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Magnetic Carbon Nanoparticles Derived from Candle soot for SALDI MS Analyses of Drugs and Heavy Metals in Latent Fingermarks

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ABSTRACT

For decades, the analysis of fingerprints (FP) has been used as the primary biometric mean of human identification. In parallel, the chemical analysis of latent fingermark (LFM) with particular reference to “touch chemistry”, offers additional intelligence to forensic examination; as such, continuous improvements in the versatility and sensitivity of detection of the molecular make up of FM is of obvious importance. In this light, we propose a facile approach to synthesize magnetic carbon nanoparticles (MCNPs) from candle soot for extraction and detection of endogenous and exogenous FM components. Initially, endogenous components of FM including fatty acids (FAs), squalene and triacylgycerols (TAGs), were successfully extracted and detected using the developed MCNPs and surface assisted laser desorption/ionization-mass spectrometry (SALDI-MS). Furthermore, the MCNPs enabled the detection of exogenous substances including antihistamine, β-blocker, antibiotic drugs and lead in contaminated FMs, whilst providing characteristic and unique fragmentation patterns for each drugs in the FM. The influence of environmental factors such as temperature on the stability of the exogenous substances in FM was investigated by exposing the contaminated FM to different temperatures over 24 hours, the findings revealed the drugs' instability at high temperatures and undergo different degrees of degradation whereas lead was more resilient to thermal stress. The detection of triprolidine, metoprolol and sulfamethoxazole from pharmaceutical tablets in FM was successfully achieved by gently touching the tablet powder. The limit of detection (LOD) values of the drugs in the tablet forms were 50, 200 and 750 ng mL^{-1} for triprolidine, metoprolol and sulfamethoxazole, respectively and their recovery rates were 91.17% for triprolidine, 94.67% for metoprolol and 120.86% for sulfamethoxazole. Finally, to create a genuine casework scenario, contaminated FM was deposited on glass and metal surfaces then subjected to extraction using MCNPs and magnet without compromising the FM impression. Substrate control experiments revealed that the glass surface exhibiting some background signal, however, they did not interfere with the analysis and satisfactory extraction efficiency of endogenous and exogenous components of the FM on both surfaces was obtained using the MCNPs. Overall, this study proves the capability of MCNPs as new SALDI-MS substrate for both extraction and detection of FM components gathering more information pertaining to the donor’s lifestyle.

Key words: Fingermark; magnetic carbon nanoparticles; extraction; SALDI-MS; endogenous, drugs; lead

1. Introduction

Fingerprints (FP) are well-recognized ridge pattern impressions obtained under controlled conditions after the fingertip comes in contact with an object. After over a century, they are considered as one of the most valuable evidence used for identification and individualization purposes. On the other hand, a latent fingermark (LFM) originates from the unintentional contact between a fingertip and a solid surface, where sweat and other substances present on the fingertip transfer onto the surface producing a distinctive ridge pattern [1]. Advances in LFM chemical and imaging analyses have been reviewed by several authors reflecting the rapid progress in this area [2, 3]. While the development of new materials to enhance the quality of the recovered print is always of great interest [4], for over a decade, several studies have focused on the chemical analysis of FM constituents offering additional supporting intelligence to forensic investigations [5].

A FM is a complex mixture composed of hundred components of natural secretions (endogenous) including organic constituents (e.g. protein, lipids, vitamins and amino acids), ions (Cl^-, K^+, Na^+, Mg^{2+}) and trace metals (Zn, Cu, Fe). In addition to exogenous substances that may have come in contact with the FM prior to the deposition (e.g. drugs, cosmetics, explosives) and semi-exogenous substances which are ingested and then excreted as metabolized or unmetabolized through sweat (e.g. drugs, medications, food and drinks components and/or their metabolites) [6]. Numerous studies have been carried out to recover/detect the endogenous species in the FM for better understanding of its chemistry and to obtain information about the donor such as age [7], gender [8, 9], health status [10, 11] and estimate the age of the FM [12]. In

parallel to that, analysis of trace exogenous substances present in FM is of paramount importance in criminal investigations as it can provide information about an individual's lifestyle. In this regard, several analytical techniques have been employed for the chemical analysis of FM such gas chromatography-mass spectrometry (GC-MS) [12], high-performance liquid chromatography coupled to mass spectrometry [13], vibrational spectroscopic methods [7] and mass spectrometry based techniques such as MALDI MS, SIMS MS, Ag-LDI and others that have been reviewed by Francese et al [14].Whilst MALDI has covered the most grounds both in terms of intelligence recoverable from FMs and compatibility with FM and blood enhancement techniques [6, 15, 16], surface assisted laser desorption/ionization mass spectrometry (SALDI-MS) has gathered considerable attention in the analysis of forensic evidence such as beverage [17, 18], fibers [19], human serum [20, 21], saliva and urine [22] utilizing several nanomaterials, inorganic monoliths, carbon-based materials and metal organic frameworks. The analysis of FM by SALDI-MS was firstly reported in 2009 by Rowell et al. [23] who employed hydrophobized silica-based dusting agent for enhancing LFM and for the detection of illicit drugs and their metabolites in spiked LFPs. Recently, additional efforts were directed towards the development of nanomaterials for the analysis and/or detection of chemical composition of FM. Of these, metallic silver was used for the detection of exogenous and endogenous compounds in LFPs [24]; Au NPs were employed for imaging FMs through the visualization of various fatty acids such as stearic and palmitic acid. Previously, we have reported that metal oxide NPs can be used as powerful SALDI substrates for the detection of exogenous drugs present on LFPs [25].

In the present study, we report the use of magnetic carbon nanoparticles (MCNPs) derived from candle soot as cost-effective and simple sorbent for extraction and detection of endogenous and exogenous components of FM using SALDI-MS. Carbon NPs (CNPs) can be easily produced

from a burning candle, one of the simple and easiest methods to obtain CNPs. CNPs are characterized by excellent absorption in the UV region and high photothermal conversion efficiency leading to enhanced LDI performance mainly *via* thermal transfer mechanism of carbon-based materials [26]. On the other hand, the distinctive properties of Fe_3O_4 NPs including the strong UV absorption and the high magnetic property warrant the nanocomposite several advantages as SALDI substrate. To the best of our knowledge, the present study demonstrates the first use of MCNPs for rapid and direct extraction of endogenous including fatty acids (FAs), squalene and triacylgycerols (TAGs) from FM. Furthermore, the MCNPs were also used to extract and detect contact drugs such as antihistamines (AHs), β-blockers (βBs) and antibiotics (ABs) in contaminated FM. Then, we have expanded the work to enable the detection of Pb from FM, thus mimicking a forensic analytical scenario related to the detection of gunshot residues. Finally, the recovery of both endogenous and exogenous components of the FM from different surfaces was achieved by manipulating the MCNPs with an external magnet.

2. Experimental

2.1. Chemicals

Iron (III) chloride ($FeCl_3$, reagent grade, 97%), iron(II) chloride ($FeCl_2$, 98%), ammonium hydroxide (NH_4OH, 28-30%), methapyrilene hydrochloride (analytical standard), triprolidine hydrochloride (≥99%), metoprolol tartrate (≥98%), labetalol hydrochloride (>98% (TLC), metronidazole (analytical standard) and sulfamethoxazole (analytical standard), ethanol (≥99.5%), lead standard (1000 mg L^{-1} Pb in nitric acid) were purchased from Sigma Aldrich (www.sigmaaldrich.com). All the chemicals were used without further purification. Double-

distilled water (DI-water) was obtained from water deionizer–Elix Milli Q used throughout all the experiments. Candles (diameter: 4 mm) were bought from a local market. Metoprolol (50 mg), triprolidine (2.5 mg) and sulfamethoxazole (800 mg) tablets were purchased from local drugstores.

2.2. Synthesis of magnetic carbon nanoparticles

Preparation of CNPs was carried out adapting previously published work [27]. In brief, candle soot was collected by placing a piece of aluminum foil on top of burning unscented candles. Subsequently, 0.5 g of the soot was mixed with 5 M HNO_3 and refluxed for 48 hours to increase the conductivity of the soot and to introduce some functional groups such as hydroxyl and carboxyl. Thereafter, CNPs were collected by centrifugation and washed several times with water and then with ethanol. Finally, the CNPs were dried in the oven at 80 ^{o}C overnight.

