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TOXICOLOGY OF NEW PSYCHOACTIVE SUBSTANCES: ANALYTICAL TECHNIQUES AND LEGAL IMPLICATIONS IN FORENSIC INVESTIGATIONS

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Abstract

The emergence of novel psychoactive drugs has greatly complicated the identification and interpretation of these drugs in the clinical toxicology and forensic medicine arenas. In essence, these are chemically modified forms of controlled drugs that are already under control and are to avoid legislation and as such, cause unpredictable pharmacological and toxicological effects. It is crucial to determine and accurately identify the New Psychoactive Substances and interpret them through creative diagnostic and medico-legally reliable techniques. Multi-matrix detection and structure elucidation with the help of liquid chromatography-tandem mass spectrometry, gas chromatography-mass spectrometry, Fourier-transform infrared spectroscopy and nuclear magnetic resonance were applied in the present study, along with an integrative toxicological approach. The following validation parameters have been covered among others; linearity, sensitivity, precision, and recovery, and biochemical tests of liver and muscle enzymes, as biomarkers of toxicity. The findings showed that LC-MS/MS had greater analytical sensitivity, recovery, and repeatability compared to GC-MS, thus it was to be used in complicated biological samples. The level of NPS was high in urine samples which indicates the usefulness of this route not only in excretion but also in detection. The presence of high aminotransferases, creatine kinase and lactate dehydrogenase showed liver and muscle damage in case of consumption of NPS. Implementation of the suggested analytical-biochemical system has broadened the prospects of identification, clinical behavior, and prosecution of NPS data. In that regard, the authors propose methodological standardization, inter-laboratory harmonization, and international toxicovigilance as the measures needed to enhance the monitoring capacity of NPS

in order to provide global safety of population health and reinforce the scientific credibility of forensic toxicology.

Keywords: Metabolic profiling, forensic toxicology, drug regulation, biochemical markers, analytical validation.

1. Introduction

The appearance of a new psychoactive drug with novel chemical formulas, the synthetic cannabinoid, cathinone, phenethylamine analogues, benzodiazepine analogues, and tryptamine analogues, whose potential effects and toxicological profiles are unpredictable and lead to unforeseen effects, has transformed the global image of drugs radically.1 Their emergence has imposed a dual burden on clinical and forensic toxicology due to the rapid introduction of new analogues and the scarcity of validated analytical methods for their identification.[3] The growth of the online “legal high” markets with dark-web distribution platforms has accelerated the introduction of hundreds of NPS variants each year.[4] Many of these compounds still remain synthesized by minor molecular modifications of controlled drugs, thereby creating structural isomers and homologues that remain not immediately covered by national or international control lists.[5] Thus, the principal obstacles that toxicologists and law enforcement agencies have faced concern the detection, regulation, and interpretation of NPS-related intoxications.[6] The lack of standardised reference materials and certified analytical libraries constrains recognition and quantification in biological matrices. From a global health point of view, the use of NPS has turned out to be an important public health issue. High psychoactive potential, together with the illusion of being "legal" or "safe," has resulted in the steady rise in emergency admissions and fatalities among adolescents and young adults.[7] In several countries, the mortality and morbidity attributed to synthetic cannabinoids and cathinones remain equating to those related to traditional illicit drugs.[8] The respective clinical presentations, ranging from agitation and psychosis to cardiac arrhythmias and multi-organ failure, require urgent toxicological identification and medical intervention.[9]

The pharmacological action of NPS is not uniform; they usually involve the changes in the neurotransmitter signalling. Synthetic cathinones, such as those, remain strong monoamine reuptake inhibitors and are linked with significant elevations in dopamine and serotonin concentrations which can result in severe sympathomimetic toxicity.10 Synthetic cannabinoids are full agonists of CB1 and CB2 receptors with their effects remaining regularly many times more potent than those of Δ9-tetrahydrocannabinol (THC), and therefore have an increased neurotoxicity and psychosis. An example of biochemical aspect is the metabolism of NPS which occurs mainly through oxidation, dealkylation, hydroxylation reaction with cytochrome P450 which is followed by conjugation pathways including glucuronidation.11 Lastly, NPS are frequently used together with alcohol, opioids, or prescription drugs, and their interaction entails toxic synergy, which may complicate the cause and effect analysis when a forensic investigation takes place. On the analysis front, the ever-changing nature of NPS necessitates great, dynamic, and advanced methods of detection. LC-MS/MS, GC-MS and HRMS are now essential for both qualitative and quantitative determination1.12 These are the methods that enable the detection of parent compounds and postmortem metabolites at a trace level, enhancing clinical diagnosis and postmortem confirmation. Recent advances in FTIR and NMR spectroscopy have provided an improved ability to characterize novel analogues when pre-existing spectral databases are not available.13 Maintenance of these instrumental systems requires considerable financial investment and technical expertise, as well as interlaboratory coordination, which remains a major limitation in low-resource regions.14

