Designer Drugs

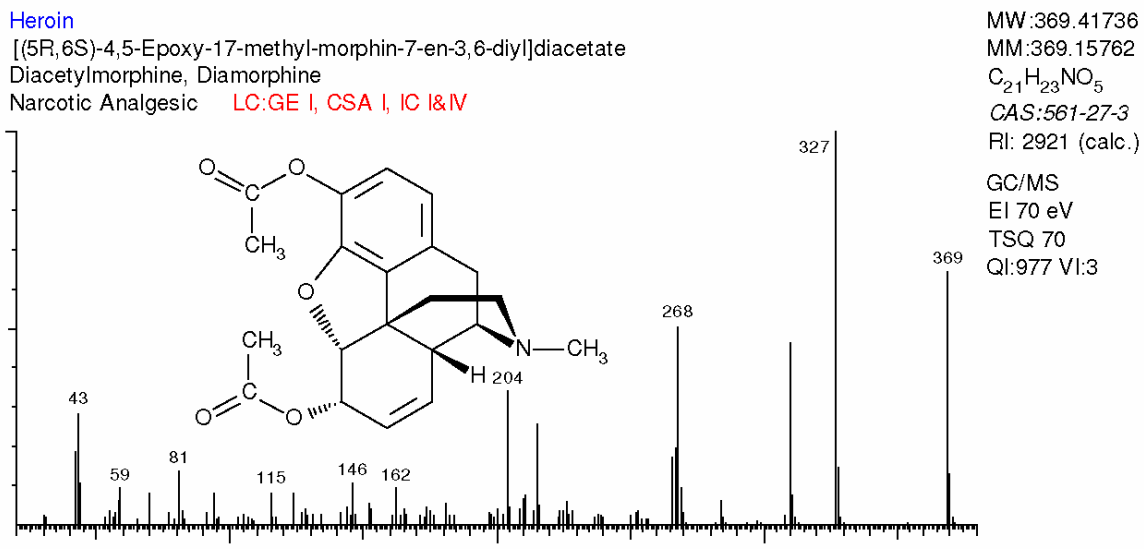
Introduction

The impressively large number and variety of clandestinely produced drugs and their increasing distribution is of concern to analytical chemists in forensic, clinical, toxicological, and university laboratories providing services to law-enforcement authorities, including identification of drugs and determination of their legitimacy. The mass spectral database Designer Drugs is the result of our efforts to collect the spectral data of legal and illegal drugs, their metabolites, precursors, natural and synthetic by products and impurities essential to scientists engaged in forensic analysis.

The database contains mass spectra of new designer drugs and other narcotic or psychotropic compounds that have appeared on the illicit market, and their metabolites, precursors, natural and synthetic byproducts, and impurities. The latest compound to be included is *N*-hydroxyethyl-3,4-methylenedioxyamphetamine, an analog of MDA seized in Luxemburg in 2005 which was previously unknown on the illicit market (REF: PIH 107). Many previously unreported phenethylamines, amphetamines, and phenylbutaneamines have been synthesized and included to facilitate identification of clandestinely produced compounds likely to appear in the future. Many compounds used world wide for pharmaceutical purposes have been included. Since the last publication in September 2004 the number of mass spectra has been increased by addition of more than 2000 new spectra, bringing the total number to more than 5500 spectra of 4739 different compounds.

Presentation of Mass Spectra

For identification of unknown compounds the mass spectra are arranged in ascending order of the nominal mass of the most intense fragment (base peak). Compounds with identical base peaks are ordered by their second intense fragment, and so forth. The mass spectra are presented as bar-graphs, the abscissa gives the nominal *m*/*z* value and the ordinate the relative intensity as a percentage.



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Predominant ions are labeled with their *m*/*z* values. The mass range below the molecular ion has been expanded if the molecular ion was of low relative intensities. These spectra are marked “expanded” and were generated from the base peak plus 1 mass up to the molecular ion region with normalized intensities. For clarity, the fragments in the mass interval below the first fragment of an expanded spectrum are not plotted. Expanded mass spectra are arranged in the same way as full mass spectra. CI spectra which proved useful for differentiation of closely related designer drugs are occasionally given.

At the top of each mass spectrum the INN (international nonproprietary name) in English is given, if available. The systematic names are found below the INN names. If several different names are used for one compound, only the IUPAC (International Union of Pure and Applied Chemistry) name is stated and, if possible, the WHO (World Health Organization) name. Synonyms (SYN) and proprietary names (PN) are only occasionally given. The information is completed by the legal category (LC) on the lists of the US Controlled Substances Act (CSA), the UN list of substances under international control (IC), and the German (GE) controlled substances list; some aspects of therapeutic or illegal use are also given. This reference does not give complete information and does not fully assess the pharmacological potential of a given drug.

