



A Facile Analytical Tool for the Simultaneous Determination of Topoisomerase Inhibitors in Human Serum and Urine

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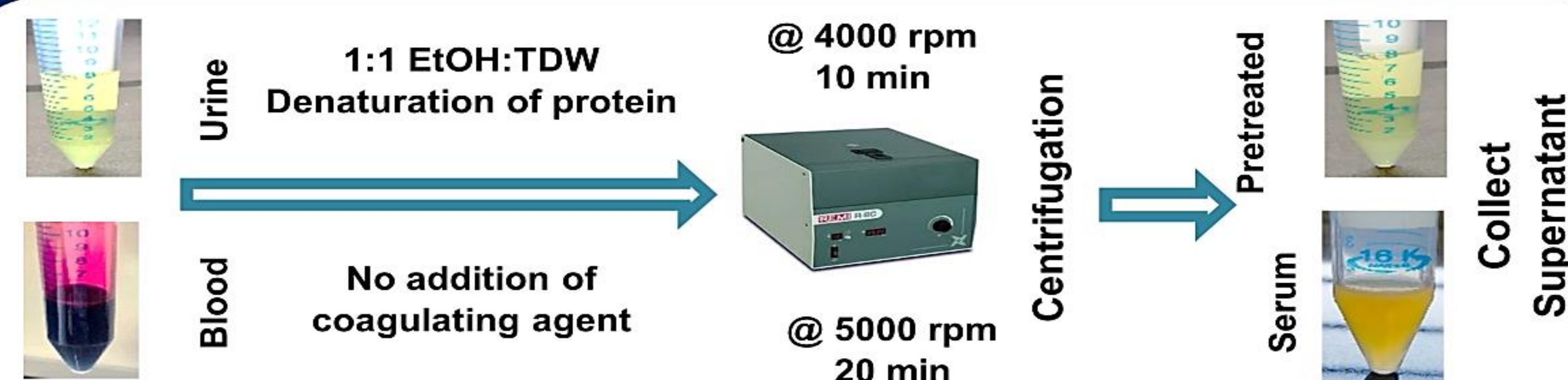
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Introduction

- Nowadays, cancer chemotherapy has upgraded from monotherapy to combination therapy, with the sequential administration of Topotecan (TOP) and Doxorubicin (DOX) exploiting dual inhibition of Topoisomerase I and II enzymes to enhance DNA damage, suppress tumour progression and improve therapeutic outcomes.
- As variations in drug concentrations can significantly influence treatment efficacy and toxicity, we need a facile analytical tool for **precise therapeutic drug monitoring**.
- Existing chromatographic techniques such as HPLC-UV/FL/MS offer excellent sensitivity. Still, they often require sophisticated instrumentation, extensive sample preparation and high operational costs, creating a demand for rapid, sensitive and accessible alternatives.
- TOP and DOX are inherently fluorescent in nature. So, a **fluorescence-based technique** can help to monitor these drugs in biological matrices.
- However, simultaneous determination of these drugs in biological matrices remains challenging because of their overlapping fluorescence signatures and the complex background fluorescence from endogenous biomolecules in serum and urine.
- To address this challenge, we developed a novel analytical methodology that integrates **Angular Sweep Total Fluorescence Spectroscopy (ASTFS)** with **Multivariate Curve Resolution-Alternating Least Squares (MCR-ALS)** chemometric modelling, enabling high resolution of spectra and accurate quantification of Topotecan and Doxorubicin in complex biological matrices with minimal sample preparation.

