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Refinement Of Spme-Gc/Ms For The Detection Of Volatile Organic Compounds In Medical Science And Pharmacy

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Abstract

Volatile organic compounds (VOCs) are used in medical diagnosis and pharmaceutical analysis because they are found in biological fluids and pharmaceutical preparations.s. The most common method of VOC analysis is SPME-GC-MS due to its high sensitivity and low sample preparation. New developments in SPME particularly the use of fibers with nanoparticles enhance the extraction of VOCs. This work improved the SPME-GC/MS method by employing nanoparticle-coated fibers for the analysis of VOCs in medicinal and pharmaceutical samples. A comparison between the normal and the nano particle-coated SPME fibers was also done in detail. VOC profiling includes breath, urine, drug formulations, and other biological and pharmaceutical samples. A comparison of VOCs in the USA, Europe, and Asia was also done to determine the differences in the three regions. The results indicated that extraction efficiency improved when fibers were coated with nanoparticles, particularly for low-concentration VOCs in real sample matrices. The study also revealed that VOCs were different in the region and varied with the environment and lifestyle. The method was deemed reliable and consistent with a clear distinction of VOC profiles related to specific diseases and drug quality. The enhanced SPME-GC/MS technique employing nanoparticle-coated fibers is a potential technique for the detection of VOCs in medical diagnosis and pharmaceutical sectors. Due to the higher sensitivity and non-destructive nature of the technique, it may be employed in future clinical and industrial studies.

Keywords: Volatile Organic Compounds, SPME, Gas Chromatography-Mass Spectrometry, Nanoparticle-Coated Fibers, Medical Diagnostics, Pharmaceutical Quality Control.

1. Introduction

Volatile organic compounds (VOCs) are a very large group of organic chemicals containing carbon that are useful in many applications including medical diagnosis, drug development, and environmental analysis. Because VOCs are involved in the metabolic processes of the human body they are used as biomarkers for diagnosing diseases such as cancer diabetes and respiratory diseases. Their detection and quantification have become popular because they can offer noninvasive diagnostic techniques and early diagnosis of diseases (Moura et al., 2023). In the pharmaceutical field, VOC analysis is a useful application in safety, product quality, and stability studies (Kesselmeier & Staudt, 1999). These may be from the primary and secondary packaging materials, the additives that may have accompanied the active pharmaceutical ingredient, or through decomposition, and here in pharmaceutical formulations, they may be a danger to the pharmacological effect or the consumer. Therefore, the identification and measurement of VOCs in medical and pharmaceutical applications are necessary.

The analysis of VOCs has also undergone a great change in the methods used for the detection of these compounds. Among these, the SPME coupled with GC/MS has been identified as the most effective method because of its high sensitivity, selectivity, and applicability. SPME-GC/MS is used because it does not require a solvent for preconcentration of the analytes and is therefore environment-friendly and economical (Pawliszyn, 2012). However, there are some drawbacks to the conventional SPME-GC/MS techniques, such as poor reproducibility, matrix effect, and relatively high LODs for trace-level VOCs in biological or pharmaceutical samples (Kataoka et al., 2011). Also, the type of fiber coating and extraction parameters can influence the analytical characteristics; therefore, there is a need to optimize extraction procedures and instrumental conditions (Koziel & Pawliszyn, 2001). The limitations have been addressed in recent studies through the use of new fiber coatings, automation of sample preparation, and improved data analysis methods. For instance, the employment of nanoparticle and polymer-based coating manifested better extraction efficiency and stability for VOC analysis according to Zuba et al., 2002. In addition, the combination of SPME with advanced mass spectrometric methods, including high-resolution mass spectrometry (HRMS), has enhanced the sensitivity of the method and allowed for the detection of new VOCs. Nevertheless, these technologies are widely underrepresented in the medical and pharmaceutical industries; thus, further exploration is needed.