Magnetic carbon nanoparticles (MCNPs) were produced by suspending 0.2 g of the CNP in 100 mL of deionized water and the suspension was sonicated for 30 min. Then, 0.75 g $FeCl_3$ and 0.25 g $FeCl_2$ were added to the suspension under vigorous stirring. Subsequently, 10 mL of NH_4OH aqueous solution (28-30%) was added dropwise to the solution to adjust the pH of the mixture to ≈ 11 then the solution was allowed to stir for 60 min at room temperature. The MCNPs were collected using an external magnet and washed several times with deionized water and finally with ethanol. The nanoparticles were dried in an oven at 80 °C overnight.

2.3. Characterization of magnetic carbon nanoparticles

Surface elemental analysis of the MCNPs was conducted using X-ray photo-electron spectroscopy (XPS) ESCALAB250 xi XPS spectrometer with an Al Kα monochromatic source

and a charge neutralizer. Fourier transform infrared spectroscopy (FTIR) was employed to characterize different functional groups present in CNPs and MCNPs using Jasco 6300 FTIR instrument in the range of 400-4000 cm^{-1}. The optical properties were studied by UV-vis spectra collected on Agilent Cary 5000 Scan UV-Vis-near-infrared (UV-Vis-NIR) spectrophotometer. Surface area analysis was carried out using Brunauer–Emmett–Teller (BET) method based on adsorption data by measuring nitrogen sorption isotherms of the samples at −195 °C on a model Gemini VII, ASAP 2020 automatic Micromeritics sorptometers (USA). The sample was degassed for 12 hours at 110 °C prior to the analysis. The morphology properties of the MCNPs were investigated using transmission electron microscopy (TEM), JEOL JEM 1230, JEOL Ltd., Japan, operating at 120 KV.

2.4 Extraction and detection of drugs and metals from LFM

For the analysis of endogenous compounds, LFM were prepared according to previously published work [28]. In brief, the donor was requested to rub the fingers on the forehead, nose and chin, five times, to eventually produce a sebum-rich mark by subsequently placing the fingertip on the surface of the target plate. For the analysis of exogenous compounds, the fingertip was dipped in solutions containing 1 mg mL^{-1}-1 fg $mL^{-1}$of drugs (β-blockers, antihistamines and antibiotics) prior to contacting the surface of the target plate. Alternatively, an artificial finger was dipped in solutions containing different concentration of Pb (1 mg mL^{-1} - 100 ng mL^{-1}). Thereafter, 2 µL of MCNPs (1 mg mL^{-1} in ethanol) was pipetted onto the FMs. A commercial magnetic wand was used to stir the suspension covering the print area in a circular motion over the surface for 10 s. Then, the wand was slowly dragged to one side of the print. The spot containing the extracted component was analyzed using MALDI-TOF-MS (Bruker ultrafleXtreme). Furthermore, the stability of the drugs contaminating the FMs which were

stored overnight was monitored at different temperatures; 25, 40, 60, 80 and 100 °C. All procedures were approved by Health Sciences Centre Ethical Committee of Kuwait University and in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

2.5 Extraction and detection of contact residues from contaminated fingermark

In this study, the fingertip made contact with 2 mg of pharmaceutical tablet powder containing triprolidine, metoprolol or sulfamethoxazole as active ingredient. Any excess substance was brushed away with the other hand so no powder was visible on the skin. The contaminated fingertip made contact with the metal target plate, glass or metallic (aluminum) surface which was thoroughly cleaned with ethanol before FM deposition, then the MCNPs were applied on top of the FM. A commercial magnetic wand was used to stir the suspension covering the print area in a circular motion over the surface for 10 s as described in section 2.4. To extract FM component from glass or metallic surface, the suspension was collected using a micropipettor with the aid of external magnet and applied on the target plate. The spot containing the extracted components was analyzed using SALDI-TOF-MS.

2.6 Analysis of fingermark using SALDI-TOF-MS and MS/MS

SALDI-TOF-MS and MS/MS were performed on a Bruker ultrafleXtreme system equipped with a Smartbeam II laser. MS spectra were obtained in positive reflectron mode using a random walk raster with a laser frequency of 2 KHz and 500 shots. The ion source voltage was set at 25 V and a reflector voltage at 26.6 kV. In MS mode, spectra were acquired over a mass range of 100–

1500 Da. The instrument was calibrated prior to the MS analyses in the specified mass range *m/z* range using ProteoMassTM calibrant. MS/MS spectra of the parent ions were acquired in positive ionization mode using ion source voltage of 7.5 kV and reflector voltage of 29.5 kV and a laser frequency of 1 KHz. Data processing was performed using Bruker flexAnalysis.

2.7 Reproducibility, limit of detection (LOD) and recovery measurement

The reproducibility of the MCNPs extraction was evaluated by acquiring 5 spectra for each sample, and the average intensities and relative standard deviations (RSDs) were calculated. For LOD determination using standard solutions, a range of analyte standard concentrations (1 mg mL^{-1} to 1 fg mL^{-1}) were analyzed and LODs were considered at 3:1 signal-to-noise (S/N) ratio. For determination of LOD from pharmaceutical tablets, the tablets containing 2.5 mg triprolidine, 50 mg metoprolol or 800 mg sulfamethoxazole were ground into fine powder and dissolved in ethanol. The solutions were centrifuged at 8000 rpm for 10 min, the supernatants were collected and the diluted to a series of solution concentrations ranging from 1 mg mL^{-1} to 100 ng mL^{-1}. Drugs contaminated FM was then prepared as described in section 2.4 and subjected for SALDI-MS analysis.

The recovery of the analytes in spiked samples was calculated using Equation 1:

$$\text{Recovery} = (C_{total} - C_{blank}/C_{spiked}) \times 100 \qquad \textbf{Equation 1}$$

Where C_{total} is the average total concentrations of seven replicates of the spiked sample, C_{blank} is the concentration of the blank solution and C_{spiked} is the original concentration of the spiked standard solution.

3. Results and discussion

3.1 Characterization of magnetic carbon nanoparticles

The chemical composition the MCNPs was studied using XPS measurements, **Figure S1A** shows the wide scan XPS spectrum of the MCNPs confirming the presence of three elements: Fe, O and C. The XPS spectrum of Fe 2p (**Figure S1B**) showed two main peaks for Fe $2p_{3/2}$ and Fe $2p_{1/2}$ which are centered at 710.6 and 724.3 eV, respectively (characteristic of Fe_3O_4) and were further deconvoluted into six peaks at 712.0, 713.9, 719.2, 725.4, 727.2 and 732.6 eV. The peaks at 712.0 and 725.4 eV are assigned to Fe^{2+} while those at 713.9 and 727.2 eV are characteristic of Fe^{3+}. The satellite peaks at 719.2 and 732.6 eV could be assigned to Fe^{3+} in the Fe_2O_3 phase. On the other hand, **Figure S1C** shows the XPS spectrum of O 1s which can be deconvoluted into three peaks at 530.1, 531.3 and 532.4 eV corresponding to Fe-O, C-O-Fe and Fe-OH, respectively. The C 1s spectrum shown in **Figure S1D** exhibited three main peaks centered at 284.6, 285.6 and 288.7 eV which are characteristics of C-C, C-O and C=O configuration, respectively [29].

In SALDI analysis, the functional groups present on the surface of the substrate play a pivotal role in SALDI analysis as it can lead to different interactions with the analyte such as hydrophobic, van der Waals, hydrogen and electrostatic forces based interactions [17]. Therefore, FTIR spectral analysis was carried out to study the functional groups present on CNPs and MCNPs as shown in **Figure S2A**. The broad peak centered at 3450 cm^{-1} is attributed to O-H stretching vibration of carboxylic acid and residual water in the CNPs, while the broad peak at 3437 cm^{-1} in the spectrum of MCNPs can be ascribed to Fe-OH vibration. Additionally, stretching vibrations of CH_2 and C=O were located at 2926-2930 cm^{-1} and 1626-1630 cm^{-1}, respectively [30] . An additional peak at 588 cm^{-1} in the spectrum of MCNPs was observed and

assigned to Fe-O magnetite phase indicating the successful formation of the MCNPs [31]. Furthermore, the ability of the substrate to absorb laser energy was studied using UV-vis spectroscopy, the UV-vis spectra for MCNPs and CNPs are shown in **Figure S2B**. The strong absorption in the range of 200-600 nm can be ascribed to the d orbital transitions of the Fe_3O_4 NPs [32], while the peak at 220 nm can be attributed to π-π* of the CNPs [33]. The surface properties of the prepared MCNPs were characterized using N_2 adsorption-desorption measurement as shown in **Figure S2C.** The obtained N_2 isotherm can be classified as type IV and the hysteresis loop can be assigned to H1/H2, indicating the mesoporous nature of the NPs [34]. The surface capacity of the MCNPs was investigated as high surface capacity of the substrate offers high loading number of the analytes molecules hence increasing the detection sensitivity [35]. The results revealed that the surface area of the prepared MCNPs was 129.2 m^2 g^{-1} with pore volume and pore diameter of 0.32 cm^3 g^{-1} and 10.01 nm, respectively. The high surface area of MCNPs can enhance the performance of SALDI-MS technique. The morphology and particles size of the MCNPs were analyzed using TEM, as shown in **Figure S2D;** the image showed that most of the particles were spherical in shape with particle size of 21.9 nm.

