A New Chemometrically Assisted UV Spectrophotometric Method for Simultaneous Determination of Tamsulosin and Dutasteride in Their Pharmaceutical Mixture

Khalid A.M. Attia,1 Ahmed Serag,1 Sherif M. Eid,2 and Ahmed Emad F. Abbas2,*

1Al-Azhar University, Faculty of Pharmacy, Pharmaceutical Analytical Chemistry Department, 11751 Nasr City, Cairo, Egypt, 2October 6 University, Faculty of Pharmacy, Analytical Chemistry Department, 6 October City, Giza 12585, Egypt

*Corresponding author's e-mail: dr.ahmedeemad@gmail.com; ahmed.emad.pha@o6u.edu.eg

Abstract

Background: Tamsulosin (TAM) and dutasteride (DUT) are ranked among the most frequently prescribed therapies in urology. Interestingly, studies have also been carried out on TAM/DUT in terms of their ability to protect against recent COVID-19. However, very few studies were reported for their simultaneous quantification in their combined dosage form and were mainly based on chromatographic analysis. Subsequently, it is very important to offer a simple, selective, sensitive, and rapid method for the quantification of TAM and DUT in their challenging dosage form.

Objective: In this study, a new chemometrically assisted ultraviolet (UV) spectrophotometric method has been presented for the quantification of TAM and DUT without any prior separation.

Method: For the calibration set, a partial factorial experimental design was used, resulting in 25 mixtures with central levels of 20 and 25 µg/mL for TAM and DUT, respectively. In addition, to assess the predictive ability of the developed approaches, another central composite design of 13 samples was used as a validation set. Post-processing by chemometric analysis of the recorded zero-order UV spectra of these sets has been applied. These chemometric approaches include partial least-squares (PLS) and genetic algorithm (GA), as an effective variable selection technique, coupled with PLS.

Results: The models' validation criteria displayed excellent recoveries and lower errors of prediction.

Conclusions: The proposed models were effectively used to determine TAM/DUT in their combined dosage form, and statistical comparison with the reported method revealed satisfactory results.

Highlights: Overall, this work presents powerful simple, selective, sensitive, and precise methods for simultaneous quantification of TAM/DUT in their dosage form with satisfactory results. The predictive ability and accuracy of the developed methods offer the opportunity to be employed as a quality control technique for the routine analysis of TAM/DUT when chromatographic instruments are not available.

Over recent years, tamsulosin (TAM), a selective α1A- and α1D- adrenoceptor antagonist (Figure 1a), and dutasteride (DUT) a 5α-reductase inhibitor (Figure 1b), are ranked among the most frequently prescribed therapies in urology, particularly for benign prostatic hyperplasia (1–4). In 2021, TAM/DUT were ranked as the 32nd and the 288th most prescribed medications in the
United States, with approximately 23 million and one million prescriptions for TAM and DUT, respectively (5). Interestingly, United States, with approximately 23 million and one million potential interaction with other COVID-19 treatments (6, 7). Fortunately, the findings indicate that immediate anti-androgen treatment with DUT may succeed to decrease inflammatory responses, viral shedding, time to remission, and severity of SARS-CoV-2 infections (8). Additionally, the findings also indicate that TAM has potential interactions with the concomitant use of lopinavir/ritonavir in patients with COVID-19, as both are potent inhibitors of CYP3A4 (9). Hence, due to the vast clinical potential of DUT/TAM, there is an urgent need for simple and economical methods to quantify DUT/TAM in their dosage form.