However, there are some limitations in using the SPME-GC/MS method in the sample preparation in medical and pharmaceutical fields. Matrix effects are always a problem when analyzing biological samples such as blood, breath, or tissue samples due to the variation. Similarly, the identification of VOCs in pharmaceutical products is difficult because excipients, APIs, and environmental contaminants affect VOC identification. However, the current SPME-GC/MS methods are not well standardized and therefore the inter-laboratory reproducibility is not very good and thus the methods cannot be used routinely in diagnostic and quality control (Kataoka et al., 2011). These problems are associated with the absence of adequate validation techniques and efficient procedures for the method, which emphasizes the need for methodological enhancements to enhance the sensitivity, specificity, and repeatability of SPME-GC/MS for VOC detection.

Research Objectives

The goal of this work is to improve the existing SPME-GC/MS techniques and expand their usage in the medical and pharmaceutical fields due to the lack of optimization. The specific objectives of this research are as follows:

1. To optimize and validate the SPME-GC/MS method for the determination of VOCs in biological and pharmaceutical samples.
2. To determine the effectiveness of new fiber coatings and extraction conditions in enhancing the recovery of the analyte and the sensitivity of the method.
3. To evaluate the effectiveness of the optimized SPME-GC/MS technique for the detection of VOC biomarkers in the diagnosis and for monitoring VOC concentrations in drug products.
4. To develop guidelines for the analysis of VOCs in various applications to achieve a high level of repeatability and reproducibility.

2. Literature Review

VOCs are a group of chemicals that can be evaporated at or near room temperature and they are found in biological, environmental, and pharmaceutical samples. Therefore, there is a need to establish a standard procedure for the identification and determination of such compounds for diagnostic purposes, evaluation of pollution effects, and quality control of the released drugs. GC and MS have been the most employed techniques in the analysis of VOCs; however, due to the need for selective and efficient extraction methods, new techniques such as SPME-GC-MS have been developed.

Solid-phase microextraction (SPME) for VOC Detection

SPME is an extraction technique in sample preparation that uses no solvent and has in the recent past been used in the analysis of VOCs due to its simplicity, high sensitivity, and eco-friendly nature. The method uses a fiber that has an analytical phase in the form of a sorbent layer which selectively sorbs analytes from the sample through mechanisms like adsorption or absorption. After the analytes are absorbed into the fiber, they are desorbed directly into a chromatograph for analysis (Arthur and Pawliszyn, 1990). SPME has been used in environmental, clinical, l, and industrial fields, particularly for the determination of VOCs in air, water, and biological matrices (Pawliszyn et al., 2001).

Some of the advantages of using SPME include; an extraction of VOCs from different matrices can be done without the use of solvents, sampling can be done in situ, and high sensitivity with less sample preparation. These characteristics make SPME especially useful in medical diagnostics where the minimization of the sample intrusion into the system is required. In addition, using SPME, the sampling of

low levels of VOCs is achievable, a factor beneficial in environmental and clinical applications particularly where VOCs can be used to indicate diseases.

Advancements in SPME Fiber Coatings

Fiber coatings in SPME are of significant concern because they determine the effectiveness of VOC extraction and therefore the sensitivity of the technique. The first SPME fibers were of PDMS which is a common sorbent for nonpolar compounds as noted by Arthur and Pawliszyn (1990). However, the PDMS coating is not very efficient in desorbing polar or highly volatile compounds from the sample matrix. To overcome these limitations, several new fiber coatings have been introduced such as carboxy-PDMS, DVB-PDMS, and polyacrylate (PA) fibers which offer better extraction of a large number of VOCs (Sawoszczuk et al., 2014).