3.2 Extraction and detection of endogenous components of FM

To avoid background signal and/or ion source contamination that may result from the use of carbon-based materials [36], minimum amount of the prepared MCNPs (1 mg mL^{-1}) was employed in this study. Extraction and detection of endogenous components was carried out on sebaceous enhanced FMs using the prepared MCNPs and detection using SALDI-MS, the spectra obtained is shown in Figure **S3** and the extracted and detected compounds are summarized in **Table S1**. Fatty acids (FAs) including oleic acid (*m/z* 283.26) and ecosenoic acid (*m/z* 311.39), which were previously reported as common components of FM [37, 38], were

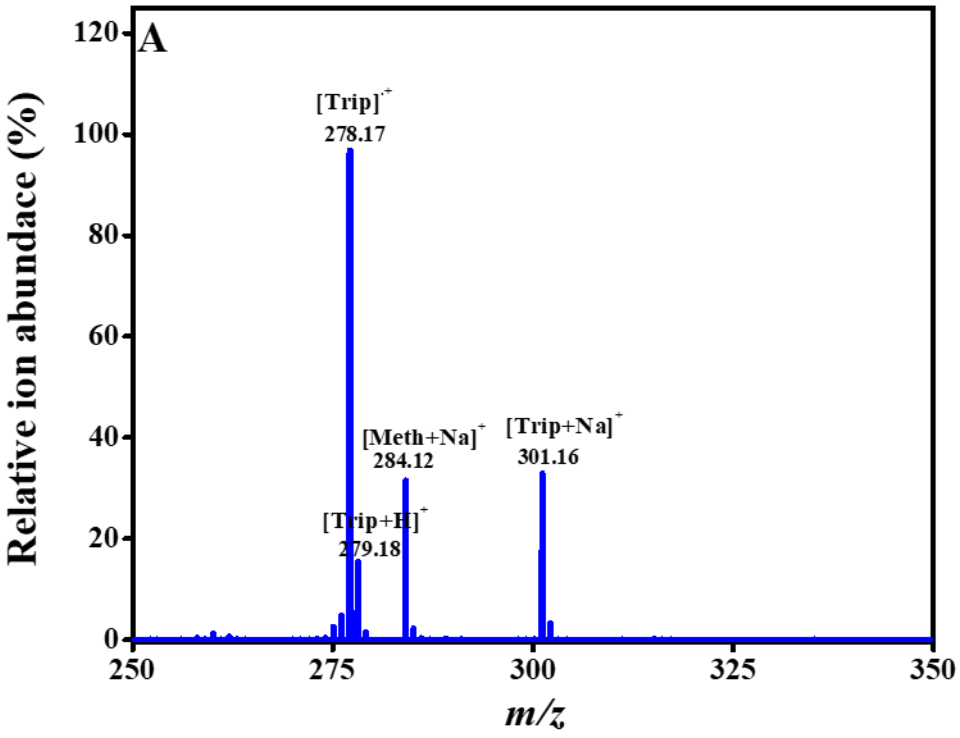
successfully extracted and detected, other lipid such triacylgycerols (TAGs) were also observed as sodiated adducts as previously illustrated by Emerson *et al.*[39]. Additionally, a peak at *m/z* 433.38 was assigned to squalene ion (sodiated adduct), which is believed to account for 10-15% of the total sebum lipid [40]. High intensity peaks were observed at *m/z* 494.56, 522.59 and 550.62; these ions have been previously assigned to dimethyldioactadecylammonium ions (DTDMAC) originating from personal and household products, as first reported in FMs as an exogenous contaminant by Wolstenholme et al. [28].

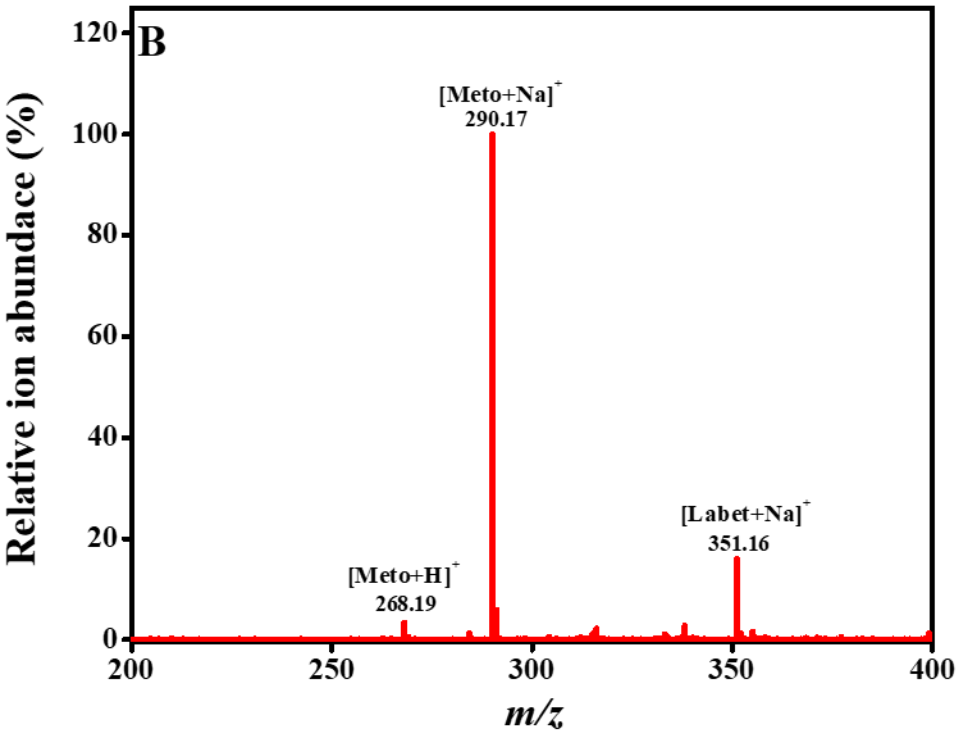
3.3 Extraction and detection of exogenous materials in FM

3.3.1 Extraction and detection of drugs in FM

The aim of this study was to investigate the potential dual use of MCNPs to extract and detect drugs of forensic interest from contaminated FM. In this regard, three classes of drugs namely; antihistamines (AHs), β-blockers (βBs) and antibiotics (ABs) were handled as a solution and the contaminated FMs were subjected extracted and SALDI analysis using the prepared MCNPs. The obtained spectra of drugs contaminated FMs depicted in **Figure 1A-C**, showed prominent signals generated by the drugs with minimum background and the extracted and detected drugs are summarized in **Table S2**. **Figure 1A,** shows the SALDI mass spectrum of the AHs at *m/z* 262.12 $[\text{methapyrilene+H}]^+$, 278.17 $[\text{triprolidine}]^{\cdot+}$, 279.18 $[\text{triprolidine+H}]^+$, 284.12 $[\text{methapyrilene+Na}]^+$ and 301.16 $[\text{triprolidine+H}]^+$ were mainly detected with mass accuracy of 2.44, 11.14, -1.50, -13.23 and -4.42 ppm, respectively. The LOD for methapyrilene and triprolidine in contaminated FM were 1 pg mL^{-1} and 10 ng mL^{-1}, respectively. For β-blockers, the SALDI MS spectrum displayed an intense peak at *m/z* 290.17 which can be assigned to the

sodiated ion adduct of metroplol (0.72 ppm) and less intense peaks at *m/z* 268.19 and 351.16 which were ascribed to protonated and sodiated ions of metroplol (2.31 ppm) and labetalol (-1.54 ppm), respectively. The LOD of metroplol drug in FM was 50 ng mL^{-1} while that of labetalol was 100 ng mL^{-1} (**Figure 1B**). Finally for the Abs, $[sulfamethoxazole+Na]^+$ ion could be observed at *m/z* 276.04 (-3.6 ppm) while the peak at *m/z* 299.03 corresponds to $[sulfamethoxazole+Na]^+$ ion; finally the metronidazole was mainly detected as sodiated ion at *m/z* 194.05 (0.82 ppm) as shown in **Figure 1C**. The LOD value was 500 ng mL^{-1} for both metronidazole and sulfamethoxazole. The relative standard deviation (RSD) values were less than 15.5% for all the extracted drugs in LFM indicating that good reproducibility can be achieved using MCNPs.




