KARAKTERISASI EKSTRAK DAN HIDROLISAT KOLAGEN DARI LIMBAH KULIT IKAN PATIN SERTA PREDIKSI POTENSI BIOAKTIVITASNYA SECARA *IN SILICO* SEBAGAI AGEN PENYEMBUH LUKA DIABETES

SKRIPSI

Diajukan untuk memenuhi sebagian syarat untuk memperoleh gelar sarjana sains
di bidang kimia

oleh:
Yunita Rachmawati
NIM 2107948

PROGRAM STUDI KIMIA
FAKULTAS PENDIDIKAN MATEMATKA DAN ILMU PENGETAHUAN ALAM
UNIVERSITAS PENDIDIKAN INDONESIA
2025

KARAKTERISASI EKSTRAK DAN HIDROLISAT KOLAGEN DARI LIMBAH KULIT IKAN PATIN SERTA PREDIKSI POTENSI BIOAKTIVITASNYA SECARA *IN SILICO* SEBAGAI AGEN PENYEMBUH LUKA DIABETES

Oleh
Yunita Rachmawati

Sebuah skripsi yang diajukan untuk memenuhi salah satu syarat memperoleh gelar Sarjana Sains pada Program Studi Kimia Fakultas Pendidikan Matematika dan Ilmu Pengetahuan Alam

Universitas Pendidikan Indonesia
Agustus 2025

HALAMAN PENGESAHAN

KARAKTERISASI EKSTRAK DAN HIDROLISAT KOLAGEN DARI LIMBAH KULIT IKAN PATIN SERTA PREDIKSI POTENSI BIOAKTIVITASNYA SECARA *IN SILICO* SEBAGAI AGEN PENYEMBUH LUKA DIABETES

oleh:

Yunita Rachmawati

2107948

Disetujui dan disahkan oleh:

Pembimbing I

Prof. Heli Siti Halimatul Munawaroh, M.Si., Ph.D.

NIP. 197907302001122002

Pembimbing II

Vidia Afina Nuraini, S.Si.,M.Sc.

NIP. 199307052020122009

Mengetahui,

Ketua Program Studi Kimia

Prof. Fitri Khoerunnisa, Ph.D.

NIP. 197806282001122001

ABSTRAK

Luka diabetes merupakan komplikasi diabetes melitus yang ditandai dengan penyembuhan luka yang lambat karena penurunan aktivitas angiogenesis. Angiogenesis berperan dalam regenerasi jaringan melalui pembentukan pembuluh darah baru. Industri pengolahan ikan patin menghasilkan limbah kulit yang dapat dimanfaatkan sebagai sumber kolagen alami untuk agen penyembuhan luka. Penelitian ini bertujuan mengevaluasi karakteristik ekstrak dan hidrolisat kolagen dari limbah kulit ikan patin serta memprediksi potensi bioaktivitasnya melalui studi *in silico* meliputi aktivitas pro-angiogenesis, antioksidan, dan antibakteri. Peptida aktif diperoleh melalui ekstraksi kolagen larut asam dan di karakterisasi dengan UV, FTIR, dan SDS-PAGE. Hidrolisat kolagen menggunakan enzim bromelin dan di karakterisasi menggunakan UV, FTIR, dan SDS-PAGE. Pengujian *in vitro* menunjukkan ekstrak kolagen mengandung protein 95,4% ± 2,00%, memiliki serapan UV khas kolagen pada 216 nm, gugus amida dan prolin/hidroksiprolin (FTIR), serta pita protein α (130 kDa) dan β (250 kDa) kolagen tipe I (SDS-PAGE). Hidrolisat kolagen menunjukkan derajat hidrolisis 63% pada 24 jam, hilangnya serapan kolagen pada 210–240 nm, pergeseran gugus (FTIR), serta pita <15 kDa (SDS-PAGE) yang menandakan *fragmentasi* menjadi peptida berukuran kecil. Hasil *in silico* menunjukkan bahwa peptida NF dan WKPEPCQICV memiliki afinitas ikatan yang tinggi terhadap VEGFR2 dan MMP-2 (pro-angiogenesis), KEAP1 (antioksidan), serta *DNA Gyrase* (antibakteri). Proses hidrolisis dapat memodifikasi struktur kolagen dan peptida aktif yang dihasilkan berpotensi dikembangkan sebagai agen terapi alami dalam merangsang pembentukan pembuluh darah baru, mengurangi stres oksidatif, dan menghambat infeksi bakteri pada luka diabetes. Validasi lanjutan secara *in vitro* terhadap bioaktivitas peptida ini direkomendasikan sebelum menuju tahap pengembangan aplikasi terapeutik.