A literature survey revealed that the main analytical technique used for DUT/TAM analysis is high-performance liquid chromatography (HPLC) (10, 11). However, the reported HPLC methods have some limitations, including the remarkable use of hazardous organic solvents in their mobile phase, such as acetonitrile, in addition to time-consuming separation procedures. Furthermore, selecting proper stationary and mobile phases for optimum peak resolution are critical parameters that must be finely tuned. Alternatively, spectrophotometric techniques can get rid of the problems above with intensified simplicity, efficacy, and accuracy for drug analysis (12, 13). These include colorimetric methods used for determination of DUT/TAM based on chemical reactions to form ion-pair complex with reagents such as bromothymol blue and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (14, 15). However, such methods suffer from a limited linearity range, a long time for the reactions to be completed, and low color stability. Other spectrophotometric methods employed for DUT/TAM determination are mathematical manipulation approaches such as univariate and bivariate methods such as first derivative, second derivative of the ratio spectra, Vierordt’s method, and area under the curve (16–19). These methods also suffer from disadvantages as these methods are inefficient to collect unused data; thus this wasteful data collection might reduce analytical methodology’s throughput. In addition, these methods have extreme sensitivity to interfering factors because of the difficulty to differentiate the signal of the analyte from an interferent when only one or two points on a data spectrum are examined. Furthermore, a calibration curve is required for each drug, and many tests are required for selecting the suitable divisor for proceeding derivative of the ratio spectra (20, 21). Thus, in recent years, chemometrics has attracted a great deal of attention as an effective post-processing technique that can tackle the aforementioned disadvantages (22, 23). Of all chemometric models, partial least-squares (PLS) has been widely used for several analytes analysis based on its ability to acquire the maximum variance and ensure that concentration and spectral variables are in a maximum correlation (24, 25). Moreover, incorporating a genetic algorithm (GA) as an effective variable selection technique extremely improves the performance of the PLS model owing to its ability to select efficient spectral regions that exclude the obsolete variables; as a consequence, models with greater stability are developed (26).

The aim of this study is to establish new simple chemometrically assisted ultraviolet (UV) spectrophotometric methods for the quantification of TAM/DUT without any prior separation in their combined dosage form. The predictive ability and accuracy of the developed methods offer the chance to be employed as a quality control technique for the routine analysis of TAM/DUT when chromatographic instruments are not available.

**Experimental**

**Reagents and Materials**

TAM and DUT were supplied by GlaxoSmithKline pharmaceutical company (Fifth District, New Cairo, Egypt), with certified purity of 99.2 ± 0.5 and 99.4 ± 0.6 for TAM and DUT, respectively. Methanol HPLC grade was purchased from Sigma-Aldrich (Germany). Duodart™ capsules (GlaxoSmithKline pharmaceutical company, Cairo, Egypt) containing 0.4 mg and 0.5 mg per capsule for TAM and DUT, respectively, were purchased from a local pharmacy.

**Instrumentation**

A UV-1601 PC double-beam Shimadzu UV-Vis spectrophotometer, with UV probe software, was used. PLS and GA were implemented in MATLAB® R2013b (8.2.0.701) employing the PLS toolbox software version 2.1.

**Standard Solutions**

Powdered TAM and DUT equivalent to 100 mg of each were transferred into two separate 100 mL volumetric flasks. Finally, methanol was used to complete each flask to 100 mL, resulting in final concentrations of 1 mg/mL. Working solutions were acquired by serial dilution using methanol. All stock and working solutions were stable enough and can be used in a dark refrigerator bottle for about a week (5° C).

**Procedures**

(a) **Experimental design.—** A well-planned experimental design is arguably a significant step to increase the probability of acquisition of representative and informative data. Ideally, for the calibration set, a partial five-level/two-factor factorial design was employed, employing five concentration levels for each of the components, resulting in 25 laboratory-prepared mixtures with different concentration...

![Figure 1. (a) Chemical structure of tamsulosin and (b) chemical structure of dutasteride.](image-url)
ranges: 12–28 μg/mL for TAM and 15–35 μg/mL for DUT. The linearity and ratio of both drugs in the pharmaceutical formulation were used to determine their concentration ranges. The main levels of the design were 20 and 25 μg/mL for TAM and DUT, respectively; the lower and upper levels for this design were 12, 28 μg/mL for TAM and 15, 35 μg/mL for DUT. To assess the predictive ability of the developed approaches, another experimental setup based on the central composite design of 13 samples was used as a validation set, as illustrated in Table 1.

Applicaton.—The weight of 20 capsules was accurately measured. Subsequently, in a dry, clean mortar, the contents were pulverized. Thereafter, in a 100 mL volumetric flask, a powder weight equivalent to 40 mg of TAM and 50 mg of DUT was separately transferred, and sufficient methanol was used to dissolve it. The solution was shaken for 10 min on a rotatory shaker followed by sonication for 30 min. The obtained solution was subjected to centrifugation at 3000 rpm for 30 min. Finally, it was filtered, and then the final volume was adapted with methanol to obtain a final concentration of 400 μg/mL TAM and 500 μg/mL DUT. Aliquots from working solutions were employed for quantification of TAM and DUT in their dosage form by directly implementing the developed method.

