diluted human serum spiked with different concentrations of methotrexate (MTX), a folate antagonist widely used for treatment of various neoplastic diseases in children, and one of the very few chemotherapeutic drugs routinely monitored in most treatment centers. The drug concentrations were chosen in a range designed to cover typical therapeutic plasmatic values (from nanomolar to millimolar) in oncological patients, and a complete methodology was implemented for developing the proposed method. The pertinent calibration was obtained by Partial Least-Squares Regression (PLSR), and the influence of the preprocessing methods on the prediction speed, robustness and accuracy performance was compared. Stability selection was employed to evaluate the capability of the PLSR model to accurately predict and extract spectral variations correlated to MTX concentration.
Such a quantitative determination is crucial for maximize the potential benefit of oncological therapies by optimizing dose regimen with TDM. Its low cost, rapid response and the possibility of obtaining spectra with simple and compact instruments, make SERS particularly apt for implementing effective *point-of-care* services. The promising results obtained in the analytical validation indicate which steps are to be taken on the way toward a clinical validation with real samples from oncological patients, for MTX as well as for other chemotherapeutic drugs.

References

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