Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

# Utilization of both UV and GC-MS spectroscopy to track the estimation of caffeine and acetaminophen in a number of paracetamol analgesic drugs

**Maha Abdallah Alnuwaiser***

*Department of Chemistry, College of Science, Princess Nourah bint Abdulrahman University, Saudi Arabia*

*Author for correspondence: maalnoussier@pnu.edu.sa

## ABSTRACT

Caffeine standard sample together with four samples; azdol, citymol, amidol and panadol were prepared so as to be studied by UV–Vis and GC–MS spectrometers. For UV–Vis the samples were prepared in a liquid form while the samples for GC–MS were prepared in a gaseous form. The UV–Vis analysis shows the existence of acetaminophen and disappearance of caffeine. For GC–MS, both acetaminophen and caffeine exists. This result may be related to the fact that the liquid state in UV–Vis analysis causes strong intermolecular interaction which causes caffeine spectrum to overlap with the host liquid. Such overlap does not exist for GC–MS where samples were studied when they are in a gaseous state. This means that caffeine exists in all samples.

**KEYWORDS**: Caffeine; paracetamol; GC–MS; UV–vis, analgesic drug.

**ملخص البحث**

**تم تحضيرعينة قياسية من الكافيين مع أربع عينات لعقار الباراستمول وهي ( أزدول ،وسيتي مول ،أيدول ، بانادول) ليتم دراستها بواسطة مطياف الكتلة و الأشعة فوق البنفسجية ، تم تحضير العينات في صورة سائلة لجهاز الأشعة فوق البنفسجية بينما تم تحضير عينات مطياف الكتلة في صورة غازيةاظهر تحليل الأشعة فوق البنفسجية وجود عقار الاسيتامينوفين واختفاء الكافيين. بالنسبة لمطياف الكتلة ،يوجد كل من الأسيتامينوفين والكافيين. قد تكون هذه النتيجة مرتبطة بحقيقة أن الحالة السائلة في التحليل بالأشعة فوق البنفسجية تسبب تفاعلًا قويًا بين الجزيئات مما يؤدي إلى تداخل طيف الكافيين مع السائل المضيف. لا يوجد مثل هذا التداخل في جهاز مطياف الكتلة حيث تمت دراسة العينات عندما تكون في حالة غازية. هذا يعني أن الكافيين موجود في جميع العينات**

**الكلمات الرئيسية: الكافيين. الباراسيتامول GC□MS .؛ UV□vis ، دواء مسكن.**

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

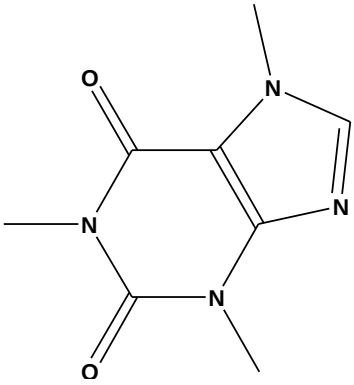
## INTRODUCTION

Paracetamol (acetaminophen) (Figure 1) with caffeine is a mixed drug specific to temporary relief of pain and discomfort associated with various conditions such as fever, headache or muscle pain [1]. Paracetamol is a derivative of p-aminophenol, possessing analgesic and antipyretic properties and weak anti-inflammatory activity [2,3]. However, recent results indicate that it has restrictive effects on cyclooxygenase (COX) enzymes, i.e. COX-1 and COX-2, with stronger selectivity for COX-2, and this leads to inhibition of prostaglandin synthesis in the central nervous system and is produced in Ultimate analgesic and analgesic effects [4]. The fixed dose combination of paracetamol and caffeine is mainly used in conditions such as migraine treatment [5]. Compared to the mixture of paracetamol and caffeine, it was found that paracetamol alone was significantly less effective in treating headaches caused by stress [6], as the moderate analgesic effect of caffeine improved synergistically and increased paracetamol action [7]. Furthermore, caffeine is used in combination therapy for medications such as a fixed dose combination with paracetamol as an effective analgesic for diseases/ diseases such as migraine, postpartum pain, dysmenorrhea, sore throat, postoperative pain, and cancer pain as well [8], to achieve better therapeutic effect and lower toxicity, it is extremely important to inhibit paracetamol and caffeine content in pharmaceutical preparations [9]. To avoid potential toxicity, paracetamol greater than 150-200 mg / kg or 7.5-10 grams should not be identified for children 1-6 years old or adults (weight 70 kg), respectively [10]. Consuming more than 400-500 mg of caffeine at a time can cause caffeine poisoning due to excessive stimulation of the central nervous system and increased caffeine overdose can lead to death [11]. While caffeine is found in various consumer products, it is difficult to obtain a typical dose [12]. A combination of paracetamol (1000 mg) with caffeine (130 mg) is a well-established analgesic mixture, as caffeine has been claimed to increase the effectiveness of paracetamol [13]. In 2010, additional Panadol tablets containing paracetamol 500 mg with caffeine became 65 mg per tablet only as a pharmacist S2. Similar to paracetamol, this preparation is indicated for the temporary relief of pain and discomfort associated with a number of cases [14].