Results and Discussion
The TAM/DUT UV spectral characteristics were determined over a wavelength region of 200–400 nm. After brief glance at these spectra, a severe overlap is observed that clearly interprets the challenge confronted for their direct simultaneous quantitative determination, as shown in Figure 2. Such overlap is clearly observed at three regions, approximately at 266, 234, and 215 nm, as both drugs are structurally related compounds and have various related chromophores, making the utilization of the multivariate calibration models inevitable. However, before employing such models, spectral data pre-processing is the crucial step that must be performed. The wavelengths from 310–400 nm were expelled as there are no absorbance values for TAM/DUT. Because of the noisy spectral composition, wavelengths below 210 nm were also eliminated. As a result, the TAM/DUT determination was performed using the presented chemometric models, PLS and GA-PLS, on 101 wavelengths ranging from 210 to 310 nm.

PLS and GA-PLS
The PLS model, a commonly used regression model, was implemented to the spectral matrix of the calibration data in order to imply it into new spaces’ dimensions known as latent variables (LVs). It was essential to carefully determine the optimal number of these LVs to avoid losing important information and any overfitting of the model due to insufficient or more LVs. As a result, the calibration set’s spectral data were submitted to a cross-validation technique that excluded one analyte at a time, and the root-mean-square error cross-validation (RMSECV) was computed after incrementally adding various LVs to the model (27). According to Haaland and Thomas’s criteria, the ideal number of LVs was chosen (28). Two LVs were optimal for modeling TAM and DUT, with RMSECV values of 0.2711 and 0.4782, respectively, as shown in Figure 3.

Interestingly, to enhance the predictive power of the PLS model, the GA procedure as an informative variable’s selection technique was used. The GA model was used on 101 variables for TAM and DUT (210 to 310 nm) to remove unnecessary variables while keeping informative ones. The adjustment of GA parameters, as shown in Table 2, is a significant issue for successful GA performance. The population size is one of the most essential elements in the use of GAs. The selection of population size is a sensitive issue. Remarkably, the proper population size for each drug was 36 as the use of smaller populations resulted in poor performance and lower accuracy of the solution. Accordingly, this meant that little search space was available. Nevertheless, the ability to seek additional spaces increased as the population size was larger than 36, resulting in premature convergence to solutions. Another important characteristic of GA was the mutation rate, as it adapted to retain the variety of genetic populations by changing a single gene or even more on the GA chromosomes, preventing quick convergence. The proper mutation rate for each drug was found to be 0.005. Other parameters include the number of subsets, the number of iterations for cross-validation at each generation, and the maximum number of LVs using the full PLS model. Interestingly, it was found that GA decreases the absorbance matrix to about 50% for TAM and 30% for DUT (53 variables for TAM and 35 variables for DUT). Interestingly, GA-PLS models for both TAM and DUT in terms of standard deviation (SD) of the % recoveries have lower values compared to the full model, as shown in Tables 3 and 4.

Models Validation
Regarding the validation of the chemometric models, we used an external validation set based on a central composite design
to test the predictive ability of the developed models. Hence, to evaluate the built models’ performance, statistical parameters such as root-mean-square error of calibration and predictions (RMSEC and RMSEP) have been calculated, as shown in Table 5. In addition, percentage of the relative root MSEP (RRMSEP) was used to measure the accuracy of the predictions (29), while bias-corrected MSEP (BCMSEP) was used to measure the precision or variance of the predictions (30), as shown in Table 5. Specificity

Figure 2. Zero-order absorption spectra of 35 µg/mL DUT and 28 µg/mL TAM show severe overlapping in the wavelength range 210–310 nm.

Figure 3. Cross-validation of (a) DUT and (b) TAM employing the full PLS model, and (c) DUT and (d) TAM employing the GA-PLS model.
of the method has been assessed using the external validation set, and good results were attained as indicated by their RMSEP. Regarding the linearity and range parameters, the experimental design of the calibration set was 12–28 μg/mL for TAM and 15–35 μg/mL for DUT. In addition, regression parameters of the predicted versus actual concentrations of the calibration set have been presented in Table 5. Interestingly, the developed models exhibit a linear pattern with slope values close to 1. Robustness of the developed models has been assessed using a central composite design with axial points outside the range of the factorial points. Such an approach can test the predictive ability of the developed models even if some concentrations were slightly outside the calibration range, thus ensuring the robustness of the developed models. LOD and LOQ of the developed models have been calculated based on the net analyte signals, and the results are presented in Table 5. Interestingly, GA-PLS models transcended the full PLS models for both TAM and DUT in terms of RMSEC, RMSEP, and other validation parameters, as indicated by their lower values compared to the full model, posing this approach as a powerful tool to enhance the performance of the multivariate models.

