ADULTERANTS FOUND IN MIXTURES OF ILLEGAL PSYCHOACTIVE DRUGS

Orlando Neves
Aluno de Graduação da Licenciatura em Análises Clínicas e Saúde Pública
Escola Superior de Saúde - UFP
orlando.neves@apdes.net

Bruno Nunes
Professor Auxiliar
Faculdade de Ciências da Saúde - UFP
bruno@ufp.pt

RESUMO

Os danos biológicos causados pelo uso de substâncias psicoactivas ilegais podem resultar não só das substâncias ilegais por si só, mas também da presença de substâncias que os traficantes lhes adicionam no sentido de aumentar o volume final de droga (substâncias de corte). O objectivo central do presente estudo consistiu na análise de substâncias psicoactivas ilegais e dos seus contaminantes/adulterantes, pela conjugação de esforços entre CHECK-IN/APDES e o Instituto Nacional de Medicina Legal do Porto. Esta colaboração permitiu comparar dados portugueses com os dados gerados pelo projecto Energy Control em Espanha, que se tem dedicado desde há mais de 10 anos à redução de riscos.

PALAVRAS-CHAVE: Análise química; cromatografia em camada fina; substâncias psicoativas; redução de danos; speed; cristal; cocaína.

ABSTRACT

The biological damages caused by the use of illicit psychoactive substances can result not only from the illegal substances themselves, but can also be due to substances that dealers had to the mixtures in order to increase the overall volume of drug (*cutting substances*). The central aim of the present study was analysing illegal psychoactive substances and their contaminants/adulterants, through the conjugation of efforts by CHECK-IN/APDES and Instituto Nacional de Medicina Legal do Porto. This cooperation allowed the comparison of Portuguese data with the data that were collected in Spain by Energy Control, a project that has been working in risk reduction for the past 10 years.

KEY-WORDS: Chemical analysis; thin layer chromatography; psychoactive substances; damage reduction; *speed*; crystal; cocaine.

1. INTRODUCTION

Since a decade ago, we witnessed an exponential growth of the use of recreational and illegal psychoactive substances. This increase has special significance among youngters, in which it was possible to systematically observe an increase in the consumption of drugs such as *speed*, crystal, ecstasy and cocaine. The increase in the use of these drugs lead to an exacerbated demand in the illegal market, which was an excellent opportunity of profit for dealers and smugglers. Additionally, dealers found a way to increase even more their profit margins, by adding other substances (adulterants) to the intoxicating mixtures, through the denominated *cutting* of the initial illicit substance. Bearing this purpose in mind, several adulterants have been found, such as pharmaceuticals, salts, sugars, solvents, portions of dry fruits, ashes, glass, silica and plastics.

The scientific core of the present study is the possibility of giving accurate scientific information to consumers of illegal substances regarding the use of adulterants incorporated into the intoxicating mixtures. With this information, consumers may them decide about the consumption of substances that can pose more serious risks to their health than the intoxicating substance that they intend to use. This approach is inserted in a policy of damage reduction, which was recently implemented in Portugal. According to this philosophy, the most effective process is to inform the usual consumer of illicit drugs with the objective of giving information about the risks inherent to his/her behaviour and to the possible toxicity of adulterants added to the intoxicating mixture. After a positive identification of adulterants in the intoxicating mixtures, the consumer is informed of their toxic effects, and is free to choose if he/she intends to use the recreational substances.

The results published in the present study result from the free cooperation of consumers of illegal substances that came to the offices of *Check-in* Project (Portugal; responsibility of Agência Piaget para o Desenvolvimento, APDES) or *Energy Control* Project (Spain) to analyse the mixtures that they intended to consume. In general terms, the procedures adopted by the Project Energy Control involved an immediate analysis of the samples, while the Portuguese Check-in Project only performed a simple colorimetric assay, with Marquis reagent, which indicated the presence of several substances. After this initial screening procedure, samples were analysed by thin layer chromatography (TLC).

The present study involved a sequence of steps, in which the first was the use of the generally described methodology and processing of samples, in order to assess the presence or absence of contaminants. The second step was a generic discussion of the obtained results, for a comparison between the here generated data and those already available for samples collected in the Iberian Peninsula, for the critical evaluation of the potential for the exertion of toxic effects by adulterants. Finally, the third step was dedicated to the analysis of the differences between the two realities, concerning the Portuguese and the Spanish scenarios of adulteration of recreational drugs.

