Tackling poor specificity of cocaine color tests by electrochemical strategies

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ABSTRACT: *This paper presents electrochemical strategies for the fast screening of cocaine and most common cutting agents found in seized drug samples. First, a study on the performance of Scott color tests on cocaine and a wide range of cutting agents is described. The cutting agents causing false positive or false negative results when in mixture with cocaine are identified. To overcome the lack of specificity of color tests, we further propose a fast screening strategy by means of square wave voltammetry on disposable graphite screen printed electrodes, which reveals the unique fingerprint of cocaine and cutting agents. By employing a forward and backward scan and by a dual pH strategy, we enrich the electrochemical fingerprint and enable the simultaneous detection of cocaine and cutting agents. The effectiveness of the developed strategies was tested for the detection of cocaine in seized cocaine samples and compared with the color tests. Moreover, we prove the usefulness of square wave voltammetry for predicting possible interfering agents in color tests, based on the reduction peak of cobalt thiocyanate. The developed electrochemical strategies allow for a quick screening of seized cocaine samples resulting in a selective identification of drugs and cutting agents.*

Cocaine is one of the most used illicit drugs, with a number of 17.1 million global users in 2015 according to United Nations Office on Drugs and Crime.[1] The use of this psychoactive drug is correlated with many health complications and deaths occurring after recreational use and abuse.[2-4] Global production of cocaine was estimated for 2015 at 1,125 tons, while the global cocaine interception rate more than doubled between 2009 and 2015 to 864 tons.[1] Cocaine continues to be trafficked primarily from South America to North America and Western and Central Europe. A great deal of attention has been focused on assessing the trafficking routes in order to reduce drug-related crime and its negative health impact. For this purpose an important role is attributed to the identification of the composition of cocaine seizures (i.e. adulterants, cutting agents and other compounds) which provides police forces with valuable information on the source of the supply and, therefore, aids tracing the illicit networks. The characterization of cutting agents and adulterants in seized cocaine samples is important from a forensic point of view in order to link different seizures to one original batch[5] as well as for the health implications some of them might have. For instance, levamisole was linked to serious adverse effects such as leukoencephalopathy.[6]

In general, police officers and custom services use field tests, i.e. color tests. A color test is a presumptive test that provides an indication of the presence or absence of a compound. Color tests are used on site as a quick and cheap screening method. They are simple, sensitive and the results can be observed visually.

The Scott color test developed by Scott in 1973[8] is the most common screening test for cocaine. The test is based on the formation of a blue complex between cocaine and cobalt thiocyanate.[9, 10] Two variants, i.e. vials and wipes, are commonly used in the field to detect the presence of cocaine in unknown samples, and are cheap in use. There are, however, two important problems associated with the color tests. Firstly, this conventional technique can be easily influenced by adding certain compounds to the cocaine mixtures, causing the test to show a false negative result. Smugglers are getting more creative each day in order to get the cargo through customs services and they mainly do this by chemically masking the cocaine with colored agents that cause the color test to be negative. Another popular technique is to mix cocaine with other solid materials like fishmeal, to hide its presence. Moreover, the color test lacks specificity. The complexation with the cobalt thiocyanate could also occur with other molecules, causing the test to turn blue, thus leading to a false positive result and possible detention of innocent people or economic burden on companies whose cargos are confiscated. Moreover, the test is influenced by temperature. At 4°C the sensitivity of the test was found to be double compared to room temperature (22°C), while temperatures over 40°C decreased the sensitivity of the test more than two fold in comparison with room temperature.[11]

Because of all these concerns, color test results need further confirmation in the laboratory by more sophisticated techniques such as chromatography or mass spectrometry which are laborious and both time consuming and costly.

Electrochemical techniques, through their simplicity, low cost, fast response and high sensitivity, offer a good alternative for on-site screening of illicit drugs in the presence of cutting agents. Several works report on the detection of cocaine in the presence of cutting agents by means of electrochemistry.[12-15] However, most of the time modification of the electrode surface is required to achieve selective cocaine detection, which can be time consuming and costly. Moreover, an extensive study on the effect of a wide range of cutting agents on the electrochemical detection of cocaine was not yet conducted.

In our previous work[12] we were able to elucidate the electrochemical fingerprint of cocaine and some of its common cutting agents, as well as their binary mixtures, on Graphite Screen Printed Electrodes (GSPE) at pH 7. Some cutting agents, i.e. levamisole, showed a suppression effect on the signal of cocaine, which might cause a false negative result if the cutting agent is present from a certain amount.

In this work a comprehensive study on cocaine detection is performed. We further investigate the influence of a broader list of cutting agents on the electrochemical signal of cocaine in solution and propose different strategies to detect cocaine in street samples, thus eliminating false negative results. Here we refer to cutting

agents as any substance found in illicit drugs at the point of purchase, thus including also adulterants, diluents and other compounds that might be present in street drug samples.

