DAFTAR PUSTAKA

Abdelazim, A.H. & Shahin, M. 2021. Different chemometric assisted approaches for spectrophotometric quantitative analysis of lesinurad and allopurinol. *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy*, 251.

Ahmad, I., Sheraz, M.A., Ahmed, S. & Anwar, Z. 2019. Multicomponent spectrometric analysis of drugs and their preparations. In *Profiles of Drug Substances, Excipients and Related Methodology*. Academic Press Inc.: 379–413.

Ashfaque-E-Alam, M., Islam, M.R. & Faria, I.J. 2017. Development and validation of a low-cost visible light spectrophotometer. In *4th International Conference on Advances in Electrical Engineering*. Dhaka, Bangladesh: Institute of Electrical and Electronics Engineers Inc.: 653–657.

BPOM, 2022. Peraturan Badan Pengawas Obat dan Makanan Nomor 14 Tahun 2022 Tentang Penarikan dan Pemusnahan Obat yang Tidak Memenuhi Standar dan/atau Persyaratan Keamanan, Khasiat, Mutu, dan Label. Badan Pengawas Obat dan Makanan.

Caro, C.A., Toledo, M. & Claudia, H. 2015. *UV/VIS Spectrophotometry-Fundamentals and Applications*. Switzerland: Mettler-Toledo AG, Analytical.

Chawla A, Chawla R, Jaggi S: Microvascular and macrovascular complications in diabetes mellitus: Distinct or continuum?. Indian J Endocr Metab. 2016, 20:546-551.

Darbandi, A., Sohrabi, M. R., & Bahmaei, M. 2020. Development of a chemometric-assisted spectrophotometric method for quantitative simultaneous determination of Amlodipine and Valsartan in commercial tablet. *Optik*, 218.

Dange, YD., Honmane, SM., Bhinge, SD., Salunkhe, VR. & Jadge, D.R. Development and Validation of UV-Spectrophotometric Method for Estimation of Metformin in Bulk and Tablet Dosage Form. *Indian Journal of Pharmaceutical Education and Research*, 51(4S): S754-760.

Depkes RI. 2020. *Farmakope Indonesia Edisi VI*. Kemenkes RI.

Dong, M.W. 2013. The Essence of Modern HPLC: Advantages, Limitations, Fundamentals, and Opportunities. *LCGC NORTH AMERICA*, 31(6): 2–7.

Dzulfianto, A., Riswanto, F.D.O. & Rohman, A. 2017. The employment of UV-spectroscopy combined with multivariate calibration for analysis of paracetamol, propyphenazone and caffeine. *Indonesian Journal of Pharmacy*, 28(4): 191–197.

Farid, J.F., Mostafa, N.M., Fayez, Y.M., Essam, H.M. & ElTanany, B.M. 2022. Chemometric quality assessment of Paracetamol and Phenylephrine Hydrochloride with Paracetamol impurities; comparative UV-spectrophotometric implementation of four predictive models. *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy*, 265.

Gupta, D., Bhardwaj, S., Sethi, S., Pramanik, S., Das, D. K., Kumar, R., Singh, P. P., and Vashistha, V. K. 2018. Simultaneous spectrophotometric determination of drug components from their dosage formulations. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 270: 1-16.

Induri, M., Raju, B., Prasad, R. & Reddy, P. 2012. Development and Validation of A Spectrophotometric Method for Quantification and Dissolution Studies of Glimepiride in Tablets. *E-Journal of Chemistry*, 9(2): 993-998.

Kalra S, Das A.K, Baruah M.P, et al.: Glucocrinology of modern sulfonylureas: Clinical evidence and practicebased opinion from an international expert group. Diabetes Ther. 2019, 10:1577-1593.

Mennickent, S. & de Diego, M. 2019. Analytical Method Validation as the First Step in Drug Quality Control. *Quality Management and Quality Control - New Trends and Developments*. IntechOpen.

Mocak, J. 2012. Chemometrics in Medicine and Pharmacy. *Nova Biotechnologica et Chimica*, 11(1): 11–26.

PERKENI. PERKENI. Pengelolaan dan Pencegah Diabetes Melitus Tipe 2 di Indonesia. 2015

Prajapati, P.R., Rathod, D.N., Modi, V.S. & Basuri, T. 2016. Chemometrics and its Applications in UV Spectrophotometry. *International Journal of Pharmaceutical Chemistry and Analysis*, 3(1): 43–48.