2. MATERIAL AND METHODS

2.1. SAMPLING

Users of recreational drugs voluntarily gave us access to samples of substances, for analysis. Offices of the *Check-in* Project were installed in youth and summer festivals and *rave* parties, during 2006 and 2007, and the users of these substances were invited to perform a simple and free test to the drugs that they possessed.

2.2. *IN LOCO* IDENTIFICATION OF DRUGS

One of the main purposes of Check-In Project is the possibility of giving results concerning the adulterants present in samples of illegal substances to consumers, in a real time scenario. This approach involved the analysis of the obtained samples with the colorimetric test, in which reagent of Marquis was added. In a few seconds, samples containing MDMA and amphetaminic derivatives were coloured. The coloured spots after adding Marquis reagent can identify MDMA or MDA (purple to black), amphetamine or methamphetamine (orange to brown), 4-bromo-2,5-dimethoxyphenethylamine (2C-B; orange to green), and dextromethorphan (DXM; gray to black). For the identification of indolamines (LSD, fungal derivatives, *foxy*, 4-ac-diptidolamins and others) and several phenilethylamines (2CT2, 2CB, 2CI, DOB, DOM and others), we added to each spot a drop of pimethylaminobenzaldehyde 5% (p-DMAB) reagent. If observed under ultraviolet light, the different substances assumed different colours. For instance, psilocybin turned reddish-purple then faded to violet, whereas psilocin yielded a strong blue color, which faded to violet. In the case of LSD, the addition of this reagent caused a deep purple coloration (National Institute of Justice, 2000).

2.3. CHROMATOGRAPHIC ASSAYS

For the detection/identification of drugs in the samples, we followed a protocol of preliminary preparation. The preparation of samples involved the use of different amounts of sample, depending on the substance to be tested. If we expected to analyse samples containing residues of cocaine, we used approximately 1.0 g of sample; if other substances were expected to be found, we sampled an amount of 4.0 g. To these amounts of samples, a small portion of methanol was added, and this mixture was stirred until total dissolution. The methodology used for the determination of the presence of adulterants was TLC – thin layer chromatoraphy. This technique is used to separate pure components in a mixture. The separation of the compounds is due to the difference of adhesion forces between the molecules of the components to a mobile phase (usually a solvent, or a mixture of solvents - elluent) and to a stationary phase (the thin layer, frequently made of silica). This difference can be shown through a higher or lower proportion of drag of each individual component along the stationery phase, allowing its separation and identification. The use of this methodology during the present work involved the preparation of cuvettes for the TLC, in which strips of absorbent paper were introduced in spectrophotometry cuvettes with distinct sizes. The solvent (elluent) employed for the separation was composed by a mixture of methanol and ammonia, in a final proportion of 29.25ml:0.75ml. Elluition of samples was allowed for 30 minutes, in a closed environment saturated with vapours of the elluent mixture. The preparation of the silica layer was performed in order to obtain a chromatofoil, with a defined number of samples and standard solutions. Standard solutions were transferred to the silica layer, through pippeting a volume of 3 µl of each standard solution. After adding each standard solution to the silica layer, the solvent was evaporated and the chromatofoil was observed in a revelation chamber with ultraviolet light, in order to assure that the applied amount of sample/standard solutions was adequate. If the transferred amounts were adequate, one can observe dark spots in the site of application; if the amount was insufficient, we should increase the amount by 1 µl, until reaching a satisfactory amount. After elluition, the solvent was evaporated and dried. Revelation and visualization of the chromatofoil was done by inserting it into a revelation chamber with iodine crystals, and the comparison of the spots resulting from samples with those resulting from standard solutions.

3. **RESULTS**

The work developed by the *Check-In* Project from APDES allowed analysing, *in situ*, a total of 15 samples, from which 10 were pills, and 5 were allegedly cocaine samples. From these two types of samples, it was possible to identify a total number of 9 different substances (including MDMA; figure 1) used to formulate pills, and cocaine samples were composed by 6 distinct products, including cocaine (figure 2).

