REFERÊNCIA

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Article

Brazilian Federal District Cocaine Chemical Profiling - Mass Balance Approach and New Adulterant Routinely Quantified (Aminopyrine)

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From a set of 159 samples seized by Brazilian Federal Police between 2010 to 2013 in the Federal District, the major component chemical profiling routine analyses revealed the presence of cocaine with purity range of 5.5 to 99.9% (mean 69.8%). Most cocaine base samples show moderately and not oxidized levels, whereas cocaine hydrochloride samples exhibit moderate to high oxidation degrees. More than 40% of the analyzed samples did not have any adulterant. Phenacetin was the most abundant adulterant (24% average purity). Aminopyrine, a new adulterant, was identified and quantified only in cocaine base samples, mainly as a trace adulterant but also as a major compound. In most samples adulterated with aminopyrine, phenacetin was also identified as a major adulterant, suggesting a possible association of the two pharmaceuticals in the cutting process. Aminopyrine was not detected in 2010 seizures, but became a common adulterant throughout the years of 2011 to 2013. A mass balance approach analysis also established that adulterants are responsible for only 12% of the mass of all seizures (i.e., 84 kg), whereas 77% (i.e., 553 kg) is due to alkaloids (cocaine and *cis*/*trans*-cinnamoylcocaine), contributing to provide forensic intelligence information to police investigators.

Keywords: chemical profiling, cocaine, aminopyrine, adulterant, mass balance

Introduction

Brazil is placed among those countries mostly affected by the illicit drugs market, due to its large population (over 200 million inhabitants) and the increasing social issues related to internal trafficking and cocaine consumption. Brazil also borders all the main coca leaf producing countries and it has the most relevant chemical industry in the South American region. The large availability of chemical products may facilitate their illegal use in the extraction, refining, dilution and adulteration (e.g., adding pharmaceutical products) of the illicit drug that reaches the Brazilian territory. Since 2006, the Brazilian Federal Police (BFP) has been implementing its own illicit drug chemical profiling program (PeQui Project). This program is designed to provide scientifically based intelligence information and forensic chemistry results, regarding both drug origin and seizure correlations by means of detailed chemical analysis.[1-3]

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The present article presents chemical profiling results of police seizures between the years of 2010 and 2013 in the Brazilian Federal District and it illustrates how sample composition information can be useful when contextualized with investigative information.[4] Cocaine samples (159) originated from 75 BFP seizures have been analyzed by gas chromatography-flame ionization detector (GC-FID). These samples correspond to a total mass of 722 kg (342 kg as cocaine hydrochloride and 380 kg as cocaine base). Major components such as cocaine, *cis*- and *trans*-cinnamoylcocaine and pharmaceutical cutting agents/adulterants (benzocaine, phenacetin, caffeine, lidocaine, levamisole, hydroxyzine, procaine, diltiazem) have been routinely quantified. Since a new adulterant (aminopyrine) has been consistently identified, it has also been quantified within the PeQui scope.

Aminopyrine (aminophenazone) is a pharmaceutical used as an analgesic, anti-inflammatory and antipyretic and it has been frequently identified in freebase forms of cocaine (e.g., coca paste and crack cocaine).[5] As aminopyrine is known to present bone marrow toxicity and

to cause agranulocytosis,[6] it becomes relevant to consider the presence of this new adulterant in the prevention of drug related diseases and in the treatment of cocaine users.

This work also focuses on a mass balance approach, which takes into consideration cocaine sample content in terms of main alkaloids and pharmaceutical adulterants, as well the total mass of police seizures. That point of view is particularly important for BFP, since it allows a more detailed analysis of international trafficking routes for high purity (low cut) cocaine feeding the internal market throughout the Brazilian Atlantic coast to Africa or Europe.[7] It also provides a diagnostic tool for the control of chemicals which may be used in the cocaine production chain.