Rena, G., Hardie, D.G. & Pearson, E.R. 2017. The mechanisms of action of metformin. *Diabetologia*, 60(9): 1577–1585.

Samosir, R.D., Salaki, D. T., & Langi, Y. 2022. Comparison of Partial Least Squares Regression and Principal Component Regression for Overcoming Multicollinearity in Human Development Index Model. *Operations Research: International Conference Series*, 3(1): 1-7.

Santos, H.T.L., de Oliveira, A.M., de Melo, P.G., Freitas, W. & de Freitas, A.P.R. 2013. Chemometrics: Theory and Application. In *Multivariate Analysis in Management, Engineering and the Sciences*. InTech.

Shah, P.S., Patel, K.G., Shah, P.A. & Gandhi, T.R. 2020. Uv-spectrophotometry-assisted chemometric methods for simultaneous determination of ambroxol hydrochloride and doxofylline in pharmaceutical formulation. *Journal of Chemical Metrology*, 14(2): 106–113.

Shantier, S.W. 2020. Drug Analysis. In Ua. J. Ahmad, ed. *Pharmaceutical Formulation Design - Recent Practices*. London: IntechOpen. www.intechopen.com.

Singh, I., Juneja, P., Kaur, B. & Kumar, P. 2013. Pharmaceutical Applications of Chemometric Techniques. *ISRN Analytical Chemistry*, 2013: 1–13.

Sivasubramanian, L. 2016. Spectrophotometric Multicomponent Analysis of Irbesartan, Hydrochlorothiazide and Ramipril in Pharmaceutical Formulations by Chemometric Techniques. *Journal of Analytical & Pharmaceutical Research*, 2(3).

Sowjanya, G., Ganapaty, S. & Almas, S. 2018. Derivative UV Spectroscopic Approaches in Multicomponent Analysis - A Review. *International Journal of Pharmacy and Pharmaceutical Sciences*, 11(2): 1–11.

Suhartati, T. 2017. *Dasar-Dasar Spektrofotometri UV-Vis dan Spektrometri Massa untuk Penentuan Struktur Senyawa Organik*. Bandar Lampung: CV. Anugrah Utama Raharja.

Supriyadi, E., Mariani, S., & Sugiman. 2017. Perbandingan Metode Partial Least Square (PLS) Dan Principal Component Regression (PCR) Untuk Mengatasi Multikolinearitas Pada Model Regresi Linear Berganda. *UNNES Journal of Mathematics*. 6(2): 117-128.

Sweetman, S.C. 2009. *Martindale : the complete drug reference*. Pharmaceutical Press.

Tangri, P., Mamgain, P., Shaffi, Verma, A.M. & Lakshmayya. 2014. In Process Quality Control: A Review. *International Journal of Industrial Pharmacy and Bio Sciences*, 1(1): 48–59. https://www.researchgate.net/publication/264129319.

Trerattanavong, K. & Tadi, P. 2022. Glimepiride. *StatPearls Publishing*. https://www.ncbi.nlm.nih.gov/books/NBK554600/ 3 April 2023.

