

Electrospray ion source interfaced to a quadruple mass analyzer apparatus which included dual Electrospray ion sources delivering ions to two separate entrance apertures of a Y shaped capillary. Positive ions created in one Electrospray source were introduced into one inlet branch of the Y shaped capillary and negative ions created from the second Electrospray ion source were introduced into the second inlet branch of the Y shaped capillary. The positive and negative ions swept into the two entrance orifices of the capillary tube began mixing where the two inlet branches of the capillary tube met well downstream of the capillary entrances located in the two ES atmospheric pressure source chambers. Dual Electrospray ionization sources or a separate ES source and a gas phase corona discharge source individually delivered ions into two entrance orifices of a Y shaped capillary. For all experiments reported, the first ES source produced ions of opposite polarity to the second ES or gas phase corona discharge source. The opposite polarity ions produced in separate ion sources were not mixed in the atmospheric pressure ion source but entered a split capillary tube at two separate entrance orifices and mixed in partial vacuum downstream in the capillary tube.

[0006] Bordoli, Woolfit and Bateman, Proceedings of the 43th ASMS Conference on Mass Spectrometry and Allied Topics, 98, 1995 described an Electrospray ion source which included a calibration ES probe configured with a second microtip (50 nl/min flow rate) sample probe interfaced to a magnetic sector mass analyzer. The sample probe included a microtip attached directly to a syringe needle. The syringe was mounted on an X-Y-Z positioning stage to optimize the position of the microtip sprayer. The calibration ES probe was configured such that it could be moved into a position when a calibration solution was sprayed at 500 nl/min while no sample flowed through the primary ES sample probe. After acquisition of a calibration mass spectrum, the calibration ES probe was retracted and the calibration solution flow turned off. The sample flow through the microtip sample ES probe was then turned on and a separate mass spectrum was acquired from the Electrosprayed ions produced. In this manner, an external calibration mass spectrum was acquired prior to acquisition of a mass spectrum of the primary sample. The calibration mass spectrum and the sample mass spectrum were then added together in the data system prior to calculating the mass assignment of the sample related peaks. For the ES source configuration reported, the two ES probes were not operated simultaneously and no gas phase mixture of calibration and sample ions was created at atmospheric pressure and no mass spectrum was acquired from a mixture of calibration and sample ions. No single mass spectrum was acquired which included sample related peaks and calibration compound related peaks with the apparatus described. Neither ES probe described was configured to operate with pneumatic nebulization assisted Electrospray. The ES calibration probe position required adjustment prior to acquiring a calibration spectrum to enable effective spraying near the orifice into vacuum. After acquisition of a calibration mass spectrum, the ES calibration probe was retracted to avoid interference prior to the mass spectrum acquisition from the sample solution delivered through the primary ES probe.

[0007] In one embodiment of the invention described, multiple samples are introduced into an API source simultaneously where ions are produced from all samples and mixed in the atmospheric pressure ion source chamber. A

portion of the gas phase ion mixture is then swept into vacuum through an orifice or capillary where the ions are mass analyzed. In this manner a solution containing calibration compounds can be ionized simultaneously with a sample solution resulting in an acquired mass spectrum containing an internal standard without mixing calibration components and sample components in solution. Higher mass accuracy's can be achieved with an internal standard when m/z assignments are calculated for sample ion related peaks in an acquired mass spectrum. In addition to independently introducing calibration compounds in an API source, multiple sample inlet probes can be used to introduce multiple samples individually or simultaneously into an API source. Mounting multiple probes in an API chamber such as ES and APCI probes, allows multiple ionization techniques to be run individually or simultaneously in a single API source assembly. Multiple Electrospray probes can be configured to collectively provide optimal performance over a wide range of sample flow rates and solution chemistries. ES probe positions can be configured to fall directly on the vacuum orifice centerline to a position angled to well over 100 degrees off the centerline. Different liquid flow rates can be delivered to separate ES or APCI probes within the same API source. ES and/or APCI probes mounted at different positions in the ES source chamber, can operate simultaneously, in pairs or in groups at different flow rates and introducing different sample solutions. The multiple ES probes may be operated with or without nebulization assist.

#### SUMMARY OF THE INVENTION

[0008] One embodiment of the invention is the configuration of an API source with multiple sample solution inlets, connected to different sample delivery systems, interfaced to a mass analyzer. Individual sample inlet probes can be operated independently or simultaneously in the same API source chamber. The composition and flow rate of solution introduced through each individual API probe can be controlled independently from other sample introduction ES, APCI or ICP probes. Multiple samples are introduced into the API source through multiple API probes without mixing separate sample components in solution prior to solution spraying and ionization. Ionization of components from multiple sample solutions occurs in the gas phase at or near atmospheric pressure. The API source may include but is not limited to Electrospray, APCI or ICP ionization means or combinations of each ionization technique. Another aspect of the invention is the technique of introducing a calibration solution into at least one API source inlet probe and the sample of interest through another API source inlet probe. Both calibration and sample solutions are introduced through separate inlet probes but are sprayed and ionized simultaneously in the API source resulting in a mixture of gas phase calibration and sample related ions. A portion of the resulting ion mixture is mass analyzed producing a mass spectrum which includes known component ion peaks that can serve as an internal standard to improve m/z measurement and even quantitation accuracy. Alternatively, multiple sample solutions can be introduced separately but simultaneously creating a mixture of ions at or near atmospheric pressure to study gas phase ion and molecule interactions and reactions. Multiple inlet probe API sources can be interfaced to any MS or MS/MS<sup>n</sup> mass analyzer type includ-