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## **ACCEPTED MANUSCRIPT**

### A new concept of efficient therapeutic drug monitoring using the highresolution continuum source absorption spectrometry and the surface enhanced Raman spectroscopy

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#### ABSTRACT

In this study, a new therapeutic drug monitoring approach has been tested based on the combination of CaF molecular absorption using high-resolution continuum source absorption spectrometry (HR-CSAS) and surface enhanced Raman scattering (SERS). HR-CSAS with mini graphite tube was successfully tested for clinical therapeutic drug monitoring of the fluorine-containing drug capecitabine in sweat samples of cancer patients: It showed advantageous features of high selectivity (no interference from Cl), high sensitivity (characteristic mass of 0.1 ng at CaF 583.069 nm), low sample consumption (down to 30 nL) and fast measurement (no sample pretreatment and less than one minute of responding time) in tracing the fluorine signal out of capecitabine. However, this technique has the disadvantage of the total loss of the drug's structure information after burning the sample at very high temperature. Therefore, a new concept of combining HR-CSAS with a non-destructive spectroscopic method (surface-enhanced Raman spectroscopy SERS) was proposed for the sensitive sensing and specific identification of capecitabine. We tested and succeed in obtaining the molecular characteristics of the metabolite of capecitabine (named 5-fluorouracil) by the non-destructive SERS technique. With the results

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