

Legal highs: a public health problem

Legal highs: um problema de saúde pública

Legal highs: un problema de salud pública

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“People now rely on drugs to cope with life’s uncertainties, decrease their anxiety, and survive in a world of turmoil. (...) Drug use is growing in a society that ignores human and emotional values and channels basic emotional needs into unbridled consumption and pleasure at any cost, where the individual always prevails over the community” ¹ (p. 52).

The world of drugs is constantly changing. Users try new drugs in search of different sensations and experiences, and manufacturers launch new products with different formulas to serve the market demand and attempt to dodge the law ².

This context includes what are known as “legal highs”: drugs designed or modified by altering the molecular structure of known illegal substances without eliminating their psychoactive effects. Recreational use targets the same effects of illicit drugs, but the prevailing legislation fails to list these new compounds as controlled substances, thereby hindering their seizure. Users can order them easily on the Internet without a medical prescription or legal restrictions ^{2,3,4}.

Legal highs are considered legal alternatives to traditional drugs, but few pharmacological or toxicological studies have demonstrated their safety in humans. Information on their use, risks, and effects is generally obtained on the Internet, at informal sites or from the manufacturers

themselves ^{2,5}. Thus, the lack or poor quality of information can fool users into mistakenly believing in the safety of such products ⁶.

Legal highs are produced by altering the molecular structure of their precursors. Classification is based on the original compound ⁷, as synthetic cathinones, piperazines, and cannabinoids, derivatives of tryptamine, phenylethylamine, pipradrol, and fentanyl, and plants containing alkaloids or terpenes with psychoactive effects ⁸.

Gaps in drug inspection and control have fostered a new market, focused mainly on sales websites for supposedly “legal” psychoactive substances that pose a public health challenge due to users’ ease in purchasing them ^{4,9}.

Another challenge for authorities is the speed with which new drugs reach the market. Following the development of a new drug, it can take just a few days or weeks to “launch” it on the market ⁸. In 2009 and 2010 alone, 65 new substances reached the European market ². This rapid entry of new drugs allows the “legal” sale of potentially harmful substances. In the European Union, adding a new substance to the list of banned drugs takes a year, while more than a hundred cannabis-like compounds await identification in Europe ^{3,8,10,11}.

According to the report by the European Observatory for Drugs and Drug Addiction, from 1997 to 2010 more than 150 new psychoactive

substances were formally reported through a rapid alert system and are now under control¹². Meanwhile, in Brazil, only seven substances were identified and added to the list of banned substances in the last five years¹³. These featured *Salvia divinorum*, salvinorin A, 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)-1-pentanone (MD-PV), ergine, 4-methylhexan-2-amine (DMAA), and methamphetamine¹⁴.

Recent studies assessed the effects of legal highs on human health^{15,16,17,18}, including users' cardiovascular, digestive, nervous, and endocrine systems. Two clinical toxicology centers in the United States reported 18 cases of acute intoxication with synthetic cathinones, detected in the blood and urine of patients exposed to "bath salts"¹⁵. Two fatal cases were reported¹⁰, besides one case of myocardial lesion after consuming a legal high containing desoxypradol (2-DPMP)¹⁸.

To ban or control a substance in Brazil, it needs to be included on one of the lists in *Ruling n. 344/98* of the National Health Surveillance Agency (ANVISA)^{4,13}. The Brazilian legislation suffers from the same shortcomings as the laws of other countries, since it requires that the chemical name of the substance be listed in the Ruling's annexes. This highlights the mismatch between market availability and legal control of these drugs. For example, the only synthetic cannabinoid banned in Brazil is JWH-018, while European officials have already seized the JWH-019, JWH-073, and JWH-250 varieties and five variations on the cyclohexylphenol series¹².

Since other countries have identified more compounds, these can be expected to enter the Brazilian market in the future⁴. Brazilian laws should thus adjust to the new reality of synthetic drugs.

The adoption of more comprehensive laws with the introduction of generic clauses that allow banning or controlling entire classes of substances could be a tool to curtail the production, marketing, and use of new synthetic drugs. The country could also enact and enforce a ban based on the pharmacological effects of the molecules and drug classes, including their salts and isomers⁴.

However, the adoption of generic clauses could lead to a "bloating" of the country's criminal legislation¹⁹, in addition to potentially preventing the sale of compounds for legitimate research purposes or therapeutic use.

The British government created a device to speed up the inclusion of new substances on the controlled lists, called "misuse of drugs: temporary class drugs". Based on a recommendation by the Advisory Council on the Misuse of Drugs,

a new compound can be included temporarily on the controlled substances list. The regulatory agency has 12 months to conduct the necessary analyses in order to move the substance from the temporary ban to the definitive list⁴. The British initiative may be the most feasible one for Brazil, since it would allow government inspection agencies to temporarily control legal highs within an established time frame. The policy would thus be in keeping with the Brazilian legal order and would not generate legal insecurity with the adoption of generic clauses.

As a way of preventing the entry of these products into Brazil, stronger cooperation is needed between the institutions responsible for seizing the compounds and their inclusion on the banned substances list. A virtual reporting system could facilitate such interaction between institutions.

International collaboration and sharing of knowledge and analytical data between specialists from forensic and clinical laboratories are also important factors, considering the size of the legal highs market.

The increasing availability of these drugs on the Internet requires comprehensive and rigorous control legislation, with a National Drug Access Program that requires accreditation for pharmacies to conduct online sales of medicines, enforcing legal penalties on all parties that engage in selling legal highs⁹.

Considering the health risk to users of legal highs, greater agility is needed in banning these substances as soon as they appear in the country, by including generic clauses in *Ruling n. 344/98*, or provisions by the Advisory Councils that temporarily ban the drug until the definitive position by the respective agency. Linkage between ANVISA and law enforcement agencies in charge of seizing and identifying these new compounds could speed up and increase the efficiency in controlling these substances.

Contributors

J. C. Honório, R. L. Kawamura, and M. M. R. Galvão conceived, organized, and revised the article. T. Herrerias participated in conceiving the article, elaborated the research instrument, assisted in the literature review, and critically revised the manuscript. E. R. Cabrera contributed to the article with a critical revision and revised the final version for publication.

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