

DAFTAR PUSTAKA

- Agustiningsih, A., 2012, Sintesis Senyawa p-Hidroksisinamil Piperidina dari Asam p-Hidroksisinamat dan Piperidin dengan Katalis Asam Borat, Skripsi tidak diterbitkan, Program Sarjana Universitas Hasanuddin, Makassar.
- Arnason, J.T., dan Bernards M.A., 2010, Impact of Constitutive Plant Natural Products on Herbivore and Pathogens, NRC Research Press, 88: 615-627
- Astuti, Y.N. (2009). Uji aktivitas penangkap radikal DPPH oleh analog kurkumin monoketon dan n-heteroalifatik monoketon. Universitas Muhammadiyah, Surakarta.
- Bahria, 2018, *Sintesis Senyawa N-Benzilkafeamida dan N-Benzilferulamida Serta Uji Bioaktivitasnya Sebagai Antikanker*, Tesis Belum Dipublikasikan, Makassar: Program Pascasarjana, Univeritas Hasanuddin
- Bhandarkar, N. S., Brown, L., & Panchal, S. K., 2018, Chlorogenic Acid Attenuates High-Carbohydrate, High-Fat Diet-Induced Cardiovascular, Liver, And Metabolic Changes In Rats. *Nutrition Research*.
- Caia, Y., Luob, Q., Sunc, M., Corkea, H., 2004. Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. *Life Sci.* 74, 2157-2184
- Chung, H. S., dan Shin, J. C., 2007, Characterization of Antioxidant Alkaloids and Phenolic Acids from Anthocyanin-pigmented Rice (*Oryza sativa*), *Food Chem.*, **104**(4): 1670-1677.
- Crozier, A., Clifford, M.N., Ashihara, H., 2006, *Plant Secondary Metabolites, Occurrence, Structure and Role in The Human Diet*, Blackwell Publishing Ltd., Oxford.
- De, P., Baltas, M., dan Bernal, F. B., 2011, Cinnamic Acid Derivatives as Anticancer Agents - A Review, *Curr. Med. Chem.*, **18**: 1672- 1703.

- De, P., Veau, D., Belval, F.B., Chassaing, S., dan Baltas, M., 2012, *Understanding Tuberculosis - New Approaches to Fighting Against Drug Resistance, Chapter 15 Cinnamic Derivatives in Tuberculosis*, In Tech, Croatia.
- Ekowati, J., Tejo, B. A., Sasaki, S., Highasiyama, K., Sukardiman, Siswandono, dan Budiati, T., 2012, Structure Modification of Ethyl *p*-Methoxycinnamate and Their Bioassay as Chemopreventive Agent Against Mice's Fibrosarcoma, *Int. J. Pharm. Pharmaceutical Sci.*, **4**(3): 528-532.
- Fischer, V., Touraud, D., Kunz, W., 2016, Eco-Friendly One Pot Synthesis Of Caffeic Acid Phenethyl Ester (Cape) Via An In-Situ Formed Deep Eutectic Solvent, *Sustainable Chemistry and Pharmacy*, **4** : 40 - 45
- Firdaus, Soekamto, N. H., Permatasari, N. U., Seniwati, Sukarti, Makmun, dan Agustiningsih, A., 2012, Sintesis Senyawa Turunan Sekunder dan Tersier *p*-Kumaramida dan Uji Aktivasnya sebagai Anti Tumor Sel Leukimia P-388, *Ind. Chim. Acta*, **5**(2): 1-7.
- Firdaus, Seniwati, Alamsyah, N., Paramita S., 2019, Synthesis And Activity Of N-(*o*-tolyl)Caffeamide And N-(*o*-tolyl)-*p*-Coumaramide Against P388 Leukemia Murine Cells, *Journal of Physics: Conference Series*, **1341**: 032005
- Firdaus, Soekamto, N. H., dan Karim, A., 2009, Sintesis Senyawa *p*-hidroksisinamamida dari Asam *p*-hidroksisinamat melalui Reaksi Esterifikasi dan Amonolisis, *Ind. Chim. Acta*, **2**(2):37-43.
- Firdaus, Soekamto, N. H., Umar, U., Dali, S., Makmun dan Agustiningsih, A., 2012, *Sintesis Derivate Senyawa p-kumaramida dan Uji Bioaktivitasnya Terhadap Sel Kanker Leukemia P-388*, Laporan Penelitian, Universitas Hasanuddin, Makassar.
- Ganiswarna, S., 1995, Farmakologi dan Terapi, edisi IV, 271-288 dan 800-810, Bagian Farmakologi Fakultas Kedokteran Universitas Indonesia, Jakarta.
- Georgiev, L., Chochkova, M., Ivanova, G., Najdenski, H., Ninova, M., dan Milkova, T., 2012 Radical Scavenging and Antimicrobial Activities of Cinnamoyl Amides of Biogenic Monoamines, *Rivista Italiana Delle Sostanze Grasse*, **89**(2): 91–102.