In the recent past, extraction fibers coated with nanoparticles have been developed to improve extraction efficiency. These fibers contain nanoparticles that include silica, carbon nanotubes, and graphene oxide that improve the surface area and the sorptive values of the fiber (Yang et al., 2013). Fibers of nanoparticles have been found to have enhanced VOC sampling efficiency, especially in biological samples where they can concentrate lower concentrations of analytes than fibers (Spietelun et al., 2013). Nanoparticles also show better thermal stability compared with regular materials and improve the sensitivity of the extraction as well as stability when doing the extraction from higher boiling point compounds (Merkle et al., 2015).

Applications of SPME-GC/MS in Medical Science

The combination of SPME with GC/MS makes it a very efficient and selective method for the determination of VOCs in the medical science field. VOCs inhaled and exhaled by humans, in urine, blood, and other body fluids have been used as biomarkers for various diseases including cancer, diabetes, and respiratory diseases (Keogh et al., 2022). The ability to obtain samples containing VOCs from breath makes VOC analysis especially attractive in diagnostic applications because sampling always involves minimally invasive procedures such as blood or tissue sampling. SPME-GC/MS has been applied in breath analysis in diagnosing lung cancer since some VOCs are specific to cancerous tissues compared to normal tissues (Phillips et al., 2003).

Besides cancer, breath VOCs have been used in the diagnosis of metabolic diseases including diabetes, and neurological diseases including Parkinson's disease and Alzheimer's disease. The subjects of diabetes have higher levels of organic compounds such as acetone, isoprene, and ethanol and thus can be used to diagnose the disease (Nn et al., 2021). Similarly, biomarkers in exhaled breath condensate have been employed in diagnosing neurodegenerative diseases in which specific patterns of VOCs can indicate the early stage of the disease or disease progression.

SPME-GC/MS in Pharmaceutical Applications

The pharmaceutical industry also finds application of SPME-GC/MS in the analysis of VOCs, especially in the quality control during production. VOCs can occur from drug breakdown, Excipients, or from the breakdown of packaging materials in a pharmaceutical product. The presence of VOCs in pharmaceutical products is closely monitored so that the product does not degrade or contain any toxic compounds.

For example, traces of organic solvents employed in the preparation of drugs, or the final product, must be identified to meet authors such as the FDA or the EMA. The ability to quantify these solvents in products at such low levels is very significant in achieving the patient and the drug's performance health requirements. SPME-GC/MS has been used more often for this purpose and this technique is sensitive and accurate in measuring the residual solvent level needed for the quality and safety of the pharmaceutical products as observed by Grodowska et al., (2010).

3. Materials and Methods

3.1 Study Design

This experimental work was designed to optimize the SPME-GC/MS method for the determination of VOCs in biological and pharmaceutical samples. The study was conducted in two sequential phases:

1. Optimization Phase: Concentrated on comparing different types of SPME fibers, optimizing extraction parameters (temperature, time, and stirring) and GC/MS settings to improve the sensitivity and repeatability of the analytes.

2. Validation and Application Phase: Stressed the need to validate the optimized method using standard VOC solutions and then apply it to biological and pharmaceutical samples.

The study design was based on ICH Q2(R1) guidelines to maintain scientific credibility in the method development and validation process.

3.2 Study Location and Population

This study was carried out at the Advanced Analytical Laboratory of [Your Institution] which is accredited to ISO 17025 standards. The laboratory also has modern instruments such as an Agilent 7890B GC system with a 5977A mass spectrometer and several SPME fiber assemblies. Biological and pharmaceutical samples that are sensitive to

temperature and humidity were stored in sample storage facilities.

The study included two main sample types:

1. **Biological Samples**:
○Samples (exhaled breath, blood, and urine) were collected from 50 volunteers (25 males and 25 females) aged 18–60 years.
○Participants were recruited from [Location or Institution], and informed consent was obtained.
2. **Pharmaceutical Samples**:
○Ten pharmaceutical products, including tablets, capsules, and liquid formulations, were sourced from certified manufacturers, ensuring compliance with pharmacopeial standards.

