Original Article

Determination of Mefenamic Acid in Aqueous Solutions Using Reverse - Continuous Flow Injection Analysis

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Abstract

This research aims to use a novel algorithm to determine the concentration of Mefenamic acid. The MA concentration in aqueous solutions was determined using this technology, and the results obtained using more conventional methods were compared to those obtained using more traditional methods. A signal detector and a specialized software spectrometer then receive the data. The maximum wavelength of the product is determined using a spectroscopic scan, a calibration curve is constructed, and measurements are made to estimate the drug's absolute concentrations in aqueous solutions. This treatment is popular because it is simple, rapid, precise, inexpensive, and adaptable.

Keywords: Mefenamic acid, NQS, Flow Injection analyses, Version 1.5 of the G-chrom software, Reverse - Continuous Flow Injection.

Introduction

It is used to treat rheumatoid arthritis, other painful musculoskeletal diseases, and post-trauma inflammation. It is derived from the amino acid [2-[(2,3-dimethyphenyl) amino] mefenamic acid, benzoic acid (MF). It functions as an anti-inflammatory, analgesic, and antipyretic agent, among other things[1-5]. MA is used to relieve mild to moderate pain, and it has been suggested for usage in the treatment of rheumatoid arthritis in the past. Like other nonsteroidal anti-inflammatory medications, MFA works by inhibiting the enzyme prostaglandin synthetase [6]. Ongoing research is being conducted to develop simple, dependable, and automated technologies for rapidly assessing therapeutic compounds in pharmaceutical formulations[7].

NQS is used to improve the limits of detection (LOD) of pharmaceutical amines and amino acids by adding chromophores or fluorophores; a derivatization phase is typically used in conjunction with chromatographic spectrophotometric spectrofluorimetric detection methods. Inorganic amines and amino acids are being determined analytically utilizing 1,2-Naphthoquinone-4-sulfonate (NQS), which is increasingly used in conjunction with ultraviolet/visible (UV-Vis) spectrophotometric detection methods.

In the presence of primary and secondary amino groups at critical medium and moderate temperatures, NQS can react to create spectrophotometrically detectable derivatives[8, 9]. In contrast to other types of analysis, flow-injection analysis (FI) is differentiated by its simplicity, quickness, cheap equipment requirements, and precision of results[10-15]. Each essay is completed in a fraction of the time manual analytical processes require, making it a critical alternative to manual analytical procedures. Its ability to control volume, mixing patterns and residence times allows it to execute chemical operations that would be unreliable if performed manually, either because the reactions do not reach equilibrium or because the reaction products are not sufficiently stable over a long time.

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Through repeatable and accurate timing, the FI approach can measure the properties of metastable and transitory species. Multiple measurements developed for clinical, pharmacological, dietary, and environmental studies have demonstrated the value of FI methods for regular analysis[10, 16-26]. When the reagents used are expensive, and the model is cheap and available in large quantities, it is preferable to reverse the injection process. In rFIA, the reagent solution is injected into the sample solution, as the latter becomes the conductive current. This technology is characterized by being economical because the used detector is small.

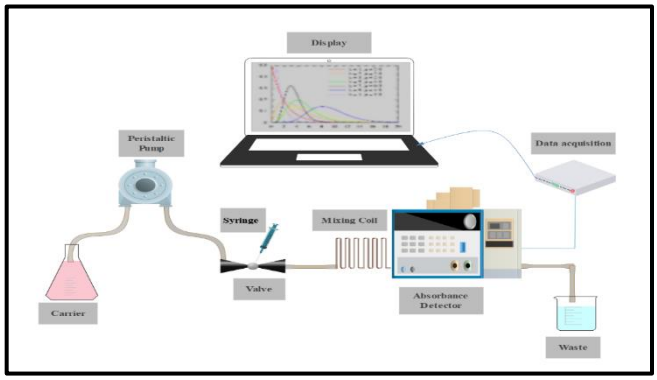

Fig. 1. It shows a flow injection system model that our laboratory designed and built.

Materials and manufacturing methods

Reagents and substances

Unless otherwise stated, all analytical-grade chemicals and double-distilled water were used for reagent dilution to sample processing. The reference of NQS provided by Aldrich and the drug was obtained from Samara, an Iraqi state-owned pharmaceutical enterprise (SDI).

