

AKTIVITAS EKSTRAK KOLAGEN DARI KULIT IKAN SALMON (*SALMO SALAR*) SEBAGAI KANDIDAT ANTIDIABETES TIPE 2 SECARA *IN VITRO* DAN *IN SILICO*

SKRIPSI

diajukan untuk memenuhi sebagian syarat untuk memperoleh gelar Sarjana Sains
Program Studi Kimia



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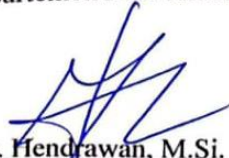
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ABSTRAK

Pengembangan inhibitor peptida banyak menarik perhatian karena spesifitasnya yang tinggi. Terdeteksinya kandungan protein kolagen yang cukup tinggi pada limbah kulit ikan memberikan alternatif sumber inhibitor alami. Pada penelitian ini dilakukan analisis aktivitas kolagen yang diekstrak dari kulit ikan Salmon (*Salmo salar*) sebagai inhibitor enzim yang berperan dalam regulasi karbohidrat untuk dijadikan kandidat antidiabetes tipe-2 secara *in vitro* maupun *in silico*. Aktivitas inhibisi ekstrak kolagen Salmon ditentukan dengan mengukur persen inhibisi relative ekstrak terhadap enzim α -amilase dan enzim DPP-IV menggunakan spektrofotometer dan *microplate reader*. Ekstrak kolagen dikarakterisasi menggunakan beberapa parameter seperti FTIR, UV-Vis, XRD dan SDS-PAGE dan menunjukkan hasil ekstrak yang diperoleh merupakan ekstrak kolagen Salmon. Hasil penelitian menunjukkan inhibisi tertinggi terhadap α -amilase menggunakan saliva non-diabetes sebesar 72,38% dan pada α -amilase saliva diabetes sebesar 76,48%. Persentase inhibisi tertinggi terhadap enzim DPP-IV diperoleh sebesar 63,45% pada konsentrasi kolagen 1000 ppm. Kajian *in silico* menunjukkan adanya interaksi antara kolagen dengan enzim α -amilase maupun enzim DPP-IV dengan afinitas pengikatan secara berturut-turut -300,38 kkal/mol, -225.67 kkal/mol dan melibatkan 113 serta 79 interaksi residu asam amino. Analisis *in silico* potensi peptida aktif dari kolagen menunjukkan bahwa afinitas pengikatan terendah dari α -amilase dihasilkan dari ligan peptida HVWFG (His-Val-Trp-Phe-Gly), WF (Trp-Phe), YW (Tyr-Trp) sebesar -9,6 kkal/mol, -9,3 kkal/mol, -9,3 kkal/mol dan kontrol positif akarbosa sebesar -9,3 kkal/mol. Afinitas pengikatan terendah dari enzim DPP-IV dihasilkan dari ligan peptida YW (Tyr-Trp), WF (Trp-Phe) sebesar -8,4 kkal/mol, -8,3 kkal/mol dan kontrol positif linagliptin sebesar -7,8 kkal/mol. Enzim α -amilase dan enzim DPP-IV memiliki jenis inhibisi kompetitif. Kolagen kulit ikan salmon dan peptida dari kolagen kulit ikan salmon memiliki potensi sebagai kandidat antidiabetes tipe 2.

Kata kunci: Antidiabetes, inhibisi, kolagen, peptida aktif, *Salmo salar*

ABSTRACT

*The development of peptide inhibitors has attracted a lot of attention because of their high specificity. The high content of collagen protein in skin fish waste provides alternative sources of natural inhibitors. In this study, an analysis of the activity of collagen extracted from the skin of Salmon (*Salmo salar*) was carried out as an inhibitor of carbohydrate-regulating enzymes which further used as a candidate for type-2 antidiabetic by using in vitro and in silico approach. The inhibitory activity of Salmon collagen extract was determined by measuring the percent inhibition of the extract relative to the α -amylase and DPP-IV enzymes using a spectrophotometer and a microplate reader. The collagen extract was characterized using several parameters such as FTIR, UV-Vis, XRD and SDS-PAGE and showed that the extract was Salmon collagen extract. The results showed the highest inhibition of α -amylase using non-diabetic saliva was 72.38% and diabetic -amylase was 76.48%. The highest percentage of inhibition of the DPP-IV enzyme was obtained at 63.45% at a concentration of 1000 ppm collagen. The in silico study showed an interaction between collagen and α -amylase and DPP-IV enzymes with binding affinities -300.38 kcal/mol, -225.67 kcal/mol, and involving 113 and 79 amino acid residue interactions, respectively. In silico analysis of the active peptide potential of collagen showed that the highest binding affinity of α -amylase produced from HVWFG (His-Val-Trp-Phe-Gly), WF (Trp-Phe), YW (Tyr-Trp) peptide ligands was -9,6 kcal/mol, -9,3 kcal/mol, -9,3 kcal/mol and positive control acarbose -9,3 kcal/mol. The highest binding affinity of the DPP-IV enzyme produced from the peptide ligand YW (Tyr-Trp), WF (Trp-Phe) -8.4 kcal/mol, -8.3 kcal/mol and positive control linagliptin -7.8 kcal/mol. The α -amylase and DPP-IV enzymes have competitive inhibition types. Salmon skin collagen and peptides from salmon skin collagen have potential as candidates for type 2 antidiabetic.*