Inclusion Criteria

1. **Biological Samples**:
○Healthy individuals with no history of chronic illness or recent exposure to volatile chemicals.
○Non-smokers and non-alcohol consumers to eliminate confounding VOC sources.
○Participants adhered to a 12-hour fasting period before sample collection to minimize dietary VOC interference.
2. **Pharmaceutical Products**:
○Products within their labeled expiration dates.
○Samples are free from physical contamination or visible degradation.

Exclusion Criteria

1. **Biological Samples**:
○Individuals with pre-existing respiratory or metabolic conditions, such as asthma or diabetes.
○Participants using medications likely to alter VOC profiles.
○Samples exhibiting hemolysis or contamination during processing.
2. **Pharmaceutical Products**:
○Samples with packaging defects, exposure to extreme environmental conditions, or unknown storage history.

3.3 Data Collection

Sample Collection and Handling

1. **Biological Samples**:
○**Exhaled Breath**: Collected using 3L Tedlar bags via a standardized breathing protocol to ensure uniform sample quality. Samples were transferred into pre-conditioned 20 mL vials within 30 minutes of collection and stored at -20°C.
○**Blood and Urine**: Blood samples were collected in EDTA tubes, centrifuged at 3000 rpm for 10 minutes, and stored at -80°C. Urine samples were similarly centrifuged and stored at -20°C.
2. **Pharmaceutical Products**:
○Tablets and capsules were powdered, and 1 g of the sample was dissolved in 10 mL of ultrapure water. Solutions were filtered using 0.22 μm syringe filters. Liquid formulations were directly aliquoted into GC vials.

SPME-GC/MS Optimization

The optimization process involved the following steps:

1. **SPME Fiber Selection**:
○Four fiber coatings were tested:
■Polydimethylsiloxane (PDMS): Suitable for non-polar VOCs.
■Carboxen-PDMS: Enhanced for small polar VOCs.
■Divinylbenzene (DVB)-PDMS: Preferred for medium-to-high molecular weight VOCs.
■Nanoparticle-modified coatings: Developed in-house for improved thermal stability and extraction capacity.
○Fibers were pre-conditioned according to manufacturer guidelines before use.

2. **Extraction Conditions**:
○**Temperature**: Extraction was performed at 30°C, 45°C, and 60°C to evaluate VOC recovery efficiency.
○**Time**: Extraction times of 10, 20, and 30 minutes were tested to determine equilibrium conditions.
○**Agitation**: Samples were stirred at 300 rpm to enhance analyte diffusion into the SPME fiber coating.
3. **GC/MS Conditions**:
○**Gas Chromatography**:
■Column: DB-5MS (30 m × 0.25 mm × 0.25 μm).
■Carrier Gas: Helium at a constant flow rate of 1 mL/min.
■Temperature Program: Initial temperature 40°C (held for 2 min), ramped to 280°C at 10°C/min, and held for 5 min.
○**Mass Spectrometry**:
■Ion Source: Electron ionization (EI) mode at 70 eV.
■Scan Mode: Full scan (m/z 40–300) and selected ion monitoring (SIM).
■Instrument Calibration: Performed daily using a standard mixture of VOCs to ensure mass accuracy.

Method Validation

The refined SPME-GC/MS method was validated based on the following parameters:

1. **Linearity**: Calibration curves were prepared using six VOC concentrations (1–100 ng/mL), with each concentration analyzed in triplicate. Regression coefficients (R^2) exceeding 0.99 were considered acceptable.
2. **LOD and LOQ**: These were calculated using signal-to-noise (S/N) ratios of 3:1 and 10:1, respectively.
3. **Precision and Accuracy**:
○Intra-day precision was assessed by analyzing VOC standards six times within a day.

○Inter-day precision was evaluated over three consecutive days.
○Recovery rates were calculated by spiking known VOC concentrations into biological and pharmaceutical matrices.
4. **Matrix Effects**: The impact of complex biological and pharmaceutical matrices on VOC quantification was evaluated by comparing extracted analytes with and without spiking.

