DOI: 10.53992/njns.v9i1.157 **NUST Journal of Natural Sciences, Vol. 9, Issue 1, 2024**

A new analytical methodology for the detection of Methamphetamine using UV-Vis, FTIR, and GC-MS techniques

Khurram Shahzad Munawar[1,2], Muhammad Sameer[3], Mohsin Javed[3], Syed Mustansar Abbas[4], Jamila Javid[5], Shabbir Hussain[6], Tauqeer Ahmad [1]

[1]Institute of Chemistry, University of Sargodha, Sargodha, Pakistan
[2]Department of Chemistry, University of Mianwali, Mianwali, Pakistan
[3]Department of Chemistry, School of Science, University of Management and Technology, Lahore, Pakistan
[4]Nanoscience and Technology Department, National Centre for Physics, QAU-Campus, 45320, Islamabad, Pakistan
[5]Department of Chemistry, University of Sialkot, Sialkot, Pakistan
[6]Institute of Chemistry, Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan, Pakistan

***Corresponding author's email:** khurramchemist@gmail.com

Abstract

Methamphetamine is one of the strongest and highly addictive stimulants of the central nervous system. It is a synthetic drug and belongs to the amphetamine-type stimulants but it is more potent as compared to amphetamines. It is illicitly manufactured in clandestine laboratories. The major precursors required for the manufacture of methamphetamine include ephedrine, pseudo-ephedrine, and phenyl-2-propanone. Its manufacturing, possession, trafficking, distribution, and sale have been restricted and controlled legally not only in Pakistan but internationally as well. The main objective is to develop and validate a new method for the detection and quantification of methamphetamine manufactured in Pakistan. The proposed method is quite easy, simple and cost-effective, and requires no complex methodology for sample preparation.A chemical spot test was used for the detection of methamphetamine as a presumptive test. The confirmation test for methamphetamine was performed using a Fourier transform infrared (FT-IR) spectrophotometer and gas chromatography-mass spectrometry (GC-MS). The quantification of methamphetamine was carried out on a UV-visible spectrophotometer. All of the parameters, like accuracy, precision, linearity, reproducibility, detection limits, quantification limits, etc., were established and validated. The proposed method is easy, simple, and accurate, and the results are so reliable that they can be used for casework in forensics and clinical drug analysis. The quantitative linearity range was from 50 µg/mL to 1000 µg/mL and the observed λ_{max} was 259 nm. The calibrators were stable for 4 days. The limit of detection was 50 µg/mL and the lower limit of quantification was also 50 µg/mL. The absorbance of methamphetamine in the UV region is due to π to π* transition because of the presence of carbon-carbon double bonds in the methamphetamine structure. FT-IR spectrum showed that the sample was 88 % pure and GC-MS results showed that the sample contained 85 % of methamphetamine.

Keywords: Methamphetamine; Method Validation; FT-IR, UV-Visible, GC-MS

Article History: **Received:** 05 September 2023, **Revised:** 03 April 2024, **Accepted**: 25 April 2024, **Published:** 30 May 2024.

Introduction

Methamphetamine (Nmethylamphetamine) is a synthetic and illegal drug [1]. Physically, it is a white crystalline powder and has a shining appearance [2]. It is one of the strong and highly addictive stimulants of the central nervous system (CNS) and belongs to the family of phenethylamines, which are closely related to amphetamine, which is also a stimulant [3]. The basic form of methamphetamine is colorless oil, which is volatile, and insoluble in water. It is odourless, and its melting point is 171-175^{o}C [4]. Hydrochloride salt is the most commonly found salt of methamphetamine, which is present in the form of white powder or crystals in Figure 1 (a) and (b).

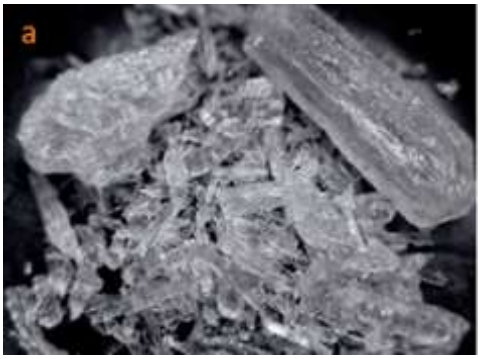


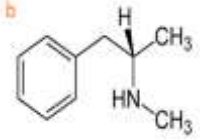
Figure 1.(a) Crystalline form of methamphetamine

Figure 1.(b) Powder form of methamphetamine

Products of methamphetamine seized by law enforcement agencies are mostly in the form of powders and also in the pure crystalline form, which is in hydrochloride salt formulations [2]. Commonly, methamphetamine is known by the street names such as "ice" or "crystal" [5]. Internationally, methamphetamine is known by its common names. Some familiar common or street names for methamphetamine are speed, ice, crank, chalk, glass, meth, crystal meth, pervitin, yaba, and shabu [6]. Methamphetamine is manufactured in clandestine laboratories throughout the world, including in China, India, the United States of America, and Pakistan [7]. Mostly it is used as a recreational drug for pleasure, enjoyment, amusement, or funny experiences, and it is very rarely used for therapeutic purposes such as the treatment of attention deficit hyperactivity disorder or the reduction of obesity in rare cases [8].

Methamphetamine exists in two of its enantiomer forms: levo methamphet- amine and dextro methamphe- tamine[9].

Figure 2 (a). Desoxyn label



(b) Structure of methamphetamine

Internationally, methamphetamine also occurs in formulations for therapeutic applications in the form of tablets and injections as well [10]. Methamphetamine is shown in Figure 2b.

