Bull. Pharm. Sci., Assiut University, Vol. 47, Issue 1, 2024, pp. 249-259.

Bulletin of Pharmaceutical Sciences
Assiut University
Website: http://bpsa.journals.ekb.eg/

BULL. PHARM. SCI. Assiut Univ.

# QUALITATIVE ANALYSIS FOR ILLICIT DRUGS AND NPS (NEW PSYCHOACTIVE SUBSTANCES) USING GC-MS

Galih Satrio Putra[1*], Sumari Sumari[1], Melanny Ika Sulistyowaty[2], Magdalena Sri Handayani[3], Farida Suhud[3], Dini Kesuma[3], Farida Anwari[4]

[1]*Department of Chemistry, Faculty of Mathematics and Natural Sciences State University of Malang,Malang-65145, Indonesia*
[2]*Department of Pharmaceutical Sciences, Faculty of Pharmacy Universitas Airlangga, Surabaya-60115, Indonesia*
[3]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Surabaya-60293, Indonesia*
[4]*Medical Laboratory Science, University of Anwar Medika, Sidoarjo 61262, Indonesia*

*This research aims to analyze 500 samples for illicit drugs and NPS (New Psychoactive Substances) using GC-MS (Gas Chromatography Mass Spectrometry) in East Java Indonesia. Sample analysis was carried out by GC-MS with HP-5 column, injection port temperature of 250°C. Column temperature was maintained at 100°C for 2 minutes. It was then raised from10°C/minute to 280°C and maintained for 5 minutes Based on the results, it was detected 244 (48.8 %) Methamphetamine (MA); 30 (6 %) 3,4-Methylenedioxymethamphetamine (MDMA); 44 (8.8 %) 3,4-Methylenedioxyethylamphetamine (MDA); 56 (11.2 %) 3,4-Methylenedioxyethylamphetamine (MDEA); 106 (21.2 %) AB-Fubinaca; 5 (1.0 %) Tramadol; 5 (1.0 %) Ketamine; and 10 (2.0 %) Mephedrone. The identification of illicit drugs and NPS in confiscated materials was successfully achieved via GC-MS. The availability of GC-MS libraries is of great assistance in the identification of new drugs. Alternatively, the study of characteristic molecule fragments combined with the determination of their accurate masses can be a useful approach to identify unknown samples that were not previously analyzed.*

***Keywords:*** *Qualitative Analysis, illicit drugs, NPS, GC-MS*

## INTRODUCTION

illicit drugs market are a troubling phenomenon in International and National scope, especially in, East Java, which remains as the second highest in Indonesia after Jakarta.[1] Similarly, the detected of New Psychoactive Substances (NPS) will increase its level in not only the national community, but international community are also likely to pose a more significant social problem in the future.[2-5] NPS (New Psychoactive Substances) are compounds that affect the central nervous system and make potential addiction. However, its use has not been regulated in the United Nations Single Convention on Narcotic Drugs of 1961, the 1971 United Nations Convention on Psychotropic Substances. There are some groups of NPS, synthetic cannabinoids derivatives, cathinones derivatives, ketamine derivatives, phenethylamines derivatives, piperazines derivatives, and plant-based substances which are deliberately developed to deceive the law.[6-8]

During the past decades, NPS has been introduced and traded through various distribution modes, including the internet. This has increased the demand and number of users throughout the world, thereby making it a serious threat to humanity.[4,8,9]

The existence of NPS in Indonesia became publicized in 2013 at the time an Indonesian actor used drugs containing 3,4-methylendioxymethcathinone. In 2015, new and unregistered evidence containing mephedrone/4-MMC was found and in early

*Received : 8/1/2024 & Accepted : 10/3/2024*

*Corresponding author: Galih Satrio Putra, E-mail: galih.satrio.fmipa@um.ac.id

2017, "blue sapphires" containing 4-chloromethcathinona/4-CMC were found in several cafes in in East Java. In 2016 and early 2017, the public was confronted by the trading of AB-Chimanaca and AB-Fubinaca in gorilla tobacco, which is a type of synthetic cannabinoids. Based on the World Drugs Report 2014, UNODC noted a 50% increase in the synthetic cannabinoids trend compared to other new substances.[1] In 2020 until 2022, AB-Fubinaca detected in Indonesia were increase, many cases reported people used it as illicit drugs.[10]

GC-MS is a method that is often used to detect the presence of NPS in powders, crystals, tablets, and tobacco samples. GC-MS is still able to detected 500 samples of NPS with high specificity, selectivity, accuracy and precision. These samples contain of synthetic cannabinoids derivatives (AB-Fubinaca); cathinones derivatives (Mephedrone); phenethylamines derivatives (amphetamine; methylamphetamine (MA); 3,4-Methylenedioxymethamphetamine (MDMA); 3,4-Methylenedioxyethylamphetamine (MDA); Phencyclidine/Ketamine derivatives, and semi opiate (tramadol). This article study showed chromatogram and mass spectra of 500 samples of NPS from some dosage form such as tablets, capsules, powders,; crystal powders, and some of simplicia.

## EXPERIMENTAL
## MATERIAL AND METHODS

All reagents and solvents such as ethyl acetate was purchased from standard commercial suppliers from Merck pro analysis grade, with samples obtained from the Surabaya Forensic Laboratory in the form of powder, crystals, tablets, capsules, crude material.

