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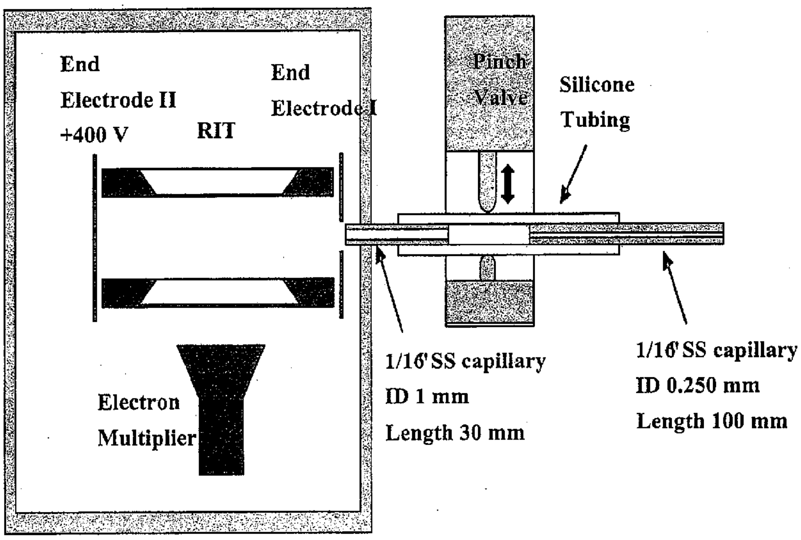

Figure 1

(57) Abstract: A method of interfacing atmospheric pressure ion sources, including electrospray and desorption electrospray ionization sources, to mass spectrometers, for example miniature mass spectrometers, in which the ionized sample is discontinuously introduced into the mass spectrometer. Discontinuous introduction improves the match between the pumping capacity of the instrument and the volume of atmospheric pressure gas that contains the ionized sample. The reduced duty cycle of sample introduction is offset by operation of the mass spectrometer under higher performance conditions and by ion accumulation at atmospheric pressure.

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DISCONTINUOUS ATMOSPHERIC PRESSURE INTERFACE

RELATED APPLICATIONS

This application claims the benefit of U.S. provisional application serial numbers 60/941,310 and 60/953,822 filed in the U.S. Patent and Trademark office June 1, 2007 and August 3, 2007 respectively, both of which are hereby incorporated by reference herein in their entireties.

GOVERNMENT SUPPORT

The present invention described herein was support at least in part by the Department of Homeland Security (grant number: HSHQPA-05-9-0033). The government has certain rights in the invention.

TECHNICAL FIELD

The invention generally relates to an improvement to ion introduction to mass spectrometers.

BACKGROUND

The atmospheric pressure interface (API) of a mass spectrometer is used to transfer ions from a region at atmospheric pressure into other regions at reduced pressures. It allows the development and use of a variety of ionization sources at atmospheric pressure for mass spectrometry, including electrospray ionization (ESI) (Fenn, J. B.; Mann, M.; Meng, C. K.; Wong, S. F.; Whitehouse, C. M. *Science* **1989**, *246*, 64-71; Yamashita, M.; Fenn, J. B. *J. Phys. Chem.* **1984**, *88*, 4451-4459), atmospheric pressure ionization (APCI) (Carroll, D. I.; Dzidic, I.; Stillwell, R. N.; Haegele, K. D.; Horning, E. C. *Anal. Chem.* **1975**, *47*, 2369-2373), and atmospheric pressure matrix assisted laser desorption ionization (AP-MALDI), (Laiko, V. V.; Baldwin, M. A.; Burlingame, A. L. *Anal. Chem.* **2000**, *72*, 652-657; Tanaka, K.; Waki, H.; Ido, Y.; Akita, S.; Yoshida, Y.; Yoshida, T.; Matsuo, T. *Rapid Commun. Mass Spectrom.* **1988**, *2*, 151-153) etc. An API not only allows the coupling of a mass spectrometer with various sample separation and sample pretreatment methods, such as liquid chromatograph, but also enables ambient preparation and treatment of ions using a variety of desirable conditions, such as the thermal production of the ions, (Chen, H.; Ouyang, Z.; Cooks, R. G. *Angewandte Chemie, International Edition* **2006**, *45*, 3656-3660; Takats, Z.; Cooks, R. G.

Chemical Communications (Cambridge, United Kingdom) **2004**, 444-445) ion-ion reactions (Loo, R. R. O.; Udseth, H. R.; Smith, R. D. *Journal of the American Society for Mass Spectrometry* **1992**, *3*, 695-705) or ion fragmentation, (Chen, H.; Eberlin, L. S.; Cooks, R. G. *Journal of the American Chemical Society* **2007**, *129*, 5880-5886) before sending them into vacuum for mass analysis. Without an API, it is also not possible to take advantage of the recent development of a new category of direct ambient ionization/sampling methods, including desorption electrospray ionization (DESI) (Takats, Z.; Wiseman, J. M.; Gologan, B.; Cooks, R. G. *Science* **2004**, *306*, 471-473), direct analysis in real time (DART) (Cody, R. B.; Laramee, J. A.; Durst, H. D. *Anal. Chem.* **2005**, *77*, 2297-2302), Atmospheric Pressure Dielectric Barrier Discharge Ionization (DBDI), and electrospray-assisted laser desoption/ionization (ELDI) (Shiea, J.; Huang, M. Z.; Hsu, H. J.; Lee, C. Y.; Yuan, C. H.; Beech, I.; Sunner, J. *Rapid Commun. Mass Spectrom.* **2005**, *19*, 3701-3704).

Since the ESI source was first successfully demonstrated for mass spectrometry (Yamashita, M.; Fenn, J. B. *J. Phys. Chem.* **1984**, *88*, 4451-4459), the configuration of API used for ESI was widely adopted and has not changed significantly. Nowadays a typical API has a constantly open channel involving a series of differential pumping stages with a capillary or a thin hole of small ID to allow ions to be transferred into the first stage and a skimmer for access to the second stage. A rough pump is usually used to pump the first region to about 1 torr and multiple turbomolecular pumps or a single pump with split flow used for pumping the subsequent regions with a base pressure in the final stage used for the mass analysis, which is usually 10^{-5} torr or below. Ion optical systems, including static electric lenses and RF guides, are also used to preserve the ion current while the neutrals are pumped away. To maximize the number of ions transferred into the final region for mass analysis, large pumping capacities are always desirable so that larger orifices can be used to pass ions from region to region. As an example, a Finnigan LTQ (Thermo Fisher Scientific, Inc., San Jose, CA) ion trap mass spectormeter has two 30 m^3/hr rough pumps for the first stage and a 400 l/s turbomolecular pump with two drag pumping stages for the next 3 stages. The highest loss in ion transfer occur at the first stage and the second stage, corresponding to a 2 orders and a 1 order of magnitude, respectively, which results in an overall efficiency lower than 0.1% for the ion transfer through an API. When an attempt is made to implement this kind of API on a portable instrument, the ion transfer efficiency is further reduced by the fact that much lower pumping capacity must be used to achieve the desirable weight and power consumption of the instruments. A recently developed Mini 10 handheld rectilinear ion trap mass spectrometer weighs only 10 kg and has miniature rough and turbo pumps of only 0.3 m^3/hr and 11 l/s, respectively. (Gao, L.; Song, Q.; Patterson, G. E.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2006**, *78*, 5994-6002)

Many efforts have been made to increase the ion transfer efficiency in laboratory scale mass spectrometers. The ion transfer through the second stage has been successfully improved by a factor of ten by replacing the skimmer with an ion funnel. (Shaffer, S. A.; Tang, K. Q.; Anderson, G. A.; Prior, D. C.; Udseth, H. R.; Smith, R. D. *Rapid Communications in Mass Spectrometry* **1997**, *11*, 1813-1817) Air-dynamic ion focusing devices (Zhou, L.; Yue, B.; Dearden, D. V.; Lee, E. D.; Rockwook, A. L.; Lee, M. L. *Anal. Chem.* **2003**, *75*, 5978-5983; Hawkridge, A. M.; Zhou, L.; Lee, M. L.; Muddiman, D. C. *Analytical Chemistry* **2004**, *76*, 4118-4122) have been employed in front of API's of mass spectrometers. Though the efficiency of API itself was not improved, the ultimate ion current reaching the mass analyzer was significance increased. However, the possibility of arcing inside the vacuum increases at high pressure, which results in high noise and short lifetime of the electron multiplier and power supplies.

There is a need for atmospheric interfaces that increase ion transfer efficiency to a mass spectrometer.

SUMMARY

An aspect of the invention herein provides a device for controlling movement of ions and the body of air or other gas in which the ions are maintained, the device including: a valve aligned with an exterior portion of a tube, in which the valve controls movement of ions through the tube; and a first capillary inserted into a first end of the tube and a second capillary inserted into a second end of the tube, in which neither the first capillary nor the second capillary overlap with a portion of the tube that is in alignment with the valve.

In a related embodiment of the device, a proximal end of the first capillary is connected to a trapping device, in which the trapping device is below atmospheric pressure. In another related embodiment, a distal end of the second capillary receives the ions from an ionizing source, in which the ionizing source is at substantially atmospheric pressure.

In certain embodiments of the device, the tube is composed of an inert plastic, for example silicone plastic. In other embodiments, the first and second capillary are composed of an inert metal, for example stainless steel. In other embodiments of the device, the first and second capillaries have substantially the same outer diameter. In alternative embodiments, the first and second capillaries have different outer diameters. In another embodiment of the device, the first and second capillaries have substantially the same inner diameter. Alternatively, the first and second capillaries have different inner diameters. In another embodiment of the device, the second capillary has a smaller inner diameter than the inner diameter of the first capillary. In another embodiment of the devices, the valve is selected from the group consisting of a pinch valve, a thin plate shutter valve, and a needle valve.

Another aspect of the invention herein provides a device for controlling movement of ions, the device including a valve aligned with an exterior portion of a tube, in which the valve controls movement of ions through the tube. In a related embodiment, a proximal end of the tube is connected to a trapping device, in which the trapping device is below atmospheric pressure. In another related embodiment, a distal end of the tube receives the ions from an ionizing source, in which the ionizing source is at substantially atmospheric pressure. In certain embodiment, a distal end of the tube receives the ions at a first pressure, and a proximal end of the tube is connected to a trapping device at a pressure reduced from the first pressure.

Another aspect of the invention herein provides a discontinuous atmospheric pressure interface system including: an ionizing source for converting molecules into gas phase ions in a region at about atmospheric pressure; a trapping device; and a discontinuous atmospheric pressure interface for transferring the ions from the region at about atmospheric pressure to at least one other region at a reduced pressure, in which the interface includes a valve for controlling entry of the ions into the trapping device such that the ions are transferred into the trapping device in a discontinuous mode. .

In a related embodiment, the system further includes at least one vacuum pump connected to the trapping device. In another related embodiment of the system, the atmospheric pressure interface further includes: a tube, in which an exterior portion of the tube is aligned with the valve; and a first capillary inserted into a first end of the tube and a second capillary inserted into a second end of the tube, such that neither the first capillary nor the second capillary overlap with a portion of the tube that is in alignment with the valve. In another embodiment of the system, the atmospheric pressure interface further includes a tube, in which an exterior portion of the tube is aligned with the valve.

In certain embodiments of the system, ions enter the trapping device when the valve is in an open position. In another embodiment of the system, ions are prevented from entering the trapping device when the valve is in a closed position. The closed position refers to complete closure of the valve, and also includes quasi-closure of the valve, i.e, the valve is substantially closed such that pumping significantly exceeds ingress of gas or vapor.

Substantially closed includes at least about 70% closed, at least about 80% closed, at least about 90% closed, at least about 95% closed, or at least about 99% closed.

In another embodiment, the system further includes a computer operably connected to the system. In another embodiment, the computer contains a processor configured to execute a computer readable program, the program controlling the position of the valve. In another embodiment, the computer contains a processor configured to execute a computer readable program, the program implementing a selected waveform inverse Fourier transformation (SWIFT) isolation algorithm to separate ions.

