



Illicit Drug Analysis: Quantification using ^{19}F qNMR

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Introduction

The Australian Forensic Drug Laboratory (AFDL) based at the National Measurement Institute Australia (NMIA) provides forensic science services to Australia's federal government agencies. Since the mid-2000s, new psychoactive substances (NPS) have posed a significant challenge for forensic drug analysis laboratories, with over 1,200 individual NPS reported to the United Nations Office on Drugs and Crime (UNODC) Early Warning Advisory.¹

While ^1H qNMR is effective for analysing pure compounds, it faces limitations when dealing with samples that contain a mixture of substances. To address this issue, NMIA has started to develop a ^{19}F qNMR method, expanding their capabilities to quantify substances containing fluorine that are unsuitable for ^1H qNMR analysis. Fluorinated analogues of drugs may exhibit increased potency, metabolic stability or increased membrane permeation when compared to their non-fluorinated counterparts.² Common fluorinated species encountered at the NMIA include *para*-fluorofuranylfentanyl, 4-fluoromethcathinone and 2'-fluoro-2-oxo-PCE (Figure 1).

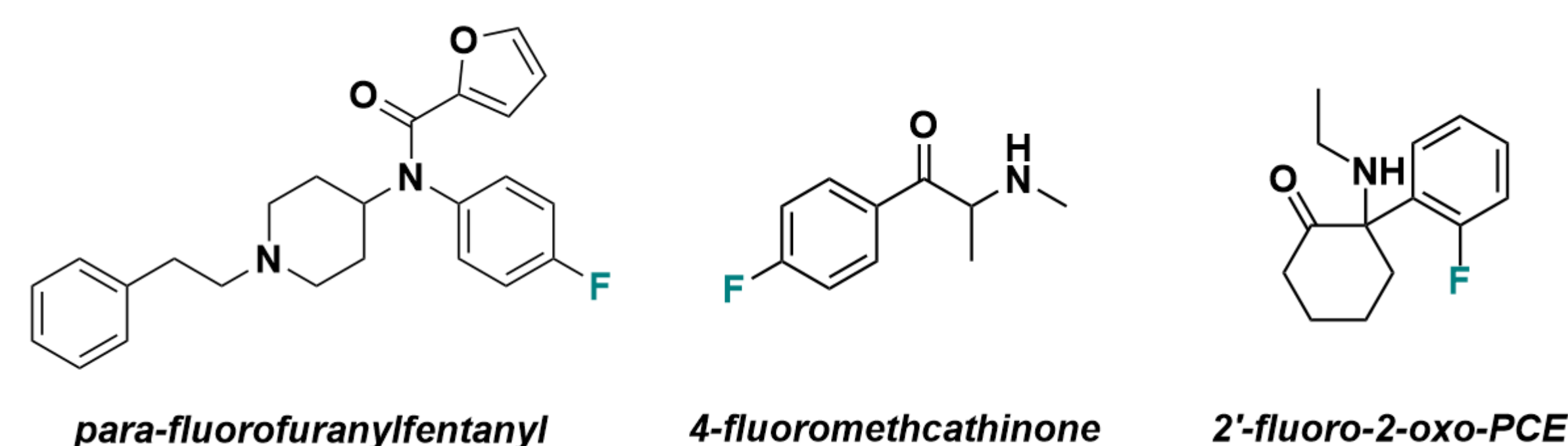


Figure 1: NPS containing fluorine.

Results and Discussion

Method validation commenced by analysing two NMIA certified reference materials (CRMs), 4-fluoroamphetamine and 4-fluoromethcathinone under ^1H and ^{19}F quantitative NMR conditions in D_2O and $\text{DMSO-}d_6$. As shown in Table 1, the calculated purities were comparable to that of the CRMs produced by mass balance.

Solvent	4-fluoromethcathinone purity via ^{19}F qNMR	4-fluoromethcathinone purity via ^1H qNMR	CRM purity (mass fraction)
D_2O	99.9%	99.7%	$99.6 \pm 0.5\%$
$\text{DMSO-}d_6$	100.0%	99.4%	

Table 1: Preliminary ^{19}F qNMR method validation results for 4-fluoroamphetamine (internal standard) and 4-fluoromethcathinone (analyte).

To demonstrate the method's applicability to other fluorinated illicit substances, two seizures containing 2'-fluoro-2-oxo-PCE (Sample A and B) were analysed under the established conditions using 4-fluoromethcathinone as the internal standard. As shown in the ^1H NMR spectrum of Sample B in Figure 2, the crowded aliphatic region restricts the availability of distinct ^1H resonances, highlighting the suitability of ^{19}F qNMR as an alternative quantitative approach. Comparable results were obtained for each sample when run under ^{19}F qNMR and ^1H qNMR conditions (Table 2).