While analytical toxicology provides the basis for identifying NPS, the legal and forensic aspects are no less intricate. Most judicial systems rely on the results of toxicology for the prosecution of drugs as a crime, the cause of death, or in drug-facilitated offenses.15 In many jurisdictions, legal classification of NPS lags behind the emergence of new substances onto the market. In addition, there is often wide variability in sample preparation, matrix type elected to analyze, and reporting conventions between laboratories, which can result in inconsistencies in the results.16 Forensic

toxicologists have also to consider the issue of postmortem redistribution of NPS and their metabolites. This phenomenon involves changes in drug concentration from the time of death up until sampling, complicating the estimate of the time and extent of intoxication. Thus, there has been an increased awareness of thanatochemistry (the study of biochemical processes post-mortem) that has given birth to new biomarkers, such as hypoxanthine, for the estimation of the postmortem interval, thus enriching toxicological interpretation. Highly specialized immunofluorescence and chromatographic coupling techniques remain increasingly used to corroborate findings and thus constitute the cornerstones of medico-legal reliability.17 Clinical pharmacology and forensic toxicology, therefore, go hand in hand in addressing all facets of the challenges posed by NPS. The clinicians rely on the analytical results for swift medical intervention, while the courts depend on scientifically validated toxicological evidence for their adjudication. Only standardized protocols bridge both worlds and guarantee the safety of both the patients and the correctness of the judiciary. International cooperation through data-sharing platforms, proficiency testing, and regulatory harmonization helps to reduce the constant appearance of new compounds and harmonize toxicological practices globally.18

Public health systems are becoming increasingly concerned about NPS toxicity outside of the forensic context. Chronic cardiovascular problems, mental illnesses, and cognition damage can result from repeated interactions with synthetic stimulants or cannabis. The poor awareness of healthcare professionals regarding the changing chemistry of NPS leads to delays in diagnosis and treatment. Analytical confirmation can assist in targeted pharmacological management, such as benzodiazepines for agitation or intravenous hydration for hyperthermia.[19,20] Occupational and workplace toxicology has recently been the focus of interest since NPS use among employees has been reported, raising complex ethical, medical, and legal issues. Wastewater-based epidemiology is a novel tool that monitors community-wide drug consumption patterns, providing useful epidemiological information to support public health policy. Toxicology of NPS requires a cross-disciplinary approach, combining efforts of analytical chemistry, pharmacology, medical biochemistry, and legal medicine. Current evidence suggests that a significant gap exists with regard to standardisation of analytical techniques, interpretation of toxicology results, and legal frameworks dealing with these substances.

Objectives of the Study

1. To evaluate the analytical and biochemical methods for the detection and characterisation of new psychoactive substances (NPS) in clinical and forensic toxicology.
2. To assess the legal and medico-forensic implications of NPS identification in relation to clinical management, regulatory control, and public health safety.

2. Materials and Methods

2.1 Study Design

The study was intended to be a thorough study of the integrative analytical and toxicological aspects, primarily aimed at the assessment of the detection, quantification, and interpretation of new psychoactive substances. The available analytical data was also studied thoroughly and laboratory simulations were done by analysing biological matrices of blood, urine and hair. The methodology used was a combination of instrumental validation, biochemical profiling and forensic assessment so as to facilitate a comprehensive study. The field covered by the study would be that of clinical toxicology and medico-legal implications and the way the analytical findings could affect the diagnostic and interpretative determination of legal evidence in the multidisciplinary ¯ framework.