Experimental

Chemicals

Cocaine base (96.1%) and *trans*-cinnamoylcocaine base (98.2%) were purchased from national metrology institute (NMI). Dipentyl phthalate (97%) and caffeine (98.0%) were provided by Acros Organics. Benzocaine (97.2%), lidocaine hydrochloride monohydrate (96.0%), procaine hydrochloride (98.7%), tetramisole hydrochloride (99.9%), diltiazem hydrochloride (98.7%), hydroxyzine dihydrochloride (98.1%) and aminopyrine (99.1%) were purchased from Sigma. Phenacetin (99.3%) was provided by TCI-EP. All working solutions were prepared by dilution of reference materials with chloroform (HPLC grade) provided by Tedia-Brazil. Dipentyl phthalate was used as internal standard dissolved in a solution of chloroform with 0.2% (v/v) of diethylamine (pa) purchased from Sigma. Helium, synthetic air, nitrogen and hydrogen (> 99.995% of purity) were supplied by IBG.

Sample preparation

All 159 cocaine samples were manually crushed and homogenized. Cocaine base samples were homogenized in the presence of liquid nitrogen as described in previous work.[1]

Amounts of 12.25 ± 0.25 mg of each crushed sample were mixed with 10.0 mL of internal standard solution (dipentyl phthalate at 0.490 mg mL^{-1} in chloroform solution with 0.2% diethylamine) and carefully stirred until dissolution. Freshly prepared solutions were transferred to 2 mL glass vials and sealed.

Qualitative and quantitative analysis of major components

Infrared spectroscopy (FTIR/ATR - Nicolet iS10 model, equipped with a SMART iTR accessory) and classical spot tests were used to stablish the cocaine form (base or hydrochloride salt).

Quantification analysis were carried out in an Agilent Technologies 6890N gas chromatograph with a flame ionization detector, using an Agilent Technologies 7683B Series autosampler. Chromatographic conditions: injection volume: 1.0 μL; split ratio 50:1; column: RXi-1MS methyl siloxane, 25 m × 200 μm (i. d.) × 0.33 μm film thickness; oven temperature program: 150 °C for 2 min, 40 °C min^{-1} to 315 °C for 4.5 min; injection port temperature: 280 °C; FID temperature: 320 °C; carrier gas flow rate: 1.0 mL min^{-1} (helium).

Major components cocaine, *cis*- and *trans*-cinnamoylcocaine and pharmaceutical cutting agents/adulterants (benzocaine, phenacetin, caffeine, lidocaine, levamisole, hydroxyzine, procaine and diltiazem) were quantified using the previous GC-FID method. Due to the gradual increase of aminopyrine as a new adulterant routinely identified, this analyte has also been included since 2014 as a part of GC-FID quantification. Analyte characterization was performed by both gas chromatography-mass spectrometry (GC-MS) and GC-FID (reference material co-injections). Analytical curves were constructed by plotting peak areas against concentration ($r^2 > 0.9999$). Other method validation figures of merit included specificity, linearity, repeatability, accuracy, working range, limit of detection (LOD) and limit of quantification (LOQ), which will be the subject of a future publication.

Cocaine sample oxidation levels were determined following a well established criterion developed by the Drug Enforcement Agency (DEA), which considers the total cinnamoylcocaine (*cis* + *trans*-cinnamoylcocaine) ratio with respect to cocaine.[8] Samples presenting a ratio less than 2% are classified as "highly oxidized"; samples presenting a ratio between 2-6% are classified as "moderately oxidized"; and samples presenting a ratio of more than 6% are classified as "minimally or not oxidized".

Seizure information and mass balance

Cocaine samples from 75 BFP seizures in the Brazilian Federal District between 2010 and 2013 correspond to a total mass of 722 kg (342 kg as cocaine hydrochloride salt form and 380 kg as freebase cocaine form). Seizure data were obtained from forensic reports in an in-house data manager system called "Criminalistica".

The percentage of each analyte in a sample was multiplied by the correspondent mass of that specific seizure, providing a mass balance of each apprehension and an estimation of both alkaloid and adulterant contents.

Results and Discussion

Chemical profiling of major components

The GC-FID quantitative analysis showed wide variations on cocaine content for the years 2010-2013, covering the purity range from 5.5% to 99.9% (Figure 1) and an overall average content of 69.8%. A substantial reduction in cocaine average purity was observed in 2013 as compared to previous periods (2010: 78.3%; 2011: 80.7%; 2012: 74.2%; 2013: 56.4%). This was mainly due to the occurrence of heavily adulterated seizures (cocaine hydrochloride with caffeine and cocaine base with phenacetin).