### Sample preparation

100 mg of the sample was dissolved in 10.0 ml ethyl acetate, and then centrifuged at 1000 rpm. It was filtered by 0.2 microns, and 1-2 µl was injected into the GC-MS instrument.

### Method of GC-MS analysis

Sample analysis was carried out by GC-MS with HP-5 column, injection port temperature of 250°C. Column temperature was maintained at 100°C for 2 minutes. It was then raised from10°C/minute to 280°C and maintained for 5 minutes. Data analysis was performed using GC-MS chromatogram approach which was determined by Library MS data from NIST or UNODC with fragmentation analysis from MS.

## RESULTS AND DISCUSSION

### Results

GC-MS are a reproducible method to quickly and accurately analyse illicit drugs and NPS (new psychoactive substances) on samples of tablets, capsules, and powder, crude material.[11] LC-MS method is commonly used for routine analysis of NPS and illicit drugs in biological fluid analysis such as urine and blood specimens.[11-13] Narcotics Schedules I-V are compounds that are classified as thermostable such as heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), peyote, methaqualone, and 3,4-methylenedioxymethamphetamine that is called ecstasy. Therefore, they could be analysed using GC-MS.[14-16.]

Some crime scene evidence for illicit drugs such as powders, tablets, capsules, and crude material consist of synthetic cannabinoids derivatives (AB-Fubinaca); cathinones derivatives (Mephedrone); phenethylamines derivatives (amphetamine; methylamphetamine (MA); 3,4-Methylenedioxymethamphetamine (MDMA); 3,4-Methylenedioxyethylamphetamine (MDA); Phencyclidine/Ketamine derivatives an and semi opiate (tramadol) could be detected with high specificity and selectivity using GC-MS instrument. Validation method for analysing illicit drugs are necessary based on criteria acceptance of International Council for Harmonisation (ICH) consisting of specificity, selectivity, accuracy and precision, LOQ (Limit of Quantification) and LOD (Limit of Detection). Illicit drugs and NPS (New psychoactive Substances) are major compounds, therefore, LOQ (limit of Quantification) and LOD (Limit of Detection) are not necessary because they does not match the analysis of traces elements (heavy metals) or organic contamination compounds such as contamination of organic solvents, and pesticides.[17]

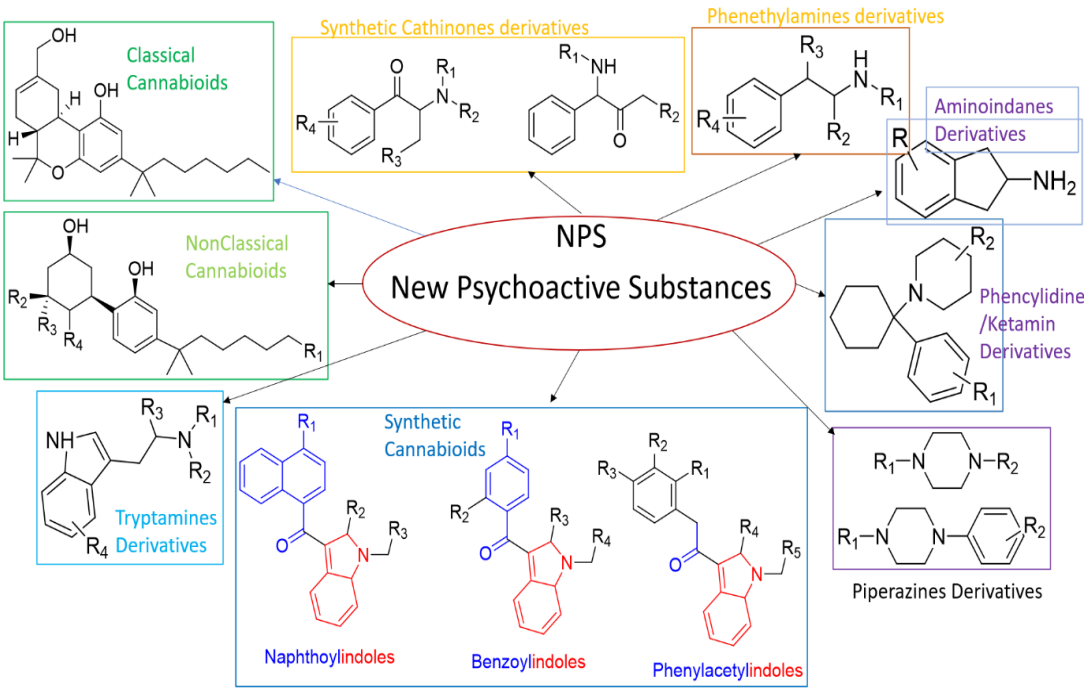
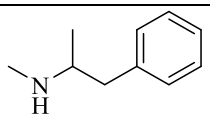
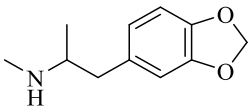
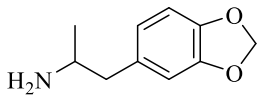
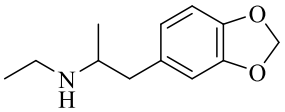
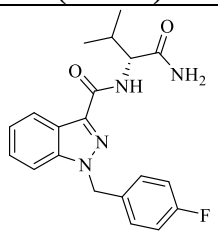
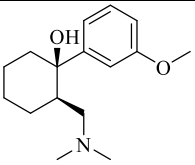
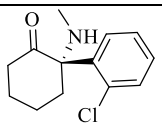
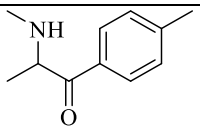