Keywords: Antidiabetic, active peptide, collagen, inhibition, *Salmo salar*

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DAFTAR PUSTAKA

- Abbas, G., Al Harrasi, A., Hussain, H., Hamaed, A., & Supuran, C. T. (2019). The management of diabetes mellitus-imperative role of natural products against dipeptidyl peptidase-4, α -glucosidase and sodium-dependent glucose co-transporter 2 (SGLT2). *Bioorganic Chemistry*, 86(February), 305–315. <https://doi.org/10.1016/j.bioorg.2019.02.009>
- Abdul, M., Khan, B., Hashim, M. J., King, J. K., Govender, R. D., Mustafa, H., & Kaabi, J. Al. (2020). *Epidemiology of Type 2 Diabetes – Global Burden of Disease and Forecasted Trends*. 10, 107–111.
- Adamiak, K., & Sionkowska, A. (2022). Spectrochimica Acta Part A : Molecular and Biomolecular Spectroscopy The influence of UV irradiation on fish skin collagen films in the presence of xanthohumol and propanediol. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 282(July), 121652. <https://doi.org/10.1016/j.saa.2022.121652>
- Afriza, D., Suriyah, W. H., & Ichwan, S. J. A. (2018). In silico analysis of molecular interactions between the anti-apoptotic protein survivin and dentatin, nordentatin, and quercetin. *Journal of Physics: Conference Series*, 1073(3). <https://doi.org/10.1088/1742-6596/1073/3/032001>
- Ainezzahira, Multri, H. D., Kiyat, W. El, Nacing, N., & Dari, D. W. (2019). Review: Pemanfaatan Enzim Alpha -amilase pada Modifikasi Pati Singkong sebagai Substitusi Gelatin Produk Marshmallow Utilization of Alpha-Amilase in Cassava Starch Modification as Gelatin Substitution at Marshmallow Product. *Jurnal Agroindustri Halal*, 5(2), 220–227.
- Alessandro, A., Howie, H., Hay, A., Dziewulska, K., Brown, B., Wither, M., Karafin, M., Stone, E., Spitalnik, S., Hod, E., Francis, R., Fu, X., Thomas, T., & Zimring, J. (2020). *Hematologic and systemic metabolic alterations due to Mediterranean class II G6PD deficiency in mice*. 4(July), 526–541.
- Allouche, A. (2012). Software News and Updates Gabedit — A Graphical User Interface for Computational Chemistry Softwares. *Journal of Computational Chemistry*, 32, 174–182. <https://doi.org/10.1002/jcc>
- Alves, A. L., Marques, A. L. P., Martins, E., Silva, T. H., & Reis, R. L. (2017).

- Cosmetic potential of Marine fish skin collagen. *Cosmetics*, 4(4), 1–16.
<https://doi.org/10.3390/cosmetics4040039>
- Amin, M. S., Saputri, F. C., & Mun'im, A. (2019). Inhibition of dipeptidyl peptidase 4 (DPP IV) activity by some Indonesia edible plants. *Pharmacognosy Journal*, 11(2), 231–236.
<https://doi.org/10.5530/pj.2019.11.36>
- Amri, E., & Mamboya, F. (2012). Papain, a plant enzyme of biological importance: A review. *American Journal of Biochemistry and Biotechnology*, 8(2), 99–104. <https://doi.org/10.3844/ajbbsp.2012.99.104>
- Astiana, I., Nurjanah, & Nurhayati, T. (2016). Characterization of Acid Soluble Collagen from Redbelly Yellowtail Fusilier Fish Skin (*Caesio cuning*). *Jurnal Pengolahan Hasil Perikanan Indonesia*, 19(1), 79–93.
<https://doi.org/10.17844/jphpi.2016.19.1.79>
- Atef, M., Ojagh, S. M., Latifi, A. M., Esmaili, M., & Udenigwe, C. C. (2020). Biochemical and structural characterization of sturgeon fish skin collagen (*Huso huso*). *Journal of Food Biochemistry*, 44(8), 1–10.
<https://doi.org/10.1111/jfbc.13256>
- Atma, Y., Lioe, H. N., Prangdimurti, E., Seftiono, H., Taufik, M., & Mustopa, A. Z. (2019). Dipeptidyl peptidase IV (DPP-IV) inhibitory activity of ultrafiltration and gel filtration fraction of gelatin hydrolyaste derived from bone of fish for antidiabetes. *International Journal on Advanced Science, Engineering and Information Technology*, 9(6), 2096–2103.
<https://doi.org/10.18517/ijaseit.9.6.10658>
- Buker, S. M., Boriack-Sjodin, P. A., & Copeland, R. A. (2019). Enzyme–Inhibitor Interactions and a Simple, Rapid Method for Determining Inhibition Modality. *SLAS Discovery*, 24(5), 515–522. <https://doi.org/10.1177/2472555219829898>
- Bernaldez, M. J. A., Billones, J. B., & Magpantay, A. (2018). In silico analysis of binding interactions between GSK983 and human DHODH through docking and molecular dynamics. *AIP Conference Proceedings*, 2045(December 2018). <https://doi.org/10.1063/1.5080886>
- Bitencourt-Ferreira, G., Veit-Acosta, M., & de Azevedo, W. F. (2019). Van der waals potential in protein complexes. *Methods in Molecular Biology*, 2053,