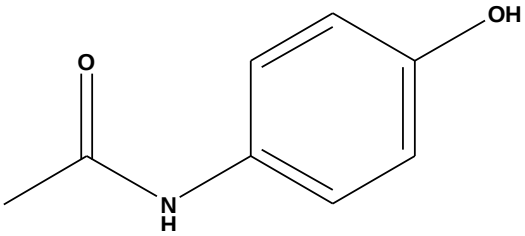
Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

To estimate paracetamol and caffeine, several authors have reported analytical methods using optical spectrophotometry [15], liquid chromatography-mass spectrometer [16], high-performance liquid chromatography (HPLC) [17], capillary electrophoresis [18], voltammetry measurement [19] and thin layer chromatography (TLC) [20]. In order to know the intrinsic stability of the drugs in the composition, as well as to determine the pathways of decomposition of drugs and their products, it is necessary to use the HPLC method that indicates stability for the simultaneous identification of many drugs and their products [21,22]. In the analysis of 30 experiments including over 10,000 patients greater analgesic activity was reported when caffeine was used in combination with analgesics (e.g., aspirin, paracetamol, aspirin plus paracetamol) in a variety of common, nonmalignant pain states. The relative potency estimate was 1.41 (95% CI 1.23–1.62); that is, to obtain the same analgesic effect without caffeine requires a dose of analgesic that is approximately 40% greater than the dose given with caffeine. Moreover, from six experiments of paracetamol/caffeine in 2,625 patients, the corresponding relative potency estimate was 1.37 (95% CI 1.13–1.70) [23]. Paracetamol (1,000 mg) when combined with caffeine (130 mg). In an experimental pain model, had shown a sustained antinociception-enhancing effect [24]. Furthermore, the combination of paracetamol and caffeine has been shown to be as efficacious as ibuprofen after periodontal surgery [25]. For the simultaneous estimation of the caffeine rate in paracetamol extra, both Spectrophotometer (UV) and Gas Chromatography–Mass Spectrometry (GC–MS) methods were used in this research.

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/




Caffeine




Paracetamol

Figure 1. Chemical structures of caffeine and paracetamol.

## MATERIALS AND METHODS

### *Collection source of samples*

Four samples of Paracetamol Extra (azdol, citymol, amidol and panadol) were collected randomly form different pharmaceutical companies in the country of Saudi Arabia.

### *Instruments*

A Shimadzou GC-MS (TQ8040) was used with capillary column (30 cm x 0.25 mm x 0.25 µm), (5% phenyl-95% dimethyl), carrier gas helium, constant flow 1 ml/min, temperature program 0.7 min at 90:35°/min to 240:8°/min, 290:25°/min to 325°- 6 min final hold [20]. A Shimadzu UV-1800 Series technique was employed wavelength range 200-400 nm having light source change wavelength (340.8 nm).

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

## RESULTS AND DISCUSSION

### *GC-MS Analysis*

**Standard solution preparation.** To prepare the reference solution, an amount of 0.001 gram of caffeine was dissolved in 100 ml of methanol (HPLC grade) in the 100 ml volumetric flask. For each analysis process, the standard solution was freshly prepared due to its instability at room temperature.