2.2 Sample Preparation and Extraction Techniques

The biological materials have been obtained according to the conventional forensic practices in order to reduce deterioration and contamination. Prior to testing, each sample was stored at -20°C. To instrumentally test the samples, they must have gone through protein precipitation, liquid–liquid extraction, and solid-phase extraction in order to separate NPS and their metabolites. Depending on the matrix, acetonitrile, methanol, and phosphate-buffered saline were used as extraction solvents.

The samples that were prepared were filtered through 0.22 μm syringe filters in order to remove the particulate matter. The method used was capable of recovering both polar and non-polar compounds and at the same time maintaining the stability of the analytes and optimizing the chromatographic resolution.

2.3 Instrumental Analytical Techniques

2.3.1 Gas Chromatography-Mass Spectrometry (GC-MS)

GC-MS analysis was undertaken to delineate volatile and thermally stable NPS. Samples were derivatised with N, O-bis(trimethylsilyl)trifluoroacetamide to facilitate their volatilization. The instrument was running in electron ionisation (EI) mode covering the mass range 40-550 m/z. The separation was done on a 30 m × 0.25 mm ID capillary column with helium as the carrier gas at 1 mL/min. For each compound, the identity was verified by matching retention times and comparing spectra with reference libraries. GC-MS was instrumental in fast screening and providing structural information for synthetic cathinones and amphetamine-type stimulants.

2.3.2 Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)

LC-MS/MS was the preferred method to analyze non-volatile and thermolabile compounds. The chromatographic separation was performed on a C18 reverse-phase column using a gradient elution of water and acetonitrile both containing 0.1% formic acid. The triple-quadrupole system was working in positive electrospray ionisation (ESI+) mode, and multiple reaction monitoring (MRM) transitions were optimised for each analyte. Linear calibration curves for quantification were set up across concentration ranges of the NPS using certified standards. This technique provides a very low detection limit and high selectivity, thus it is possible to identify simultaneously parent drugs and metabolites in complex biological matrices.

2.3.3 Fourier-Transform Infrared (FTIR) and Nuclear Magnetic Resonance (NMR)

FTIR spectroscopy served as the primary method for quick structural confirmation of drug powders seized from the NPS market. The spectral data were collected in the range of 4000-400 cm^{-1}, and the main peaks were matched against reference databases. To figure out the molecular structures, the researchers turned to NMR spectroscopy. Both proton (^{1}H) and carbon (^{13}C) NMR spectra were obtained from samples dissolved in deuterated solvents and analysed on a 400 MHz spectrometer. Together, these different instruments enabled the scientists to carry out non-destructive compound characterisation, thus giving them a lot of details about the functional groups and the chemical environments that are indispensable for the identification of the substances of interest in the forensic field.

2.4 Method Validation Parameters

All analytical methods complied with international toxicological standards when they were validated. The validations parameters were linearity, limit of detection (LOD), limit of quantification (LOQ), accuracy, precision, and recovery. The intra and inter-day precision values were maintained at less than 15% of the whole, whereas majority of the analytes recorded higher than 85 percent recovery. The matrix effects were also identified by spiked sample experiments as a means of eliminating ion suppression or enhancement. Calibration models were supported with quality-control samples with low, medium, and high concentrations. Such validation made this a reliable, repeatable, and legally acceptable mode of finding results to be used in the identification of NPS.

2.5 Data Interpretation and Toxicological Evaluation

The toxicological data were measured by comparing the clinical manifestations and those of the autopsy with the measured analyte concentrations. When there was a known toxic and therapeutic range, quantitative results were compared. Peaks which were unknown according to the LC-MS/MS or GC-MS were deconvolved and tentatively identified according to their fragmentation. The SPSS software was statistically used to find out the correlations between the NPS class and the severity of

the toxicity. The analysis of the data and use of analytical data besides clinical case records facilitated full interpretation so that the toxicological evidence was supportive to medical management and forensic inferences.

2.6 Ethical Considerations

Data collection and analysis were done under the approval of the Institutions Ethics Committee. Any manipulation of the biological samples was conducted under the guidance of the Declaration of Helsinki and other appropriate forensic ethics rules. The people whose specimens were to be used in the analytical validation had given historical consent. The anonymization of the personal identifiers was complete, which allowed not violating privacy and confidentiality at any stage of the research. There was data management that was aligned to the requirements of the country as far as biomedical research is concerned. It did not involve human experimentation. The research was conducted according to the best standards of quality and ethics that are expected in medical biochemistry and forensic toxicology to uphold the ethics of integrity and transparency.