Akira Ogata synthesized amine for the first time in Japan in 1919. In 1920, Burroughs Wellcome & Company patented, manufactured, and then launched methamphetamine on the market for the first time in the form of hydrochloride salt with the brand name “Methedrine”. During 1920-1930, both the medicinal importance and abuse of methamphetamine increased in Europe and generally in the West [12]. Methamphetamine has been used for therapeutic applications, for example, it was used for the treatment of depression, frustration, and other behavioral problems in the United States, but its use as a stimulant and psychoactive drug was also initiated by various individuals in the United States [13]. The side effects of methamphetamine use for non-medical purposes comprise a descrease in appetite, high blood pressure, frustration, depression, high blood pressure, behavioral changes, and psychiatric disrurbances and physiological changes that have been reported since 1930 [14].

In 1938, a pharmaceutical company named Temmler in Berlin initiated the methamphetamine, naming it "Pervitin" [15]. During World War II, it was provided in bulk quantities to the German armed forces to increase their performance and enhance focus. Because of this, methamphetamine was called "Pilot’s salt" and "Pilot’s chocolate" in Germany [16]. In the 1990s, the use of methamphetamine increased continuously in the West and Northwest. In the general population, its use has increased from below 2 % of the total young generation in 1994 to 5 % of the total young generation in the year 2000 [17]. Monitoring the Future reported that the use of methamphetamine has persisted continuously and became stable over the last decade of the nineteenth century [18].

Methamphetamine is used in various ways. It can be taken orally, snorted, smoked with a cigarette, or injected (Figure 3 (a) to (c)) [19].

(a) Injection (b) Smoking (c) Snorting
Figure 3. Different ways to intake methamphetamine

The crystalline, or salt, form of methamphetamine is volatile and can be used directly in cigarettes [20]. "Control of Narcotic Substances Act 1997," which has been in effect all over the country since 1997 [21]. Section 9 of the_CNSA (1997) deals with narcotics and controlled substances. This law is based upon the quantity of the seized substance; the greater the quantity or weight of the seized material, the harsher the punishment and the higher the fine assessed against the accused.The objective of the present research work is to establish qualitative as well as quantitative analytical methodology using three different instrumentations for the identification and analysis of methamphetamine that should be quite easy, simple, sensitive, accurate, and reproducible. Previously, highly sophisticated and costly instruments were in use for qualitative as well as quantitative analysis, but all of those procedures are quite expensive, secondly, these methods require a complex methodology for sample preparation and extraction of drugs from different formulations. So, to overcome the complexity of these expensive techniques, here we developed a very easy, cheap, reproducible, and sensitive method that

neither requires tedious sample preparation steps nor other complex methods of extraction. The proposed method is quite simple, and the instruments used are easily accessible in Pakistan.

Methamphetamine entered Pakistan in 2010, and since that time, no work has been performed on this drug, either for quantitative analysis or qualitative analysis. This proposed method uses FT-IR and GC-MS for the detection and qualitative analysis of methamphetamine and a UV-visible spectrophotometer for quantitative analysis with proper validation including all the parameters like precision, accuracy, rapidity, stability, standard deviation, reproducibility, and sensitivity. The current method can be used for routine casework in forensic analysis.

Methodology

Chemicals and instruments:

Different kinds of reagents like methamphetamine (Sigma-Aldrich, USA), sodium hydroxide (Acros Organics), chloroform(Universal Chemical California USA), potassium permanganate (Yuanrun Chemicals China), methylsulfonylmethane (Chaitanya Chemicals), isopropylbenzyl-amine(Sigma-Aldrich), magnesium sulfate (Veckridge Chemicals),methylphenidate (Watson Pharmaceuticals), fluoxetine (Wilshire Laboratories), talcum powder (Jd labs USA), lactose (Agri Dairy), sucrose (Agri Dairy), pseudoephedrine (Abbott), caffeine (Siemens), inositol (ABH pharma), distilled water and methanol(Southern Chemical Corporation) were used in their purest form.

A GC-MS (GC 7890B-MS 5977B, Agilent Technologies) was used to record spectra. Infrared spectra from 400-4000 cm^{-1} were taken on a FT-IR spectrophotometer (Thermo-Fischer Scientific Model 10). The λ_{max} was detected using a UV-visible spectrophotometer, the Evolution 300, with a Xenon lamp (Thermo-Fisher Scientific Model EVO 300 PC, Software Visionpro).

Quality Check of Methamphetamine:

Initially, the sample was checked for the presence of methamphetamine. For this purpose, FT-IR and GC-MS were used. For every sample, we always ran blanks before and after the sample.

Quantification of methamphetamine by UV-Vis studies:

The following are the steps involved in the quantification of methamphetamine:

1.Making suitable dilutions for UV-Vis spectrophotometric analysis
2.Determination of λ_{max}
3.Developing standard calibration graph
4.Validation of the calibration method
5.Stability study
6.Finding accuracy and precision
7.Taking reading and quantification performed

Preparation of standard solution and calibrators

The standard solution of methamphet-amine was prepared by dissolving 10 mg of it in methanol to make the final volume of 10 mL. Then five calibrators of 50 µg/mL, 200 µg/mL, 400 µg/mL, 800 µg/mL, and 1000 µg/mL were prepared. Important calibration parameters checked for the quantification of methamphetamine are given in Table 1.