79–91. https://doi.org/10.1007/978-1-4939-9752-7_6

- Borawska-Dziadkiewicz, J., Darewicz, M., & Tarczynska, A. S. (2021). Properties of peptides released from salmon and carp via simulated human-like gastrointestinal digestion described applying quantitative parameters. *PLoS ONE*, *16*(8 August), 1–23. <https://doi.org/10.1371/journal.pone.0255969>
- Buker, S. M., Boriack-Sjodin, P. A., & Copeland, R. A. (2019). Enzyme–Inhibitor Interactions and a Simple, Rapid Method for Determining Inhibition Modality. *SLAS Discovery*, *24*(5), 515–522. <https://doi.org/10.1177/2472555219829898>
- Bulusu, G., & Desiraju, G. R. (2020). Strong and Weak Hydrogen Bonds in Protein–Ligand Recognition. *Journal of the Indian Institute of Science*, *100*(1), 31–41. <https://doi.org/10.1007/s41745-019-00141-9>
- Cao, J., Duan, Q., Liu, X., Shen, X., & Li, C. (2019). Extraction and Physicochemical Characterization of Pepsin Soluble Collagens from Golden Pompano (*Trachinotus blochii*) Skin and Bone. *Journal of Aquatic Food Product Technology*, *28*(8), 837–847. <https://doi.org/10.1080/10498850.2019.1652216>
- Chen, J., Li, L., Yi, R., Xu, N., Gao, R., & Hong, B. (2016). Extraction and characterization of acid-soluble collagen from scales and skin of tilapia (*Oreochromis niloticus*). *LWT - Food Science and Technology*, *66*, 453–459. <https://doi.org/10.1016/j.lwt.2015.10.070>
- Chinh, N. T., Manh, V. Q., Trung, V. Q., Lam, T. D., Huynh, M. D., Tung, N. Q., Trinh, N. D., & Hoang, T. (2019). Characterization of collagen derived from tropical freshwater carp fish scale wastes and its amino acid sequence. *Natural Product Communications*, *14*(7). <https://doi.org/10.1177/1934578X19866288>
- Chuaychan, Sira; Benjakul, Soottawat; Kishimura, Hideki. (2015). Characteristics of acid- and pepsin-soluble collagens from scale of seabass (*Lates calcarifer*). *LWT - Food Science and Technology*, *63*(1), 71–76. doi:10.1016/j.lwt.2015.03.002
- Dandekar, P. D., Kotmale, A. S., Chavan, S. R., Kadlag, P. P., Sawant, S. V., Dhavale, D. D., & Ravikumar, A. (2021). Insights into the Inhibition Mechanism of Human Pancreatic α -Amylase, a Type 2 Diabetes Target, by Dehydrodieugenol B Isolated from *Ocimum tenuiflorum*. *ACS Omega*, *6*(3),

- 1780–1786. <https://doi.org/10.1021/acsomega.0c00617>
- Damián-Medina, K., Salinas-Moreno, Y., Milenkovic, D., Figueroa-Yáñez, L., Marino-Marmolejo, E., Higuera-Ciapara, I., Vallejo-Cardona, A., & Lugo-Cervantes, E. (2020). In silico analysis of antidiabetic potential of phenolic compounds from blue corn (*Zea mays* L.) and black bean (*Phaseolus vulgaris* L.). *Heliyon*, 6(3). <https://doi.org/10.1016/j.heliyon.2020.e03632>
- Dachriyanus. 2014. Analisis Struktur Senyawa Organik secara Spektroskopi. Padang: LPTIK.
- Dawson, P., Al-Jeddawi, W., & Remington, N. (2018). Effect of Freezing on the Shelf Life of Salmon. *International Journal of Food Science*, 2018. <https://doi.org/10.1155/2018/1686121>
- Decroli, eva. 2019. Diabetes Mellitus Tipe 2 edisi 1. Padang. Bagian Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Andalas.
- Devita, L., Nurilmala, M., Lioe, H. N., & Suhartono, M. T. (2021). Chemical and Antioxidant Characteristics of Skin-Derived Collagen Obtained by Acid-Enzymatic Hydrolysis of Bigeye Tuna (*Thunnus obesus*). *Marine Drugs*, 19(4). <https://doi.org/10.3390/md19040222>
- Doak, B. C., & Kihlberg, J. (2017). Drug discovery beyond the rule of 5 - Opportunities and challenges. *Expert Opinion on Drug Discovery*, 12(2), 115–119. <https://doi.org/10.1080/17460441.2017.1264385>
- Guo, H., Richel, A., Hao, Y., Fan, X., Everaert, N., Yang, X., & Ren, G. (2020). Novel dipeptidyl peptidase-IV and angiotensin-I-converting enzyme inhibitory peptides released from quinoa protein by in silico proteolysis. *Food Science and Nutrition*, 8(3), 1415–1422. <https://doi.org/10.1002/fsn3.1423>
- Engel, M., Hoffmann, T., Wagner, L., Wermann, M., Heiser, U., Kiefersauer, R., Huber, R., Bode, W., Demuth, H. U., & Brandstetter, H. (2003). The crystal structure of dipeptidyl peptidase IV (CD26) reveals its functional regulation and enzymatic mechanism. *Proceedings of the National Academy of Sciences of the United States of America*, 100(9), 5063–5068. <https://doi.org/10.1073/pnas.0230620100>
- Engwa, G. A., Nwalo, F. N., Chibuzor, G. E., Ejiagha, E. C., Abonyi, M. C., Ugwu, T. E., Ikechukwu Obiudu, K., Agbafor, K. N., Oyejide Ojo, O., & Ewa Ubi,