The block of information at the right of the spectrum is divided in two parts. The upper part contains compound-specific data – the molecular weight (MW) and the weight of the molecular ion (MM). The molecular ion is calculated on the basis of the isotopes with the greatest natural abundance. The nuclide masses and isotopic abundance used for calculation of the mass of the molecular ion were taken from the literature [1]. This follows the empirical formula, a verified Chemical Abstracts registry number (CAS), if available, and the measured or calculated gas chromatographic Kovats retention index (RI) [2–4] for an SE 30 (DB1, OV-1, OV-101) column. It is not claimed the calculated RI values are exact; they do, however, aid location of a compound in gas or total-ion chromatograms in situations where no measured or published Kovats retention index is available.

The lower part of the information block contains information about the conditions used to record the spectra, for example interface type (GC–MS, DI–MS), the mode of ionization (EI 70 eV), and the type of spectrometer data system used (i.e. TSQ 70). In the last line of the recording information block a quality field is given in which the quality index (*QI*) and the verification index (VI) of the mass spectrum can be found.

Recording of Mass Spectra

Electron impact (EI) mass spectra were acquired with an ionization energy of 70 eV. Chemical ionization (CI) mass spectra with methane as reagent gas were recorded at a pressure of 130 pa (1 torr) using an ionization energy of 70 eV. Unless otherwise stated compounds were transferred via an SE 30 or OV-1 capillary column into the mass spectrometer. The was source maintained at 150°C. If necessary the samples were eluted directly (DI) into the mass spectrometer source.

The bulk of mass spectra were recorded on quadrupole mass spectrometers. A small number were acquired on ion-trap or magnetic-sector mass spectrometers. Because EI mass spectra recorded on different types of mass spectrometer may be very different in appearance, spectra acquired using different types of mass spectrometer have been collected for each compound, to avoid errors arising from use of different spectra and MS search algorithms.

Quality of Mass Spectra

As far as possible, all spectra were verified by use of standard mass spectra libraries [5–9] and checked by use of mass spectral interpretations. When no molecular ion was obtained under EI conditions the spectrum was also acquired under CI conditions.

Comparison of unknown and reference mass spectra is a key step in the mass spectral identification of chemical compounds by automated systems. The quality of reference mass spectra is very dependent on operating procedures and sample purity. All electron-impact mass spectra therefore were given a numerical quality index rating on the scale proposed by D. Speck, R. Venkataraghavan, and F.W. McLafferty [10]. The quality index (*QI*) is a numerical value between 0 and 1000 and the product of seven quality factors:

1. the source of the spectrum
2. the ionization conditions
3. high-molecular-mass impurities
4. illogical neutral losses
5. isotope abundance accuracy
6. number of peaks
7. lower mass limit of peaks

The software Chemograph Plus [11] was developed to calculate these quality factors . The overall quality index *QI* is given for all the mass spectra is presented. The software has been found useful in finding "garbage" spectra and preparing a high-quality mass-spectral data base. Electron-impact mass spectra judged to be unsatisfactory ($QI < 900$) by the software were eliminated; only for ion-trap mass spectra, very rare drugs, metabolites, very compact molecules, or uncommon substance-specific fragmentation was a $QI < 900$ accepted. Chemical ionization mass spectra having a quality index of 0, by definition, were also accepted. A high quality factor is indicative of the absence of standard errors in the spectrum. Some serious errors, for example rearrangement of ions before dissociation, cannot, however, be detected by this method [12]. This type of error can be detected only by mass spectroscopists who are knowledgeable about ionic fragmentation processes.

In addition to the quality index, a verification index (VI) is given, if possible. The number behind the verification index gives the number of standard mass spectral libraries [5–9] in which this mass spectrum corresponds to a reference mass spectrum with a similarity equal to or larger than 90%. Approximately 13% of all mass spectra in Designer Drugs 2006 were verified in this way. This low verification rate is indicative of the large number of mass spectra which can be found in Designer Drugs 2006 only.

An important aspect of the quality of reference mass spectra is use of a pure sample free from chemical noise. If possible, therefore, mass spectra were added to the collection only when the signal-to-noise ratio of the peak in the total-ion current chromatogram was larger than 10.

Accurate intensity information is crucial to identification of chemical compounds by library-search processes. Small intensity differences between two mass spectral peaks of almost equal intensity may result in a total failure of compound identification by standard presearch library-search processes. To avoid distorted intensity data from saturated peaks we rejected mass spectra with an overall intensity of more then 10 million counts. By addressing the problem in this way we produced library mass spectral data with more accurate intensity information enabling more definitive library matches.

Statistical Data of Designer Drugs 2006

Number of mass spectra: 5584
Number of structures: 5584
Number of different compounds: 4739
Average number of peaks per spectrum: 150
Average quality index of spectra: 921
Replicate spectra: 42
Number of GC–MS spectra: 5467
Number of direct insertion probe mass spectra: 117
Number of verified mass spectra: 722 (12.9%)

Structural and Empirical Formulas

Structural formulas are uniformly drawn in their precise stereochemical representation. The elements of empirical formula are arranged according to Hill [13]:

1. Number of carbon atoms
2. Number of hydrogen atoms
3. Alphabetical order of the other elements
4. Increasing number of elements