For this purpose, the specificity of the commercially available Scott test towards the detection of cocaine in the presence of a range of common cutting agents was first investigated. This part delivers valuable information about the flaws of color tests, which are even upon this point in time not widely documented in literature. The focus was put on the problem of false positive results of color tests and the alternative of employing electrochemical methods to address this issue. A screening of cocaine in the presence of the most common cutting agents by means of square wave voltammetry (SWV) is included. The problem of false negative results obtained by the proposed electrochemical method is further addressed by two approaches: (1) employing a double scan and (2) a dual pH strategy by adjusting the pH of the detection buffer from pH 7 to 12. We refer to "double scan" as a SWV scan performed by first sweeping the potential in the negative direction, followed by a potential sweep in the positive direction, while a "single scan" refers to performing directly a potential sweep in the positive direction. Moreover we demonstrate the usefulness of electrochemical techniques to predict the possible presence of interfering agents in color tests, based on the change in the electrochemical reduction signal of Co (II) in cobalt thiocyanate upon interaction with cocaine and cutting agents.

Experimental section

Cocaine HCl and heroin HCl standards were purchased from Lipomed (Arlesheim, Switzerland). Standards of phenacetine, diltiazem, lidocaine, procaine, hydroxyzine, benzocaine, ephedrine, dextromethorphan, dextropropoxyphene, bupivacaine and paracetamol were purchased from Sigma-Aldrich (Diegem, Belgium). Standards of benzoic acid, chlorpromazine, promethazine, diphenhydramine and levamisole were purchased from Acros Organics (Geel, Belgium). Standards of caffeine and boric acid were purchased from VWR Chemicals (Leuven, Belgium).

Color tests (M.M.C. International B.V, The Netherlands) were performed according to the producers instructions, by adding more than 1 mg sample powder to the test vial, homogenizing for 10 seconds and observing the color visually. The street samples were provided by the National Institute of Criminalistics and Criminology (NICC) of Belgium and were previously analyzed qualitatively and quantitatively by gas-chromatography-mass spectrometry and gas chromatography-flame ionization detection, respectively.

SWV measurements were performed using an Autolab potentiostat/galvanostat (PGSTAT 302N, ECOCHEMIE, The Netherlands) controlled by NOVA software. Phosphate buffer (KH_2PO_4) 20mM containing 100mM KCl (PBS) of pH 7 or pH 12 was prepared and used as supporting electrolyte for electrochemical measurements. The pH of the solutions was adjusted by using a 100 mM KOH solution.. 50 mM stock solutions of the pure compounds and mixtures were prepared in Milli Q water and stored at 6°C. These stock solutions were further diluted to the desired concentration with the prepared buffer solutions immediately before measurement. 50 µL of solution was applied immediately after preparation onto the surface of ItalSens graphite screen-printed electrodes (GSPE) containing a graphite working electrode (3 mm diameter), a carbon counter electrode and a (pseudo)silver reference electrode (PalmSens, The Netherlands). The single scan SWV parameters were as follows: potential range -0.1V to 1.5V, step potential 5mV, amplitude 25mV and frequency 10 Hz. For the SWV double scan the potential was firstly swept from 1.5V to -0.1V, before scanning back from -0.1V to 1.5V. All results obtained by SWV were presented after baseline correction using the mathematical algorithm "moving average" (window = 1) contained within NOVA 1.11 software. Concerning the investigation of complex formation with cobalt thiocyanate, the SWV parameters were as follows: potential range -0.8 to -1.2V, step potential -5mV, amplitude -75mV and frequency 10 Hz. The solutions containing cobalt thiocyanate were deoxygenated by purging nitrogen for 10 minutes prior to the experiments.

The specificity of each test was quantitatively determined as the ratio of the number of true negative (N) samples and the sum of the number of true negative samples and false positive (FP) samples. True negative is considered the number of cases that the test declares negative and that are truly negative, while false positive is the number of cases that the test declares positive but are in fact negative. The sensitivity of each test was quantitatively determined as the ratio of the number of true positives (P) samples and the sum of the number of true positive samples and false negative (FN) samples. True positive is considered the number of cases that the test declares positive and that are truly positive, while false negative is the number of cases that the test declares negative but are in fact positive.

Results and Discussion

Performance of color tests on pure compounds

In order to identify which molecules may interfere with the commercially available Scott color test, a selection of compounds that are commonly used as cutting agents for cocaine samples and other compounds that might be present in drug samples were analyzed. The selection of compounds was made according to the most popular cutting agents of cocaine according to data delivered by the European Drug Report 2017[16], as well as the data delivered by the NICC in Belgium. In addition, some compounds claimed in other literature[10, 17] to be false positive compounds for the cocaine color test were also added. All selected compounds are white powders. The results of the Scott test are presented in Figure 1. A positive result was considered when discoloration to blue occurred, even when only a few particles were colored in blue.