Kata Kunci: Peptida Aktif, Kulit Ikan Patin, Kolagen, Hidrolisat Kolagen, Luka Diabetes, *In* Silico, Angiogenesis

ABSTRACT

Diabetic wounds are a complication of diabetes mellitus characterized by slow wound healing due to decreased angiogenesis activity. Angiogenesis plays a role in tissue regeneration through the formation of new blood vessels. The catfish processing industry produces skin waste that can be utilized as a natural source of collagen for wound healing agents. This study aims to evaluate the characteristics of collagen extracts and hydrolysates from catfish skin waste and predict their potential bioactivity through in silico studies including pro-angiogenesis, antioxidant, and antibacterial activities. Active peptides were obtained through acid soluble collagen extraction and characterized by UV, FTIR, and SDS-PAGE. Collagen hydrolysate using bromelain enzyme and characterized using UV, FTIR, and SDS-PAGE. In vitro testing showed that the collagen extract contained 95.4% ± 2.00% protein, had typical collagen UV absorption at 216 nm, amide and proline/hydroxyproline groups (FTIR), and α (130 kDa) and β (250 kDa) protein bands of type I collagen (SDS-PAGE). The collagen hydrolysate showed 63% hydrolysis degree at 24 hours, loss of collagen absorption at 210-240 nm, cluster shift (FTIR), and <15 kDa band (SDS-PAGE) indicating fragmentation into small-sized peptides. In silico results showed that NF and WKPEPCQICV peptides have high binding affinity to VEGFR2 and MMP-2 (pro-angiogenesis), KEAP1 (antioxidant), and DNA Gyrase (antibacterial). The hydrolysis process can modify the structure of collagen and the resulting active peptides have the potential to be developed as natural therapeutic agents in stimulating the formation of new blood vessels, reducing oxidative stress, and inhibiting bacterial infection in diabetic wounds. Further in vitro validation of the bioactivity of these peptides is recommended before moving towards the development stage of therapeutic applications.

Keyword: *Active Peptides, Catfish Skin, Collagens, Collagen Hydrolysate, Diabetic Wounds, In Silico, Angiogenesis*

DAFTAR ISI

DAFTAR GAMBAR

DAFTAR TABEL

DAFTAR SINGKATAN

AGEs	: *Advanced Glycation End-Products*
Akt	: Protein Kinase B
Ala	: Alanin
Arg	: Arginine
ASC	: *Acid Soluble Collagen*
ATP	: *Adenosin Trifosfat*
CF	: *Cysteine–Phenylalanine*
CR	: *Cysteine–Arginine*
DM	: Diabetes melitus
DNA	: Asam Deoksiribonukleat
ECH	: *Enoyl-CoA Hydratase*
ECM	: Matriks Ekstraseluler
eNOS	: *endothelial Nitric Oxide Synthase*
FAO	: *Food and Agriculture Organization of the United Nations*
FTIR	: *Fourier Transform Infrared Spectroscopy*
Gly	: Glisin
GyrB	: *Gyrase* B
HCl	: Asam Klorida
HIF-1	: *Hypoxia-Inducible Factor* 1
HO-1	: *Heme Oxygenase*-1
Hyp	: Hidroksiprolin
IDF	: *International Diabetes Federation*
KEAP1	: *Kelch-like ECH-associated protein* 1
MF	: *Methionine–Phenylalanine*
MG	: *Methionine–Glycine*
MMP2	: *Matrix Metalloproteinase* 2
MPG	: *Methionine–Proline–Glycine*
MR	: *Methionine–Arginine*
NaOH	: Natrium Hidroksida
NF	: *Asparagine–Phenylalanine*
NPWT	: *Negative Pressure Wound Therapy*
NQO1	: NAD(P)H:*quinone oxidoreductase* 1
PDPF	: *Proline–Aspartic acid–Proline–Phenylalanine*
PG	: *Proline–Glycine*
Phe	: Fenilalanin
PI3K	: Phosphoinositide 3-kinase
PMG	: *Proline–Methionine–Glycine*
PPG	: *Proline–Proline–Glycine*
Pro	: Prolin
PSC	: *Pepsin Soluble Collagen*
QF	: *Glutamine–Phenylalanine*
RMSD	: *Root Mean Square Deviation*
RNA	: Asam Ribonukleat
ROS	: *Reactive Oxygen Species*