Method validation parameters

For the method validation, there are various important parameters, which were checked according to the rules and regulations of the International Conference

on Harmonization (ICH), according to the recommendations of SWGDRUG [23] and

Table.1 Calibration parameters of UV-Visible spectrophotometer

Sr. No.	Parameters	
1	**Wavelength mode for quantification**	**Single wavelength mode**
2	Selected wavelength	259 nm
3	Lamp type	Xenon
4	Bandwidth set point	2.0 nm
5	Calibrators	5
6	No. of replicates	3
7	Calibration curve mode	Linear
8	Unit of concentration	µg/mL
9	Conc. Dec Places	3

according to guidelines of IUPAC [24]. Important parameters like wavelength, accuracy, precision, repeatability, reproducibility, and photometric accuracy were checked and validated. The wavelength accuracy and reproducibility were checked over the UV-visible range for the determination λ_{max}. At least two samples of different concentrations were run. The maximum deviation was found to be ±1.0 nm.

λ_{max}

Initially, all the calibrators were run on a UV-visible spectrophotometer to find out the λ_{max}. A UV-visible spectrophotometer in the range 225-350 nm against methanol as a blank, and the wavelength corresponding to maximum absorbance was observed which was 259 nm.

Linearity and Concentration Range

Linearity refers to how well a plot of the analytical response (absorption of the analyte) versus the concentration of interest (concentration of methamphet-amine) follows a linear or straight line. Absorption is directly proportional to the concentration of analyte in samples of methamphetamine. Five calibrators having

different concentrations (50 µg/mL, 200 µg/mL, 400 µg/mL, 800 µg/mL, and 1000 µg/mL) were made by using the stock solution.

Accuracy and Precision

The analyst must measure the "true" value and may have some sort of error associated with every measurement. So, after finding out the associated errors, the accuracy of the method can be determined. The percentage recovery of the proposed method was also determined. A solution having a concentration of 100 µg/mL was selected to study the accuracy of the method.

If the measured results are very close to each other, then our measurement is precise. The measured values should be repeatable and reproducible under the same conditions and on the same instrument. Precision depends upon the concentration, so precision should be checked at different concentrations within the range of linearity. SD can be calculated as follows:

$$s = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}(x_i - \bar{x})^2}$$

Intra inter-day precision

Intra-day precision was checked by running the same solution on the same instrument three times a day. The inter-day precision was checked by running the same solution on the same instrument on three different days at different times.

Limit of detection (LOD) and limit of quantitation (LOQ)

The smallest concentration of analyte can be detected, and its value is different from

the blank to check for impurities contaminating the sample. Different concentrations of methamphetamine were made to study LOD and LOQ, i.e., 50 µg/mL-1000 µg/mL. The concentration of an analyte that can be quantitated with reliable accuracy is said to be the limit of quantification, including both the lower limit of quantification (LLOQ) and the upper limit of quantification (ULOQ).

Standard calibration curve

All the calibrators were run on UV-visible spectrophotometers, and the calibration curve was drawn. A standard calibration curve was obtained by drawing a calibration graph between the absorption and concentration of calibrators having different concentrations (50 µg/mL, 200 µg/mL, 400 µg/mL, 800 µg/mL, and 1000 µg/mL).

For validation of the developed method and checking the parameters of validity, a blank that has no analyte and two solutions of samples labeled as POS1 and POS2 of known concentrations (50 µg/mL and 150 µg/mL) were also run on a UV-visible spectrophotometer.

Stability, repeatability and reproducebility of the solution

The stability of results can be measured by using the same concentration of a single solution at different time intervals. It is necessary to check in the sample whether degradation products are present or not. Under the same conditions and with the same instrument, the absorbance and λ_{max} of all calibrators were checked continuously for seven days for confirmation of stability. Some readings were taken in the morning, others during the day, and still others in the evening to ensure that the solutions were stable enough. The repeatability of the methamphetamine samples was determined by recording the absorbance of samples ten times a day. The reproducibility of the method was checked by measuring the absorbance of ten replicates of 400 µg/mL of methamphetamine.

Specificity of solution

Specificity tells us about the substances that can interfere with our desired analyte, and these substances also have effects on the identification and quantification of the drug. Specificity was determined by measuring the absorbance of adulterants and diluents of methamphetamine using a UV-visible spectrophotometer. These adulterants and diluents were observed while analyzing methamphetamine by GC-MS and were added to methamphetamine in clandestine laboratories. As the street samples are being submitted for analysis these adulterants and diluents are very common in street samples which are being added in methamphetamine samples to increase the bulk of drugs and enhance the stimulant effects of the drugs. It was calculated and confirmed that the selected wavelength of 259 nm was specific for the estimation of methamphetamine. In Table 2, adulterants and diluents are mentioned as being used to check out the specificity of methamphetamine.

Table 2. Adulterants and diluents used for the determination of specificity

Sr No	Compounds
1	Methylsulfonylmethane
2	Isopropylbenzylamine
3	Magnesium sulfate (Epson salt)
4	Methylphenidate
5	Talcum powder
6	Lactose
7	Sucrose
8	Pseudoephedrine
9	Caffeine
10	Dextrose
11	Inositol

Results and Discussion

Spot test

Methamphetamine in crystalline form was analyzed qualitatively as well as quantitatively.Initially, for the presumptive testing, color tests were performed so that we could say whether our sample contained methamphetamine or not. For screening, the Marquis, Sodium Nitroprusside and Liebermann reagents were used, which indicated the presence of methamphetamine. For the Marquis color test, a small quantity of sample was placed on a spot plate, and then two drops of Marquis reagent were added. An orange-brown color was produced, which indicated the presence of methamphetamine in the sample. For the sodium nitroprusside test, a small quantity of sample was placed on a spot plate, and two drops of reagent were added. The resultant blue color indicated that methamphetamine was present in our sample. Similarly, for the Liebermann test, a small quantity of sample was placed on a spot plate, and two drops of reagent were added. Gold-yellow or orange color indicated the presence of methamphetamine in the sample. Similarly, for quantitative analysis, we used a UV-visible spectrophotometer proposed method was validated, and all the parameters like lambda max, linearity range, accuracy, precision, etc. were checked.