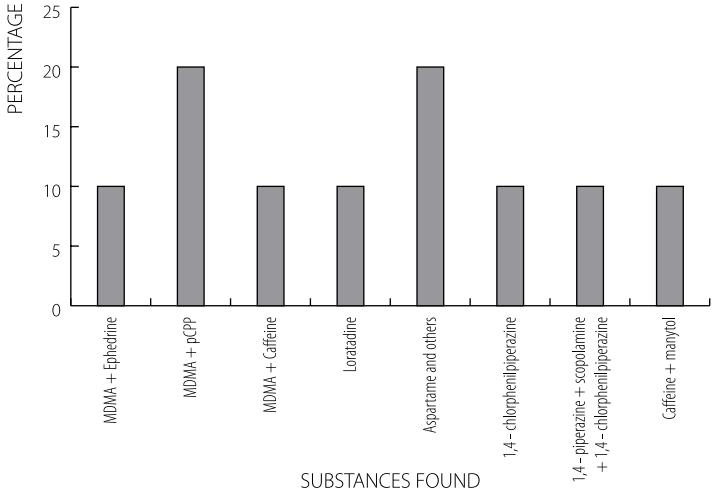

Figure 1. Results obtained after analysis of pills (n=10)

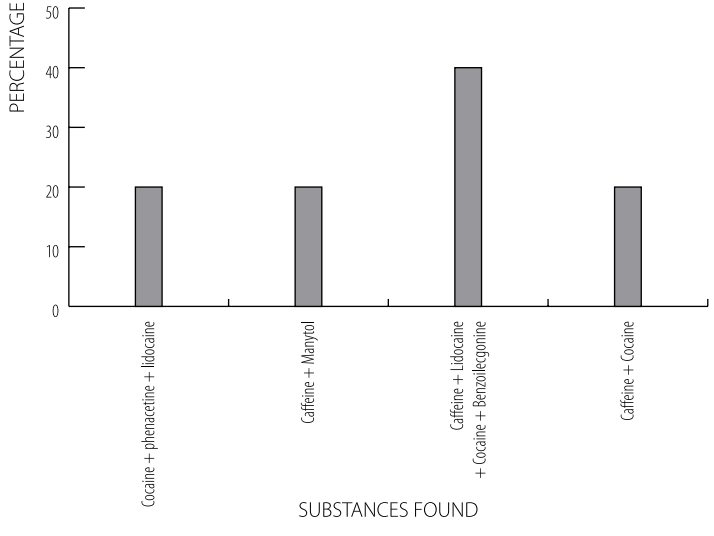

Figure 2. Results obtained after analysis of cocaine (n=5)

Results obtained during the *Energy Control* Project are depicted in figures 3, 4, 5 and 6, and illustrate the adulteration of speed, cocaine, crystal and pills samples, respectively, in Spain, also during 2006 and 2007.

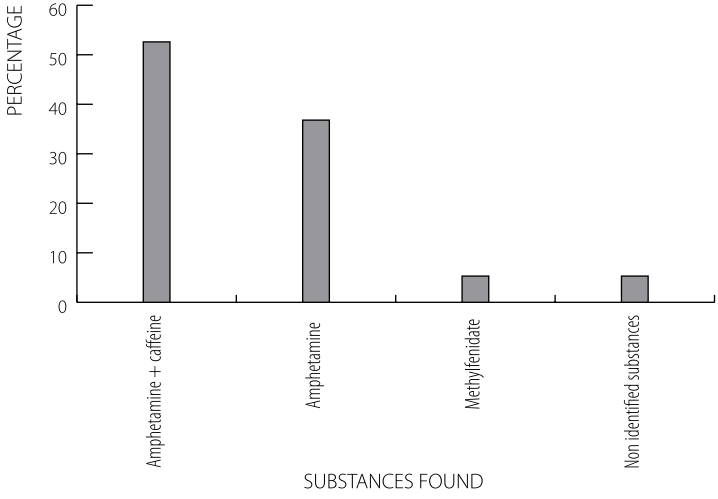

Figure 3. Results obtained after the analysis of *speed* samples in Spain, by *Project Energy Control* during 2006 and 2007 (n=19).