SDS-PAGE	: *Sodium Dodecyl Sulfate–Polyacrylamide Ge*l
SOD2	: *Superoxide Dismutase* 2
Trp	: Tripsin 44
Tyr	: Tirosin 44
UV-Vis	: *Ultraviolet–Visible Spectrophotometry*
VEGFR2	: *Vascular Endothelial Growth Factor Receptor*-2
WF	: *Tryptophan–Phenylalanine*
WG	: *Tryptophan–Glycine*
WKPEPCQICV	: *Tryptophan–Lysine–Proline–Glutamic acid–Proline – Cysteine–Glutamine–Isoleucine–Cysteine–Valine*

DAFTAR LAMPIRAN

DAFTAR PUSTAKA

Abbas, A. A., Shakir, K. A., & Walsh, M. K. (2022). Functional Properties of Collagen Extracted from Catfish (Silurus triostegus) Waste. *Foods*, *11*(5), 633. https://doi.org/10.3390/foods11050633

Abuzenadah, A. M., Al-Sayes, F., Mahafujul Alam, S. S., Hoque, M., Karim, S., Hussain, I. M. R., & Tabrez, S. (2022). Elucidating Antiangiogenic Potential of Rauwolfia serpentina: VEGFR-2 Targeting-Based Molecular Docking Study. *Evidence-Based Complementary and Alternative Medicine*, *2022*, 1–10. https://doi.org/10.1155/2022/6224666

Adejumo, A. L., Azeez, L., Ajayi, E., Atere, T. G., Aderibigbe, F. A., & Adetoro, R. O. (2022). Characterisation, Amino Acid Composition and Denaturation status of Acid Soluble Collagen from Catfish (Clarias gariepinus) Skin. *West Indian Journal of Engineering*, *44*(2), 14–19. https://doi.org/10.47412/oymi4758

Afifah, A., Suparno, O., Haditjaroko, L., Tarman, K., Setiyono, A., & Nugraha, A. W. (2024). Isolation and characterization of collagen from salmon (Salmo salar) skin using papain enzyme. *Jurnal Pengolahan Hasil Perikanan Indonesia*, *27*(6), 536–552. https://doi.org/10.17844/jphpi.v27i6.53285

Agu, P. C., Afiukwa, C. A., Orji, O. U., Ezeh, E. M., Ofoke, I. H., Ogbu, C. O., Ugwuja, E. I., & Aja, P. M. (2023). Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management. *Scientific Reports*, *13*(1). https://doi.org/10.1038/s41598-023-40160-2

Ahmed, R., Haq, M., & Chun, B.-S. (2019). Characterization of marine derived collagen extracted from the by-products of bigeye tuna (Thunnus obesus). *International Journal of Biological Macromolecules*, *135*, 668–676. https://doi.org/10.1016/j.ijbiomac.2019.05.213

Ahuja, I., Dauksas, E., Remme, J. F., Richardsen, R., & Løes, A.-K. (2020). Fish and fish waste-based fertilizers in organic farming – With status in Norway: A review. *Waste Management*, *115*, 95–112. https://doi.org/10.1016/j.wasman.2020.07.025

Aitcheson, S. M., Frentiu, F. D., Hurn, S. E., Edwards, K., & Murray, R. Z. (2021). Skin Wound Healing: Normal Macrophage Function and Macrophage Dysfunction in Diabetic Wounds. *Molecules*, *26*(16), 4917. https://doi.org/10.3390/molecules26164917

Al Hajj, W., Salla, M., Krayem, M., Khaled, S., Hassan, H. F., & El Khatib, S. (2024). Hydrolyzed collagen: Exploring its applications in the food and beverage industries and assessing its impact on human health – A comprehensive review. Dalam *Heliyon* (Vol. 10, Nomor 16). Elsevier Ltd. https://doi.org/10.1016/j.heliyon.2024.e36433