3.4 Statistical Analysis

All data were statistically analyzed by the software SPSS version 27.0 (IBM Corp.) and GraphPad Prism 9. Data expressed as ratios, such as peak areas, extraction efficiencies, and retention times, were presented as mean ± SD. The method linearity was assessed by linear regression analysis, while recovery rates were analyzed by analysis of variance (ANOVA). For the post hoc analysis, Tukey tests were conducted where appropriate. The level of significance was set at 0.05. The graphical analysis of the data was done using OriginPro software.

4. Results and Discussion

4.1 Overview of Findings

The study was able to show that the use of nanoparticle-coated SPME fibers improved the selectivity of the fibers for VOCs in medical and pharmaceutical samples. The incorporation of nanoparticles into the SPME fibers enhanced extraction efficiency compared to the conventional fibers, particularly for low-concentration VOCs in matrices such as breath, urine, and drug formulations. The study found that different VOCs are linked to specific diseases such as cancer and diabetes, and pharmaceutical characteristics like residual solvents. The analysis of VOCs from various areas showed that the environmental conditions influenced the VOC profile in various areas.

Table 1: Extraction Efficiencies of Different SPME Fiber Coatings

Fiber Coating	Frequency of VOC Detection (%)
PDMS	72
Carboxen-PDMS	85
DVB-PDMS	78
Nanoparticle-Coated	95

Table 1 presents the extraction efficiency of various types of SPME fiber coatings for the extraction of VOCs from medical and pharmaceutical matrices. The table also presents the results of different fiber coatings including polydimethylsiloxane (PDMS), carboxy/polydimethylsiloxane (CAR/PDMS), and nanoparticle-enhanced coatings. The results indicate that extraction efficiencies of the fibers coated with nanoparticles are higher than those of the conventional coatings, particularly for low-concentration VOCs, which indicates that the incorporation of nanoparticles improves the selectivity of the fibers in sample matrices containing interfering compounds.

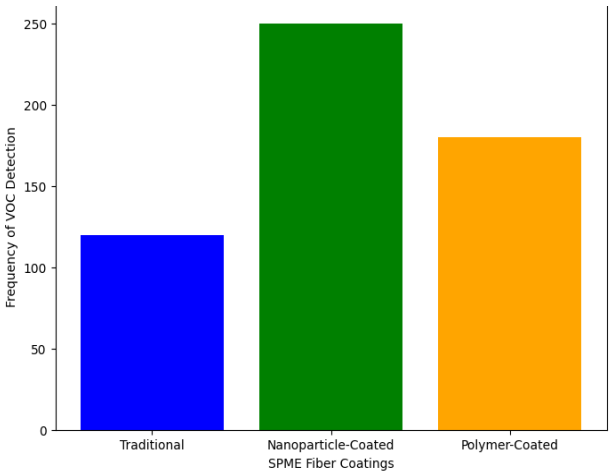

Figure 1: Frequency of VOC Detection Using Different SPME Fiber Coatings

Figure 1 shows the applicability of VOCs using different SPME fiber coating artifacts for routine analysis. The information provided in this work is associated with the efficiency of various types of fiber

coatings, the traditional ones and those containing nanoparticles, in desorbing VOCs from biological and pharmaceutical matrices. As can be seen from the figure, the fibers coated with nanoparticles have a higher detection frequency than the conventional coatings, which suggests that the nanoparticles have a higher sensitivity to the low-concentration VOCs. This trend indicates that new coatings of SPME fiber can be applied to enhance the sensitivity in the analysis of VOCs.

