

### Illicit drugs, legal highs and over-consumption of psychoactive medicines: the many faces of a public health problem

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Drogas ilícitas, drogas legales y el consumo excesivo de medicamentos psicoactivos: las múltiples caras de un problema de salud pública

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Dear Editors,

In a previous issue of CSP, Honório et al. <sup>1</sup> addressed the instigating question of “legal highs”, or psychoactive drugs that are not prohibited by Brazil’s laws. Although many traditionally used substances such as alcohol, solvents (*e.g.*, glue, toluene and gasoline sniffing), indigenous plants, nicotine (in tobacco) and others could fit into this category, the term “legal highs” is generally used to refer to an entirely new class of products (also known as “designer drugs” and “herbal highs”) that have recently emerged in the recreational drug market. These “new players in the old drama”, as Zawilska <sup>2</sup> called them, are plant-derived and synthetic drugs including amphetamine- and ecstasy-like psychostimulants, hallucinogens, phencyclidine analogs and synthetic cannabinoids (“spice”).

Banned drugs and those put under strict control are described by their chemical names and thus restrictive legal provisions can be bypassed by structural modifications that alter the chemical identity but do not change the targeted psychopharmacological effects. Since they are not listed in national regulations (in Brazil, *SVS/MS Directive 344/98* and its annexes), “legal highs” are unregulated and can be freely sold, possessed and used.

The emergence of “designer drugs” as a public health problem was boosted by the internet revolution and, as highlighted by Carrol et al. <sup>3</sup>, by modern advancements in medicinal chemistry. In their excellent overview, Carrol et al. <sup>3</sup> described how clandestine chemists took advantage of the abundant literature on the pharmacological properties and synthesis of psychoactive agents (psychostimulants, narcotics, hallucinogens, anxiolytics, hypnotics, cannabinoids,

and other drugs) to produce analogs that circumvent the law. Inevitably, regulation lists are at least one-step behind the changes in the dynamic market for legal highs. Honório et al.’s <sup>1</sup> suggestion of “banning or controlling entire classes of substances”, however, would negatively affect the development of new therapeutic drugs and thus would be more of a problem than a solution.

While listing a drug among banned substances paves the way for repressive actions, it does not eliminate the problem. The same compound and similar psychoactive substances can be bought on the clandestine market of recreational drugs. Methamphetamine (“crystal meth”) and methylene-dioxy-methamphetamine (MDMA or “ecstasy”) are examples along this line. Methylone, a drug banned by the Brazilian National Health Surveillance Agency (ANVISA) in February 2014, is an analog of MDMA, the psychostimulant effects of which are very similar to those of its prototype.

It is of note that recreational drugs were also synthesized and produced by pharmaceutical companies. Methamphetamine was first synthesized (from ephedrine) in Japan in 1893 and was widely used by armies on both sides during World War II. In the 1950s, methamphetamine was marketed by pharmaceutical companies as an appetite suppressant and nasal decongestant. MDMA was first synthesized by Merck Darmstadt in 1912 and its pharmacological effects were investigated by the German company in 1927 and in the 1950s (it was used as a precursor in the synthesis of other drugs) <sup>4</sup>. Another example is the piperidine derivative desoxypropylololol (2DPMP), a norepinephrine and dopamine reuptake inhibitor, that was synthesized by CIBA (now Novartis) in the 1950s <sup>5</sup> and researched as a drug for attention deficit hyperactivity disorder (its development was abandoned because the company found that methylphenidate was a better drug for ADHD).

The health risks posed by “legal highs” were emphasized by Honório et al. <sup>1</sup> who cited some case reports. Most of the reported toxic effects are consistent with those exhibited by the illicit prototype compounds. Cardiovascular injury and heart arrhythmias, and an elevated risk of sudden deaths are expected from amphetamine and MDMA-related compounds. Methamphetamine and amphetamine-like drugs are a leading cause of admissions to psychiatric units, and hallucinogenic agents have been implicated in the onset of schizophrenia in susceptible individuals. Developmental risks for the unborn baby cannot be ignored as well.