Alahmad, K., Xia, W., Jiang, Q., & Xu, Y. (2022). Effect of the Degree of Hydrolysis on Nutritional, Functional, and Morphological Characteristics of Protein Hydrolysate Produced from Bighead Carp (Hypophthalmichthys nobilis) Using Ficin Enzyme. *Foods*, *11*(9), 1320. https://doi.org/10.3390/foods11091320

Al-Hassan, J. M., Hinek, A., Renno, W. M., Wang, Y., Liu, Y. F., Guan, R., Wen, X. Y., Litvack, M. L., Lindenmaier, A., Afzal, M., Paul, B., Oommen, S., Nair, D., Kumar, J., Khan, M. A., Palaniyar, N., & Pace-Asciak, C. (2020). Potential Mechanism of Dermal Wound Treatment With Preparations From the Skin Gel of Arabian Gulf Catfish: A Unique Furan Fatty Acid (F6) and Cholesta-3,5-Diene (S5) Recruit Neutrophils and Fibroblasts to Promote Wound Healing. *Frontiers in Pharmacology*, *11*. https://doi.org/10.3389/fphar.2020.00899

Ali Arsyad, M., Rusli dan Rosmaladewi Program Studi Pengolahan dan Penyimpanan Hasil Perikanan, A., & Pertanian Negeri Pangkajene Kepulauan Jl, P. (2024). Karakteristik Kimiawi Kolagen Larut Asam Dari Cangkang Bulu Babi Chemical Characteristics Of Acid-Soluble Collagen From Sea Urchin Sheel. *Jurnal Segara*, *19*(2), 107–114. https://doi.org/10.15578/segara.v19i2.14673

Alsedfy, M. Y., Ebnalwaled, A. A., Moustafa, M., & Said, A. H. (2024). Investigating the binding affinity, molecular dynamics, and ADMET properties of curcumin-IONPs as a mucoadhesive bioavailable oral treatment for iron deficiency anemia. *Scientific Reports*, *14*(1), 22027. https://doi.org/10.1038/s41598-024-72577-8

Ameji, P. J., Uzairu, A., Shallangwa, G. A., & Uba, S. (2024). Retraction Note: Molecular docking simulation, drug-likeness assessment, and pharmacokinetic study of some cephalosporin analogues against a penicillin-binding protein of Salmonella typhimurium. *The Journal of Antibiotics*, *77*(2), 128–128. https://doi.org/10.1038/s41429-023-00684-1

American Diabetes Association. (2020). Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2021. *Diabetes Care*, *44*(Supplement_1), S111–S124. https://doi.org/10.2337/dc21-S009

Amirrah, I. N., Lokanathan, Y., Zulkiflee, I., Wee, M. F. M. R., Motta, A., & Fauzi, M. B. (2022). A Comprehensive Review on Collagen Type I Development of Biomaterials for Tissue Engineering: From Biosynthesis to Bioscaffold. Dalam *Biomedicines* (Vol. 10, Nomor 9). MDPI. https://doi.org/10.3390/biomedicines10092307

Ampitiya, A. G. D. M., Gonapinuwala, S. T., Fernando, C. A. N., & de Croos, M. D. S. T. (2023). Extraction and characterisation of type I collagen from the skin offcuts generated at the commercial fish processing centres. *Journal of Food Science and Technology*, *60*(2), 484–493. https://doi.org/10.1007/s13197-022-05630-x

Andini, A., Handajani, R., Koesnowidagdo, S., Ichsan, M. Z., & Pighinelli, L. (2020). In vivo Effectivity of Collagen Extract from Clarias gariepinus (Burchell, 1822) 'Sangkuriang' on Formation of Malondialdehyde and Macrophages in Burn Healing: Effectivity of Collagen Extract from Clarias gariepinus in Burn Healing. *Proceedings of the Pakistan Academy of Sciences: B. Life and Environmental Sciences*, *57*, 35–0. http://www.ppaspk.org/index.php/PPAS-B/article/view/5

Angelina Natalia Ricardo. (2024). *Pengaruh Aplikasi Gel Kolagen Patin Siam (Pangasius Hypophthalmus) Terhadap Penyembuhan Luka Pasca Ekstraksi Gigi* [Universitas Sriwijaya]. http://repository.unsri.ac.id/167374/4/RAMA_11106_04112682327003_0030089002_0028128304_01_front_ref.pdf