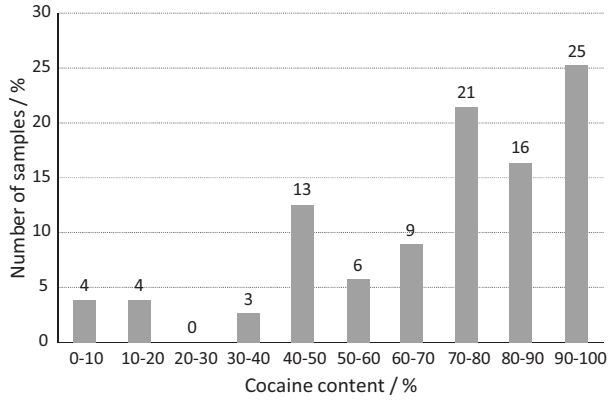

Figure 1. Histogram of cocaine content distribution (base and hydrochloride) 159 samples, years 2010 to 2013.

The total cinnamoylcocaine to cocaine ratio (the oxidation level indicator) revealed that most cocaine base samples underwent either moderate oxidation processes (20%) or were not oxidized at all (76%). On the other hand, most cocaine hydrochloride samples experienced moderate (64%) to high (30%) oxidation processes.

More than 40% of the analyzed samples (63) did not contain any adulterant, which is coherent with the high purity international seizures usually performed by BFP. Among the pharmaceutical products identified as cutting agents, phenacetin was the most abundant one (present in 26% of samples = 41 samples). Levamisole (19% = 30 samples), caffeine (14% = 23 samples), aminopyrine (12% = 19 samples), lidocaine (11% = 18 samples), benzocaine (5% = 8 samples) and diltiazem (5% = 8 samples) were also identified.

The results show a prevalence of phenacetin as the main quantified adulterant (mean purity of 24%, Table 1). Previous BFP routine analysis also identified phenacetin as a key adulterant, found mainly in cocaine base seizures, all over the country. Table 2 shows that about half of cocaine base samples (53%) contains phenacetin as a detected adulterant and for the most part as a major adulteration (> 5% content). This kind of analysis has been performed for each identified adulterant as a forensic intelligence tool in the core of the PeQui project (Figure 2).

Aminopyrine was found in 8 seizures (19 cocaine base samples, 25% of the total cocaine base analyzed), mainly as a trace adulterant (14 samples with < 2% of purity), but also as a major compound (3 samples with purity between 2-5%; 1 sample with purity of 5.8%; and 1 sample with purity of 26.0% - Figure 3). In 15 cocaine base samples adulterated with aminopyrine, phenacetin was also identified as a

Table 1. Adulterant distribution, all samples (base and hydrochloride cocaine)

	Adulterant									
	Overall	Benzo	Phena	Caff	Lido	Amino	Leva	Proc	Hydro	Diltia
Number of adulterated samples	96	8	41	23	18	19	30	0	0	8
Adulterant incidence / %	–	5	26	14	11	12	19	0	0	5
Adulterant mean content in adulterated samples / %	23.7	0.6	24.0	37.2	9.7	3.1	6.3	0	0	2.5

Overall: sum of adulterants; Benzo: benzocaine; Phena: phenacetin; Caff: caffeine; Lido: lidocaine; Amino: aminopyrine; Leva: levamisole; Proc: procaine; Hydro: hydroxyzine; Diltia: diltiazem.

Table 2. Adulterant distribution, base cocaine

	Adulterant									
	Overall	Benzo	Phena	Caff	Lido	Amino	Leva	Proc	Hydro	Diltia
Number of adulterated samples	53	8	40	8	3	19	0	0	0	0
Adulterant incidence / %	–	11	53	11	4	25	0	0	0	0
Adulterant mean content in adulterated samples / %	19.7	0.6	24.6	0.6	3.3	3.1	0	0	0	0

Overall: sum of adulterants; Benzo: benzocaine; Phena: phenacetin; Caff: caffeine; Lido: lidocaine; Amino: aminopyrine; Leva: levamisole; Proc: procaine; Hydro: hydroxyzine; Diltia: diltiazem.