In certain embodiments of the system, the ionizing source operates by a technique selected from the group consisting of: electrospray ionization, nano-electrospray ionization, atmospheric pressure matrix-assisted laser desorption ionization, atmospheric pressure chemical ionization, desorption electrospray ionization, atmospheric pressure dielectric barrier discharge ionization, atmospheric pressure low temperature plasma desorption ionization, and electrospray-assisted laser desorption ionization. In another embodiment of the system, the trapping device is selected from the group consisting of a mass analyzer of a mass spectrometer, a mass analyzer of a handheld mass spectrometer, and an intermediate stage storage device.

In another embodiment of the system, the mass analyzer is selected from the group consisting of: a quadrupole ion trap, a rectalinear ion trap, a cylindrical ion trap, a ion cyclotron resonance trap, and an orbitrap. In another embodiment of the system, the intermediate storage device is coupled with a mass analyzer of a mass spectrometer or a mass analyzer of a handheld mass spectrometer. In a related embodiment, the mass analyzer is selected from the group consisting of: a mass filter, a quadrupole ion trap, a rectalinear ion trap, a cylindrical ion trap, a ion cyclotron resonance trap, an orbitrap, a time of flight mass spectrometer, and a magnetic sector mass spectrometer. In yet another embodiment, the system further includes an ion accumulating surface connected to a distal end of the second capillary. In yet another embodiment, the system further includes an ion accumulating surface connected to a distal end of the tube. In another embodiment of the system, the tube of the atmospheric interface is composed of an inert plastic, for example silicone plastic. In another embodiment of the system, the first and second capillary of the atmospheric interface are composed of an inert metal, for example stainless steel.

In certain embodiments of the system, the valve operates to control entry of ions in a synchronized manner with respect to operation of the mass analyzer. In another embodiment of the system, the configuration of the discontinuous atmospheric pressure interface and the mass analyzer is off-axis. In another embodiment of the system, an ion optical element, for example, a focusing tube lens, is located between the discontinuous atmospheric pressure interface and the mass analyzer to direct the ions into the mass analyzer. In another embodiment, the system further includes an ion optical element located between the ionization source and the discontinuous atmospheric pressure interface to direct the ions into the mass analyzer.

Another aspect of the invention provides a kit including the above devices and a container. Another aspect of the invention provides a kit including the above system and a container. In certain embodiments, the kits include instructions for use.

Another aspect of the invention provides a method of discontinuously transferring ions at atmospheric pressure into a trapping device at reduced pressure, the method including: opening a valve connected to an atmospheric pressure interface, such that opening of the valve allows for transfer of ions substantially at atmospheric pressure to a trapping device at reduced pressure; and closing the valve connected to the atmospheric pressure interface, such that closing the valve prevents additional transfer of the ions substantially at atmospheric pressure to the trapping device at reduced pressure.

In certain embodiments, prior to opening the valve, the method further includes converting molecules to gas phase ions. In other embodiments, the converting step is selected from the group consisting of: electrospray ionization, nano-electrospray ionization, atmospheric pressure matrix-assisted laser desorption ionization, atmospheric pressure chemical ionization, desorption electrospray ionization, atmospheric pressure dielectric barrier discharge ionization, atmospheric pressure low temperature plasma desorption ionization, and electrospray-assisted laser desorption ionization.

In another embodiment of the method, the opening and the closing of the valve is controlled by a computer operably connected to the atmospheric pressure interface. In another embodiment of the method, the trapping device is selected from the group consisting of a mass analyzer of a mass spectrometer, a mass analyzer of a handheld mass spectrometer, and an intermediate stage storage device. In another embodiment of the method, the mass analyzer is selected from the group consisting of: a quadrupole ion trap, a rectalinear ion trap, a cylindrical ion trap, a ion cyclotron resonance trap, and an orbitrap. In another embodiment of the method, the intermediate storage device is coupled with a mass analyzer of a mass spectrometer or a mass analyzer of a handheld mass spectrometer. In a related embodiment, the mass analyzer is selected from the group consisting of: a mass filter, a quadrupole ion trap, a rectalinear ion trap, a cylindrical ion trap, a ion cyclotron resonance trap, an orbitrap, a time of flight mass spectrometer, and a magnetic sector mass spectrometer.

In certain embodiments of the method, electrical voltage of the mass analyzer is set to ground when the valve is open. In other embodiments of the method, subsequent to the ions being transferred into the mass analyzer and the valve being closed, the ions are retained by the mass analyzer for further manipulation. In another embodiment of the method, prior to further manipulation, the ions are cooled and the pressure is further reduced. In yet another embodiment of the method, further manipulation includes mass analysis of the ions.

In certain embodiments of the method, the computer synchronizes the opening and the closing of the valve with a sequence of mass analysis of the ions in the mass analyzer. In a related embodiment of the method, the computer synchronizes the opening and the closing of the valve with a sequence of steps that allow tandem mass analysis of the ions in the mass analyzer.

In another embodiment of the method, the atmospheric pressure interface further includes: a tube, in which an exterior portion of the tube is aligned with the valve; and a first capillary inserted into a first end of the tube and a second capillary inserted into a second end of the tube, such that neither the first capillary nor the second capillary overlap with a portion of the tube that is in alignment with the valve. In another embodiment of the method, the atmospheric pressure interface further includes: a tube, in which an exterior portion of the tube is aligned with the valve. In related embodiments of the method, the valve is selected from the group consisting of a pinch valve, a thin shutter plate valve, and a needle valve.

In another embodiment of the method, after converting the molecules to ions, the ions are stored on a functional surface connected to the distal end of the second capillary at atmospheric pressure, in which the functional surface is continuously supplied with ions from a continuously operated ion source. In another embodiment of the method, after converting the molecules to ions, the ions are stored on a functional surface connected to the distal end of the tube at atmospheric pressure, in which the functional surface is continuously supplied with ions from a continuously operated ion source. In related embodiments, the ions stored on the functional surface are subsequently transferred by the atmospheric pressure interface to the trapping device.

In another embodiment of the method, the first and second capillary of the atmospheric interface have substantially the same outer diameter. Alternatively, the first and second capillary of the atmospheric interface have different outer diameters. In another embodiment of the method, the first and second capillary of the atmospheric interface have substantially the same inner diameter. Alternatively, the first and second capillary of the atmospheric interface have different inner diameters. In another embodiment of the method, the second capillary has a smaller inner diameter that the inner diameter of the first capillary.

Another aspect of the invention provides a method of discontinuously transferring ions into a mass spectrometer, the method including: opening a valve connected to an atmospheric pressure interface, such that opening of the valve allows for transfer of ions substantially at atmospheric pressure to a mass analyzer at a reduced pressure in the mass spectrometer; and closing the valve connected to the atmospheric pressure interface, such that closing the valve prevents additional transfer of the ions substantially at atmospheric pressure to the mass analyzer at the reduced pressure in the mass spectrometer.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic view of a discontinuous atmospheric pressure interface coupled in a miniature mass spectrometer with rectilinear ion trap.

Figure 2a is a horizontal time graph of a typical scan function used for mass analysis using a discontinuous atmospheric pressure interface.

Figure 2b is a horizontal time graph of a manifold pressure measured during scanning, with an open time of 20ms and a close time of 800ms for the DAPI.

Figure 3a is a nano ESI mass spectrum recorded using a DAPI for a 5 ppm solution of caffeine and cocaine, 20 ms ion introduction time and 500 ms cooling time, including a detail of a portion of that spectrum.

Figure 3b is a nano ESI mass spectrum recorded using a DAPI for a 50 ppb mixture solution of methylamphetamine, cocaine and heroin, 25 ms ion introduction time and 500 ms cooling time.

Figure 4a is a nano ESI mass spectrum of a 500 ppb mixture solution of methylamphetamine, cocaine and heroin.

Figure 4b is a MS/MS mass spectra of molecular ions of methylamphetamine m/z 150, SWIFT notch 300 to 310 kHz and excitation AC at 100kHz.

Figure 4c is a MS/MS mass spectra of molecular ion of cocaine m/z 304, SWIFT notchth 300 to 310 kHz and excitation AC at 100kHz.

Figure 4d is a MS/MS mass spectra of molecular ion of heroin m/z 370, SWIFT notch 300 to 310 kHz and excitation AC at 100kHz.

Figure 5a is a ESI mass spectrum with 20 ms ion introduction of a 500ppb lysine solution.

Figure 5b is a APCI mass spectrum with 20 ms ion introduction of a 50 ppb DMMP in air.

Figure 6 is a DESI mass spectrum of cocaine on Teflon surface with 15ms ion introduction time and 500ms cooling time, background subtracted.

Figure 7a is a DESI mass spectrum of direct analysis of black ink from BIC Round Stic ballpoint pen.

Figure 7b is a DESI mass spectrum of direct analysis of blue ink from BIC Round Stic ballpoint pen.

Figure 8 is a nano ESI mass spectrum of a 400 ppt mixture solution of methamphetamine, cocaine and heroin.

Figure 9a is a schematic elevation view of a discontinuous atmospheric pressure interface coupled with a miniature mass spectrometer and nano electrospray ionization source.

Figure 9b is a schematic elevation view of a discontinuous atmospheric pressure interface coupled with a miniature mass spectrometer and atmospheric pressure chemical ionization using corona discharge.

Figure 10 is an APCI mass spectrum of naphthalene vapor.

Figure 11 a schematic elevation view of an off-axis configuration for the combination of discontinuous API and RIT, which avoids direct gas jet into RIT. A focusing tube lens is used to direct the ion beam into the RIT.

Figure 12 is a schematic elevation view of a discontinuous atmospheric pressure interface coupled via a tubing with an functional inner surface for ion accumulation and release. The Ions are accumulated for a given time on this inner surface before they are sent through the discontinuous atmospheric pressure interface into the mass analyzer.

DETAILED DESCRIPTION OF THE INVENTION

For ion trap type mass spectrometers, the pumping capability is not efficiently used with a traditional constantly open API. The ions are usually allowed to pass into the ion trap for only part of each scan cycle but neutrals are constantly leaked into the vacuum manifold and need to be pumped away to keep the pressure at the low levels typically needed for mass analysis. Although the mass analysis using an ion trap usually requires an optimal pressure at several milli-torr or less, ions can be trapped at a much higher pressure. (Shaffer, S. A.; Tang, K. Q.; Anderson, G. A.; Prior, D. C.; Udseth, H. R.; Smith, R. D. *Rapid Communications in Mass Spectrometry* **1997**, *11*, 1813-1817) Taking advantage of this characteristic of an ion trap, an alternative atmospheric pressure interface, discontinuous atmospheric pressure interface (DAPI), is proposed here to allow maximum ion transfer at a given pumping capacity for mass spectrometers containing an ion trapping component. The concept of the discontinuous API is to open its channel during ion introduction and then close it for subsequent mass analysis during each scan. An ion transfer channel with a much bigger flow conductance can be allowed for a discontinuous API than for a traditional continuous API. The pressure inside the manifold temporarily increases significantly when the channel is opened for maximum ion introduction. All high voltages can be shut off and only low voltage RF is on for trapping of the ions during this period. After the ion introduction, the channel is closed and the pressure can decrease over a period of time to reach the optimal pressure for further ion manipulation or mass analysis when the high voltages can be is turned on and the RF can be scanned to high voltage for mass analysis.

A discontinuous API opens and shuts down the airflow in a controlled fashion. The pressure inside the vacuum manifold increases when the API opens and decreases when it closes. The combination of a discontinuous atmospheric pressure interface with a trapping device, which can be a mass analyzer or an intermediate stage storage device, allows maximum introduction of an ion package into a system with a given pumping capacity.

Much larger openings can be used for the pressure constraining components in the API in the new discontinuous introduction mode. During the short period when the API is opened, the ion trapping device is operated in the trapping mode with a low RF voltage to store the incoming ions; at the same time the high voltages on other components, such as conversion dynode or electron multiplier, are shut off to avoid damage to those device and electronics at the higher pressures. The API can then be closed to allow the pressure inside the manifold to drop back to the optimum value for mass analysis, at which time the ions are mass analyzed in the trap or transferred to another mass analyzer within the vacuum system for mass analysis. This two-pressure mode of operation enabled by operation of the API in a discontinuous fashion maximizes ion introduction as well as optimizing conditions for the mass analysis with a given pumping capacity.

