



## Poison in party pills is too much to swallow

The harm caused by designer drugs justifies the law's attempts to keep pace with underground chemists, says Mike Cole.

Europe's underground chemists have been busy. According to a report last month from the European Monitoring Centre for Drugs and Drug Addiction in Lisbon, the alarming rise in the appearance and abuse of drugs continues. In 2008, some 13 new substances were reported. In 2009, this figure rose to 24, and in 2010, the highest ever number of new drugs was reported, a total of 41 new substances.

Most were cathinones — related to amphetamines — or synthetic cannabinoids. All must have been made by skilled chemists as a deliberate challenge to drug-control laws.

Should we try to keep ahead of those who make and use these materials? Is the effort and expense required for chemists such as myself to develop tests for new drugs, and to work with legal professionals to increase the number of banned substances, really worth it? The simple answer is yes. I have seen the effects that these chemicals can have on those who take them. In addition to damaging medical conditions, these drugs can induce dangerous or violent changes in mood and behaviour. I believe that society has a duty to intervene.

Prosecuting a drug case requires a compound to be identified and shown to be illegal — not always an easy task. Some laws control drugs by name and chemical class, thereby outlawing a broad family of related chemicals. Others ban only specific isomers, opening the door to 'designer' drugs manufactured to mimic the effects but not the structure of an illegal compound. The Internet has facilitated international trade in these materials.

One such new drug is benzylpiperazine, or BZP. Developed by the Wellcome Research Laboratories in Beckenham, UK, in 1944 as an anthelmintic drug to combat parasitic worms in livestock, it was subsequently investigated as a potential antidepressant. It entered the party scene a decade or so ago as a legal alternative to ecstasy (MDMA), producing similar effects but not illegal at that time. Today, ecstasy tablets bought on the streets of London or San Francisco are as likely to contain BZP as MDMA.

BZP exemplifies the problems that new drugs and 'legal highs' pose for law-makers. Widespread use led to the compound being banned in the United States and much of Europe, yet it remains legal in other places, such as Canada.

Work in my laboratory has shown that BZP is not, as many users believe, safe. We treated immortalized cell lines from the liver and kidney — the excretory organs that clear drugs from the body — and fibroblasts, cells involved in wound-healing, with BZP, its precursor chemicals and its reaction by-products. We tested both the compounds and the impurities

created in their manufacture in isolation, as mixtures and as drug blends synthesized to mimic street samples. The concentrations used represented those recorded in the body during drug use.

All these chemicals were hugely toxic to both liver and kidney cell lines. The major impurity in BZP, dibenzylpiperazine, is especially toxic to the kidneys. One of the starting materials, piperazine hexahydrate, some of which can make it into the final product, is extremely toxic to the liver. These results start to explain the symptoms of renal and hepatic failure observed in people who use BZP.

Toxicity depends on the composition and concentration of the mixtures, and the effects are hard to predict. Other side effects include insomnia, anxiety attacks, nausea, vomiting and serious palpitations that frequently go unreported. These effects become worse when the drugs are mixed with alcohol. In short, the effect on individuals is potentially significant, long-lasting and even fatal.

Control of such drugs brings its own problems. Synthesis of a compound is driven underground. BZP is easily manufactured from piperazine hexahydrate and benzyl chloride, but the level of impurities depends on the precise quantities of starting materials, the reaction conditions and the procedures used to extract the drug from the reaction mixture. This presents a paradox common in drug control: the safest option is for people not to ingest the chemicals, which is the aim of making them illegal. But making them illegal can make them more dangerous.

In response to this conundrum, people on both sides of the debate over whether to criminalize drugs often cite the economic benefit of their approach, but this argument is a red herring.

Both sides have costs. Outpatient treatment after the ingestion of BZP costs hundreds of pounds per patient per visit. In-patient care, including treatment in an intensive-care unit, costs thousands of pounds a day. Society has a right to frown on and to seek to outlaw such costly behaviour. Yet the science behind a strategy of drug prohibition — quality-control methods in an analytical lab and access to forensic services — is expensive too.

So, returning to the original question: should we continue to outlaw recreational drugs, and compounds such as BZP in particular? The evidence is mounting that even pure drugs are toxic and do harm, both in the short and in the longer term. When public health and safety is at risk then surely it is socially responsible to ban these substances, and to provide a legislative and forensic-science system that supports such bans. ■

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Mike Cole is professor of forensic science at Anglia Ruskin University in Cambridge, UK.  
e-mail: [Michael.cole@anglia.ac.uk](mailto:Michael.cole@anglia.ac.uk)