- Gouthamchandra, K., Sudeep, H. V., Venkatesh, B. J., Shyam Prasad, K., 2017, Chlorogenic Acid Complex (CGA7), Standardized Extract From Green Coffee Beans Exerts Anticancer Effects Against Cultured Human Colon Cancer Hct-116 Cells, *Food Science and Human Wellness*, **6**(3), 147–153.
- Guzman, J. D., 2014, Synthetic Derivatives and Hybrids with Antimicrobial Activity, *Molecules*, **19**: 19292-19349.
- Hartanti, L. dan Setiawan, H.K., 2009, Inhibitor Potential of Some Synthetic Cinnamic Acid Derivatives Towards Tyrosinase Enzyme, *Indo J.Chem.*, **9**(1): 158-168.
- Helm, R. F., Ralph, J., dan Hatfield, R. D., 1992, Synthesis of Feruloylated and *p*-Coumaroylated Methyl Glycosides, *Carbohydr. Res.*, **229**: 183-194
- Hermawan, A., Hana, W. dan Wiwiek, T., 2007. Pengaruh Ekstrak Daun Sirih (*Piper betle* L.) terhadap Pertumbuhan *Staphylococcus aureus* dan *Escherichia coli* dengan Metode Diffusi Disk. Surabaya: Unair.
- Ilyas, A., 2008, *Isolasi dan Identifikasi Metabolit Sekunder dari Ekstrat Etilasetat Kulit Akar Tumbuhan *Kleinhovia hospita* Linn. (*Paliasa*) dan Uji Toksisitasnya Terhadap *Artemia salina* Leach*, Tesis tidak dipublikasikan, Program Pascasarjana Universitas Hasanuddin, Makassar.
- Jitareanu, A., Tataringa, G., Zbancioc, M., Tuchilus, C., Balan, M., dan Stanescu, U., 2013, Cinnamic acid Derivatives and 4-Aminoantipyrine Amides – Synthesis and Evaluation of Biological Properties, *Res. J. Chem. Sci.*, **3**(3): 9-13.
- Julianus, J., Luckyvano, E., 2014, Sintesis Asam Sinamat dari Benzaldehida dan Asam Malonat dengan Katalis Dietilamina, *Jurnal Farmasi Sains dan Komunitas*, **11**(1) : 1 – 6.
- Kylli, P., Nousiainen, P., Biely, P., Sipila, J., Tenkanen, M., Heinonen, M., 2008. Antioxidant potential of hydroxycinnamic acid glycoside esters. *J. Agric. Food Chem.* **56** (12), 4797–4805.
- Kusmayati dan Agustini, N.W.R. 2007. Uji Aktivitas Senyawa Antibakteri dari Mikroalga (*Porphyridium cruentum*), *J Biod.* **8**(1) : 48– 53.

- Koumenis, C., dan Naczki, C., 2004, Method of Using Caffeic Acid Phenethyl Ester and Analogs There of as Radiation Sensitizers, *U.S.A. Patent*.
- Lim, J.Y., Ishiguro, K., Kubo, I., 1999. Tyrosinase inhibitory p-coumaric acid from ginseng leaves. *Phytother. Res.* 13, 371-375.
- Lou, Z., Wang, H., Rao, S., Sun, J., Ma, C., & Li, J. (2012). p-Coumaric acid kills bacteria through dual damage mechanisms. *Food Control*, 25(2), 550–554. doi:10.1016/j.foodcont.2011.11.022
- Lu, F., dan Ralph, J., 1998, Facile Synthesis of 4-Hydroxycinnamyl *p*-Coumarates, *J. Agric. Food Chem.*, 46: 2911–2913.
- Madigan, M.T., J.M. Martinko, and J. Parker., 2009. *Biology of Microorganisms*. 12th ., New York: Prentice Hall International.
- Marwati, J. S., 2012, *Sintesis Senyawa Potensial Anti Kanker Turunan Asam Sinamat*, Tesis Tidak Diterbitkan, Magister Sains Ilmu Kimia, Program Pascasarjana, UI, Depok.
- Montalbetti, C. A. G. N., dan Falque, V., 2005, Amide Bond Formation and Peptide Coupling, *Tetrahedron*, **61**: 10827-10852.
- Morishita, H., dan Ohnishi, M., 2001, Absorption, Metabolism and Biological Activities of Chlorogenic Acids and Related Compounds, *Stud. Nat. Prod. Chem.*, **25**: 919-953.
- Nagasaka, R., Chotimar, C., Shafiqul, I. M., Hori, M., Ozaki, H., and Ushio, H., 2007, Anti-Inflammatory Effect of Hydroxycinnamic Acid Derivatives, *Biochem. Biophys. Res. Commun*, 35: 615-619.
- Naz, S., Ahmad, S., Rasool, S.A., Sayeed, S.A., dan Siddiqi, R., 2006, Antibacterial Activity Directed Isolation of Compounds from *Onosma hispidum*, *Microbiol. Res.*, **161**(1): 43-48.
- Nomura, E., Kashiwada, A., Hosoda, A., Nakamura, K., Morishita, H., Tsuno, T., dan Taniguchi, H., 2003, Synthesis of Amide Compounds of Ferulic Acid, and Their Stimulatory Effects on Insulin Secretion In Vitro, *Bioorg. Med. Chem.*, **11**: 3807-3813.
- Nong, W., Zhao, A., Wei, J., Lin, X., Wang, L., dan Lin, C., 2017, Synthesis and biological evaluation of a new series of cinnamic acid amide derivatives as potent haemostatic agents containing a 2-aminothiazole substructure, *Bioorganic & Medicinal Chemistry Letters*, **27**(18), 4506–4511.