LAMPIRAN

Lampiran 1. Skema Kerja

Skema 1. Preparasi larutan stok

```
┌─────────────────────────────────────┐
│   Baku glimepirid dan metformin      │
└─────────────────────────────────────┘
                    │
                    │   -  Ditimbang masing-masing 25 mg
                    │      glimepirid dan metformin
                    │   -  Dilarutkan dan kemudian
                    │      dicukupkan dengan aquadest
                    │      hingga tanda batas
                    ▼
┌─────────────────────────────────────┐
│            Larutan stok              │
└─────────────────────────────────────┘
```
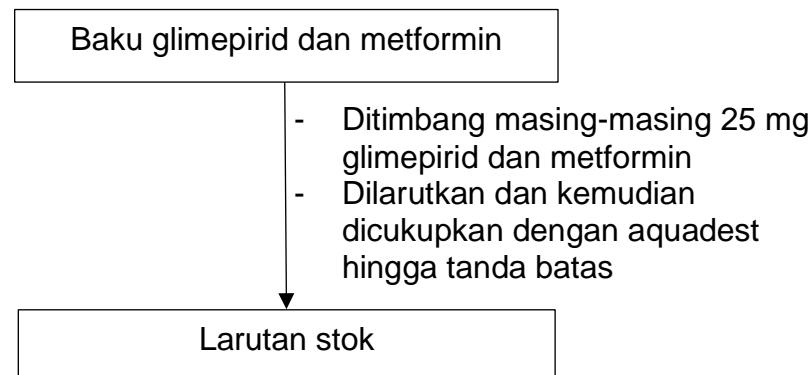
Skema 2. Penentuan panjang gelombang maksimum

```
┌─────────────────────────────────────┐
│            Larutan stok              │
└─────────────────────────────────────┘
                    │
                    │   -  Diencerkan hingga konsentrasi 200
                    │      bpj untuk glimepirid dan 50 bpj
                    │      untuk metformin
                    │   -  Dicukupkan dengan aquadest pada
                    │      labu tentukur 5 ml hingga tanda
                    │      batas
                    ▼
┌─────────────────────────────────────┐
│         Spektrofotometer UV-Vis      │
└─────────────────────────────────────┘
                    │
                    │   -  Diukur pada panjang gelombang
                    │      200-400 nm dengan interval 2 nm
                    ▼
┌─────────────────────────────────────┐
│   Data panjang gelombang maksimum    │
└─────────────────────────────────────┘
```
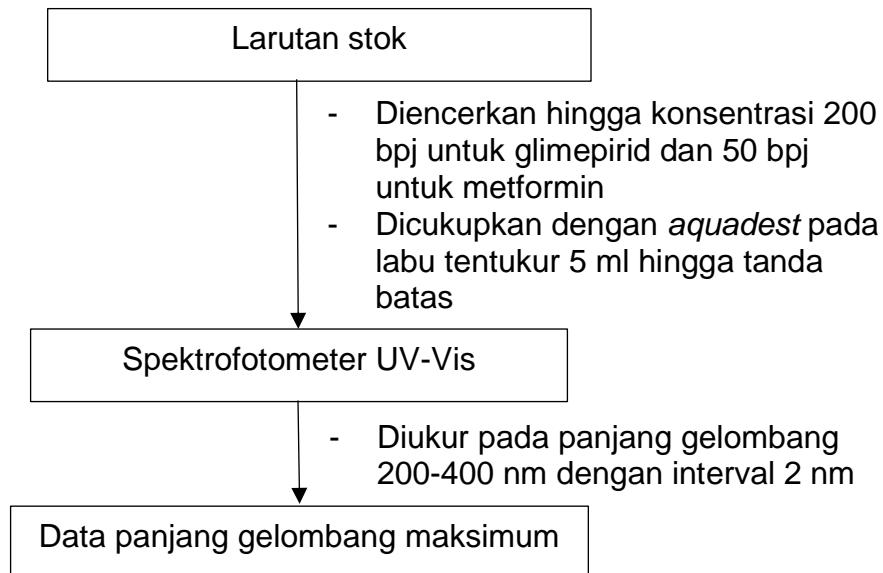
Skema 3. Pembuatan kurva baku

```
┌─────────────────────────────────────┐
│            Larutan stok              │
└─────────────────────────────────────┘
                  │     -  Diencerkan hingga konsentrasi 3-15
                  │        bpj untuk glimepirid dan 5-25 bpj
                  │        untuk metformin
                  │     -  Dicukupkan dengan aquadest pada
                  │        labu tentukur 5 ml hingga tanda
                  │        batas
                  ▼
┌─────────────────────────────────────┐
│        Spektrofotometer UV-Vis       │
└─────────────────────────────────────┘
                  │     -  Diukur pada panjang gelombang
                  │        200-400 nm dengan interval 2 nm
                  │     -  Absorbansi yang diperoleh diplot ke
                  │        dalam grafik dan diregresikan untuk
                  │        memperoleh persamaan regresi
                  │        linear
                  ▼
┌─────────────────────────────────────┐
│             Kurva baku               │
└─────────────────────────────────────┘
```

