Determination and Characterization of Psychoactive Drugs. Elucidation of their Metabolic Processes

Vojtěch Hrdlička[1], Radek Jerga[2], Marta Choińska-Młynarczyk[1], Jana Skopalová[2], Jan Langmaier[1], Renáta Šelešovská[3], Tomáš Navrátil[1,*]

[1]J. Heyrovský Institute of Physical Chemistry of the Czech Academy of Sciences, Prague, Czech Republic
[2]Department of Analytical Chemistry, Faculty of Science, Palacký University Olomouc, Olomouc, Czech Republic
[3]University of Pardubice, Faculty of Chemical Technology, Institute of Environmental and Chemical Engineering, Pardubice, Czech Republic
*E-mail: tomas.navratil@jh-inst.cas.cz

ABSTRACT

Psychoactive drugs (PDs) belong generally to the most commonly (mis)used substances worldwide. Determination and monitoring of their active pharmaceutical ingredients (APIs) and their respective metabolites in body fluids and environmental matrices present a challenge for analytical chemists. Our research is focused on the most frequently prescribed and on newly introduced psychoactive drugs of specified structures and/or defined properties. Emphasis was placed on the investigation of the reaction mechanisms of metabolite formation. New and alternative methods to the commonly used electroanalytical methods applicable for the analysis and characterization of target compounds in the pure state, in body fluids, wastewaters, or other matrices, have been developed. If possible, the applied electrochemical techniques are combined with others (mass spectroscopy, chromatography, etc.). To improve the chemometric parameters and sensing characteristics, attention is paid to the construction of new electrochemical sensors and detectors.

Keywords: Active pharmaceutical ingredient (API); Electrochemistry; Environment; Metabolites; Psychoactive drugs; Body fluids.

INTRODUCTION

A psychoactive drug (PD), psychopharmaceutical, psychoactive agent, or psychotropic drug, is a chemical substance that changes functions of the nervous system and results in alterations in perception, mood, consciousness, cognition, or behavior. These substances may be used medically, recreationally, or spiritually to purposefully improve performance or alter one's consciousness, as entheogens for ritual, spiritual, or shamanic purposes, or for research. Misuse of PDs can lead to addiction. Therefore, their manufacture, prescription, and distribution are mostly under governmental control.

More than 200 drugs, discovered and developed during the last 60 years, are available for the treatment of psychiatric and neurologic patients. From the medical and toxicological point of view, their applications present a huge problem. The active ingredients of drugs are classified (according to the organ or system on which they act, their therapeutic intent or nature, and their chemical characteristics) in the Anatomical Therapeutic Chemical (ATC) drug classification system. PDs belong mostly to the nervous system (N)-group.

OBJECTIVE

The presented research was focused on the development of new/alternative electrochemical methods (possibly combined with other analytical techniques). The results can be applied in the determination or

monitoring of selected psychoactive substances and their metabolites in their pure state, body fluids, and other matrices.

METHODOLOGY

The realization of the above-mentioned goals was divided into several interconnected aims:

Development of suitable working electrodes

The material of the working electrode plays a crucial role in any electroanalytical technique. Among others, we used and developed the following types of electrodes:

a) **Mercury-based - amalgam - electrodes.** Relatively cheap bare or modified solid amalgam electrodes are suitable to replace the liquid mercury electrodes in the elucidation of reaction mechanisms, metabolite formations, enzymatic reactors, etc. (Yosypchuk et al.)
b) **Boron-doped diamond electrodes (BDDEs).** Some of the disadvantages of mercury-based electrodes can be solved by replacing them with BDDEs with a wide potential window. Some properties can be changed by their modifications (e.g., using nanoparticles of Au, Ag, and Pd) (Matvieiev et al.).
c) **3D printed electrodes.** 3D printing (or additive manufacturing) belongs to the most promising approaches toward simple, rapid, and inexpensive production of various sensors, electrodes, and cells, with prospective use for the determination of various PDs and their metabolites (Choinska et al.).

Analysis of real samples, separation techniques - Hollow-fiber microextraction

Various matrix components present in complex biological samples (urine, blood, blood serum or plasma) can cause a huge complication interfering with API determination. One of the ways of their removal and simultaneously sample preconcentration is the application of hollow-fiber microextraction (HF-LPME) (Hrdlicka, Barek and Navratil).

Additional data on analytes - ion transfer voltammetry

There is a lack of information on the bioavailability and physicochemical parameters of the investigated drugs, especially, atypical and newly synthesized ones. This data can be collected using ion transfer voltammetry at supported room-temperature ionic liquids. This technique can provide a broad range of both theoretical and practical results of the electrochemical or analytical significance (estimation of partition coefficients, dissociation constants, etc.) (Skalova et al.).

Investigated drugs

We focus our attention on the most frequently prescribed psychoactive, modern, newly introduced drugs, and some atypical antipsychotics. From the chemical point of view, we paid our attention to the electrochemically active compounds; drugs containing nitrogen heterocycles or quaternary (nitrogen) bases; extractable using HF-LPME; complexable using some heavy metal cations (e.g., Cu^{2+}, Cu^{+}, Ag^{+}, Au^{+}, Au^{3+}).

RESULTS AND DISCUSSIONS

In our contribution, the results achieved in the following areas will be presented:

- Development and characterization of novel screen-printed sensors with chemically deposited boron-doped diamond; their application in the analysis of selected PDs (Matvieiev et al.).
- Investigation of chemical and structural stability of four non-conductive 3D printing materials (Elastic, Clear, PET, and PLA) in 17 various solvents (e.g. acetone, acetonitrile, chloroform, cyclohexanone). Characterization and application of carbon fiber polylactic acid 3D printed electrodes (Choinska et al.).

- Development of methods for the determination of cancer biomarkers (e.g., 5-hydroxyindoleacetic acid) using hollow-fiber-based microextraction at different BDDEs (Hrdlicka, Barek and Navratil).
- Characterization of some physicochemical parameters of selected PDs (e.g., venlafaxine or cocaine) using ion transfer voltammetry and the TDMA-TFPB membrane cell (Skalova et al.).
- Elucidation of reaction mechanisms and analyte transformations using a combination of various analytical techniques (electrochemical, mass spectrometry, liquid chromatography, etc.) (Selesovska et al.).
- Application of the elimination voltammetry with linear scan to reveal the reaction mechanisms (e.g., controlling processes), increase the sensitivity of signal recording, improve the separation of recorded signals, etc.).

CONCLUSIONS

The development of new sensors/electrodes/cells/systems and hyphenated systems for the characterization and analysis of PDs and their metabolites is one of the most important trends in modern analytical chemistry. The electrochemical methods can be extremely suitable not only as alternative analytical methods, but also, e.g., in the elucidation of reaction mechanisms of PDs and the formation of their metabolites in human bodies. They can be characterized by low running costs, simplicity, and low investment. Among their important advantages in the analysis of PDs belongs their applicability in point-of-care devices.

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