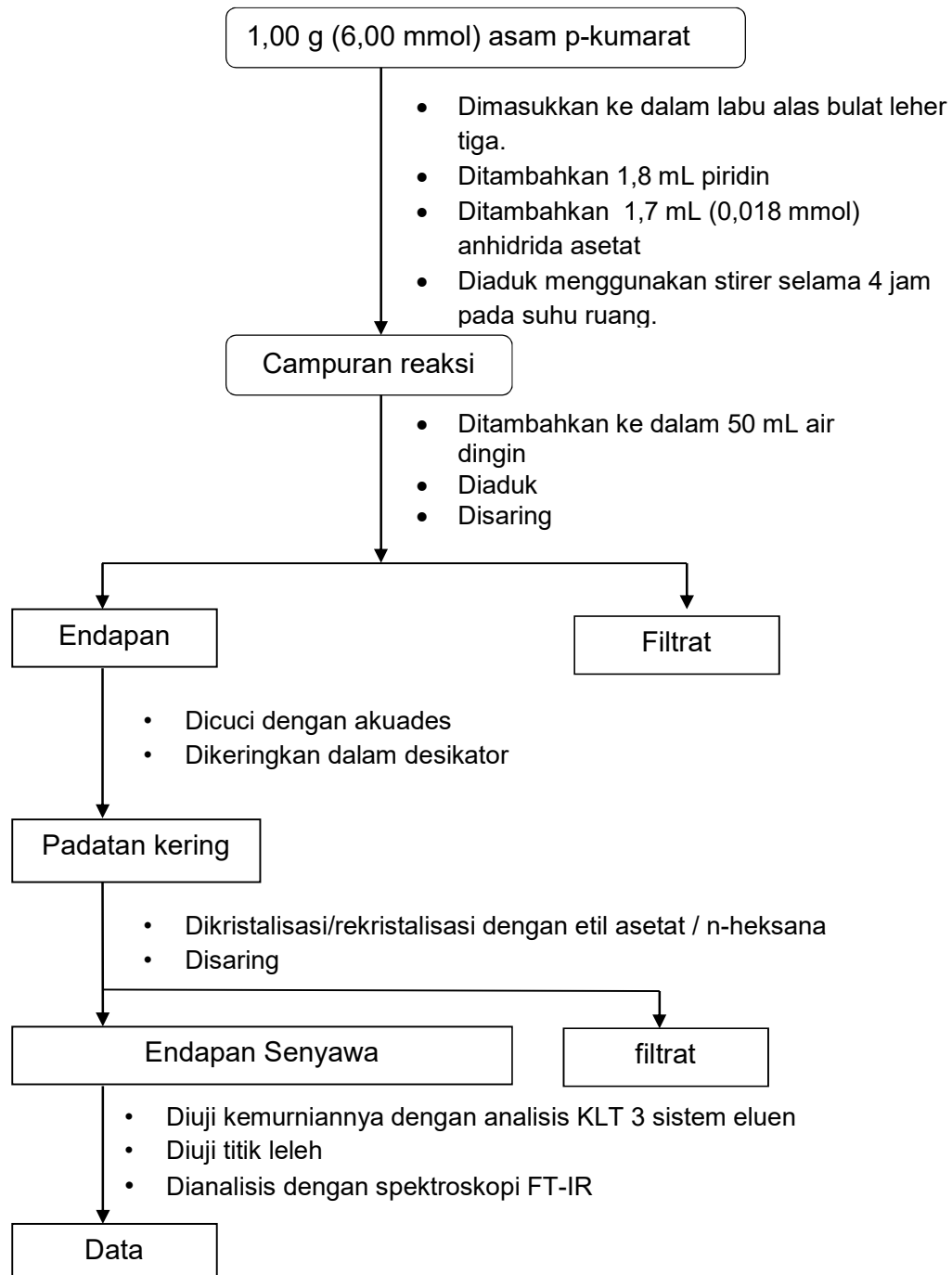
- Parveen, I., Threadgill, M. D., Hauck, B., Donnison, I., Winters, A., 2011, Isolation, Identification and Quantitation of Hydroxycinnamic acid Conjugates, Potential Platform Chemicals, in the Leaves and Stems of *Miscanthus giganteus* Using LC-ESI-MS, *Phytochemistry*, **72** : 2376 - 3284
- Pelczar, Michael J. ECS. Chan., 2008. Dasar-dasar Mikrobiologi. Jakarta. UI Press.
- Rajan, P., Vedernikova, I., Cos, P., Berghe, D. V., Augustynsa, K., dan Haemers, K., 2001, Synthesis and Evaluation of Caffeic Acid Amides as Antioxidants, *Bioorg. Med. Chem. Lett.*, **11**: 215-217.
- Sharma, P., 2011, Cinnamic Acid Derivatives: A New Chapter of Various Pharmacological activities, *J. Chem. Pharm. Res.*, **3**(2) : 403-423.
- Shargel, L., dan Yu, A., 1988, *Biofarmasetika dan Farmakokinetika*, Diterjemahkan Oleh Fasih dan Siti Syamsiah, 2004, Edisi II, Universitas Airlangga Press, Surabaya.
- Silva, T., Oliveira C., Borges, F., 2014, Caffeic Acid Derivatives, Analogs And Applications: A Patent Review (2009 -- 2013), *Expert Opin. Ther. Patents*, **24**(11) : 1 – 14.
- Slavchev, I., Dobrikov, G. M., Valcheva, V., Ugrinova, I., Pasheva, E., dan Dimitrov, V., 2014, Antimycobacterial activity generated by the amide coupling of (-)-fenchone derived aminoalcohol with cinnamic acids and analogues, *Bioorganic & Medicinal Chemistry Letters*, **24**(21), 5030–5033.
- Stankova, I., Chuchkov, K., Shishkov, S., Kostova, K., Mukova, L., dan Galabov, A. S., 2009, Synthesis, Antioxidative and Antiviral Activity of Hydroxycinnamic Acid Amides of Thiazole Containing Amino Acid, *Amino Acids*, **37**: 383–388.
- Sulistyo. 1971. Farmakologi dan Terapi. Yogyakarta: EKG
- Tang, 2005, Boroc Acid Catalyzed Amide Formation From Carboxylic Acid and Amines *N*-Benzyl-4-Phenylbutyramide, *Org. Syn.*, **81**: 262.