**Fig. 1 :** The groups of New Psychoactive Substances (NPS).

The result of qualitative analysis on 500 samples consisting of tablets, capsules, powder, and crude material is shown in **Fig. 2**. Based on the results, it was detected 244 (48.8%) Methamphetamine (MA); 30 (6 %) 3,4-Methylenedioxymethamphetamine (MDMA); 44 (8.8%) 3,4-Methylenedioxyethylamphetamine (MDA) ;56 (11.2%) 3,4-Methylenedioxyethylamphetamine (MDEA); 106 (21.2) AB-fubinaca ; 5 (1.0 %) tramadol; 5 (1.0%) ketamine; 10(2.0%) mephedrone that is shown in **Table 1**.


**Fig. 2:** The samples of Drugs of Abused and NPS.

**Table 1:** The result of Qualitative analysis on Drugs of Abuse and NPS Using GS-MS Instrument.

| Samples | % Samples | Compound | TR (Retention Time) | Similarity Index |
|---|---|---|---|---|
| 244 | 48.8 |  Methamphetamine (MA) | 5.7 | 100% |
| 30 | 6 |  3,4-Methylenedioxymethamphetamine (MDMA) | 10.92 | 100% |
| 44 | 8.8 |  3,4-Methylenedioxyethylamphetamine (MDA) | 7.05 | 100% |
| 56 | 11.2 |  3,4-Methylenedioxyethylamphetamine (MDEA) | 17.5 | 100% |
| 106 | 21.2 |  AB-Fubinaca | 27.5 | 100% |
| 5 | 1 |  Tramadol | 24.01 | 99% |
| 5 | 1 |  Ketamine | 23.12 | 98% |
| 10 | 2 |  Mephedrone | 17.5 | 99% |
| 500 | 100 % | Total samples | | |

AB-Fubinaca contains cigarette or tobacco or simplicia. Samples were detected at 27.5 minutes (time retention) followed by other phytochemicals such as eugenol and caffeine with chromatogram profile that is shown ion **Fig. 3**, and while their mass profile spectra that is shown in **Fig. 4**. AB-Fubinaca is an NPS from synthetic cannabinoids derivatives laced on plant material that has been encountered by law enforcement in recent years. These products laced with synthetic cannabinoids which are smoked for their psychoactive effects.[18] Based on reported data UNODC 2022 and National Narcotics Board, there were a signification increased of illicit drugs from and NPS from synthetic cannabinoids derivatives such as AB-Fubinaca. AB-Fubinaca was previously reported in a patent by Pfizer in 2009. There are no commercial or medical uses for this substance. AB-Fubinaca has a high affinity binding as agonist to the CB1 receptor.[5,18] AB-Fubinaca is a synthetic cannabinoid that is recently encountered on the designer drug market and has been found laced on plant material and marketed under the guise of herbal incense products.

Phenethylamines derivatives such as Methamphetamine (MA); Methylenedioxymethamphetamine (MDMA); Methylenedioxyethylamphetamine (MDA); and Methylenedioxyethylamphetamine (MDEA) are commonly detected for illicit drugs. Methamphetamine (MA) is a compound that dominates illicit drugs and often found in tablet dosage forms like candies, not only Methamphetamine (MA), but also Methylenedioxymethamphetamine (MDMA) (ecstasy); Methylenedioxyethylamphetamine (MDA); and Methylenedioxyethylamphetamine (MDEA) that is shown in **Fig. 5 and Fig. 6**. MA; MDMA; MDA dan MDEA are narcotic schedule that have strong activity as analgesic nevertheless these have strong addiction side effect. Because of the strong addiction side effect, MA and MDMA were never used as medicine on clinical practices.

Ketamine and tramadol are medicines on clinical practices. Ketamine has strong analgesic and general anaesthesia with moderate addiction side effect. Ketamine is a class of Phencyclidine derivatives which are often used as illicit drugs. Tramadol is a medicine that has strong analgesic with mild addiction side effect. Tramadol is classified as semi-opioid medicine that is often used as illicit drugs. Tramadol is often detected in tablets or caplet dosage form and ketamine is often detected in white crystal powders dosage form that is shown in **Fig. 7**.

Mephedrone (4-MMC) was also found in the drug market. Mephedrone is a group of synthetic cathinone derivatives. Mass profile spectra of Mephedrone can be shown in **Fig. 8**. Mephedrone exhibits high abuse liability. It has earlier onset and shorter duration of effects probably related to its short elimination of half-life compared to MDMA, and this, could explain a more compulsive pattern of use as described by the user's illicit drugs users.[19]

