

## DAFTAR PUSTAKA

- Adams, G. 2020. A beginner's guide to RT-PCR, qPCR and RT-qPCR. *Biochem. Lond.* 42(3).
- Alipour Jenagrad, P., Daghig Kia, H., Moghaddam, G., Ebrahimi, M. 2018. Evaluating caffeine antioxidant properties on Ghezel ram sperm quality after freeze-thawing. *Rev. Med. Vet. (Toulouse)*. 169, 233–240.
- Arulselvan, P., Fard, M.T., Tan, W.S., Gothai, S., Fakurazi, S., Norhaizan, M.E., Kumar, S.S. 2016. Role of Antioxidants and Natural Products in Inflammation. *Oxid. Med. Cell. Longev.* 2016.
- Charroux, B., Capo, F., Kurz, C.L., Peslier, S., Chaduli, D., Viallat-lieutaud, A., Royet, J. 2018. Cytosolic and Secreted Peptidoglycan-Degrading Enzymes in Drosophila Respectively Control Local and Systemic Immune Responses to Microbiota. *Cell Host Microbe* 23, 215-228.e4.
- Fischer, R., Maier, O. 2015. Interrelation of oxidative stress and inflammation in neurodegenerative disease: Role of TNF. *Oxid. Med. Cell. Longev.* 2015.
- Gloire, G., Legrand-Poels, S., Piette, J. 2006. NF- $\kappa$ B activation by reactive oxygen species: Fifteen years later. *Biochem. Pharmacol.* 72, 1493–1505.
- Hoffman, H.M. 2009. Therapy of autoinflammatory syndromes. *J. Allergy Clin. Immunol.* 124, 1129–1138.
- Iatsenko, I., Kondo, S., Mengin-Lecreux, D., Lemaitre, B. 2016. PGRP-SD, an Extracellular Pattern-Recognition Receptor, Enhances Peptidoglycan-Mediated Activation of the Drosophila Imd Pathway. *Immunity* 45, 1013–1023.
- Kany, S., Vollrath, J.T., Relja, B. 2019. Cytokines in inflammatory disease. *Int. J. Mol. Sci.* 20, 1–31.
- Kastner, D.L., Aksentijevich, I., Goldbach-Mansky, R. 2010. Autoinflammatory Disease Reloaded: A Clinical Perspective. *Cell* 140, 784–790.
- Khansari, N., Shakiba, Y., Mahmoudi, M. 2009. Chronic Inflammation and Oxidative Stress as a Major Cause of Age- Related Diseases and Cancer. *Recent Pat. Inflamm. Allergy Drug Discov.* 3, 73–80.