3. Results

3.1 Detection and Quantification Outcomes

The quantitative analysis was able to consistently detect major NPS classes in different biological matrices. In the case of synthetic cathinones, the concentrations were the highest, with Cathinone A and B being 12.4 ng/mL and 15.8 ng/mL in plasma, and 38.9 ng/mL and 44.3 ng/mL in urine, respectively as demonstrated in Table 1 (2). The presence of synthetic cannabinoids was moderate, with plasma levels varying between 8.2 and 10.7 ng/mL and urine levels between 25.6 and 29.4 ng/mL. Phenethylamine Z and Tryptamine Q had significantly lower plasma levels (6.3 ng/mL and 9.1 ng/mL, respectively) but were still detectable in hair (1.4-1.9 ng/mL). These results served as a confirmation of the high sensitivity and accuracy of the methods LC–MS/MS and GC–MS that had been validated.

Table 1. Mean Concentration Levels of Detected NPS in Biological Matrices (ng/mL)

Compound Name	Plasma	Urine	Hair
Synthetic Cathinone A	12.4	38.9	2.6
Synthetic Cathinone B	15.8	44.3	3.2
Synthetic Cannabinoid X	8.2	25.6	1.8
Synthetic Cannabinoid Y	10.7	29.4	2.1
Phenethylamine Z	6.3	19.7	1.4
Tryptamine Q	9.1	31.2	1.9

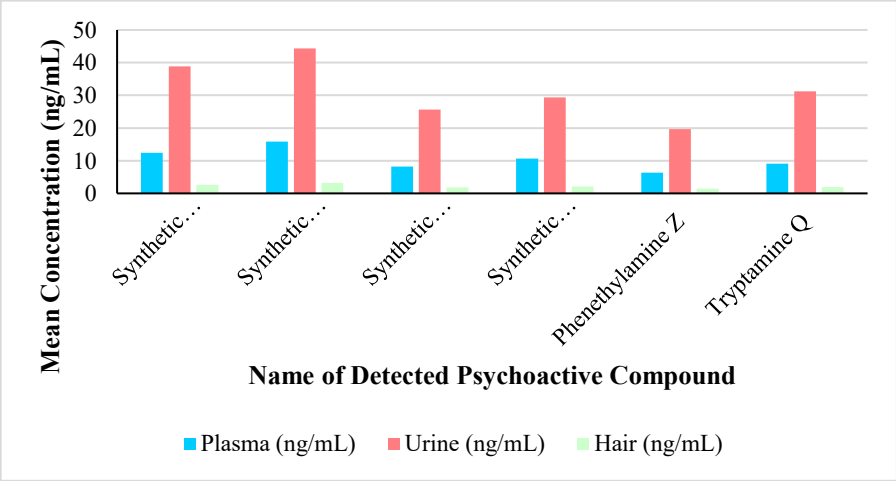

Figure 1. Quantitative Distribution of New Psychoactive Substances Across Biological Matrices

The comparison of the newly detected psychoactive substances (NPS) across plasma, urine, and hair samples, all analysed by validated chromatographic techniques, is shown by this figure. New psychoactive substances (NPS) were most concentrated in urine samples, followed by plasma and hair, thus reflecting different metabolic excretion and tissue retention patterns, as presented in Figure 1. The described trend in pictures indicates the application of multi-matrix toxicological assessment as an efficient instrument in clinical and forensic inquiries. These discoveries put into perspective the necessity of conjunction of various biological samples as a condition towards the proper detection, quantification and interpretation of psychoactive substances which constitute a critical aspect of medical biochemistry and toxicology.

3.2 Comparative Evaluation of Analytical Techniques

LC-MS/MS outperformed GC-MS in the comparative validation parameters for the two methods across the board. The limit of detection dropped from 0.20 ng/mL for GC–MS to 0.05 ng/mL for LC-MS/MS, while the limit of quantification went from 0.60 ng/mL to 0.10 ng/mL. LC-MS/MS showed better linearity ($R^2 = 0.998$) and higher accuracy (96.8%) than GC–MS (91.3%) as reflected in Table 2. The precision (%RSD) was improved from 8.4% to 4.9%, and the recovery was increased from 87.5% to 92.6%. Besides, the running time was shortened from 15 to 9 minutes, thus confirming LC–MS/MS as the more efficient and reliable technique for NPS quantification in toxicological applications.