In addition to health risks posed by the psychoactive substances themselves, unexpected toxic effects may also arise from uncharacterized contaminants. The licit and illicit recreational drugs produced by clandestine laboratories operating under poor manufacturing practices often contain highly toxic contaminants. A dramatic example along this line is MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), a potent neurotoxin generated accidentally during a clandestine production of MPPP (1-Methyl-4-phenyl-4-propionoxypiperidine), a synthetic opioid with morphine (and pethidine)-like effects. In the 1980s, at least six cases of Parkinson disease-like symptoms of sudden onset and great severity were di-

agnosed in narcotic drug users (“the frozen addicts”) who had injected themselves with MPPP contaminated with MPTP<sup>6</sup>.

Although illicit drugs are commonly referred to as toxicants (“tóxicos”) in Brazil, toxicity and addictive properties are only part of the problem. Abuse of drugs is associated with distress in social relationships, with domestic violence, criminal behavior, accidents and problems at work, at home and at school. Overconsumption of psychoactive substances for non-therapeutic purposes, whether they be licit or illicit drugs, is also a major problem. Anti-anxiety and anti-depressive agents, for instance, are among the most consumed prescription medicines. Benzodiazepines have been increasingly used for coping with stressful experiences and anxiety in everyday life, while fluoxetine (Prozac) has been commonly used to “treat” minor depression symptoms and sadness elicited by ordinary events such as the loss of beloved friends or relatives. The scenario of a society in which drugs modulate basic human emotions is worrisome. Aldous Huxley in his novel *Brave New World*, published in 1931, decades before benzodiazepines and fluoxetine gave us a glimpse of such a futuristic world where a psychoactive drug (soma) played a central role. In a drugged society, soma (a name taken from a ceremonial drink used in ancient India) was the pharmacological solution for stress, frustration, emotional pain and unhappiness, and served as social control tool as illustrated by this quotation from the book: “*And if ever, by some unlucky chance, anything unpleasant should somehow happen, why, there's always soma to give you a holiday from the facts. And there's always soma to calm your anger, to reconcile you to your enemies, to make you patient and long-suffering. In the past you could only accomplish these things by making a great effort and after years of hard moral training. Now, you swallow two or three half-*

*gramme tablets, and there you are*” (<http://www.idph.com.br/conteudos/ebooks/BraveNewWorld.pdf>, p. 161-2). Reading Huxley's masterpiece makes us reflect on whether we would indeed enjoy living in such a “perfect” world where apparently safe, psychoactive drugs are freely available for hedonistic purposes and to tame our unpleasant emotions.

### Contributors

Both authors collaborated equally in the writing of the paper.

1. Honorio JC, Kawamura RL, Galvão MMR, Hererías T, Cabrera ER. Legal highs: a public health problem. *Cad Saúde Pública* 2014; 30:228-30.
2. Zawilska JB. “Legal highs”: new players in the old drama. *Curr Drug Abuse Rev* 2011; 4:122-30.
3. Carroll FI, Lewin AH, Mascarella SW, Seltzman HH, Reddy PA. Designer drugs: a medicinal chemistry perspective. *Ann NY Acad Sci* 2012; 1248:18-38.
4. Freudenmann RW, Oxler F, Bernschneider-Reif S. The origin of MDMA (ecstasy) revisited: the true story reconstructed from the original documents. *Addiction* 2006; 101:1241-5.
5. Tripod J, Sury E, Hoffmann K. Zentralerregende Wirkung eines neuen Piperidinderivates. *Experientia* 1954; 10:261-2.
6. Langston JW, Ballard P, Tetrud JW, Irwin I. Chronic Parkinsonism in humans due to a product of meperidine-analog synthesis. *Science* 1983; 219: 979-80.

Submitted on 24/Mar/2014

Approved on 27/Mar/2014