**Samples processing.** A 0.01 grams of each tablets was weighed and placed in a 100 ml volumetric flask. 100 ml of methanol (HPLC grade) was added to each sample. The contents of each sample was mixed by magnetic stirrer. The mixture was filtered, then the filtrate was subjected to GC-MS analysis. For each sample, 1 µl was injected and chromatography run was made. The chromatogram data was scanned and recorded in Figures 2 and 3. The retention time was measured for each sample and compared with that of the standard solution. The retention time (Rt) values were calculated for each sample and their results are given in Table 1.

Table 1. Retention time (Rt) and M/z values of analyzed caffeine samples

| No. | Sample | Rt | M/z |
|---|---|---|---|
| 1 | Caffeine STD | 11.608 | 194,109,82,67,55 |
| 2 | Azdol | 11.608 | 194,109,82,67,55 |
| 3 | Citymol | 11.608 | 194,109,82,67,55 |
| 4 | Amidol | 11.608 | 194,109,82,67,55 |
| 5 | Panadol | 11.608 | 194,109,82,67,55 |

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

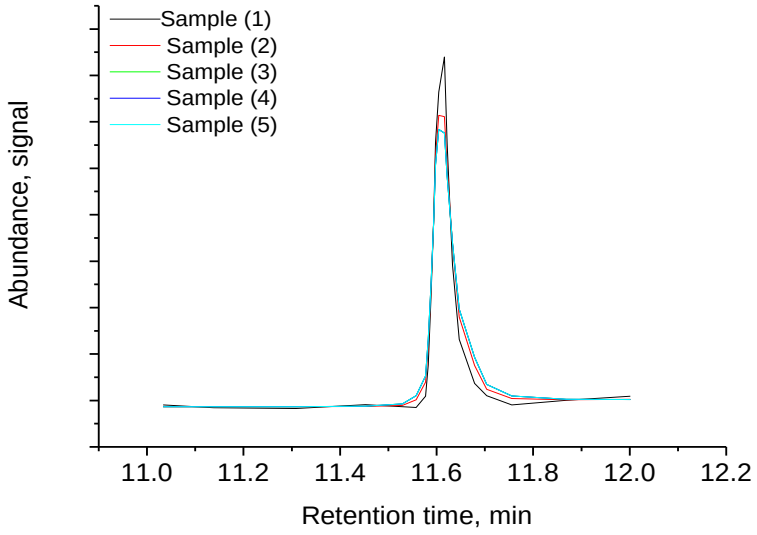



Figure 2. Retention time spectra of caffeine samples 1- caffeine standard, 2- Azdol, 3- Citymol, 4- Amidol, and 5- Panadol by GC–MS.

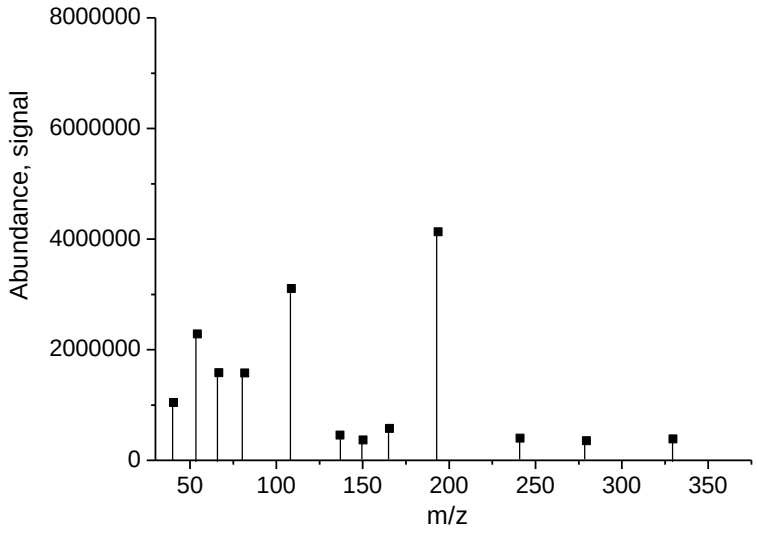



Figure 3. GC–/MS chromatographic spectra of Azdol sample.