- B. (2018). Relationship between Type 2 Diabetes and Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency and Their Effect on Oxidative Stress. *Journal of Diabetes & Metabolism*, 09(08). <https://doi.org/10.4172/2155-6156.1000800>
- Exler, J., & Pehrsson, P. R. (2007). Nutrient content and variability in newly obtained salmon data for USDA Nutrient Database for Standard Reference. *The FASEB Journal*, 21(5), 20705. <https://doi.org/10.1096/fasebj.21.5.a315-b>
- Fakih, T. M., & Dewi, M. L. (2020). Identifikasi Peptida Bioaktif dari Protein Kedelai sebagai Inhibitor Enzim α -glukosidase untuk Kandidat Antidiabetes. *Pharmacon: Jurnal Farmasi Indonesia*, 17(2), 101–109. <https://doi.org/10.23917/pharmacon.v17i2.10635>
- Giorgino, F., Laviola, L., & Leonardini, A. (2005). Pathophysiology of type 2 diabetes: Rationale for different oral antidiabetic treatment strategies. *Diabetes Research and Clinical Practice*, 68(SUPPL. 1), 22–29. <https://doi.org/10.1016/j.diabres.2005.03.012>
- Girardi, E., Sañé Schepisi, M., Goletti, D., Bates, M., Mwaba, P., Yeboah-Manu, D., Ntoumi, F., Palmieri, F., Maeurer, M., Zumla, A., & Ippolito, G. (2017). The global dynamics of diabetes and tuberculosis: the impact of migration and policy implications. *International Journal of Infectious Diseases*, 56, 45–53. <https://doi.org/10.1016/j.ijid.2017.01.018>
- GORNALL, A. G., BARDAWILL, C. J., & DAVID, M. M. (1949). Determination of serum proteins by means of the biuret reaction. *The Journal of Biological Chemistry*, 177(2), 751–766. [https://doi.org/10.1016/s0021-9258\(18\)57021-6](https://doi.org/10.1016/s0021-9258(18)57021-6)
- Han, Y., Ahn, J. R., Woo, J. W., Jung, C. K., Cho, S. M., Lee, Y. B., & Kim, S. B. (2010). Processing optimization and physicochemical characteristics of collagen from scales of yellowfin tuna (*Thunnus albacares*). *Fisheries and Aquatic Sciences*, 13(2), 102–111. <https://doi.org/10.5657/fas.2010.13.2.102>
- Hartina, U., R, M., Annuar, Q., H, Izzreen, N. Q., N, M., & M, H. (2019). *PROPERTIES OF HYDROLYSED COLLAGEN FROM THE SKIN OF MILKFISH (Chanoschanos) AS AFFECTED BY DIFFERENT ENZYMATIC TREATMENTS*. 6(2), 34–41. <https://doi.org/10.5281/zenodo.2572454>
- Harnedy-Rothwell, P. A., Khatib, N., Sharkey, S., Lafferty, R. A., Gite, S.,

- Whooley, J., O'harte, F. P. M., & Fitzgerald, R. J. (2021). Physicochemical, nutritional and in vitro antidiabetic characterisation of blue whiting (*Micromesistius poutassou*) protein hydrolysates. *Marine Drugs*, *19*(7). <https://doi.org/10.3390/md19070383>
- Harnedy-Rothwell, P. A., McLaughlin, C. M., O'Keeffe, M. B., Le Gouic, A. V., Allsopp, P. J., McSorley, E. M., ... Fitzgerald, R. J. (2020). Identification and characterisation of peptides from a boarfish (*Capros aper*) protein hydrolysate displaying in vitro dipeptidyl peptidase-IV (DPP-IV) inhibitory and insulinotropic activity. *Food Research International*, *131*, 108989. <https://doi.org/10.1016/j.foodres.2020.108989>.
- Harnedy, P. A., Parthsarathy, V., McLaughlin, C. M., O'Keeffe, M. B., Allsopp, P. J., McSorley, E. M., ... Fitzgerald, R. J. (2018a). Atlantic salmon (*Salmo salar*) coproduct-derived protein hydrolysates: A source of antidiabetic peptides. *Food Research International*, *106*, 598–606. <https://doi.org/10.1016/j.foodres.2018.01.025>
- Harnedy, P. A., Parthsarathy, V., McLaughlin, C. M., O'Keeffe, M. B., Allsopp, P. J., McSorley, E. M., ... Fitzgerald, R. J. (2018b). Blue whiting (*Micromesistius poutassou*) muscle protein hydrolysate with in vitro and in vivo antidiabetic properties. *Journal of Functional Foods*, *40*, 137–145. <https://doi.org/10.1016/j.jff.2017.10.045>.
- Herschlag, D., & Pinney, M. M. (2018). Hydrogen Bonds: Simple after All? *Biochemistry*, *57*(24), 3338–3352. <https://doi.org/10.1021/acs.biochem.8b00217>
- Hevener, K. E., Zhao, W., Ball, D. M., Babaoglu, K., Qi, J., White, S. W., & Lee, R. E. (2009). Validation of *molecular docking* programs for virtual screening against dihydropteroate synthase. *Journal of Chemical Information and Modeling*, *49*(2), 444–460. <https://doi.org/10.1021/ci800293n>
- Hidayat, B., Ramadani, R. V., Rudijanto, A., Soewondo, P., Suastika, K., & Siu Ng, J. Y. (2022). Direct Medical Cost of Type 2 Diabetes Mellitus and Its Associated Complications in Indonesia. *Value in Health Regional Issues*, *28*, 82–89. <https://doi.org/10.1016/j.vhri.2021.04.006>
- Horowitz, S., & Trievel, R. C. (2012). Carbon-oxygen hydrogen bonding in