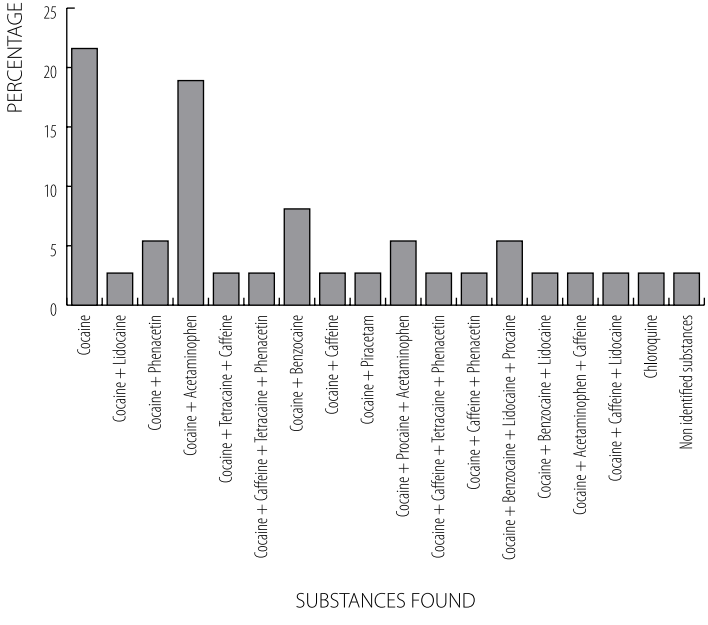

Figure 4. Results obtained after the analysis of cocaine samples in Spain, by *Project Energy Control* during 2006 and 2007 (n=36).

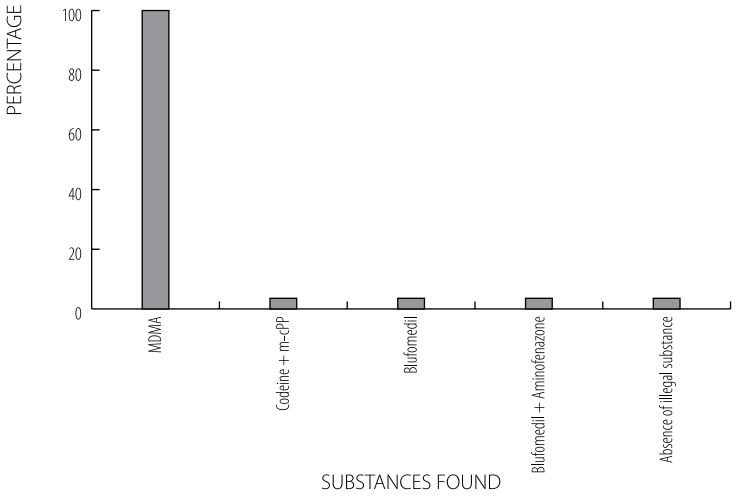

Figure 5. Results obtained after the analysis of *crystal* samples in Spain, by *Project Energy Control* during 2006 and 2007 (n=32).

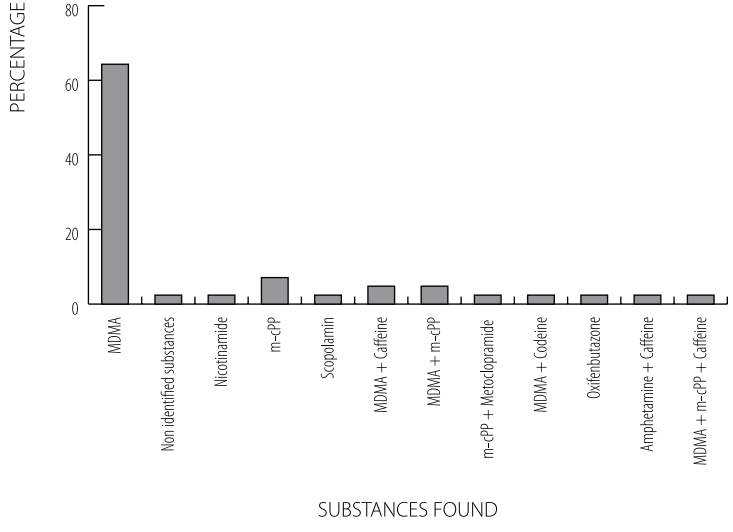

Figure 6. Results obtained after the analysis of pills samples in Spain, by *Project Energy Control* during 2006 and 2007 (n=42).