### Application of the Described Models for Quantitative Analysis of Duodart Capsules

The proposed chemometrically assisted UV spectrophotometric method was used and was successful in the quantification of TAM and DUT in Duodart capsules. The results of the developed methods were statistically compared to those acquired by the

### Table 2. Optimized parameters implemented for the GA applied for variable selection selected for TAM and DUT full spectral data

| Parameters                                   | Optimum values |
|----------------------------------------------|----------------|
| Population size                              | 36             |
| Maximum generations                          | 100            |
| Mutation rate                                | 0.005          |
| % wavelength used at initiation              | 15             |
| The number of variables in a window          | 2              |
| Percent of population (% of convergence)     | 80             |
| Cross-type                                   | Double         |
| Maximum number of latent variables           | 2              |
| Cross-validation                             | Random         |
| Number of subsets to divide data into cross-validation | 4             |
| Number of iterations for cross-validation at each generation | 2              |

### Table 3. Different statistical parameters for TAM and DUT in the calibration set by the described models

| Calibration mixture | PLS | GAPLS |
|---------------------|-----|-------|
|                     | TAM | DUT   | TAM | DUT |
| 1                   | 103.03 | 103.66 | 102.47 | 99.72 |
| 2                   | 100.88 | 100.56 | 100.86 | 101.04 |
| 3                   | 100.30 | 100.67 | 100.33 | 101.41 |
| 4                   | 98.57  | 100.49 | 100.86 | 101.05 |
| 5                   | 102.52 | 103.59 | 102.40 | 99.12 |
| 6                   | 99.72  | 99.95  | 97.91  | 99.25 |
| 7                   | 100.88 | 100.56 | 100.86 | 101.04 |
| 8                   | 100.30 | 100.67 | 100.33 | 101.41 |
| 9                   | 100.88 | 100.49 | 100.86 | 101.05 |
| 10                  | 98.57  | 100.26 | 98.28  | 100.42 |
| 11                  | 98.34  | 99.74  | 97.40  | 98.80 |
| 12                  | 98.34  | 98.81  | 98.42  | 99.51 |
| 13                  | 99.41  | 97.77  | 99.60  | 99.59 |
| 14                  | 99.20  | 97.72  | 99.31  | 99.17 |
| 15                  | 100.96 | 100.37 | 100.95 | 100.47 |
| 16                  | 101.93 | 103.81 | 101.59 | 101.10 |
| 17                  | 100.09 | 100.14 | 99.97  | 99.77 |
| 18                  | 99.54  | 99.89  | 99.54  | 100.20 |
| 19                  | 100.50 | 99.16  | 100.48 | 98.94 |
| 20                  | 102.23 | 101.30 | 102.12 | 100.94 |
| 21                  | 99.74  | 100.89 | 99.72  | 100.81 |
| 22                  | 101.84 | 100.97 | 101.78 | 99.87 |
| 23                  | 98.95  | 100.03 | 99.04  | 100.08 |
| 24                  | 100.39 | 101.31 | 100.26 | 99.96 |
| 25                  | 101.25 | 100.07 | 101.14 | 100.06 |
| Mean                | 100.28 | 100.48 | 100.24 | 100.13 |
| SD                  | 1.325  | 1.875  | 1.232  | 0.910 |