### *UV–vis Analysis*

**Standard solution preparation.** A 0.7 gram of caffeine was weighed and put into 100 ml volumetric flask. The volume was completed to 100 ml of water solution. 5 ml of this solution was transferred into 50 ml volumetric flask and again diluted up to the mark of the flask using the water solution. Scanning and read the absorption in UV–Vis device (Table 2 & Fig. 4A).

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

Table 2. The wavelength and absorbance data of caffeine samples at different states

| No. | Sample | Wavelength, nm | Absorbance |
|---|---|---|---|
| 1 | Caffeine STD | 272.60 | 1.346 |
| 2 | Caffeine STD with HCl | 271.60 | 0.030 |
| 3 | Caffeine STD with $H_2O_2$ | - | - |
| 4 | Caffeine STD using UV lamp | 269 | 3.884 |
| 5 | Caffeine STD using temp 60 $^oC$ | 269 | 3.899 |

**Samples processing.** A 0.7 gram of each sample was weighed and put into 100 ml volumetric flask. The volume was completed to 100 ml of water solution (sample A). 5 ml of this solution was transferred into 50 ml volumetric flask and again diluted up to the mark of the flask using the water solution (sample B). Scanning and read the absorption in UV−Vis device.

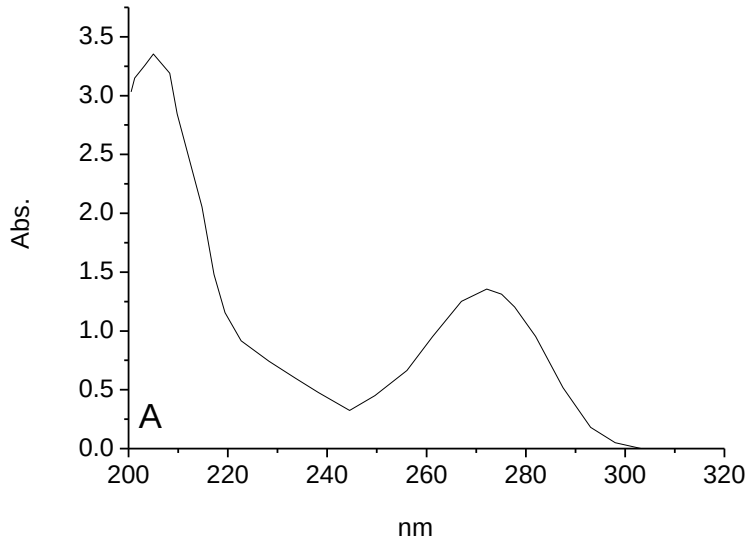



Figure 4A. UV−Vis spectrum of Caffeine STD.

Take 4.8 ml from solution (B) in 50 ml volumetric flask and add 0.2 ml of HCl 0.1 M then complete to the mark using water and rimming 24 hrs before read in UV−Vis device (Fig. 4B).

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

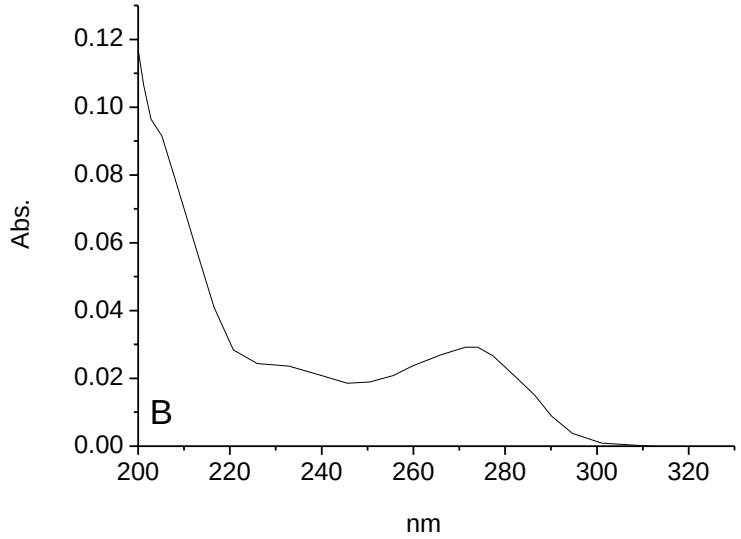



Figure 4B. UV−Vis spectrum of Caffeine STD with HCl.