As standard solutions, prepare Mefenamic acid, NQS, and any required buffer solutions

All of the dilutions shown below were created using freshly produced working solutions. By dissolving it in 50 mL of distilled water, sodium 1,2-Naphthoquinone-4-Sulfonic (NQS) 5 mg (0.005gm) of the reagent was freshly prepared as a stock solution containing 100 parts per million (ppm). It was possible to make mefenamic acid (MA) at a concentration of 50ppm by dissolving 5mg (0.005gm) of MA in 25mL distilled water and diluting the solution with distilled water 100mL in a volumetric flask. 0.2M sodium hydroxide is used in this recipe. To make it, dissolve 1.6gm sodium hydroxide in 25ml distilled water in a volumetric flask and dilute to 200mL with more distilled water. 0.2M Potassium Chloride is used in this experiment. To make a standard solution, dissolve 2.858gm in 20ml distilled water in a volumetric flask and dilute it with distilled water to 200mL in a volumetric flask. 0.2M Boric acid is used in this recipe. It was necessary to prepare a standard solution of 1.2366gm by dissolving it in 25ml of distilled water and diluting it to 100mL in a volumetric flask before using it.

Solution of sodium hydroxide and boric acid as a buffer 50mL distilled used water to dissolve the boric acid, then combined with 4.15mL sodium hydroxide (0.2M) in a 100mL volumetric flask to form a solution and after that, diluted the answer with distilled water until it reached the desired concentration.

pH 10 buffer solution containing (boric acid, potassium chloride, and sodium hydrochloride) A 100mL volumetric flask containing 25mL boric acid (0.2M), 25mL potassium chloride (0.2M), and 21.85mL sodium hydroxide (0.2M) was used to prepare the solution, which was then diluted with distilled water to the desired concentration.

pH 12 buffer solution containing sodium hydroxide and potassium chloride in a 100mL volumetric flask, combine 50mL potassium chloride (0.2M) and 24mL sodium hydroxide (0.2M) and dilute with distilled water to the specified concentration.

pH 13 buffer solution containing sodium hydroxide and potassium chloride in a 100mL volumetric flask, combine 25 mL potassium chloride (0.2M) and 65mL sodium hydroxide (0.2M) and dilute with distilled water at the specified concentration.

Instruments

All flow injection analyses were conducted utilizing a Rabbit peristaltic pump, a Rheodyne valve 7725, a BioLogic QuadTec UV-Vis Detector, and a Sartorius CPA2P Competence Analytical Balance. G-Chrom V1.5 Loop Volume: 40 µL for appropriate analytical methods that can be designed and developed for a variety of purposes, such as qualitative analysis, formulation, conservatism content, and estimating analyte concentrations in biological or non-biological fluids, the software designer is responsible for scanning, calibration, measurements, and report editing for the methods.

I decided to use Accumulate Peak Analysis (APA) because of its precision, quick analysis, and ability to graph data. The data produced from the technique were screened and compared to the standard solution with the help of an equation that was expressly created for this purpose. This step will aid the analyst in gaining a complete understanding of the parameters that influence the performance of the analysis during the next stage. As shown in Fig. 1, the FIA injection system comprises a peristaltic pump and an injection valve joined together by a single low-load link to deliver the fluid. Operation is comparable to a standard six-way valve operating in two directions, widely applied in the spectrum analysis of injection techniques, except that this system only works in one order. The injection ring comprises a single input and output connected by many channels. A two-link valve regulates the condition of the injection system and helps to enhance modelling by controlling the flow of fluid. The diameter of the injection ring (the loading link) used in this experiment, 50 µL, determines the sample's size.

Results

Determine the maximum wavelength (max)

1mL of a standard solution containing 50ppm MA was transferred to a 10mL volumetric flask, followed by 1mL of buffer solution (pH 12) and 1mL of NQS solution, followed by the addition of 1mL of a standard solution containing 50ppm MA (100ppm). To achieve thorough mixing, mixed and diluted the components with distilled water.

A study was conducted to investigate the absorption spectra of mefenamic acid compared to water and discovered that mefenamic acid exhibits a maximum absorption peak at 285 nm. It was determined that there was no absorption interference between the reagent and the sample by examining the absorption spectrum of NQS against water in the range of wavelengths used in the experiment (385-580). After then, the absorption spectra of the product were compared to those of water (to confirm that there was no effect of the reagent in this range). Finally, the absorption spectra of the result were compared to those of the reagent to determine their differences. The maximum absorption wavelength of the product was determined to be 477nm in length, Fig .2 & Table.1.

