Toxicological analysis of cocaine adulterants in blood samples

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Introduction

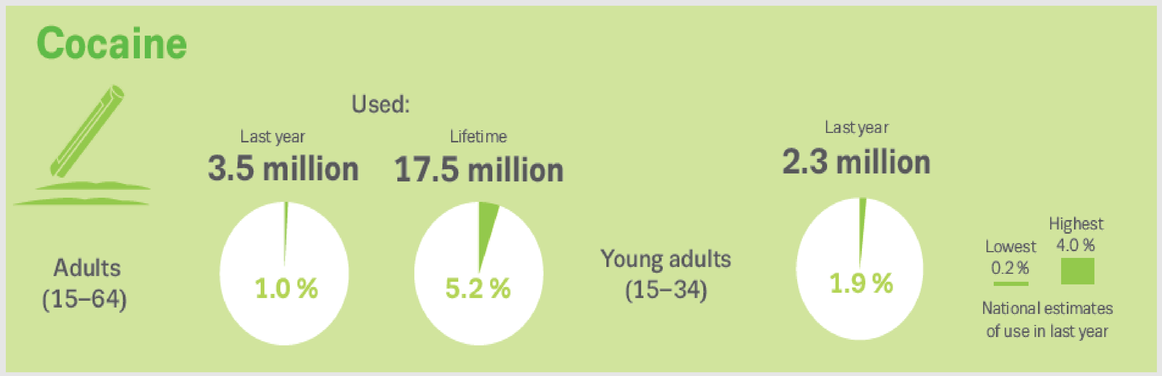


Figure 1. Estimates of cocaine use in the European Union in 2016 and lifetime, between adults and young adults [1].

In Portugal, according to data collected in 2012 [1], cocaine was consumed by 1.2% of the population between 15 and 64 years old once in their lifetime. More recently, it was found that 0.4% of the Portuguese population between 15 and 34 years old consumed cocaine in 2016 [2]. This drug is commonly related to diluting agents, contaminants and adulterants, pharmacologically active substances developed for medical purposes (analgesics, local anesthetics, antihistamines, anthelmintics and others), with the purpose of increasing profits due to their low cost and availability, but also to augment or emulate the stimulant and analgesic effect of cocaine [3,4]. Cocaine illegal use causes well-known toxic effects at the cardiovascular and respiratory levels, however, there is little knowledge about the influence of its adulterants in the human body, such as an increase of cocaine toxicity even in non-toxic concentrations [5].

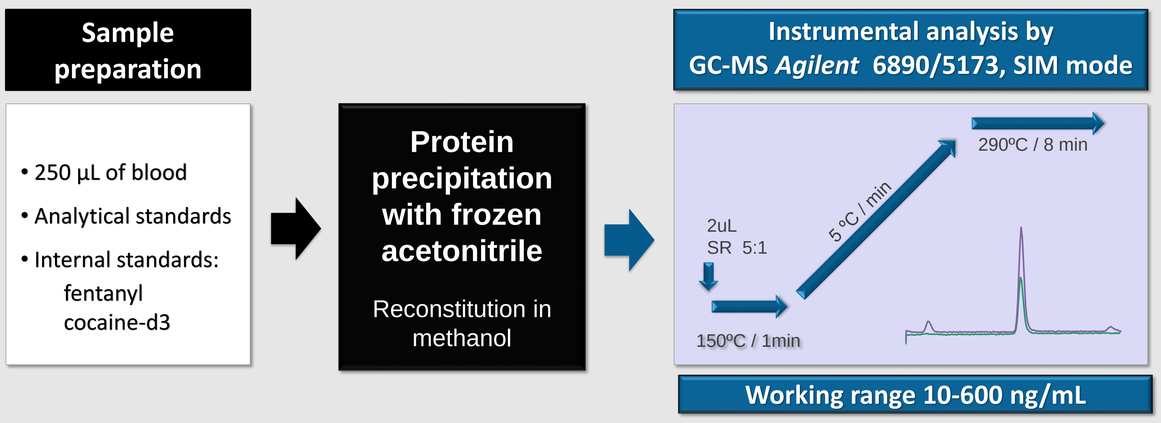
Aims

The objective of this work was to validate a method that allows the identification, confirmation and quantification of cocaine adulterants in blood samples collected *in vivo* or post-mortem, based on the criteria defined by SWGTOX and the methodology in force in the Laboratory of Forensic Chemistry and Toxicology of the National Institute of Legal Medicine and Forensic Sciences (SQTF). The studied substances (atropine, phenacetin, hydroxyzine, ketamine, lidocaine and tetramisole) were selected taking into account the literature review, the available analytical standards and technical conditions. It was also intended to make a retrospective study of the prevalence of these substances in cases with a positive result for cocaine or its metabolites, as well as their relative concentrations.

Methods

97 blood samples positive for cocaine and/or its metabolites, admitted between January 2015 and December 2016

- **52** collected *in vivo* during the supervision of DUI of psychotropic substances
- **45** post-mortem



Results and discussion

The method was fully validated in accordance with parameters and criteria implemented in the SQTF and SWGTOX recommendations (selectivity, interference studies, recovery, limit of detection, limit of quantification, linearity and calibration model, repeatability, reproducibility, accuracy and carryover) (Table 1).