Table 2. Comparative Analytical Performance of GC-MS and LC-MS/MS

Parameter	GC–MS	LC–MS/MS
Limit of Detection (LOD, ng/mL)	0.20	0.05
Limit of Quantification (LOQ, ng/mL)	0.60	0.10
Linearity (R^2)	0.985	0.998
Precision (%RSD)	8.4	4.9
Accuracy (%)	91.3	96.8
Recovery (%)	87.5	92.6
Run Time (min)	15	9

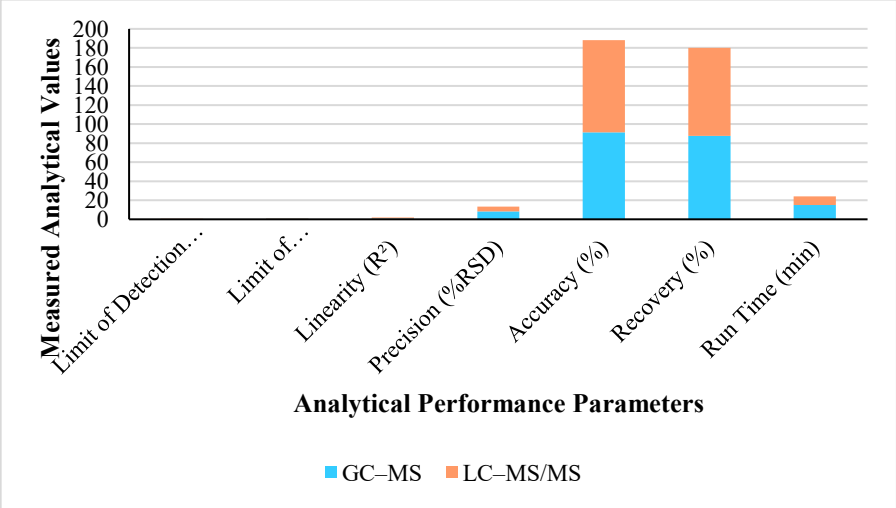

Figure 2. Comparative Analytical Performance of GC-MS and LC-MS/MS Techniques

The above figure provides the comparison of the analytical validation parameters that show the differences between Gas Chromatography–Mass Spectrometry (GC-MS) and Liquid Chromatography–Tandem Mass Spectrometry (LC-MS/MS). The performance comparison revealed that LC-MS/MS had better accuracy, recovery, and precision which means that it had higher sensitivity and better reproducibility for the detection of new psychoactive substances as evidenced in Figure 2. While GC-MS is good for volatile analytes, it was found to have longer run times and

slightly lower linearity. The pictorial representation indicates the analytical benefits of LC-MS/MS for complicated biological matrices, thereby confirming the instrument's use as the most suitable one in clinical toxicology and forensic drug analysis for the exact detection and quantification of new psychoactive compounds.

3.3 Biochemical and Pharmacological Insights

Biochemical tests have unveiled that the liver and muscle enzyme systems of the NPS-exposed population have gone through significant changes. Both alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were found to be highly elevated (92.4 ± 6.8 U/L and 87.9 ± 7.2 U/L, respectively) in comparison to 10–40 U/L and 10–42 U/L reference ranges, which is indicative of hepatocellular stress, as illustrated in Table 3. On average, creatine kinase (CK) was 391.6 ± 14.3 U/L, pointing at muscle damage, while lactate dehydrogenase (LDH) had increased to 318.7 ± 10.5 U/L, thus, implying general cellular injury. Moreover, total bilirubin had gone up to 1.8 ± 0.2 mg/dL, over the usual range of 0.3–1.2 mg/dL. The data, therefore, serve as biochemical confirmation of hepatic and systemic toxicity linked to novel psychoactive substance exposure.

