



Molecular Ionization from Carbon Nanotube Paper**

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Dedicated to Professor C. N. R. Rao on the occasion of his 80th birthday.

Abstract: Ambient ionization is achieved by spraying from a carbon nanotube (CNT)-impregnated paper surface under the influence of small voltages (≥ 3 V). Organic molecules give simple high-quality mass spectra without fragmentation in the positive or negative ion modes. Conventional field ionization is ruled out, and it appears that field emission of microdroplets occurs. Microscopic examination of the CNT paper confirms that the nanoscale features at the paper surface are responsible for the high electric fields. Raman spectra imply substantial current flows in the nanotubes. The performance of this analytical method was demonstrated for a range of volatile and nonvolatile compounds and a variety of matrices.

Recent progress in mass spectrometry has depended heavily on advances in the methods of ion formation. The creation of stable molecular ions of complex molecules with minimum internal energy has been a primary goal of such experiments. The most widely used methods to achieve this are electrospray ionization (ESI) and matrix-assisted laser desorption/ionization (MALDI). More recently developed ambient ionization methods,^[1] such as desorption electrospray ionization (DESI),^[2] allow samples to be examined in their native state with minimal or no sample pre-treatment. These advantages and the resulting speed of analysis have led to the introduction of about fifty different variants of ambient ionization. Direct analysis in real time (DART),^[3] extractive electrospray ionization (EESI),^[4] desorption atmospheric pressure chemical ionization (DAPCI),^[5] desorption atmospheric pressure photoionization (DAPPI),^[6] laser ablation electrospray ionization (LAESI)^[4b] and paper spray ionization,^[7] are some of the methods that have been introduced

over the past decade. Herein, we show that ionization can be achieved from a substrate that is coated with carbon nanotubes (CNTs) at a potential of just a few volts. It is suggested that the high electric fields that are produced at the small CNT protrusions are responsible for low-voltage ionization, which appears to occur by field emission of charged microdroplets.^[8] With this “nanotube spray” method, various analytes, which are applied to the tip of the coated substrate, are detectable in small amounts. Neutral molecules typically appear as either their protonated or deprotonated forms, whereas salts yield both positive and negative ions. The fact that a high voltage (HV) is not needed sets this method apart from other ambient spray ionization methods, except for easy ambient spray ionization (EASI).^[9]

Experiments were done with triangles of CNT-coated filter paper, which were wetted with MeOH/water and connected to a 3 V battery (Figure 1A,B; see also the Experimental Section). Mass spectra that were recorded for triphenylphosphine (TPP) using the CNT paper and a 3 V battery source (Figure 1C) exhibited a peak at m/z 263, which is due to protonated triphenylphosphine, $[M+H]^+$. Spectra could be collected for two to three seconds using 2 μ L of the sample solution. When the voltage on the paper was reduced

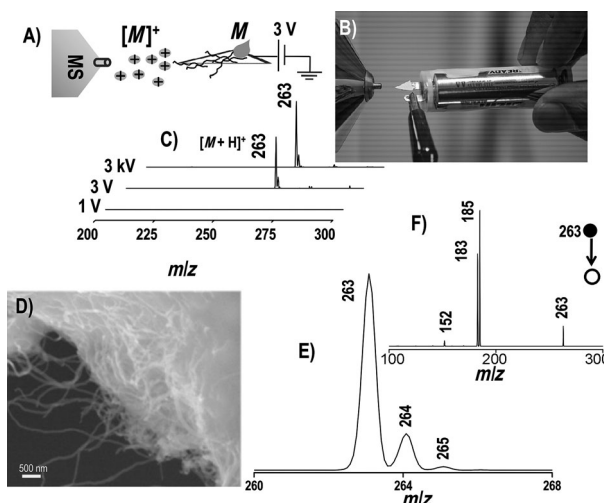


Figure 1. A) Schematic representation of the ionization process from CNT paper. B) Photograph of the ionization source showing paper triangle and battery along with a grounding electrical connection. C) Mass spectra of triphenylphosphine (M) at 3 kV, 3 V, and 1 V from wet CNT paper. D) Field emission scanning electron microscopy (FE-SEM) image of CNT-coated paper. E) Isotope distribution of the protonated molecule at 3 V. F) MS² spectrum of the parent ion at m/z 263.