4. **DISCUSSION**

4.1. **CRYSTAL AND SPEED**

The size of the global sampled substances in Spain, during the period of 2006 and 2007, was much larger than the samples analysed in Portugal, during the same period; consequently, all comparisons may be biased and may not reflect a complete assessment of the Portuguese scenario. However, and after the observation of the compiled data from the Iberian Peninsula during 2006 and 2007, the general conclusion pointed to a marked similarity between the adulterants found in both countries (Portugal and Spain). However, caffeine is the most common adulterant found in *crystal* and *speed* samples. Caffeine is a central nervous system stimulant, depending on its ability to reduce adenosine transmission in the brain (Fisone et al, 2004). Other studies point to the involvement of different pathways that may be triggered by caffeine, as a central nervous stimulant. Murphy et al. (2004) observed that systemically administered caffeine was capable of activating orexin neurons (which play a critical role in arousal) over non-orexin neurons. The same study showed that this compound might also be responsible by increased locomotion activity after acute exposure. Furthermore, caffeine can have a pronounced effect on metabolism, as shown by Haller et al (2004): its us was responsible for increased systolic blood pressure and plasma free fatty acid and urinary epinephrine concentrations. In spite of causing these biological modifications, caffeine may be used as an adulterant of illegal mixtures since users misinterpret its energizing properties, believing that these effects are the desired consequences of the use of the illegal psychoactive substances. An average of 53% of all samples of *speed* and *crystal* contained caffeine as adulterant; according to the sensitivity of the consumer, and to the concentration of caffeine present in the intoxicating mixture, we can anticipate that users may suffer potential health risks. The study by Haller et al. (2004) showed that an association of caffeine and another stimulant (such as ephedrine) can result in severe physiological modifications, such as increased systolic blood pressure and heart rate, and raised fasting glucose, insulin, free fatty acid, and lactate concentrations. These modifications, along with the impairment of specific neuronal functions, may present an additional risk to consumers of illegal drugs contaminated with adulterants such as the one here found.

4.2. **COCAINE**

The adulteration of cocaine samples is a common issue among the illegal drug markets around the globe. King (1999) showed that the mean degree of purity of cocaine samples in the United Kingdom reached only 51%. Spanish cocaine samples were usually adulterated with caffeine, in a percentage of about 69%; in Portugal, this percentage was generally much higher, reaching 75%. These data lead us to the conclusion that caffeine is again a major adulterant of cocaine samples, and was present in the majority of analysed samples. 16% of all cocaine samples in Spain were adulterated with another compound, lidocaine, which was also observed in Portugal. Again the level of adulteration of cocaine in Portugal was much higher, since 75% of cocaine samples contained lidocaine. This pattern of adulteration is not exclusive of the Portuguese reality; in fact, Brazilian cocaine samples, tested for the presence of adulterants, showed similar results, since adulteration of cocaine with caffeine and lidocaine was also common (Bernardo et al, 2003). Fucci and De Giovanni (1998) screened samples of cocaine sold in the illegal market of the streets of Rome (Italy), and also concluded that caffeine and lidocaine were common adulterants. Lidocaine is a local anaesthetic that has been held responsible for cardiotoxic and neurotoxic adverse events, as described by Marra et al (2006) and by Takahashi et al (2006). The direct contact of lidocaine with the eye can also result in lidocaine toxicity, as shown by Doat et al (2006). The oral intake of lidocaine-containing paediatric preparations was the causative agent for a toxic syndrome described by Yamashita et al (2002). Our samples of cocaine were also adulterated with a third substance,

the analgesic/antipyretic paracetamol (acetaminophen). This is a well-known toxic compound, which in high doses (well above the therapeutic dosage) is frequently fatal (Davies, 2007). This pharmaceutical compound is the commonest cause of fulminant hepatic failure in most western countries (McGregor et al, 2003); its use, as and adulterant of cocaine, may result in fatal intoxication, since cocaine is frequently used in high amounts during the events in which sampling took place.