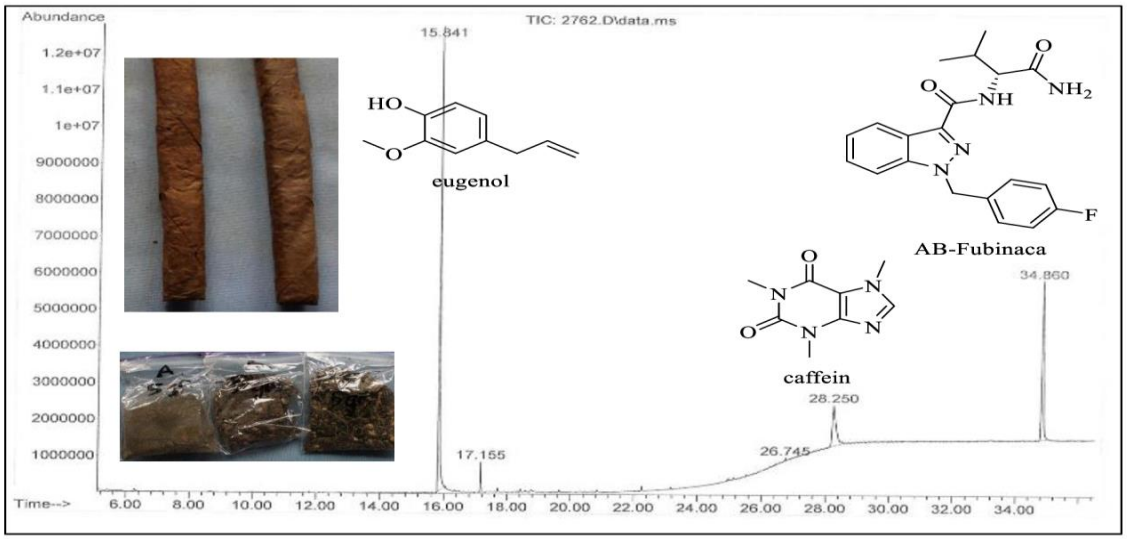



**Fig. 3:** Chromatogram profile of cigarette or tobacco or simplicia samples.

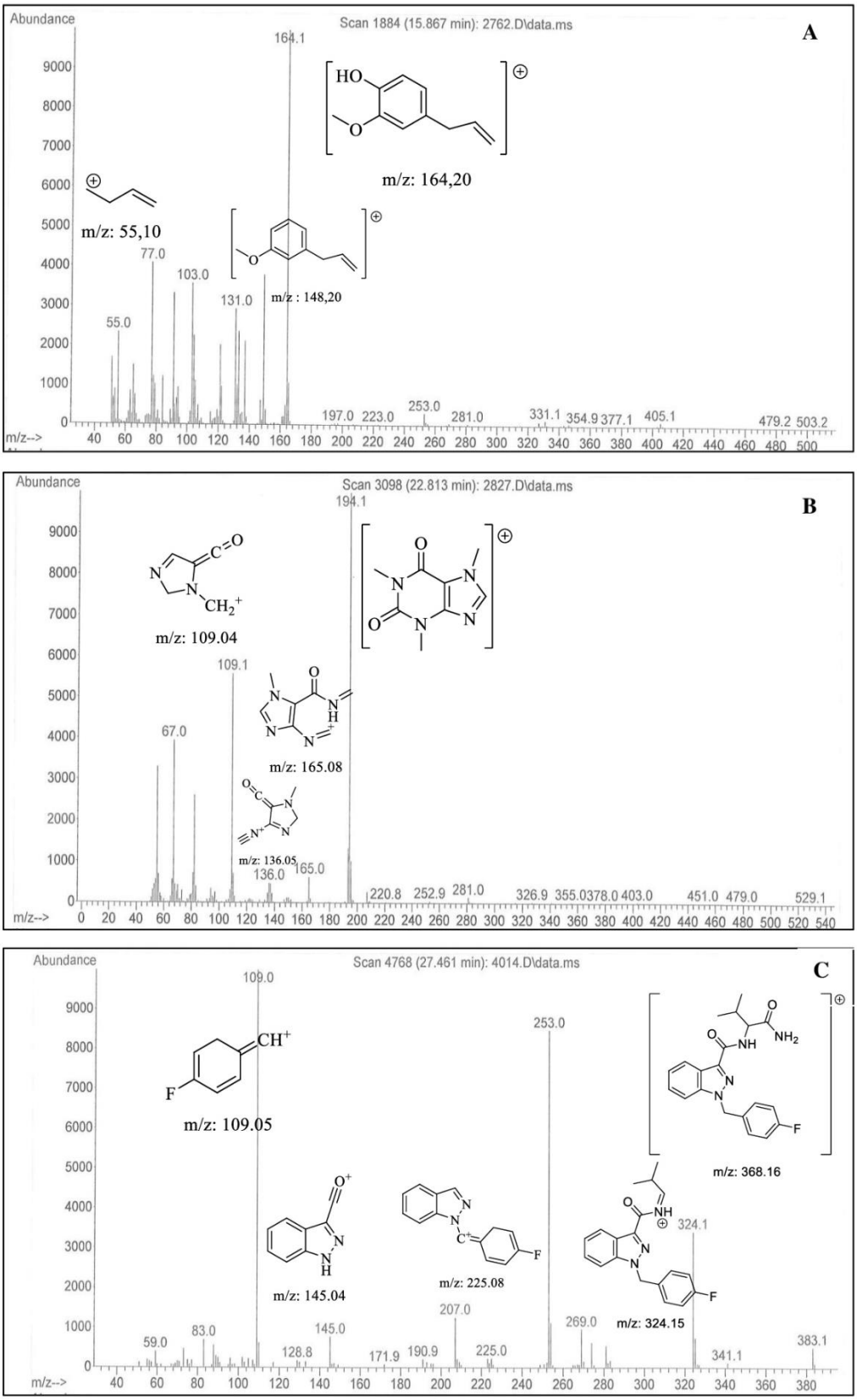



**Fig. 4:** Mass profile spectra of **A**.eugenol, **B**.caffeine . **C**.AB-Fubinaca.

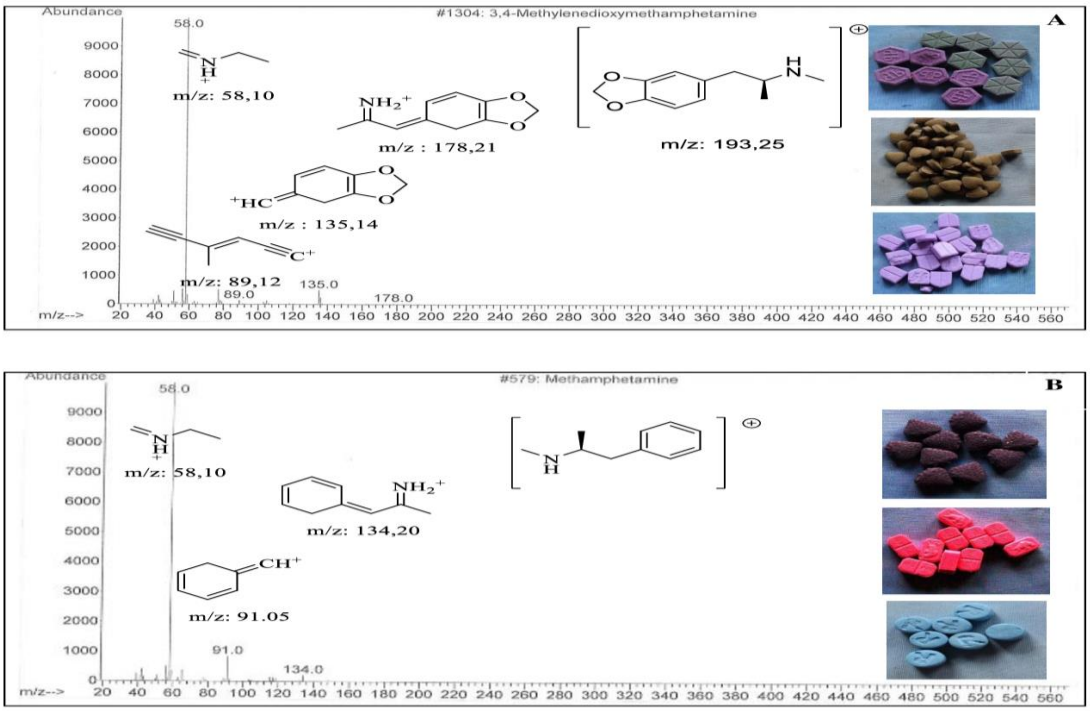