Antar, S. A., Ashour, N. A., Sharaky, M., Khattab, M., Ashour, N. A., Zaid, R. T., Roh, E. J., Elkamhawy, A., & Al-Karmalawy, A. A. (2023). Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. *Biomedicine & Pharmacotherapy*, *168*, 115734. https://doi.org/https://doi.org/10.1016/j.biopha.2023.115734

Arda, A. G., Syaifie, P. H., Ramadhan, D., Jauhar, M. M., Nugroho, D. W., Kaswati, N. M. N., Noviyanto, A., Safihtri, M., Rochman, N. T., Andrianto, D., & Mardliyati, E. (2024). Activity of propolis compounds as potential MMP1 and MMP2 inhibitors by in silico studies in wound healing application. *Journal of Pharmacy & Pharmacognosy Research*, *12*(2), 264–285. https://doi.org/10.56499/jppres23.1719_12.2.264

Arifin, A., & Kurnia, A. (2022). Aplikasi Penerapan Lidah Buaya (Aloe Vera) Dalam Penyembuhan Luka Ulkus Diabetes Melitus. *Holistic Nursing Care Approach*, *2*(2), 54. https://doi.org/10.26714/hnca.v2i2.9330

Asnawi, A., Febrina, E., Aligita, W., Aman, L. O., & Razi, F. (2024). Molecular docking and molecular dynamics study of 3-hydroxybutyrate with polymers for diabetic ketoacidosis-targeted molecularly imprinted polymers. *Journal of Pharmacy & Pharmacognosy Research*, *12*(5), 822–836. https://doi.org/10.56499/jppres23.1926_12.5.822

Atef, M., Ojagh, S. M., Latifi, A. M., Esmaeili, M., & Udenigwe, C. C. (2020). Biochemical and structural characterization of sturgeon fish skin collagen

(Huso huso). *Journal of Food Biochemistry*, *44*(8). https://doi.org/10.1111/jfbc.13256

Baheramsyah. (2021, Desember 12). *Dongkrak Produktivitas, KKP Siapkan Patin Pustina*. Info Publik Portal Berita Info Publik. https://infopublik.id/kategori/nasional-politik-hukum/589049/dongkrak-produktivitas-kkp-siapkan-patin-pustina?video=

Burgess, J. L., Wyant, W. A., Abujamra, B. A., Kirsner, R. S., & Jozic, I. (2021). Diabetic wound-healing science. Dalam *Medicina (Lithuania)* (Vol. 57, Nomor 10). MDPI. https://doi.org/10.3390/medicina57101072

C, S., S., D. K., Ragunathan, V., Tiwari, P., A., S., & P, B. D. (2022). Molecular docking, validation, dynamics simulations, and pharmacokinetic prediction of natural compounds against the SARS-CoV-2 main-protease. *Journal of Biomolecular Structure and Dynamics*, *40*(2), 585–611. https://doi.org/10.1080/07391102.2020.1815584

Cabral-Pacheco, G. A., Garza-Veloz, I., Castruita-De la Rosa, C., Ramirez-Acuña, J. M., Perez-Romero, B. A., Guerrero-Rodriguez, J. F., Martinez-Avila, N., & Martinez-Fierro, M. L. (2020). The Roles of Matrix Metalloproteinases and Their Inhibitors in Human Diseases. *International Journal of Molecular Sciences*, *21*(24), 9739. https://doi.org/10.3390/ijms21249739

Cao, Z., Chen, J., Cannon, J., Meyer, Z., Li, Y., Ouyang, W., Baker, J., & Wang, S. H. (2024). Nanoemulsion is an effective antimicrobial for methicillin-resistant Staphylococcus aureusin infected swine skin burn wounds. *Microbiology Spectrum*, *12*(11). https://doi.org/10.1128/spectrum.01378-24

Carpio, K. C. R., Bezerra, R. S., Cahú, T. B., Do Monte, F. T. D., Neri, R. C. A., da Silva, J. F., Dos Santos, P. R., Carvalho, R. P., Galeno, D. M. L., & Inhamuns, A. J. (2023). Extraction and characterization of collagen from the skin of Amazonian freshwater fish pirarucu. *Brazilian Journal of Medical and Biological Research*, *56*. https://doi.org/10.1590/1414-431X2023e12564