The design goal is to have largest opening while keeping the optimum vacuum pressure for the mass analyzer, which is between 10^{-3} to 10^{-10} torr depending the type of mass analyzer. The larger the opening in an atmospheric pressure interface, the higher is the ion current delivered into the vacuum system and hence to the mass analyzer.

A device of simple configuration was designed to test the concept of the discontinuous API with a Mini 10 handheld mass spectrometer. A Mini 10 handheld mass spectrometer is shown in Gao, L.; Song, Q.; Patterson, G. E.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2006**, *78*, 5994-6002. In comparison with the pumping system used for lab-scale instruments with thousands watts of power, the Mini 10 has a 18 W pumping system with only a 5 L/min (0.3 m^3/hr) diaphragm pump and a 11 L/s turbo pump. The discontinuous API was designed to connect the atmospheric pressure region directly to the vacuum manifold without any intermediate vacuum stages. Due to the leakage of a relatively large amount of air into the manifold during ion introduction, traps with relatively good performance with air as buffer gas are preferred as the mass analyzer for the discontinuous API. A rectilinear ion trap was used in Mini 10 for mass analysis, for which the performance with air buffer gas had been demonstrated previously. (Gao, L.; Song, Q.; Patterson, G. E.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2006**, *78*, 5994-6002) Various atmospheric pressure ionization methods, including ESI, APCI and DESI, were coupled to the Mini 10 and limit of detection (LOD) comparable with lab-scale instruments was achieved while unit resolution and tandem mass spectrometry efficiency were also retained.

A first embodiment is shown in Figure 1, in which a pinch valve is used to open and shut off the pathway in a silicone tube connecting the regions at atmospheric pressure and in vacuum. A normally-closed pinch valve (390NC24330, ASCO Valve Inc., Florham Park, NJ) was used to control the opening of the vacuum manifold to atmospheric pressure region. Two stainless steel capillaries were connected to the piece of silicone plastic tubing, the open/closed status of which is controlled by the pinch valve. The stainless steel capillary connecting to the atmosphere is the flow restricting element, and has an ID of 250μm, an OD of 1.6 mm (1/16") and a length of 10cm. The stainless steel capillary on the vacuum side has an ID of 1.0 mm, an OD of 1.6 mm (1/16") and a length of 5.0 cm. The plastic tubing has an ID of 1/16", an OD of 1/8" and a length of 5.0 cm. Both stainless steel capillaries are grounded. The pumping system of the mini 10 consists of a two-stage diaphragm pump 1091-N84.0- 8.99 (KNF Neuberger Inc., Trenton, NJ) with pumping speed of 5L/min (0.3 m^3/hr) and a TPD011 hybrid turbomolecular pump (Pfeiffer Vacuum Inc., Nashua, NH) with a pumping speed of 11 L/s.

When the pinch valve is constantly energized and the plastic tubing is constantly open, the flow conductance is so high that the pressure in vacuum manifold is above 30 torr with the diaphragm pump operating. The ion transfer efficiency was measured to be 0.2%, which is comparable to a lab-scale mass spectrometer with a continuous API. However, under these conditions the TPD 011 turbomolecular pump can not be turned on. When the pinch valve was de-energized, the plastic tubing was squeezed closed and the turbo pump could then be turned on to pump the manifold to its ultimate pressure in the range of 1x 10^{-5} torr.

The sequence of operations for performing mass analysis using ion traps usually includes, but is not limited to, ion introduction, ion cooling and RF scanning. After the manifold pressure is pumped down initially, a scan function shown in Figure 2a was implemented to switch between open and close modes for ion introduction and mass analysis. During the ionization time, a 24 V DC was used to energize the pinch valve and the API was open. The potential on the RIT end electrode I was also set to ground during this period. A minimum response time for the pinch valve was found to be 10 ms and an ionization time between 15 ms and 30 ms was used for the characterization of the discontinuous API. A cooling time between 250 ms to 500 ms was implemented after the API was closed to allow the pressure to decrease and the ions to cool down via collisions with background air molecules. The high voltage on the electron multiplier was then turned on and the RF voltage was scanned for mass analysis.

During the operation of the discontinuous API, the pressure change in the manifold can be monitored using the micro pirani vacuum gauge (MKS 925C, MKS Instruments, Inc. Wilmington, MA) on Mini 10. With an open time of 20 ms and a close time of 850 ms, the reading of the pirani gauge was recorded and is plotted as shown in Figure 2b. A pressure variation between 8 x 10^{-2} torr to 1 x 10^{-3} torr was measured. Capillaries with different flow conductance were tested as the flow restricting element, including 10 cm capillaries with a 127 μm ID and 500 μm ID. It was found that the sensitivity significantly decreased with the former and a much longer cooling time, 2 to 3s, was required for pressure to drop with the latter.

Different atmospheric ionization sources were used with the mini 10 mass spectrometer to verify the performance of this discontinuous atmospheric pressure interface. A scan speed of 5000 m/z per second was used for mass analysis with a resonance ejection AC of 350 kHz and an electron multiplier voltage of -1600V was used for ion detection. Sample solutions used for ESI and nano ESI were prepared using 1:1 methanol water with 0.5% acetic acid. A 250ppm standard acetonitrile drug mixture solution (Alltech-Applied Science Labs, State College, PA) of methamphetamine, cocaine and heroin was diluted for preparation of samples at various concentrations.

The discontinuous API on the Mini 10 was first characterized with a nano ESI source, which was set up using a nano spray tip prepared in house. (Wilm, M.; Mann, M. *Anal.*

Chem. **1996**, *68*, 1-8; Pan, P.; Gunawardena, H. P.; Xia, Y.; Mckuckey, S. A. *Anal. Chem.* **2004**, *76*, 1165-1174) A spray voltage between 1.3 and 2.5 kV was applied. A sample solution containing 5 ppm caffeine and cocaine were analyzed using the Mini 10 with the discontinuous API. The RF voltage was set at a low mass cut-off (LMCO) of m/z 60 corresponding to about 160 $V_{0\text{-}p}$, during the 20 ms ion introduction of the DAPI and was scanned to m/z 450 (1200 $V_{0\text{-}p}$) to record a spectrum as shown in Figure 3a. The protonated molecules m/z 195 from caffeine and m/z 304 from cocaine were observed. Though the ion introduction was at much higher pressure, the mass analysis was performed at about 5 milli-torr and unit resolution was obtained. Another sample solution containing 50 ppb methamphetamine, heroine and cocaine was also analyzed with a 20 ms ion introduction time (Figure 3b). The signal-to-noise ratio is lower for this sample due to the much lower concentration used but a LOD lower than 50 ppb was indicated to be achievable for this sample. Another sample solution containing 400 ppt methamphetamine, cocaine and heroin was also analyzed (Figure 8), indicating the limit of detection is lower than 400 ppt.

Tandem mass spectrometry can also be performed with a discontinuous API using an altered scan function with two additional periods for ion isolation and ion excitation between the cooling and the RF scan. The ions was first isolated by applying a SWIFT waveform and subsequently fragmented via collision induced dissociation (CID) by applying an excitation AC. (Gao, L.; Song, Q.; Patterson, G. E.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2006**, *78*, 5994-6002) After 20 ms ion introduction and a 500 ms cooling period, the pressure inside the manifold is in the milli-torr range, a condition for CID that is identical to what was previously used without an atmospheric pressure interface. (Gao, L.; Song, Q.; Patterson, G. E.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2006**, *78*, 5994-6002) No additional collision gas was added and the air left in the manifold was used as the collision gas. A sample solution containing 500 ppb methamphetamine, cocaine and heroin was analyzed using MS/MS with nano ESI source and discontinuous API. A waveform with a notch window between 300 to 310 kHz was used for the isolation of the precursor ions and an excitation AC at 100 kHz was used for CID. The MS spectrum for the mixture and the MS^2 spectra for each of the component were recoded and shown in Figure 4. Typical fragment patterns were observed for the protononated molecular ions of these three compounds.

For tandem mass analysis, additional operations including ion isolation, ion excitation and ion cooling are added between the ion introduction and final RF scanning steps. The operation of the pinch valve is synchronized with the operation of the ion optics and the RIT scan. The pinch valve is open for around 20 ms in this particular case, during which time ions are allowed to enter the vacuum manifold by setting the voltage on end electrode I of the RIT to ground to allow the ions to enter RIT; during this time the pressure inside the manifold increases. After the pinch valve is shut off, the ions are trapped in the RIT for hundreds of milliseconds and the pressure inside the manifold graduate decreases to optimum values for mass analysis. The high voltages for ion detectors are then turned on, the RF applied on RIT is scanned to mass selectively eject ions and the auxiliary AC for resonance ejection can also be applied at the same time. This sequence of mass analysis steps can be repeated.

The analysis of amino acids was performed with an ESI source using the discontinuous API and Mini 10. The spray direction was angled at 30° with respect to the stainless steel tubing of the interface to minimize the introduction of the neutral droplets into the vacuum system. The sample was sprayed at a flow rate of 0.5μl/min with a high voltage of 3kV applied and a sheath gas pressure was 80 psi. An ESI-MS spectrum was recorded with 20 ms ion introduction for a solution containing 500 ppb lysine, as shown in Figure 5a. The protonated molecule $[M+H]^+$ (m/z 147) and protonated dimer $[2M+H]^+$ (m/z 293) were observed.

In addition to ESI (Figure 9a), this experiment setup can also be used with other ionization methods. An atmospheric pressure chemical ionization source using a platinum wire for corona discharge was used with the discontinuous atmospheric pressure interface, as shown in Figure 9b. The vapor from a moth ball was the sample and a spectrum of naphthalene and other chemicals was recorded as shown in Figure 10.

Gas sample analysis with the discontinuous API was demonstrated using the chemical warfare simulant dimethyl methylphosphonate (DMMP) and an APCI source, which was set up for use with the Mini 10 using a stainless steel corona discharge pin as previously described. (Carroll, D. I.; Dzidic, I.; Stillwell, R. N.; Haegele, K. D.; Horning, E. C. *Anal. Chem.* **1975**, *47*, 2369-2373; Laughlin, B. C.; Mulligan, C. C.; Cooks, R. G. *Anal. Chem.* **2005**, *77*, 2928-2939) The discharge pin was placed about 5mm away from the stainless steel capillary inlet with 3kV voltage applied on it. A 10 ml flask containing 50 ppb DMMP in air was place under the discharge pin and the stopper was removed from the flask to allow the sample to escape. A spectrum was recorded with a 20 ms ion introduction as shown in Figure 5b. The protonated molecule $[M+H]^+$ (m/z 125) and proton-bound dimer $[2M+H]^+$ (m/z 249) were observed. Good signal-to-noise ratio was obtained for the analysis of this sample at a concentration of 50 ppb. In another experiment, a signal-to-noise ratio of 50 was observed for an air sample containing 10 ppb DMMP, based on which the LOD is estimated to be below 1 ppb.

As a demonstration of the use of the discontinuous API for the direct ambient sampling methods, a DESI source was set up for analysis of samples directly from surfaces. A sample was prepared by depositing 5 μl methanol/water (1:1) solution containing 5 ppm cocaine onto a 2 x 3 mm area on a Teflon surface. After the sample had dried in air, it was analyzed using Mini 10 with DESI and the discontinuous API. Methanol water solvent at a ratio of 1:1 was sprayed at a flow rate of 10 ml/min with a spray voltage of 3 kV to generate the sampling charged droplets. A spray angle of 55° and a take-off angle of 10° were applied and a sheath gas pressure 120 psi was used. The distance between the spray tip and the Teflon surface is about 2 mm and the sampling area was estimated to be 1 mm^2. The sample area and a blank area on the Teflon surface were analyzed with 15 ms ion introduction and the spectrum recorded for latter was used for background subtraction. The solid cocaine on surface was desorbed and ionized by DESI and the protonated molecule m/z 304 was observed (Figure 6).