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to 1 V, the spectrum disappeared completely. The full-range mass spectrum of TPP on CNT-coated paper (Supporting Information, Figure S1) is similar to the conventional ESI mass spectrum recorded at 3 kV (Figure S2). Although the intensity of the molecular ion at 3 V is as much as 10^4 times lower than that in the ESI spectrum, the conditions are less harsh; in particular, the oxidation product of triphenylphosphine at m/z 279 as well as the oxidation product of a trace homologous impurity (product at m/z 293) are not observed, nor are their fragmentation products at m/z 203 and m/z 219. Moreover, the mass spectrum shows a well-defined isotopic pattern (Figure 1 E) of the molecular ion, and its structure was confirmed by a tandem mass spectrum, which showed the expected benzene loss and further loss of H_2 (Figure 1 F).

An increase in the applied potential increases the ion intensity, until it is saturated at 4 kV; at this point, the signal was almost of the same magnitude as the ESI signal. However, no additional features were observed. The two paper spray spectra (at 3 kV and 3 V, both from CNT-coated paper) that are shown in Figure 1 C are identical in terms of the ions observed but the signal/noise ratio is higher at 3 V. A minimum applied voltage of 3 V is essential for detectable ion signals. Control experiments confirmed the fact that CNTs were essential for the ionization process at 3 V. Filter paper without the CNT coating, but cut similarly and using the same solvent did not produce detectable ions with a range of analytes, even at up to 500 V (Figure S3 A). A closer examination of the edge of the coated paper revealed protruding nanotubes (Figure 1 D). From these results and the experiments described below, we suggest that field emission of microscale solution droplets containing analyte occurs at these nanoscale protrusions, and this is responsible for the observed ionization event.

Additional experiments were conducted to explore the mechanism of ionization. Clearly, the absence of fragment ions in the mass spectrum may be attributed to the occurrence of soft ionization events. The occurrence of ionization at 3 V strongly implies a process that is associated with a very high electric field. The field must be due to the small conductive CNT structures (Figure 1 D) that protrude from the surface of the filter paper and act as electrodes.^[10] The voltage (from the battery) that is applied at the CNT electrode induces an electric field between the paper tip and the mass spectrometer inlet. The field intensity is high at the paper tip, where ionization occurs.

To differentiate the contributions of the protruding CNT structures from the macroscopic paper point to ionization, in another experiment, a rectangle of CNT-coated paper was held in front of the mass spectrometer inlet (with one of the long sides facing the MS inlet), and ionization of TPP was attempted. All other parameters except the shape of the paper were held constant. The mass spectra showed ionization of TPP at 3 V from this paper rectangle (Figure S3 D). This confirms that in this case, the pointed paper tip is not involved in the ionization, but that the protruding CNTs are responsible for this process. Furthermore, the complete absence of molecular ion peaks when using a similarly cut filter paper without the CNT coating revealed the role of the nanoscale features in providing a field strength that is high enough to

cause field emission. Figure S3 E and S3 F show the change in intensity of the molecular ion peak with voltage for CNT-coated and normal paper triangles, respectively. The ion signals for both of these papers saturate at high voltages, but with CNTs, the onset of ion ejection occurs much earlier. Therefore, it is reasonable to conclude that at lower voltages CNTs play a role in ionization, and that with the increase in voltage a Taylor cone forms at the paper tip so that the macroscopic electric field is responsible for ionization.

In conventional field ionization,^[11] vapor-phase molecules that are placed in a strong electric field lose an electron to form positively charged radical cations. Many of the analytes used are simple volatile organic molecules, which are expected to give M^+ radical cations when ionized by this mechanism, for example, m/z 262 in the case of triphenylphosphine, not the observed m/z 263. To test whether field ionization of vapor-phase compounds might contribute, triethylamine (vapor pressure: $p = 57$ torr at 20°C) was dissolved in acetone ($p = 184.5$ torr at 20°C) and introduced into the field (the gap between the CNTs and the MS inlet) as a vapor, and ionization was attempted at low voltages. It was found that the use of analyte vapors did not lead to a detectable amount of ionization. We thus conclude that field emission occurs from a solvated analyte or droplet, as in all cases, only the $[M+H]^+$ ion and not the radical cation M^+ was detected.

To further investigate the proposed mechanism, which involves field emission of charged droplets, the experiment with TPP and three other analytes was repeated in the presence and absence of a protic acid.^[9] Addition of acid will generate the salt and should inhibit simple field ionization (to give M^+), but it should increase the field emission from droplets (to give $[M+H]^+$). Therefore, analytes that contain basic functional groups (phosphines and amines) were selected, and they were analyzed before and after the addition of dilute acid (0.01 N HCl). The relative intensities of the peaks that correspond to the protonated molecules are enhanced after the addition of dilute acid to the analytes with basic functional groups (Figure 2). This enhancement supports the hypothesis that ionization of a solvated species has occurred.