GC-MS Studies

For the confirmation of methamphetamine, we used the gas chromatography-mass spectrometry technique. Before running the sample, the standard and blank were also run so that there would be no impurity in the column and we would get a contamination-free result. The compounds were searched in libraries. The library search report match was 85 % methamphetamine. The spectra of the blank run before the sample, the lchromatogram of the sample showing the principle peak of methamphetamine and the MS spectrum of major ions are presented in Figures 4-6.

The major ions observed in the mass spectrum of methamphetamine were at m/z = 148, 134, 91, 77, 65, and 43. The peak at m/z = 148 was due to the $(M^{+}-1)$ ion; the peak at m/z = 134 was observed because of the $(C_9H_{12}N)^{+}$ ion; and the peak at m/z = 91 was due to the $(C_6H_5CH_2)^{+}$ ion. The peak at m/z = 77 was detected due to the $(C_6H_5)^{+}$ ion, the peak at m/z = 65 was due to the $(C_5H_5)^{+}$ ion, the peak at m/z = 58 was due to the $(C_3H_8N)^{+}$ ion and the peak at m/z = 43 was observed because of the $(C_2H_5N)^{+}$ ion. The library search report showed that the sample contained 85% methamphetamine. The fragmentation pattern of methamphetamine is shown in Figure 7.

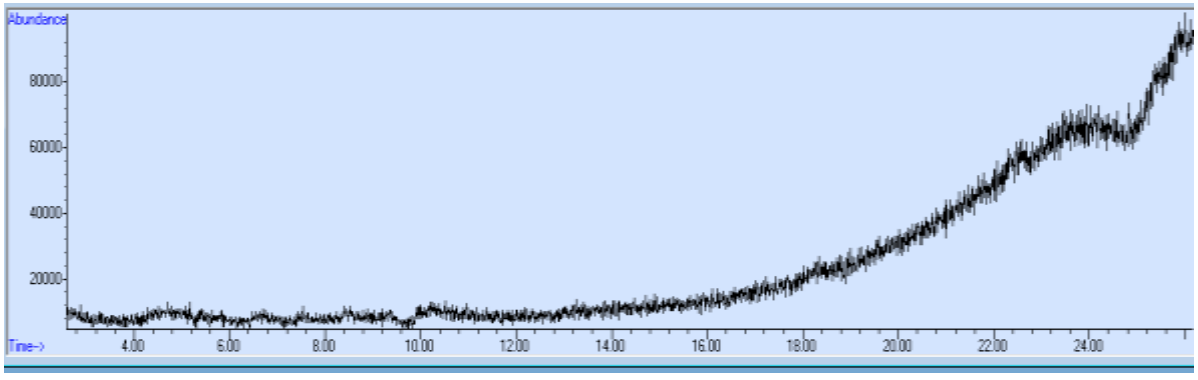


Figure 4. Chromatogram of methanol (Blank run)

