

DAFTAR PUSTAKA

- Abukhalil, M.H., Althunibat, O.Y., Aladaileh, S.H., Al-Amarat, W., Obeidat, H.M., Al-Khawakde, A.A.A., Hussein, O.E., Alfwuaires, M.A., Algerare, A.I., Alanazi, K.M., Al-Swailmi, F.K., Arab, H.H., & Mahmoud, Y.M. 2021. Galangin Attenuates Diabetic Cardiomyopathy Through Modulating Oxidative Stress, Inflammation and Apoptosis in Rats. *Biomedicine & Pharmacotherapy*, 138.
- Ambion. 2012. PureLink[®] RNA Mini Kit. Carlsbad, CA USA. <https://www.thermofisher.com/order/catalog/product/12183018A>. Diakses pada 19 Oktober 2023.
- Aviles-Pagan, E.E. & Orr-Weaver, T.L. 2018. Activating Embryonic Development in *Drosophila*. *Seminars in Cell & Development Biology*, 11.
- Base, N.H., Murdifi, M., & Nainu, F. 2019. Pengujian Ekstrak Keluwak Terhadap Aktivitas Reproduksi dengan Model *Drosophila melanogaster*. *Majalah Farmasi dan Farmakologi*, 23(1), 35-37.
- Berbudi, A., Rahmadika, N., Tjahjadi, A.I., & Ruslami, R. 2020. Type 2 Diabetes and Its Impact on The Immune System. *Current Diabetes Review*, 16, 442-449.
- Bequer, L., Gomez, T., Molina, J.L., Alvarez, A., Chaviano, C., & Clapes, S. 2018. Experimental Diabetes Impairs Maternal Reproductive Performance in Pregnant Wistar Rats and Their Offspring. *System Biology in Reproductive Medicine*, 64(1): 60-70.
- Bilous, R., Donnelly, R., & Idris, I. 2021. *Handbook of Diabetes*. Edisi 5. United Kingdom: John Wiley & Sons.
- Ceccatelli, S. 2012. *Methylmercury and Neurotoxicity*. USA: Springer.
- Chyb, S. & Gompel, N. 2013. *Athlas of Drosophila Morphology*. UK: Elsevier.
- Deepthi, B., Sowjanya, K., Lidiya, B., Bhargavi, R.S., & Babu, P.S. 2017. A Modern Review of Diabetes Mellitus: An Annihilatory Metabolic Disorder. *Journal of In Silico & In Vitro Pharmacology*, 3(1): 4.
- Ekengren, S. & Hultmark, D. 2001. A Family of Turandot-Related Genes in Humoral Stress Response of *Drosophila*. *Biochemical and Biophysical Research Communication*, 284, 998-1003.
- Felix-Martinez, G.J., Azpiroz-Leehan, J., Avila-Pozos, R., & Fernandez, J.R.G. 2014. Effect of Impaired ATP Production and Glucose Sensitivity on Human β -Cell Function: A Simulation Study. *Rev. Mex. Ing. Biomed*, 35(2).