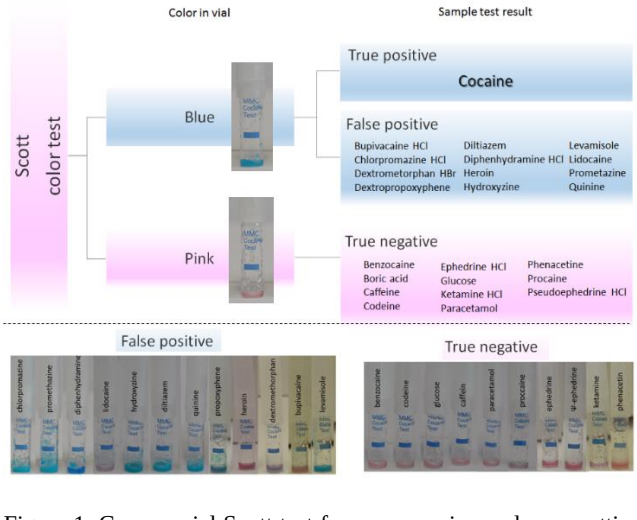


Figure 1. Commercial Scott test for pure cocaine and pure cutting agents.

As shown in Figure 1, besides cocaine, the test also colors blue when other compounds such as lidocaine, heroin and bupivacaine are present in the sample giving false positive results. A possible explanation might be that, as stated by Oguri *et al*[9], the complex

formed between cocaine and cobalt thiocyanate is most likely due to the complexation of cobalt with a carbonyl group and tertiary amine group of cocaine. The benzoyloxy group is not taken into consideration since the complex is not formed in atropine, which has the benzoyloxy group but lacks the other carbonyl group. Several studies were performed on the complexation of the Scott-agent and cocaine[9, 18, 19], but a well-defined structure has never been fully proven, while the 2:1 complex structure is assumed to be the most plausible. While it is easy to assume the cobalt thiocyanate reagent will only form a complex with the tertiary amine group and carbonyl group of cocaine, it is to be expected that a metal complex could be formed with other ligands as well, that being the reason for these false positive results of the color test. Many molecules contain similar functional groups as cocaine (see Figure S1 in s*upplementary material*). Lidocaine, heroin, bupivacaine, diltiazem and dextropropoxyphene all contain tertiary amine and carbonyl groups, which present pairs of nonbonding electrons that can form an interaction with the metal ion (electron donor groups). The carbonyl groups are missing for chlorpromazine, promethazine, diphenhydramine, dextromethorphan, levamisole and hydroxyzine, suggesting the complexation could also occur with different ligands via another mechanism. The only constant in each molecule present is the tertiary amine group, which acts as an electron donor group. Of all tested substances, only procaine and codeine gave a negative result with the color test while containing a tertiary amine group. For codeine, the main reason for the negative result can be related to the position of the tertiary amine group in the molecule. It can be assumed that the position of the amine results in steric hindrance and blocks the coordination of codeine to cobalt. The presence and the position of the carbonyl group seems to create a suitable environment for coordination of heroin (quite similar molecule with codeine). The negative result of procaine can be related to the distance between the carbonyl and the tertiary amine group. This distance might block the coordination of procaine with the cobalt ion.

The specificity of the color test was determined, focusing on the pure compounds, and was calculated to be 0.478, much lower than what is expected for a well performing screening test. A test is perfect when the specificity is 1, equivalent to a random draw when the specificity is 0.5, while if the specificity is below 0.5, the test is counter performing. Since these powders are all white, the confusion will be major, and the goods will be confiscated, while the carrier will be detained, although he or she might not be transporting anything illegal. With lidocaine, hydroxyzine, diltiazem and certainly levamisole as important cutting agents[1, 16], this presents a major problem.

Performance of color tests on binary mixtures of cocaine and cutting agents

Another important issue related to the Scott color test is the significant amount of false negative (FN) results that may occur. In this sense, the influence of certain agents on the analysis of cocaine samples with the commercial color test was further investigated. For this purpose, an equal amount of cocaine and another compound was mixed and added to the color test vial. The results are presented in Figure 2. The test turns blue for mixtures of cocaine with levamisole, diltiazem, dextromethorphan, promethazine, chlorpromazine, and benzocaine (true positive), while no discoloration is observed for mixtures of cocaine and procaine, codeine and quinine, leading to false negative results.

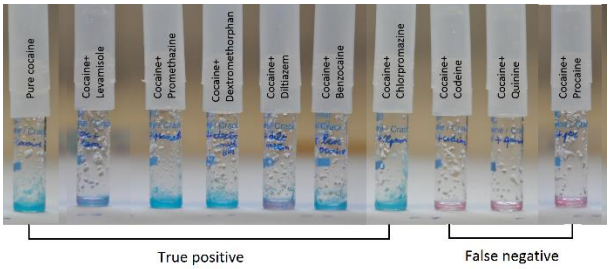
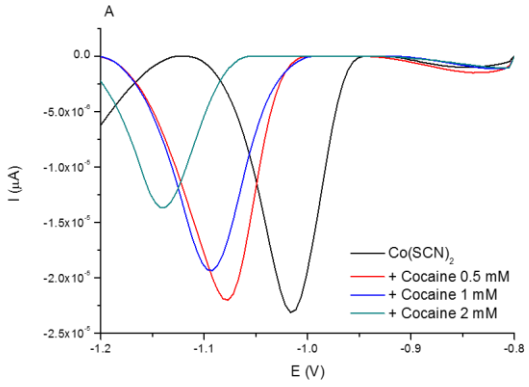


Figure 2. Color test for binary mixtures (1:1) of cocaine and cutting agents.