Teixeira, J., Gaspar, A., Garrido, E. M., Garrido, J., Borges, F., 2013, Hydroxycinnamic Acid Antioxidants: An Electrochemical Overview, *BioMed Research International*, 1–11.

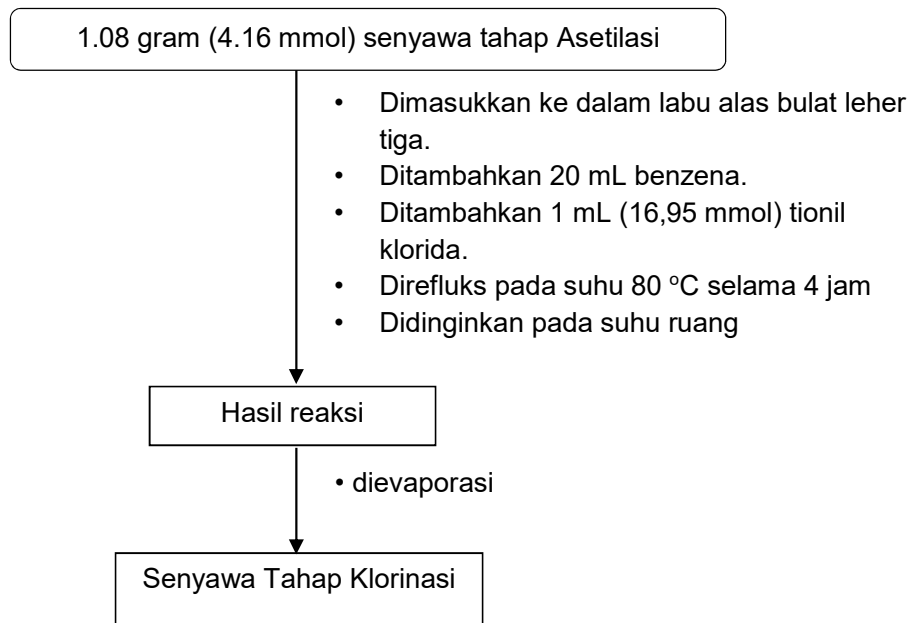
Winarsih, H., 2005, *Antioksidan Alami dan Radikal Bebas*, Penerbit Kanisius, Yogyakarta