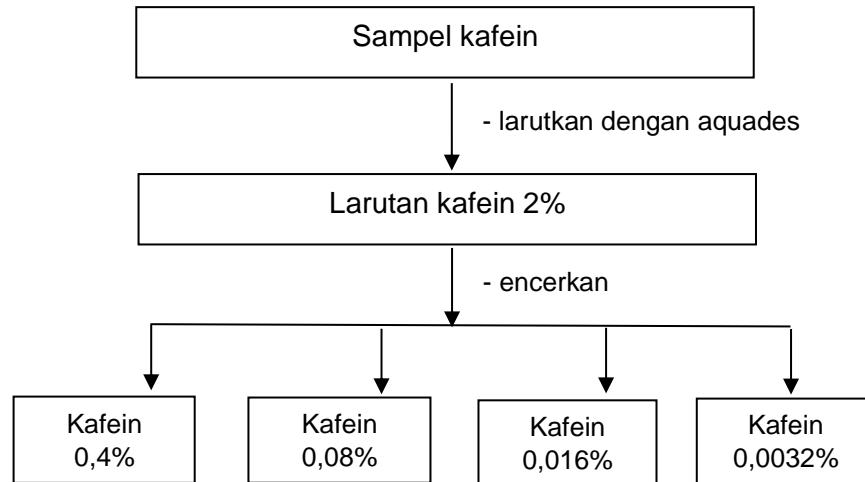
- Kounatidis, I., Chtarbanova, S., Cao, Y., Hayne, M., Jayanth, D., Ganetzky, B., Ligoxygakis, P. 2017. NF-κB Immunity in the Brain Determines Fly Lifespan in Healthy Aging and Age-Related Neurodegeneration. *Cell Rep.* 19, 836–848.
- Kralik, P., Ricchi, M. 2017. A basic guide to real time PCR in microbial diagnostics: Definitions, parameters, and everything. *Front. Microbiol.* 8, 1–9.
- Landis, G. N., & Tower, J. 2005. Superoxide Dismutase Evolution and Life Span Regulation. *Mechanisms of Ageing and Development*, 126 (3), 365–379.
- Lee, J., Song, C.H. 2021. Effect of reactive oxygen species on the endoplasmic reticulum and mitochondria during intracellular pathogen infection of mammalian cells. *Antioxidants* 10.
- Lee, S.H., Min, K.J. 2019. Drosophila melanogaster as a model system in the study of pharmacological interventions in aging. *Transl. Med. Aging* 3, 98–103.
- Liu, R., Gang, L., Shen, X., Xu, H., Wu, F., Sheng, L. 2019. Binding characteristics and superimposed antioxidant properties of caffeine combined with superoxide dismutase. *ACS Omega* 4, 17417–17424.
- Liu, Z., Ren, Z., Zhang, J., Chuang, C.C., Kandaswamy, E., Zhou, T., Zuo, L. 2018. Role of ROS and nutritional antioxidants in human diseases. *Front. Physiol.* 9, 1–14.
- Matos, T.C., Terreri, M.T.R.A., Petry, D.G., Barbosa, C.M., Len, C.A., Hilário, M.O.E. 2009. Autoinflammatory syndromes: Report on three cases. *Sao Paulo Med. J.* 127, 314–316.
- Meier-Schiesser, B., French, L.E. 2021. Autoinflammatory syndromes. *J. Dtsch. Dermatol. Ges.* 19, 400–426.
- Minatel, I.O., Francisqueti, F.V., Corrêa, C.R., Pereira Lima, G.P. 2016. Antioxidant activity of γ-oryzanol: A complex network of interactions. *Int. J. Mol. Sci.* 17.
- Mittal, M., Siddiqui, M.R., Tran, K., Reddy, S.P., Malik, A.B. 2014. Reactive oxygen species in inflammation and tissue injury. *Antioxidants Redox Signal.* 20, 1126–1167.
- Mohammed, M.J., Al-Bayati, F.A. 2009. Isolation, identification and purification of caffeine from Coffea arabica L. and Camellia sinensis L.:

- A combination antibacterial study. *Int. J. Green Pharm.* 3, 52–57.
- Mutsuddi, M., Mukherjee, A. 2019. Insights into human neurodegeneration: Lessons learnt from drosophila, Insights into Human Neurodegeneration: Lessons Learnt from Drosophila.
- Nainu, F. 2018. Review : Penggunaan Drosophila melanogaster Sebagai Organisme Model Dalam Penemuan Obat. *J. Farm. Galen.* 4, 50–67.
- Neckameyer, W.S., Bhatt, P. 2016. Protocols to study behavior in drosophila. *Methods Mol. Biol.* 1478, 303–320.
- Ong, C., Yung, L.Y.L., Cai, Y., Bay, B.H., Baeg, G.H. 2015. Drosophila melanogaster as a model organism to study nanotoxicity. *Nanotoxicology* 9, 396–403.
- Pandey, U.B., Nichols, C.D. 2011. Human Disease Models in. *Pharmacol. Rev.* 63, 411–436.
- Paredes, J.C., Welchman, D.P., Poidevin, M., Lemaitre, B. 2011. Negative regulation by Amidase PGRPs shapes the drosophila antibacterial response and protects the Fly from innocuous infection. *Immunity* 35, 770–779.
- Pham-Huy, L.A., He, H., Pham-Huy, C. 2008. Free radicals, antioxidants in disease and health. *Int. J. Biomed. Sci.* 4, 89–96.
- Pisoschi, A.M., Pop, A. 2015. The role of antioxidants in the chemistry of oxidative stress: A review. *Eur. J. Med. Chem.* 97, 55–74.
- Rahman, M.T., Uddin, M.S., Sultana, R., Moue, A., Setu, M. 2013. Polymerase Chain Reaction (PCR): A Short Review. *Anwer Khan Mod. Med. Coll. J.* 4, 30–36.
- Rodak, K., Kokot, I., Kratz, E.M. 2021. Caffeine as a factor influencing the functioning of the human body—friend or foe? *Nutrients* 13.
- S.A. Deepak, K.R. Kottapalli, R. Rakwal, G. Oros, K.S. Rangappa, H. Iwahashi, Y. Masuo, G.K. Agrawal. 2007. Real-Time PCR: Revolutionizing Detection and Expression Analysis of Genes. *Curr. Genomics* 8, 234–251.
- Shalmashi, A., Golmohammad, F. 2010. Solubility of caffeine in water, ethyl acetate, ethanol, carbon tetrachloride, methanol, chloroform, dichloromethane, and acetone between 298 and 323 K. *Lat. Am. Appl. Res.* 40, 283–285.