Performance of electrochemical methods for the investigation of complex formation with cobalt thiocyanate

In a first step we studied the usefulness of electrochemical methods to predict possible interfering agents in color tests. For this purpose, the interaction between cocaine and cobalt thiocyanate was investigated via a reductive scan by SWV. Reductive scans of cocaine solution in PBS pH 7 at GSPE did not reveal any peak for cocaine. By sweeping the potential from -0.8V to -1.4V cobalt thiocyanate shows a reductive peak at around -1V at GSPE in PBS pH 7 corresponding to the reduction of Co(II). This is in good agreement with previous research reporting on the appearance of a reduction peak for a cobalt thiocyanate solution pH 6.8 in differential pulse polarography scans.[20] The formation of a complex between cocaine and cobalt thiocyanate was studied by spiking the 1mM cobalt thiocyanate solution with different concentrations of cocaine and recording the SWV. A decrease in the cathodic peak current together with a negative shift of the peak potential at around -1V was observed when the concentration of cocaine increased from 0.5 mM to 2 mM, which confirms the formation of a stable complex (Figure 3A). The peak corresponds to the free metal ion during the titration with the ligand. As a control experiment the interaction between cobalt thiocyanate and phenacetine (true negative in color tests) was investigated in the same way. No significant shifts in the peak potential or peak current were observed in this case (Figure 3B), proving that phenacetine does not form a complex with cobalt thiocyanate. This provides a platform for investigating possible interfering agents in color tests (false positives) by means of electrochemistry.



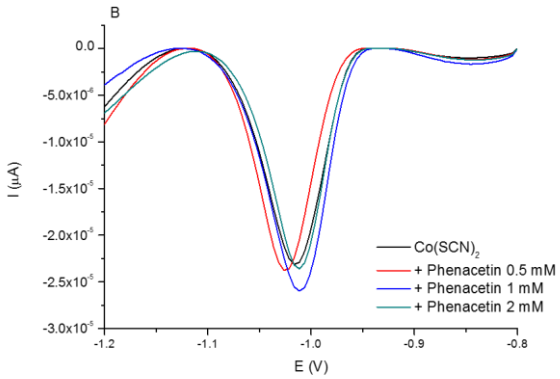


Figure 3. Square wave voltammograms of the titration of 1 mM cobalt thiocyanate solution in PBS pH 7 with 0.5, 1 and 2 mM cocaine (A) and phenacetine (B).

Taking into consideration the problems of false positives and false negatives caused in the color test, electrochemical methods were further developed and optimized as a screening alternative for cocaine in order to overcome the suppression effect of some cutting agents on the cocaine electrochemical signal, as was observed earlier by our group[12]. Firstly, measurements with a single SWV scan in PBS buffer pH 7 were performed for collecting information about the presence of cocaine and most cutting agents. In addition, by performing a SWV double scan and by adjusting the pH of the buffer to 12, we were able to detect cocaine in the presence of most cutting agents and exclude the false negative results.

Electrochemical response of cocaine and cutting agents at pH 7 by SWV single scan

In a first step, the influence of common cutting agents on the electrochemical signal of cocaine was studied at pH 7. For this purpose binary mixtures of cocaine and cutting agents were analyzed by SWV and compared with the SWV of the pure compounds (SWV for pure compounds in Figure S3 of the *supplementary material*). Cocaine gives rise to an oxidation peak at 1.04V in PBS pH 7 (see Figure 4 and Table S1 in *supplementary material*) due to the oxidation of the tertiary amine.[12]

As seen in Figure 4, phenacetine, paracetamol, lidocaine, ephedrine and caffeine show no significant influence on the oxidation signal of cocaine, allowing the simultaneous detection by means of one quick SWV scan at pH 7 and automated peak recognition (1.04V ± 10mV). The peak potentials of standards of common cutting agents at pH 7 are presented in Table S1 in *supplementary material*.

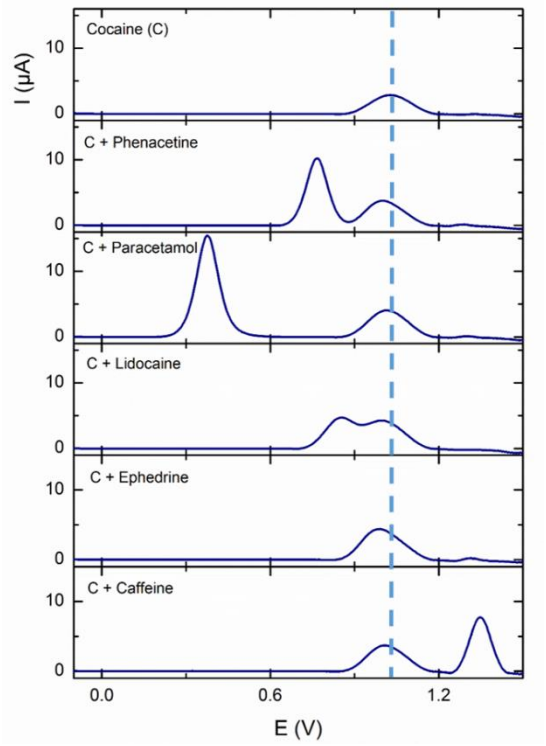


Figure 4. Forward SWV single scans of cocaine (C, 0.5 mM) and binary mixtures of cocaine (0.5mM) with common cutting agents (0.5mM) that have no significant influence on the cocaine electrochemical signal. Supporting electrolyte PBS pH 7. The dotted line represents the characteristic redox potential of cocaine at 1.04V± 10mV at pH 7.