**Fig.5:** Mass profile spectra of **A.** Methamphetamine (MA) and **B.**Methylendioxymethamphetamine (MDMA).

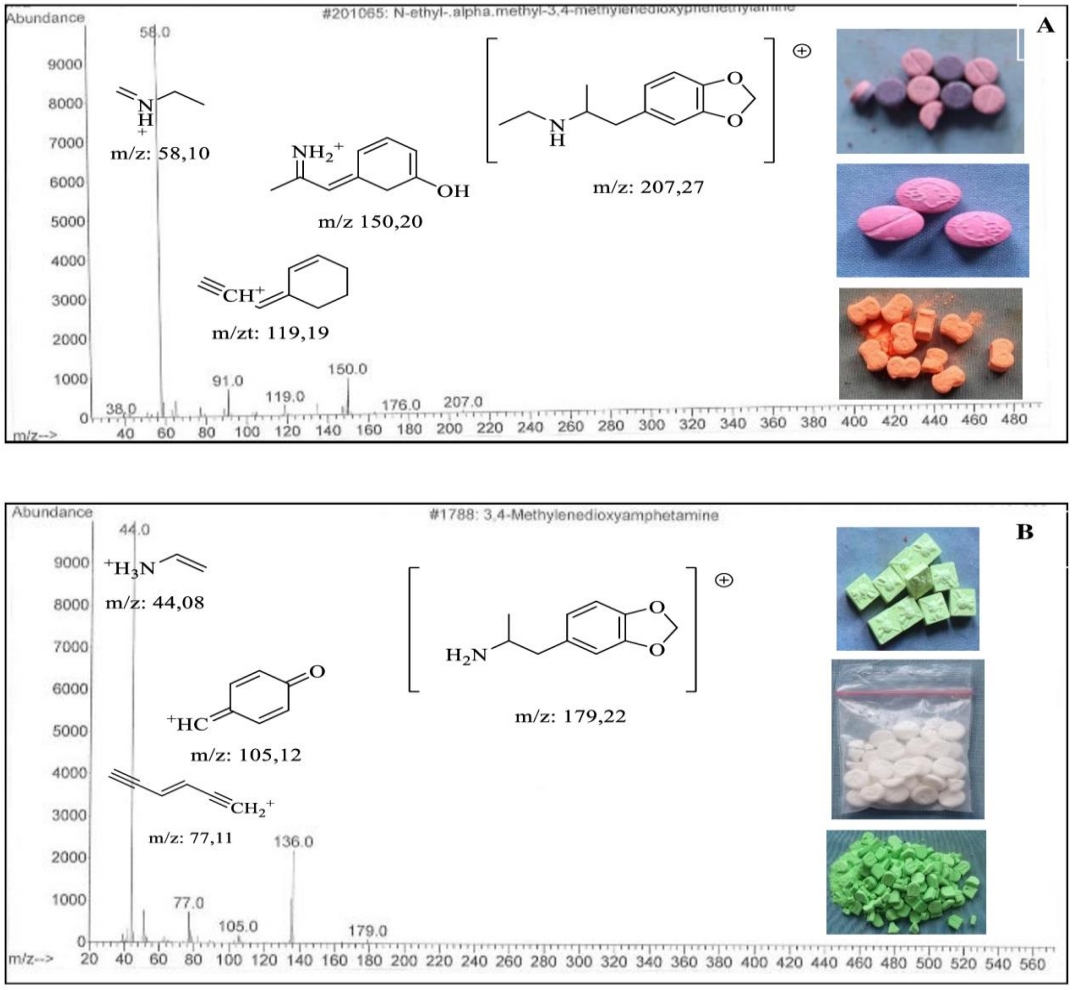



**Fig. 6 :** Mass profile spectra of **A.** Methylenedioxyethylamphetamine (MDEA) and **B.** Methylenedioxyethylamphetamine (MDA).