Take 4.8 ml from solution (B) in 50 ml volumetric flask and add 0.2 ml of $H_2O_2$ 3% then complete to the mark using water and rimming 24 hrs before read in UV−Vis device (Fig. 4C).

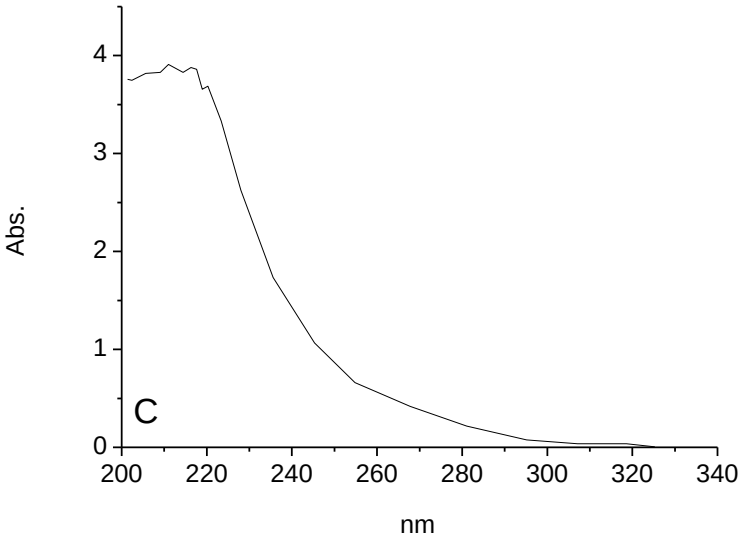



Figure 4C. UV−Vis spectrum of Caffeine STD with $H_2O_2$.

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

Exposure amount of powder in UV lamp 24 hrs and take 0.7 gram from powder and dissolve in 100 ml of water then take 5 ml and complete volume to 50 ml using water and read in UV−Vis device (Fig. 4D).

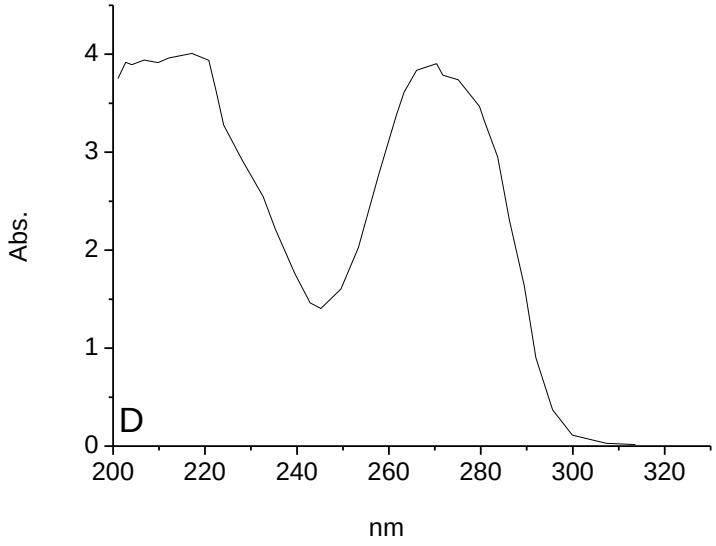



Figure 4D. UV−Vis spectrum of Caffeine STD using UV lamp.

Exposure amount of powder in temperature 60 $^{o}$C 24 hrs and take 0.7 gram from powder and dissolve in 100 ml of water then take 5ml and complete volume to 50 ml using water and read in UV−Vis device (Fig. 4E).