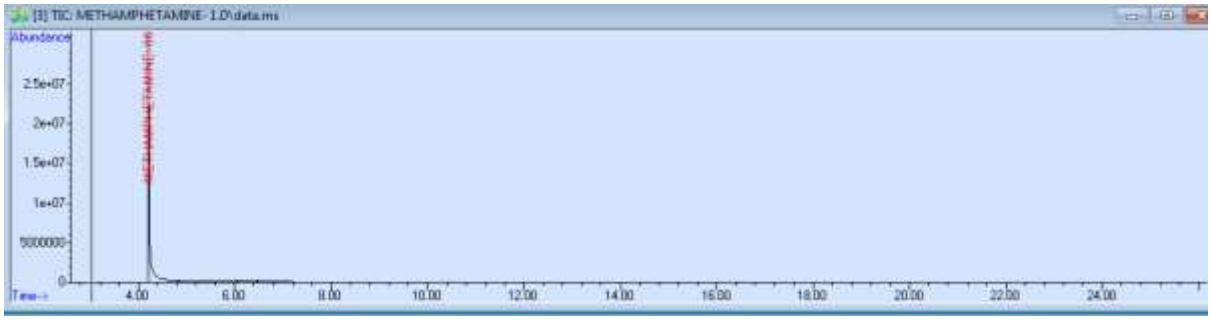


Figure 5. Chromatogram of methamphetamine

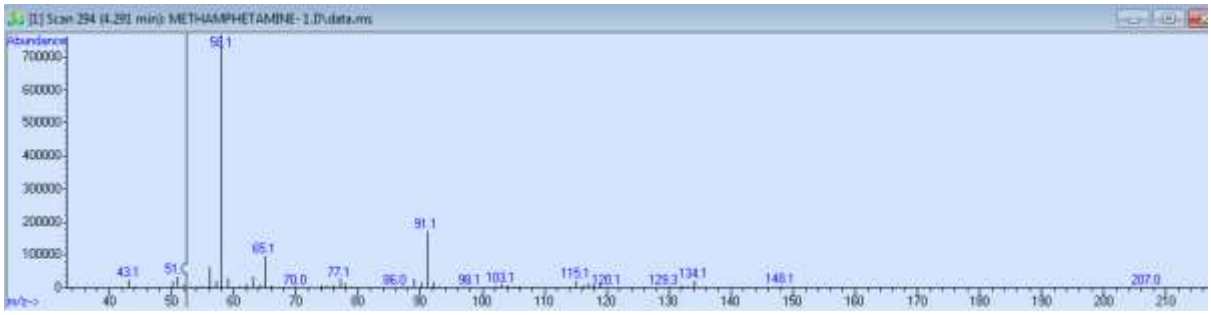


Figure 6. The mass spectrum of methamphetamine shows major peaks

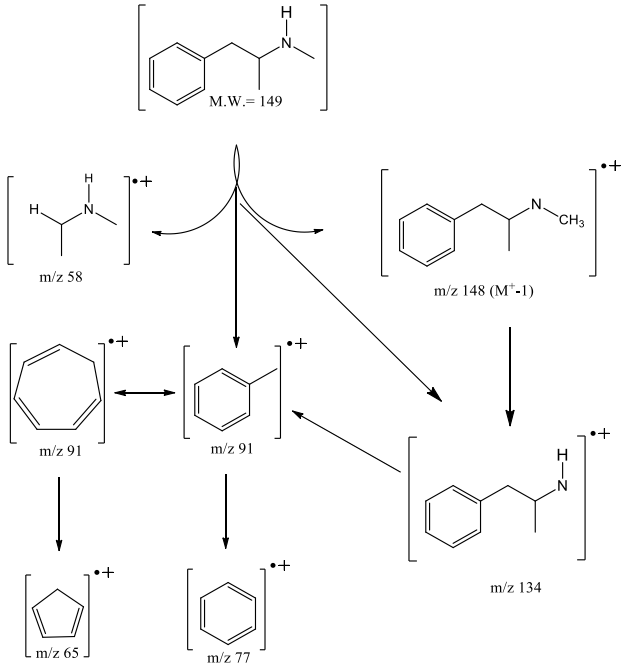


Figure 7. Fragmentation pattern of methamphetamine.

Fourier Transform Infrared (FTIR) details

The crystalline form of the sample was further analysed by using a Fourier transorm infrared spectrophotometer for confirmation of methamphetamine. Before running the sample, the background was checked and cleared so that no interference should be observed. The library search report match was 88 %. The spectrum of the sample is shown in Figure 8, and the library search report is shown in Figure 9.

The peak at 3021 cm^{-1} was due to C-H bond stretching in the aromatic ring, and the peak at 2966 cm^{-1} was because of the aliphatic C-H stretching. The peak at 1453 cm^{-1} was due to the bending vibrations of C=C [25].

UV-Visible spectroscopy

The quantification of methamphetamine was done with the help of a UV-Visible spectrophotometer. Before using the spectrophotometer, the instrument was calibrated using potassium dichromate standards to ensure the proper working of the instrument. Initially, a standard solution with a concentration of 1 mg/mL was prepared, and then calibrators having different concentrations were prepared to check the λ_{max}. The blank was run, and then the sample was scanned from 200 to