### Table 4. Different statistical parameters for TAM and DUT in the validation set by the described models

| Validation mixture | PLS | GAPLS |
|--------------------|-----|-------|
|                    | TAM | DUT   | TAM | DUT |
| 1                  | 102.06 | 104.91 | 101.47 | 101.20 |
| 2                  | 100.08 | 99.32  | 100.02 | 98.76  |
| 3                  | 99.41  | 98.42  | 99.54  | 99.30  |
| 4                  | 101.57 | 99.89  | 101.55 | 99.27  |
| 5                  | 100.46 | 98.93  | 100.49 | 98.80  |
| 6                  | 100.23 | 98.91  | 100.45 | 100.94 |
| 7                  | 101.31 | 102.59 | 102.19 | 101.97 |
| 8                  | 99.13  | 100.87 | 99.36  | 100.28 |
| 9                  | 100.18 | 99.42  | 100.20 | 99.98  |
| 10                 | 101.76 | 101.81 | 101.61 | 100.19 |
| 11                 | 100.33 | 99.51  | 100.18 | 98.32  |
| 12                 | 98.51  | 98.08  | 98.64  | 99.44  |
| 13                 | 99.85  | 101.68 | 99.87  | 102.03 |
| Mean               | 100.45 | 100.33 | 100.42 | 99.99  |
| SD                 | 1.164  | 1.952  | 1.023  | 1.223  |

### Table 5. Assay validation sheet of TAM and DUT by the proposed models

| Validation parameters | PLS | GAPLS |
|-----------------------|-----|-------|
|                      | TAM | DUT   | TAM | DUT |
| RMSEC<sup>a</sup>     | 0.2519 | 0.4963 | 0.2343 | 0.2131 |
| RMSEP<sup>b</sup>     | 0.2419 | 0.5303 | 0.2159 | 0.3262 |
| RRMSEP<sup>c</sup>    | 1.2096 | 1.9284 | 1.0795 | 1.18636 |
| BCRMSEP<sup>d</sup>   | 0.0585 | 0.2812 | 0.0466 | 0.1064 |
| r<sup>e</sup>         | 0.9991 | 0.9979 | 0.9992 | 0.9996 |
| Intercept<sup>f</sup> | –0.2997 | –0.7627 | –0.2495 | –0.1950 |
| Slope<sup>e</sup>     | 1.0139 | 1.0283 | 1.0116 | 1.0072 |
| LOD<sup>f</sup>       | 3.2017 | 4.2483 | 2.9653 | 4.1189 |
| LOQ<sup>f</sup>       | 10.5657 | 14.0196 | 9.7856 | 13.5924 |

<sup>a</sup> Root-mean-square error of calibration.
<sup>b</sup> Root-mean-square error of prediction.
<sup>c</sup> Relative root-mean-square error of prediction.
<sup>d</sup> Bias-corrected mean square error of prediction.
<sup>e</sup> Data of the straight line plotted between predicted concentrations versus actual concentrations of the calibration set.
<sup>f</sup> The LOD and LOQ calculations are based on the net analyte signals.
HPLC reported methods (31), indicating that there are no significant differences, as shown in Table 6.

### Conclusions

In this work, a simple, sensitive, and precise chemometrically assisted UV spectrophotometric method, PLS, and GA-PLS for the quantification of TAM/DUT without any prior separation in their pharmaceutical dosage forms has been presented with satisfactory results. In terms of the results reported in this research, the proposed methods can be confidently ranked between selective and accurate methods. The predictive ability and accuracy of the developed method offer the chance to be employed as a quality control technique for the routine analysis of TAM/DUT when chromatographic instruments are not available. Furthermore, the results presented in this paper provide an outlook for exploiting the chemometric techniques for the quantification of pharmaceuticals using simple, readily available, and low-cost instruments devices such as the UV spectrophotometer regarding the number of samples, number of interfering components, or severely overlapped spectra.

### Conflict of Interest

All authors declare no conflict of interest.