Direct ink analysis from surface was also carried as a demonstration of the fast in-situ analysis using an instrument package of DESI, discontinuous API and Mini 10. Two 2 mm×3 mm dots were drawn on a piece of printer paper (Xerox Corporaton, Rochester, NY) using BIC Round Stic black ball pen and blue ball pen, respectively. The experimental condition for DESI was identical to that described above except the methanol water ratio of the solvent was 9:1. The two sample areas on the paper were analyzed with a 15 ms ion introduction and the spectra were recorded as shown in Figure 7. Basic violet 3, corresponding to the peak m/z 372, was found in the black ball pen ink (Figure 7a) while both basic violet 3 and basic blue 26 (m/z 470) were found in the blue ball pen ink (figure 7b). The peak m/z 358 and 344 observed for both black and blue ball pen ink were reported to be the products of oxidative demethylation of basic violet 3. (Ifa, D. R.; Gumaelius, L. M.; Eberlin, L. S.; Manicke, N. E.; Cooks, R. G. *Analyst* **2007**, *132*, 461-467; Grim, D. M.; Siegel, J.; Allison, J. *J. Forensic Sci.* **2002**, *47*, 1265-1273).

Various arrangements of a discontinuous atmospheric pressure interface can be used to transfer ions between two regions at different pressures that opens to allow ions to be transferred and shuts off after the ion transfer to allow different pressures to be established thereby achieving high efficiency ion transfer between differential pressure regions with limited pumping capacity.

While these features have been disclosed in connection with the illustrated preferred embodiments, other embodiments of the invention will be apparent to those skilled in the art that come within the spirit of the invention as defined in the following claims. All references, including issued patents and published patent applications, are incorporated herein by reference in their entireties.

What is claimed is:

1. A device for controlling movement of ions, the device comprising:

a valve aligned with an exterior portion of a tube, wherein the valve controls movement of ions through the tube; and

a first capillary inserted into a first end of the tube and a second capillary inserted into a second end of the tube, wherein neither the first capillary nor the second capillary overlap with a portion of the tube that is in alignment with the valve.

2. The device according to claim 1, wherein a proximal end of the first capillary is connected to a trapping device, wherein the trapping device is below atmospheric pressure.

3. The device according to claim 1, wherein a distal end of the second capillary receives the ions from an ionizing source, wherein the ionizing source is at substantially atmospheric pressure.

4. The device according to claim 1, wherein the tube is composed of an inert plastic.

5. The device according to claim 4, wherein the inert plastic is silicone plastic.

6. The device according to claim 1, wherein the first and second capillary are composed of an inert metal.

7. The device according to claim 6, wherein the inert metal is stainless steel.

8. The device according to claim 1, wherein the first and second capillary have substantially the same outer diameter.

9. The device according to claim 1, wherein the first and second capillary have different outer diameters.

10. The device according to claim 1, wherein the first and second capillary have substantially the same inner diameter.

11. The device according to claim 1, wherein the first and second capillary have different inner diameters.

12. The device according to claim 10, wherein the second capillary has a smaller inner diameter that the inner diameter of the first capillary.

13. The device according to claim 1, wherein the valve is selected from the group consisting of a pinch valve, a thin plate shutter valve, and a needle valve.

14. A discontinuous atmospheric pressure interface system comprising:

an ionizing source for converting molecules into gas phase ions in a region at about atmospheric pressure;

a trapping device; and

a discontinuous atmospheric pressure interface for transferring the ions from the region at about atmospheric pressure to at least one other region at a reduced pressure, wherein the interface comprises a valve for controlling entry of the ions into the trapping device such that the ions are transferred into the trapping device in a discontinuous mode.

15. The system according to claim 14, further comprising at least one vacuum pump connected to the trapping device.

16. The system according to claim 15, wherein the atmospheric pressure interface further comprises:

a tube, wherein an exterior portion of the tube is aligned with the valve; and

a first capillary inserted into a first end of the tube and a second capillary inserted into a second end of the tube, wherein neither the first capillary nor the second capillary overlap with a portion of the tube that is in alignment with the valve.

17. The system according to claim 15, wherein the atmospheric pressure interface further comprises a tube, wherein an exterior portion of the tube is aligned with the valve.

18. The system according to claim 14, wherein the valve is selected from the group consisting of a pinch valve, a thin plate shutter valve, and a needle valve.

19. The system according to claim 14, wherein ions enter the trapping device when the valve is in an open position.

20. The system according to claim 14, wherein ions are prevented from entering the trapping device when the valve is in a closed position.

21. The system according to claim 14, further comprising a computer operably connected to the system.

22. The system according to claim 21, wherein the computer contains a processor configured to execute a computer readable program, the program controlling the position of the valve.

23. The system according to claim 21, wherein the computer contains a processor configured to execute a computer readable program, the program implementing a waveform inverse Fourier transformation (SWIFT) isolation algorithm to separate~~s~~ ions.

24. The system according to claim 14, wherein the ionizing source operates by a technique selected from the group consisting of: electrospray ionization, nano-electrospray ionization, atmospheric pressure matrix-assisted laser desorption ionization, atmospheric pressure chemical ionization, desorption electrospray ionization, atmospheric pressure dielectric barrier discharge ionization, atmospheric pressure low temperature plasma desorption ionization, and electrospray-assisted laser desorption ionization.

25. The system according to 14, wherein the trapping device is selected from the group consisting of a mass analyzer of a mass spectrometer, a mass analyzer of a handheld mass spectrometer, and an intermediate stage storage device.

26. The system according to claim 25, wherein the mass analyzer is selected from the group consisting of: a quadrupole ion trap, a rectalinear ion trap, a cylindrical ion trap, a ion cyclotron resonance trap, and an orbitrap.

27. The system according to claim 25, wherein the intermediate storage device is coupled with a mass analyzer of a mass spectrometer or a mass analyzer of a handheld mass

spectrometer.

28. The system according to claim 27, wherein the mass analyzer is selected from the group consisting of: a mass filter, a quadrupole ion trap, a rectalinear ion trap, a cylindrical ion trap, a ion cyclotron resonance trap, an orbitrap, a time of flight mass spectrometer, and a magnetic sector mass spectrometer.

29. The system according to claim 16, further comprising an ion accumulating surface connected to a distal end of the second capillary.

30. The system according to claim 17, further comprising an ion accumulating surface connected to a distal end of the tube.

31. The system according to either of claims 16 or 17, wherein the tube is composed of an inert plastic

32. The system according to claim 29, wherein the inert plastic is silicone plastic.

33. The system according to claim 16, wherein the first and second capillary are composed of an inert metal.

34. The system according to claim 16, wherein the inert metal is stainless steel.

35. The system according to claim 16, wherein the first and second capillary have substantially the same outer diameter.

36. The system according to claim 16, wherein the first and second capillary have different outer diameters.

37. The system according to claim 16, wherein the first and second capillary have substantially the same inner diameter.

38. The system according to claim 16, wherein the first and second capillary have different inner diameters.

39. The system according to claim 16, wherein the second capillary has a smaller inner diameter that the inner diameter of the first capillary.

40. The system according to claim 25, wherein the valve operates to control entry of ions in a synchronized manner with respect to operation of the mass analyzer.

41. The system according to claim 25, wherein the configuration of the discontinuous atmospheric pressure interface and the mass analyzer is off-axis.

42. The system according to claim 14, further including an ion optical element located between the discontinuous atmospheric pressure interface and the mass analyzer to direct the ions into the mass analyzer.

43. The system according to claim 42, wherein the ion optical element is a focusing tube lens.

44. The system according to claim 14, further including an ion optical element located between the ionization source and the discontinuous atmospheric pressure interface to direct the ions into the mass analyzer.

45. A kit comprising the device according to claim 1 and a container.

46. A kit comprising the system according to claim 14 and a container.

47. The kit according to either of claims 45 or 46 further comprising instructions for use.

48. A method of discontinuously transferring ions at atmospheric pressure into a trapping device at reduced pressure, the method comprising:

opening a valve connected to an atmospheric pressure interface, wherein opening of the valve allows for transfer of ions substantially at atmospheric pressure to a trapping device at reduced pressure; and

closing the valve connected to the atmospheric pressure interface, wherein closing the valve prevents additional transfer of the ions substantially at atmospheric pressure to the trapping device at reduced pressure.

49. The method according to claim 48, wherein prior to opening the valve, the method further comprises converting molecules to gas phase ions.

50. The method according to claim 49, wherein said converting step is selected from the group consisting of: electrospray ionization, nano-electrospray ionization, atmospheric pressure matrix-assisted laser desorption ionization, atmospheric pressure chemical ionization, desorption electrospray ionization, atmospheric pressure dielectric barrier discharge ionization, atmospheric pressure low temperature plasma desorption ionization, and electrospray-assisted laser desorption ionization.

51. The method according to claim 48, wherein the opening and the closing of the valve is controlled by a computer operably connected to the atmospheric pressure interface.

52. The method according to claim 48, wherein the trapping device is selected from the group consisting of a mass analyzer of a mass spectrometer, a mass analyzer of a handheld mass spectrometer, and an intermediate stage storage device.

53. The method according to claim 52, wherein the mass analyzer is selected from the group consisting of: a quadrupole ion trap, a rectalinear ion trap, a cylindrical ion trap, a ion cyclotron resonance trap, and an orbitrap.

54. The method according to claim 52, wherein the intermediate storage device is coupled with a mass analyzer of a mass spectrometer or a mass analyzer of a handheld mass spectrometer.

55. The method according to claim 54, wherein the mass analyzer is selected from the group consisting of: a mass filter, a quadrupole ion trap, a rectalinear ion trap, a cylindrical ion trap, a ion cyclotron resonance trap, an orbitrap, a time of flight mass spectrometer, and a magnetic sector mass spectrometer.

56. The method according to claim 52, wherein electrical voltage of the mass analyzer is set to ground when the valve is open.

57. The method according to claim 56, wherein subsequent to the ions being transferred into the mass analyzer and the valve being closed, the ions are retained by the mass analyzer for further manipulation.

58. The method according to claim 57, wherein prior to further manipulation, the ions are cooled and the pressure is further reduced.

59. The method according to claim 57, wherein further manipulation comprises mass analysis of the ions.

60. The method according to claim 59 wherein the computer synchronizes the opening and the closing of the valve with a sequence of mass analysis of the ions in the mass analyzer.

61. The method according to claim 59, wherein the computer synchronizes the opening and the closing of the valve with a sequence of steps that allow tandem mass analysis of the ions in the mass analyzer.

62. The method according to claim 48, wherein the valve is selected from the group consisting of a pinch valve, a thin plate shutter valve, and a needle valve.

63. The method according to claim 48, wherein the atmospheric pressure interface further comprises a tube, wherein an exterior portion of the tube is aligned with the valve.

64. The method according to claim 48, wherein the atmospheric pressure interface further comprises:

a tube, wherein an exterior portion of the tube is aligned with the valve; and

a first capillary inserted into a first end of the tube and a second capillary inserted into a second end of the tube, wherein neither the first capillary nor the second capillary overlap with a portion of the tube that is in alignment with the valve.

65. The method according to claim 64, wherein after converting the molecules to ions, the ions are stored on a functional surface connected to the distal end of the second capillary at atmospheric pressure, wherein the functional surface is continuously supplied with ions from a continuously operated ion source.

66. The method according to claim 65, wherein the ions stored on the functional surface are subsequently transferred by the atmospheric pressure interface to the trapping device.

67. The method according to claim 63, wherein after converting the molecules to ions, the ions are stored on a functional surface connected to the distal end of the tube at atmospheric pressure, wherein the functional surface is continuously supplied with ions from a continuously operated ion source.

68. The method according to claim 67, wherein the ions stored on the functional surface are subsequently transferred by the atmospheric pressure interface to the trapping device.