4.3. **PILLS**

The number of adulterants found in pills is extremely high. Among the most common adulterants, one can find piperazine, which is a pharmaceutical drug used as antiparasitic (Boonmars et al, 2005). This drug has also been used by consumers of illegal substances (namely MDMA) since they mimic the effect of MDMA in the brain (Sheridan et al, 2007; Staack, 2007; Baumann et al, 2005). However, several derivatives of this substance may also exert stimulant or psychedelic effect, since they can act directly on the central nervous system (Matsumoto et al, 2007; Sadashiva et al, 2006). This chemical is highly toxic for the liver and kidneys, and its use may result in severe failure of these organs, and consequent death. Several other compounds were added to the tested samples, such as the anti-inflammatory drug oxifenbutazon, nicotinamide (vitamin B3), and codeine. Codeine is an opioid, and is added to cough syrups; its use is not limited to therapeutics, since drugs addicted individuals use it simultaneously with cocaine and crack for abuse/recreational purposes (Peters et al, 2007). Several samples were contaminated by scopolamine, an hallucinogenic substance, found in plants of the *Solanaceae* family, which interferes with cholinergic function in the central nervous system, resulting in impaired behavioral performance, and, in the hippocampus, disrupted conditioned stimulus-evoked field potential, high frequency shift in field activity, and paired presentation-induced hyperexcitability (Múnera et al, 2000). Scopolamine is also an antispasmodic, used in peptic, duodenal and colic ulcers, and also in motion sickness (Nachum et al, 2006). In spite of its therapeutic use, this is a highly toxic compound, which must be used in small amounts, since it may cause delirium, paralysis, coma or even death. Its long-term use can lead to serious metabolic disturbances, as shown by Piva et al (2007); this study assessed the effects of prolonged exposure of pigs to scopolamine, and the authors observed gastro-intestinal alterations, where the mucous membrane showed lymphocytic infiltration and a loss of epithelium; villi were necrotic and replaced by dystrophic regeneration. Several samples were tested and revealed that another adulterant was ephedrine, which is a simpaticomimetic stimulant substance (Haller et al, 2004). This compound has been used in several pharmaceutical preparations to fight overweight, but has been identified as a causative agent for strong dependence (Arnold and Yager, 2007; Miller and Waite, 2003). Loratadine was also found in the tested samples, and this is an anti-histaminic drug that acts through the blockade of H1 (histamine) receptors. The sweetener aspartame was found among the identified adulterants, and may be used in order to give the convenient consistency to the manufactured pills. Several other chemicals were found, but it was not possible to perform a positive identification. However, we have indications that, similarly to what was found in other samples (results not shown), these adulterants may be other psycho-active compounds, dry and powdered fruits, silica, salts, sugars and other organic compounds.

5. **CONCLUSIONS**

The nature of the adulteration can be partial, when a single substance or a mixture of substances was added to the formulation, but one can still detect the presence of the initial illegal substance; however, it can also be total, when not event the desired substance can be found in the mixture, and the formulation is only composed by adulterants. After the attainment of the proposed objectives, we can assume that 100% of all Portuguese samples tested were adulterated, a scenario that was not observed in Spain.

In fact, the percentage of tested Spanish samples that was found adulterated was much lower, and a percentage comprised between 42 to 58% of samples from this country may be considered pure. These facts lead us to the conclusion that, in spite of the extremely small number of tested samples, the use of recreational drugs is far less subjected to adulteration in Spain. This consideration may be partly explained due to the existence, in Spain, of a risk reduction policy for more than 15 years, through the contribution of projects such as *Energy Control*. The recent adoption of similar measures in Portugal, that took place only five years ago, can also be a valuable contribution for a much-needed change concerning this issue. One of the most important factors to consider in the near future is the broadening and enlargement of the sampling universe, in order to allow the identification of more contaminants, and also to permit a larger number of samples being analysed. These two complimentary trends will certainly contribute for a more comprehensive and coherent service to consumers of these types of substances, always bearing in mind the inherent philosophy or risk reduction.

REFERENCES

ARNOLD KK, Yager J (2007). A case of unexpected and selective remission of a 20-year history of ephedrine dependence following treatment with low-dose aripiprazole. *Journal of Clinical Psychiatry*. 68 (10):1620-1.

BAUMANN MH, Clark RD, Budzynski AG, Partilla JS, Blough BE, Rothman RB (2005). N-substituted piperazines abused by humans mimic the molecular mechanism of 3,4-methylenedioxymethamphetamine (MDMA, or 'Ecstasy'). *Neuropsychopharmacology*. 30(3): 550-60

BERNARDO NP, Siqueira MEPB, de Paiva MJN, Maia PP (2003). Caffeine and other adulterants in seizures of street cocaine in Brazil. *The International Journal of Drug Policy* 14 (4): 331-334.

BOONMARS T, Khunkitti W, Sithithaworn P, Fujimaki Y (2005). In vitro antiparasitic activity of extracts of Cardiospermum halicacabum against third-stage larvae of *Strongyloides stercoralis*.
Parasitololgy Research 97(5): 417-9.

DAVIES DS (2007). Paracetamol toxicity: A 40 year odyssey. Toxicology 240 (3): 149-150.