However, the presence of other cutting agents interferes with the electrochemical detection of cocaine as seen in Figure 5. Quinine and codeine for example exhibit an oxidation peak around 1.04 V, overlapping the peak of cocaine at 1.04 V and thus leading to false positive results if cocaine wouldn't have been present. Other cutting agents suppress or shift the peak of cocaine, thus leading to false negative results: benzocaine, chlorpromazine, dextromethorphan, dextropropoxyphene, diltiazem, hydroxyzine, bupivacaine, levamisole, procaine and promethazine.

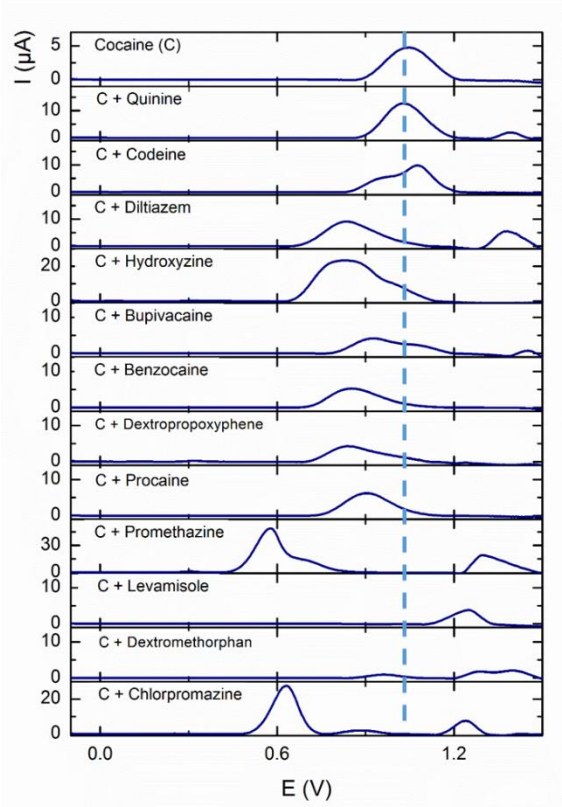


Figure 5. Forward SWV single scans of cocaine (C, 1 mM) and binary mixtures of cocaine (1 mM) and cutting agents (0.5 mM) that have an influence on the cocaine electrochemical signal. Supporting electrolyte PBS pH 7. The dotted rectangle represents the characteristic redox potential of cocaine at 1.04V± 10mV at pH 7.

To overcome the issues related to overlapping or suppressing signals we further investigated the effect of SWV double scan and pH 12 on the electrochemical response of binary mixtures.

Electrochemical response of cocaine and cutting agents at pH 7 by SWV double scan

A double SWV scan was performed for all cocaine-cutting agents solutions that led to suppression of the cocaine signal in single SWV. A conditioning potential of 1.5V was initially applied for 5 seconds, followed by a first scan sweeping the potential negatively from 1.5V to -0.1V. Afterwards, the usual forward SWV scan was performed. This step allows to reveal the oxidation peak of cocaine in binary mixtures with codeine, diltiazem, hydroxyzine, bupivacaine, benzocaine and dextropropoxyphene, solving the problem of false negatives that occurred in the previous section for these compounds. Applying this double scan approach allows an easier detection of cocaine in certain mixtures because of the lower signal intensity for irreversible compounds and, more importantly, the narrower signals they produce in this oxidation scan. This allows a better distinguishability between the cocaine signal and these other compounds. Using the double scan approach also allows to better identify certain cutting agents, since for some compounds, new products are formed during oxidation, resulting in extra peaks in the oxidation scan of the double scan SWV.[21-23] As seen in Figure 6, the peak of cocaine is slightly shifted in binary mixtures (dotted line), however, this does not pose a problem for automated cocaine detection. Quinine, however, still influences the signal of cocaine, due to overlapping signals. With regard to codeine, codeine shows a second oxidation peak at around the same potential as cocaine (1.05V). Although the intensity of the peak at 1.05V is increasing in the mixture with cocaine (and can thus be attributed to the presence of cocaine in the sample), in case of a fast screening it is difficult to discriminate whether the peak is due to the presence of cocaine or codeine. It is, however, important to notice that quinine and codeine are not common cutting agents in cocaine street samples, but are present mostly in heroin street samples. Therefore, finding these compounds in combination with cocaine is unlikely. Moreover, Quinine can be distinguished from cocaine and other compounds because of its very small grain size and bad solubility in basic conditions. Running a reverse scan before the forward SWV scan can contribute to an improved signal by reduction and/or desorption of any possible impurities present at the electrode surface and improvement of the electrocatalytic effect.[24] For procaine, promethazine, levamisole, dextromethorphan and chlorpromazine, there is no added value of a double scan, as the signal of cocaine is still suppressed.