- biological structure and function. *Journal of Biological Chemistry*, 287(50), 41576–41582. <https://doi.org/10.1074/jbc.R112.418574>
- IDF (International Diabetes Federation).2017. idf Diabetes Atlas. Edisi 8. International Diabetes Federation
- Isfa, M., & Walid, M. (2019). Uji Kombinasi Antidiabetik antara Ekstrak Kulit Durian dan Acarbose dengan Perhitungan Combination Index dalam Penghambatan Kerja Enzim α -Amilase. *PHARMACY: Jurnal Farmasi Indonesia (Pharmaceutical Journal of Indonesia)*, 16(1), 85. <https://doi.org/10.30595/pharmacy.v16i1.4482>
- Iswariya, S., Velswamy, P., & Uma, T. S. (2018). Isolation and Characterization of Biocompatible Collagen from the Skin of Puffer Fish (*Lagocephalus inermis*). *Journal of Polymers and the Environment*, 26(5), 2086–2095. <https://doi.org/10.1007/s10924-017-1107-1>
- Jafari, H., Lista, A., Siekapen, M. M., Ghaffari-Bohlouli, P., Nie, L., Alimoradi, H., & Shavandi, A. (2020). Fish collagen: Extraction, characterization, and applications for biomaterials engineering. *Polymers*, 12(10), 1–37. <https://doi.org/10.3390/polym12102230>
- Jaziri, A. A., Shapawi, R., Mokhtar, R. A. M., Noordin, W. N. M., & Huda, N. (2022). Biochemical analysis of collagens from the bone of lizardfish (*Saurida tumbil* Bloch, 1795) extracted with different acids. *PeerJ*, 1–22. <https://doi.org/10.7717/peerj.13103>
- Jowett, L. A., Ricci, A., Wu, X., Howe, E. N. W., & Gale, P. A. (2019). Investigating the influence of steric hindrance on selective anion transport. *Molecules*, 24(7). <https://doi.org/10.3390/molecules24071278>
- Jakobsen, J., Smith, C., Bysted, A., & Cashman, K. D. (2019). Vitamin D in wild and farmed atlantic salmon (*salmo salar*)-what dowe know? *Nutrients*, 11(5), 1–14. <https://doi.org/10.3390/nu11050982>
- Kaale, L. D., & Eikevik, T. M. (2016). Changes of proteins during superchilled storage of Atlantic salmon muscle (*Salmo salar*). *Journal of Food Science and Technology*, 53(1), 441–450. <https://doi.org/10.1007/s13197-015-1979-9>
- Kaur, N., Kumar, V., Nayak, S. K., Wadhwa, P., Kaur, P., & Sahu, S. K. (2021). Alpha-amylase as molecular target for treatment of diabetes mellitus: A

- comprehensive review. *Chemical Biology and Drug Design*, 98(4), 539–560. <https://doi.org/10.1111/cbdd.13909>
- Kęska, P., Stadnik, J., Bak, O., & Borowski, P. (2019). Meat proteins as dipeptidyl peptidase iv inhibitors and glucose uptake stimulating peptides for the management of a type 2 diabetes mellitus in silico study. *Nutrients*, 11(10). <https://doi.org/10.3390/nu11102537>
- Khirzin, M. H., Hilmi, M., Prastujati, A. U., Mawardi, N., & Rahayu, R. (2020). *AKTIVITAS PENGHAMBATAN ALFA AMILASE (α -AMYLASE INHIBITOR) HIDROLISAT GELATIN TULANG ITIK*. 6(1), 1200–1208.
- Kumar, L. V., Shakila, R. J., & Jeyasekaran, G. (2019). In vitro anti-cancer, anti-diabetic, anti-inflammation and wound healing properties of collagen peptides derived from unicorn leatherjacket (*Aluterus monoceros*) at different hydrolysis. *Turkish Journal of Fisheries and Aquatic Sciences*, 19(7), 551–560. https://doi.org/10.4194/1303-2712-v19_7_02
- Laemmly. (1970). © 1970 Nature Publishing Group. *Nature Publishing Group*, 228, 1979.
- Lauritano, C., & Ianora, A. (2016). Marine organisms with anti-diabetes properties. *Marine Drugs*, 14(12). <https://doi.org/10.3390/md14120220>
- Lee, J., Chang, I., & Yu, W. (2019). Atomic insights into the effects of pathological mutants through the disruption of hydrophobic core in the prion protein. *Scientific Reports*, 9(1), 1–14. <https://doi.org/10.1038/s41598-019-55661-2>
- Li, K., Yao, F., Xue, Q., Fan, H., Yang, L., Li, X., Sun, L., & Liu, Y. (2018). Inhibitory effects against α -glucosidase and α -amylase of the flavonoids-rich extract from *Scutellaria baicalensis* shoots and interpretation of structure–activity relationship of its eight flavonoids by a refined assign-score method. *Chemistry Central Journal*, 12(1), 1–11. <https://doi.org/10.1186/s13065-018-0445-y>
- López, A. L., Peñaloza, A. M., Juárez, V. M. M., Torres, A. V., Zeugolis, D. I., & Álvarez, G. A. (2019). Hydrolyzed Collagen—Sources and Applications. *Molecules*, 24, 1–16.
- Los Huertos, M. (2020). Conservation and Restoration. In *Ecology and Management of Inland Waters*. <https://doi.org/10.1016/b978-0-12-814266->

