The identification and analysis of Canadian designer drugs

WILLIAM L WILSON

Bureau of Drug Research, Health and Welfare Canada, Ottawa, Ontario, Canada K1A OL2

One may wonder what could possibly be significant enough about designer drugs in Canada that would make them different from anyone else's. It is a fact of life that we often see new, clandestinely produced drugs before they appear elsewhere. My presentation will address some of the reasons why this occurs. For the purposes of this presentation, any substance, synthesized for the specific purpose of circumventing regulatory nomenclature in the area of controlled substances, qualifies as a designer drug. The responsibility for administering Canada's drug regulations rests with the federal minister of Health and Welfare. The administrative functions, such as the disposition of all seizures which is done at our national level, and our international commitments, are handled by the Bureau of Dangerous Drugs. The analysis of all drug seizures is carried out in the laboratories of the federal department of Health and Welfare. It is primarily the responsibility of the five regional laboratories of the Field Operations Directorate. The Bureau of Drug Research, to which I belong, has the responsibility for method development and provision of authenticated reference substances to be used by the regional laboratories. Research projects such as sample linking or impurity profiling and international collaboration with the UNDND and other various national agencies falls within BDR's mandate. All drug seizures are to be submitted for analysis to Health and Welfare by police officers. The number of exhibits has steadily increased to almost 70,000 last year and there has been a dramatic increase in the number of cocaine samples (Table 1). The criminal elements involved in the designer drug field in Canada are mainly motorcycle gangs although some trained chemists appear to be independently involved.

Canadian drug legislation is governed by two Acts which are administered by Health and Welfare. The Narcotic Control Act and Regulations, is patterned after the UN 1961 Single Convention. The schedule includes sections on opium, cannabis, coca, fentanyls and PCP, among others. These are substances for which a medical use is, or had at one time been, approved. Parts 3 and 4 of the Food and Drug Act deal with Controlled and Restricted drugs. Schedule H is where the majority of designer drugs are

listed. These are substances for which no medical use is allowed. Schedule G lists controlled substances such as amphetamine, methamphetamine, methaqualone and the barbiturates. Schedule F contains prescription drugs including meprobamate and the benzodiazepines which must be moved up to a level of control such as schedule G, now that Canada has signed the 1971 Psychotropic Convention. Canada has always had a fast track system in which a substance could be added to the schedule within a matter of 2 to 3 days provided there is no acceptable medical use and there is evidence of abuse. In addition, our courts have not been as strict in their interpretation of what is a "derivative" and substances such as the reversed esters of meperidine and the fentanyls have always been considered as included in the NCA schedule. Nevertheless, we felt it was time for a complete overhaul of the legislation to take account of scientific advances and incorporate our new requirements under the 1971 Psychotropic Convention. The Psychoactive Substance Control Bill was tabled in the last Parliament, but died on the order paper because of the election. Its reintroduction awaits the government agenda. Consideration is being given to providing for the seizure of any substance with psychoactive properties which is misused. There may be more inclusive scheduling and provisions to control precursors.

TABLE 1. Summary of police exhibits analysed by Health and Welfare Canada

	1978–1979	*1983–1984*	*1988–1989*
Cannabis	37241	30969	36370
Heroin	847	843	1183
Cocaine	1190	4050	16079
PCP	566	658	571
LSD	1497	1775	886
Psilocybin	0	914	942
Other*	2992	1460	1878
Total violative	44333	40669	57909
Total non-violative	6587	5778	6319
Total analysed	50920	46447	64228
Total quantitated	1445	2445	6123

* includes less common substances

Each year, the appearance of the new crop of designer drugs is one of the events which adds to the interest of our work. In addition, there is the challenge of trying to predict what will be the next drug or class of drugs to appear or re-appear. Every summer for the last few years, it seems, we have

been presented with a fresh test by our clandestine chemists. Over the past 5 years, approximately 50 labs have been investigated. PCP, methamphetamine and hydroponic set-ups for cannabis are seen regularly, as well as cocaine base labs. The older amphetamine analogs are rarely seen today. There have been two labs which have prepared a multitude of designer amphetamines. Fentanyl analogs have never been reported in Canada. One lab preparing U4EUH has been dismantled. Of the meperidine reverse ester analogs, MPPP has been submitted as exhibits but no lab operation has been found. OP5 was a recent encounter which will be discussed later. I will not spend much time describing methamphetamine and MDA since these reallly are old designer drugs and the procedures for their preparation have been extensively described in the literature. Our concern is that precursors such as benzaldehyde, P-2-P, ephedrine, piperonal and safrole are not subject to control in Canada. Quantities of up to 200 lbs per batch have been prepared in makeshift labs.

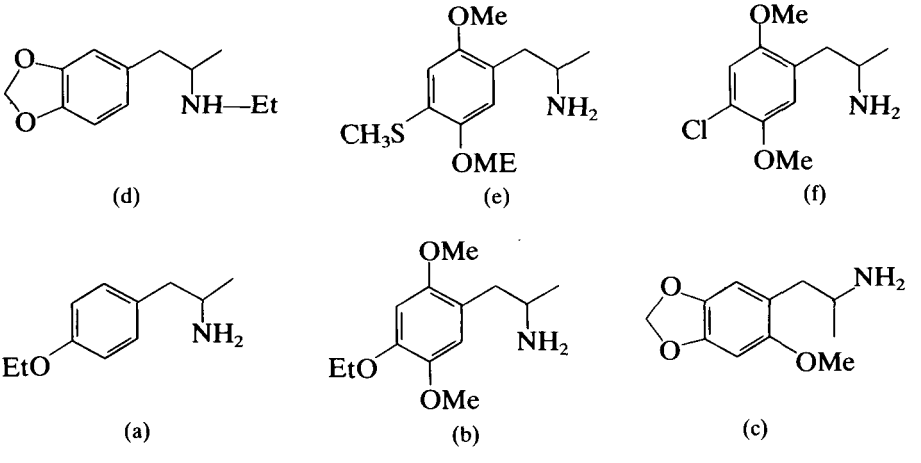

FIGURE 1 Designer amphetamines. (a) PEA; (b) MEM; (c) MMDA-2; (d) MDEA; (e) THIO—TMA; (f) DOC.