B
[Meto+Na]+
290.17
[Meto+H]+
268.19
[Labet+Na]+
351.16
Relative ion abundace (%)
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40
60
80
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120
200
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400

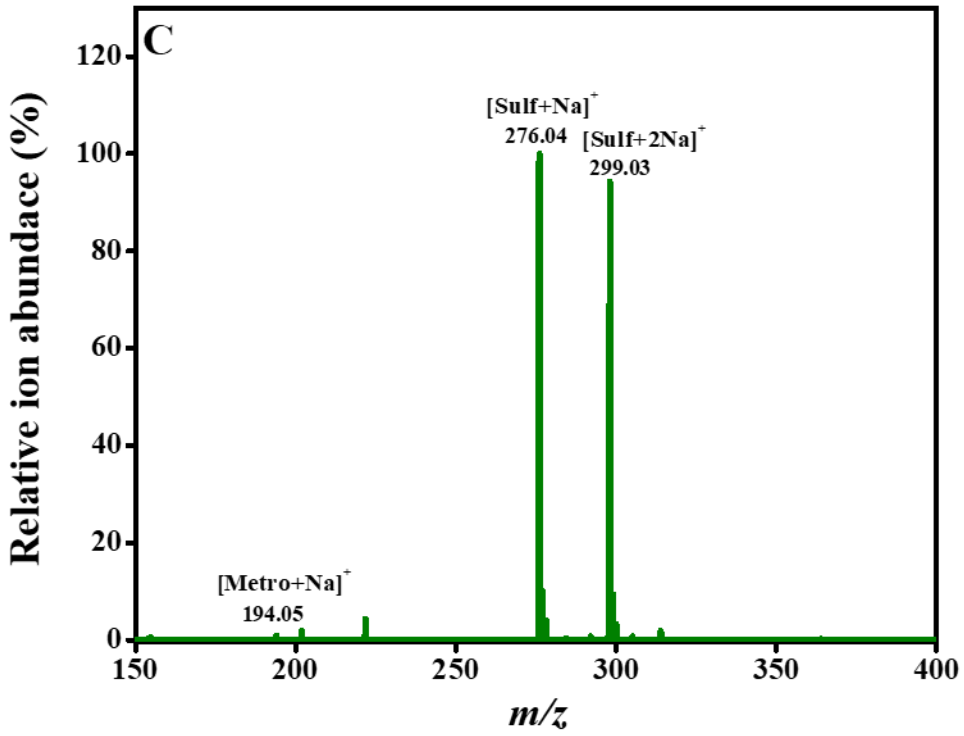
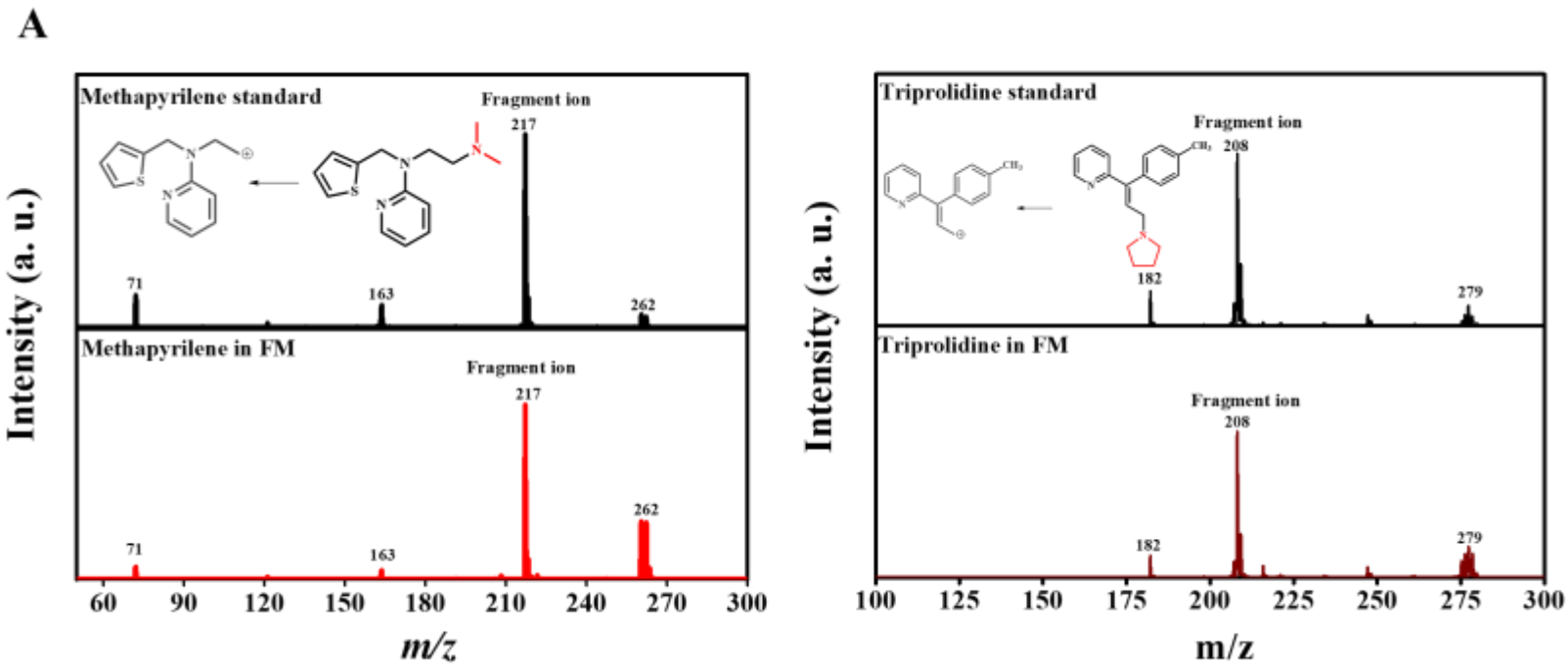


Figure 1: SALDI MS spectra acquired from fingermark contaminated with A) antihistamines; Methapyrilene [Meth] and Triprolidine [Trip] B) β-blockers; Metoprolol [Meto] and Labetalol [Labet] and C) antibiotics; Metronidazole [Metro] and Sulfamethoxazole [Sulf], drugs obtained using MCNPs.

Furthermore, MS/MS was employed to confirm the presence of all six drugs in the LFM by comparing the product ions of the drugs in the FM to those generated by the drugs standards. MS/MS spectra for the product ions derived from the collision induced dissociation of the drugs on FM corresponded very well with those obtained from the drugs standard solutions (**Figure 2A-C**). **Figure 2A** shows the fragment ion at *m/z* 217.08 (-2.75 ppm) in the MS/MS spectrum of

methapyrilene can be ascribed to the loss of tertiary amine group in the molecule. Similarly, a significant product ion fragment observed for triprolidine at *m/z* 208.11 (-6.5 ppm) resulting from the loss of the tertiary amine group in the drug molecule which is in good agreement with previous data [41]. Furthermore, **Figure 2B** reports MS/MS spectra of metroprolol; the peak at *m/z* 116.10 (-0.94 ppm), which is characteristic to the substructure of isopropyl amine group (secondary amine), can be easily protonated and detected [42]. The prominent ion fragment at *m/z* 311.17 (-9.6 ppm) in the spectrum of labetalol can be ascribed to the loss of hydroxyl group in the molecule (**Figure 2B**). In contrast, **Figure 2C** shows metronidazole with its nitroimidazole core and major ion fragment at *m/z* 128.04 (5.0 ppm) indicating that the ion underwent loss of hydroxyethyl group while smaller ion fragment at *m/z* 125.07 (6.7 ppm) resulted from the loss of nitro group [43]. The stable ion fragment of sulfamethoxazole at *m/z* 156 resulted from the elimination of NH_2 bonded to oxazole moiety as illustrated in **Figure 2C** which supports the findings obtained by Mistri *et al.* [44].