Skema 4. Analisis secara kemometrik

```
┌─────────────────────────────────────┐
│              Sampel                  │
└─────────────────────────────────────┘
                  │     -  Buat model campuran
                  ▼
┌─────────────────────────────────────┐
│        Spektrofotometer UV-Vis       │
└─────────────────────────────────────┘
                  │     -  Diukur pada panjang gelombang
                  │        200-400 nm dengan interval 2 nm
                  ▼
┌─────────────────────────────────────┐
│        Data absorbansi sampel        │
└─────────────────────────────────────┘
                  │     -  Analisis PLS menggunakan
                  │        software RStudio®
                  ▼
┌─────────────────────────────────────┐
│           Nilai recovery             │
└─────────────────────────────────────┘
```
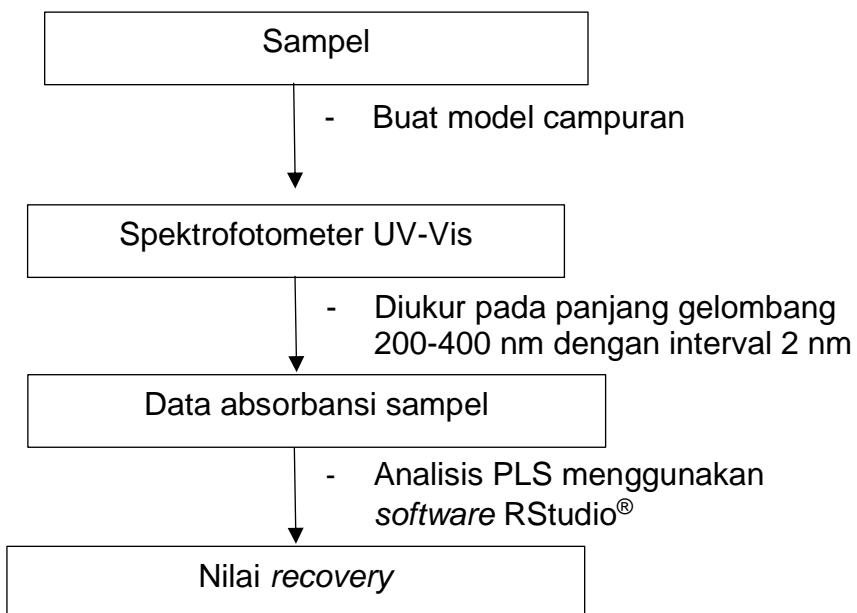
Lampiran 2.   Kurva Baku Glimepirid dan Metformin pada Replikasi Lainnya

Lampiran 2.1 Kurva Baku Glimepirid

Replikasi 1

y = 0.0456 + 0.0588x
R² = 0.9992

Replikasi 3

y = 0.0816 + 0.0574x
R² = 0.9978
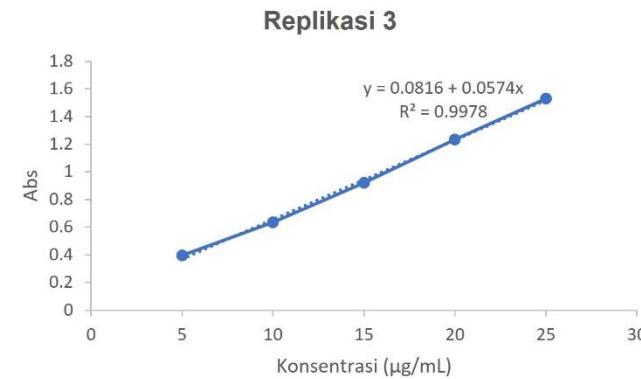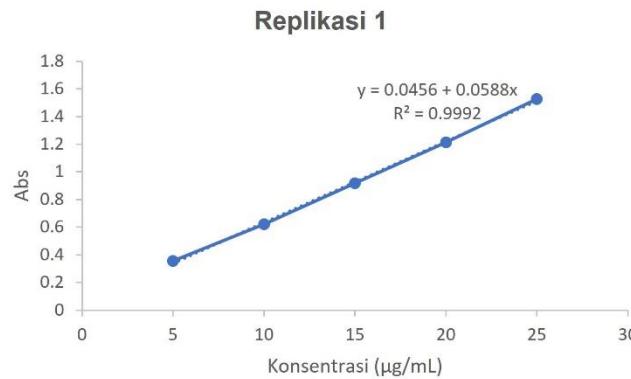
Lampiran 2.2 Kurva Baku Metformin