Lampiran 1. Bagan Prosedur Penelitian

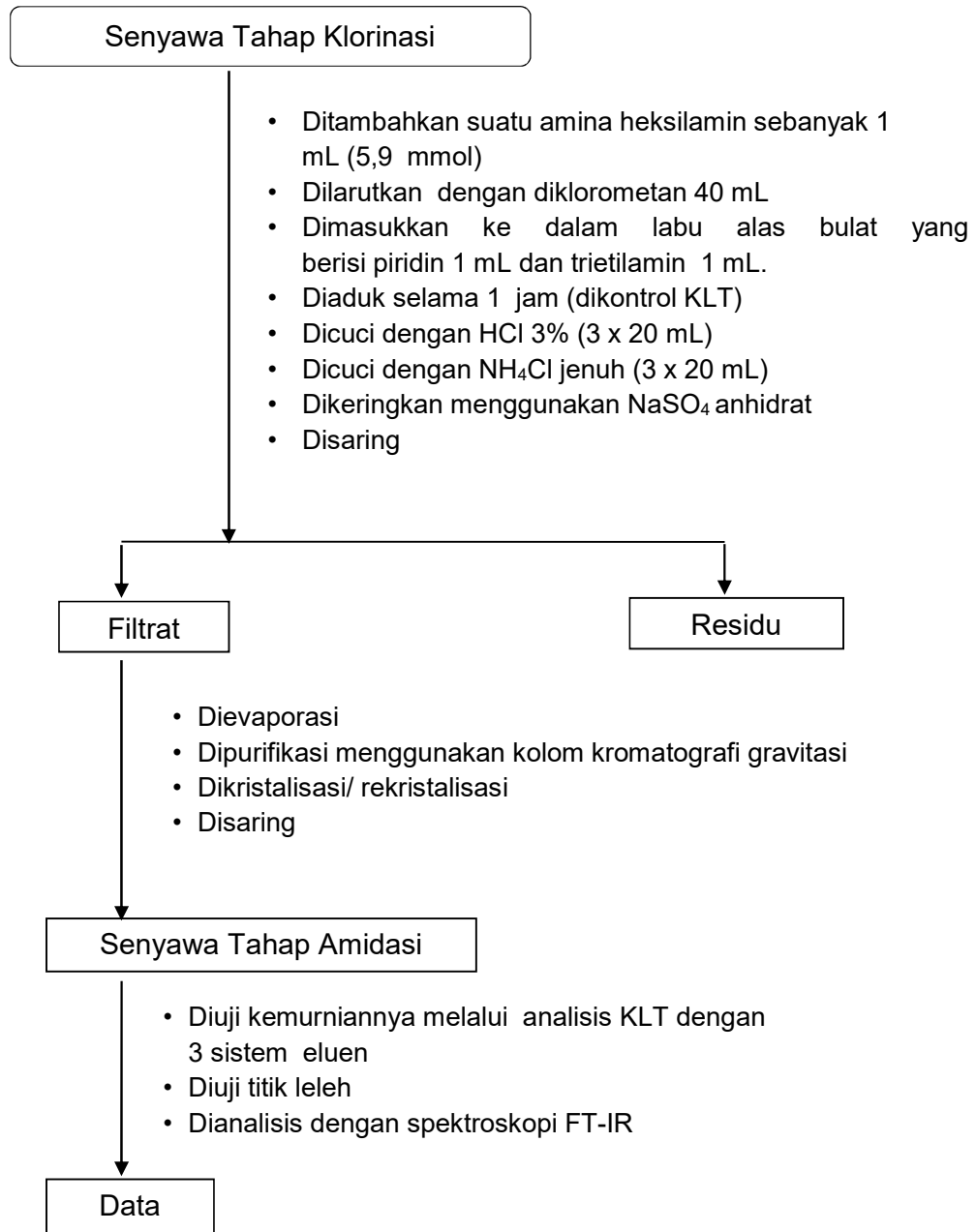
A. Prosedur Asetilasi



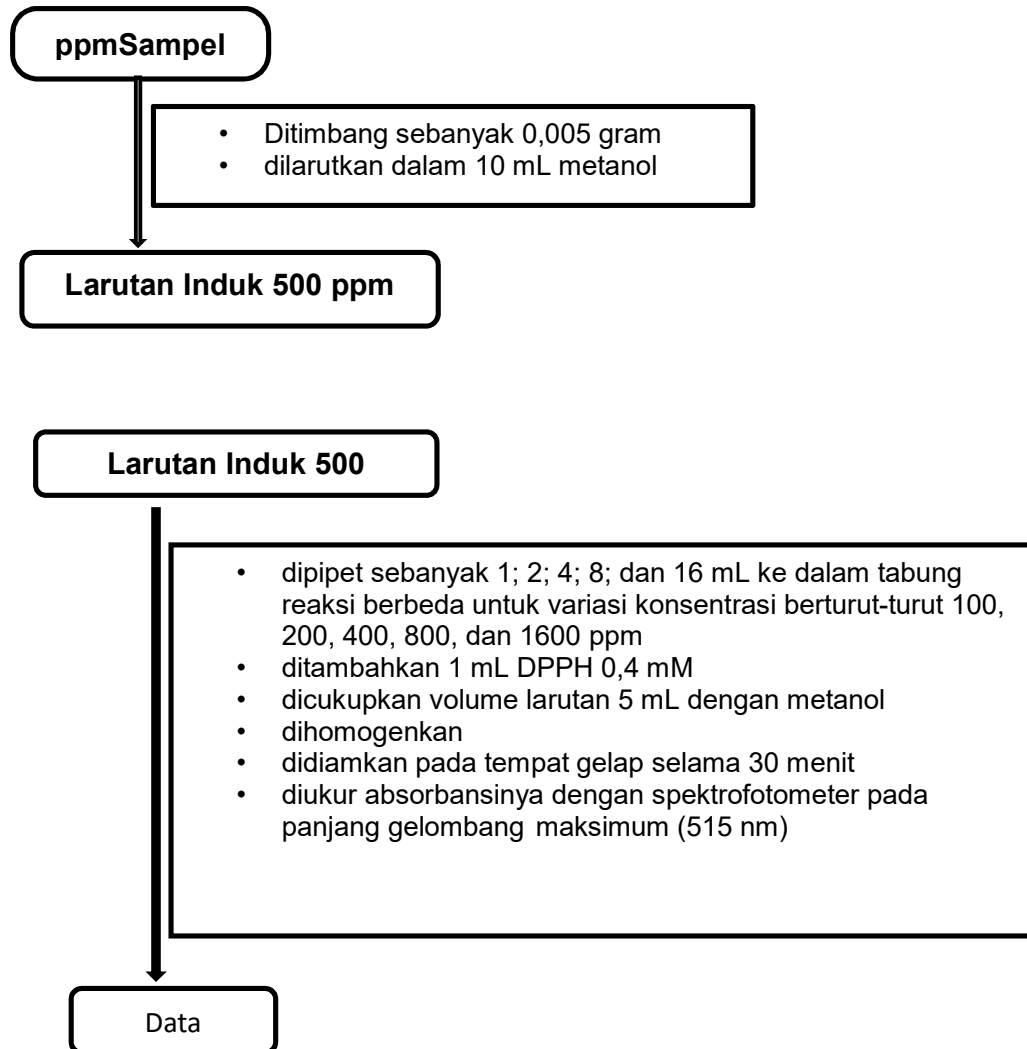
B. Prosedur Klorinasi



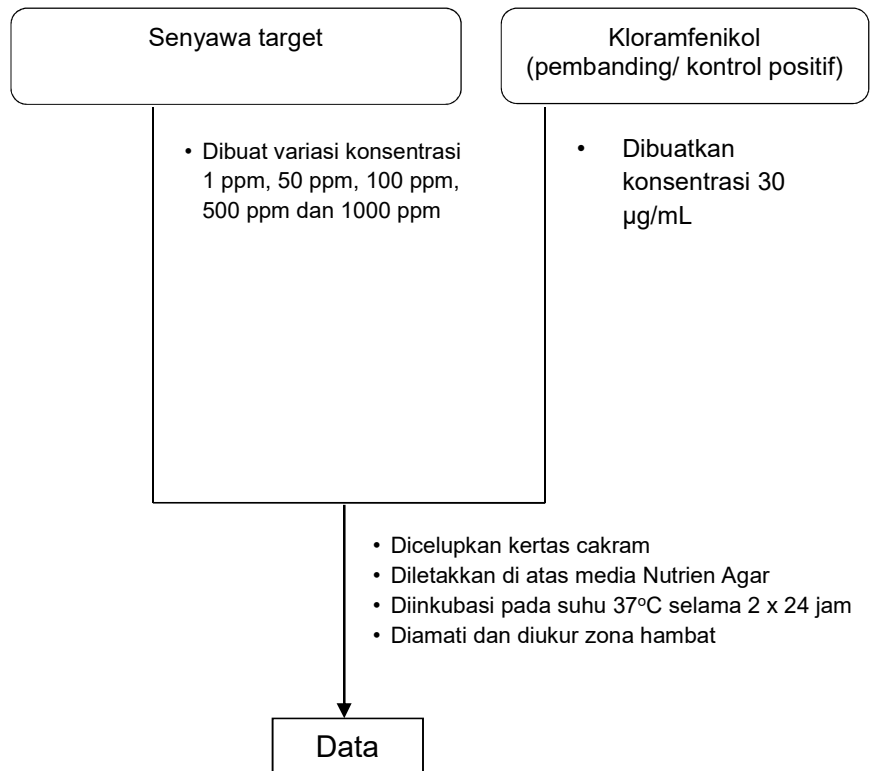
C. Prosedur Amidasi



D. Uji Bioaktivitas sebagai Antioksidan



E. Uji bioaktivitas antibakteri



Lampiran 2. Perhitungan Reaktan

1. Sintesis Senyawa asam 3-(4-asetoksifenil)akrilat

1.1 Asam *p*-kumarat

$$\begin{aligned} \text{mol asam } p\text{-kumarat} &= \frac{\text{massa asam } p\text{-kumarat}}{\text{Mr asam } p\text{-kumarat}} \\ &= \frac{1,00 \text{ g}}{164,16 \text{ g/mol}} \\ &= 0,006 \text{ mol} \\ &= 6,0 \text{ mmol} \end{aligned}$$

1.2 Anhidrida Asetat

$$\begin{aligned} \text{mol anhidrida asetat} &= 3 \text{ kali mol asam } p\text{-kumarat} \\ &= 3 \times 0,006 \text{ mol} \\ &= 0,018 \text{ mol} \\ &= 18 \text{ mmol} \end{aligned}$$

$$\begin{aligned} \text{massa anhidrida asetat} &= \text{mol anhidrida asetat} \times \text{Mr anhidrida asetat} \\ &= 0,018 \text{ mol} \times 102,09 \text{ g/mol} \\ &= 1,84 \text{ g} \end{aligned}$$

$$\begin{aligned} \text{volume anhidrida asetat} &= \frac{\text{massa anhidrida asetat}}{\rho \text{ anhidrida asetat}} \\ &= \frac{1,84 \text{ g}}{1,082 \text{ g/mL}} \\ &= 1,7 \text{ mL} \end{aligned}$$