A
Methapyrilene standard
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Methapyrilene in FM
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Intensity (a. u.)
60 90 120 150 180 210 240 270 300
m/z
Triprolidine standard
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Intensity (a. u.)
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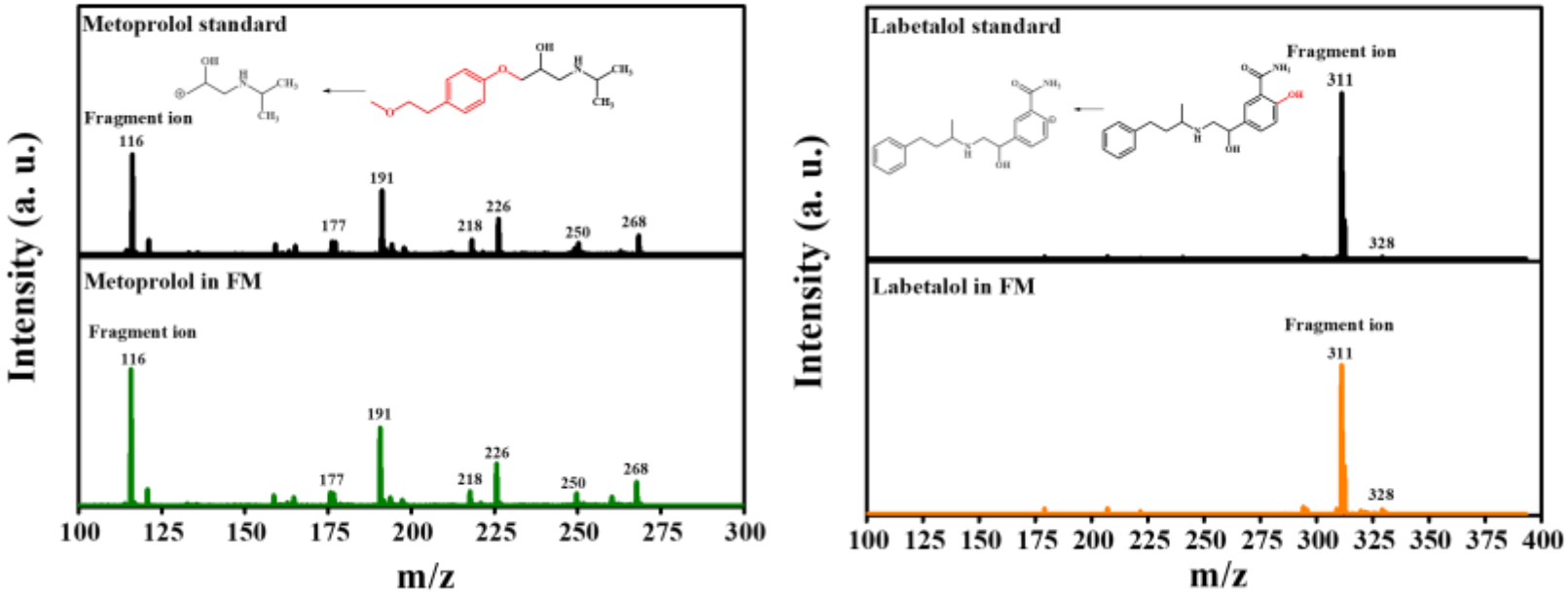
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Intensity (a. u.)
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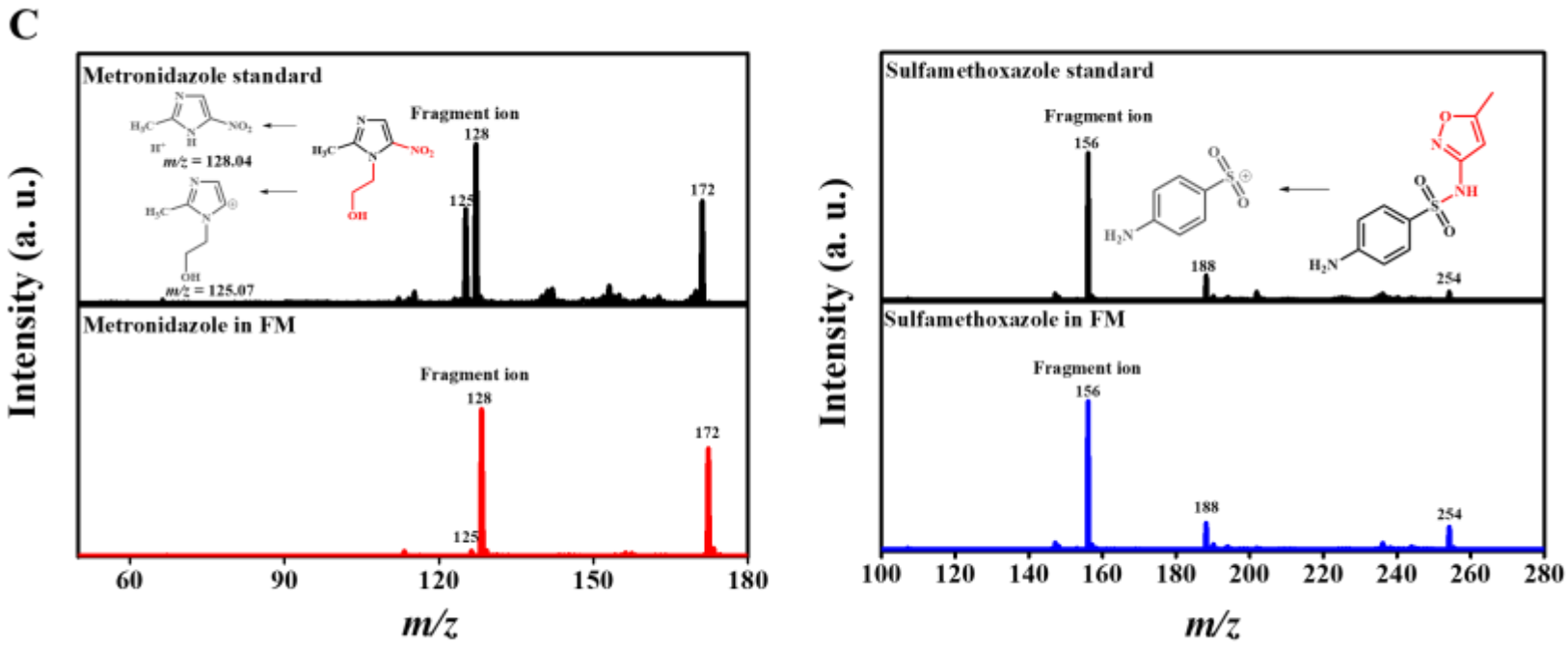


Figure 2: SALDI MS/MS spectra confirmation of the identity of the six drugs used in this study; methapyrilene, triprolidine, metoprolol, labetalol, metronidazole and sulfamethoxazole. MS/MS experiments were performed on the drug standards and on their corresponding exogenous form in fingermark. Spectra obtained for ions with A) *m/z* 262.13 (methapyrilene) and 279.18 (triprolidine), B) *m/z* 268.19 (metoprolol) and 328.17 (labetalol) and C) *m/z* 172.07 (metronidazole) and 254.06 (sulfamethoxazole).

The stability of FM discovered and/or recovered in the crime scene is of great importance in criminal investigation, sometimes crimes are reported after minutes, hours or even days depending on when the crime was reported and consequently the time of FM discovery. Therefore a preliminary assessment of the influence of environmental condition, specifically temperature on the stability of the exogenous contaminants in FM and consequently their detection in contaminated FM was investigated. Temperature can cause some irrevocably changes to physical evidence, particularly drugs as they can undergo oxidation/reduction or hydrolysis reactions [45].Our group has previously explored the influence of time and temperature on the detection of illicit drugs on LFP using Fe_2O_3 NPs as SALDI-MS substrate [25]. Thus, we further extended this study to investigate the stability of drugs contaminated FM stored overnight at different temperatures using MCNPs as SALDI substrate. The analysis of contaminated FMs stored at 25, 40, 60, 80 and 100 ^{o}C was carried out and the relative ion intensity of each drug was monitored and plotted against temperature as shown in **Figure S4A-C**. **Figure S4A** displays the effect of temperature on the stability of AH drugs; at mild temperatures of 25 and 40 ^{o}C, the drugs showed similar intensities suggesting that the molecules maintained their integrity and did not undergo any significant degradation at these temperatures. However, the signal intensities of the drugs decreased at higher temperatures (60 and 80 ^{o}C) and the degradation became more prominent at 100 ^{o}C indicating the instability of the drugs at higher temperatures. Similarly, as illustrated in **Figure S4B**, the stability of β-blockers drugs was affected to a greater extent at temperatures above 40 ^{o}C and the signal intensities decreased to less than 50% with significant reduction at 100 ^{o}C. Moreover, the ABs drugs metronidazole and sulfamethoxazole underwent different degrees of degradation when subjected to thermal stress as shown in **Figure S4C**. Notably, metronidazole was unstable at moderate and high temperature

and it was completely degraded at 100 ^{o}C, while sulfamethoxazole was relatively stable even at high temperature. Thus, this study suggests that most of the drugs are unstable at elevated temperatures and undergo different degrees of degradation when subjected to thermal stress subsequently temperature can significantly impact the stability of exogenous compounds such as drugs that might present in FM.

