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OPTIMIZATION OF PLASMA-ASSISTED DESORPTION/IONIZATION-MASS SPECTROMETRY FOR ANALYSIS OF IBUPROFEN

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In medical practice, nonsteroidal anti-inflammatory drugs (NSAIDs) are often used to treat osteoarthritis and rheumatoid arthritis. Ibuprofen is a well-known NSAID, analgesic, and antipyretic medication. This chemical is an active ingredient of several oral medications that are offered in tablet, gel pellet, and syrup forms and has higher efficacy, tolerance, and side effect rates than other compounds, including pyrazolone derivatives. We present a unique plasma-assisted desorption/ionization mass spectrometry (PADI-MS) approach for improving pharmaceutically important solids using an ibuprofen tablet as a model solid sample. The goal of the study is to create an innovative mass spectrometric method that could be used for quick and accurate analysis in the development of pharmaceutically relevant compounds. Sniffer tubes were used to route sample ions into a single quadrupole MS, with each acquisition lasting for 1 minute. Without any prior preparation, samples of ibuprofen tablets were directly exposed to PADI plasma for one minute at an atmosphere pressure. The approach is rapid, easy to use, and needs little to no sample preparation. In this study, the settings were improved by optimization of several parameters, such as plasma power, plasma-to-sample distance, and inner/outer flows of helium carrier gas, which were found to be 8 W, 2 mm, and 284 mL/min, respectively. The PADI-MS method provides a real-time information about structural features on the compounds. Ibuprofen tablets were used as a paradigm for pharmaceutically significant materials and direct PADI-MS analysis without a preliminary sample -treatment appeared to be successful: according to PADI-MS data a medication can be examined after one minute of plasma exposure.

Keywords: plasma-assisted desorption ionization-mass spectrometry; optimization; ibuprofen.

Introduction

Pharmaceuticals and pharmaceutically active substances are now classified as emerging environmental pollutants due to their unavoidable rise in consumption and increasing presence in a variety of environmental compartments. Due to their potential for being hazardous to both aquatic and terrestrial environments, these pharmaceutically active chemicals and their metabolites have since turned into pollutants of concern [1 – 3]. Nonsteroidal anti-inflammatory drugs (NSAIDs) and their metabolites are widely used in human medicine. The treatment of osteoarthritis and rheumatoid arthritis with NSAIDs is common in medicine [4]. Ibuprofen (IBU) is a well-known NSAID, analgesic, and antipyretic medication. This chemical is the active ingredient in a number of oral medications that are offered in tablet, gel pellet, and syrup forms and has higher efficacy, tolerance, and adverse effect rates than other substances, including pirazolonic derivatives [5]. The pharmaceutical substances that show up most frequently as pollutants in soils, sediments, and waterways include analgesics and NSAIDs, such as IBU [6 – 9]. Even though illegally disposed of medications, waste from pharmaceutical enterprises, etc., can also produce pharmaceutical pollutants, pharmaceuticals discharged into sewage remain the most common source of pharmaceuticals discovered in the environment. Often, intact drugs or their derivatives that were used in treatments but not yet metabolized might be found in the urine and feces [8, 10 – 12].

Pharmaceutical solid substances have been evaluated using nuclear magnetic resonance (NMR), infrared (IR) spectroscopy, and high-performance liquid chromatography (HPLC) [13]. The IBU aqueous solution has been analysed using many techniques, including biofiltration [14], biodegradation [15], oxidation [16], photo-degradation [17], electrochemical degradation [18], extraction [19], and adsorption [20]. Recently, IBU and other NSAID medications have also been evaluated using capillary electrophoresis and isotachophoresis [21 – 25]. Worldwide, HPLC-based IBU analysis is used for pharmaceutical quality control. The method

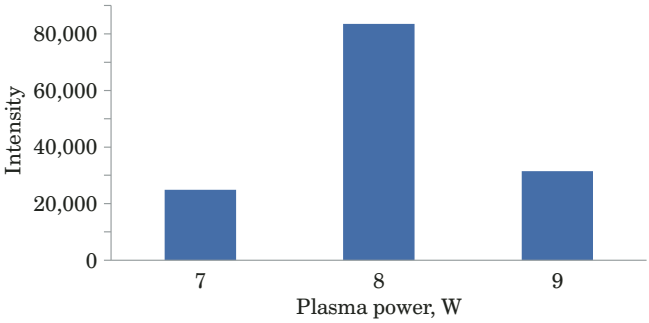

Fig. 1. Ibuprofen tablet signal intensity measured against various values of plasma power