In the designer amphetamine series, all of those shown in Figure 1 have been, or were in the process of being, prepared by two clandestine chemists. Derivatives of 2,5-dimethoxyamphetamine have been particularly popular recently, including the 4-ethoxy-, the 4-chloro-, and, perhaps most interesting of all in this group, the 4-methylthio-derivative. The chemistry involved is not elaborate, because the appropriate starting material, methylthiodimethoxybenzene is commercially available. Looking at the notebook seized at the scene of this laboratory, it is obvious that the chemist was familiar with Canadian drug regulations and synthesized analogs which he knew were outside the legislation. This disturbing trend illustrates the need for

harmonization of drug legislation so that, because of subtle differences in regulation, one country does not become the branch plant source of drugs for another.

The future possibilities in amphetamine chemistry are almost limitless, and a part of our activity has been to try to predict, from the literature and other sources, what will be the likely candidates for future production. We have already synthesized a number of prime prospects, and this crystal-ball gazing stood us in good stead two years ago. When 4-ethoxyamphetamine first made its appearance on the street, we were on the point of carrying out the final reaction to make the standard, as we had earlier predicted its future appearance as being very likely. This particular compound is now in the process of being tested to evaluate its toxicity and psychoactive properties. Again, the starting materials are commercially available. Our approach to the identification and analysis of these amphetamines has been to use a combination of capillary GC-MS and proton magnetic resonance spectroscopy. Conclusive identification of the actual positional isomer sometimes requires synthesis of all the possible isomers for spectroscopic comparison. Sufficient quantities are then synthesized for method development work.

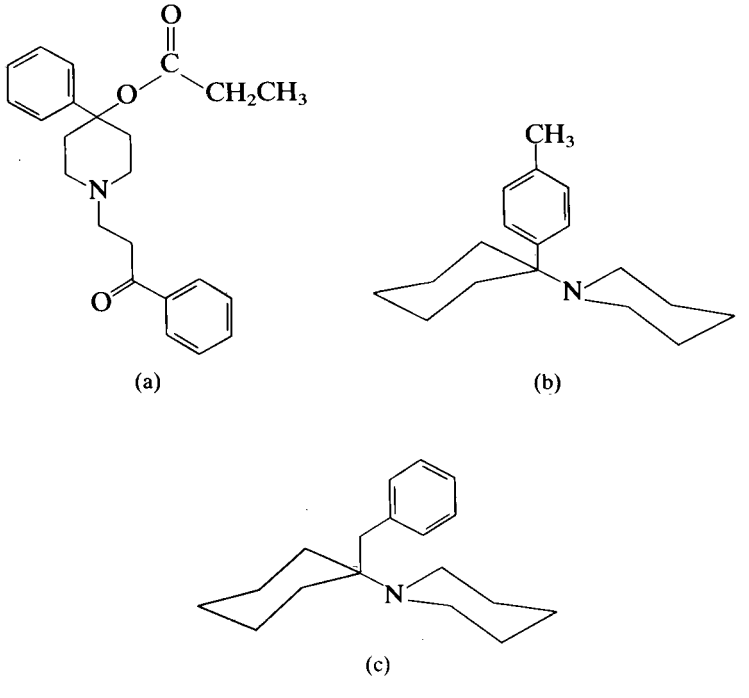

FIGURE 2 Some other designer drugs. (a) OP5; (b) tolcyclidine; (c) benzcyclidine.

Two years ago produced a complete surprise for us in the appearance of the substance which came to be known as OP5 (Figure 2a), as we had never even considered the possibility of such a compound. With 1300 times the analgesic activity of meperidine, the implications of this drug being sold on the street were profound, as the dose would be in the same order as that of LSD, and the possibility of not finding any drug in a sample when it first appears is very real. We were fortunate in that the incident was intercepted before the main batch of drug was synthesized, although we subsequently learned that a sample of 1 gram had been made and test marketed in California. There was enough material for about 500,000 doses to be made and the chemistry was not elaborate. The greatest danger from such a drug would probably have been from the very real possibility of a tetrahydropyridine, similar to MPTP, being inadvertently produced during the synthesis. The paper which the chemist had been following dated from 1962. The case led to a subsequent investigation in co-operation with the US Drug Enforcement Agency resulting in the arrests of 4 people and the seizure of an operational lab in California. Sixty grams of OP5 were seized.

This year's crop of designer drugs was no less of a surprise than the previous years' had been. The drug PCP is a regional one in Canada, the vast majority of exhibits submitted for analysis to our labs coming from the province of Quebec. Tolcyclidine and benzcyclidine (Figure 2b, c) are the paramethylphenyl (paratolyl) and phenylmethyl (benzyl) homologs of PCP. Although informal police assistance is offered by most reputable chemical suppliers in Canada, our current legislation does not provide a mechanism similar to the piperidine reporting and purchaser identification scheme found in the US. Who knows which class of drugs will become the next designer drug candidate. We are concentrating our efforts on the synthesis of the n-substituted analogs of the various ethoxyamphetamines and becoming more involved in the neuropsychopharmacological assessment of these substances. It is very important that close collaboration continue among the scientific staff from all national labs so that an early warning system is available when the next designer drug makes its appearance.