DOAT M, Pierre-Kahn V, Bejjani RA, Bourges JL, Renard G, Chauvaud D (2006). Inadvertent intravitreal lidocaine injection following subcutaneous palpebral anesthesia: retinal toxicity of lidocaine? *Journal of French Ophthalmology* **29**(2):176-80.

FUCCI N, De Giovanni N (1998). Adulterants encountered in the illicit cocaine market. *Forensic Science International* **95**(3): 247-52.

FISONE G, Borgkvist A, Usiello A (2004). Caffeine as a psychomotor stimulant: mechanism of action. *Cell and Molecular Life Sciences* **61**(7-8): 857-72.

HALLER CA, Jacob P 3rd, Benowitz NL (2004). Enhanced stimulant and metabolic effects of combined ephedrine and caffeine. *Clinical Pharmacology and Therapeutics* 75(4): 259-73.

KING LA (1999). Drug content of powders and other illicit preparations in the UK. *Forensic Science International* 85 (2): 135-147.

MCGREGOR AH, More LJ, Simpson KJ, Harrison DJ (2003). Liver death and regeneration in paracetamol toxicity. *Human Experimental Toxicology* 22(4):221-7.

MARRA DE, Yip D, Fincher EF, Moy RL (2006). Systemic toxicity from topically applied lidocaine in conjunction with fractional photothermolysis. *Archives of Dermatology* 142(8):1024-6.

MATSUMOTO RR, Pouw B, Mack AL, Daniels A, Coop A (2007). Effects of UMB24 and (+/-)-SM 21, putative sigma2-preferring antagonists, on behavioral toxic and stimulant effects of cocaine in mice. Pharmacology, Biochemistry and Behaviour 86(1): 86-91.

MILLER SC, Waite C (2003). Ephedrine-type alkaloid-containing dietary supplements and substance dependence. *Psychosomatics* 44(6): 508-11.

MURPHY JA, Deurveilher S, Semba K (2003). Stimulant doses of caffeine induce c-FOS activation in orexin/hypocretin-containing neurons in rat. *Neuroscience 121*(2): 269-275.

NACHUM Z, Shupak A, Gordon CR (2006). Transdermal scopolamine for prevention of motion sickness: clinical pharmacokinetics and therapeutic applications. *Clinical Pharmacokinetics* 45(6): 543-66.

National Institute of Justice, Color Test Reagents/Kits for Preliminary Identification of Drugs of Abuse NIJ Standard–0604.01. (2000) *Law Enforcement and Corrections Standards and Testing Program.* U.S. Department of Justice, Office of Justice Programs.

PETERS RJ Jr, Williams M, Ross MW, Atkinson J, Yacoubian GS Jr (2007). Codeine cough syrup use among African-American crack cocaine users. *Journal of Psychoactive Drugs*. 39(1):97-102.

PIVA G, Morlacchini M, Pietri A, Fusaric A, Corradi A, Piva A (1997). Toxicity of dietary scopolamine and hyoscyamine in pigs. *Livestock Production Science* 51 (1): 29-39.

SADASHIVA CT, Narendra Sharath Chandra JN, Ponnappa KC, Veerabasappa Gowda T, Rangappa KS (2006). Synthesis and efficacy of 1-[bis(4-fluorophenyl)-methyl]piperazine derivatives for acetylcholinesterase inhibition, as a stimulant of central cholinergic neurotransmission in Alzheimer's disease. Bioorganic & Medicinal Chemistry Letters 16(15): 3932-6.

SHERIDAN J, Butler R, Wilkins C, Russell B (2007). Legal piperazine-containing party pills--a new trend in substance misuse. *Drug Alcohol Rev* 26(3): 335-43

STAACK RF (2007). Piperazine designer drugs of abuse. *Lancet* 369(9571): 1411-3

TAKAHASHI R, Oda Y, Tanaka K, Morishima HO, Inoue K, Asada A (2006). Epinephrine increases the extracellular lidocaine concentration in the brain: a possible mechanism for increased central nervous system toxicity. *Anesthesiology* 105(5): 984-9.

YAMASHITA S, Sato S, Kakiuchi Y, Miyabe M, Yamaguchi H (2002). Lidocaine Toxicity During Frequent Viscous Lidocaine Use for Painful Tongue Ulcer. *Journal of Pain and Symptom Management* 24 (5): 543-545.