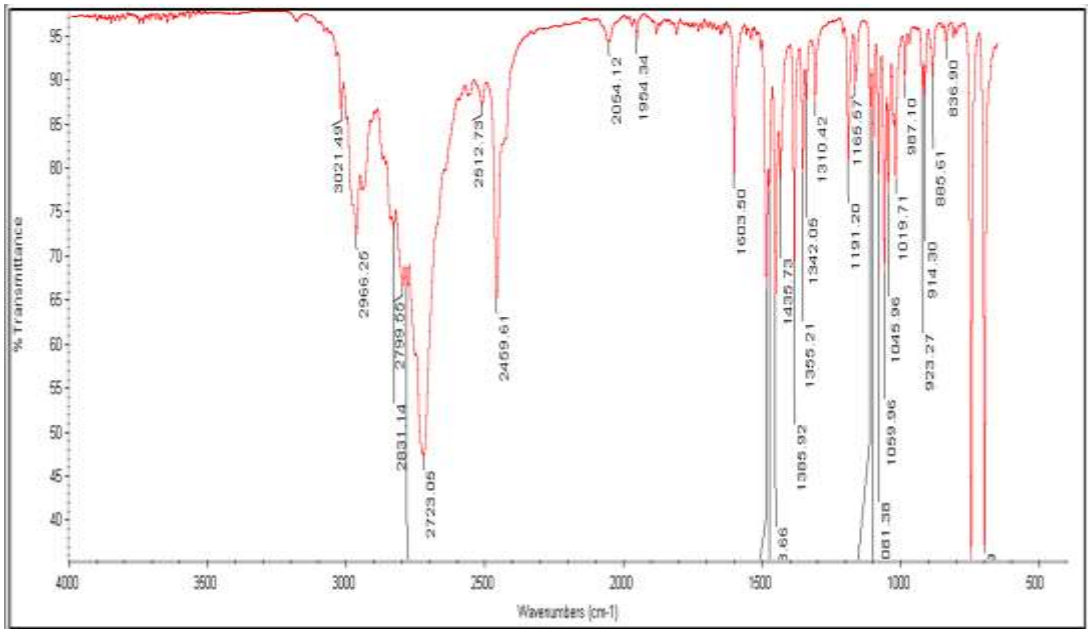


Figure 8. FTIR spectrum for methamphetamine

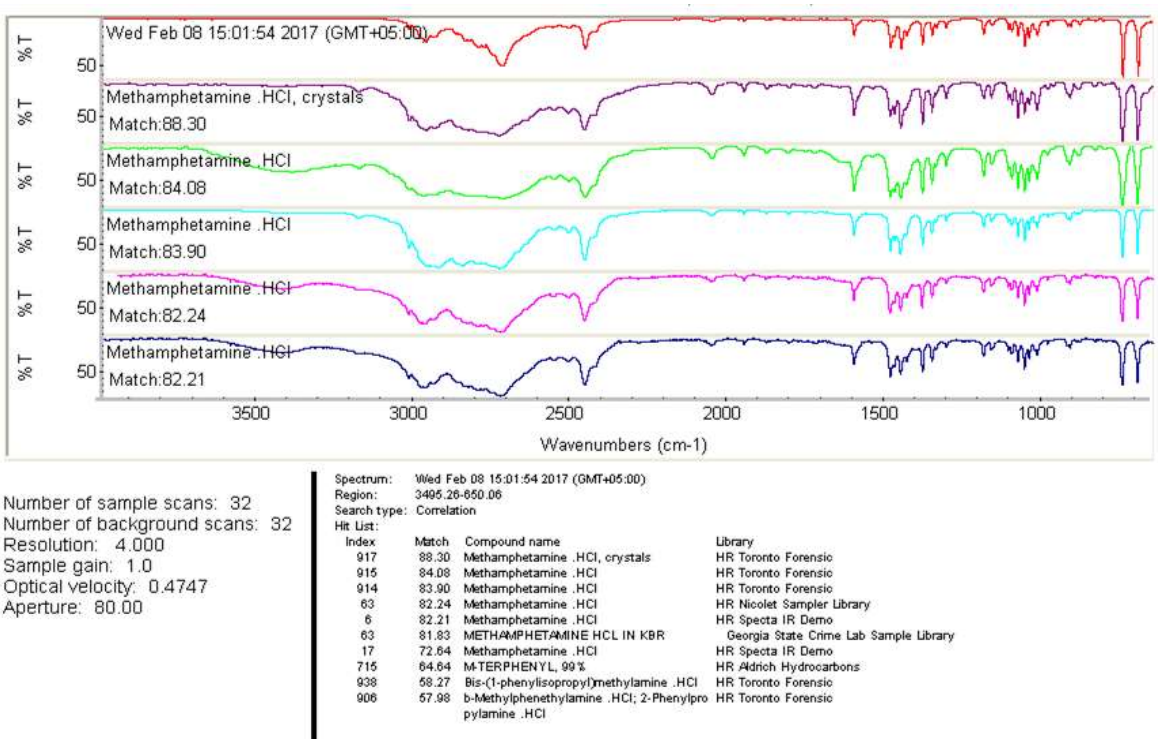


Figure 9. Library search report

600 nm. Then all the samples were scanned again from 225 to 350 nm to find the λ_{max}, which comes out to be 259 nm (Figure 10).

A total of five calibrators with concentrations of 50 µg/mL, 200 µg/mL, 400 µg/mL, 800 µg/mL, and 1000 µg/mL were prepared. For all the calibrators, absorbance was measured, and a calibration curve was also drawn, which came out to be linear. All the calibrators follow the Beer Lambert law in the range from 50 µg/mL to 1000 µg/mL.

The absorbance of methamphetamine at 259 nm is due to π- π* transition because of the presence of carbon-carbon double

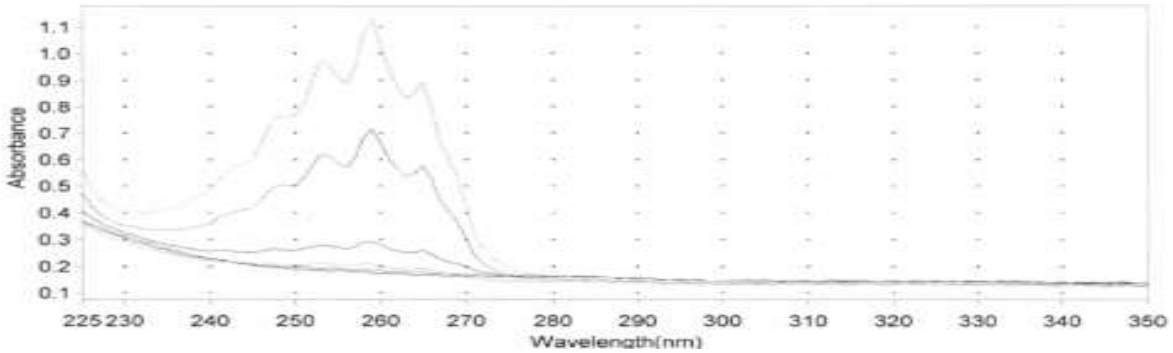


Figure 10. Stacked spectrum showing λ_{max} of methamphetamine

bonds in the methamphetamine structure. The calibrators were kept in the lab to ensure their stability and reproducibility. The absorbance of all the calibrators was measured continuously for seven days to snsure that they were stable enough. The calibration curve was drawn, and the following parameters were checked for the validation of the method for the quantification of methamphetamine.

λ_{max}

The wavelength corresponding to the maximum absorbance for methamphetamine was noted, which is known as λ_{max}, i.e., at 259 nm.