Sample	2'-fluoro-2-oxo-PCE purity via ^{19}F qNMR*	2'-fluoro-2-oxo-PCE purity via ^1H qNMR*
A	78.8%	78.5%
B	85.6%	85.7%

Table 2: Preliminary ^{19}F qNMR method validation results for 4-fluoromethcathinone (internal standard) and 2'-fluoro-2-oxo-PCE (analyte). *Purity expressed as 2'-fluoro-2-oxo-PCE free base.

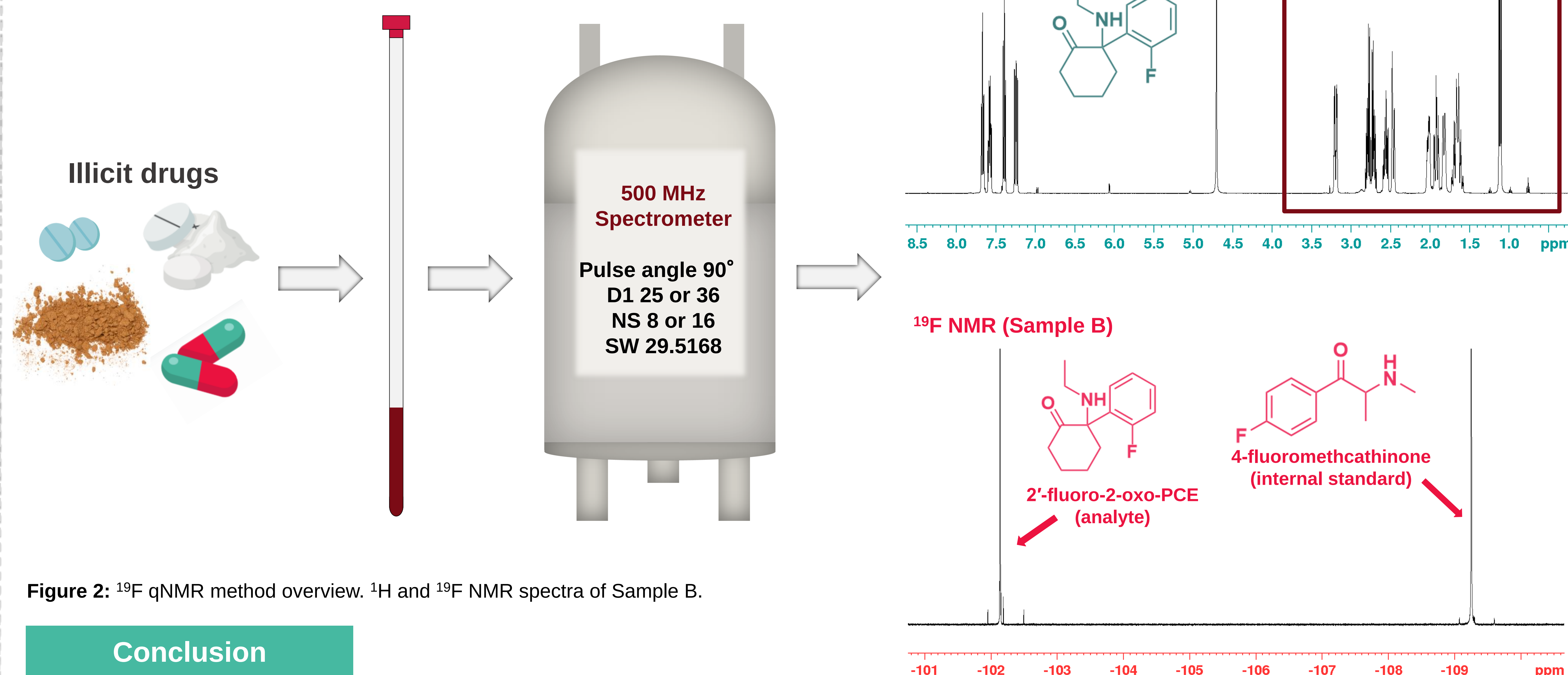


Figure 2: ^{19}F qNMR method overview. ^1H and ^{19}F NMR spectra of Sample B.

Conclusion

This study highlights the advantage of ^{19}F qNMR for the quantification of illicit drugs such as 2'-fluoro-2-oxo-PCE. Quantification via this primary analytical technique provides several advantages, including quick sample preparation, short run time, and enables analysis of multiple analytes with a single certified reference material. Furthermore, when a sample is compatible with both ^1H and ^{19}F qNMR, the combined use of these techniques provides a powerful, complementary approach to quantification, requiring only one sample preparation and two experimental setups. This ongoing innovation enhances the AFDL's ability to accurately identify and quantify a broad range of NPS, contributing significantly to forensic science and public health efforts. Efforts are underway to finalise the validation of this method, with plans to expand its application to other fluorinated-illicit substances and fluorinated CRMs.

1. United Nations Office on Drugs and Crime (UNODC) Current NPS Threats, Volume VII, July 2024.
2. Pharmaceuticals (Basel). 2023 Aug 15;16(8):1162.