3.3.2 Extraction and detection of lead in FM

Detection and identification of gunshot residue (GSR) is valuable in shooting related investigations. Residue generated in GSR, either organic or inorganic, can easily adhere to the hand, hair, face, clothes, nasal mucous of a shooter and other object or person nearby. Analysis of these residues can help to investigate whether the shooting has actually occurred and estimate the shooting distance [46]. Additionally, metallic GSR originating from ammunition (Pb, Sb, Ba, etc..) can stick to LFM which may enable the link between the biometric information and the circumstances of the offence. In this context, MCNPs was used to extract and detect Pb in contaminated FM mimicking a forensic analytical scenario involving gunshots. To the best of our knowledge, this work demonstrates the first use of magnetic NPs to extract and detect lead from contaminated FM using SALDI-MS. **Figure 3A** reports a positive ion mass spectrum of Pb contaminated FM extracted using the MCNPs. The proposed substrate enabled the detection of the isotopic distribution of Pb at *m/z* = 205.97, 206.97, and 207.97 for Pb^{206}, Pb^{207} and Pb^{208}, respectively. The results revealed that the mass of Pb^{2+} ion on FM were accurate to within 11.74 ppm of its theoretical mass with isotopic distribution close to the predicted isotopic pattern (**Figure 3A)**. Spot-to-spot reproducibility was assessed using MCNPs and the RSD value for ions collected from 5 different spectra was less than 20% with LOD value of 100 ng mL^{-1}.

Furthermore, the stability of lead contaminated FM stored overnight at different temperatures was explored as shown in **Figure 3B**. Unlike the drugs in FM showing exponential decay in the ion intensity with increasing the temperature, lead in FM maintained its stability even at the highest temperature tested (100 ºC). Albeit the analysis of Pb in environmental and biofluid samples was previously reported by Chih-Ching Huang and coworkers [47, 48] using Au NPs as SALDI-MS substrate, the present study offers a new approach to extract and detect Pb from FM which could be adopted in the future to extract and detect both organics and inorganics generated in GSR.

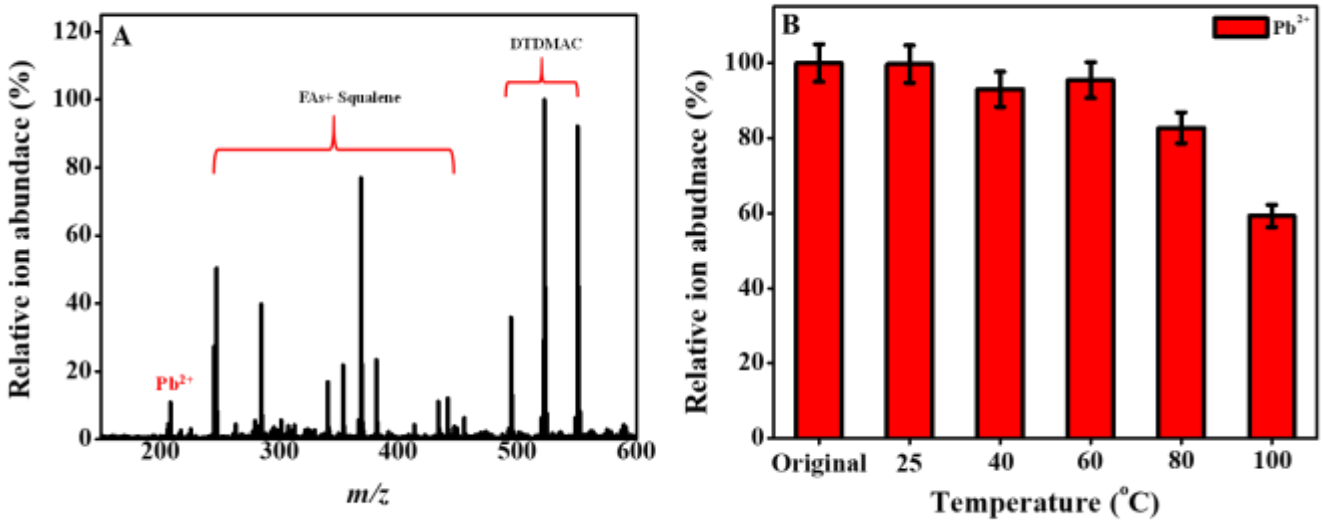


Figure 3: Detection of lead in contaminated fingermark A) SALDI-MS spectrum of fingermark contaminated with lead and B) effect of temperature on the analysis of lead contaminated fingermark. Error bars represent standard deviation for five replicates.

3.4 Extraction and detection of contact residues from FM

In this study, the presence of residues following contact with pharmaceutical tablet containing triprolidine, metoprolol or sulfamethoxazole was compared with that of the standard solution. Characteristic peaks corresponding to protonated and sodiated ions of triprolidine were clearly observed at *m/z* 279.18 and 301.16, respectively (**Figure 4A)**. Additional peaks at *m/z* 166.12 and 188.10 were assigned to the protonated and sodiated ions of pseudoephedrine, respectively, which is the second active ingredient in the drug tablet (60 mg). It is of interest to note that the peak at *m/z* 208.10 is related to the fragment ion of triprolidine as previously shown in MS/MS spectra (**Figure 2A**). Similarly, as demonstrated in **Figure 4B** the respective protonated and sodiated ions of metoprolol were detected at *m/z* 268.18 and 290.17, in addition to peaks at *m/z* 365.10 and 381.07 which can be ascribed to sodium and potassium adducts of lactose (an excipient in the tablet), respectively. **Figure 4C** shows the SALDI spectrum of the extracted FM following contact with sulfamethoxazole tablet powder, the corresponded peaks of sulfamethoxazole ionss were clearly observed at *m/z* 254.05 $[M+H]^+$, 276.04 $[M+Na]^+$ and 292.01 $[M+K]^+$. It is noteworthy that the LOD values of the drugs in the tablet forms were 50, 200 ng mL^{-1} and 750 ng mL^{-1} for triprolidine, metoprolol and sulfamethoxazole, respectively which are slightly higher than the values obtained using standard drug solution. This can be attributed to the complexity of the tablet formulation and the presence of multiple excipients. Additionally, spot-to-spot reproducibility was evaluated for ions collected from 5 spectra and the RSD values were in the range of 3.6-10.3%, 10.8-12.1% and 11.9-17.5% for extracted FM contaminated with triprolidine, metoprolol and sulfamethoxazole residues, respectively.

To assess the accuracy of the results, recovery rates were calculated by spiking known concentration of drug standard solution on top of FM sample. Following the same extraction procedure, the drugs were separated using MCNPs and subjected to SALDI-MS analysis. The

linear dynamic range was evaluated by analyzing different concentrations of triprolidine, metoprolol and sulfamethoxazole; the calibration plots were built by linear regression of signal intensities of all the ions detected against the concentrations of the analytes standard solution as shown in **Figure S5A-C**. The concentration of triprolidine, metoprolol or sulfamethoxazole in spiked FM sample was determined according to linear fitting equation and the recovery of the analytes in spiked FM samples was calculated using **equation 1**. The obtained recoveries reported in **table 1** were 91.17% for triprolidine, 94.67% for metoprolol and 120.86% for sulfamethoxazole indicating that the proposed MCNPs can be effectively used to extract and detect contact residues from FM matrix with satisfactory recovery.