Replikasi 1

y = 0.033 + 0.0689x
R² = 0.9986

Replikasi 3

y = -0.0118 + 0.0797x
R² = 0.9975
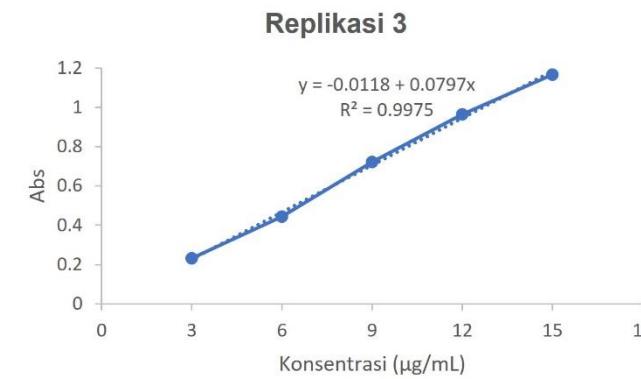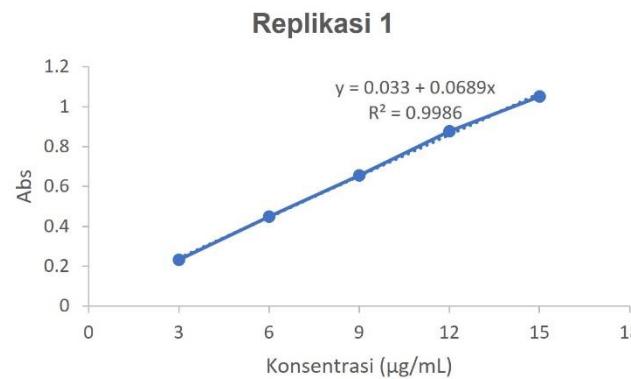
Lampiran 3. Analisis PLS pada Model Campuran Glimepirid dan Metformin

Tabel 5. Analisis PLS pada model campuran glimepirid

| Konsentrasi Metformin (ppm)	Konsentrasi Glimepirid (ppm)	Absorbansi (y_1) pada panjang gelombang tertentu (x)										Prediksi Konsentrasi (ppm)	Persentase *Recovery* (%)
		206	226	230	240	254	258	297	299	303	309		
3	5	0,446	0,417	0,437	0,368	0,097	0,063	0,009	0,008	0,020	0,018	2,97	99,0
3	10	0,603	0,533	0,545	0,430	0,106	0,065	0,007	0,007	0,019	0,018	2,99	99,6
3	15	0,691	0,709	0,725	0,548	0,137	0,088	0,013	0,013	0,024	0,023	3,01	100,3
3	20	0,912	0,935	0,944	0,688	0,175	0,116	0,018	0,017	0,028	0,026	3,00	99,9
3	25	1,005	1,078	1,097	0,806	0,203	0,134	0,035	0,034	0,046	0,046	2,99	99,8
6	5	0,468	0,453	0,490	0,437	0,101	0,058	0,010	0,010	0,022	0,021	6,07	101,2
6	10	0,654	0,633	0,667	0,557	0,132	0,081	0,014	0,013	0,025	0,023	5,92	98,6
6	15	0,809	0,800	0,833	0,661	0,155	0,094	0,011	0,011	0,023	0,022	6,01	100,1
6	20	0,877	0,958	0,993	0,767	0,170	0,100	0,005	0,005	0,017	0,016	6,06	101,0
6	25	1,022	1,135	1,176	0,897	0,201	0,119	0,008	0,007	0,019	0,018	5,96	99,3
9	5	0,681	0,603	0,660	0,626	0,163	0,103	0,045	0,045	0,057	0,055	8,93	99,2
9	10	0,701	0,709	0,772	0,691	0,154	0,087	0,019	0,019	0,030	0,029	9,10	101,1
9	15	0,919	0,925	0,983	0,832	0,199	0,122	0,031	0,031	0,042	0,040	8,95	99,5
9	20	0,960	1,056	1,120	0,913	0,191	0,105	0,004	0,004	0,016	0,015	8,84	98,2
9	25	1,087	1,242	1,304	1,044	0,227	0,130	0,010	0,010	0,021	0,019	9,03	100,3
12	5	0,745	0,713	0,797	0,772	0,180	0,105	0,037	0,036	0,048	0,046	12,04	100,3
12	10	0,826	0,823	0,908	0,829	0,170	0,090	0,011	0,010	0,022	0,019	11,93	99,4
12	15	0,992	1,019	1,103	0,967	0,216	0,124	0,018	0,018	0,029	0,026	12,11	100,9
12	20	1,095	1,184	1,263	1,068	0,227	0,126	0,012	0,012	0,023	0,021	12,22	101,8
12	25	1,224	1,334	1,430	1,173	0,244	0,133	0,003	0,003	0,015	0,014	12,21	101,7
15	5	0,831	0,785	0,891	0,881	0,194	0,105	0,029	0,029	0,040	0,037	14,83	98,9
15	10	0,900	0,940	1,056	1,013	0,245	0,144	0,010	0,010	0,022	0,019	15,21	101,4
15	15	1,012	1,069	1,174	1,059	0,216	0,112	0,011	0,011	0,023	0,021	14,97	99,8
15	20	1,197	1,274	1,387	1,204	0,255	0,140	0,019	0,019	0,030	0,028	15,15	101,0
15	25	1,276	1,425	1,542	1,295	0,264	0,140	0,006	0,005	0,017	0,016	14,79	98,6

