

Short communication

Comparison of gampi paper and nanofibers to chromatography paper used in paper spray-mass spectrometry



Pei-Hua Lai^a, Pei-Chun Chen^a, Ya-Wei Liao^a, Ju-Tsung Liu^a, Chien-Chung Chen^{b,**},
Cheng-Huang Lin^{a,*}

^a Department of Chemistry, National Taiwan Normal University, 88 Sec. 4, Tingchow Road, Taipei 11677, Taiwan

^b Graduate Institute of Biomedical Materials and Tissue Engineering, Taipei Medical University, 250 Wu-Hsing St., Taipei, Taiwan

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ABSTRACT

Two series of “papers” that were made from natural fibers and synthetic fibers, respectively, were examined for use in paper-spray mass spectrometry and the results were compared to chromatography paper that is currently being used. In the former case, four types of papers were used, including gampi paper, tengujou paper, glassine paper and cicada paper, and the findings show that the limit of detection can be improved when gampi paper was used. This is because gampi paper is very tough and extremely thin (thickness, <20 μm), which permits sample molecules to be translated and evaporated nearly instantly. Since ionization occurs within a very short period, an abundance of ions is formed, leading to a dramatic improvement in the limit of detection. Meanwhile, a series of tough, thin synthetic fibers, including a microarray membrane (hollow and fibrous) and nanofibers, were also tested. The papers were prepared from polycarbonate, polylactic acid and poly-L-lactic acid (PLLA), respectively, by means of a co-axial electrospinning technique. The findings show that the limit of detection also can be improved, when a PLLA nanofiber was used. This is because this type of paper-like nanofiber is also very thin, tough and hydrophobic, which permits to ionization to occur within a very short period. Detailed information on methods for synthesizing these fibers and their use in the analysis of a real sample are also reported.

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1. Introduction

A wide variety of ionization methods have recently been developed. Among these methods, ambient sampling/ionization mass spectrometry is in widespread use, because it greatly simplifies and increases the speed of a mass-spectrum analysis [1–10]. Among these methods, since its debut in 2010 [11], the use of a triangular shaped section of chromatography paper, so-called paper spray-mass spectrometry (paper-spray MS), has opened new insights in the field of mass spectrometric analysis, and as a result, it has now become a quite popular and important method for use in mass spectrometry. Although various types of paper have been evaluated for use in this area [11,12], chromatography paper continues to be the most commonly used material for this technique. As is well known, the paper and pulp papermaking process were developed in ancient China; Washi is a style of paper that was first made in Japan. The Washi name comes from *wa* meaning Japanese and *shi*

meaning paper. It is manufactured using fibers from the bark of the gampi tree, as well as other natural materials, including bamboo, hemp, rice, wheat, etc. Although it was made by hand in the traditional manner, gampi paper is the highest grade of Washi. It has insect repelling properties and was used in preparing valuable documents and paper currency in ancient times. Beside, cicada paper, tengujou paper and glassine paper were also used for comparison in this study. In contrast to these “real” papers, a series of synthetic “papers” were also developed by means of an electrospinning technique [13–20]. In fact, the synthetic “papers”, look like a traditional type of paper. The materials that are currently used for fabricating these fibers/membranes include polycarbonate (PC), polylactic acid (PLA) and poly-L-lactic acid (PLLA), polyvinylidene fluoride (PVDF) and nylon, respectively [20–24].

In this study, we report on a comparison of the chromatography paper that is currently used in paper-spray MS to two series of “paper-like fibers”, including papers that were made from natural fibers and from synthetic fibers, respectively. A series of designer drugs, including *p*-chloroamphetamine were selected as model samples, since the data obtained in this study could be compared to previously acquired data collected in our laboratory, using the same mass spectrometer. Details of the procedures for

* Corresponding author. Tel.: +886 2 77346170; fax: +886 2 29324249.

** Corresponding author.

E-mail address: chenglin@ntnu.edu.tw (C.-H. Lin).

preparing synthetic paper-like fibers used for paper-spray mass spectrometric analysis are also reported.