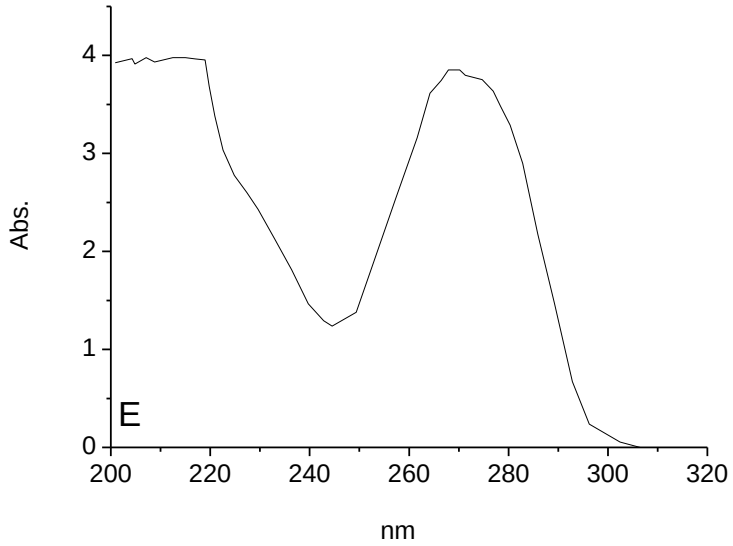



Figure 4E. UV−Vis spectrum of Caffeine STD using temp 60 $^{o}$C.

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

For each sample of azdol, citymol, amidol and panadol, take amount of sample solution was injected for UV–Vis device. The absorbance and wavelength was measured (Fig. 5). A comparison between standard solutions, the absorbance was calculated and displayed in Table 3 and Figure 5.

Table 3. The wavelength and absorbance data of different panadol samples.

| No. | Sample | Wavelength nm | Absorbance |
|---|---|---|---|
| 1 | Citymol | 242.80 | 1.368 |
| 2 | Amidol | 242.80 | 0.884 |
| 3 | Azdol | 241.80 | 3.797 |
| 4 | Panadol | 242.80 | 1.656 |

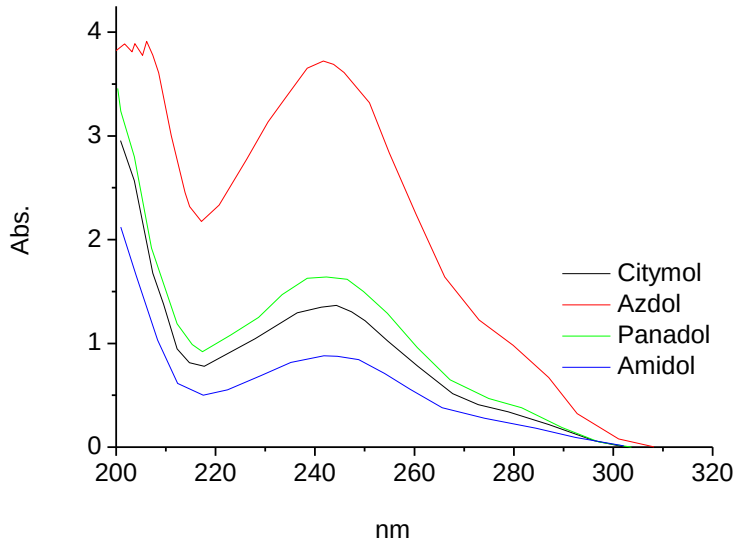



Figure 5. UV–Vis spectra of different panadol samples.

## CONCLUSION

The results of UV–Vis spectra doesn't show a positive result concerning caffeine, while it shows a positive results for acetaminophen active material due to the existence of its characteristic wavelength at about 242 nm. The disappearance of caffeine in UV–Vis spectrum is attributed to the strong intermolecular interactions of the samples.