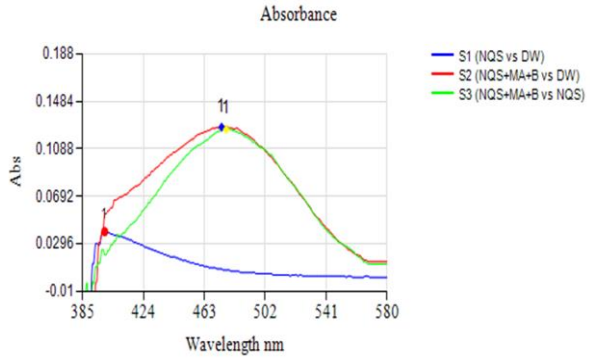

Fig. 2. The spectrum of NQS and product

Table.1. Result of Lambda max

Result Table

Lembda	S1	Lembda	S2	Lembda	S3
399	0.04	474	0.127	477	0.125

Optimization of Experimental Conditions:

Monitored a single parameter and the effect on the absorbance of the coloured species to identify the best possible experimental conditions for the experiment.

The influence of flow rate:

Explored the effect of flow rate on the formation of the coloured product by altering the flow rate (1 = 0.5 6 = 3) ml/min and measuring the absorbance of the coloured product produced. The study discovered that the optimal flow rate is 3 = 1.5 ml/min, generating the best beak shape and the most significant absorption. Two picked over the other options because of the more excellent time required by speed, Fig 3.

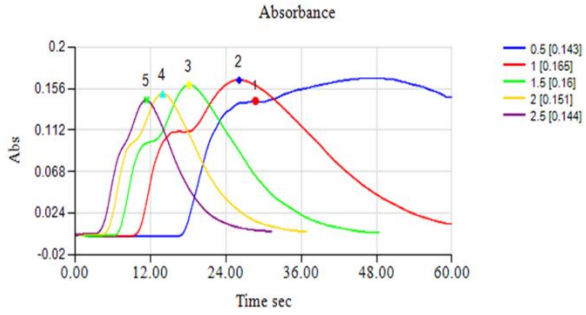

Fig.3. Shows the effect of flow rate

The following is the effect of the length of the mixing coil

The effect of altering the length of the reaction coil was explored and compared. The results were those obtained without using a mixing loop in the experiment. Several sizes (100, 75, 50, and 25) cm were used to test the response without using a response coil; the highest absorbency value and the best shape for the peak using a reaction coil with a length of 75 cm were obtained after the double-top rise (which indicates that the mixing was not complete) was eliminated, with a low peak indicating insufficient mixing and a high height indicating adequate mixing being obtained, Fig.4.

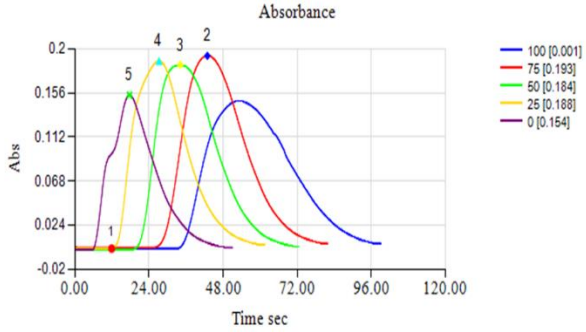

Fig.4. The impact of the reaction coil is depicted

The following is the effect of the base type and the quantity added

Various base solutions, such as sodium hydroxide and numerous buffer solutions with variable pH values (pH9, pH10, pH12, and pH13), were used to determine the maximum absorbance intensity. In the following study, NaOH is utilized since it has a higher sensitivity and repeatability than methanol, Fig.5. The best sodium hydroxide concentration for achieving the most incredible colour intensity, on the other hand, was discovered to be (3= 0.15 ml for each 20 ml sample) 0.75mL for each 100ml model, which was found to be the case, Fig.6.