69. The method according to either of claims 63 or 64, wherein the tube is composed of an inert plastic

70. The method according to claim 69, wherein the inert plastic is silicone plastic.

71. The method according to claim 64, wherein the first and second capillary are composed of an inert metal.

72. The method according to claim 71, wherein the inert metal is stainless steel.

73. The method according to claim 64, wherein the first and second capillary have substantially the same outer diameter.

74. The method according to claim 64, wherein the first and second capillary have different outer diameters.

75. The method according to claim 64, wherein the first and second capillary have substantially the same inner diameter.

76. The method according to claim 64, wherein the first and second capillary have different inner diameters.

77. The method according to claim 64, wherein the second capillary has a smaller inner diameter that the inner diameter of the first capillary.

78. A method of discontinuously transferring ions into a mass spectrometer, the method comprising:

opening a valve connected to an atmospheric pressure interface, wherein opening of the valve allows for transfer of ions substantially at atmospheric pressure to a mass analyzer at a reduced pressure in the mass spectrometer; and

closing the valve connected to the atmospheric pressure interface, wherein closing the valve prevents additional transfer of the ions substantially at atmospheric pressure to the mass analyzer at the reduced pressure in the mass spectrometer.

79. A device for controlling movement of ions, the device comprising:

a valve aligned with an exterior portion of a tube, wherein the valve controls movement of ions through the tube.

80. The device according to claim 79, wherein a proximal end of the tube is connected to a trapping device, wherein the trapping device is below atmospheric pressure.

81. The device according to claim 79, wherein a distal end of the tube receives the ions from an ionizing source, wherein the ionizing source is at substantially atmospheric pressure.

82. The device according to claim 79, wherein a distal end of the tube receives the ions at a first pressure, wherein a proximal end of the tube is connected to a trapping device at a pressure reduced from the first pressure.

83. The device according to claim 79, wherein the tube is composed of an inert plastic.

84. The device according to claim 83, wherein the inert plastic is silicone plastic.

85. The device according to claim 79, wherein the valve is selected from the group consisting of a pinch valve, a thin plate shutter valve, and a needle valve.

86. A kit comprising the device according to claim 79 and a container.

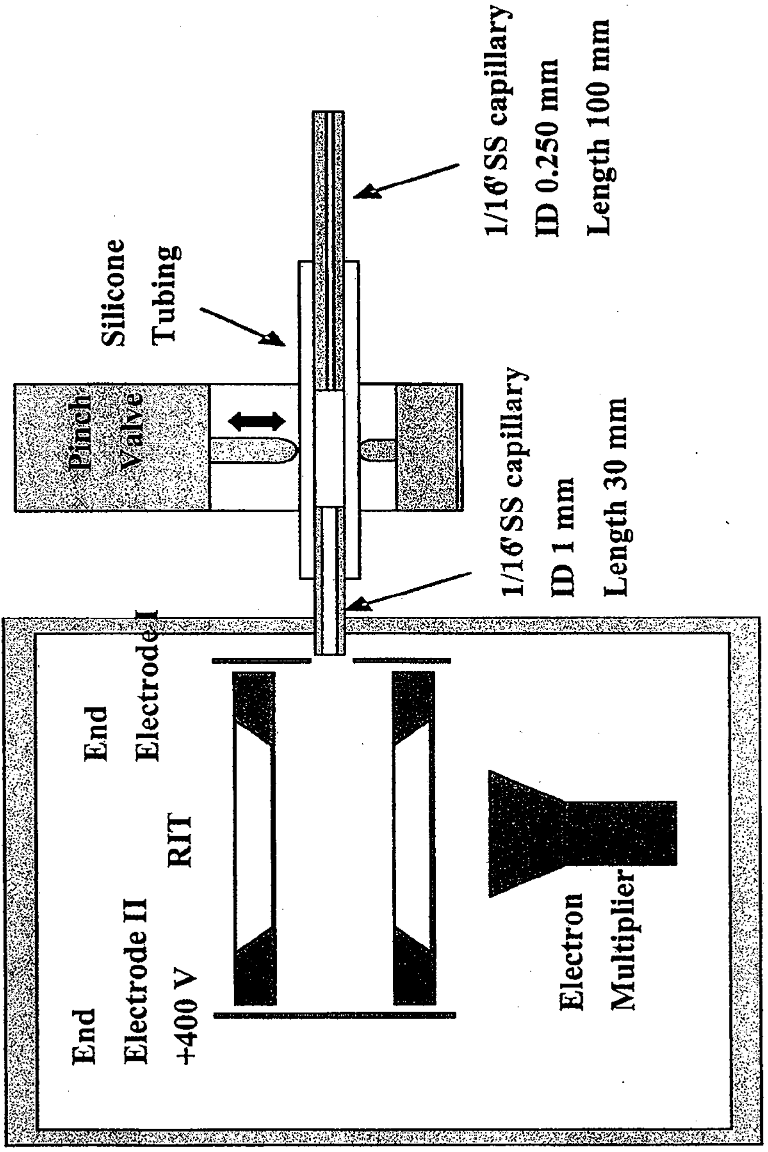
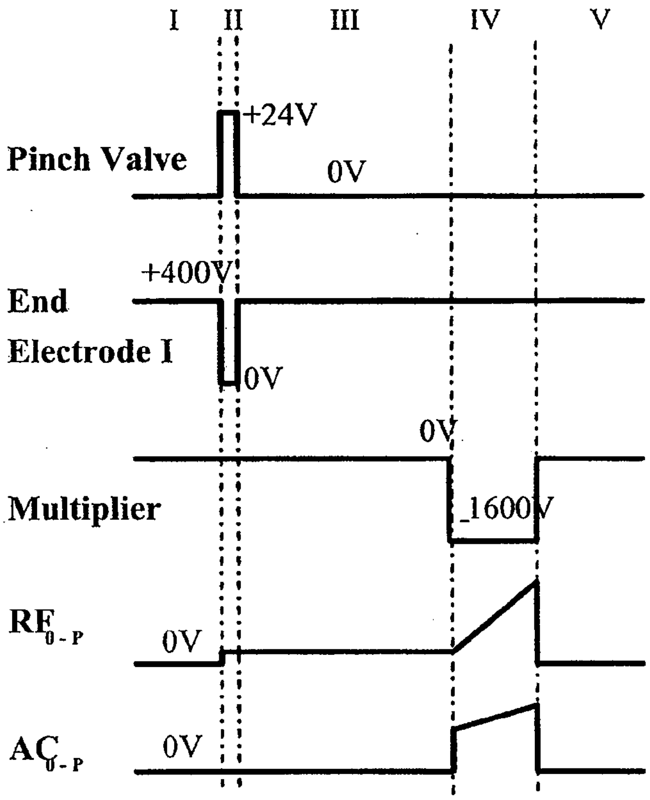

End
Electrode II
+400 V
RIT
End
Electrode I
Electron
Multiplier
Pinch
Valve
Silicone
Tubing
1/16' SS capillary
ID 1 mm
Length 30 mm
1/16' SS capillary
ID 0.250 mm
Length 100 mm

Figure 1



I. Preionization

II. Ionization (ion transfer allowed) 15-30 ms

III. Cooling, 250 – 500 ms

IV. Scan, 100 ms

V. Postscan

Figure 2a

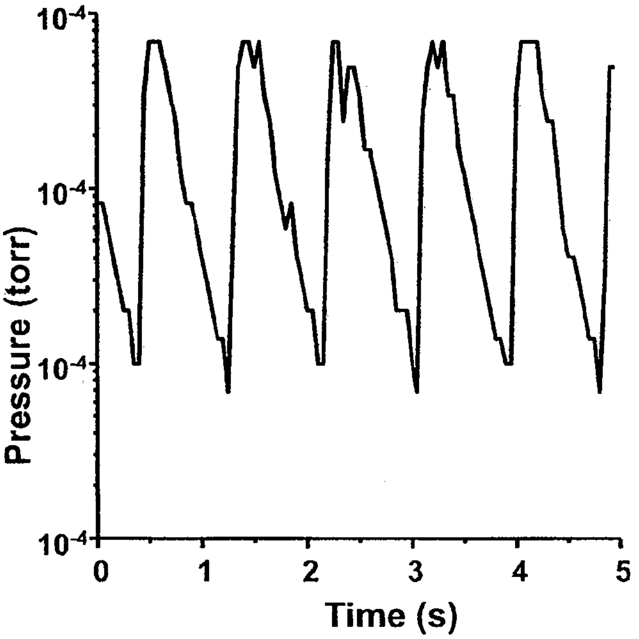


Figure 2b

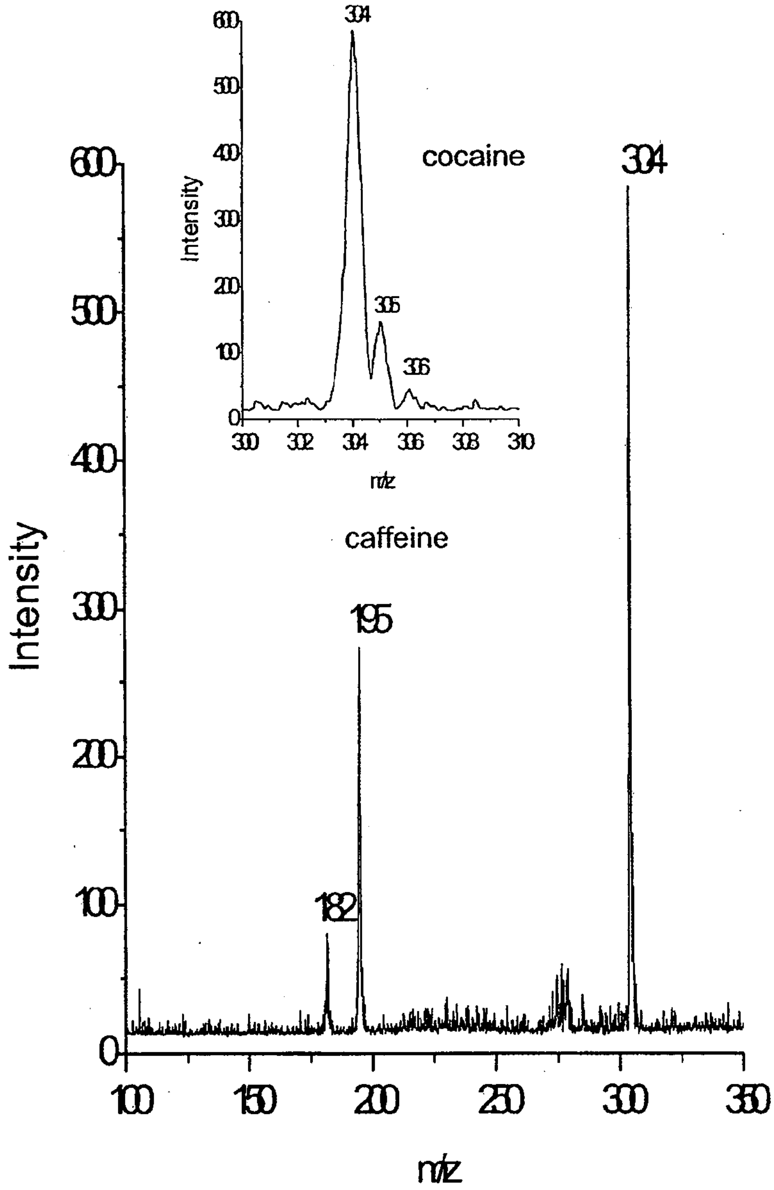

600
500
400
300
200
100
0
Intensity
100
150
200
250
300
350
m/z
182
195
caffeine
304
cocaine
Intensity
m/z
300
302
304
306
308
310
305
306