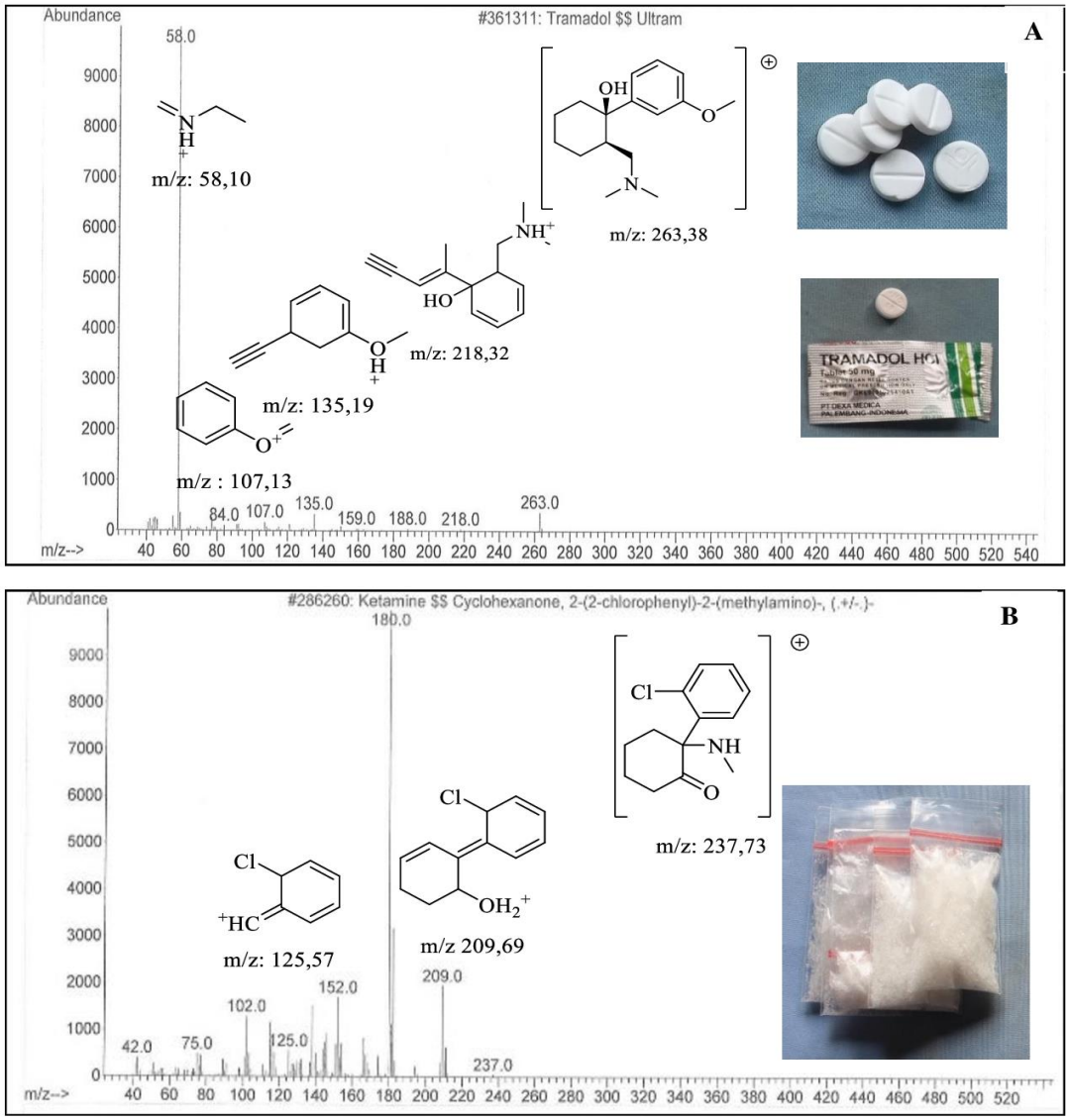



**Fig. 7:** Mass profile spectra of **A.** Tramadol and **B.** Ketamin.

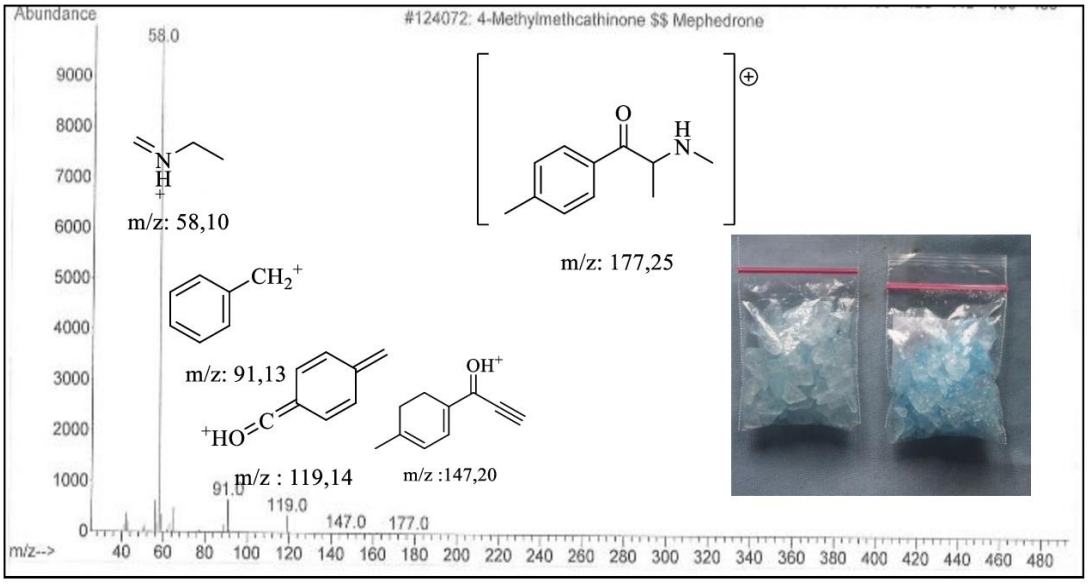



**Fig. 8:** Mass profile spectra of Mephedrone.

## Conclusion

GC-MS is a method that can detect the presence of NPS with high specificity and selectivity. From 500 samples, it was detected 244 (48.8%) Methamphetamine (MA); 30 (6%) 3,4-Methylenedioxymethamphetamine (MDMA); 44 (8.8%) 3,4-Methylenedioxyethylamphetamine (MDA) ; 56 (11.2%) 3,4-Methylenedioxyethylamphetamine (MDEA); 106 (21.2%) AB-fubinaca; 5 (1.0%) Tramadol; 5 (1.0%) ketamine; and 10 (2.0%)mephedrone

## Acknowledgement

This research was funded by Lembaga Penelitian dan Pengabdian Masyarakat (LPPM) University of Surabaya.

## REFERENCES

1. B.N.N. Health Research on Drug Abuse Effect. Research, Data, and Information Center National Narcotics Board of the Republic of Indonesia : Jakarta. ISBN : 978-623-93034-1-9 (2019).
2. A. M. Araújo, M. J. Valente, M. Carvalho, D. D. Silva, H. Gaspar, F. Carvalho, M. L. Bastos and P. G. Pinho, "Raising awareness of new psychoactive substances: chemical analysis and in vitro toxicity screening of 'legal high' packages containing synthetic cathinones", ***Arch Toxicol***, 89 (5),757-771 (2014).
3. T. Seddon, "Drug policy and global regulatory capitalism: the case of new psychoactive substances (NPS). International Journal of Drug Policy", ***Int J Drug Discov***, 25(5), 1019-1024 (2014).
4. J. Mounteney, P. Griffiths, R. Sedefov, A. Noor, J. Vicente and R. Simon, "The drug situation in Europe: an overview of data available on illicit drugs and new psychoactive substances from European monitoring in 2015", ***Addiction,*** 111 (1) 34-48 (2015).
5. A. C. Moffat, M. D. Osselton, B. Widdop, 2011. Clarke's Analysis of Drugs and Poisons in pharmaceuticals, body fluids and postmortem material. 4th edition. London : Pharmaceutical Press.