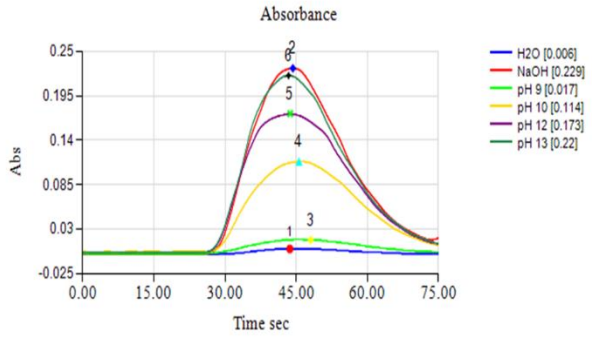

Fig.5. The Influence of the Base Type

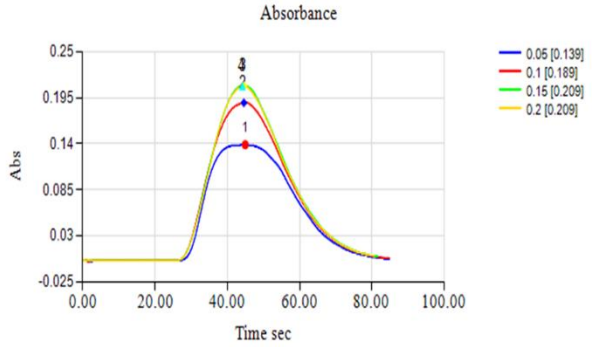

Fig.6. Effect of base concentration on the results

Effect of NQS concentration

This study evaluated the effect of changing the reagent concentration on the reaction. Used a range of NQS concentrations (10-100) ppm to collect data, and the results revealed that the best absorbance occurs when the reagent concentration is 50ppm, Fig.7.

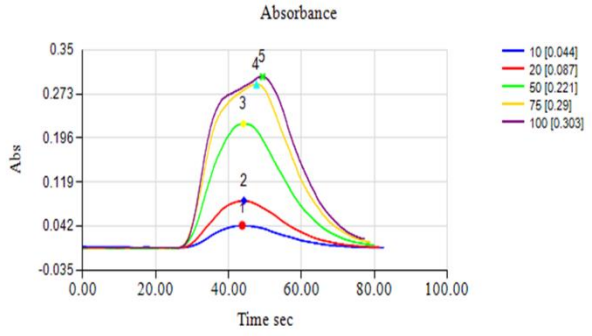

Fig.7. The Influence of NQS Concentration

General procedures and the calibration curve are discussed below.

20-mL volumetric flasks with a capacity of 0.15mL sodium hydroxide solution were used to prepare solutions of varied MA concentrations for flow as carrier solution with 50ppm NQS injected in the loop, 75 cm of reaction coil, and a flow rate of 1.5 mL/min. The calibration curve shown below was created using the following steps, Fig.8 & 9.

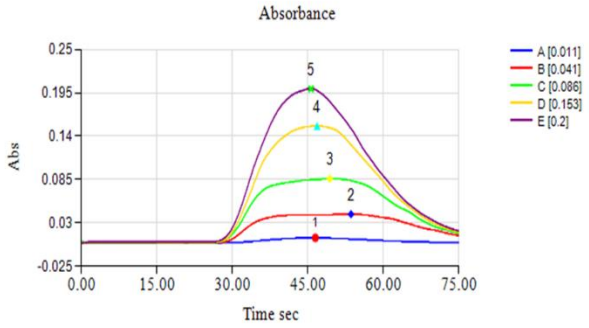

Fig.8. Shows (1–30) ppm spectrum of mefenamic acid.

Table.2. Result of absorbance

Result Table

Index	Sample	MA ppm	Peak Height
1	A	1	0.011
2	B	5	0.041
3	C	10	0.086
4	D	20	0.153
5	E	30	0.2

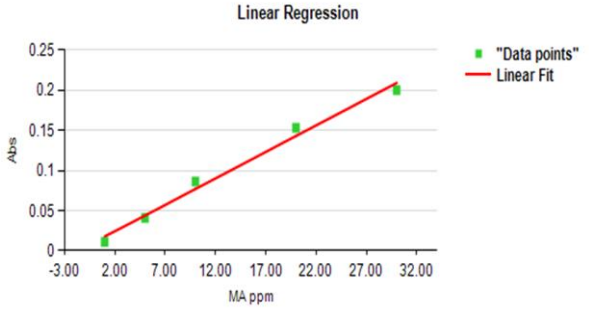

Fig.9. Calibration curve of mefenamic acid

Table .3. Equation & R-squared value with ideal values of a calibration curve

MA ppm	Abs	QR
1	0.011	0.018
5	0.041	0.044
10	0.086	0.077
20	0.153	0.143
30	0.2	0.209

$y = 0.007x + 0.011$

$R^2 = 0.9869$

Repeatability

Discovered the reproducibility of the proposed method was highly high by performing repeated analyses on six sample solutions containing 30 ppm MA. The approach displayed highly high repeatability, Fig.10.