Figure 3a

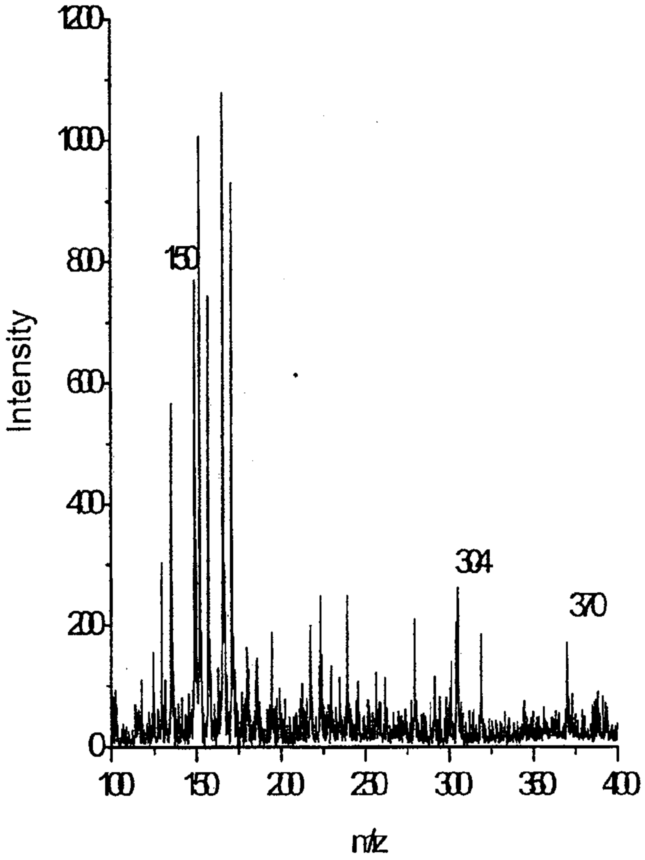

Intensity
1200
1000
800
600
400
200
0
150
304
370
100
150
200
250
300
350
400
m/z

Figure 3b

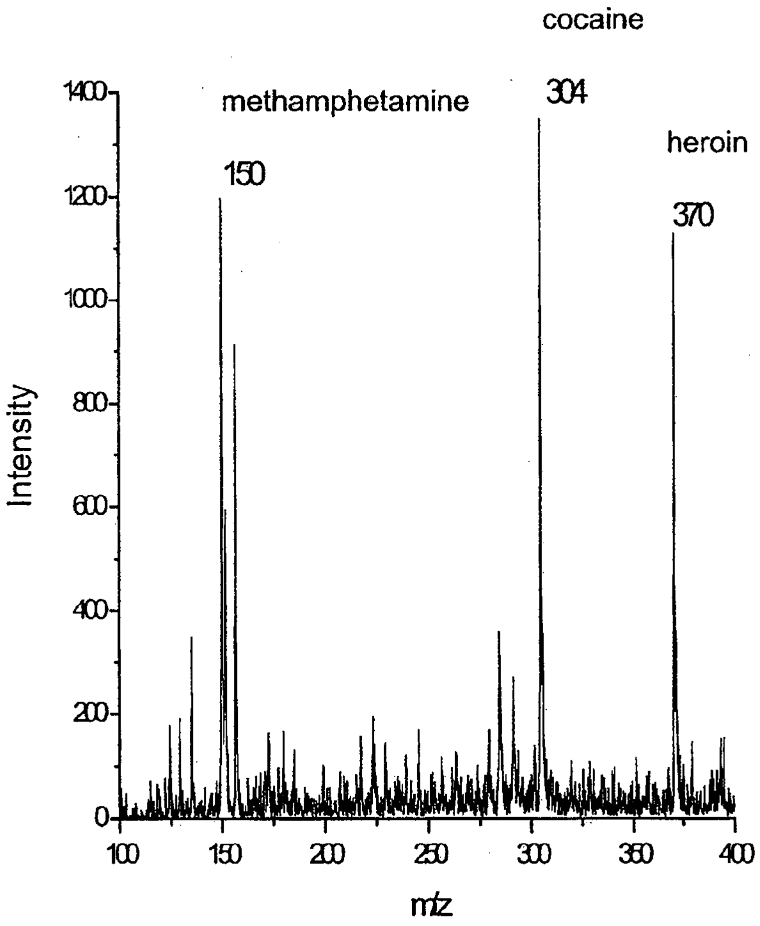

cocaine
304
methamphetamine
150
heroin
370
Intensity
0
200
400
600
800
1000
1200
1400
100
150
200
250
300
350
400
m/z

Figure 4a

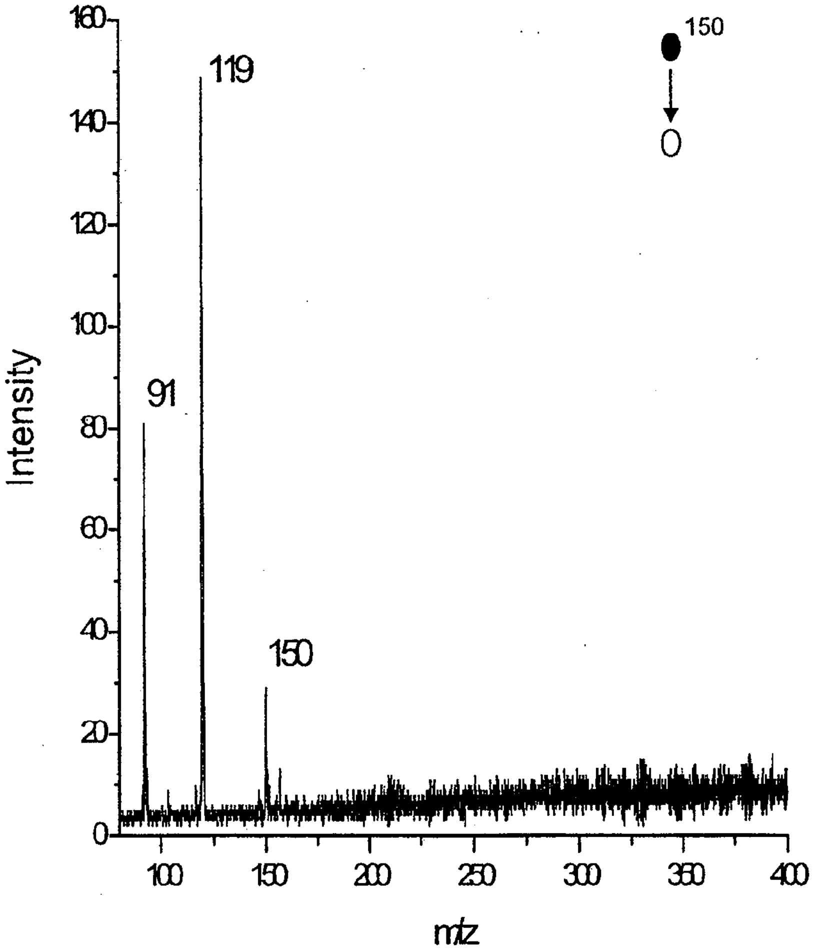

150
0
119
91
150
Intensity
160
140
120
100
80
60
40
20
0
100
150
200
250
300
350
400
m/z

Figure 4b

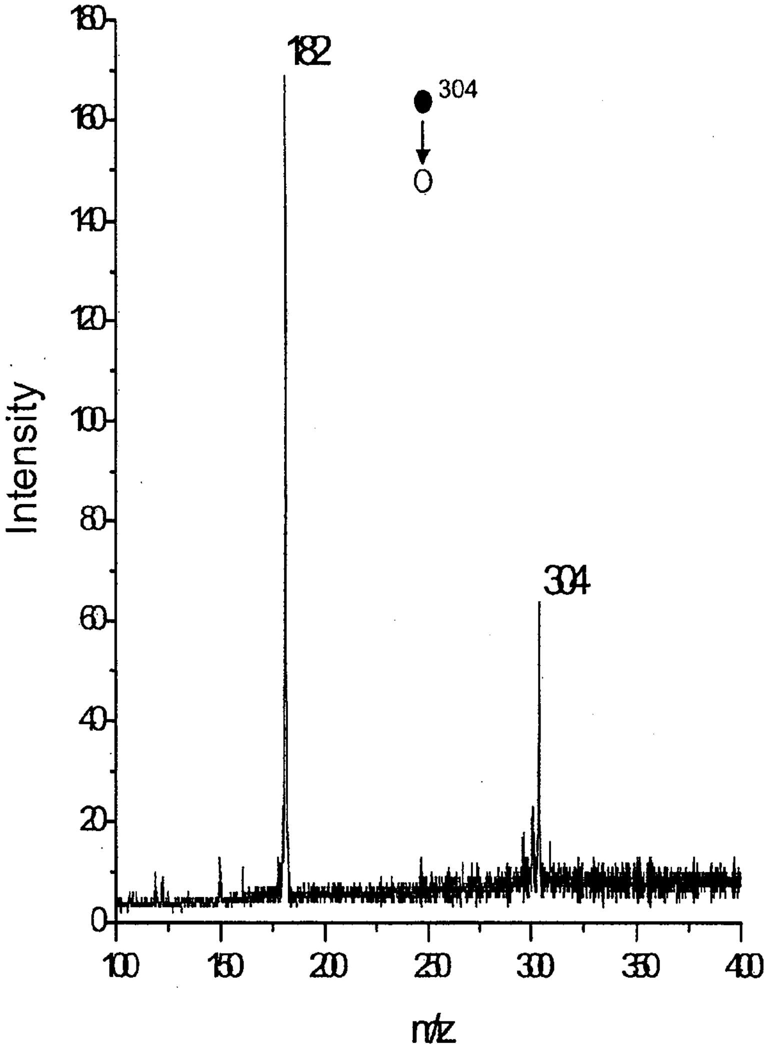

182
304
304
0
Intensity
m/z
180
160
140
120
100
80
60
40
20
0
100
150
200
250
300
350
400

Figure 4c

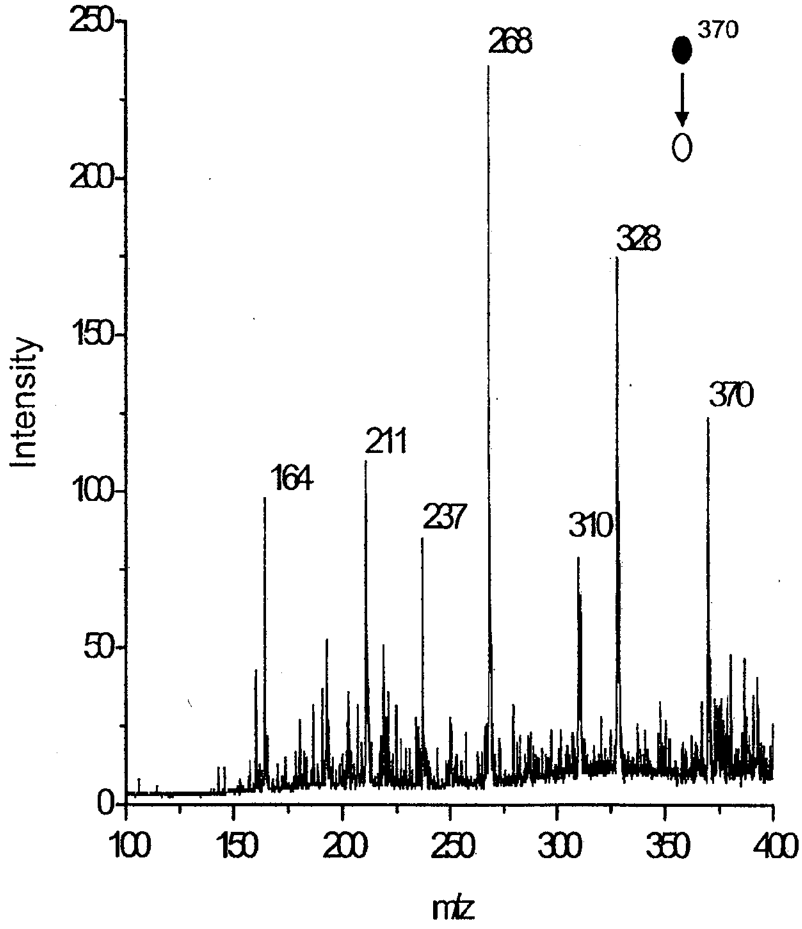

370
0
268
328
370
211
164
237
310
Intensity
250
200
150
100
50
0
100
150
200
250
300
350
400
m/z