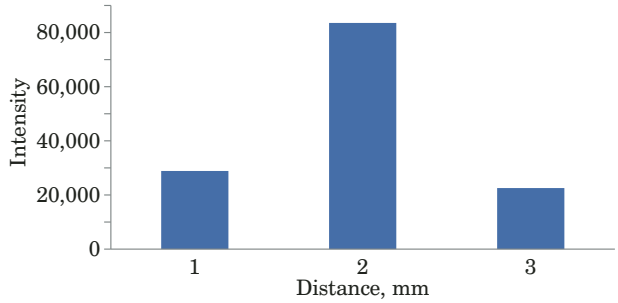

Fig. 2. Ibuprofen tablet signal intensity measured at various plasma-to-sample distances

makes the analysis of IBU and degradation products such as 4-isobutyl acetophenone possible by this method [26, 27]. It may be difficult to pre-treat the sample to determine whether the excipients or active component is soluble in the mobile phase. Isotachophoresis and capillary electrophoresis are simple, useful, and reliable methods for IBU analysis. Non-ionic species, such as those found in excipients, also have no impact on the analysis, however, the technique requires skilled technicians [5]. Although infrared spectroscopy is used in the pharmacopoeia's method for identifying IBU, there has only been one study that employs IR spectroscopy to determine the amount of IBU [5].

Although spectrophotometric methods can be more advantageous for identifying biological materials because they are less expensive and easier to use [28 – 30], there has been a recent rise in interest in ambient mass spectrometry (AMS). Samples are instantly desorbed from surfaces using AMS techniques and ionized under air pressure. The plasma-assisted desorption ionisation-mass spectrometry (PADI-MS) equipment utilized in this study was developed internally based on an earlier design by Ratcliffe et al. [31]. PADI uses a very low-power plasma with a very straightforward, reliable design that can quickly provide diagnostic mass spectra from a variety of materials. It is also generally insensitive to sample geometry [32]. A non-thermal visible plasma source is used in PADI, a contemporary ambient ionization technique, to create ions from the surfaces of molecules. This method has the benefit of lacking the drawbacks of other analytical techniques, including sensitivity, time-consuming nature, and sample pre-treatment. Plasmas are essential to numerous scientific and industrial operations. Reactive species such as $(H_2O)_nH^+$, He*, $\bar{e}$, and N_2^+ are formed when the plasma used in this study interacts with the surrounding atmosphere. The surface atoms from the sample interact with these species [33].

The aim of the study was to develop a novel ambient mass spectrometric technique that might be utilized to swiftly and precisely assess the emergence of molecules with potential for medicinal applications.

Experimental

The front end of the Micromass ZQ, Manchester, UK, single quadruple used in the PADI-MS apparatus was removed to make room for a Stoffels-designed plasma pen ionization source employing a 13.56 MHZ RF power source [31]. To support coaxial dual gas flow, The plasma pencil included a quartz glass tube with an inner ceramic tube inside of it. The PADI-MS parameters for all of the samples in this experiment were found to be 8 W of plasma power, 284 ml/min of the inflow, and a 2 mm distance between the plasma flame and sample using preliminary analysis. Tesco Stores Ltd. provided ibuprofen tablets with a 200 mg dose per tablet, Welwyn Garden City al7 1ga, UK. British Oxygen Company (BOC) Gases, UK, provided the helium gas (99% purity). Deionized water was supplied using a pure lab option LGA, model Ultra Clear TWF UV, with a resistivity of 18 MΩ/cm. Ibuprofen tablet samples were directly exposed for 1 min at air pressure to PADI plasma without any prior preparation. Direct PADI-MS analysis of an ibuprofen tablet sample was performed under ideal conditions with a total duration of 1 min.