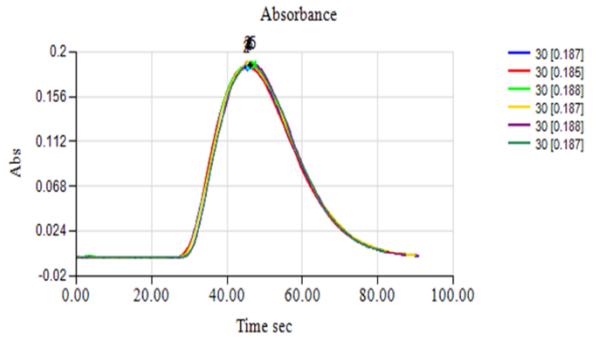

Fig.10. Depicted the reproducibility of mefenamic acid

Dead volume

As a result of the two results indicating that no interaction occurred when eliminated the reagent or sample with the base, the dead volume was calculated to ensure the system's high quality, Fig.11.

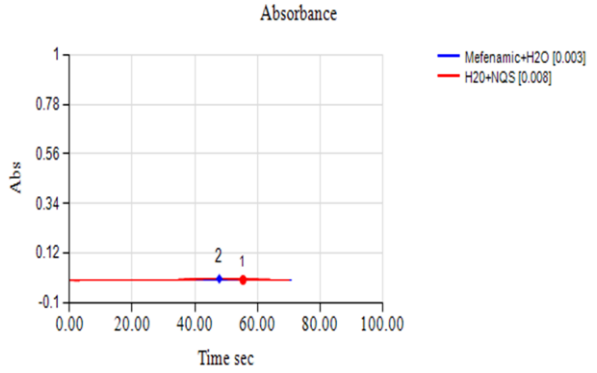

Fig.11. The dead volume of mefenamic acid

The determination of dispersion

The acid mefenamic acid is present in 30 parts per million. Two experiments were carried out to estimate the dispersion value within the sample zone. First, a concentration of Mefenamic acid (30 ppm) flows into the FIA for the first experiment. This experiment represents the sample's intensity response that passes into the investigation (H max). The reaction is constant after the reactants (Mefenamic acid and NQS) have been mixed and passed through a manifold unit, demonstrating no dispersion effect due to convection or diffusion. This illustration depicts (Ho). It is possible to compute dispersion (D) by applying the following equation: D ° = Ho/H max ((D=1.18). The distribution of these figures is restricted to a small range, Fig.12.

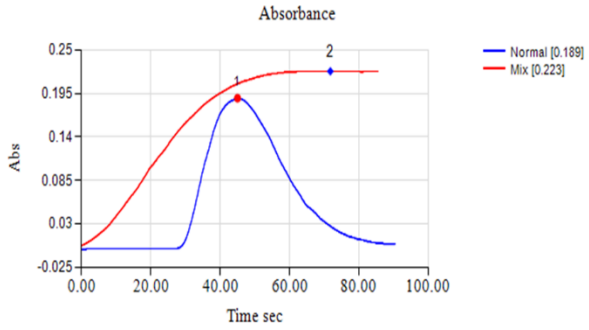

Fig.12. Dispersion

In aqueous solutions, mefenamic acid can be determined as follows

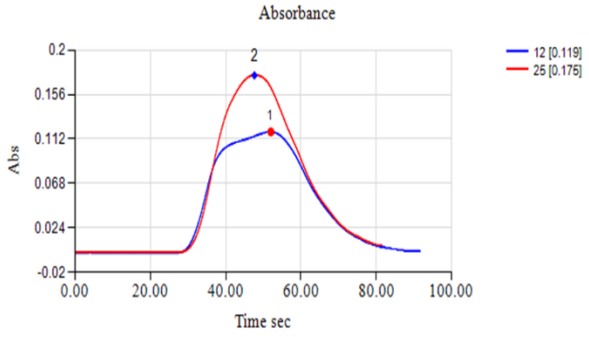

Fig.13. The spectrum of possible applications

Table 4. Value of sample application

Result Table

Index	Sample (Taken)	Mefenamic acid (founded)	Peak Height
1	12	16.358	0.119
2	25	24.889	0.175