0.00026-x

- Makrilakis, K. (2019). The role of dpp-4 inhibitors in the treatment algorithm of type 2 diabetes mellitus: When to select, what to expect. *International Journal of Environmental Research and Public Health*, 16(15). <https://doi.org/10.3390/ijerph16152720>
- Margono, R. S., & Sumiati, T. (2019). Potensi Tanaman Indonesia sebagai Antidiabetes melalui Mekanisme Penghambatan Enzim α -glukosidase. *Jurnal Farmamedika (Pharmamedica Journal)*, 4(2), 86–92. <https://doi.org/10.47219/ath.v4i2.84>
- Martinez-Gonzalez, A. I., Díaz-Sánchez, Á. G., De La Rosa, L. A., Vargas-Requena, C. L., Bustos-Jaimes, I., & Alvarez-Parrilla, E. (2017). Polyphenolic compounds and digestive enzymes: In vitro non-covalent interactions. *Molecules*, 22(4). <https://doi.org/10.3390/molecules22040669>
- Mohamed, M. A., Jaafar, J., Ismail, A. F., Othman, M. H. D., & Rahman, M. A. (2017). Fourier Transform Infrared (FTIR) Spectroscopy. In *Membrane Characterization*. Elsevier B.V. <https://doi.org/10.1016/B978-0-444-63776-5.00001-2>
- Moreno, H. M., Montero, M. P., Gómez-Guillén, M. C., Fernández-Martín, F., Mørkøre, T., & Borderías, J. (2012). Collagen characteristics of farmed Atlantic salmon with firm and soft fillet texture. *Food Chemistry*, 134(2), 678–685. <https://doi.org/10.1016/j.foodchem.2012.02.160>
- Muchtar, R. S. U., Murniasih, E., Purba, M. K., Samosir, M. K., Patmono, & Widarti. (2022). *EDUKASI DIABETES MELLITUS DAN SENAM DIABETES DALAM UPAYA PENCEGAHAN PENYAKIT DIABETES MELLITUS DI WILAYAH KERJA PUSKESMAS TANJUNG UNCANG KOTA BATAM TAHUN 2021*.
- National Center for Biotechnology Information (2022). PubChem Compound Summary for CID 6913668, Collagen I, alpha chain (98-110). Retrieved February 7, 2022 from https://pubchem.ncbi.nlm.nih.gov/compound/Collagen-I_-alpha-chain-_98-110.
- Nilsuwan, K., Fusang, K., Pripatnanont, P., & Benjakul, S. (2022). Properties and

- Characteristics of Acid-Soluble Collagen from Salmon Skin Defatted with the Aid of Ultrasonication. *Fishes*, 7(1), 1–14. <https://doi.org/10.3390/fishes7010051>
- Nining, N. (2020). Pemanfaatan Kolagen Laut dalam Sistem Penghantaran Obat. *Majalah Farmasetika*, 5(5), 245. <https://doi.org/10.24198/mfarmasetika.v5i5.28866>
- Nugraha, M. R., & Hasanah, A. N. (2018). Metode Pengujian Aktifitas Antidiabetes. *Farmaka*, 16(3), 28–34.
- Nurubhasha, R., Sampath Kumar, N. S., Thirumalasetti, S. K., Simhachalam, G., & Dirisala, V. R. (2019). Extraction and characterization of collagen from the skin of *Pterygoplichthys pardalis* and its potential application in food industries. *Food Science and Biotechnology*, 28(6), 1811–1817. <https://doi.org/10.1007/s10068-019-00601-z>
- Nur, S., Wierson, Y., Sami, F. J., Megawati, Gani, S. A., Aisyah, A. N., Yulia, & Marwati. (2021). Characterization, antioxidant and α -glucosidase inhibitory activity of collagen hydrolysate from lamuru (*caranx ignobilis*) fishbone. *Sains Malaysiana*, 50(8), 2329–2341. <https://doi.org/10.17576/jsm-2021-5008-16>
- Nurilmala, M., Suryamarevita, H., Husein Hizbullah, H., Jacob, A. M., & Ochiai, Y. (2022). Fish skin as a biomaterial for halal collagen and gelatin. *Saudi Journal of Biological Sciences*, 29(2), 1100–1110. <https://doi.org/10.1016/j.sjbs.2021.09.056>
- Nurjanah, TI, B., & Nurhayati, T. (2021). Ekstraksi Kolagen Kulit Ikan Tuna Sirip Kuning (*Thunnus albacares*) menggunakan Enzim Pepsin dan Papain. *Jurnal Pengolahan Hasil Perikanan Indonesia*, 24(2), 174–187. <https://doi.org/10.17844/jphpi.v24i2.35410>
- Odularu, A. T. (2020). Worthwhile Relevance of Infrared Spectroscopy in Characterization of Samples and Concept of Infrared Spectroscopy-Based Synchrotron Radiation. *Journal of Spectroscopy*, 2020. <https://doi.org/10.1155/2020/8869713>
- OECD. (2017). Safety Assesment of Transgenic Organism in the Environment Volume 7: Atlantic Salmon
- Olasupo, S. B., Uzairu, A., Shallangwa, G. A., & Uba, S. (2020). Profiling the

- antidepressant properties of phenyl piperidine derivatives as inhibitors of serotonin transporter (SERT) via cheminformatics modeling, *molecular docking* and ADMET predictions. *Scientific African*, 9, e00517. <https://doi.org/10.1016/j.sciaf.2020.e00517>
- Prastyo, D. T., Trilaksani, W., & Nurjanah. (2020). Aktivitas Antioksidan Hidrolisat Kolagen Kulit Ikan Nila (*Oreochromis niloticus*). *Jurnal Pengolahan Hasil Perikanan Indonesia*, 23(3), 423–433. <https://doi.org/10.17844/jphpi.v23i3.31732>
- Pham, A., Ky, X., Vy, B., Ha, V., Khanh Hy, H., Hong, T., Thiet, T., Anh, P., Xuan Ky, P., Bao Vy, P., Viet Ha, D., Ho Khanh Hy, L., Thu Hong, N., Thi Thiet, D., & Phuong Anh, N. (2018). Investigation of protein patterns and antioxidant activity of collagen hydrolysates from skin of Fan-bellied leatherjacket *Monacanthus chinensis* by various enzymes Item Type Journal Contribution INVESTIGATION OF PROTEIN PATTERNS AND ANTIOXIDANT ACTIVITY OF COLLAGEN HYDROLYSATES FROM SKIN OF FAN-BELLIED LEATHERJACKET *Monacanthus chinensis* BY VARIOUS ENZYMES. *Journal of Marine Science and Technology*, 18(4A), 141–150. <https://doi.org/10.15625/1859-3097/18/4A/13642>
- Purnomo, Y., Soeatmadji, D. W., Sumitro, S. B., & Widodo, M. A. (2015). Anti-diabetic potential of *Urena lobata* leaf extract through inhibition of dipeptidyl peptidase IV activity. *Asian Pacific Journal of Tropical Biomedicine*, 5(8), 645–649. <https://doi.org/10.1016/j.apjtb.2015.05.014>
- Primada, C., Anugrahini, H., & Wahyuni, A. S. (2021). Narrative Review : Aktivitas Antidiabetes Tanaman Tradisional Di pulau Jawa. *Pharmacon: Jurnal Farmasi Indonesia. Edisi Khusus (Rakerda - Seminar IAI Jateng)*, 120–131.
- Qiao, M., Tu, M., Chen, H., Mao, F., Yu, C., & Du, M. (2018). Identification and in silico prediction of anticoagulant peptides from the enzymatic hydrolysates of *mytilus edulis* proteins. *International Journal of Molecular Sciences*, 19(7). <https://doi.org/10.3390/ijms19072100>
- Ramadhan, A. H., Nawas, T., Zhang, X., Pembe, W. M., Xia, W., & Xu, Y. (2018). Purification and identification of a novel antidiabetic peptide from Chinese