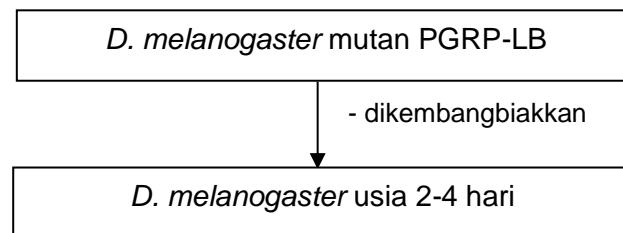
- Simanjuntak, E.J., Zulham, Z. 2020. Superoksid Dismutase (Sod) Dan Radikal Bebas. *J. Keperawatan Dan Fisioter.* 2, 124–129.
- Suh, H.J., Shin, B., Han, S.H., Woo, M.J., Hong, K.B. 2017. Behavioral changes and survival in *Drosophila melanogaster*: Effects of ascorbic acid, taurine, and caffeine. *Biol. Pharm. Bull.* 40, 1873–1882.
- Sutphin, G.L., Bishop, E., Yanos, M.E., Moller, R.M., Kaeberlein, M. 2012. Caffeine extends life span, improves healthspan, and delays age-associated pathology in *Caenorhabditis elegans*. *Longev. Heal.* 1.
- Swinbourne, A.M., Kind, K.L., Flinn, T., Kleemann, D.O., van Wettere, W.H.E.J. 2021. Caffeine: A potential strategy to improve survival of neonatal pigs and sheep. *Anim. Reprod. Sci.* 226, 106700.
- Tartey, S., Kanneganti, T.D. 2020. Inflammasomes in the pathophysiology of autoinflammatory syndromes. *J. Leukoc. Biol.* 107, 379–391.
- Tewabe Gebeyehu, B. 2015. Determination of Caffeine Content and Antioxidant Activity of Coffee. *Am. J. Appl. Chem.* 3, 69.
- Touitou, I., Koné-Paut, I. 2008. Autoinflammatory diseases. *Best Pract. Res. Clin. Rheumatol.* 22, 811–829.
- Tsang, C.K. wa., Liu, Y., Thomas, J., Zhang, Y., Zheng, X.F.S. 2014. Superoxide dismutase 1 acts as a nuclear transcription factor to regulate oxidative stress resistance. *Nat. Commun.* 5, 3446.
- Weydert, C.J., Cullen, J.J. 2010. Measurement of superoxide dismutase, catalase and glutathione peroxidase in cultured cells and tissue. *Nat. Protoc.* 5, 51–66.
- Yashin, A., Yashin, Y., Wang, J.Y., Nemzer, B. 2013. Antioxidant and antiradical activity of coffee. *Antioxidants* 2, 230–245.
- Yasui, K., Baba, A. 2006. Therapeutic potential of superoxide dismutase (SOD) for resolution of inflammation. *Inflamm. Res.* 55, 359–363.