Chemical Warfare Agents

The threat of chemical weapons has become real since the terrorist attacks in Tokyo and New York. The authors therefore decided to add electron-impact mass spectra of all important chemical warfare agents and explosives. The most important class of chemical weapons is the nerve agents, which are mainly derivatives of the cholinesterase inhibitor insecticides. The agents enter the body mainly by inhalation and percutaneous absorption. Because many of these compounds are readily hydrolyzed at the monovalent phosphorus bond the mass spectra of several degradation products were added [14]. The former IG Farben discovered the organophosphorus compound Tabun. Originally synthesized as an insecticide it rapidly became adopted for battlefield use soon after related compounds such as Sarin and Soman were developed. The three compounds Tabun, Sarin and Soman were given the military codes GA, GB, and GD respectively. Other high toxic nerve agents were synthesized in the US Edgwood Arsenal laboratories in Maryland. These agents are named according to the military code – EA (origin) and number 1701 (current number) e.g. EA 1701 for VX [15].V in VX probably describes a physical property – viscous liquid of low volatility. It has a tendency to cling to everything it comes into contact with and is the most insidious threat of all nerve agents. Russia and China developed VX analogues which are known as V-gases (VR and VC, respectively).

Indexing

An alphabetical index of names and synonyms with page information for the corresponding full, expanded and CI spectrum is provided.

Abbreviation	**Meaning**
A	Artifact
AC	Acetylated
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft code
CI	Chemical ionization
CSA	US Controlled-substances Act
CAS	Chemical Abstracts Registry Number
DEA	US Drug Enforcement Administration
DI	Direct insert
DMBS	Dimethylbutylsilylated
ECF	Ethyl chloroformate
EI	Electron impact
ET	Ethylated
eV	Electron volt = 96,487 kJ mol^{-1} = 23.06 kcal mol^{-1}
FORM	Formylated
GE	German Controlled Substances Act (BtMG)
GCQ	GCQ Ion Trap Mass Spectrometer, Finnigan/Thermoquest
HCF	Hexyl chloroformate
HFIP	Hexafluoroisopropanol
HP 5972	HP 5972 Quadrupole mass spectrometer, Agilent
MCF	Methyl chloroformate
IBCF	*iso*-Butyl chloroformate
INN	International Nonproprietary Name
IND	Indication or use i-PROP iso-propylated
IUPAC	International Union of Pure and Applied Chemistry
IC	UNO Substances under International Control
LC	Legal category (GE German, CSA US Controlled Substances Act, IC International Control)
LIT	Literature
M	Metabolite
ME	Methylated
MM	Molecular weight calculated with the isotopes of greatest natural abundance (corresponds to the weight of the molecular ion)
MW	Molecular weight
NH	In NMR spectra: exchangeable protons of amine and ammonium groups
PECSS	Perkin–Elmer Lambda Series UV–visible spectrometer
PFO	Perfluorooctanoylated
PFB	Pentafluorobenzylated
PFP	Pentafluoropropionylated
PN	Proprietary name
PROP	Propionylated
REF	Reference to psychoactive compounds included in PiHKAL [16] (PIH:) or TiHKal [17] (TIK:)
RI	Gas chromatographic Kovats retention index
TBDMS	*tert*-Butyldimethylsilylated
TFA	Trifluoroacetylated
TFP	Trifluoroacetylpropylated
TMSH	Trimethylsulfoniumhydroxide
TMS	Trimethylsilylated

TRACE	TRACE DSQ Single Quadrupole Mass Spectrometer, Finnigan/Thermoquest TSQ
TSQ 700	Triple Quadrupole Mass Spectrometer, Finnigan/ Thermoquest
WHO	World Health Organization

Pesticide abbreviations

Ins	Insecticide
Aca	Acaricide
Fun	Fungicide
Rod	Rodenticide
Bac	Bactericide
Alg	Algicide
Rep	Repellent
Nem	Nematicide
Her	Herbicide
Mol	Molluscicide

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Internet Addresses

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4 http://www.erowid.org/library/books_online/pihkal/pihkal.shtml
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7 http://www.poppies.org
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9 http://www.apgea.army.mil\safty\msds
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An electronic library of mass spectra named “Designer Drugs 2006” is also available in all major MS library formats which can be used directly with different mass spectrometer systems. Because of the large amount of data a computer with at least 500 MByte RAM is recommended

The graphics in this manual were prepared with the Windows computer software Chemograph Plus Version 6.4 (www.Chemograph.de) [11].*

The structural and spectral data in this manual are also available in an electronic form which can be accessed by the computer software Chemograph Plus under all Windows 32 bit operating systems. Because of the large amount of data a computer with at least 500 MByte RAM is recommended.

This manual has been prepared with the greatest care. Because of the extremely large amount of data, however, the possibility errors cannot be completely discounted and no legal responsibility can be accepted for any inaccuracies of statements, data, illustrations, procedural details, or other items. Users are requested to report any error found or other suggestions by E-mail to P.Roesner@t-online.de or by Fax: 0049 431/32723. In forthcoming editions suggestions will be included and errors will be corrected.

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We hope that this compilation of mass spectral data will be useful also to other analytical chemists in forensic, clinical, or university laboratory in the analysis of new drugs and other drug related compounds.

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