Linearity range

Five calibrators having different concentrations (50 µg/mL, 200 µg/mL, 400 µg/mL, 800 µg/mL, and 1000 µg/mL) were made by using the stock solution. For checking the linearity range, a standard calibration curve was drawn by plotting the absorption versus concentrations of five calibrators. The linearity range of methamphetamine is 50 µg/mL-1000 µg/mL.

Accuracy and precision

The calibrator, which has a concentration of 50 µg/mL, was selected to study the accuracy of the methamphetamine quantification method. Similarly, the calibrator having a concentration of 500 µg/mL was selected to study the precision of the methamphetamine quantification

method. The accuracy of the method was established by comparing the analytical amount determined with the known amount spiked at 2 mg, 4 mg, and 6 mg drug concentrations. Table 3 shows the data for the calculation of accuracy, while Table 4 shows the method for the calculation of precision.

Table.3 Determination of accuracy at a concentration of 50 µg/mL

Sr. No.	Spiked amount(mg)	Recovered amount(mg)	Percentage recovery	Mean value	SD	Percentage RSD
1.	2	1.94	96.50	98.49	1.90	1.93
2.	2	1.92	95.50			
3.	2	1.98	98.50			
4.	4	3.98	99.00			
5.	4	3.94	98.00			
6.	4	3.91	98.75			
7.	6	5.98	99.33			

8.	6	5.94	98.50			
9.	6	6.15	102.33			

Table 4 Determination of precision at a concentration of 500 µg/mL

Sr. No.	Recovered concentration (µg/mL)	Percentage Recovery	Mean Percentage Recovery	SD	Percentage RSD
1	499.66	99.932	98.29	0.175	0.17
2	500.77	100.154			
3	500.77	100.154			
4	500.77	100.154			
5	499.66	99.932			
6	499.66	99.932			
7	499.66	99.932			
8	498.55	99.71			
9	500.77	100.154			
10	498.55	99.71			

Correlation coefficient

The correlation coefficient refers to the linear relationship between two variables. It tells us how two variables are related to each other. In this case, the correlation coefficient is 0.9997.

Limit of detection (LOD) and limit of quantification (LOQ)

To investigate the limit of detection and limit of quantification, different concentrations of methamphetamine ranging from 50 µg/mL to 1000 µg/mL were prepared. The LOD for methamphetamine was 50 µg/mL. The LLOQ for methamphetamine was 50 µg/mL, and the ULOQ was 1000 µg/mL.

Calibration curve

A standard calibration graph was obtained by drawing a calibration graph between the absorption and concentration of calibrators having different concentrations (50 µg/mL, 200 µg/mL, 400 µg/mL, 800 µg/mL, and 1000 µg/mL). Table 5 shows the values of absorbance for all the calibrators, and Figure 11 shows the standard calibration curve.

Table.5 Absorbance of calibrators

Sr. No.	Concentration (µg/mL)	Absorbance
1	50	0.185
2	200	0.783
3	400	1.617
4	800	3.322
5	1000	4.079

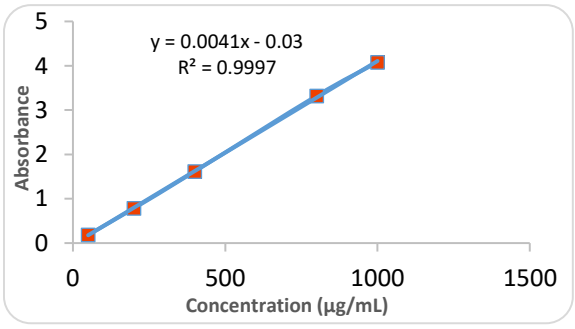


Figure 11. Standard calibration curve of methamphetamine

The detector response was recorded, and it was observed that the response was linear for these solutions as well, giving a correlation coefficient value of 0.9997 at a wavelength of 259 nm.

Solution stability

The absorbance and λ_{max} of all the calibrators were checked continuously for seven days for confirmation and stability. Some of the readings were taken in the morning, some in the daytime, and some in the evening so that it could be confirmed that the solutions were stable enough, and it was confirmed that the calibrators were stable for 4 days. The results of all the parameters that have been checked for method validation are listed in Table 6.

Table.6 Method validation parameter resul results

Validated parameters	
Calibration range	50-1000 µg/mL
Calibration Slope	0.0009
Calibration intercept	0.1653
Coefficient r^2	0.9997
λ_{max}	259 nm
Solution Stability	≤ 4 days
Precision	98.29 ± 0.17
Accuracy	98.49 ± 1.90
Mean Recovery	98.29 ± 0.17
LOD	50 µg/mL
LLOQ and ULOQ	50 µg/mL and 1000 µg/mL

Conclusion

In conclusion, we can say that the proposed method is quite easy, simple, sensitive, reproducible, and cost-effective as well. As such, no complex methodology for sample preparation is required. The results are very accurate and reliable. The library search report of methamphetamine in the FT-IR spectrum was 88 %, and that of GC-MS was 85 %. The linearity range in UV-visible spectrophotometer is from 50 µg/mL to 1000 µg/mL. The intraday and interday stability of calibrators were checked for four days. The λ_{max} of methamphetamine was 259 nm. The absorbance showed by methamphetamine in the UV-Visible range is due to π to π* transition because of the presence of carbon-carbon double bonds in methamphetamine structure. The proposed method can be used for the forensic analysis of not only methamphetamine but also other narcotic drugs. This was the initiative, and it will help the researchers find out how we can prevent our youngsters from abusing these types of stimulants and illicit drugs. If we don't take the initiative and take serious steps regarding the manufacturing, use, trafficking, distribution, and sale of this drug, a day will come when none of us will remain to save from the effects and consequences of this illicit, clandestinely manufactured, life-threatening drug. Although our legislation is strong enough and its production, use, carrying, purchase, sale, and distribution are restricted, still we are facing very serious issues regarding its use in our young generation.

