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Review article

The role of alkylsilyl derivatization techniques in the analysis of illicit drugs by gas chromatography

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ABSTRACT

Alkylsilylations are the most powerful derivatization techniques used for the identification and quantification of organics with reactive proton containing functional groups: providing volatile derivatives of excellent mass spectrometric properties (high selectivity, outstanding sensitivity). These derivatives proved to be excellent candidates also for illicit drug analyses: for species from the simple (γ-hydroxybutyric acid) up to the complex structures (amphetamines, opiates, cannabinoids, etc.), mostly by one injection, simultaneously.
In this paper the possibilities of illicit drug analyses by gas chromatography (GC) are reviewed: performing analyses without derivatization and applying alkylsilyl derivatizations. Further sorting was based on the alkylsilylation reagent type, on the examined matrix, enrichment, derivatization, acquisition protocols, limit of detection (LOD), and limit of quantitation (LOQ) data, and on the target illicit drug(s) to be identified and quantified. Special attention was paid to the selectivity and sensitivity properties of methods. Analytical performance characteristics were documented in details and commented.

Contents

1. Introduction

The relevancy and continued interest towards illicit drugs' chromatographic analyses can be explained by the exponential extent of illicit drug use and by their contribution to the global burden of several diseases associated with their appearance in numerous biological and even in environmental matrices [1]. Thus, the need of improved sensitivity, selectivity, reliability and reproducibility of chromatographic methods – suitable for the simultaneous identification and quantification of compounds with different functional groups – is not questionable.

Literature overview of proposals, published mainly in the last two decades, revealed considerable GC contributions to the field (41% of the total of papers, summed up on ScienceDirect basis).

It is worth mentioning that the last review concerning the comparison of GC–MS analytical techniques for illicit drugs was published in 1979 [2]. This fact can be explained with the huge amounts of proposals regarding a single matrix, only. Consequently, to refresh the advancements to this field, in a wide scale remain of interest and importance. Recent reviews [3–12] were related to the quantification of selected groups [3–6], like *Cannabis* products [3], lysergic acid diethylamide [4], heroine and cocaine seizures [5], cocaine with its metabolites [6], or summing up the analysis

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of several groups of drugs of abuse in selected matrices (blood [7], or hair [8], or sweat [9]). The challenges of new psychoactive drugs' analysis were compiled, recently [10]. Special approaches were devoted to illicit drugs' mapping as environmental pollutants: estimating illicit drug consumption also from wastewater analysis data applying 'back calculations' [11]. Recently, amphetamine drug profiling was performed by GC [12].

The present compilation focuses on those relevant papers – without completeness – in which GC technique was used for illicit analysis either without derivatization or subsequent to alkylsilylation derivatizations. Further classifications were listed according to the matrix as they had to be extracted from and to the detailed protocol they were subjected to, prior to their analysis by GC.

1.1. Sample and method selection

The aim of this compilation, following matrix specific proposals and basic researches, was to assess the involvement of the biological matrix of drug abusers, or drug abuse in general, focusing on the efficient sample and method selections. The distribution of matrices reveals that the most frequently analyzed sample types vary from 28.0% (urine) to 1.2% (breath, nail, tooth, placenta, skin, muscle), expressed in total of our selection (Fig. 1).

From methodological point of view, regarding species of diverse origin and structure [13–80] — we preferred to examine various alkylsilylation techniques [33–80] because their many-sided suitability and unique efficiency, as introduced by Pierce [81], were also confirmed in our earlier experiences [82–94].

2. GC of illicit drugs

In general, it is worth mentioning that derivatization does have a particular importance in the GC based protocols. This time consuming and tedious process, by many application chemists, was and still regarded as the main disadvantage of sample preparation, needed prior to GC analyses. However, this so called 'disadvantage' is dwarfed in comparison to several advantages associated with the GC analysis of derivatized compounds (increased selectivity, sensitivity and the possible identification and quantification of numerous species on a single column, simultaneously).

Comparing the limited selectivity and sensitivity properties in the GC quantification of illicit drugs in their initial forms [13–32] with the variously derivatized species [33–80], manifesting considerable bettered analytical performance characteristics, the need of derivatization proved to be evident and advantageous. The list of species reviewed in this paper, along with their abbreviations, is shown in Table 1.