6. D. Favretto, J. P. Pascali and F. Tagliaro, "New challenges and innovation in forensic toxicology: Focus on the "New Psychoactive Substances", ***J Chromatogr A***, 1287, 84-95 (2013).
7. S, Elliott and J. Evans, "A 3-year review of new psychoactive substances in casework", ***Forensic Sci Int,*** 243(1), 55-60 (2014).
8. UNODC, 2013. Global Smart Programme : New Psychoactive Substances.
9. S. S. Rossi, S. Odoardi, A. Gregori, G. Peluso, L. Ripani, G. Ortar, G. Serpelloni and F. S. Romolo, " An Analytical Approach to the Forensic Identification of Different Classes of New Psychoactive Substances (NPS) in Seized Materials**",** ***Rapid Commun. Mass Spectrom***, 28(17), 1904-1916 (2014).
10. S. M. Handajani, R. R. Risthanti, A. A. Setiawan and G. S. Putra, "Trends in drug abuse in the East Java region in 2016-2017", ***J-PhAM***, 4 (1), 58-70 (2021)
11. M. P. Elie, L. E. Elie and M. G. Baron, "Keeping pace with NPS releases: fast GC-MS screening of legal high products. Drug Testing and Analysis", ***Drug Test Anal***, 5(5), 281-90 (2013).
12. C. Bell, C. George, A.T. Kicman and A. Traynor, "Development of a rapid LC-MS/MS method for direct urinalysis of designer drugs", ***Drug Test Anal,*** 3(7-8), 496-504 (2013)
13. A. A. Aldubayyan, E. Castrignanò, S. Elliott and V. Abbate, "A Quantitative LC–MS/MS Method for the Detection of 16 Synthetic Cathinones and 10 Metabolites and Its Application to Suspicious Clinical and Forensic Urine Samples", ***Pharmaceuticals,*** 15(5),1-22 (2022).
14. DEA "Drug Enforcement Administration", 2020 AB-FUBINACA, Diversion Control Division Drug & Chemical Evaluation Section
15. B. Byrska and D. Zuba, "Application of Fast Gas Chromatography to Routine Analysis of Narcotic Drugs and Psychotropic Substances", ***Probl Forensic Sci,*** 79 (LXXIX); 303-313. (2009)
16. S. Assi, A. Guirguis, S. Halsey, S. Fergus and J.L. Stair, "Analysis of 'legal high' substances and common adulterants using