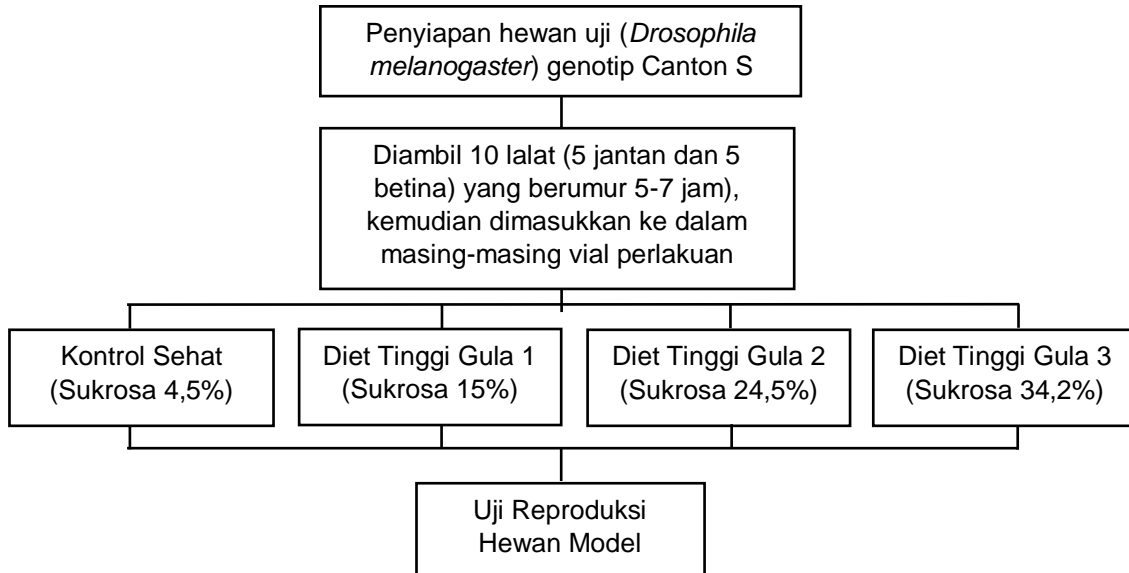
- Furman, B.L. 2015. Streptozotocin-Induced Diabetic Models in Mice and Rats. *Current Protocols in Pharmacology*. 5.47.1-5.47.20.
- Garibyan, L. & Avashia, N. 2013. Polymerase Chain Reaction. *Journal of Investigative Dermatology*, 133.
- Harikumar, K., Kumar, B.L., Hemalatha, G.J., Kumar, M.B., & Lado, S.F.S. 2015. A Review on Diabetes Mellitus. *Int J Novel Trends Pharm Sci*, 5, 201-217.
- Hoffmann, J., Romey, R., Fink, C., & Roeder, T. 2013. Drosophila: A Model to Study Metabolic Disorder. *Adv Biochem Eng Biotechnol*. 135: 42-61.
- Joshi, M. & Deshpande, J.D. 2010. Polymerase Chain Reaction: Methods, Principles and Application. *Journal of Biomedical Research*. 1(5): 81-97.
- Kharroubi, A.T. & Darwish, H.M. 2015. Diabetes Mellitus: The Epidemic of The Century. *Worlds J Diabetes*, 6, 850-867.
- Kinoshita, Y., Shiratsuchi, N., Araki, M., & Inoue, Y.H. 2023. Anti-Tumor Effect of Turandot Proteins Induced via the JAK/STAT Pathway in the mxc Hematopoietic Tumor Mutant in *Drosophila*. *Cells*, 12, 2047.
- Liguori, F., Mascolo, E., & Verni, F. 2021. The Genetics of Diabetes: What We Can Learn from *Drosophila*. *Int. J. Mol. Sci.* 22(20): 11295.
- Magdalena, L.M., Coipan, E.C., Vladimirescu, A.F., Savu, L., Costache, M., & Gavrilă, L. 2012. Downregulation of *hsp22* Gene Expression in *Drosophila melanogaster* from Sites Located Near Chemical Plants. *Genetics and Molecular Research*, 11(1), 739-745.
- Mo, Y., Wan, R., & Zhang, Q. 2012. Application of Reverse Transcription-PCR and Real-Time PCR in Nanotoxicity Research. *Methods Mol Biol*. 926: 99-112.
- Morrow, G., Pecheur, M.L., & Tanguay, R.M. 2015. *Drosophila melanogaster* Mitochondrial *hsp22*: A Role in Resistance to Oxidative Stress, Aging, and The Mitochondrial Unfolding Protein. *Biogerontology*, 17(1): 61-70.
- Morrow, G. & Tanguay, R.M. 2015. *Drosophila melanogaster hsp22*: A Mitochondrial Small Heat Shock Protein Influencing The Aging Process. *Front. Genet.* 6: 103.
- Musselman, L.P., Fink, J.L., Narzinski, K., Ramachandran, P.V., Hathiramani, S.S., Cagan, R.L., & Baranski, T.J. 2011. A High-Sugar Diet Produces Obesity and Insulin Resistance in Wild-Type *Drosophila*. *Disease Models & Mechanism*, 4: 842-849.