Figure 4d

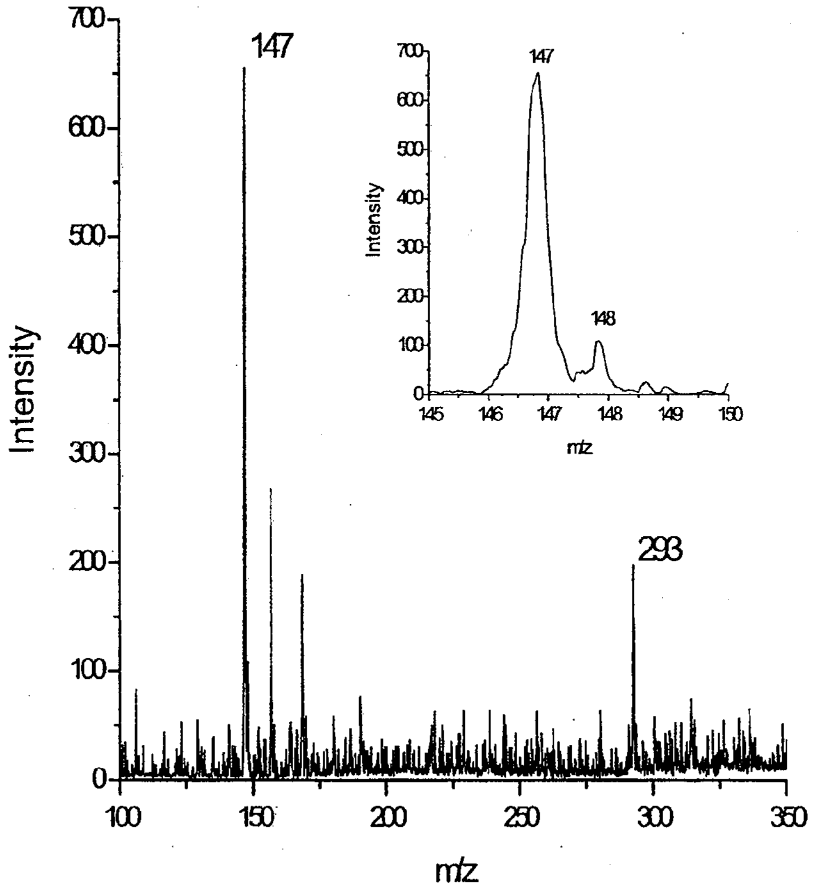

147
293
Intensity
m/z
0
100
200
300
400
500
600
700
100
150
200
250
300
350
147
148
145
146
147
148
149
150

Figure 5a

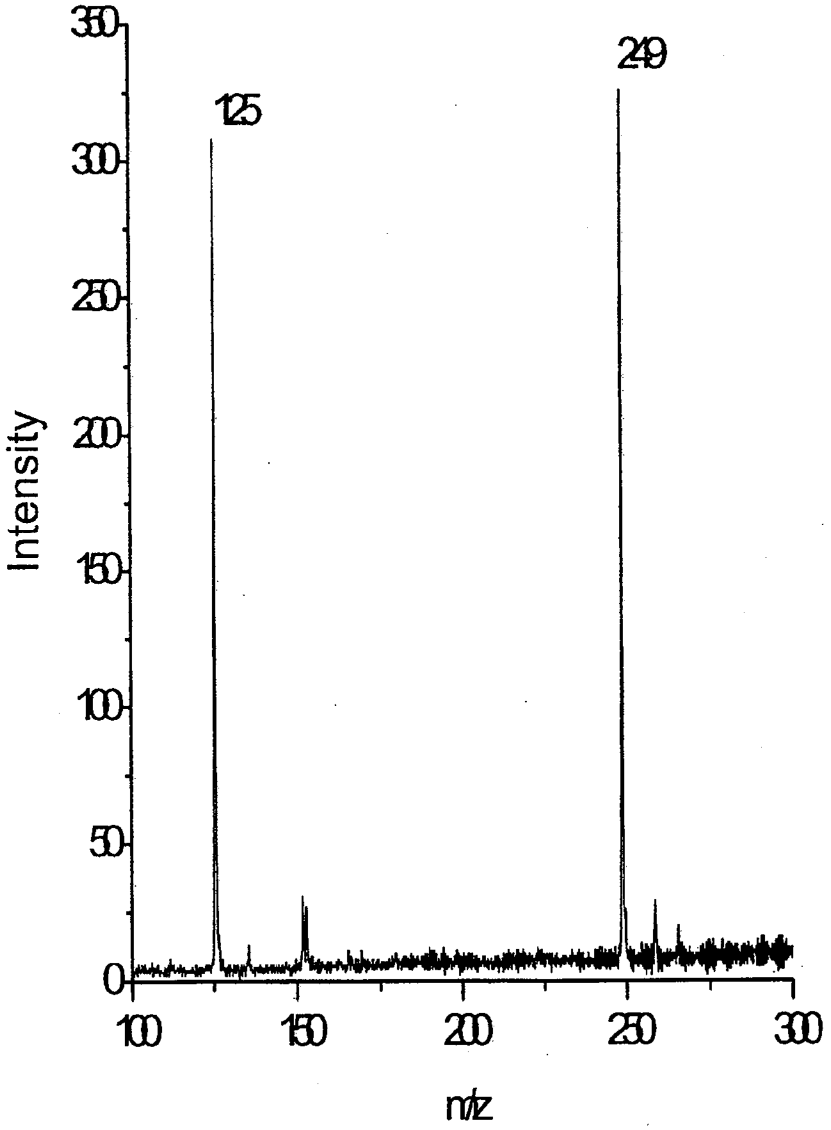

Intensity
350
300
250
200
150
100
50
0
125
249
100
150
200
250
300
m/z

Figure 5b

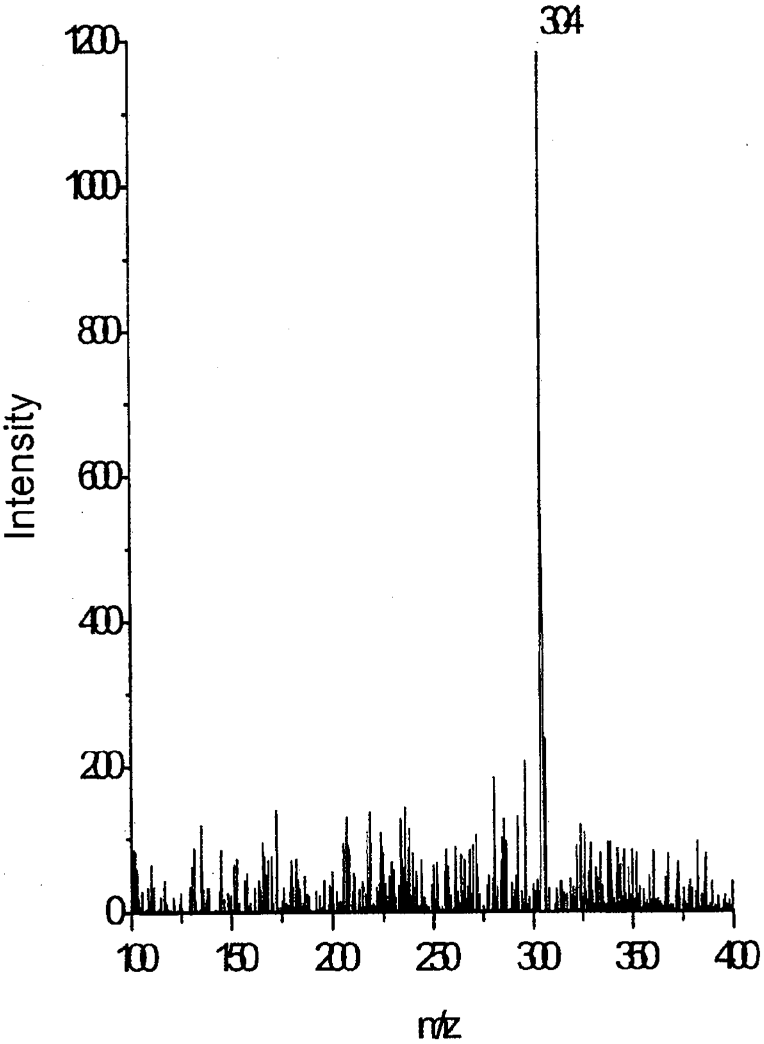

304
1200
1000
800
600
400
200
0
Intensity
100
150
200
250
300
350
400
m/z

Figure 6

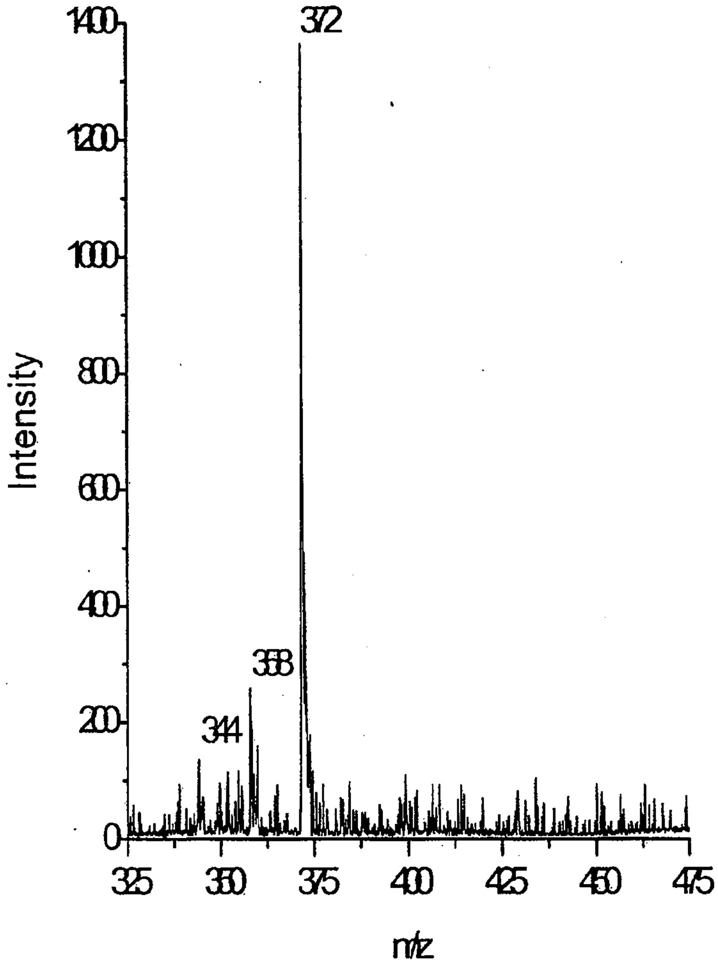

1400
1200
1000
800
600
400
200
0
Intensity
372
358
344
325
350
375
400
425
450
475
m/z