handheld spectroscopic techniques", ***Anal Methods***, 7(2),736–746 (2012).
17. ICH "International Conference on Harmonisation". (2005) Validation of Analytical Procedures: Text And Methodology Q2(R1).
18. Drug Enforcement Administration (DEA). ***US Department of Justice***, Part 1308 — schedules of controlled substances. Link to an amendment published at 85 FR 5322, Jan, 30, (2020).
19. E. Papaseit, C. Pérez-Mañá, J.A. Mateus, M. Pujadas, F. Fonseca, M. Torrens, E. Olesti, R. Torre and M. Farré, "Human Pharmacology of Mephedrone", in Comparison with MDMA ***Neuropsychopharmacol***, 41(11), 2704-2713 (2016).

Bull. Pharm. Sci., Assiut University, Vol. 47, Issue 1, 2024, pp. 249-259.

نشرة العلوم الصيدلية
جامعة أسيوط

BULL. PHARM. SCI. Assiut Univ.

# تحليل الأدوية التي اسئ استخدامها مع مواد نفسية نشطة جديدة باستخدام التحليل الغازي الكروماتوجرافي مع طيف الكتلة

**جاليه ساتريو بوترا[1*] – سوماري سوماري[1] – ميلاني إيكا سوليستيواتي[2] – ماجدالينا سري هانداياني[3] – فريدة سهود[3] – ديني كيسوما[3] – فريدة أنواري[4]**

[1]قسم الكيمياء ، كلية الرياضيات والعلوم الطبيعية ، جامعة مالانج الحكومية، مالانج ٦٥١٤٥ ، إندونيسيا

[2]قسم العلوم الصيدلانية ، كلية الصيدلة، جامعة إيرلانجا، سورابايا ٦٠١١٥ ، إندونيسيا

[3]قسم الكيمياء الصيدلية ، كلية الصيدلة، سورابايا ٦٠٢٩٣ ، إندونيسيا

[4]علوم المختبرات الطبية ، جامعة أنور ميديكا، سيدوارجو ٦١٢٦٢ ، إندونيسيا

يهدف هذا البحث إلى تحليل ٥٠٠ عينة للمخدرات غير المشروعة و المواد ذات التأثير النفسي الجديدة باستخدام التحليل الغازي الكروماتوجرافي مع طيف الكتلة في جاوة الشرقية بإندونيسيا. تم إجراء تحليل العينة بواسطة GC-MS مع عمود HP-5، ودرجة حرارة منفذ الحقن ٢٥٠ درجة مئوية. تم الحفاظ على درجة حرارة العمود عند ١٠٠ درجة مئوية لمدة دقيقتين. ثم تم رفعها من ١٠ درجة مئوية / دقيقة إلى ٢٨٠ درجة مئوية والحفاظ عليها لمدة ٥ دقائق. وبناء على النتائج، تم الكشف عن ٢٤٤ (٤٨,٨٪) من الميثامفيتامين (MA)؛ ٣٠ (٦%) ٣،٤–ميثيلين ديوكسي ميثامفيتامين (MDMA)؛ ٤٤ (٨,٨%) ٣،٤–ميثيلين ديوكسي إيثيلامفيتامين (MDA)؛ ٥٦ (١١,٢%) ٣،٤–ميثيلين ديوكسي إيثيلامفيتامين (MDEA)؛ ١٠٦ (٢١,٢%) أب–فوبيناكا؛ ٥ (١,٠%) ترامادول؛ ٥ (١,٠%) كيتامين؛ و١٠ (٢,٠%) ميفيدرون. تم بنجاح التعرف على المخدرات غير المشروعة وNPS في المواد المصادرة عبر GC-MS. يعد توفر مكتبات GC-MS بمثابة مساعدة كبيرة في تحديد الأدوية الجديدة. وبدلاً من ذلك، يمكن أن تكون دراسة أجزاء الجزيء المميزة جنبًا إلى جنب مع تحديد كتلتها الدقيقة طريقة مفيدة لتحديد العينات غير المعروفة التي لم يتم تحليلها مسبقًا.