Chen, H., Yin, B., Hu, B., Zhang, B., Liu, J., Jing, Y., Fan, Z., Tian, Y., Wei, X., & Zhang, W. (2021). Acellular fish skin enhances wound healing by promoting angiogenesis and collagen deposition. *Biomedical Materials*, *16*(4), 045011. https://doi.org/10.1088/1748-605X/abef7a

Chen, J., Qin, S., Liu, S., Zhong, K., Jing, Y., Wu, X., Peng, F., Li, D., & Peng, C. (2023). Targeting matrix metalloproteases in diabetic wound healing. *Frontiers in Immunology*, *14*. https://doi.org/10.3389/fimmu.2023.1089001

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

Coppola, D., Lauritano, C., Palma Esposito, F., Riccio, G., Rizzo, C., & de Pascale, D. (2021). Fish Waste: From Problem to Valuable Resource. *Marine Drugs*, *19*(2), 116. https://doi.org/10.3390/md19020116

Coscueta, E. R., Brassesco, M. E., & Pintado, M. (2021). Collagen-based bioactive bromelain hydrolysate from salt-cured cod skin. *Applied Sciences (Switzerland)*, *11*(18). https://doi.org/10.3390/app11188538

Dănilă, E., Stan, R., Kaya, M. A., Voicu, G., Marin, M. M., Moroşan, A., Titorencu, I., & Ţuţuianu, R. (2022). Valorization of Cyprinus Carpio Skin for Biocompatible Collagen Hydrolysates with Potential Application in Foods, Cosmetics and Pharmaceuticals. *Waste and Biomass Valorization*, *13*(2), 917–928. https://doi.org/10.1007/s12649-021-01569-w

Das, A., Abas, M., Biswas, N., Banerjee, P., Ghosh, N., Rawat, A., Khanna, S., Roy, S., & Sen, C. K. (2019). A Modified Collagen Dressing Induces Transition of Inflammatory to Reparative Phenotype of Wound Macrophages. *Scientific Reports*, *9*(1), 14293. https://doi.org/10.1038/s41598-019-49435-z

de Almeida, L. G. N., Thode, H., Eslambolchi, Y., Chopra, S., Young, D., Gill, S., Devel, L., & Dufour, A. (2022). Matrix Metalloproteinases: From Molecular Mechanisms to Physiology, Pathophysiology, and Pharmacology. *Pharmacological Reviews*, *74*(3), 714–770. https://doi.org/10.1124/pharmrev.121.000349

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

Dikel, Ç., & Yanar, Y. (2025). Characterization of Acid-Soluble Collagen From By-Product Bones of European Sea Bass (Dicentrarchus labrax and Common Carp (Cyprinus carpio). *Food Science & Nutrition*, *13*(4). https://doi.org/10.1002/fsn3.70059

Diller, R. B., & Tabor, A. J. (2022). The Role of the Extracellular Matrix (ECM) in Wound Healing: A Review. *Biomimetics*, *7*(3), 87. https://doi.org/10.3390/biomimetics7030087

Dimitrov, I., Bangov, I., Flower, D. R., & Doytchinova, I. (2014). AllerTOP v.2—a server for in silico prediction of allergens. *Journal of Molecular Modeling*, *20*(6), 2278. https://doi.org/10.1007/s00894-014-2278-5

Duong, T. Y., Pham, L. T. K., Le, X. T. K., Nguyen, N. T. T., Nor, S. A. M., & Le, T. H. (2023). Mitophylogeny of Pangasiid Catfishes and its Taxonomic Implications for Pangasiidae and the Suborder Siluroidei. *Zoological Studies*, *62*. https://doi.org/10.6620/ZS.2023.62-48

El Masry, M. S., Chaffee, S., Das Ghatak, P., Mathew-Steiner, S. S., Das, A., Higuita-Castro, N., Roy, S., Anani, R. A., & Sen, C. K. (2019). Stabilized collagen matrix dressing improves wound macrophage function and epithelialization. *The FASEB Journal*, *33*(2), 2144–2155. https://doi.org/10.1096/fj.201800352R

Escott, G. M., da Silveira, L. G., Cancelier, V. da A., Dall'Agnol, A., & Silveiro, S. P. (2021). Monitoring and management of hyperglycemia in patients with advanced diabetic kidney disease. *Journal of Diabetes and its Complications*, *35*(2), 107774. https://doi.org/https://doi.org/10.1016/j.jdiacomp.2020.107774