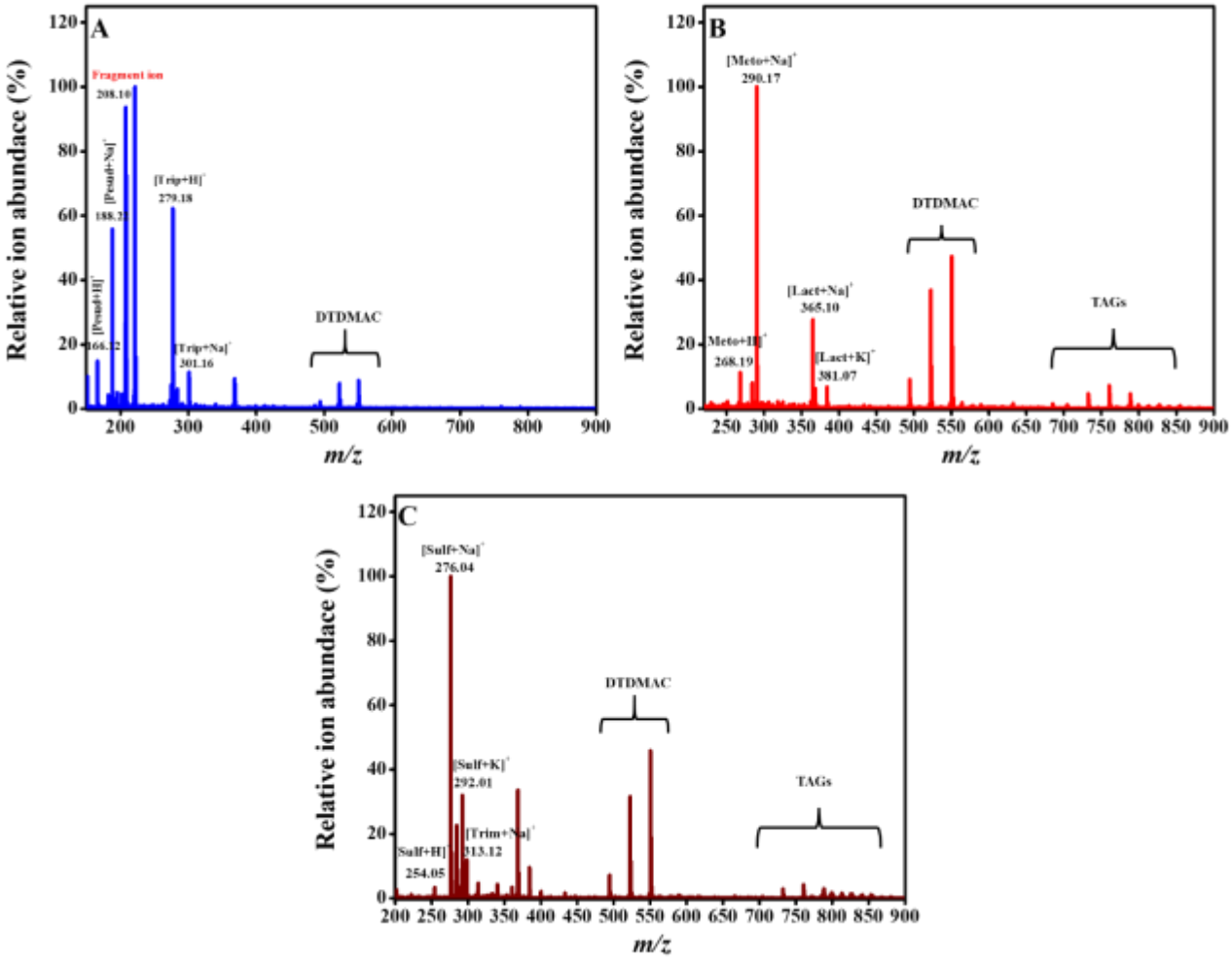


Figure 4: SALDI spectra acquired from fingermark following contact with A) triprolidine [Trip] and B) metoprolol [Meto] and C) sulfamethoxazole [Sulf] tablets. Other excipients present in the tablets were also detected including pesudoephedrin [Pesud], lactose [Lact] and trimethoprim [Trim].

Table 1: Compounds extracted from fingermark contaminated with tablets containing triprolidine, metroprol and sulfamethoxazole using MCNPs and SALDI-MS. Average intensities, RSD, LOD and percentage recovery values are presented.

Triprolidine Tablet									
Detected m/z	**Experimental m/z**	**m/z error (ppm)**	**Possible species**	**Intensity**	**%RSD**	**Spiked concentration[a] (ng mL^{-1})**	**Detected[b] (ng mL^{-1})**	**Recovery (%)**	**LOD** (ng mL^{-1})
166.1236	166.12264	-5.78	Pesudoephedrine+H]$^{+}$	27528.2	11.4	-	-	-	-
188.1023	188.10513	15.04	Pesudoephedrine+Na]$^{+}$	61937.9	7.9				
279.1877	279.18558	-5.65	[Triprolidine+H]$^{+}$	9601.6	3.6	200	182.35	91.17	50
301.1678	301.16807	0.90	Triprolidine+Na]$^{+}$	2734.0	10.3				
Metoprolol Tablet									
Detected m/z	**Experime**	**m/z**	**Possible species**	**Intensity**	**%RSD**	**Spiked**	**Detected[b]**	**Recovery**	**LOD**

	ntal m/z	error (ppm)				concentration[a] (ng mL^{-1})	(ng mL^{-1})	(%)	
268.1911	268.19072	-1.42	[Metoprolol+H]$^{+}$	6229.3	12.1	300	284.52	94.67	200
290.1733	290.17321	-0.34	[Metoprolol+Na]$^{+}$	30545.9	10.8				
365.1038	365.10598	5.86	[Lactose+Na]$^{+}$	5139.3	5.6	-	-	-	-
381.0750	381.07992	12.9	[Lactose+K]$^{+}$	403.4	11.8				
Sulfamethoxazole Tablet									
Detected m/z	**Experimental m/z**	**m/z error (ppm)**	**Possible species**	**Intensity**	**%RSD**	**Spiked concentration[a] (ng mL^{-1})**	**Detected[b] (ng mL^{-1})**	**Recovery (%)**	**LOD**
254.0587	254.05994	4.88	[Sulfamethoxazole+H]$^{+}$	1297.6	11.9	1000	1209	120.86	750 ng

276.0428	276.04188	3.33	[Sulfamethoxazole+Na]$^{+}$	50697.8	15.1				mL^{-1}
292.0144	292.01582	4.86	[Sulfamethoxazole+K]$^{+}$	25400.5	17.5				
313.1247	313.12766	9.45	[Trimethoprim+Na]$^{+}$	535.8	2.7	-	-	-	-

a. Spiked concentration from drug standard on FM

b. Detected concentration from calibration plot

SALDI-MS analysis of FM components has garnered a considerable amount of attention over the last decades. These analyses are of great importance to obtain some characteristic details about the donor, reconstruct the crime scene hence, providing prosecutorial evidentiary data. On this point, Rowell and coworkers have employed several silica-based particles for the detection of exogenous substances including drugs, nitro-organic and peroxide explosives in FM [23, 49-51] whilst Ag-Au alloy was used to probe endogenous components of FM. In the current study, we report the use of MCNPs to extract both endogenous and exogenous components of FMs and the potential of using this approach to extract these substances from different surfaces. Additionally, the proposed method offers satisfactory LODs and the recovery rates for these drugs in FM sample as reported in **Table 2** indicating this proposed method can be a potential alternative in forensic laboratories.

Table 2: Summary of some substrates used in SALDI-MS for the detection of components.