### References

1. Dunn, C.J., Matheson, A., & Faulds, D.M. (2002) Drugs Aging 19, 135–161. doi: 10.2165/0002512-20021902-00004
2. Keam, S.J., & Scott, I.J. (2008) Drugs Aging 68, 463-485. doi: 10.2165/0002512-200868040-00008
3. Attia, K.A.M., Abdell-Raoof, A.M., Serag, A., Eid, S.M., & Abbas, A.E. (2022) RSC Adv. 12, 17536–17549. doi: 10.1039/D2RA01962K
4. Abbas, A. (2021) Al-Azhar J. Pharm. Sci. 64, 93–108. doi:10.21608/ajsips.2021.187763
5. The Top 300 of 2021, https://clincalc.com/DrugStats/Top300Drugs.aspx (accessed June 21, 2021)
6. Montopoli, M., Zumerle, S., Vettor, R., Rugge, M., Zorri, M., Catapano, C.V., Carbone, G.M., Cavalli, A., Pagan, F., Ragazzi, E., Prayor-Galetti, T., & Alimonti, A. (2020) Ann. Oncol. 31, 1040–1045. doi:10.1007/ann onc.2020.04.479
7. Rezaee, H., Pourkarm, F., Pourtaghi-Anvarian, S., Entezari-Maleki, T., Asvadi-Kermani, T., & Nouri-Vaskeh, M. (2020) Pharmaceut. Res. Perspect. 9, 1–18. doi:10.1002/prp2.705
8. Cadegiani, F.A., McCoy, J., Gustavo Wambier, C., & Goren, A. (2021) Cureus 13, 1–13. doi:10.7759/cureus.13047
9. Brandariz-Nuñez, D., Correas-Sanahuja, M., Guarc, E., Picón, R., Garcia, B., & Gil, R. (2020) Med. Clin. (Barc). 1–6. doi:10.1016/j.medcli.2020.06.026
10. Barut, B.B., Erkmen, C., Gumustas, A., Gumustas, M., Ozkan, S.A., & Uslu, B. (2020) J. Iran. Chem. Soc. 17, 1457–1465. doi:10.1007/s13738-020-01871-9
11. Chaudhari, R., Mohanraj, K., & Shiras, V. (2014) Int. J. Pharm. Sci. Res. 5, 1–9. doi:10.13040/IJPSR.0975-8232.5(7).2791-06
12. Elsonbaty, A., Serag, A., Abdulwahab, S., Hassan, W.S., & Eissa, M.S. (2020) Spectrochim. Acta A Mol. Biomol. Spectrosc. 238, 118415. doi:10.1016/j.saa.2020.118415
13. Attia, K.A.M., El-Abasawi, N.M., El-Olemy, A., & Serag, A. (2018) Spectrochim. Acta A Mol. Biomol. Spectrosc. 190, 1–9. doi:10.1016/j.saa.2017.08.066
14. Lakshmi Prasanna, I., Naidu, G.T., Fathima, N., Chakravathy, I.E., & Huq, G.A. (2018) Int. J. Res. Trends Innov. 3, 6–11
15. Lakshmi Prasanna, I., Naidu, G.T., Fathima, N., Chakravathy, I.E., & Huq, G.A. (2018) Am. J. PharmTech Res. 8, 211–220
16. Choudhari, V.P., Gite, S.R., Raut, R.P., Hable, A.A., Pareek, S.R., & Kuchekar, B.S. (2010) Int. J. Pharm. Sci. Res. 2, 63–67
17. Choudhari, V.P., Hable, A., Bolegaonkar, S.S., & Suryawanshi, S.S. (2012) Der Pharma Chemico 3, 989–995
18. Giriraj, P., & Sivakkumar, T. (2017) Arab. J. Chem. 10, S1862–S1867. doi:10.1016/j.arabjc.2013.07.013
19. Pande, V.V., Jadhav, J.N., & Chandorkar, J.G. (2009) Arab. J. Chem. 2, 17536–17549. doi:10.1039/D2RA01962K
20. Fayez, Y.M., Tawakkol, S.M., Fahmy, N.M., Lotfy, H.M., & Elsayef, I.E., & Huq, G.A. (2018) Int. J. PharmTech Res. 119626. doi:10.1016/j.saa.2021.119626
27. Serag, A., Hasan, M.A., Tolba, E.H., Abdelzaher, A.M., & Elmaaty, A.A. (2022) Spectrochim. Acta A Mol. Biomol. Spectrosc. 264, 120334. doi:10.1016/j.saa.2021.120334
28. Haaland, D.M., & Thomas, E.V. (1988) Anal. Chem. 60, 1193–1202
29. Elmasry, M.S., Serag, A., Hassan, W.S., El-Mammli, M.Y., & Badrawy, M. (2022) J. AOAC Int. 105, 309–316. doi:10.1093/jaoacint/qsab105
30. Westad, F., & Marini, F. (2015) Anal. Chim. Acta 893, 14–24. doi:10.1016/j.aca.2015.06.056
31. Chandrasekhar, K., & Manikandan, A. (2021) Rasayan J. Chem. 14, 665–671. doi:10.31788/RJC.2021.1425740