References:

1. Gooyit M, Miranda PO, Wenthur CJ, Ducime A, Janda KD. Influencing antibody-mediated attenuation of methamphetamine CNS distribution through vaccine linker design. ACS chemical neuroscience. 2017 Mar 15;8(3):468-72.
2. Mehling R, Triggle DJ. Methamphetamine. Infobase Publishing; 2008.
3. Shi S, Chen T, Zhao M. The crosstalk between neurons and glia in methamphetamine-induced neuroinflammation. Neurochemical Research. 2022 Apr;47(4):872-84.
4. Adam P, Natakankitkul S, Sirithunyalug J, Aramrattana A. Physico-chemical profiles of methamphetamine tablets. CMU. Journal. 2005;4(1):65.
5. Bunting PJ, Fulde GW, Forster SL. Comparison of crystalline methamphetamine ("ice") users and other patients with toxicology-related problems presenting to a hospital

emergency department. Medical Journal of Australia. 2007 Nov;187(10):564-6.
6. Alam Mehrjerdi Z. Crystal in Iran: methamphetamine or heroin kerack. DARU Journal of Pharmaceutical Sciences. 2013 Dec; 21:1-3.
7. Shukla RK, Crump JL, Chrisco ES. An evolving problem: Methamphetamine production and trafficking in the United States. International Journal of Drug Policy. 2012 Nov 1;23(6):426-35.
8. Grant P. Evaluation of children removed from a clandestine methamphetamine laboratory. Journal of Emergency Nursing. 2007 Feb 1;33(1):31-41.
9. Mendelson J, Uemura N, Harris D, Nath RP, Fernandez E, Jacob III P, Everhart ET, Jones RT. Human pharmacology of the methamphetamine stereoisomers. Clinical Pharmacology & Therapeutics. 2006 Oct;80(4):403-20.
10. Rothman T, Sward K. Studies in Pharmacological Psychotherapy: 1. Treatment of Refractory Psychoneuroses and Personality Disorders with Thiopental (Pentothal) Sodium and Methamphetamine (Desoxyn). AMA Archives of Neurology & Psychiatry. 1956 Jan 1;75(1):95-105.
11. Oyler JM, Cone EJ, Joseph Jr RE, Moolchan ET, Huestis MA. Duration of detectable methamphetamine and amphetamine excretion in urine after controlled oral administration of methamphetamine to humans. Clinical chemistry. 2002 Oct 1;48(10):1703-14.
12. Daraei B, Sahraei E, Aghazadeh E. Investigation of Methamphetamine as a Stimulant with Side Effects and Methods of Synthesis and Impurities in any Way. Modares Journal of Biotechnology. 2019 Dec 10;10(4):665-71.
13. Iritani BJ, Hallfors DD, Bauer DJ. Crystal methamphetamine use among young adults in the USA. Addiction. 2007 Jul;102(7):1102-13.
14. Wu LT, Pilowsky DJ, Schlenger WE, Galvin DM. Misuse of methamphetamine and prescription stimulants among youths and young adults in the community. Drug and alcohol dependence. 2007 Jul 10;89(2-3):195-205.
15. Griffiths P, Mravcik V, Lopez D, Klempova D. Quite a lot of smoke but very limited fire—the use of methamphetamine in Europe. Drug and alcohol review. 2008 May;27(3):236-42.
16. Defalque RJ, Wright AJ. Methamphetamine for Hitler's Germany: 1937 to 1945. Bulletin of anesthesia history. 2011 Apr 1;29(2):21-4.
17. Hoffmann L, Schumann N, Fankhaenel T, Thiel C, Klement A, Richter M. Methamphetamine use in Central Germany: protocol for a qualitative study exploring requirements and challenges in healthcare from the professionals' perspective. BMJ open. 2016 Jun 1;6(6): e011445.
18. Johnston LD, O'Malley PM, Bachman JG. Monitoring the future: National results on adolescent drug use: Overview of key findings. Focus. 2003 Apr;1(2):213-34.
19. Barr AM, Panenka WJ, MacEwan GW, Thornton AE, Lang DJ, Honer WG, Lecomte T. The need for speed: an update on methamphetamine addiction. Journal of psychiatry and neuroscience. 2006 Sep 1;31(5):301-13.
20. Petit A, Karila L, Chalmin F, Lejoyeux M. Methamphetamine addiction: a review of the literature. Journal of Addiction Research & Therapy S. 2012; 1:1-6.
21. Khaled A. Pakistan Measures In Controlling Narcotics TRADE. Annals of the University of Oradea, Economic Science Series. 2013 Dec 1;22(2).
22. Chohan M. Role of Punjab Police in Control of Narcotics A Comparison with ANF and Customs. Pakistan Journal of Criminology. 2012 Apr 1.
23. Brown HM, McDaniel TJ, Fedick PW, Mulligan CC. The current role of mass spectrometry in forensics and prospects.

Analytical Methods. 2020;12(32):3974-97.
24. Thompson M, Ellison SL, Wood R. Harmonized guidelines for single-laboratory validation of methods of analysis (IUPAC Technical Report). Pure and applied chemistry. 2002 Jan 1;74(5):835-55.
25. Pavia DL, Lampman GM, Kriz GS, Vyvyan JR. Introduction to spectroscopy.