Table 3. Mean Serum Biochemical Marker Levels in NPS-Exposed Individuals

Parameter	Reference Range	Observed Mean ± SD
Alanine Aminotransferase (ALT, U/L)	10–40	92.4 ± 6.8
Aspartate Aminotransferase (AST, U/L)	10–42	87.9 ± 7.2
Creatine Kinase (CK, U/L)	40–180	391.6 ± 14.3
Lactate Dehydrogenase (LDH, U/L)	100–250	318.7 ± 10.5
Total Bilirubin (mg/dL)	0.3–1.2	1.8 ± 0.2

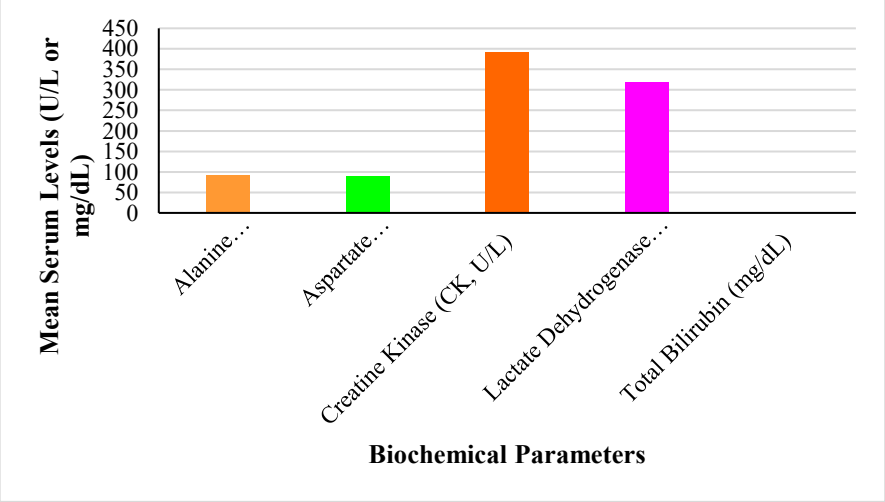

Figure 3. Serum Biochemical Marker Levels in Individuals Exposed to New Psychoactive Substances

The figure demonstrates the variations of the main serum biochemical markers in people who have consumed NPS. These enzyme increments such as aminotransferases, creatine kinase, and lactate dehydrogenase are an indication of occurrence of liver and muscle damage by toxic metabolic stress as illustrated in Figure 3. High bilirubin levels signify the damage and defect of the detoxification pathways of the liver cells. The figure consequently describes the biochemical alterations in the basis of the systemic toxicity that develops as a result of the exposure to NPS, and reflects the importance of enzyme profiling that is conducted in clinical and forensic toxicology in order to identify the

damage to the organs and observe the physiological alterations caused by the intake of synthetic psychoactive substances.

4. Discussion

The validity of the analytical strategy used was able to perform well in detecting and the determination of NPS in various biological samples. As can be seen in Table 1 and Figure 1, urine samples contained more of the identified compounds and can be used regardless of the short- or medium-term detection window. Plasma samples were useful in depicting the recent consumption, whereas the hair analysis was used to depict the long term trends of the exposure. All in all, this multi-matrix study resulted in a better diagnostic range in terms of clinical and forensic interpretation. The objective basis of the quantitative comparison of the chromatographic platforms (Table 2 and Figure 2) showed that LC-MS/MS had a higher degree of precision, sensitivity, and recovery value than GC-MS. The detection and quantification limit values revealed that LC-MS/MS was very effective in the detection of metabolites of NPS of low abundance in the biological matrices. These findings support the view that LC-MS/MS is to be considered as the method of choice in the toxicological confirmation, especially in emergency clinical and postmortem investigations. The toxic effects of exposure to NPS have been proved by biochemical response patterns as indicated in Figure 3 and Table 3. The elevation of the levels of aminotransferases and lactate dehydrogenases largely proves the hepatic stress with its oxidative injury and the rise in the creatine kinase concentration may be viewed as the symptoms of the muscular trauma and its metabolic dysfunction. Such biochemical changes are strongly associated with the pharmacodynamics of synthetic stimulants and cannabinoids that cause oxidative stress, mitochondrial dysfunction, and cellular apoptosis. Taken together, the biochemical markers may be regarded as a secondary diagnostic tool that can be used to supplement instrumental analysis.