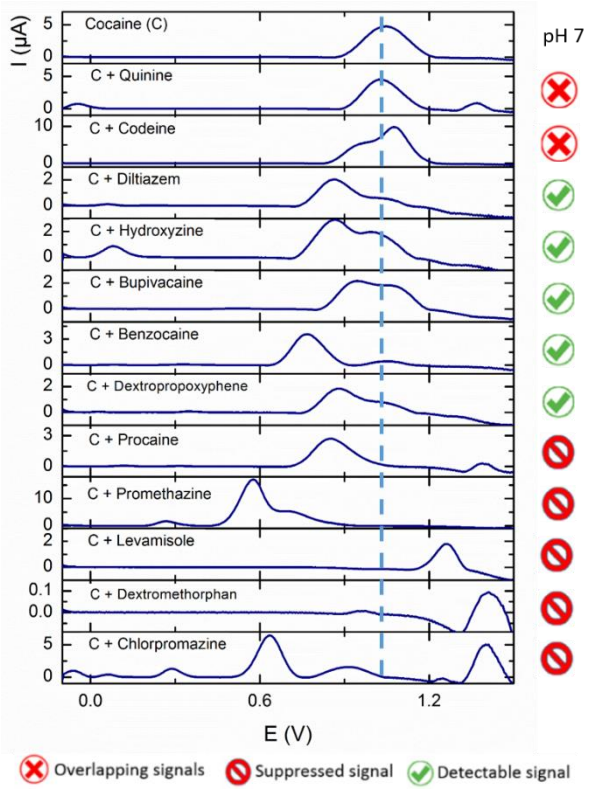


Figure 6. Double SWV scans of cocaine (1 mM) and binary mixtures of cocaine (1 mM) with cutting agents (0.5 mM) that have an influence on the cocaine electrochemical signal. Supporting electrolyte PBS pH7. The dotted rectangle represents the characteristic redox potential of pure cocaine at 1.04V ± 10mV at pH 7.

Electrochemical response of cocaine and cutting agents at pH 12

The pH of the electrolyte solution has an influence on the electrochemical behavior of certain compounds. When the pH increases from 7 to 12 the peak current of cocaine is increasing and the peak potential shifts to a less positive value (from 1.04V to 0.83V) (Table S1 of the *supplementary material*). Taking that into consideration, we studied the electrochemical behavior at pH 12 of the cutting agents that have an influence on the cocaine signal at pH 7, as pure compounds and in binary mixtures with cocaine (Figure 7). Altering the pH of the electrolyte allows to reveal the oxidation

peak of cocaine in binary mixtures with several cutting agents, after a single SWV scan: bupivacaine, dextropropoxyphene, promethazine, levamisole, dextromethorphan, chlorpromazine, while for diltiazem and procaine the signal of cocaine in the mixture is only detectable at pH 12 after performing a double SWV scan. A double scan at pH 12 was performed in an effort to reveal the characteristic peaks of cocaine and cutting agents for which a single scan did not perform well at pH 12. Quinine and codeine present overlapping signals with cocaine also at pH 12, in both single and double scans, however as previously mentioned, they are not common cutting agents in cocaine street samples as is sometimes reported incorrectly. Adjusting the pH to 12 did not show any improvement in the analysis of cocaine-hydroxyzine and cocaine-benzocaine mixtures. The hydroxyzine oxidation signal overlaps with the cocaine signal, while benzocaine suppresses it, both in a single and a double scan. However, the detection of cocaine in their presence is possible by performing a double scan at pH 7 as previously shown. The peak potentials of standard solutions of cocaine and of cutting agents at pH 12 are presented in Table S1 in *supplementary material*.

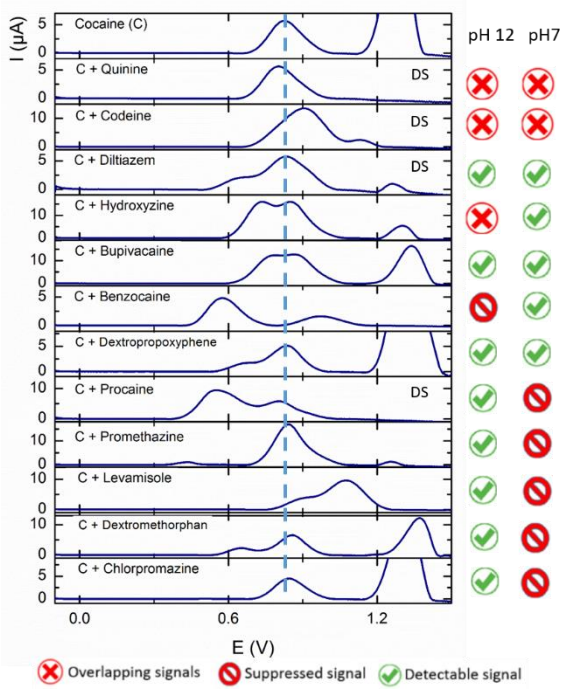


Figure 7. SWV scans of cocaine (1 mM) and binary mixtures of cocaine (1 mM) with cutting agents (0.5 mM) that have an influence on the cocaine electrochemical signal. DS: double scan. Supporting electrolyte PBS pH 12. The dotted rectangle represents the characteristic redox potential of pure cocaine at 0.83V ± 10mV at pH 12.