Tabel 6. Analisis PLS pada model campuran metformin

Konsentrasi Metformin (ppm)	Konsentrasi Glimepirid (ppm)	Absorbansi (y_1) pada panjang gelombang tertentu (x)										Prediksi Konsentrasi (ppm)	Persentase *Recovery* (%)
		206	226	230	240	254	258	297	299	303	309		
3	5	0,465	0,421	0,442	0,371	0,098	0,063	0,010	0,010	0,021	0,019	4,95	99,1
3	10	0,579	0,535	0,546	0,429	0,108	0,067	0,007	0,006	0,019	0,018	9,87	98,7
3	15	0,687	0,709	0,725	0,548	0,137	0,088	0,013	0,013	0,024	0,023	14,84	98,9
3	20	0,912	0,935	0,944	0,688	0,175	0,116	0,018	0,017	0,028	0,026	19,97	99,9
3	25	1,005	1,078	1,097	0,806	0,203	0,134	0,035	0,034	0,046	0,046	24,71	98,8
6	5	0,475	0,447	0,485	0,434	0,097	0,054	0,006	0,007	0,019	0,018	4,97	99,3
6	10	0,639	0,631	0,664	0,555	0,131	0,080	0,013	0,013	0,025	0,023	10,10	101,0
6	15	0,819	0,800	0,833	0,661	0,155	0,094	0,011	0,011	0,023	0,022	14,86	99,1
6	20	0,881	0,958	0,993	0,767	0,170	0,100	0,005	0,005	0,017	0,016	20,21	101,0
6	25	1,015	1,135	1,176	0,897	0,201	0,119	0,008	0,007	0,019	0,018	24,68	98,7
9	5	0,684	0,603	0,660	0,626	0,163	0,103	0,045	0,045	0,057	0,055	4,95	99,0
9	10	0,692	0,709	0,772	0,691	0,154	0,087	0,019	0,019	0,030	0,029	9,93	99,3
9	15	0,919	0,925	0,983	0,832	0,199	0,122	0,031	0,031	0,042	0,040	14,82	98,8
9	20	0,960	1,056	1,120	0,913	0,191	0,105	0,004	0,004	0,016	0,015	19,80	99,0
9	25	1,093	1,242	1,304	1,044	0,227	0,130	0,010	0,010	0,021	0,019	25,21	100,8
12	5	0,745	0,713	0,797	0,772	0,180	0,105	0,037	0,036	0,048	0,046	5,03	100,7
12	10	0,819	0,823	0,908	0,829	0,170	0,090	0,011	0,010	0,022	0,019	9,93	99,3
12	15	0,990	1,019	1,103	0,967	0,216	0,124	0,018	0,018	0,029	0,026	14,82	98,8
12	20	1,095	1,184	1,263	1,068	0,227	0,126	0,012	0,012	0,023	0,021	19,95	99,7
12	25	1,228	1,334	1,430	1,173	0,244	0,133	0,003	0,003	0,015	0,014	25,21	100,8
15	5	0,831	0,785	0,891	0,881	0,194	0,105	0,029	0,029	0,040	0,037	4,95	99,0
15	10	0,900	0,940	1,056	1,013	0,245	0,144	0,010	0,010	0,022	0,019	9,94	99,4
15	15	1,012	1,069	1,174	1,059	0,216	0,112	0,011	0,011	0,023	0,021	14,79	98,6
15	20	1,197	1,274	1,387	1,204	0,255	0,140	0,019	0,019	0,030	0,028	19,92	99,6
15	25	1,276	1,425	1,542	1,295	0,264	0,140	0,006	0,005	0,017	0,016	25,19	100,8