2. Experimental

2.1. Materials

Poly(lactic acid (PLA; Mw. 10 kDa), polycarbonate (PC; Mw. 2.25 kDa), polyethylene glycol (PEG; Mw. 35 kDa), polyethylene oxide (PEO; Mw. 900 kDa) and nylon 6 were purchased from Sigma–Aldrich (MO, USA). Poly-L-lactic acid (PLLA; Mw. 300 kDa) and poly(vinylidene fluoride (PVDF; Solef® 21216 copolymer, Mw. 600 kDa) were purchased from Polyscience (PA, USA) and Solvay Plastics (Belgium), respectively. *p*-Chloro-amphetamine and clandestine tablets were provided by the Military Police Command, Forensic Science Center, Taiwan. Tablet samples were ground and dissolved in methanol before use. Chromatography paper was obtained from Advantec (Japan); Gampi paper was purchased from PAPER NAO (Japan; <http://www.papernao.com>); cicada paper, tengujou paper and glassine paper were obtained from the KUO-TAI FINE ART SERVICE (Taiwan). All other chemicals were of analytical grade and were obtained from commercial sources.

2.2. Apparatus

The mass spectrometer (Finnigan LCQ Classic LC/MS/MS) used in this study was the same instrument that was used in our previous studies [25,26]. A commercially available electrospinning machine, purchased from MECC Co., Ltd. (Japan), was used for making various types of microarray membranes, and a co-axial electrospinning head was manufactured by our machine shop. Using of this machine, it was possible to prepare an A4 sized sheet of a paper-like microarray membrane or nanofibers. A scanning electron microscope (SEM; JSM-6510, JEOL Ltd.) was also used for surface observation.

2.3. Preparation for a microarray membrane and nanofibers

2.3.1. Microarray membrane

A hollow, poly(lactic acid fiber, i.e. a microarray membrane, was produced using the above described co-axial electrospinning head. In this preparation, the outside layer tubing was filled with a 15 wt% solution of PLA in a dichloromethane/dimethylformamide (v/v: 7/3) mixed solvent, whereas the inner tubing was prepared using a 10 wt% solution of PEO/PEG (v/v: 1/1) in distilled water. A 6.5 kV high voltage was applied for electrospinning and the feed rate of the inner and outer tubes was 4.0 mL/h, respectively. The distance between the spinneret and roller was 30 mm and the roller rotational speed was 108 rpm.

2.3.2. Nanofibers

Instead of using the co-axial electrospinning head, a standard stainless needle (O.D./I.D.: 0.6/0.2 mm) was used. A polycarbonate fiber membrane was produced using an 18 wt% solution of polycarbonate in a mixed solvent (dichloromethane/tetrahydrofuran; v/v: 9/1). The voltage used was 10 kV and the feed rate was 1.0 mL/h. The distance between the spinneret and roller was 50 mm and the rotational speed of the roller was 2000 rpm.

A Nylon fiber membrane was produced using a 12.5 wt% solution of nylon (solvent: foracid). The voltage and feed rate was 28 kV and 0.2 mL/h, respectively. The distance between the spinneret and roller and the rotational speed of the roller were 150 mm and 3000 rpm, respectively.

A PLLA fiber membrane was produced using a 10 wt% PLLA solution (solvent, hexafluoro-2-propanol). In this preparation, the voltage and feed rate was 20 kV and 0.5–1.0 mL/h, respectively. The

distance between the spinneret and roller and the rotational speed of the roller were also 150 mm and 3000 rpm, respectively.

The PVDF fiber membrane was produced using a 12.5 wt% PVDF solution in a mixed solvent, dimethylformamide/acetone; v/v: 6/4. The voltage and feed rate was 20 kV and 1.0 mL/h, respectively. The distance between the spinneret and roller and the rotational speed of the roller were the same was used for the PLLA membrane.

2.4. Experimental conditions

A nib-assisted paper spray method was identical to that used in our previous studies [25,26] and is abbreviated herein. Briefly, a piece of paper, either gampi-, nanofiber- or chromatography-paper, was cut into a triangular shape, 5 mm in length and 3 mm wide. The sample solution was dropped on the triangular spray-paper, and then directly placed on the nib, in which a 3 kV was applied. The nib was made from brass and was designed to easily connect with a capillary (I.D. 0.25 mm). As a result, it was possible to continuously elute the paper with methanol at a rate of 6 μ L/min.