Various preformed ions (derived from the salts tetramethylammonium chloride, tetramethylammonium bromide, tetramethylammonium nitrate, and tetrabutylammonium iodide) were studied under the same conditions. In accordance with the proposed mechanism, both positive and negative ions were observed in the CNT-derived mass spectra (Figure S4 and S5). No fragmentation was observed, and the extreme softness of the process, even compared to other soft ionization methods, is indicated by the presence of hydrated halide anions. These studies showed that preformed ions can also be ejected from the surface in droplets, and that conventional field ionization is not responsible for ion formation.

To further investigate the applicability of the CNT ionization technique, this method was employed for the qualitative analysis of various analytes, including pesticides, antibiotics, and amino acids. All of these compounds gave characteristic mass spectra; therefore, it has been shown that

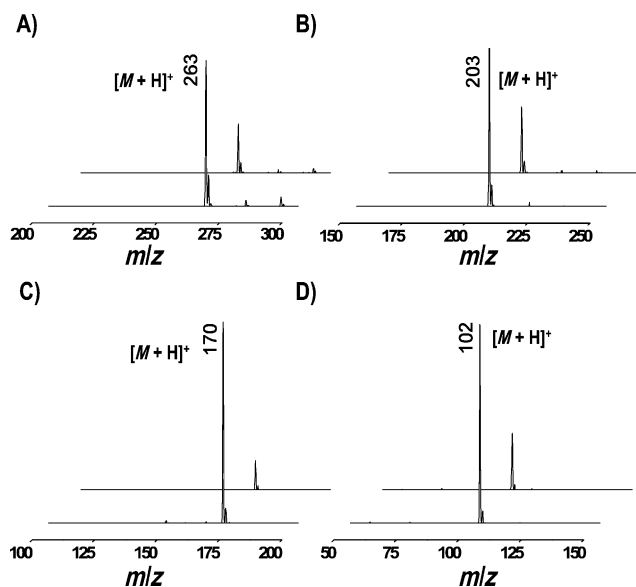


Figure 2. A–D) Intensity enhancement upon the addition of dilute HCl for various analytes (*M*) at 3 V, namely triphenylphosphine (A), tributylphosphine (B), diphenylamine (C), and triethylamine (D). The upper and lower traces in each plot are on the same scale and show spectra that were recorded before and after HCl addition, respectively. The y axes correspond to the intensity.

this low-voltage ionization method is useful for diverse analytical needs. Direct analysis of various contaminants on fruit is possible with this method. Three common insecticides (carbofuran, methyl parathion, and parathion) that are used for the protection of fruit were applied on the surface of an orange at a concentration of 50 ppm. Then, CNT-coated paper was rubbed on the surface and held in front of the MS inlet for analysis. The molecular ion peaks of different pesticides that were obtained using the battery-powered spray MS method are shown in Figure 3. In reality, the amount of sample extracted from the fruit surfaces during rubbing may be several orders of magnitude lower than the applied quantity, and therefore, the limit of detection is much lower than the applied sample concentration. The molecular ion peaks of each of these pesticides are shown in Figure S6.

The same method was used to analyze medicines. CNT-coated paper was rubbed on the surfaces of three commercially available tablets, namely Crocin, Combiflam, and Xyzal (trade names), and held in front of the MS inlet with the 3 V battery set-up. Both Crocin and Combiflam contain paracetamol (acetaminophen) as the major ingredient (Figure S7). Direct analysis of these tablets using the CNT-coated paper gave a peak corresponding to protonated paracetamol. The other tablet, Xyzal, is a non-sedative antihistamine and contains levocetirizine dihydrochloride as the active ingredient. Analysis of this tablet (Figure S7B) under the same conditions gave a peak in the mass spectrum that corresponds to protonated levocetirizine. The identity of the analytes was confirmed by MS² studies (Figure S7, insets).