**Lampiran 4. Dokumentasi Selama Penelitian**

Gambar 10. Proses penimbangan bahan obat
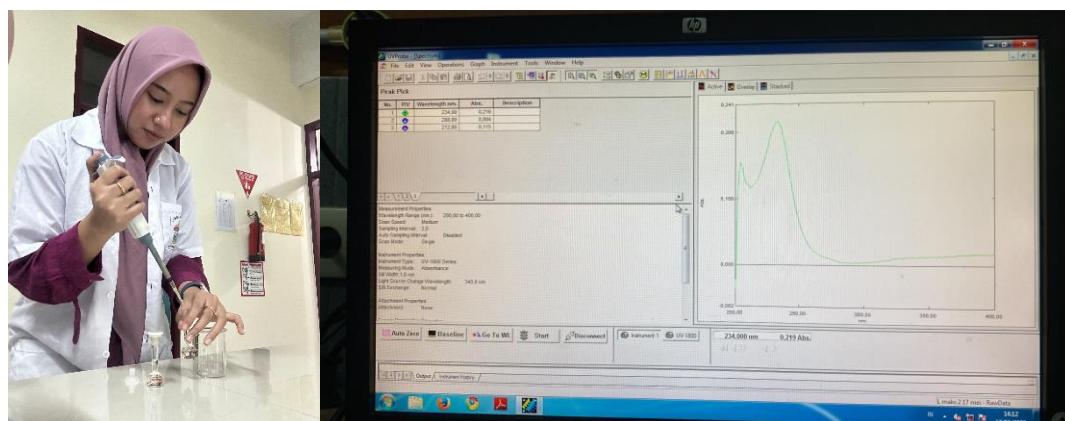
Gambar 11. Pengukuran panjang gelombang maksimum

Gambar 12. Pembuatan seri konsentrasi
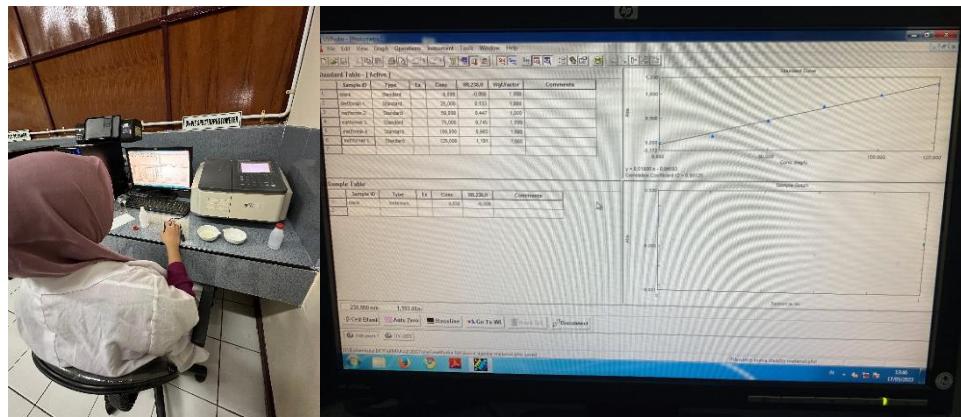
Gambar 13. Pengukuran seri konsentrasi untuk pembuatan kurva baku

Gambar 14. Pembuatan set kalibrasi untuk metformin dan glimepirid
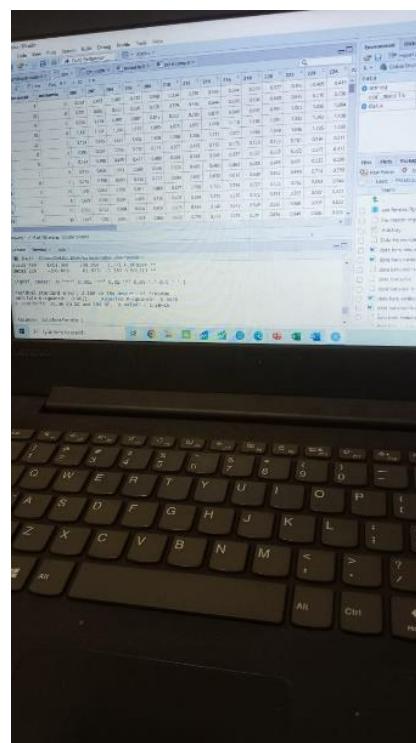
Gambar 15. Pengolahan data menggunakan *software*