- giant salamander (*Andrias davidianus*) protein hydrolysate against α -amylase and α -glucosidase. *International Journal of Food Properties*, 20(3), S3360–S3372. <https://doi.org/10.1080/10942912.2017.1354885>
- Ramadhan, B., & Wikandari, P. R. (2021). Aktivitas enzim amilase dari bakteri asam laktat (karakteristik dan aplikasi). *UNESA Journal of Chemistry*, 10(2), 109–120.
- Rohmah, M. K. (2018). STUDI IN SILICO POTENSI SENYAWA ALLIUM BAWANG PUTIH (*Allium sativum*) SEBAGAI INHIBITOR DPP-4 PADA DIABETES MELLITUS. *Jurnal Ilmiah Medicamento*, 4(1), 13–17. <https://doi.org/10.36733/medicamento.v4i1.873>
- Rudeekulthamrong, P., & Kaulpiboon, J. (2012). Kinetic inhibition of human salivary alpha-amylase by a novel cellobiose-containing tetrasaccharide. *Journal of the Medical Association of Thailand = Chotmaihet Thangphaet*, 95 Suppl 1, 102–108.
- Sagu, S. T., Zimmermann, L., Landgräber, E., Homann, T., Huschek, G., Özpinar, H., Schweigert, F. J., & Rawel, H. M. (2020). Comprehensive characterization and relative quantification of α -amylase/trypsin inhibitors from wheat cultivars by targeted HPLC-MS/MS. *Foods*, 9(10), 1–25. <https://doi.org/10.3390/foods9101448>
- Sembiring Timbangan, Dayana Indri, Rianna Martha. Alat Penguji Material. 2019. Bogor: Guepedia.
- Shukla, K., Singh, P., Singh Mahatma, R., Chitrakoot, G., Vishwavidyalaya, G., & Sharma, R. (2015). Amylases: an overview with special reference to alpha amylase Molecular characterization of Geminivirus/es and their management View project. *Article in Journal of Global Biosciences*, January 2017. www.mutagens.co.in
- Sinulingga, S., Subandrate, S., & Safyudin, S. (2020). Uji Fitokimia dan Potensi Antidiabetes Fraksi Etanol Air Benalu Kersen (*Dendrophloe petandra* (L) Miq). *Jurnal Kedokteran Dan Kesehatan*, 16(1), 76. <https://doi.org/10.24853/jkk.16.1.76-83>
- Sobczak-Kupiec, A., Drabczyk, A., Florkiewicz, W., Głab, M., Kudłacik-Kramarczyk, S., Słota, D., Tomala, A., & Tylińczak, B. (2021). Review of

- the applications of biomedical compositions containing hydroxyapatite and collagen modified by bioactive components. *Materials*, 14(9). <https://doi.org/10.3390/ma14092096>
- Song, J. J., Wang, Q., Du, M., Ji, X. M., & Mao, X. Y. (2017). Identification of dipeptidyl 614 peptidase-IV inhibitory peptides from mare whey protein hydrolysates. *Journal of Dairy 615 Science*, 100, 6885-6894
- Stanzione, F., Giangreco, I., & Cole, J. C. (2021). Use of *molecular docking* computational tools in drug discovery. *Progress in Medicinal Chemistry*, 273–343. doi:10.1016/bs.pmch.2021.01.004
- St. Maryam, Suhaena, A., & Amrullah, N. F. (2020). Uji Aktivitas Penghambatan Enzim α -Glukosidase Ekstrak Etanol Biji Buah Alpukat Sangrai (*Persea americana* Mill .) Secara In Vitro. *Jurnal Farmas*, 12(1), 51–56.
- Sulaiman, A. W., & Sarbon, N. M. (2020). Characterization of acid soluble collagen (Asc) and pepsin soluble collagen (psc) extracted from shortfin scad (*decapterus macrosoma*) waste. *Food Research*, 4(6), 2272–2280. [https://doi.org/10.26656/fr.2017.4\(6\).267](https://doi.org/10.26656/fr.2017.4(6).267)
- Sundarram, A., & Murthy, T. P. K. (2014). α -Amylase Production and Applications : A Review. *Journal of Applied & Environmental Microbiology*, 2(4), 166–175. <https://doi.org/10.12691/jaem-2-4-10>
- Taylor, W. H. (1957). Formol titration: An evaluation of its various modifications. *The Analyst*, 488, 488–498. <https://doi.org/10.1039/AN9578200488>
- Tiwari Anshul & Singh Sakshi. (2022). Chapter 13 - Computational approaches in drug designing. *Bioinformatics*, 207-217.
- Tri Ari Penia Kresnowati, M., Rahayu Affandi, C., & Pratiwi, C. (2021). Preliminary Evaluation of Halal Protein Hydrolysate Production in Indonesia. *IOP Conference Series: Materials Science and Engineering*, 1143(1), 012040. <https://doi.org/10.1088/1757-899x/1143/1/012040>
- Truong, T. M. T., Nguyen, V. M., Tran, T. T., & Le, T. M. T. (2021). Characterization of acid-soluble collagen from food processing by-products of snakehead fish (*Channa striata*). *Processes*, 9(7), 1–11. <https://doi.org/10.3390/pr9071188>

