# Detection and quantification of drugs using ToF-SIMS

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## 1. Introduction

Detection and quantification of licit drugs and illicit drugs in biological samples is often time consuming due to the need of extensive sample preparation before analysis. A fast accurate method for simultaneous detection and quantification with minimal work-up of the specimen would be an important progress in emergency situations and routine analysis of urine and serum specimens.

Many methods for drug analysis are used, but almost all of them include a drug extraction process before analysis. The most popular being GC/MS [1-2], GC/FID [3] and HPLC [4-5]. Immunoassays generally do not need special preparation but they only give semi-quantitative results or analyse drug classes (e.g. benzodiazepines).

High performance time of flight secondary ion mass spectrometry (ToF-SIMS) characterised by high mass resolution and extreme sensitivity has been applied to the detection of cocaine in methanol and urine [6].

We here describe preliminary results using time of flight mass spectrometry for the detection of bromazepam and morphine in methanol solution. Detection limit is less than 0.01 mg/L for morphine. The quantification range is in the same order of magnitude.

## 2. Experimental

Methanol solutions containing 0.01, 0.1, 1, 10 and 100 mg/L of morphine in methanol have been prepared. Some microliters of these solutions have been deposited on silver substrates in order to obtain a mono or submono layer.

The analysis are performed using a high mass resolution time-of-flight SIMS instrument (TOF III), which combines the high sensitivity of the TOF analyser with high mass resolution [6] and parallel detection of the entire spectrum. This instrument is composed of a mass resolved pulsed primary ion gun (10 keV $Ar^+$, pulse width 1 ns, repetition rate 5 kHz), a reflectron TOF analyser on the secondary column, an ion-electron-photon converter detector system and a registration system with an 800 MHz time to digital converter (TDC).

During the measurement the sample was bombarded by $Ar^+$ primary ion beam over a area of 500x500 $\mu m^2$ with an average current of 1 pA during 200 seconds. The total primary ion doses were < $10^{12}$ ions/$cm^2$. Typical mass resolutions M/ΔM (Full Width at Half Maximum) for the spectra at around 50 amu were on the order of 6000-7000.

### 3. Results and discussion

Optimum emission of secondary ions is obtained from silver substrates covered by only a mono or submono-layer of molecules (figure 1).

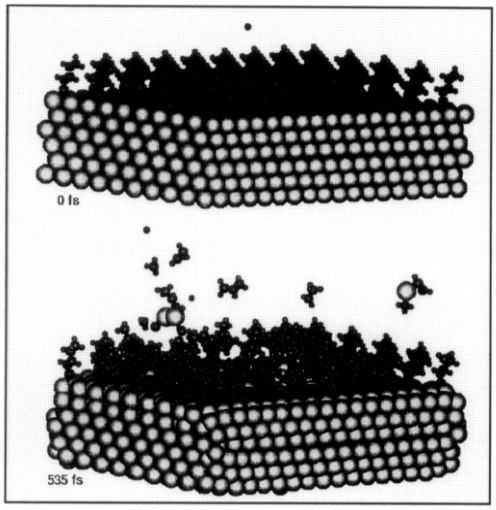


Figure 1: Emission of secondary ions of organic molecules after bombardment by $Ar^+$ (primary) ions.

(a) Drug absorbed on silver substrate

(b) Drug-ionisation under primary bombardment

ToF-SIMS spectra of bromazepam and morphine in methanol solution are represented in figures 2 and 3. The predominant peak of morphine is situated at m/e 286 $(M+H)^+$ (figure 2), the silver cationized $(M+Ag)^+$ species of bromazepam show higher intensity than the corresponding protonated cluster $(M+H)^+$.

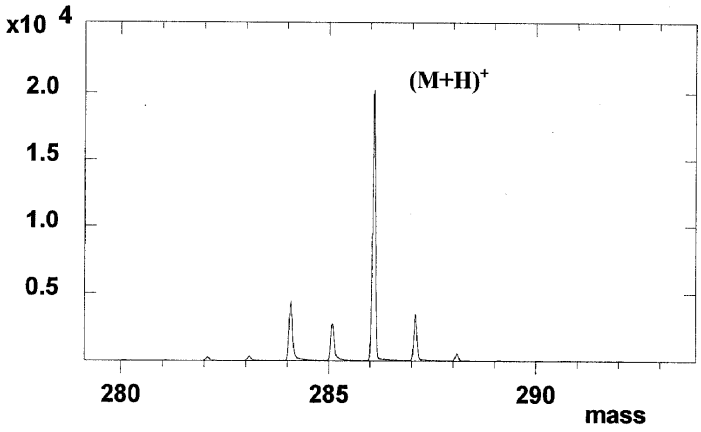


Figure 2: Positive secondary-ion mass spectrum of sample containing morphine in methanol solution deposited on silver substrate.