- Nagy, T., Fisi, V., Frank, D., Katai, E., Nagy, Z., & Miseta, A. 2019. Hyperglycemia-Induced Aberrant Cell Proliferation; A Metabolic Challenge Mediated by Protein O-G1cNAc Modification. *Cells*, 8, 999.
- Nainu, F. 2018. Review: Penggunaan *Drosophila melanogaster* sebagai Organisme Model dalam Penemuan Obat. *Jurnal Farmasi Galenika (Galenika Journal of Pharmacy)*, 4(1), 50-67.
- Ong, K.L. 2021. Global, Regional, and National Burden of Diabetes from 1990 to 2021, with Projections of Prevalence to 2050: A Systematic Analysis for The Global Burden of Disease Study 2021. *The Lancet*, 402. 203-234.
- Piero, M.N., Nzaro, G.M., & Njagi, J.M. 2014. Diabetes Mellitus – A Devastating Metabolic Disorder. *Asian J Biomed Pharm Sci*, 4, 1-7.
- Prawitasari, D.S. 2019. Diabetes Melitus dan Antioksidan. *Jurnal Kesehatan dan Kedokteran*, 1(1), 48-52.
- Punthakee, Z., Goldenberg, R., & Katz, P. 2018. Definition, Classification and Diagnosis of Diabetes, Prediabetes, and Metabolic Syndrome. *Can J Diabetes*, 42, 10-15.
- Rosa, R.A., Latada, N.P., Asbah, A., Mu'arif, A., Yulianty, R., & Nainu, F. 2021. Eksplorasi Efek Etanol terhadap Survival dan Status Imunitas *Drosophila melanogaster*. *Jurnal Farmasi Indonesia*. 13(2), 146-153.
- Saputri, R. D. 2020. Komplikasi Sistemik pada Pasien Diabetes Melitus Tipe 2. *Jurnal Ilmiah Kesehatan Sandi Husada*, 9(1), 1.
- Seiglie, J.A., Marcus, M.E., Ebert, C., Prodromidis, N., Geldsetzer, P., Theilmann, M., Agoudavi, K., Andall-Brereton, G., aryal, K.K., Bicaba, B.W., Bovet, P., Brian, G., Dorobantu, M., Gathecha, G., Gurung, G.S., Guwatudde, D., Msaidie, M., Houehanou, C., Houinato, D., & Manne-Goehler, J. 2020. Diabetes Prevalence and Its Relationship with Education, Wealth, BMI in 29 Low-Middle-Income Countries. *Diabetes Care*, 43(4), 767-775.
- Spellman, F.R. 2008. *The Science of Water*. Edisi 2. USA: CRC Press.
- Sun, X., Siri, S., Hurst, A., & Qiu, H. 2022. Heat Shock Protein 22 in Physiological and Pathological Hearts: Small Molecule, Large Potential. *Cells*, 11, 114.
- Tennessee, J.M., Barry, W., Cox, J., & Thummel, C.S. 2014. Methods for Studying Metabolism in *Drosophila*. *Methods*, 68(1), 105-115.
- Warr, C.G., Shaw, K.H., Azim, A., Piper, M.D.W., & Parsons, L.M. 2018. Using Mouse and *Drosophila* Models to Investigate the Mechanistic Links between Diet, Obesity, Type II Diabetes, and Cancer. *Int. J. Mol. Sci.* 19, 4110.