Direct analysis of amino acids is also possible by spraying from CNT-coated paper. Several amino acids (30 ppm) were dropped onto the tip of the CNT-coated paper with a micro-

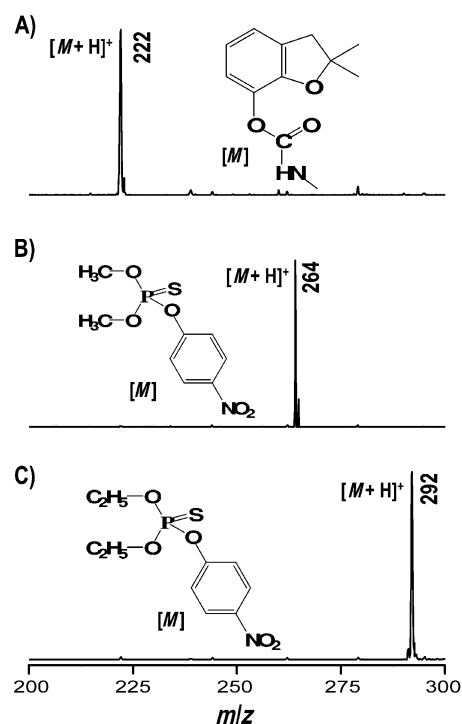


Figure 3. A–C) Detection of pesticides that were examined individually from the surface of an orange; carbofuran (A), methyl parathion (B), and parathion (C). The y axes correspond to the intensity.

pipette (injected volume: 3 μ L, which corresponds to a total loading of 10 ng). Intense peaks that correspond to the protonated amino acids were observed by mass spectrometry (Figure S8). The zwitterionic nature of amino acids may lead to easy extraction of ions from the nanotube tips in the electric field.

To probe the effect of the ionization event on the paper electrode itself, Raman spectra of CNT-coated paper were recorded before and after a series of experiments (ionization of TPP at 3 V over a period of 20 min with continuous sampling (50 times) using 3 μ L of solution each time; Figure 4A).^[12] The data revealed a large red shift^[13] of the D and G bands, which implies the acquisition of electrons by the CNT during ionization in the positive ion mode.^[14] It appears that as the ionization occurs, a charge builds up, as would be expected for field-assisted ionization.^[11] However, there appears to be electron transfer from the developing microdroplet to the CNT, which is effectively a polarization of the electrons in the long thin CNT fiber (see Figure 1D) that is driven by the high field, the mobility of electrons in the CNTs, and their large electron affinity.^[15] As the positively charged droplet breaks away, the residual charge appears to lead to a reduction of the CNTs, which is reflected by the red-shifted D and G bands in the Raman spectrum. The hypothesis that electron transfer from the charged solvent microdroplet to CNT occurs was supported by a blank experiment, where only solvent and potential were applied to CNT-coated paper for the same period of time; afterwards, the CNT paper was studied by Raman spectroscopy. The recorded spectrum revealed red-shifted D and G bands.

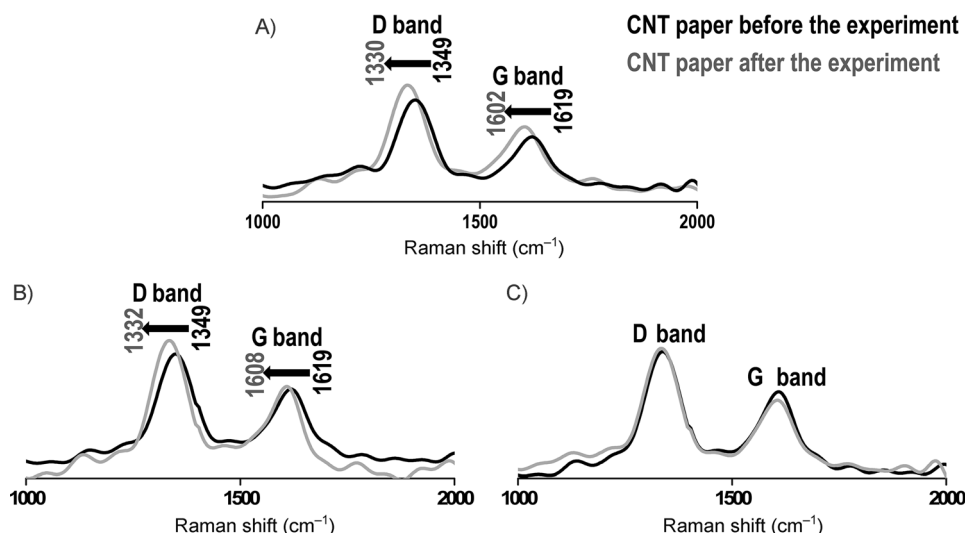


Figure 4. Raman spectra of CNT-coated paper before and after ionization for A) neutral molecules (30 ppm TTP in MeOH/H₂O) and preformed ions (tetramethylammonium bromide) in the B) positive and C) negative ion modes. The y axes correspond to the intensity.