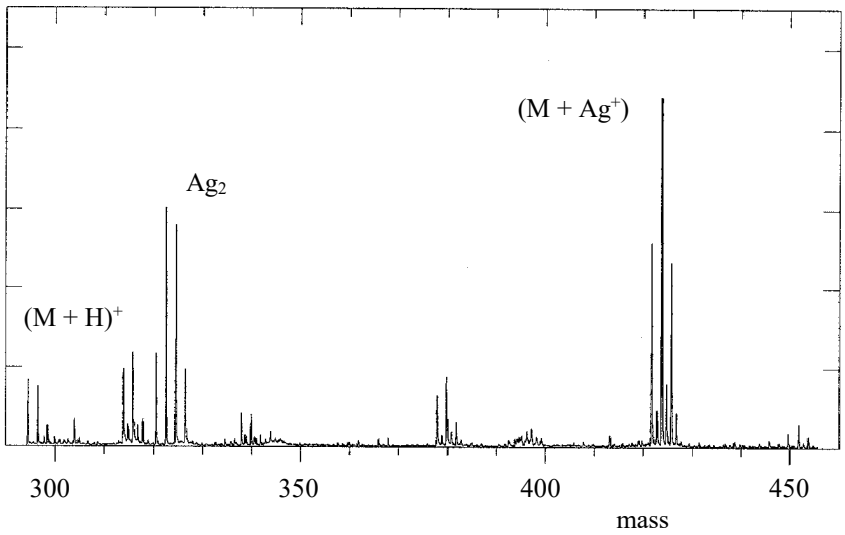


Figure 3: Positive secondary-ion mass spectrum of sample containing brom azepam in methanol solution deposited on silver substrate.

The limit of detection for morphine and bromazepam has been found to be less than 0.01 mg/L. The quantification range of morphine covers several orders of magnitude, starting at 0.01 mg/L up to 100 mg/L in methanol (figure 4).

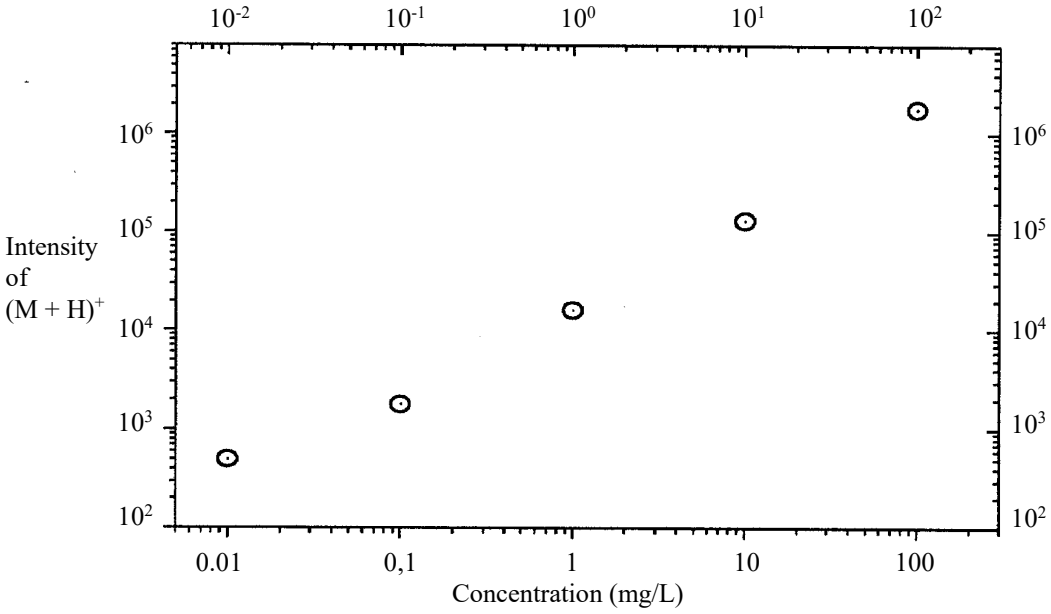


Figure 4: Quantification range of morphine in methanol.

## 4. Conclusion

The preliminary ToF SIMS analysis of morphine and bromazepam in methanol shows characteristic spectra for these drugs, a high reproducibility of the experiments and a quantification range of morphine from 0.01 mg/L to 100 mg/L. The main advantages of the ToF SIMS technique are :

* no work - up and direct analysis of the specimen,
* low limit of detection(< 0.01 mg/L) and quantification range and
* the possibility to simultaneously analyse several different drugs in one "run".

Further studies will be extended to other licit and illicit drugs and their metabolites in serum and urine. Deuteriated internal standards will be used for direct quantification.

## References


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