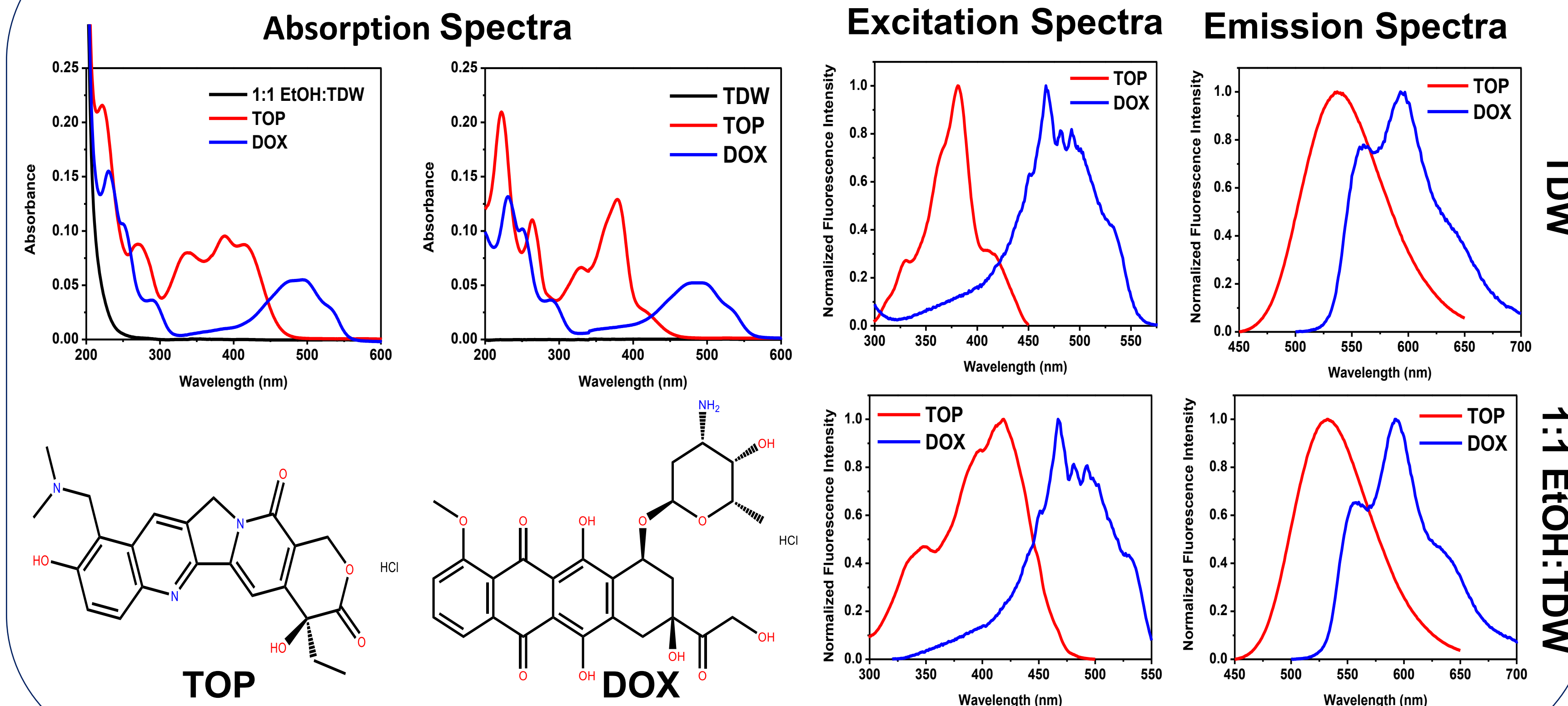
Sample Preparation



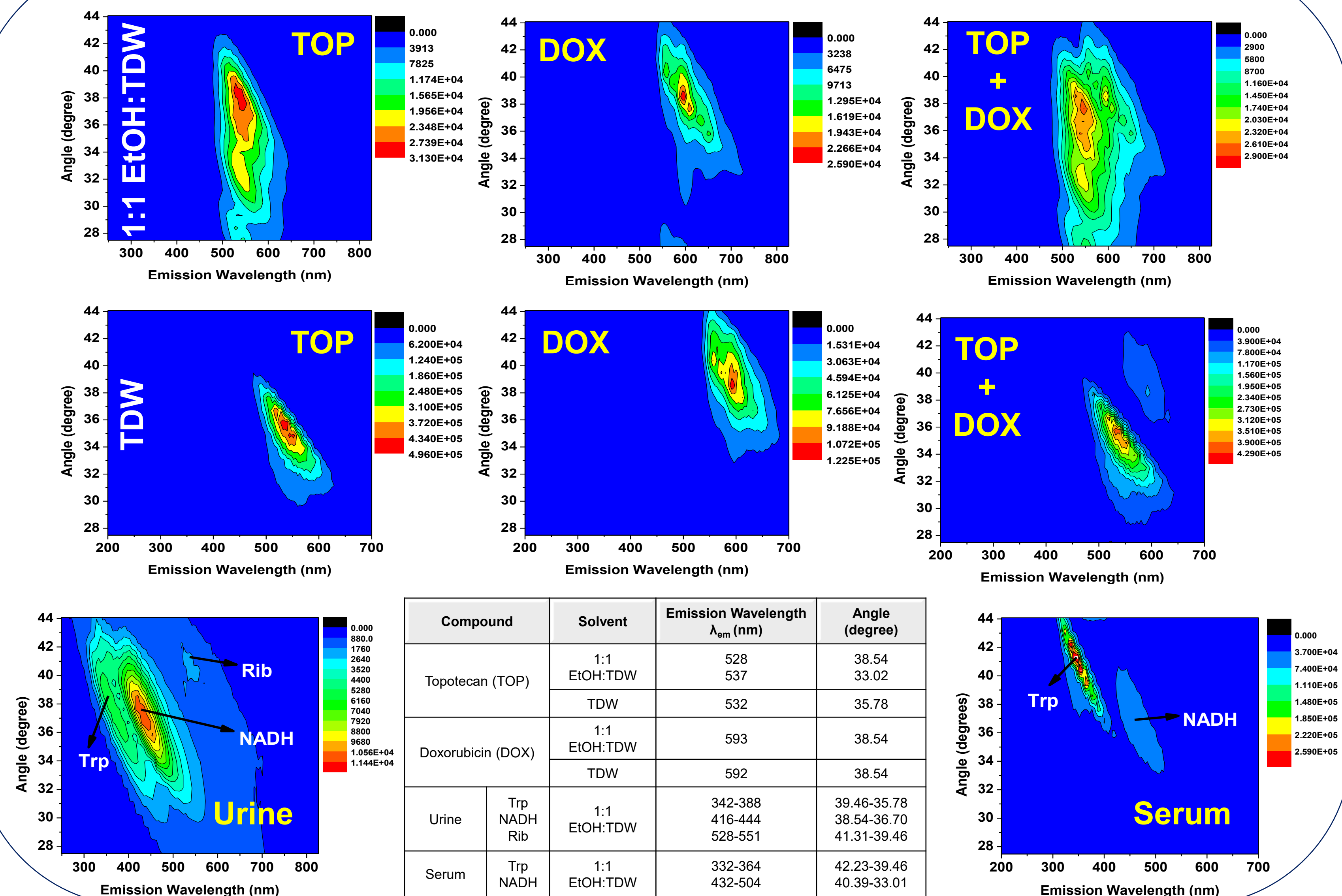
Methodology



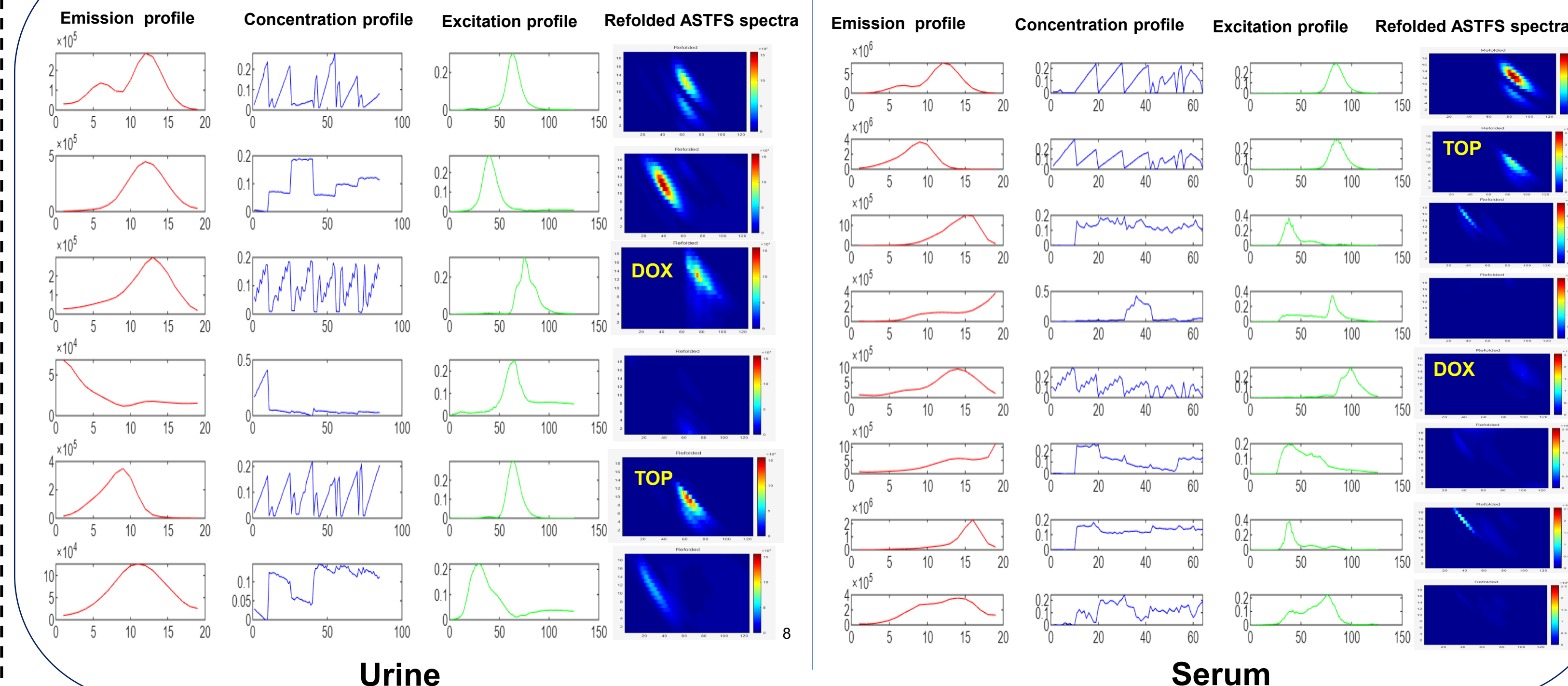
Photophysical characterization



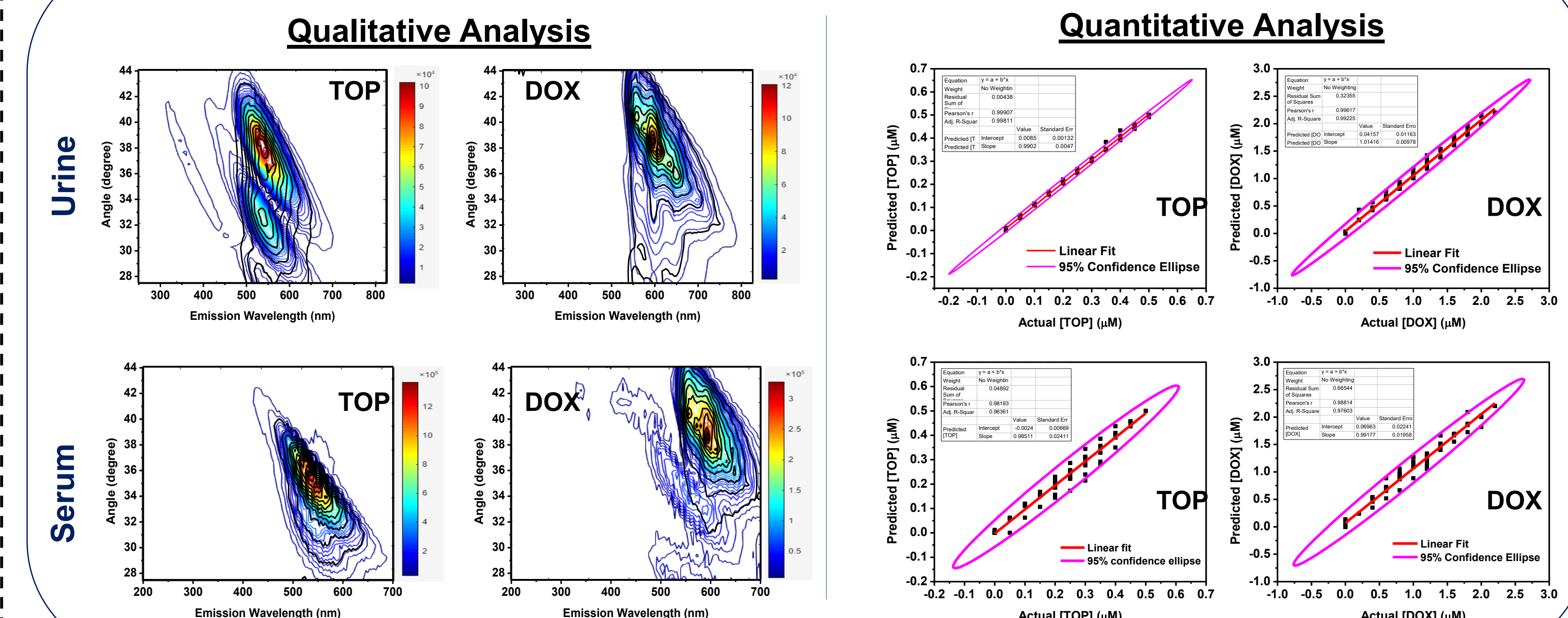
ASTFS Characteristics of Tis & Matrices



MCR-ALS Modelling



MCR-ALS Analysis



Conclusion

- A single-step ethanol-based pre-treatment was followed for the urine and direct serum was taken for the study.
- We optimised the experimental and chemometric parameters to improve sensitivity and selectivity in resolving overlapping fluorescence signatures of multiple anti-cancer drugs in two different biomatrices.
- The model performance was evaluated and the 6-component and 8-component MCR-ALS models for the ASTFS dataset in urine and serum, respectively, can resolve the TIs and matrix with good figures of merit.

References

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Acknowledgement