Table 1. Main results obtained in the method validation for the selected adulterants.

Compound	RT (min)	Ions (m/z)	Mean Recovery (%)	LOD (ng/mL)	CV (%)	BIAS (%)
Atropine	16.4	124, 140, 289	93	10	6.3	2.7
Hydroxyzine	27.0	201, 299, 374	100	25	6.2	3.0
Ketamine	10.5	182, 209, 166	115	25	13.0	7.8
Lidocaine	10.9	86, 120, 234	101	25	7.9	3.4
Phenacetine	7.6	179, 137, 180	103	10	8.0	3.4
Tetramisole	12.5	148, 203, 204	102	10	8.5	4.5

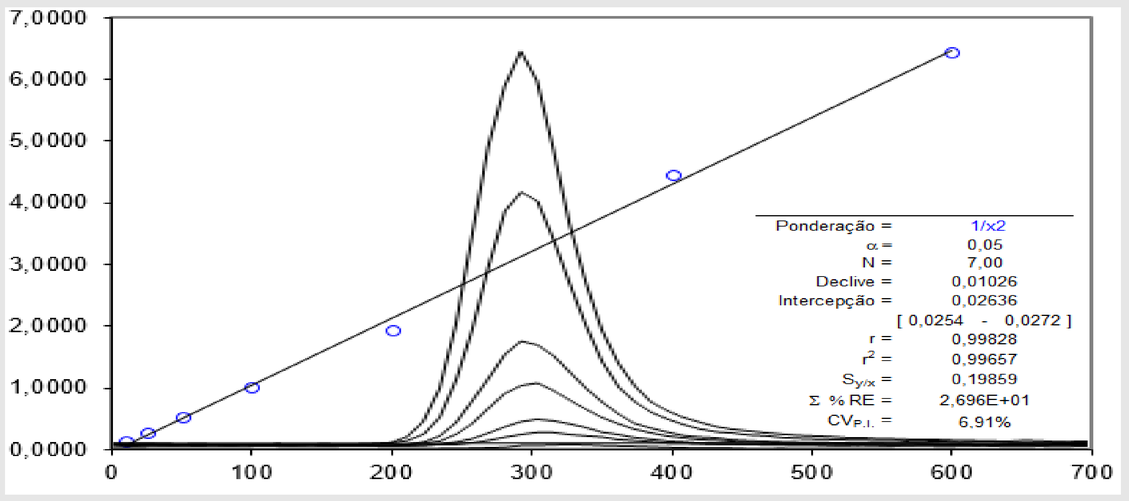


Figure 2. GC-MS chromatogram of tetramisole calibrators and respective calibration curve.

It was possible to identify and quantify the presence of at least one adulterant in 31 samples (approximately one third), 18 of which were post-mortem samples and 13 samples collected *in vivo*, and only 8 samples had more than one adulterant present.

Table 2. Concentration of the studied adulterants found in the analysed samples.

Adulterant	Concentration (ng/mL)		Positive samples (%)
	In vivo	Post-mortem	
Hydroxyzine	-	29	1
Lidocaine	47-215	164-414	8
Phenacetine	14-166	28-1151	15
Tetramisole	50 (1 case)	10-1106	19

Tetramisole was the most prevalent adulterant and was present almost exclusively in post-mortem samples. Lidocaine was more prevalent in samples collected *in vivo* (75%). Phenacetin was evenly distributed between post-mortem and *in vivo* samples. Adulterant concentrations were higher in post-mortem samples for all compounds analysed (Table 2).

The adulterants found in the analyzed samples are in agreement with the several studies carried out [3,4]. Regarding post-mortem concentrations, they are higher than the values presented in the study by Pawlik [5]. Lidocaine is a common local anesthetic and is being used as an adulterant because of its cocaine-like effects. It may enhance the oral numbness, mimicking the high cocaine quality [6]. In turn, phenacetin is an analgesic that can be used as a cocaine adulterant due to its slightly euphoric effects [5]. Finally, tetramisole is an anthelmintic that has become an important subject for forensic scientists in the last two decades because of its high presence in cocaine preparations. Among the possible reasons for its use as an adulterant are the inhibition of monoamine oxidase in nicotine receptors, increasing dopamine transmission and the euphoric effect of cocaine [7]; inhibition of cholinesterase, decreasing cocaine metabolism and increasing its half-life [6]; and tetramisole being metabolized to aminorex, a drug of stimulant behavior similar to amphetamines [8]. Although little is known about the concomitant use of cocaine and adulterants, it is known to be associated with more side effects of cocaine use [9].

Conclusions

The validated method allows rapid, precise, accurate and economic analysis of selected compounds and requires smaller sample aliquots which can be important in post-mortem cases. One third of the analysed samples were positive for at least one of the adulterants, with the most detected being tetramisole, phenacetin and lidocaine. The information collected can be important in future studies of correlation between the presence of adulterants and cocaine toxicity.

References

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