Thus, the problem of overlapping or suppressed cocaine signals because of the presence of cutting agents has been overcome by two electrochemical strategies: (1) By performing a double SWV scan at pH 7 or (2) by adjusting the pH of the supporting electrolyte to pH 12. The peaks of both cocaine and the cutting agents can be revealed using these strategies, allowing the reliable detection of cocaine in adulterated street samples.

Electrochemical methods versus color tests for the analysis of cocaine street samples

The final goal is to determine the presence of cocaine in authentic samples encountered on the street, in harbors or airports. Therefore, several confiscated street samples were tested with the developed electrochemical strategies and compared to the color test in order to determine the presence of cocaine and investigate any possible false negative samples. Firstly, authentic street samples were analyzed with the color tests in order to assess the specificity of the color test and identify false negatives and false positives. The complete color tests study is provided in *supplementary material,* Table S2 and Figure S2. Several samples were selected and further investigated by means of electrochemical methods (full electrochemical data is available in *supplementary material* Figure S4). For this purpose, more than 1 mg of street sample was dissolved in 1 mL PBS buffer pH 7 and pH 12, respectively and analyzed by SWV. As seen in Table 1, the color tests reveal the presence of cocaine in samples 1-8 and 16. Moreover, cocaine can also be easily detected in these samples by a fast SWV scan at either pH 7 or pH 12. In sample 5, due to the presence of levamisole which is suppressing the peak of cocaine at pH 7, cocaine can only be detected by running a double scan at pH 7 or by adjusting the pH to 12. In sample 6 the amount of levamisole is more than five folds less than the amount of cocaine whilst phenacetine and mannitol have no influence on the oxidation peak of cocaine. Thus, cocaine can be easily identified in this sample by a single SWV scan and/or by adjusting the pH to 12. Sample 7 contains levamisole and benzocaine, both of which have an influence on the oxidation signal of cocaine as shown in section 3.3. Thus, when SWV is performed at pH 7, only a small shoulder can be observed for cocaine, while the detection of cocaine at pH 12 is more straightforward. Cocaine in sample 8 could not be detected probably due to the low amount of cocaine 7% (m/m) compared to levamisole (around six times more), which is the reason of peak suppression at both pH 7 and pH 12. The positive color test in this case might be due to the presence of levamisole in high amount which was shown to give a false positive in color tests (Figure 1). Color tests give false negative results for samples 9-14 and it should be noted that four of these samples are colored (Table S2 in the *supplementary material*). The color test just assumes the color of the powder, again emphasizing one of the weaknesses of the color test. Most of these problems can, however, be easily resolved by analyzing the sample with SWV, proving the utility of the electrochemical method in overcoming the drawbacks of color tests. Sample 9 gives a false negative SWV result at pH 12 probably due to the higher amount of lidocaine present in the sample. Experiments on a mixture of lidocaine:cocaine 1:1 at pH 12 showed only one broad peak at 0.8V, instead of two separate peaks at 0.6V (lidocaine) and 0.8V (cocaine). Thus, the concentration of cocaine in the sample and the cocaine/cutting agent ratio may have an influence on the outcome of the electrochemical measurements. However, the proposed SWV strategy can be applied to most cocaine street samples as the average minimum purity between all EU countries for confiscated cocaine samples was 14% in 2015.[16]

The remaining negative samples, which could visually be mistaken for cocaine, 17-22 did not present a problem for both the color test and the electrochemical approach. Sample 15 tested false positive for both the color test and electrochemical tests, but since heroin is another major illegal drug, the overlap of its signal with the cocaine signal does not present a major problem.

Table 1. Color tests versus SWV results obtained for the analyses of cocaine street samples.

No	Sample composition		Color test	SWV	
	Compounds	wt%		pH 7	pH 12
1	Cocaine	98	P	P	P
2	Cocaine block	100	P	P	P

3	Cocaine Caffeine Hydroxyzine Lidocaine	76 3 10 <1	P	P	P
4	Cocaine Phenacetine	73 17	P	P	P
5	Cocaine Levamisole	70 23	P	P, DS	P
6	Cocaine Levamisole Phenacetine Manitol	31 6 3 *	P	P, SS	P
7	Cocaine Phenacetine Caffeine Lidocaine Levamisole Benzocaine	22 8 16 12 2 *	P	P, DS	P
8	Cocaine Phenacetine Caffeine Lidocaine Levamisole	7 11 23 3 41	P	FN	FN
9	Cocaine Levamisole Lidocaine Caffeine	22 9 * <1	FN	P	P
10	Cocaine Paracetamol Levamisole	19 73 2	FN	P	P
11	Cocaine Boric acid	30 *	FN	P	P
12	Cocaine in fishmeal	17	FN	P	P
13	Cocaine in Sirup bottle	*	FN	P	FN
14	Cocaine Levamisole	26 9	FN	P	P
15	Heroin Caffeine 6-mam Papaverine Noscapine	58 13 8 <1 2	FP	FP	FP
16	Cocaine Amphetamine sulphate Caffeine Phenacetine Lidocaine	10 42 2 11 2	P	P, SS	P
17	Glucose Chlortetracycline	* *	N	N	N
18	Wash powder	*	N	N	N
19	Boric Acid	*	N	N	N
20	Phenacetine Lidocaine	37 7	N	N, DS	N
21	Flour	*	N	N	N
22	Phenacetine	100	N	N	N

DS, double scan; SS, single scan; N, true negative; P, true positive; FN, false negative; FP, false positive *, compound was identified, but not quantified.