2. Sintesis Senyawa 4-(3-chloro-3-oxopropenyl)phenyl acetate

2.1 Hasil Senyawa 4-(3-chloro-3-oxopropenyl)phenyl acetate

$$\begin{aligned} \text{mol senyawa} &= \frac{\text{massa senyawa } \mathbf{1}}{\text{Mr senyawa } \mathbf{1}} \\ &= \frac{1,0846 \text{ g}}{206,20 \text{ g/mol}} \\ &= 0,005 \text{ mol} \end{aligned}$$

$$= 5 \text{ mmol}$$

2.2 Tionil Klorida

$$\text{mol tionil klorida} = 5 \times \text{mol senyawa 1}$$

$$= 5 \times 0,005 \text{ mol}$$

$$= 0,025 \text{ mol}$$

$$= 25 \text{ mmol}$$

$$\text{massa tionil klorida} = \text{mol tionil klorida} \times \text{Mr tionil klorida}$$

$$= 0,005 \text{ mol} \times 118,97 \text{ g/mol}$$

$$= 2,9743 \text{ g}$$

$$\text{volume tionil klorida} = \frac{\text{massa tionil klorida}}{\text{densitas tionil klorida}}$$

$$= \frac{2,9743 \text{ g}}{1,678 \text{ g/mL}}$$

$$= 1,7 \text{ mL}$$

3. Sintesis Senyawa 4-(3-hexylamine-3-oxopropenyl)phenyl acetate

3.1 Heksilamin

$$\text{mol heksilamin} = 1,1 \times \text{mol senyawa 4-(3-hexylamine-3-oxopropenyl)phenyl acetate}$$

$$= 1,1 \times 0,005 \text{ mol}$$

$$= 0,0055 \text{ mol}$$

$$= 5,5 \text{ mmol}$$

$$\text{massa heksilamin} = n \text{ butilamin} \times \text{Mr heksilamin}$$

$$= 0,0055 \text{ mol} \times 289 \text{ g/mol}$$

$$= 1,5895 \text{ g}$$

$$\text{volume heksilamin} = \frac{\text{massa heksilamin}}{\text{densitas heksilamin}}$$

$$= \frac{1,5895 \text{ g}}{0,77 \text{ g/mL}}$$

$$= 2,1 \text{ mL}$$

3.2 Piridin

$$\begin{aligned}\text{mol piridin} &= 0,25 \times \text{mol senyawa 1} \\ &= 0,25 \times 0,005 \text{ mol} \\ &= 0,00125 \text{ mol} \\ &= 0,1 \text{ mmol} \\ \text{massa piridin} &= 0,00125 \text{ mol} \times 79,1 \text{ g/mol} \\ &= 0,09888 \text{ g} \\ \text{volume piridin} &= \frac{\text{massa piridin}}{\text{densitas piridin}} \\ &= \frac{0,09888 \text{ g}}{0,9819 \text{ g/mL}} \\ &= 0,100 \text{ mL}\end{aligned}$$

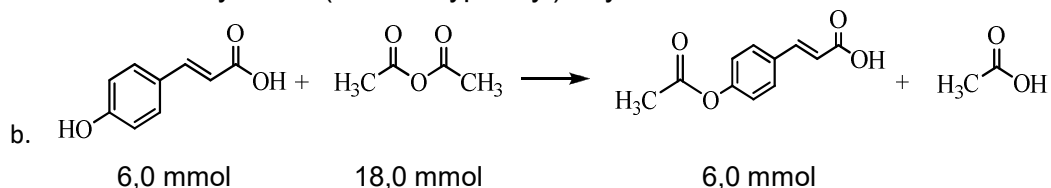
3.3 Trietilamin

$$\begin{aligned}\text{mol trietilamin} &= 0,8 \times \text{mol senyawa 1} \\ &= 0,8 \times 0,005 \text{ mol} \\ &= 0,004 \text{ mol} \\ \text{massa trietilamin} &= 0,004 \text{ mol} \times 101,19 \text{ g/mol} \\ &= 0,4048 \text{ g} \\ \text{volume trietilamin} &= \frac{\text{massa trietilamin}}{\text{densitas trietilamin}} \\ &= \frac{0,4048 \text{ g}}{0,7255 \text{ g/mL}} \\ &= 0,6 \text{ mL}\end{aligned}$$

Perhitungan rendemen

A. Perhitungan Rendemen 3-(4-acetoxyphenyl)acrylic acid

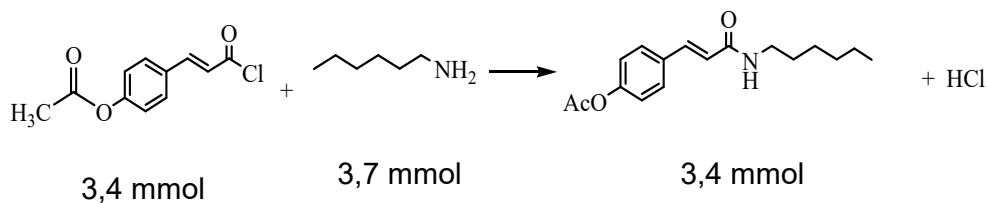
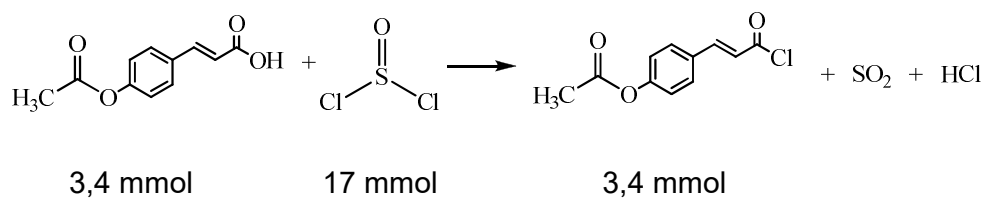
a. Sintesis senyawa 3-(4-acetoxyphenyl)acrylic acid