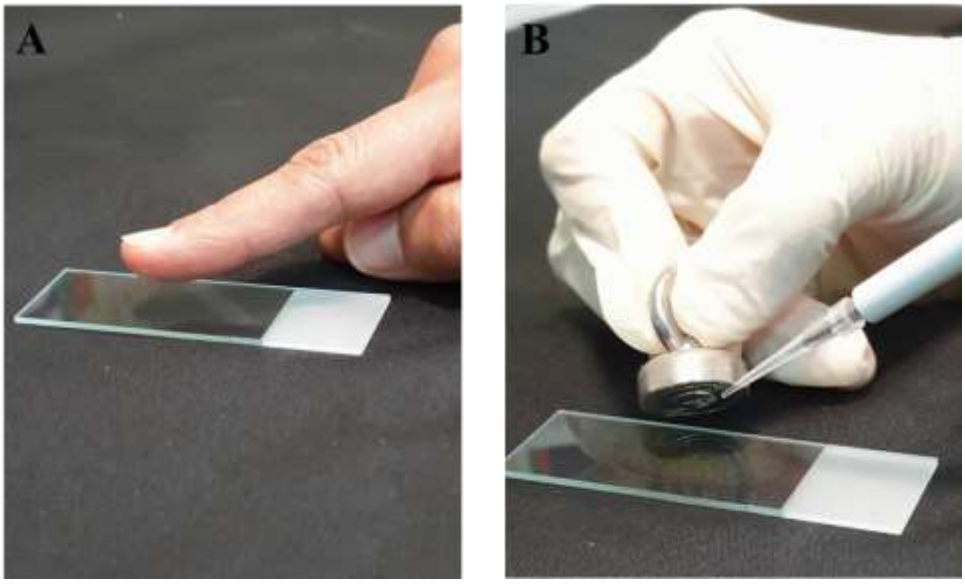
Substrate	**Application**	**Analyte(s)**	**LOD/LOQ**	**% Recovery**	**Ref.**
Hydrophobic silica dusting agent	Detection of drugs in spiked FM	Codeine, diacetylmorphine and methadone	-	-	[23]
Hydrophobic silica particles	Detection of nicotine and cotinine in dusted FM of smokers	Nicotine and cotinine	-	-	[49]
Hydrophobic silica nanopowder	Detection environmental nicotine FM of smokers	Nicotine	-	-	[52]
Silica-CB particles	Detection of drugs in spiked FM	Heroin, methadone, nicotine, noscapine and 6-monoacetylmorphine	Detection level of range of 2-200 ng on	-	[53]

			different surfaces		
ROAR black magnetic powder	Detection of nitro-organic and peroxide explosives in doped FM	TNT, tetryl (N-methyl-N,2,4,6-tetranitroaniline), HMx, RDX, TNG and PETN	-	-	[50]
ARRO SupraNano™ MS black magnetic powder	Detection of drugs in dusted FM	Cocaine, methadone, aspirin, paracetamol and caffeine	-	-	[51]
Commercial black powder	Detection of drug cross contamination in dusted FM	Cocaine, methadone, aspirin, paracetamol and caffeine	-	-	[54]
Ag-Au alloy nanoparticles	Detection of endogenous components of FM	Endogenous components of FM including FAs	-	-	[55]
Metal oxide NPs	Detection of drugs in spiked FM	Nortriptyline, amitriptyline, nortriptyline and promazine	-	-	[25]
MCNPs	Detection of drugs and heavy metals in contaminated FM	Antihistamines; methapyrilene and triprolidine, β-blockers; metoprolol and labetalol antibiotics; metronidazole and sulfamethoxazole drugs in addition to Pb^{2+} ion.	50-750 ng mL^{-1}	91.17-94.67%	This work

3.5 Extraction and detection of contact residues from different surfaces

In the present study, MCNPs have been successfully exploited for extraction and subsequent detection of substances from both "natural" and contaminated FMs using SALDI-MS. The ability of SALDI-MS to detect exogenous components of FM was considered in several studies employing different materials to assist the ionization/desorption process. This substantiates the growing interest in the analysis of FM using SALDI-MS for example, doped silica NPs have been previously used as SALDI-substrate for the analysis of terbinafine in FM [56]. In two different studies, hydrophobic silica coupled with SALDI-MS have been utilized for the detection codeine, diacetylmorphine (heroin), methadone nicotine and cotinine in FM [23, 49]. However, at crime scenes, FM residues can be found on different surfaces, traditionally, these marks are recovered from the surfaces using different tape or gelatine lifts following the application of the most appropriate enhancement technique, mainly for physical comparison of the FP ridges. Thus, as a proof-of-principle study, we propose the use of MCNPs to extract and detect FM components from different surfaces without affecting the FM ridge pattern or the need for developing agent. In the last effort of this study, MCNPs was employed to extract components of FM generated by contamination of the fingertip with pharmaceutical tablets from different surfaces to test its versatility. For this purpose, contaminated FMs on glass slide and aluminum surfaces were investigated as example of common surfaces where FM can be found, then components of the contaminated FM were extracted as described in **section 2.5**. Initially, as substrate control experiments, SALDI MS spectra of the surfaces in the absence of the FM are displayed in **Figure S6A-B**. Subsequently, a fingertip contaminated with 2 mg of pharmaceutical powder tablet (containing metoprolol, as representative drug) was contacted on a clean glass or aluminum surface and extracted using MCNPs as illustrated in **Figure 5A-B**. The mass spectrum

obtained from extraction of FM following contact with metoprolol tablet on glass slide is shown in **Figure 5C;** the sodiated adduct of metoprolol at *m/z* 290.17 in addition to several endogenous components of the FM such as TAGs were detected. Unlike the glass surface which showed a significant background interference, extraction of contaminated FM on aluminum surface permitted the facile detection of sodium ion of metoprolol in addition to peaks corresponding to TAGs (**Figure 5D)**. As can be seen, these preliminary results indicate that the surface can have a significant impact on FM analysis yet utilizing the MCNPs enabled the extraction and detection of FM endogenous and exogenous components from different surfaces.



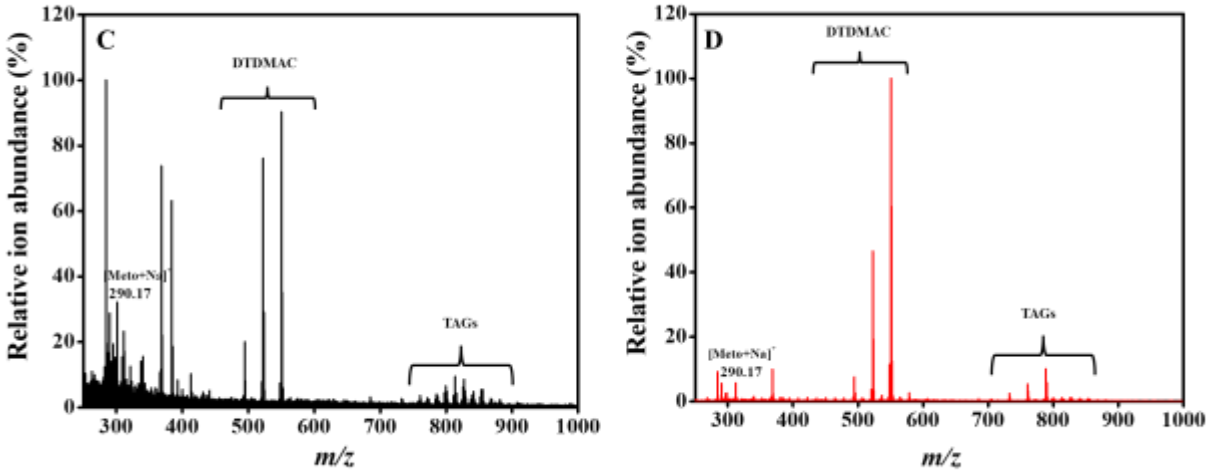


Figure 5: A) Deposition of fingermark following contact with metoprolol [Meto] containing tablet on glass slide (as an example) B) collection of MCNPs from the glass slide using micropipettor and an external magnet, SALDI spectra acquired from fingermark following contact with metoprolol tablet on C) glass surface and D) aluminum surface using the MCNPs.

Conclusions and outlook

In the present study, we propose a facile approach for synthesizing magnetic carbon NPs from candle soot. The prepared material was fully characterized using several analytical techniques which confirmed the successful formation of the MCNPs. The MCNPs enabled extraction and detection of endogenous components of FM including FAs, squalene and TAGs in addition to exogenous substances such as antihistamines, β-blockers, antibiotics drugs and Pb. Thermal stability study suggested that the drugs are prone to degradation, yet the presence of parent drug ion was confirmed even at elevated temperatures indicating decent stability of the physical evidence. Quantitative analysis of contact residues on finger for parent drugs was investigated

and recovery rates of 91.17, 94.67 and 120.86% were obtained for triprolidine, metoprolol and sulfamethoxazole, respectively. Finally, a proof-principle study was conducted to extract and detect components of FM, following contact with metoprolol tablet residue from metal and glass surfaces. Ultimately, the proposed method offered satisfactory extraction and detection of FM components on aluminum and glass surfaces, however, some background interferences were observed in the mass spectra when FM was extracted from a glass surface. Despite the presence of few techniques for FM chemical analysis, combining magnetic material with SALDI-MS for extraction and detection of FM components could offer a valid alternative. A potential extension of this approach may include the analysis of FM on several porous and nonporous surfaces and the detection of a broader range of exogenous compounds in FM under different conditions. Finally, an in-depth study is required to understand the decay mechanisms of FM endogenous components which is important for the development of FM dating technology.

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Conflict of interest

The authors declare that they have no competing interests.

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