- Ubaidillah, Z., Pratama, P. L., Susanto, N. A., & Ariani, T. A. (2021). Analisis Faktor Hiperglikemia Tidak Terkontrol Pada Klien Diabetes Melitu Tipe 2. *Jurnal Keperawatan*, *13*(1), 213–226.
- Venkatesan, J., Anil, S., Kim, S. K., & Shim, M. S. (2017). Marine fish proteins and peptides for cosmeceuticals: A review. *Marine Drugs*, *15*(5), 1–18. <https://doi.org/10.3390/md15050143>
- Villaret, A., Ipinazar, C., Satar, T., Gravier, E., Mias, C., Questel, E., Schmitt, A. M., Samouillan, V., Nadal, F., & Josse, G. (2019). Raman characterization of human skin aging. *Skin Research and Technology*, *25*(3), 270–276. <https://doi.org/10.1111/srt.12643>
- Vilsbøll, T., & Knop, F. K. (2007). DPP IV inhibitors - Current evidence and future directions. *British Journal of Diabetes and Vascular Disease*, *7*(2), 69–74. <https://doi.org/10.1177/14746514070070020401>
- Wardani, N. A. K., Andini, Indriani, P. T., & Sarinastiti, D. I. (2018). Enzim α -Amilase Inhibitor Pada Ekstrak Air Kacang Merah (*Phaseolus vulgaris* L.) Untuk Penanggulangan Diabetes Melitus. *Jurnal Ilmu Pangan Dan Hasil Pertanian*, *1*(2), 50–59. <https://doi.org/10.26877/jiphp.v1i2.1900>
- Wang, H., Zhang, W., Xu, J., & Guo, Z. (2018). Advances in Polar Materials for Lithium–Sulfur Batteries. *Advanced Functional Materials*, *28*(38). <https://doi.org/10.1002/adfm.201707520>
- Wang, S. S., Yu, Y., Sun, Y., Liu, N., & Zhou, D. Q. (2019). Comparison of Physicochemical Characteristics and Fibril Formation Ability of Collagens Extracted from the Skin of Farmed River Puffer (*Takifugu obscurus*) and Tiger Puffer (*Takifugu rubripes*). *Marine Drugs*, *17*(8). <https://doi.org/10.3390/md17080462>
- Weichenberger, C. X., Byzia, P., & Sippl, M. J. (2008). Visualization of unfavorable interactions in protein folds. *Bioinformatics*, *24*(9), 1206–1207. <https://doi.org/10.1093/bioinformatics/btn108>
- Xiong, Q., Hu, L. X., Liu, Y. S., Wang, T. T., & Ying, G. G. (2019). New insight into the toxic effects of chloramphenicol and roxithromycin to algae using FTIR spectroscopy. *Aquatic Toxicology*, *207*(November 2018), 197–207.

<https://doi.org/10.1016/j.aquatox.2018.12.017>

- Yandri, Nadila, N., Suhartati, T., Satria, H., & Hadi, S. (2020). PENINGKATAN KESTABILAN ENZIM α -AMILASE DENGAN PENAMBAHAN GLISEROL. *Analit: Analytical and Environmental Chemistry*, 5(02), 143–154.
- Yuniarto, A., & Selifiana, N. (2018). Aktivitas Inhibisi Enzim Alfa-glukosidase dari Ekstrak Rimpang Bangle (*Zingiber cassumunar* Roxb.) secara In vitro. *MPI (Media Pharmaceutica Indonesiana)*, 2(1), 22–25. <https://doi.org/10.24123/mpi.v2i1.1299>
- Yuniastuti, A., Susanti, R., & Iswari, R. S. (2018). Efek Infusa Umbi Garut (*Marantha arundinaceae* L) Terhadap Kadar Glukosa dan Insulin Plasma Tikus yang Diinduksi Streptozotocyn. *Jurnal Mipa*, 41(1), 34–39.
- Yuniati, R., Pradigdo, S. F., & Rahfiludin, M. Z. (2017). Hubungan Konsumsi Karbohidrat, Lemak Dan Serat Dengan Kadar Glukosa Darah Pada Lanjut Usia Wanita (Studi Di Rumah Pelayanan Sosial Lanjut Usia Pucang Gading Kota Semarang Tahun 2017). *Jurnal Kesehatan Masyarakat (e-Journal)*, 5(4), 759–767.
- Zaelani, B. F. D., Safithri, M., Tarman, K., Setyaningsih, I., & Meydia, M. (2019). Collagen isolation with acid soluble method from the skin of Red Snapper (*Lutjanus* sp.). *IOP Conference Series: Earth and Environmental Science*, 241(1).
- Zhou, X., Chai, L., Wu, Q., Wang, Y., Li, S., & Chen, J. (2021). Anti-diabetic properties of bioactive components from fish and milk. *Journal of Functional Foods*, 85, 104669. <https://doi.org/10.1016/j.jff.2021.104669>