Fagnani, L., Bellio, P., Di Giulio, A., Nazzicone, L., Iorio, R., Petricca, S., Franceschini, N., Bertarini, L., Tondi, D., & Celenza, G. (2024). Mechanism of non-competitive inhibition of the SARS-CoV-2 3CL protease dimerization: Therapeutic and clinical promise of the lichen secondary metabolite perlatolinic acid. *Heliyon*, *10*(19), e38445. https://doi.org/10.1016/j.heliyon.2024.e38445

Farooq, S., Ahmad, M. I., Zheng, S., Ali, U., Li, Y., Shixiu, C., & Zhang, H. (2024). A review on marine collagen: sources, extraction methods, colloids properties, and food applications. *Collagen and Leather*, *6*(1), 11. https://doi.org/10.1186/s42825-024-00152-y

Fitrianingsih, Sauriasari, R., Yunir, E., & Saptaningsih, A. B. (2025). In-hospital costs of diabetic foot infection at a national referral hospital in Jakarta, Indonesia. *Heliyon*, *11*(2). https://doi.org/10.1016/j.heliyon.2024.e41263

Fu, K., Zheng, X., Chen, Y., Wu, L., Yang, Z., Chen, X., & Song, W. (2022). Role of matrix metalloproteinases in diabetic foot ulcers: Potential therapeutic targets. *Frontiers in Pharmacology*, *13*. https://doi.org/10.3389/fphar.2022.1050630

Fu, Z., Akula, S., Thorpe, M., & Hellman, L. (2021). Marked difference in efficiency of the digestive enzymes pepsin, trypsin, chymotrypsin, and pancreatic elastase to cleave tightly folded proteins. *Biological Chemistry*, *402*(7), 861–867. https://doi.org/10.1515/hsz-2020-0386

Gaikwad, S., & Kim, M. J. (2024). Fish By-Product Collagen Extraction Using Different Methods and Their Application. *Marine Drugs*, *22*(2), 60. https://doi.org/10.3390/md22020060

Galeano, M., Pallio, G., Irrera, N., Mannino, F., Bitto, A., Altavilla, D., Vaccaro, M., Squadrito, G., Arcoraci, V., Colonna, M. R., Lauro, R., & Squadrito, F. (2021). Polydeoxyribonucleotide: A Promising Biological Platform to Accelerate Impaired Skin Wound Healing. *Pharmaceuticals*, *14*(11), 1103. https://doi.org/10.3390/ph14111103

Gao, D., Guo, P., Cao, X., Ge, L., Ma, H., Cheng, H., Ke, Y., Chen, S., Ding, G., Feng, R., Qiao, Z., Bai, J., Nordin, N. I., & Ma, Z. (2020). Improvement of chicken plasma protein hydrolysate angiotensin I-converting enzyme inhibitory activity by optimizing plastein reaction. *Food Science and Nutrition*, *8*(6), 2798–2808. https://doi.org/10.1002/fsn3.1572

Gea, R., Zai, R., Perjuangan Lombu, F., Dwista Telaumbanua, D., Cerdas Lase, R., Juwita Dawolo, A., Dewi Zebua, R., Studi Sumber Daya Akuatik, P., & Sains dan Teknologi, F. (2025). Analisis Kinerja Pertumbuhan Ikan Patin (Pangasius Sp.) pada Sistem Budidaya dengan Kolam Terpal. *Ilmu Kedokteran Hewan*, *3*, 63–72. https://doi.org/10.62951/zoologi.v3i1.102

Geahchan, S., Baharlouei, P., & Rahman, M. A. (2022). Marine Collagen: A Promising Biomaterial for Wound Healing, Skin Anti-Aging, and Bone Regeneration. Dalam *Marine Drugs* (Vol. 20, Nomor 1). MDPI. https://doi.org/10.3390/md20010061

Geindreau, M., Ghiringhelli, F., & Bruchard, M. (2021). Vascular Endothelial Growth Factor, a Key Modulator of the Anti-Tumor Immune Response. *International Journal of Molecular Sciences*, *22*(9), 4871. https://doi.org/10.3390/ijms22094871

Gianino, E., Miller, C., & Gilmore, J. (2018). Smart wound dressings for diabetic chronic wounds. Dalam *Bioengineering* (Vol. 5, Nomor 3). MDPI AG. https://doi.org/10.3390/bioengineering5030051

Girsang, V., Reveny, J., & Nainggolan, M. (2020). Isolation and Characterization Collagen Of Patin Fish Skin (Pangasius Sp.). *Asian Journal of Pharmaceutical Research and Development*, *8*(1), 47–51. https://doi.org/10.22270/ajprd.v8i1.661

Goshev, I., & Nedkov, P. (1979). *Extending the Range of Application of the Biuret .Reaction: Quantitative Determination of Insoluble Proteins*.