Results and Discussion

The approach was improved by enhancing the peak of the chemical using ibuprofen tablets. The appropriate conditions for PADI-MS sample analysis were found through repeated measurements of the component. The PADI-MS parameters of interest were the plasma power, the separation between the visible plasma and the sample surface, and the flow rate of the helium carrier gas. It was found that when the plasma power was 8 W, the main ions in the sample had the highest intensity (or the least noise). As shown in Fig. 1, this was found to be the best option for all samples. As expected, the noise increased as the plasma power increased (to >8 W). This is because a strong plasma flame, spe-

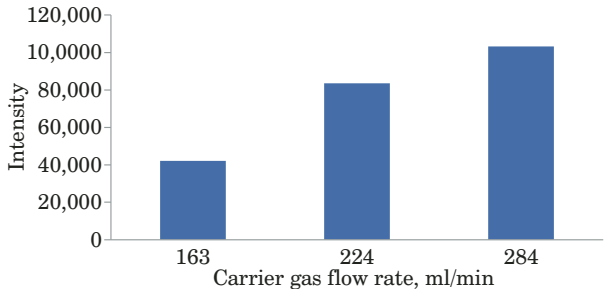

Fig. 3. The signal intensity of an ibuprofen tablet measured at various gas flow rates

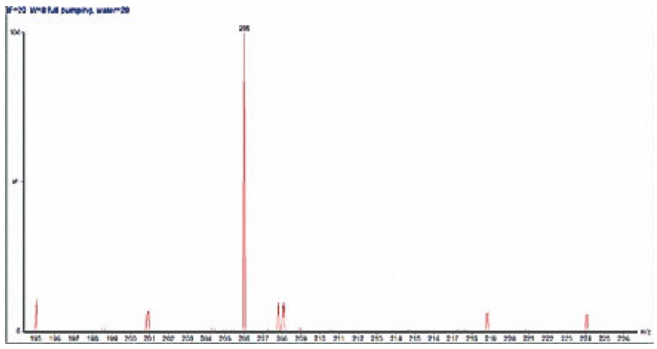

Fig. 4. PADI-MS spectra of an ibuprofen tablet using 8 W plasma power, 2 mm distance, and 284 m/min helium flow rate

cifically one greater than 8 W, may cause more harm to the sample. Molecular intensities also dropped when using less plasma energy (8 W). As shown in Fig. 2, it was also found that the sample had the highest intensity at a distance of 2 mm from the plasma flame. The same problems that were previously addressed could arise when the plasma pencil's distance from the sample was more than or less than 2 mm. The carrier gas flow that produced the highest intensity of the sample ions was found to be 284 ml/min for both the inner flow and the outer flow (Fig. 3). The same problems as previously discussed could arise when the carrier gas flow rate was more or less than 284 ml/min.

Following optimization of a coaxially organized supply with inner and outer flow rates of 284 ml/min for each, helium and water were delivered close to the needle tip. The sample was placed 2 mm away from the visible plasma flame. These conditions led to primary ions in the sample with the maximum signal-to-noise ratio, and it was found that these conditions were ideal for all solid samples. As anticipated, the noise increased with a tighter plasma pencil to sample (2 mm). In order to minimise sample damage and ion intensity as the distance between the plasma pencil and the sample increased (> 2 mm), the ideal compromise between the two was a distance of 2 mm. This may be due to the sample being more severely harmed by the reactive species in the plasma. When helium and water vapor are employed as the gas flow, as shown in Fig. 4, the ibuprofen $[M^+]$ m/z at 206 is higher.

Conclusion

The purpose of this work was to develop an ambient mass spectrometric method that may be used to evaluate compounds that have the potential to be used in pharmaceuticals. This method should be novel, simple to use, rapid, sensitive, and affordable. This study states the use of PADI-MS for direct analysis of solids, as well as how frequently it takes little to no setup effort, little to no sample preparation, and rapid analytical times. The PADI-MS approach additionally provides instantaneous structural information on the molecules. The use of ibuprofen tablets as a paradigm for pharmaceutically important materials resulted in successful results from direct PADI-MS analysis without sample pre-treatment. According to PADI-MS results, the drug can be analyzed after 1 min of plasma exposure.

Future applications of the strategy presented here could be in the biomedical, food, and environmental sectors. To demonstrate the findings of this study, future studies should compare this non-thermal plasma of PADI with other plasmas while analyzing pharmaceutical tablets.

Conflict of interests

The author has no conflict of interest to declare.

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