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

Constituents which are in a liquid phase, this interaction affect strongly the caffeine spectrum and cause it to disappear due to its overlap with the source back ground and acetaminophen spectrum. However the results of GC–MS spectrometer are positive. This is since it shows the existence of both acetaminophen and caffeine spectrum for different retention time and different bonding breaking related to the ratio M/z. The appearance of caffeine spectrum is related to the fact that the samples are studied in a gaseous state. This prevents intermolecular interaction, thus allows the pure spectrum of each compound to appear the final results thus show the existence of caffeine in the studied samples.

## ACKNOWLEDGEMENTS

This research was funded by the deanship of scientific Research at Princess Nourah bint Abdulrahman University through the Fast–track Research Funding program.

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

## REFERENCES

1- K. Brune, B. Renner, G. Tiegs, JAMPS, 5(3) (2016) 1-18
2- S.C. Sweetman, Martindale: The Complete Drug Reference, 36th, Pharmaceutical Press.**(2009**)
3- M. Jozwiak-Bebenista, J.Z. Nowak, Acta Pol. Pharm., 71 (2014) 11-23.
4- N.V. Chandrasekharan, H. Dai, K.L.T. Roos, N.K. Evanson, J. Tomsik, T.S. Elton, D.L. Simmons, Proc. Natl. Acad. Sci. U.S.A., 99 (2002) 13926-13931.
5- M.D. Ferrari, K.I. Roon, R.B. Lipton, P.J. Goadsby, Lancet, 358 (2001) 1668-1675.
6- J.R. Migliardi, J.J. Armellino, M. Friedman, D.B. Gillings, W.T. Beaver, Clin. Pharmacol. Ther., 56 (1994) 576-586.
7- J. Goldstein, Inflammopharmacology, 9 (2001) 51-61.
8- A. Straube, B. Aicher, B.L. Fiebich, G. Haag, BMC Neurol., 11 (2011) 43.
9- A. Safavi, M. Tohidi, J. Pharma. Biomed., 44 (2007) 313-318.
10- Diagnostic and statistical manual of mental disorders. 4th ed., Washington (DC): American Psychiatric Association, 1994.
11- P. Holmgren, L. Norden-Pettersson, J. Ahlner, Foren. Sci. Int., 139(1) (2004)71-3.
12- D.M. Mrazik, Reconsidering caffeine: An awake and alert new look at America's most commonly consumed drug. (**2004**) 7-14
13- A.H. Aktaş, F. Kitiş, Croat. Chem. Acta, 87 (2014) 69-74.
14- A. Wang, J. Sun, H. Feng, S. Gao, Z. He, Chromatographia, 67 (2008) 281-285.
15- A. Acheampong, W.O. Gyasi, G. Darko, J. Apau, S. Addai-Arhin, Springerplus, 5 (2016) 625.
16- Clarkes analysis of drugs and poisons "third edition, by Anthony C. Moffat, M. David Osselton, Brian Widdop **.2 (2004) 1391-1392**
17- M.L. Altun, Turk. J. Chem., 26 (2002) 521-528.
18- S.H. Youssef, D. Mohamed, M.A.M. Hegazy, A. Badawey, BMC Chem., 13(1) (2019) 78.
19- M. Amare, W. Teklay, Cogent Chemistry, 5 (2019) 1576349.
20- A. Ambekar, B. Kuchekar, J. Chromatogr. Sep. Technol., 7 (2016) 324-334.
21- T. Belal, T. Awad, R. Clark, J. Chromatogr. Sci., 47 (2009) 849-854.

Multi-Knowledge Electronic Comprehensive Journal For Education And Science Publications ( MECSJ )
Issue (40),2021
ISSN: 2616-9185
www.mecsj.com/

22- H. Sharma, K. Vishakha, K.V. Kumar, H.P. Bhatta, Int. J. Pharm. Sci. Res., 7 (2016) 316-324.
23- A. Nazir, Y. Naseer, R. Shahid, S. Raza, Sci. Int., 28 (2016) 2497.
24- H. Li, C. Zhang, J. Wang, Y. Jiang, J.P. Fawcett, J. Gu, J. Pharm. Biomed. Anal., 51 (2010) 716-722.
25- V. Stoynova, I. Getov, J. Clin. Med., 3 (2010) 41-50.