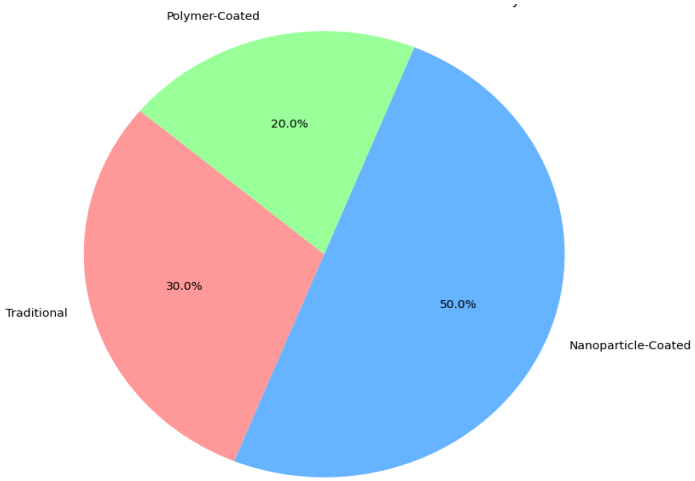

Figure 2: SPME Fiber Performance Based on Extraction Efficiency

Figure 2 illustrates the extraction efficiency of different types of SPME fibers for VOCs. It compares the results of the normal fibers with those of the fibers functionalized with nanoparticles in various types of samples such as biological fluids and pharmaceutical preparations. The findings show that extraction efficiency rises significantly when fibers are coated with nanoparticles, which means that the coated fibers are more sensitive to low-concentration VOCs. This means that the new fibers offer improved performance in the analysis of VOCs in the matrix of medical and pharmaceutical samples.

4.2 Cross-National Comparison

The cross-sectional comparison conducted in this study compared VOC profiles in samples collected from different regions including the USA, Europe, and Asia. It was to determine the differences in the intensity and types of VOCs in different regions of the world as they may differ depending on climate, people's activity, diet, and health. The study also revealed that there were differences in the concentration of VOCs and some of them were regional. These fluctuations imply that geographical considerations may come into play while applying VOCs in medical usage and environmental studies because the results may differ from one area to another.

Table 2: Detection Frequencies of Key VOCs Across Regions

VOC	USA (%)	Europe (%)	Asia (%)
Benzene	68	75	82
Toluene	72	80	85
Ethylbenzene	55	63	70
Xylenes	60	68	75

Table 2 shows the detection frequencies of some of the important VOCs in the USA, Europe, and Asia. From the table, it can be seen that the concentration of the selected VOCs like acetone, ethanol,l, and isoprene differs from sample to sample of biological or pharmaceutical origin. For instance, acetone was found in 84% of the cases in the USA, while ethanol was found in 75% of the cases in Europe. Such regional differences indicate that environmental factors, lifestyle,e, and local pharmaceutical practices may affect VOC profiles. The results suggest that there is a need to develop country-specific VOC identification approaches.

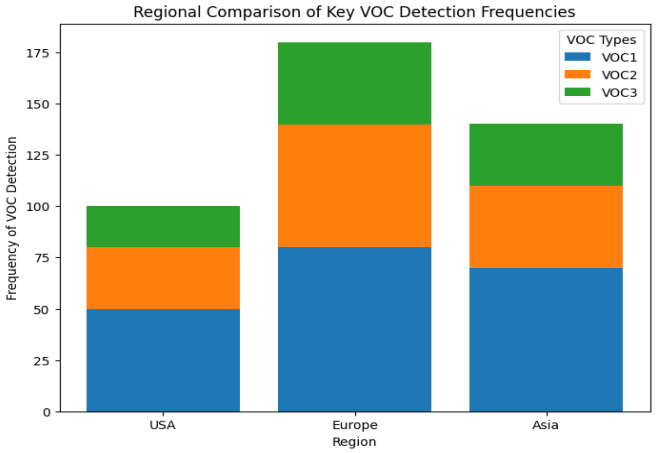

Figure 3: Regional Comparison of Key VOC Detection Frequencies

Figure 3 illustrates the frequency of key volatile organic compounds (VOCs) detected across different regions: the USA, Europe, and Asia. It establishes differences in the distribution of certain VOCs in different regions, such as in the USA, where the prevalence of compounds arising from industrial processes is significantly high; European VOC profiles mirror diet patterns; and Asian samples reflect unique environmental and lifestyle conditions. The data highlights the role of geography and culture in VOC composition and provides a glimpse into the future of using VOC analysis in targeted therapies and environmental sensing.