Figure 7a

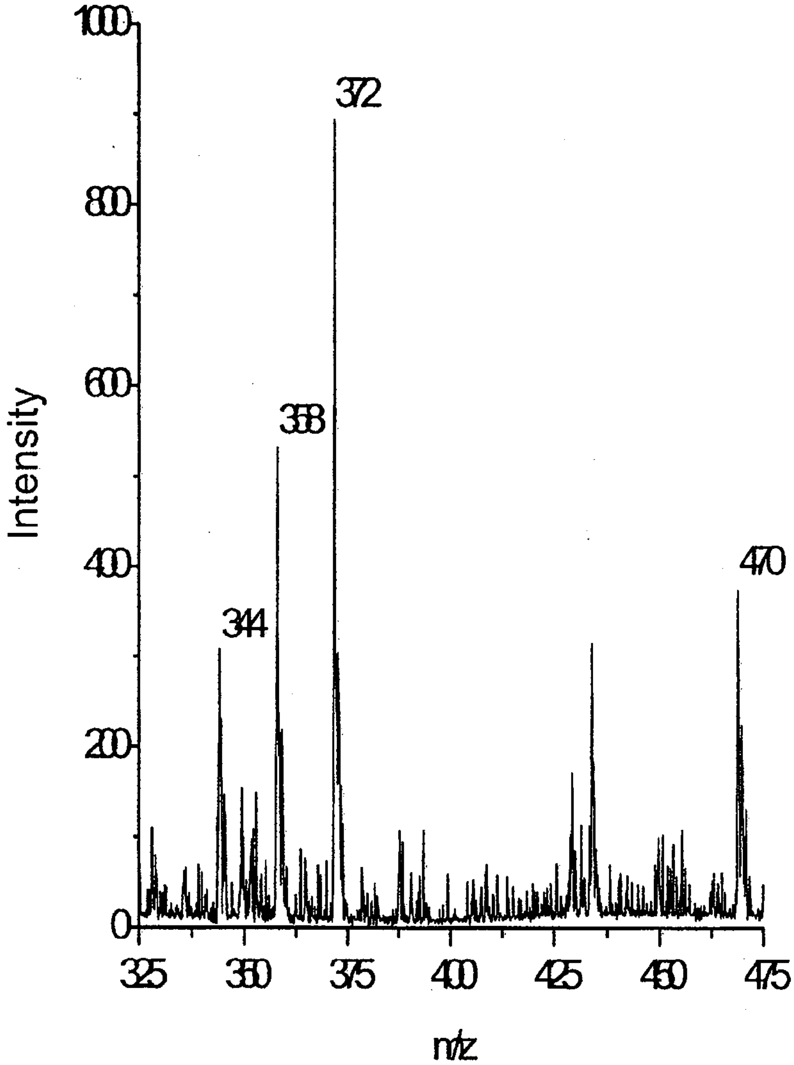

1000
800
600
400
200
0
Intensity
372
358
344
470
325
350
375
400
425
450
475
m/z

Figure 7b

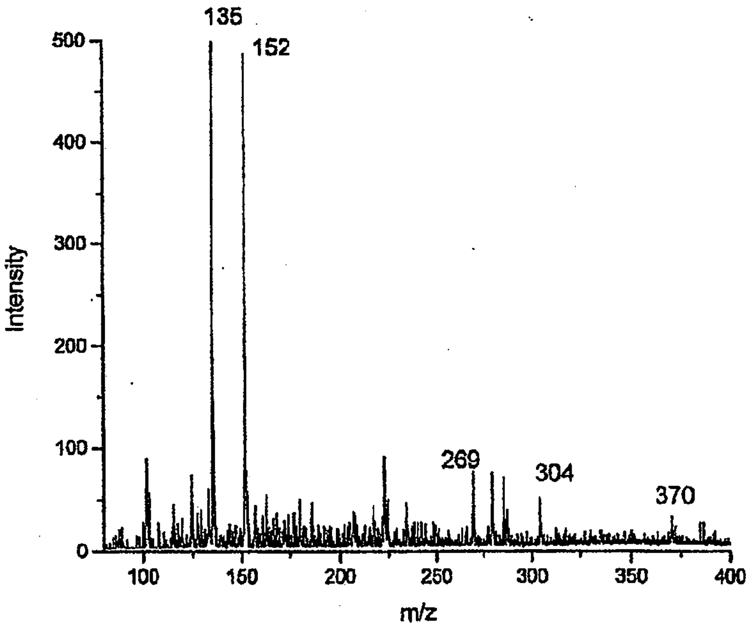

135
152
269
304
370
500
400
300
200
100
0
Intensity
100
150
200
250
300
350
400
m/z

Figure 8

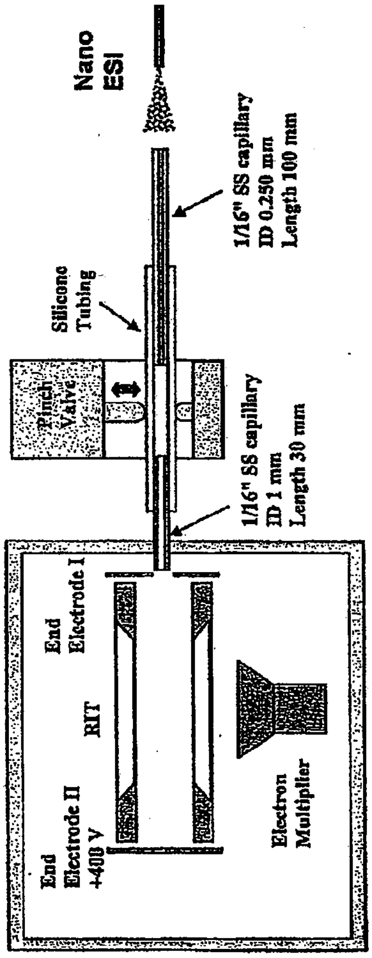

Nano ESI
1/16" SS capillary ID 0.250 mm Length 100 mm
Silicone Tubing
Pinch Valve
1/16" SS capillary ID 1 mm Length 30 mm
End Electrode I
RIT
End Electrode II +400 V
Electron Multiplier

Figure 9a

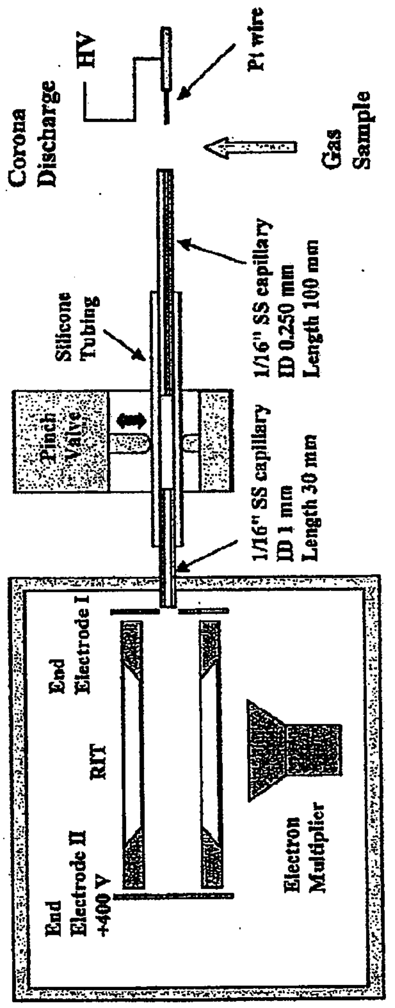

End
Electrode II
+400 V
RIT
End
Electrode I
Electron
Multiplier
Pinch
Valve
Silicone
Tubing
1/16" SS capillary
ID 1 mm
Length 30 mm
1/16" SS capillary
ID 0.250 mm
Length 100 mm
Corona
Discharge
HV
Pt wire
Gas
Sample

Figure 9b

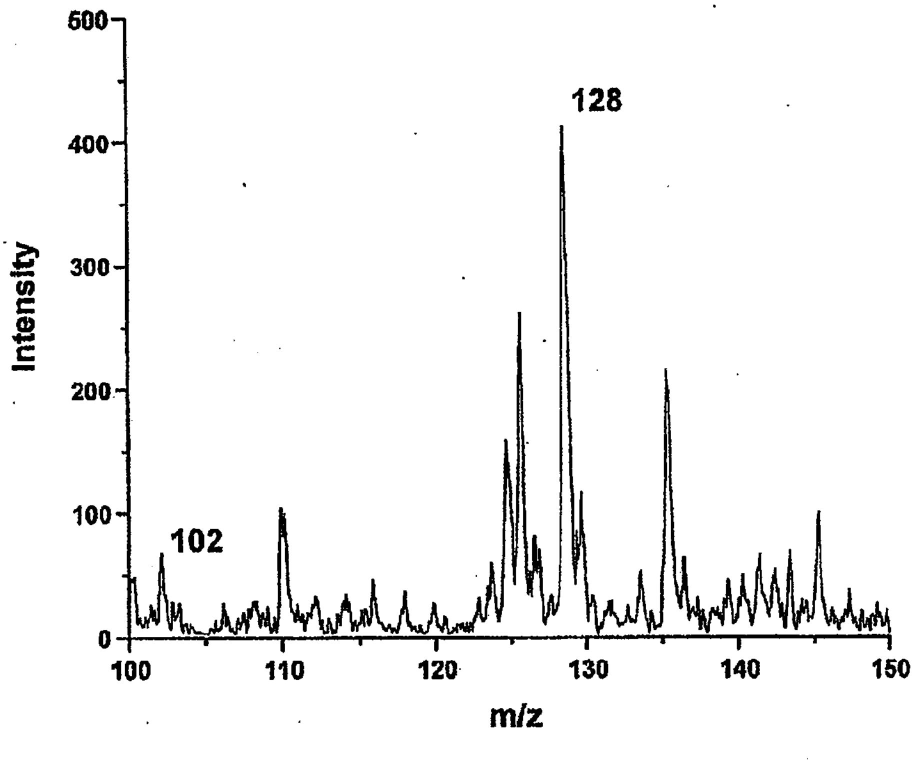

600
400
300
200
100
0
Intensity
128
102
100
110
120
130
140
150
m/z

Figure 10

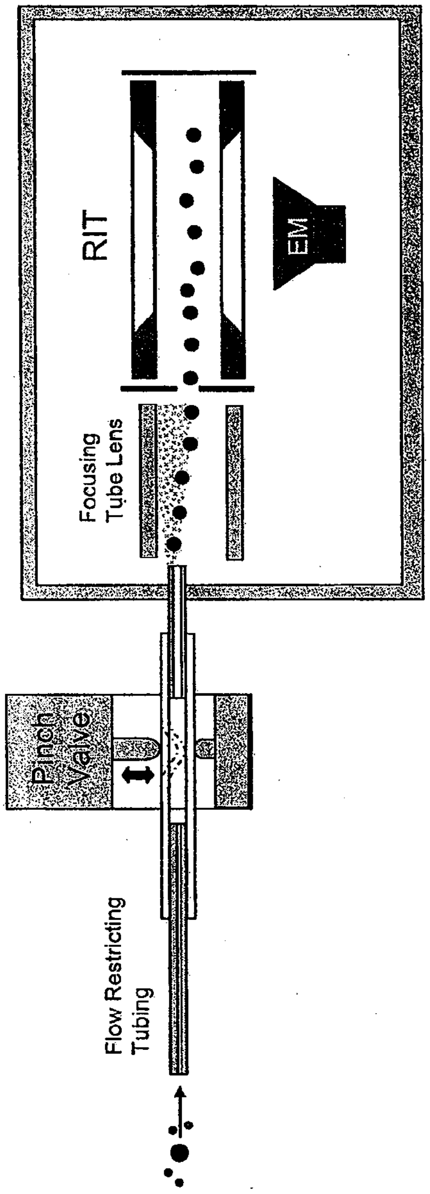

RIT
EM
Focusing Tube Lens
Pinch Valve
Flow Restricting Tubing

Figure 11

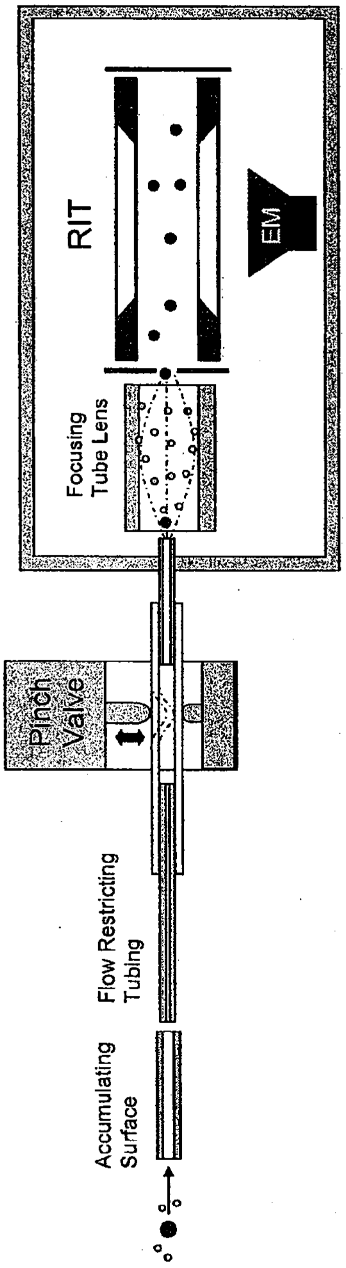

RIT
EM
Focusing Tube Lens
Pinch Valve
Flow Restricting Tubing
Accumulating Surface

Figure 12