Raman spectra of the nanotube sample were also recorded before and after ionization of the salt tetramethylammonium bromide in both the positive and negative ion modes. When preformed ions were employed, a red shift of the D and G bands for the CNT-coated paper was only observed for the measurement in the positive ion mode (Figure 4B). As before, this may be due to the high electric field that is needed to cause the ejection of solvated ions in microdroplets. Such a reduction did not occur during the negative ion mode measurement, as Raman spectra showed unshifted D and G bands (Figure 4C), presumably because the CNTs are already electron-rich under these conditions, and the field replenishes the lost charge. These measurements also confirm the reusability of the nanotube-coated electrodes.

The results presented herein suggest a versatile strategy for the direct analysis of diverse chemical species. This method can be modified to suit various analytical requirements. Nanoscale surfaces have previously been used for ionization in matrix-free laser-based techniques.^[17] Replacement of the high-voltage power supply with a 3 V battery simplifies mass spectrometry through ion formation from a nanoscale antenna. This nanotube ionization method has been applied to analyze a variety of samples from different sources, including fruit surfaces, tablets, and a range of organic molecules, including amino acids, antibiotics, and pesticides, at relatively low concentrations.^[18]

Experimental Section

Most of the experiments were carried out using multi-walled carbon nanotubes (MWNTs), referred to as CNTs. They were dispersed in water (2 mg in 25 mL water) assisted by sodium dodecyl sulfate (6 mg) as a surfactant using a probe sonicator.^[16] This stable CNT suspension was drop-cast onto Whatman 42 (particle retention: 2.5 µm) filter paper (3 µL of the CNT suspension coating 5 mm²). The uniformity of this dispersion and its consequent stability are essential aspects of the success of the experiment. The paper was

dried in air and cut into triangles with dimensions of 2 × 5 mm (base × height). As mentioned in the text, a triangular shape is not essential. The CNT-coated paper triangle was connected to a 3 V battery and held close (2 mm) to the mass spectrometer inlet. Then it was loaded with sample (typically as 30 ppm solutions). The volume of solvent used was 2 µL, and repeated measurements using the same paper used the same aliquot of pure solvent. All routine measurements were made at 3 V. Mass spectra were recorded in the positive ion mode for all analytes, except for preformed ions. For preformed ions that are derived from salts, both positive and negative ion mode spectra were recorded at ± 3 V. Spectra were recorded under the following experimental conditions: solvent: methanol/water (1:1); source voltage: ± 3 V; capillary temperature: 150 °C; capillary voltage: ± 15 V; and tube lens voltage: ± 55 V. Single-walled carbon nanotubes (SWNTs) were also used for measurements, but no detectable enhancement of the signal was seen. The following parameters were used for all ESI experiments: Source voltage: −5 kV; sheath gas (nitrogen) flow rate: 8 (manufacturer's unit); solvent flow rate: 2 µL min^{−1}; all other parameters were the same as for the paper spray experiments. All ESI mass spectra correspond to an average of 100 scans.

SWCNTs and MWCNTs were purchased from Nanocyl s.a, USA; SDS from RFCL Ltd., Gujarat, India; triphenylphosphine from Spectrochem Pvt. Ltd., Mumbai, India; tributylphosphine from Wako Pure Chemical Industries Ltd.; diphenylamine and triethylamine from Merck Ltd., Mumbai, India. The pesticides carbofuran, methyl parathion, and parathion were purchased from Sigma Aldrich, India. All of the tablets used (Crocine, Combiflam, and Xyzal, all trade names) were purchased from a local pharmacy. Amino acids used in the experiments were purchased from Sisco Research Laboratories Pvt. Ltd., Mumbai, India. All analytes (other than pesticides and tablets) were used at concentrations of 30 ppm. HPLC-grade methanol (Sigma Aldrich) and MeOH/water (1:1) were used as the solvents.

The probe sonicator (750 W, model number VCX 750) was obtained from M/s Sonics, USA. All mass spectra were recorded using an ion trap LTQ XL (Thermo Scientific, San Jose, California). MS² analysis using collision-induced dissociation was performed to confirm the identity of the ions. Raman measurements were made using a Witec GmbH Confocal Raman microspectrometer, Germany with 532 nm and 633 nm laser excitations. A field emission scanning electron microscope by FEI was used to image the CNT-coated paper samples.

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