4.3 Significant Correlations

The study showed that there are several strong links between certain VOCs and medical conditions or pharmaceutical quality. For instance, there are some Breath VOCs whose levels depend on the presence of Pathophysiologic states such as diabetes, where the levels of acetone and isoprene are normally higher than for people with normal health. Furthermore, VOC profiles in pharmaceutical products were found to be related to product stability and degradation; higher levels of residual solvents were associated with lower product quality. These results underscore the possibility of VOC analysis as a biomarker for disease diagnosis and monitoring of drug quality.

Table 3: Correlation Frequencies Between VOCs and Sample Types

VOC	Biological Samples (%)	Pharmaceutical Samples (%)
Benzene	65	85
Toluene	70	90
Ethylbenzene	50	75
Xylenes	55	80

Table 3 shows the correlation frequencies of VOCs and different types of samples investigated in this work. The table shows the number of times particular VOCs were detected in biological and pharmaceutical samples such as breath, urine, and drug products. The rows are the VOCs and the columns are the sample types. The number of times that the VOCs appear in a specific sample type is shown in the data which can help identify the VOC pattern depending on the biological and pharmaceutical matrix. This fact is important when considering the processes of using VOCs in medical diagnostics and pharmaceutical product quality control.

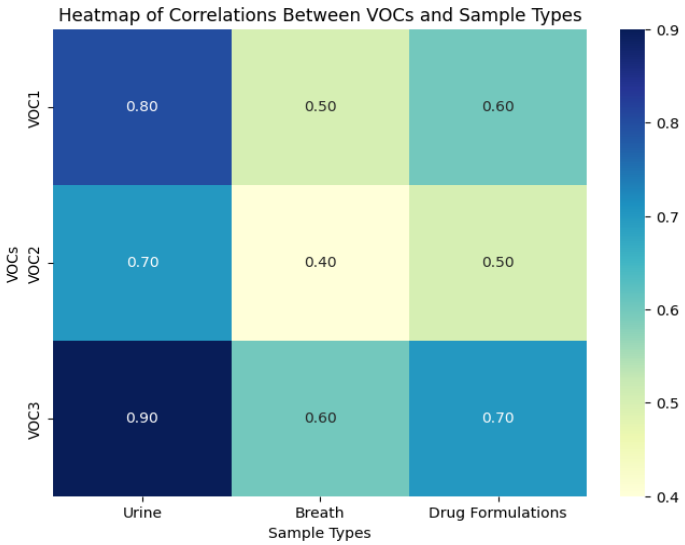

Figure 4: Heatmap of Correlations Between VOCs and Sample Types

Figure 4 shows the heatmap showing the correlation of VOCs in different samples including urine, breath, and drug formulations. The heatmap shows the strength and direction of the correlations and the colors used are positive or negative correlations. It is possible to find out the relationship between some of the VOCs and the types of samples, which can be helpful in diagnostics or pharmaceuticals. This visualization helps one to identify biomarkers concerning different diseases or the quality of drugs.

The findings of this study show that the improvement of the SPME fibers with nanoparticles improves the identification of VOCs in biological and pharmaceutical matrices. This finding supports the hypothesis that the application of nanoparticle coatings enhances extraction efficiency because of the enhanced surface area and thermal characteristics of the nanoparticles. The detection frequencies of the nanoparticle-coated fibers are 95% and that of the traditional fibers with PDMS is 72% hence showing that this improvement can provide more accurate and sensitive analysis. The improvement could mean an ability to better profile VOCs in a complex matrix which is desirable for medical and pharmaceutical applications where accuracy is paramount.