## LAMPIRAN

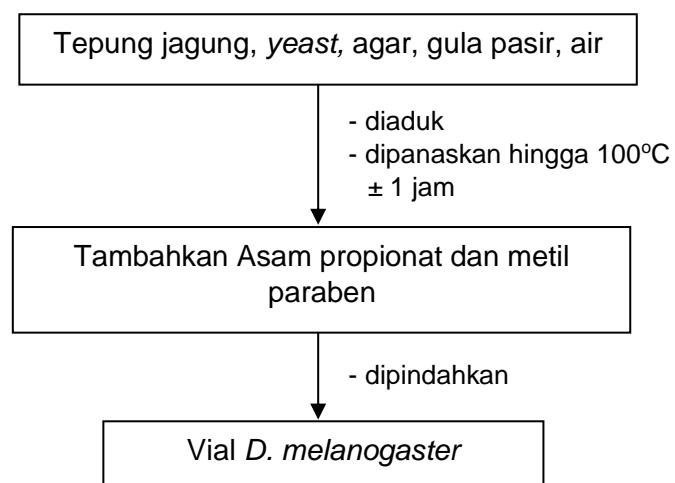
### Lampiran 1. Preparasi Sampel



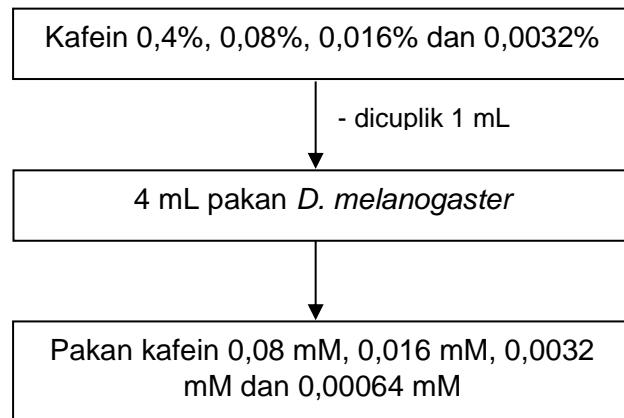
### Lampiran 2. Penyiapan Hewan Uji



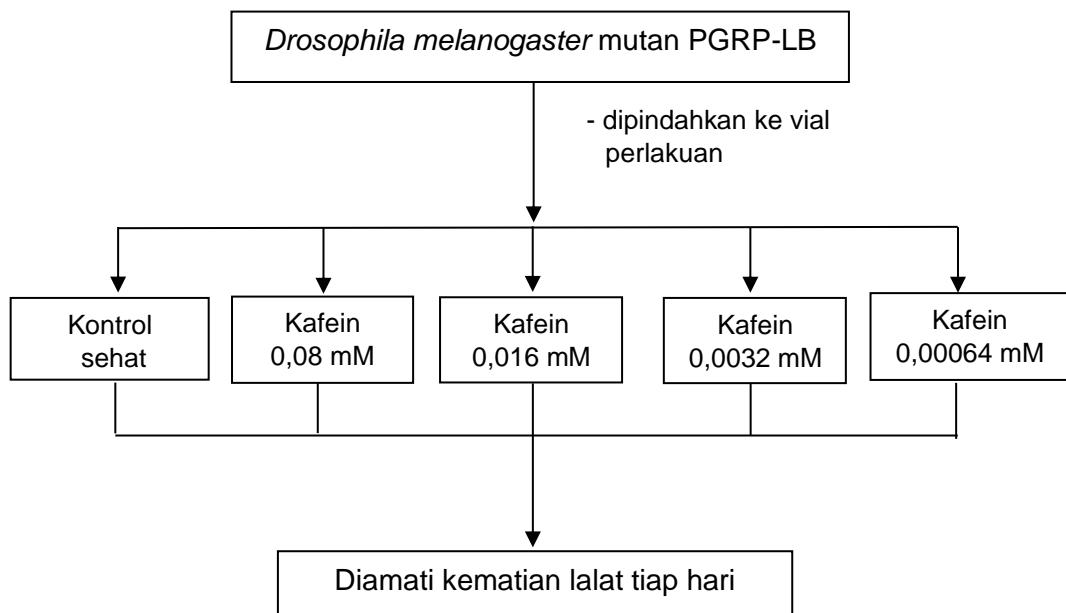