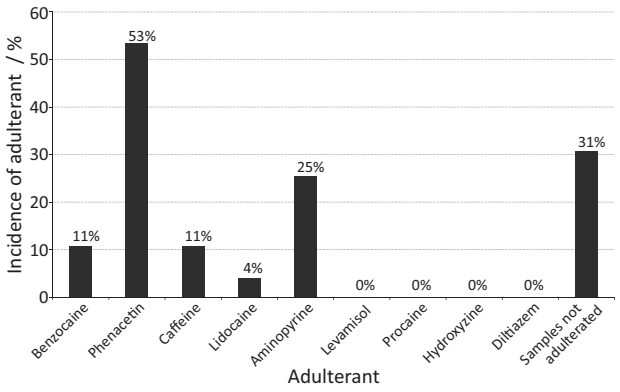

Figure 2. Pharmaceutical adulterants incidence (%) in cocaine base (76 samples).

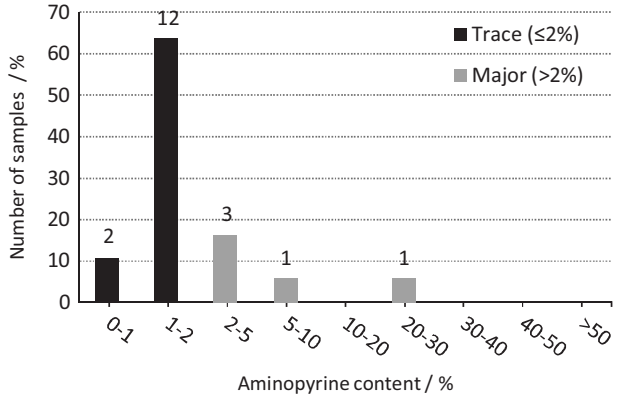

Figure 3. Histogram of aminopyrine content distribution (cocaine base samples).

major adulterant (8 to 40% of purity), suggesting a possible association of the two pharmaceuticals in the cutting process. In none of the cases, aminopyrine was found as an adulterant in cocaine hydrochloride.

It was also noted that aminopyrine was present only in samples seized after 2010 (2011: 3 samples; 2012: 5 samples; 2013: 11 samples), indicating a growth tendency during that period. Finally, it's important to note that the association of phenacetin/aminopyrine in drug samples have been identified not only in Federal District, but also in other Brazilian States around the country. To the best of our knowledge, those results have not yet been published in articles related to drug profiling.

Mass balance

A mass balance approach can be also proposed to supply forensic intelligence information to police investigators. As an example, it's possible to infer that adulterants in 2010-2013 seizures amount to 12% on a mass basis (i.e., 85 kg), and that alkaloids (cocaine and *cis*/*trans*-cinnamoylcocaine) amount to 77% (i.e., 553 kg) (Table 3). This picture is coherent with the high purity cocaine international trafficking profile found in BFP routine seizures, for which most of the samples have their composition reasonably described by the quantification of 12 major components (centesimal > 88%).

Table 3. Individual and overall mass balance of quantified adulterants and alkaloids

Adulterant			
Adulterant	Mass / kg	(Adulterant mass/Σ adulterant mass) / %	(Adulterant mass/seizure mass) / %
Benzocaine	0.22	0	0.0
Phenacetin	41.22	49	5.7
Caffeine	20.69	24	2.9
Lidocaine	15.01	18	2.1
Levamisol	4.02	5	0.6
Procaine	0.00	0	0.0
Hydroxyzine	0.00	0	0.0
Diltiazem	0.13	0	0.0
Aminopyrine	3.54	4	0.5
Σ Adulterants	84.83	100	11.7
Alkaloid			
Alkaloid	Mass / kg	(Alkaloid mass/seizure mass) / %	
Cocaine	522.41	72.3	
cis-Cinnamoylcocaine	16.58	2.3	
trans-Cinnamoylcocaine	13.90	1.9	
Σ Alkaloids	552.89	76.5	
Summation			
	Mass / kg	Centesimal[a]	
Σ (alkaloids + adulterants)	637.72	88.3	
Total seized	722.61	–	

[a]Σ (alkaloids + adulterants) mass/seizures total mass (in %).