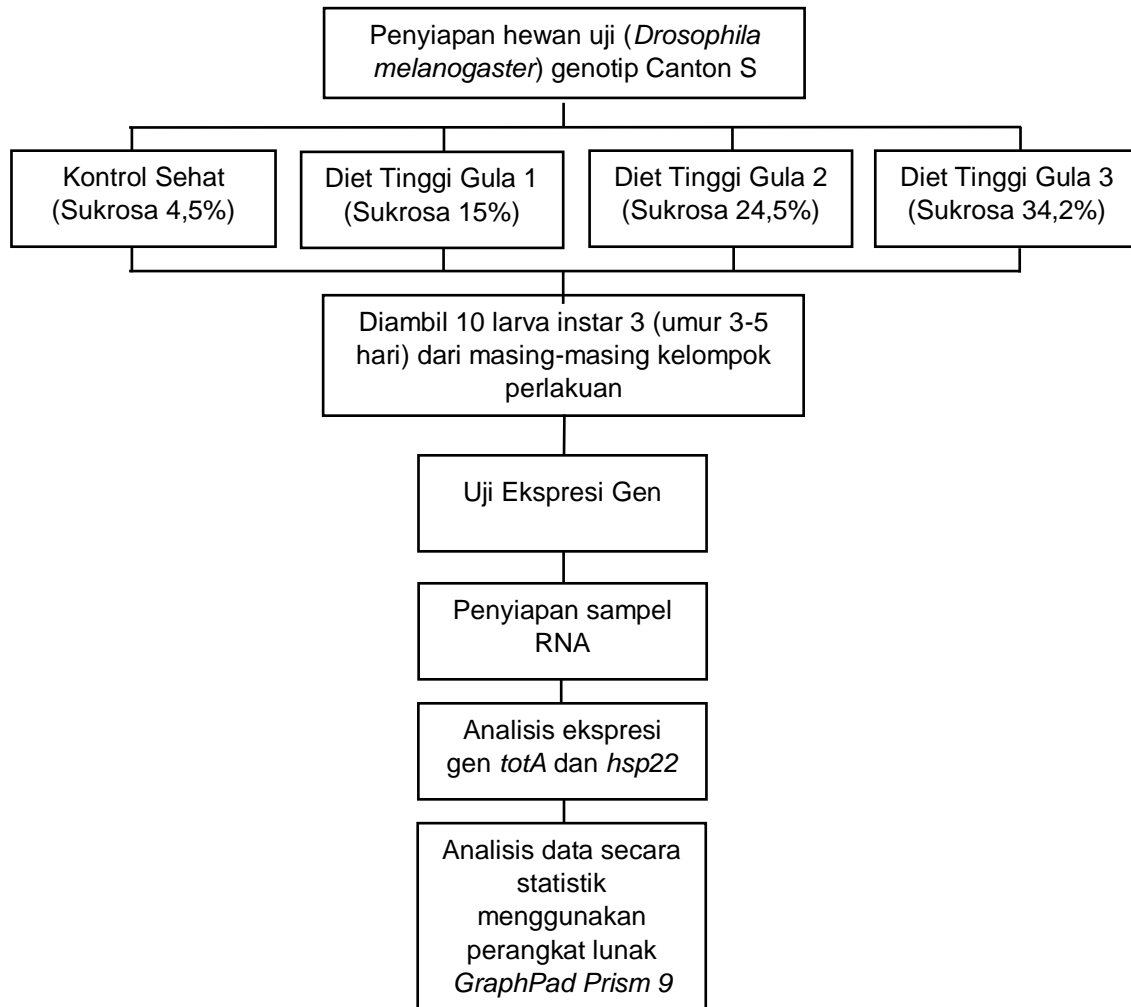
- Yamaguchi, M. 2018. *Drosophila Models for Human Diseases*. Japan: Springer.
- Yu, J., Chen, B., Zheng, B., Qiao, C., Chen, X., Yan, Y., Luan, X., Xie, B., Liu, J., Shen, C., He, Z., Hu, X., Liu, M., Li, H., Shao, Q., & Fang, J. 2019. ATP Synthase is Required for Male Fertility and Germ Cell Maturation in *Drosophila* Testes. *Molecular Medicine Report*, 19, 1561-1570.
- Yu, L., Liang, Q., Zhang, W., Liao, M., wen, M., Zhan, B., Bao, H., & Cheng, X. 2019. *hsp22* Suppresses Diabetic-Induced Endothelial Injury by Inhibiting Mitochondrial Reactive Oxygen Species Formation. *Redox Biol*, 21,1-13.