2.1. Quantitation of illicit drugs in their initial forms, without derivatization (Table 2)

Proposals were sorted in line of matrices, enrichment protocols – samples were subjected to – before performing GC analyses [13–32].

Various types of solid phase microextractions (SPME) [13–23], polymer monolith microextraction (PMME) [24], solvent microextraction (SME) [25] and liquid/liquid/extraction (LLE) [26–30] were used for species enrichment. Acceptable LOQ values were obtained with SIM acquisitions [13–15,17,19,21,24,28,29]: independent on the samples' biological matrix.

Automated solid phase extraction (ASPE) followed by tandem mass spectrometry (GC–MS–MS) resulted in simultaneous analysis of COC and its metabolites in saliva [23].

The PMME process proved to be a useful tool in the quantitation of THC content in saliva [24].

SME by chloroform was suitable to detect amphetamine contents in urine, with LOD values in the range of 15–500 ng/mL, applying pulsed discharge helium ionization detection (PDHID) [25].

A simple extraction by toluene, followed by two dimensional separations (GC × GC) and a pixel based chemometric processing, led to suitable markers for future analysis of illicit drug seizures [26].

Solvent selection study for toxicological screening of urine samples revealed the optimum mixture of *n*-butyl chloride (*n*-BuCl)/*i*-propanol (*i*-PrOH) = 4/1 (v/v), resulting in excellent LOD characteristics: 1–25 ng/mL for 54 drugs [27].

LLE of A, MA, E, norE, COD, dihyCOD, COC, BE, and EME from urine and saliva [28] and six amphetamines from urine [29] were performed with *tert*.butyldimethyl ether (TBME). Quantifications, based on GC–MS-SIM acquisition protocols [28,29], resulted in poor analytical performance characteristics: chemical ionization (CI) with methanol [29] had no effect.

FA enrichment was carried out from rat plasma by *n*-BuCl extraction; quantitation with nitrogen phosphorus detection (NPD) [30] provided

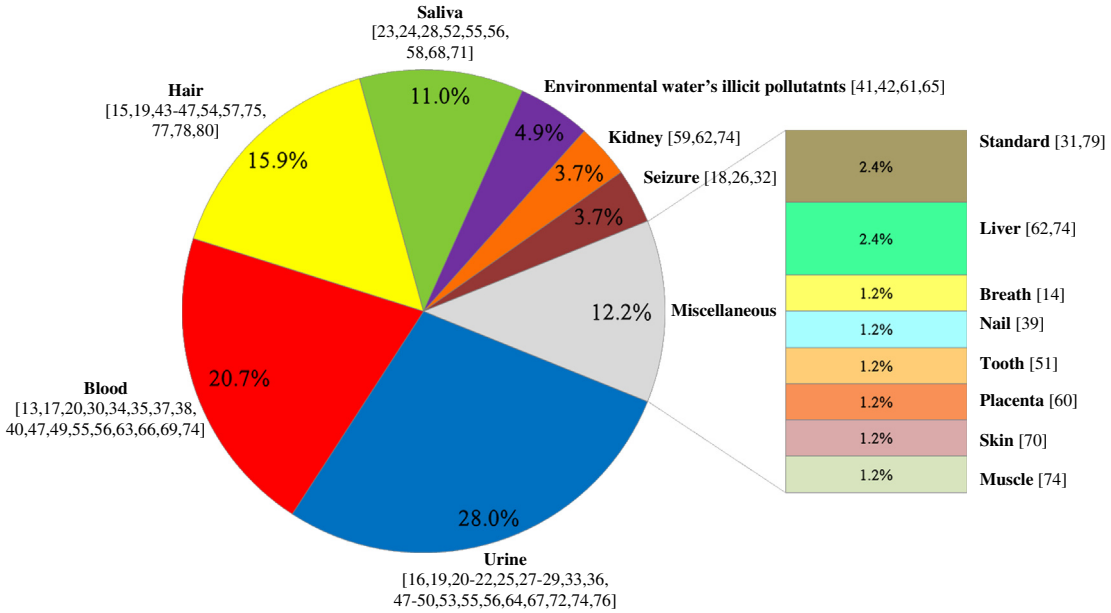

Fig. 1. Distribution of the most frequently analyzed sample types of biological and environmental matrices analyzed by gas chromatography.