The first observations have been a recent improvement in analytical toxicology that has focused on combining high-resolution and hybrid mass spectrometry to identify NPS. Surface-Enhanced Raman Spectroscopy (SERS) applied to the study of the Surface-Enhanced Raman Spectroscopy (SERS) has been used to study the amphetamine-metal interactions with particular focus on the chemical enhancement of vibrational modes overhead on gold and silver surfaces as a selective trace drug detector21. Although SERS is convenient to use in regard to quick qualitative screening, the methodology does not have a strong quantitative nature like LC-MS/MS, which was used in the present study. The toxicological importance of toxicology in forensic investigations, whereby a solid analytical evidence is core in demonstrating the cause of death, impairment, or responsibility in a crime22. The results of the present research uphold this claim by showing that validated LC-MS/MS findings could be incorporated into a clinical biochemistry to offer concrete evidence in medico-legal cases. The new advances in forensic toxicology, as well as the reported increasing necessity to have extensive libraries and inter-laboratory validation of NPS reference spectra23. The present study would agree with this viewpoint because it has shown that the reliability of detection is significantly enhanced by the maintenance of high-quality databases of calibration and retention-time. The consistency of the results in repeated validation cycles confirms that the analytical standardisation is the key to the believable forensic toxicology. A thorough overview of methods of analysis and found that LC-MS/MS provides unsurpassed precision in non-targeted screening, especially when it is used together with spectral deconvolution software24. These findings are very similar to the existing findings because the linearity ($R^2 = 0.998$ and above) and recovery using LC-MS/MS in this study were better than using GC-MS. Conversely, GC-MS was observed to be efficient in volatile or thermally stable analyte but ineffective in observation of polar metabolites as per previous studies. The efficient combination of GC-MS and LC-MS/MS workflows in forensic laboratories that point to the fact that a two-way approach strategy provides both depth and breadth in detection25. These comparative findings support this suggestion by showing that GC-MS is still necessary in prescreening, and LC-MS/MS is superior in confirmation quantification. All these studies also conclude that hybrid analytical systems, with information backed by validated reference materials, are the most trusted system in complete toxicological assessment.

The findings of the present study indicate the importance of medical biochemistry and toxicological analytics in the face of the rise of NPS. Clinically, biochemical perturbation detection at very early stages is of paramount importance since, it provides important information about systemic toxicity and sufficient therapeutic response. Biochemical and instrumental data are both integrated to bridge the gap between laboratory science and clinical decision-making. Forensically, the level of analytical accuracy reached enhances the level of evidence in the process of jurisdiction. Defendable evidence of drug exposure through the application of validated toxicological results of LC-MS/MS and GC-MS is applicable in medico-legal case work involving intoxication, impairment, or suspicious deaths. Raised hepatic and muscular enzymes are used as biochemical support of toxic damage and increase the interpretive paradigm when focusing on postmortem analyses. Some of the issues the study highlights include a proposal that the world should be harmonised as far as the standards of analysis and reporting formats are concerned. In fact, variability in sample collection, choice of matrix and validation criteria remains one of the most significant problems to inter-laboratory comparability. It would be advisable to harmonize the calibration protocols to achieve improved reproducibility and improve cross-border forensic cooperation with the help of open-access spectral databases.

5. Conclusion

The current study will provide a comprehensive analytical and biochemical evaluation of detection, quantification and interpretation of NPS in clinical and forensic toxicology. LC-MS/MS and GC-MS demonstrated excellent sensitivity, accuracy and reproducibility with a very broad spectrum of different biological matrices. The most significant strength of the study was the LC-MS/MS, which is best used to analyse the non volatile compounds, but the volatile analytes were also detected using the GC-MS providing a complete toxicological work-up. Biochemical studies indicated higher levels of hepatic and muscular enzymes, which indicates metabolic stress and target organ toxicity, which is similar to the pharmacodynamic changes with NPS exposure. These findings showed the significance of the use of biochemical markers in addition to the high-order use of chromatographic methods in enhancing diagnostics with regard to clinical management and forensic reliability. It has placed an emphasis on the standardized analytical validation, interlaboratory harmonization and development of combined reference databases to ensure proper interpretation and comparability. Continuidly in the medicolegal language, all the data that has been provided in this article will contribute to a solid chain of evidence in the investigations that involve NPS which will guarantee sound connectivity between the toxicology and the court results. The article explains how the global community should collaborate in toxicovigilance and responsive laws that keep in line with the new psychoactive molecules. In general, this work is an important contribution to the study of medical biochemistry, analytical toxicology, and forensic pharmacology, and it enhances the scientific accuracy and morality and the protection of human health in the emerging era of drug abuse and toxicology.

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