LAMPIRAN

Lampiran 1. Skema Kerja Perlakuan Uji



Lampiran 2. Skema Kerja Analisis Ekspresi Gen



Lampiran 3. Data Statistika

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

| <i>ANOVA summary</i> | <i>Value</i> |
|--|--------------|
| F | 366,6 |
| P Value | <0,0001 |
| P Value summary | **** |
| Significant diff among means (P<0,05)? | Yes |
| R square | 0,9964 |

Tabel 4. Hasil uji lanjutan *Tukey's Test* ekspresi gen *totA*

| Tukey's Multiple Comparison Test | Mean Diff | Summary | Adjusted P Value |
|--|-----------|---------|------------------|
| Kontrol vs Diet Tinggi Gula 1 | 0,480 | * | 0,0195 |
| Kontrol vs Diet Tinggi Gula 2 | 1,005 | ** | 0,0013 |
| Diet Tinggi Gula 1 vs Diet Tinggi Gula 2 | 0,5250 | * | 0,0399 |

Tabel 5. Hasil *one-way anova* ekspresi gen *hsp22*

| <i>ANOVA summary</i> | <i>Value</i> |
|--|--------------|
| F | 245,5 |
| P Value | <0,0001 |
| P Value summary | **** |
| Significant diff among means (P<0,05)? | Yes |
| R square | 0,9946 |

Tabel 6. Hasil uji lanjutan *Tukey's Test* ekspresi gen *hsp22*

| Tukey's Multiple Comparison Test | Mean Diff | Summary | Adjusted P Value |
|--|-----------|---------|------------------|
| Kontrol vs Diet Tinggi Gula 1 | 0,3125 | # | 0,0618 |
| Kontrol vs Diet Tinggi Gula 2 | -1,332 | *** | 0,0003 |
| Diet Tinggi Gula 1 vs Diet Tinggi Gula 2 | -1,645 | *** | 0,0009 |

Tabel 7. Hasil *one-way anova* uji reproduksi (pupa)

| <i>ANOVA summary</i> | <i>Value</i> |
|--|--------------|
| F | 315,7 |
| P Value | <0,0001 |
| P Value summary | **** |
| Significant diff among means (P<0,05)? | Yes |
| R square | 0,9885 |

Tabel 8. Hasil uji lanjutan *Tukey's Test* uji reproduksi (pupa)

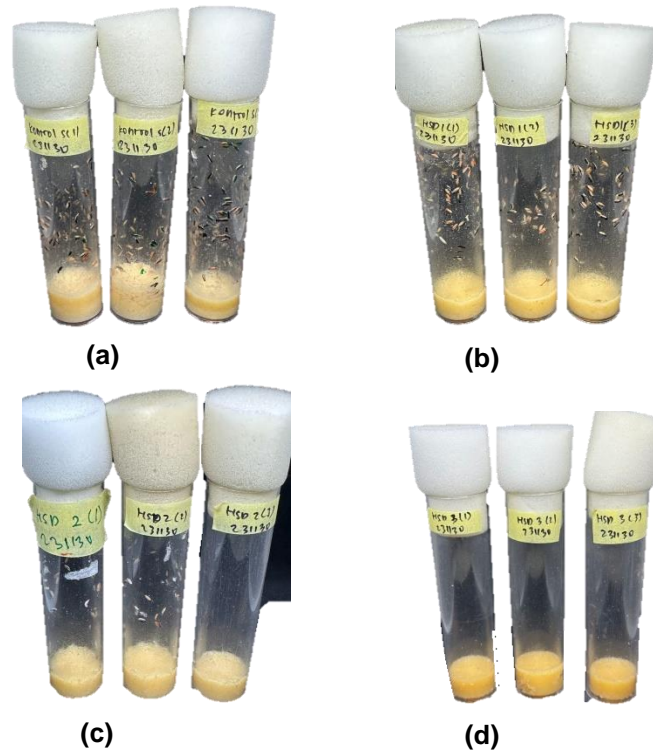
| Tukey's Multiple Comparison Test | Mean Diff | Summary | Adjusted P Value |
|--|------------------|----------------|-------------------------|
| Kontrol vs Diet Tinggi Gula 1 | 17,00 | ns | 0,1503 |
| Kontrol vs Diet Tinggi Gula 2 | 77,67 | **** | <0,0001 |
| Kontrol vs Diet Tinggi Gula 3 | 166,7 | **** | <0,0001 |
| Diet Tinggi Gula 1 vs Diet Tinggi Gula 2 | 60,67 | **** | <0,0001 |
| Diet Tinggi Gula 1 vs Diet Tinggi Gula 3 | 149,7 | **** | <0,0001 |
| Diet Tinggi Gula 2 vs Diet Tinggi Gula 3 | 89,00 | **** | <0,0001 |