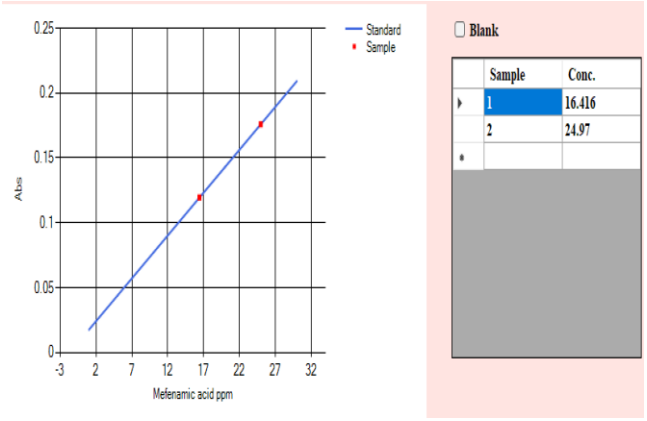

Fig.14. Determination of sample unknown on a calibration curve

Discussion

The technique is based on the physical characteristics of electromagnetic radiation. The study's findings indicated that

the injection technique is simple and can detect drug concentrations in aqueous solutions. According to the results, the detection limit was determined to be LOD = 0.021 ppm, the limit of quantification was determined to be LOQ = 0.071 ppm, the straight-line equation for drug concentration versus absorption was determined to be y = 0.012 x + 0.007, and the correlation equation for the standard specification 0.9869 linearity was determined to be (1-30) ppm. The calibration curve's results indicated a high correlation coefficient with linearity, implying a solid relationship between peak height and concentration, relevant to the study's aims. G-Chrome is Peak Accumulated Analysis (APA) for this type of analysis. Conducted the research was based on a single reading. This procedure has been demonstrated to be both rapid and precise.

Along with the standard deviation (SD) and relative standard deviation (RSD%), this method gave the analyst greater latitude in computing the standard deviation (SD). They are combined the data, graphs, and tables into a final, exceptionally reliable report by calculating the equations of straight and linear lines without referring to standard Excel computations. Compared to non-destructive methods and near-infrared spectroscopy, the results from this method are acceptable (NIRS).

MA does not have a long-term or lethal effect, but it may create health concerns if consumed in excess. MA has been shown to interfere with the anticoagulant activity of Aspirin. Some studies have linked anti-inflammatory medications to an increased incidence of stomach ulcers. When used with diuretics, the efficacy of the diuretics is decreased, and the risk of kidney damage increases. In the United States, the Food and Drug Administration (FDA) has ordered a review of all non-steroidal anti-inflammatory drugs to warn about the risk of renal problems in neonates. Several techniques are employed in drug detection and identification, including differential pulse polarization, thin layer chromatography, adsorption voltammetry, and differential spectroscopy. When constructed on measurements, the laboratory and G-Chrome programs are more precise, adaptable, and time-efficient. This technique cumulatively records the individual measurements of each sample throughout time. This technique requires less analysis time than gathering all the statistical data necessary to publish the final report. This pattern might be appropriate for indicators. Routine measurements are utilized in spectroscopic analysis to determine flow and injection. Finally, the newly developed G-Chrome method is inapplicable to solid samples. On the other hand, solid samples can be dissolved in a solvent that has been tested against G-Chrome. CONCLUSIONS: A paradigm shift has occurred in the visual evolution of FI-UV.

Unlike previous instruments, the new one employs a novel, entirely constructed, in-lab planned, and in-lab managed G-Chrome flow-injection software to determine the spectroscopic approach. This system is straightforward to use, and data transmission is automatic. Due to the internal architecture of the software utilized in this technique, injecting the sample and then repeating it at an intersection or modifying the selection is straightforward. Additionally, I discovered that the data acquired was accurate and equivalent to that produced using more complex instruments. This system is differentiated by its cost and convenience of use, its high degree of flexibility, precision, and control over the results, and, most crucially, the analyst's ability to build and improve the system and approach.

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