3. Results and discussion

Fig. 1 shows SEM (scanning electron microscope) images of samples of chromatography paper, gampi paper, PLLA nanofibers and the PLA microarray membrane (frames, A–D), respectively. As can be seen, in frame (A), the chromatography paper is comprised of disorganized-fibers. In contrast to this, gampi paper (frame B) is of more uniform, straighter fibers that are smaller in diameter, and more compact. The paper skin is smooth and has the natural color (light yellow) of the cream, with a unique desirable luster. To be on the safe side, we measured the average thickness of cicada paper, tengujou paper and glassine paper. We also investigated electrospray ionization efficiency, using *p*-chloroamphetamine (concentration level, 5 μ g/mL) as the test sample. These findings are summarized in Table 1. The average thickness of gampi paper that was used in this study was about 19 μ m and the limit of detection of *p*-chloroamphetamine was determined to be 0.04 μ g/mL; linearity was found from 0.04 to 25 μ g/mL and the LOD (at $S/N = 3$). Tengujou paper is also very thin, but it is too soft to use. Since a thin and tough type of paper is preferable for use in paper-spray MS, we synthesized a series of thin and tough fibers, i.e. nanofibers, for comparison. One more reason for this is that gampi paper is made by hand in the traditional manner, which may result in differences in the final product, depending on the location where it is manufactured. Furthermore, it may not be easily obtained in other countries. As it can be seen in frame (C), the PLLA nanofiber is comprised of a regularly arrayed nanofibers. Actually, it resembles very thin A4 paper. The inset (in frame C) shows a cross section image. The average diameter of this single fiber is about 0.91 μ m. We were curious as to whether the use of a material comprised of hollow fibers would improve ionization efficiency, so we synthesized a series of microarray membranes for comparison. Frame (D) shows a SEM image of a PLA microarray membrane. The inset (in frame D) shows an expanded surface image, showing a surface with a large number of small holes. Almost all of these

Table 1
Limit of detection (μ g/mL) values for *p*-chloroamphetamine for five different types of paper.

Type of papers	Average thickness (μ m)	LOD ($n = 3$)	R^2
Chromatography paper	130	0.10	0.9952
Gampi paper	19	0.04	0.9976
Cicada paper	43	0.08	–
Tengujou paper	19	0.23	–
Glassine paper	22	0.15	–

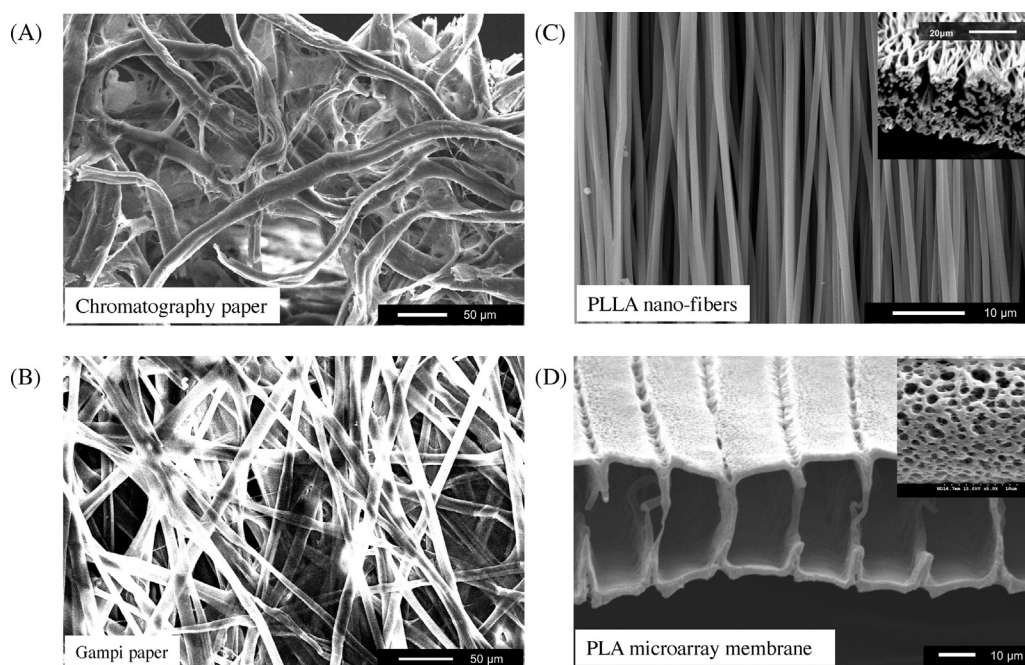


Fig. 1. SEM (scanning electron microscope) images of samples of chromatography paper (A), gampi paper (B), PLLA nanofiber (C) and PLA microarray membrane (D), respectively. The insets (in frames C and D) show an expanded cross section image the surface, respectively.