Tabel 9. Hasil *one-way anova* uji reproduksi (lalat dewasa)

| ANOVA summary | Value |
|--|--------------|
| F | 101,9 |
| P Value | <0,0001 |
| P Value summary | **** |
| Significant diff among means (P<0,05)? | Yes |
| R square | 0,9745 |

Tabel 10. Hasil uji lanjutan *Tukey's Test* uji reproduksi (lalat dewasa)

| Tukey's Multiple Comparison Test | Mean Diff | Summary | Adjusted P Value |
|--|------------------|----------------|-------------------------|
| Kontrol vs Diet Tinggi Gula 1 | 10.00 | # | 0,7204 |
| Kontrol vs Diet Tinggi Gula 2 | 72.33 | *** | 0,0003 |
| Kontrol vs Diet Tinggi Gula 3 | 145.7 | **** | <0,0001 |
| Diet Tinggi Gula 1 vs Diet Tinggi Gula 2 | 62,33 | *** | 0,0008 |
| Diet Tinggi Gula 1 vs Diet Tinggi Gula 3 | 135,7 | **** | <0,0001 |
| Diet Tinggi Gula 2 vs Diet Tinggi Gula 3 | 73,33 | *** | 0,0002 |

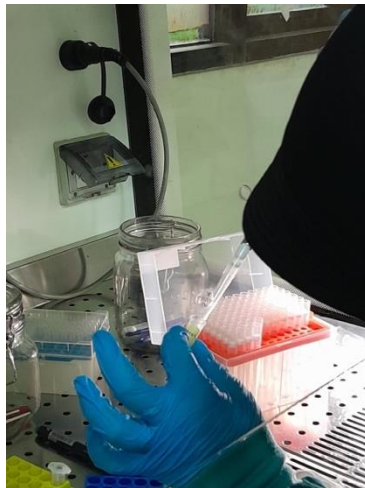
Lampiran 4. Gambar Hasil Uji Penelitian**Gambar 9. Hasil uji reproduksi; (a) Kontrol, (b) DTG 1, (c) DTG 2, (d) DTG 3.****Gambar 10. Hasil perhitungan jumlah RNA isolat**

Lampiran 5. Dokumentasi

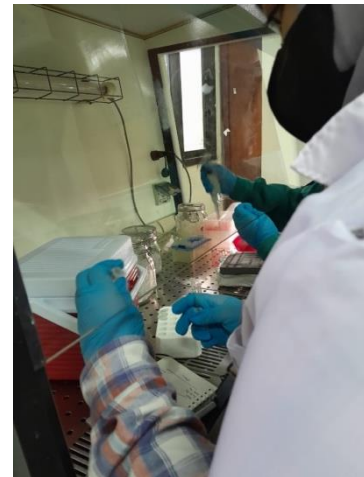
Gambar 11. Pemisahan jantan dan betina



Gambar 12. Pengukuran jumlah isolat RNA



Gambar 13. Proses isolasi RNA



Gambar 14. Preparasi analisis qRT-PCR



Gambar 15. Proses analisis qRT-PCR