### Lampiran 3. Pembuatan Pakan



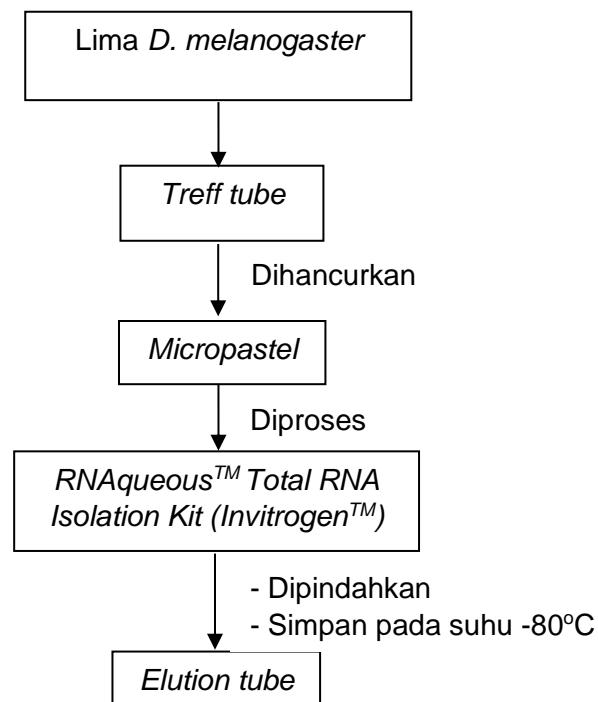
#### Lampiran 4. Penyiapan Pakan Pengujian



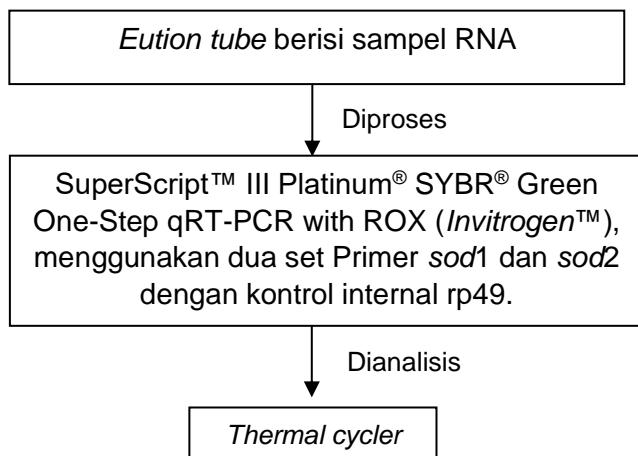
#### Lampiran 5. Skema Kerja Uji Survival