holes penetrate through the tube wall; the pipe thickness is about 2–5 μm . However, these properties failed to result in an improvement in the limit of detection. Table 2 summarizes the average ϕ values for the microarray membrane and nanofibers. The limit of detection values for *p*-chloroamphetamine, when used in paper-spray MS are also summarized. As can be seen, the results for PLLA nanofibers are similar to those for gampi paper. Thus, we conclude that either gampi paper or PLLA nanofiber is superior to chromatography paper for use in paper-spray MS analyses. We also propose the reason for this. Fig. 2 shows the relationship between the paper-spray ion intensity (total ion current; m/z : 169.05–170.05) and the period of successive ion occurring (time; s). In the case of chromatography paper, the ion intensity decreased very slowly (black line). About ~ 101 s (time of $I_{1/2}$) are required for the ion intensity to drop to one half of the maximum, after the sample solution (3 μL) was dropped. However, when gampi paper (red line) and PLLA nanofibers (blue line) were used, the values of $I_{1/2}$ are only 2.7 and 1.5 s, respectively. The mechanism of paper-spray MS has been reported previously [27] and is not repeated in this report. Based on our data, it is clear that, after dropping the sample molecules on a thin and tough paper, they are translated and evaporated immediately, and, as a result, many more sample molecules can be detected in a very short period of time.

Thus far, the use of gampi paper is quite convenient. If it is difficult to obtain, the synthesis of a nanofiber support is an alternate

Table 2
Limit of detection ($\mu\text{g}/\text{mL}$) values for *p*-chloroamphetamine for six types of fibers.

	Averaged ϕ (μm)	LOD ($n=3$)	R^2
<i>Microarray membrane</i>			
Poly(lactic acid) (PLA)	36.2	0.30	0.9726
<i>Nanofiber</i>			
Poly(vinylidene fluoride) (PVDF)	0.45	0.10	0.9801
Nylon	0.17	0.30	0.9363
Poly(L-lactic acid) (PLLA)	0.91	0.04	0.9849
Random PLLA	0.71	0.1	0.9795
Polycarbonate (PC)	3.0	0.05	0.9973

choice. Finally, we used gampi paper to detect two types of clandestine tablets, in order to examine whether the combination of gampi paper and paper-spray MS is actually more useful and faster than that of GC/MS, a traditional method. Fig. 3 shows the mass spectra for the components of the two types of clandestine tablets. As can be seen in frame (A), the clandestine tablet I contains MDMA (3,4-methylenedioxy-*N*-methylamphetamine) caffeine and ketamine, respectively. The inset shows the results obtained by GC/MS. The internal standard (I.S.) used was methoxyphenamine hydrochloride. Typically, more time is required to process a clandestine tablet for analysis, since a series of pretreatment steps are needed. Frame (B) shows a different type of clandestine tablet; it contains methamphetamine, norephedrine, ephedrine, caffeine and ketamine, respectively. The inset shows the result obtained by a GC/MS, which

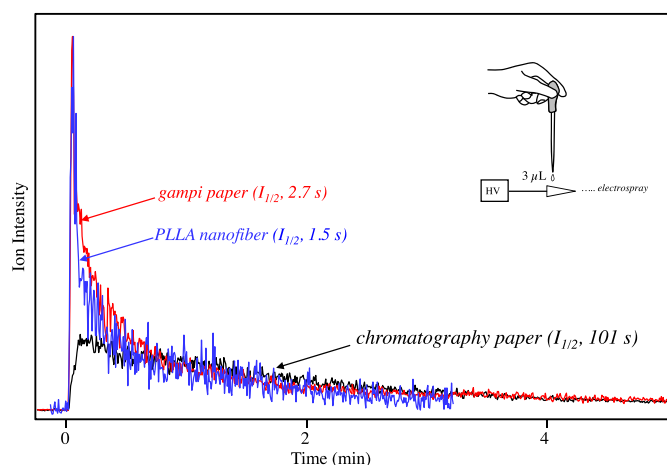


Fig. 2. The relationship between paper-spray ion intensity (total ion current; m/z : 169.05–170.05) and the period of successive ion occurring (time; s). Results obtained using chromatography paper, gampi paper and PLLA nanofibers, are shown as black, red and blue lines, respectively. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