Additional correlation analysis involving contents and mass information may be performed considering cocaine form (e.g., base or hydrochloride, Figure 4), place or date of apprehension, etc. That kind of analysis may help to identify trends and changes in cocaine traffic dynamics.

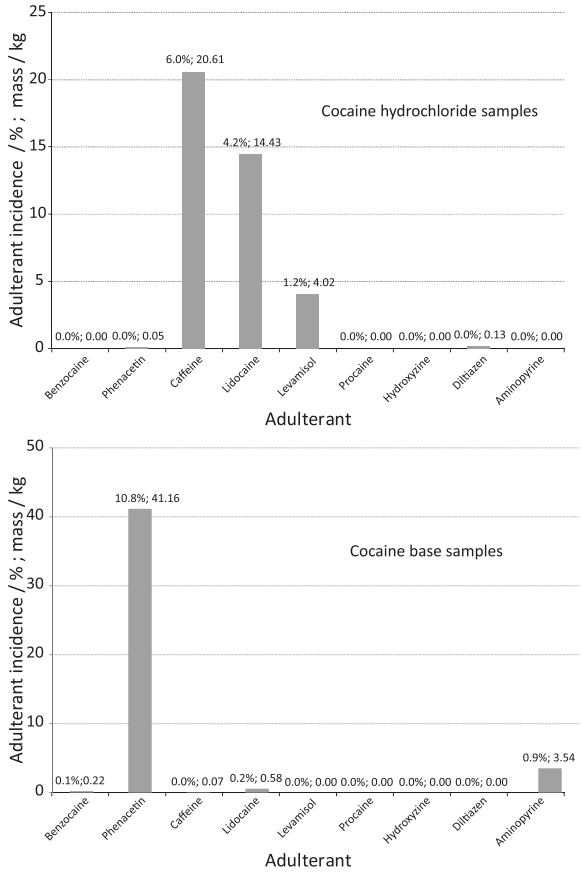

Figure 4. Adulterant mass balance in cocaine hydrochloride and base [incidence of adulterant in seizures (%) and equivalent mass in kg].

Conclusions

From a set of 159 samples seized by Federal Police between 2010 and 2013 in the Brazilian Federal District, the major component chemical profiling routine analyses of the PeQui project revealed the presence of cocaine with purity range of 5.5 to 99.9% (mean 69.8%). Most cocaine base samples show moderately (20%) and not oxidized (76%) levels, whereas cocaine hydrochloride samples exhibit moderate (64%) to high (30%) oxidation degrees.

More than 40% of the analyzed samples did not have any adulterant, which is coherent with the cocaine international trafficking seizures performed by the Brazilian Federal Police in a relative high purity scenario. Among the pharmaceuticals identified as cutting agents, phenacetin was the most abundant one (53% of cocaine base samples with 24% average purity).

Aminopyrine, a new adulterant found in the PeQui project scope, was identified and quantified only in cocaine base samples (8 seizures, 19 samples), mainly as a trace adulterant but also as a major compound in 3 samples. In most samples adulterated with aminopyrine, phenacetin was also identified as a major adulterant, suggesting a possible association of the two pharmaceuticals in the cutting process. Aminopyrine was not detected in 2010 seizures, but became a common adulterant throughout the years of 2011 to 2013.

A mass balance approach analysis established that adulterants are responsible for only 12% of the mass of all seizures (i.e., 84 kg), whereas 77% (i.e., 553 kg) is due to alkaloids (cocaine and *cis*/*trans*-cinnamoylcocaine).

Chemical profiling results proved to be relevant to supply scientifically based information to the Brazilian Federal Police investigators and to identify how traffic dynamics could possibly have changed, as a result of the utilization of new pharmaceutical adulterants, the concentration of analytes and seizure mass balance.

Acknowledgements

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