$$\begin{aligned} \text{Bobot teoritis} &= \text{mol produk} \times \text{Mr produk} \\ &= 0,006 \text{ mol} \times 206 \text{ g/mol} \\ &= 1,236 \text{ g} \end{aligned}$$

$$\begin{aligned} \text{Rendemen} &= \frac{\text{bobot praktek}}{\text{bobot teoritis}} \times 100\% \\ &= \frac{1,0846}{1,236} \times 100\% \\ &= 87,75\% \end{aligned}$$

c. Sintesis senyawa 4-(3-hexylamine-3-oxopropenyl)phenyl acetate



$$\begin{aligned} \text{Bobot teoritis} &= \text{mol produk} \times \text{Mr produk} \\ &= 0,0034 \text{ mol} \times 261 \text{ g/mol} \\ &= 0,887 \text{ g} \end{aligned}$$

$$\begin{aligned}\text{Rendemen} &= \frac{\text{bobot praktek}}{\text{bobot teoritis}} \times 100\% \\ &= \frac{0,1527}{0,887} \times 100\% \\ &= 15,59\%\end{aligned}$$

Lampiran 3. Kriteria rendamen reaksi

Persentase(%)	Kriteria
100	kuantitatif
>90	hebat
>80	Sangat baik
>70	Baik
>50	Cukup baik
>40	buruk

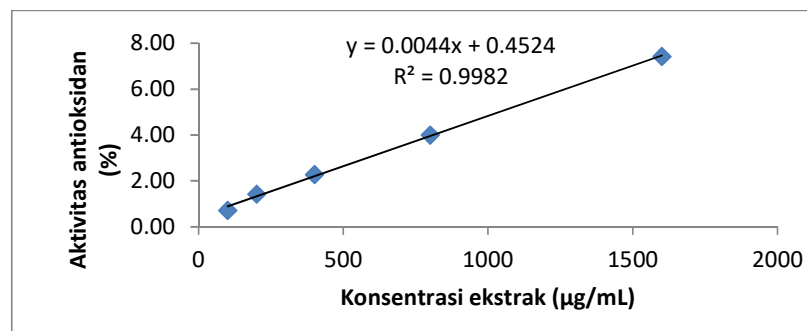
(Vogel et al., A.I., 1996)

**Lampiran 4. Data Hasil Pengukuran Aktivitas Antioksidan senyawa
4-(3-hexylamine-3-oxopropenyl)phenyl acetate**

1. SEMPLO

No	Konsentrasi (µg/mL)	Absorbansi (A) λ = 515 nm	Aktivitas Antioksidan (%)
1	100	0.695	0.71
2	200	0.690	1.43
3	400	0.684	2.29
4	800	0.672	4.00
5	1600	0.648	7.43
6	kontrol	0.700	

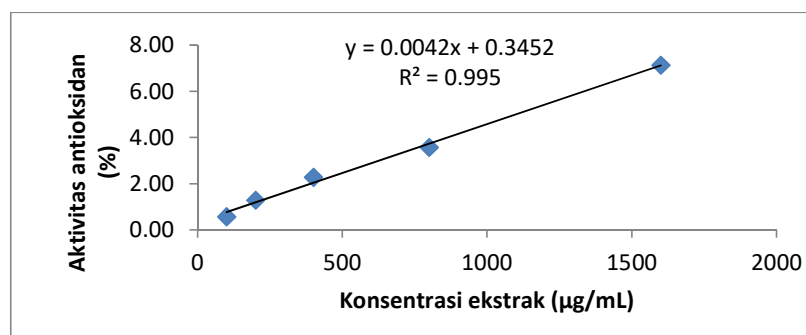
No	Konsentrasi (µg/mL)	Aktivitas Antioksidan (%)	Nilai IC-50 (µg/mL)
1	100	0.71	11260.8182
2	200	1.43	
3	400	2.29	
4	800	4.00	
5	1600	7.43	



2. DUPLO

No	Konsentrasi (µg/mL)	Absorbansi (A) λ = 515 nm	Aktivitas Antioksidan (%)
1	100	0.696	0.57
2	200	0.691	1.29
3	400	0.684	2.29
4	800	0.675	3.57
5	1600	0.650	7.14
6	kontrol	0.700	

No	Konsentrasi (µg/mL)	Aktivitas Antioksidan (%)	Nilai IC-50 (µg/mL)
1	100	0.57	11822.5714
2	200	1.29	
3	400	2.29	
4	800	3.57	
5	1600	7.14	



3. TRIPLO

No	Konsentrasi (µg/mL)	Absorbansi (A) λ = 515 nm	Aktivitas Antioksidan (%)
1	100	0.695	0.71
2	200	0.691	1.29
3	400	0.683	2.43
4	800	0.675	3.57
5	1600	0.648	7.43
6	kontrol	0.700	

No	Konsentrasi ($\mu\text{g/mL}$)	Aktivitas Antioksidan (%)	Nilai IC-50 ($\mu\text{g/mL}$)
1	100	0.71	11275.7045
2	200	1.29	
3	400	2.43	
4	800	3.57	
5	1600	7.43	