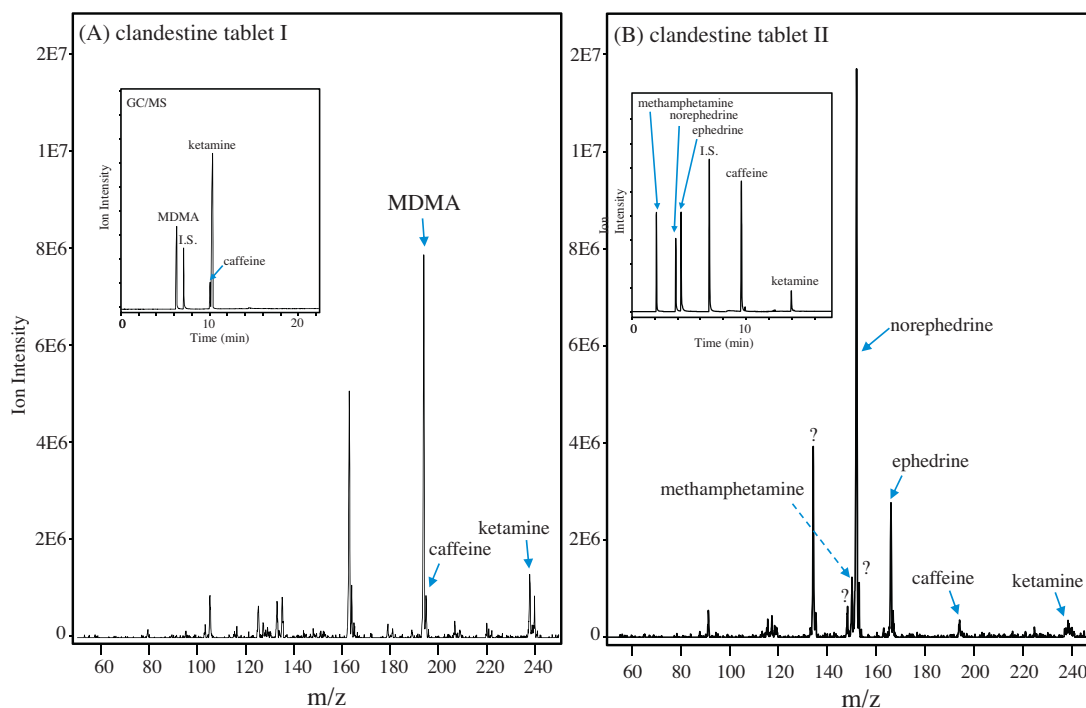


Fig. 3. Mass spectra of two types of clandestine tablets. The inset shows the results obtained by GC/MS.

verifies that the results obtained by paper-spray MS are valid. In general, methamphetamine can be synthesized from ephedrine or pseudoephedrine, and, as shown in this case; norephedrine is a decomposition product produced from methamphetamine. Hence, we conclude that either gampi paper or a nanofiber is more suitable for paper spray-MS better than chromatography paper, and, under most circumstances, this technique is the most favorable rapid “drug-screening” method for use under ambient conditions.

4. Conclusions

The development of novel materials for paper-spray mass spectrometry is described. Gampi paper proved to be superior to regular chromatography paper, cicada paper, tengujou paper and glassine paper. Among the synthesized papers, i.e. nanofibers and a microarray membrane, the poly-L-lactic acid nanofiber was better than polylactic acid, polycarbonate, polyvinylidene fluoride or nylon. This method is simple and economical, and is suitable for use in the rapid screening of drugs, since it has a high degree of sensitivity, the operating procedure is simple and an ion signal can be observed immediately. We believe this method has the potential for use in practical analyses and can also be regarded as a helpful tool for use, not only in forensic and clinical analysis, but also biomolecules.

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