The fingerprint of the cutting agents can also be revealed in the analyzed samples. Figure 8 presents the exemplary results obtained for sample 6 and 12. The square wave voltammograms of sample 6 (Figure 8A) clearly show that cocaine (peak 1) can be detected in adulterated street samples at both pH 7 and pH 12, with higher peak intensity at pH 12. The electrochemical oxidation signal of the cutting agents phenacetine (peak 2) and levamisole (peak 3) can also be detected. Figure 8B proves that cocaine can be detected by means of SWV at pH 7 and pH 12 even in more complex matrices were color test fail, such as fishmeal samples. The peaks at around 1.45V are due to the electrode material.

As a validation method, the sensitivity and specificity of the color test and the electrochemical method were determined for these street samples. The samples giving a debatable color test result (Table S2 and Figure S2 of the *supplementary material*) were considered positive. The sensitivity of the color test was found to be 0.68, while the specificity was found to be 0.75. For the 22 samples tested with the electrochemical approach, the sensitivity of the electrochemical test was found to be 0.93 and the specificity 0.86. The electrochemical approach scores significantly better for sensitivity and even the specificity is already improved, despite the fact that almost none of the measured negative street samples contain false positive compounds for the color test that were identified earlier, in absence of cocaine.

In conclusion, the proposed electrochemical approaches can provide a useful on-site screening tool for cocaine samples adulterated with various compounds, even in complex matrices such as syrup or fishmeal.

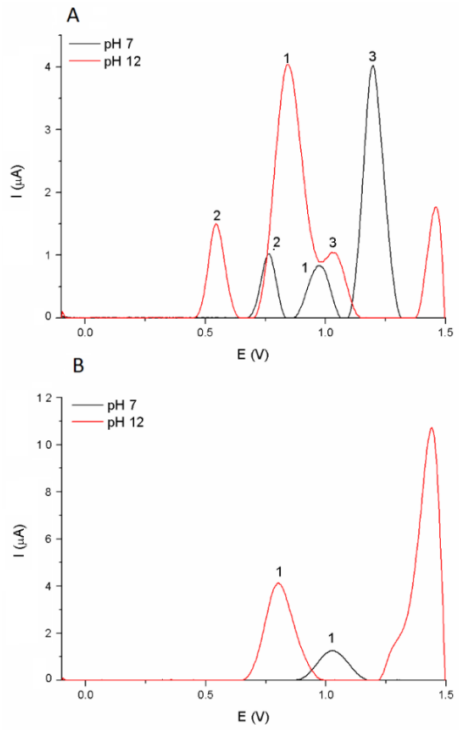


Figure 8. SWV response at pH 7 and pH 12 of seized street samples revealing the peak of cocaine (peak 1) in the presence of (A) phenacetine (peak 2) and levamisole (peak 3) in sample 6 and (B) fishmeal in sample 12.

Conclusion

The presence of cutting agents in cocaine samples can seriously affect the specificity of Scott's color tests. Taking into consideration all the false positives and false negatives that were given by the color test, we proposed an electrochemical screening approach by SWV at pH 7 using disposable GSPE. Although cocaine has a well-defined oxidation peak at GSPE at pH 7, the presence of several compounds in the sample may overlap or suppress the peak of cocaine interfering in the analysis e.g. benzocaine, chlorpromazine, dextromethorphan, dextropropoxyphene, diltiazem, hydroxyzine, bupivacaine, levamisole, procaine, promethazine. We addressed this problem by employing a double SWV scan (by running a reverse scan before the forward scan) and by a dual pH strategy by adjusting the pH of the detection buffer to pH 12. These strategies

allow to detect cocaine in the presence of most cutting agents and were applied successfully in street samples containing low amounts of cocaine (19-22%), however were not effective for samples containing only 7% of cocaine in presence of high amount of levamisole.

In order to expand their practical application the established electrochemical strategies were further applied to seized cocaine samples, resolving most of the false negatives given by color tests. Moreover, the usefulness of electrochemical techniques in predicting possible interfering agents in color tests has been successfully demonstrated. With the major advantages of superior specificity, speed, simplicity and low cost, the developed strategies offer a promising alternative for on-site screening of seized cocaine samples, since the instrumentation can also be easily miniaturized and mobilized.

ASSOCIATED CONTENT

Supporting Information. Chemical structures of cocaine and cutting agents; Peak potentials of cocaine and cutting agents at pH 7 versus pH 12; Street samples analyzed by color tests. This material is available free of charge via the Internet at http://pubs.acs.org.

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