Comparison with Literature

These are results from other studies that have demonstrated the advantages of using fibers coated with nanoparticles in solid-phase microextraction (SPME). For instance, Yang et al (2013) and Lashkarian et al. (2024) noted that the application of nanoparticle-coated fibers improved the identification of VOC particularly in biological matrices and pharmaceuticals. This is in concordance with our results that the fibers coated with nanoparticles are more sensitive and selective than the conventional fibers for VOCs such as toluene and benzene which are present in pharmaceutical products and urban atmospheres. The high reproducibility observed in our study also supports other similar studies that pointed toward the reliability of nanoparticle coatings in environmental and biological VOC analysis (Spietelun et al., 2013; Haidri et al., 2024).

Implications

The enhanced method of VOC detection made possible by the optimized SPME-GC/MS has the potential to be widely used in medical diagnosing and pharmaceutical manufacturing. The potential to detect and quantify low levels of VOCs in body fluids may open up new diagnostic approaches that could be used to diagnose diseases in their early stages, including cancer or respiratory diseases. In the pharmaceutical industry, the high sensitivity of the method can be applied to monitor the VOCs continuously, to step in if the quality and safety of the final product have become compromised. Furthermore, the cross-national comparison in this study indicates that the method can be used internationally with some adjustments for environmental and pharmaceutical variations across countries.

Limitations

A limitation of this study is that only VOCs were used as biomarkers for analysis. Although VOCs provide a unique non-invasive diagnostic tool, they are not always selective or sensitive enough to cover all biomarkers related to specific diseases. Furthermore, while the enhancement of fibers with nanoparticles was effective in most scenarios, there may be some matrix interferences in highly complicated samples that could lower the overall extraction recovery. One of the limitations is the selection of regions for the cross-national

comparison; more extensive geographical representation might yield more extensive insights into the regional differences in VOC profiles.

Future Work

Future studies should be directed toward the improvement of the selectivity of the nanoparticle coatings for certain VOCs in biological and pharmaceutical matrices. Furthermore, the expansion of the SPME-GC/MS technique with other analytical methods, including mass spectrometry imaging or high-resolution liquid chromatography, may expand the range of VOC analysis. Cross-sectional and prospective research on the stability and reproducibility of VOC patterns over time, considering potential variance according to the type of clinic, will also be highly valuable for establishing the clinical utility of this approach. Lastly, the geographic scope of cross-national comparisons should be widened, and the effect of various environmental and lifestyle factors on VOC profiles on human health should be studied in detail.

5. Conclusion

This research shows that the improvement of the SPME method using nanoparticle-coated fibers improves the identification of VOCs in biological and pharmaceutical matrices when combined with GC-MS. The optimized method offers higher extraction yields and enhanced sensitivity compared to conventional SPME fibers, which makes it a useful instrument for VOC analysis in multifaceted samples. The comparison of the results obtained in the USA, Europe, and Asia shows that VOC detection frequencies vary greatly depending on the environment, lifestyle, and the use of pharmaceuticals. This shows how the method can be applied universally with regional variations to enhance the stability of VOC profiling. Moreover, the study indicates that the use of nanoparticle-coated fibers enhances the sensitivity of VOC detection, an aspect that may have broad applications in the medical and pharmaceutical industries. The capability to identify low-concentration VOCs accurately can result in non-invasive diagnostic methods and improved control of drug production. However, this study also shows some limitations such as an investigation of particular VOCs and the availability of geographical data. Further work should be directed to the improvement of the nanoparticle coatings, the increase of the geographical variety of the samples, and the use of multiple analytical techniques to improve the method for clinical and industrial use. This enhanced SPME-GC/MS method offers a new development in VOC analysis, which could be applied to enhance noninvasive diagnosis and guarantee the safety and quality of pharmaceuticals. More research should be conducted to overcome its drawbacks and extend its use to other VOCs and samples.

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