### Lampiran 6. Penyiapan Sampel RNA



### Lampiran 7. Analisis Ekspresi Gen



## Lampiran 8. Hasil Uji Survival

**Tabel 2. Data Hasil Uji Survival**

No	Tanggal	Kontrol tanpa perlakuan	Kafein 0,08 mM	Kafein 0,016 mM	Kafein 0,0032 mM	Kafein 0,00064 mM
1	211113	10/10	10/10	10/10	10/10	10/10
2	211114	10/10	10/10	10/10	10/10	10/10
3	211115	9/10	10/10	10/10	10/10	10/10
4	211116	9/10	10/10	10/10	10/10	10/10
5	211117	9/10	10/10	10/10	10/10	10/10
6	211118	9/10	10/10	10/10	10/10	10/10
7	211119	9/10	10/10	10/10	10/10	10/10
8	211120	9/10	10/10	10/10	10/10	10/10
9	211121	9/10	10/10	10/10	10/10	10/10
10	211122	9/10	9/10	10/10	10/10	10/10
11	211123	8/10	9/10	10/10	9/10	10/10
12	211124	8/10	9/10	10/10	9/10	10/10
13	211125	7/10	7/10	10/10	9/10	10/10
14	211126	7/10	7/10	10/10	9/10	10/10
15	211127	7/10	6/10	10/10	9/10	10/10
16	211128	7/10	6/10	10/10	9/10	10/10
17	211129	7/10	5/10	10/10	9/10	10/10
18	211130	7/10	5/10	10/10	9/10	10/10
19	211201	7/10	5/10	10/10	9/10	10/10
20	211202	7/10	5/10	10/10	9/10	10/10
21	211203	6/10	5/10	10/10	9/10	9/10
22	211204	6/10	4/10	10/10	9/10	9/10
23	211205	6/10	3/10	10/10	9/10	9/10
24	211206	6/10	3/10	10/10	9/10	9/10
25	211207	6/10	3/10	10/10	9/10	9/10
26	211208	6/10	3/10	10/10	9/10	9/10
27	211209	6/10	2/10	10/10	8/10	9/10
28	211210	6/10	1/10	10/10	8/10	9/10
29	211211	6/10	0/10	10/10	8/10	9/10
30	211212	6/10	0/10	10/10	8/10	9/10
31	211213	6/10	0/10	10/10	8/10	9/10
32	211214	6/10	0/10	10/10	8/10	9/10

## Lampiran 9. Data Statistik

**Tabel 3. Hasil one-way anova ekspresi gen sod1**

<b>ANOVA summary</b>	<b>Value</b>
F	12,22
P value	0,0086
P value summary	**
Significant diff. among means ( $P < 0.05$ )?	Yes
R squared	0,9072

**Tabel 4. Hasil uji lanjutan dunnet ekspresi gen sod1**

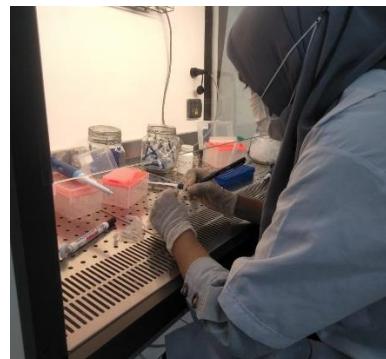
<b>Dunnett's Multiple Comparisons Test</b>	<b>Mean Diff</b>	<b>Summary</b>	<b>Adjusted P Value</b>
Tanpa Perlakuan vs. Kafein 0,08 mM	-7,865	ns	0,0037
Tanpa Perlakuan vs. Kafein 0,016 mM	-5,340	*	0,0196
Tanpa Perlakuan vs. Kafein 0,0032 mM	-4,251	*	0,0486
Tanpa Perlakuan vs. Kafein 0,00064 mM	-2,385	ns	0,2638

**Tabel 5. Hasil one-way anova ekspresi gen sod2**

<b>ANOVA summary</b>	<b>Value</b>
F	0,6948
P value	0,6270
P value summary	ns
Significant diff. among means ( $P < 0.05$ )?	No
R squared	0,3572

**Tabel 6. Hasil uji lanjutan dunnett ekspresi gen sod2**

<b>Dunnett's Multiple Comparisons Test</b>	<b>Mean Diff</b>	<b>Summary</b>	<b>Adjusted P Value</b>
Tanpa Perlakuan vs. Kafein 0,08 mM	-0,2900	ns	0,6897
Tanpa Perlakuan vs. Kafein 0,016 mM	-0,3250	ns	0,6156
Tanpa Perlakuan vs. Kafein 0,0032 mM	-0,02500	ns	0,9999
Tanpa Perlakuan vs. Kafein 0,00064 mM	-0,02000	ns	0,9999

**Lampiran 10. Gambar Penelitian****Gambar 13. Pembuatan Pakan****Gambar 14. Pemisahan Lalat Jantan****Gambar 15. Uji Suvival****Gambar 16. Isolasi RNA****Gambar 17. *Running real time PCR***