Gupta, S., Kapoor, P., Chaudhary, K., Gautam, A., Kumar, R., & Raghava, G. P. S. (2013). In Silico Approach for Predicting Toxicity of Peptides and Proteins. *PLoS ONE*, *8*(9), e73957. https://doi.org/10.1371/journal.pone.0073957

Hadfi, N. H., & Sarbon, N. M. (2019). Physicochemical properties of silver catfish (Pangasius sp.) skin collagen as influenced by acetic acid concentration. *Food Research*, *3*(6), 783–790. https://doi.org/10.26656/fr.2017.3(6).130

Harris, M., Potgieter, J., Ishfaq, K., & Shahzad, M. (2021). Developments for collagen hydrolysate in biological, biochemical, and biomedical domains: A comprehensive review. *Materials*, *14*(11). https://doi.org/10.3390/ma14112806

Hartina, U., Razali, M., Mamat, H., & Qhairul, N. (2019). *Properties Of Hydrolysed Collagen From The Skin Of Milkfish (Chanoschanos) As Affected By Different Enzymatic Treatments*. https://doi.org/10.5281/zenodo.2572454

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

Hilliard, G. M., Wilkinson, T. S., Harris, L. G., Jenkins, R. E., & Shornick, L. P. (2024). PCL-gelatin honey scaffolds promote Staphylococcus aureus agrA expression in biofilms with Pseudomonas aeruginosa. *Frontiers in Microbiology*, *15*. https://doi.org/10.3389/fmicb.2024.1440658

Hong, H., Zheng, Y., Song, S., Zhang, Y., Zhang, C., Liu, J., & Luo, Y. (2020). Identification and characterization of DPP-IV inhibitory peptides from silver carp swim bladder hydrolysates. *Food Bioscience*, *38*. https://doi.org/10.1016/j.fbio.2020.100748

Horie, Y., Suzuki, T., Inoue, J., Iso, T., Wells, G., Moore, T. W., Mizushima, T., Dinkova-Kostova, A. T., Kasai, T., Kamei, T., Koshiba, S., & Yamamoto, M. (2021). Molecular basis for the disruption of Keap1–Nrf2 interaction via Hinge-amp; Latch mechanism. *Communications Biology*, *4*(1), 576. https://doi.org/10.1038/s42003-021-02100-6

Hossain, M. J., Al-Mamun, M., & Islam, M. R. (2024). Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. Dalam *Health Science Reports* (Vol. 7, Nomor 3). John Wiley and Sons Inc. https://doi.org/10.1002/hsr2.2004

Hou, N. T., & Chen, B. H. (2023). Extraction, purification and characterization of collagen peptide prepared from skin hydrolysate of sturgeon fish. *Food Quality and Safety*, *7*. https://doi.org/10.1093/fqsafe/fyad033

Hsieh, C. H., Shiau, C. Y., Su, Y. C., Liu, Y. H., & Huang, Y. R. (2016). Isolation and characterization of collagens from the skin of giant grouper (Epinephelus lanceolatus). *Journal of Aquatic Food Product Technology*, *25*(1), 93–104. https://doi.org/10.1080/10498850.2013.828145

Idramsyah, I., Dahrizal, D., Ruran, M., & Nair, H. K. R. (2024). Enhancing Diabetic Foot Ulcer Healing: The Role of Channa striata Extract Nutrition in Accelerating Inflammatory, Proliferative, and Maturation Phases. *IJNP*

(Indonesian Journal of Nursing Practices), *8*(2), 99–104. https://doi.org/10.18196/ijnp.v8i2.20740

Iragavarapu-Charyulu, V., Wojcikiewicz, E., & Urdaneta, A. (2020). Semaphorins in Angiogenesis and Autoimmune Diseases: Therapeutic Targets? *Frontiers in Immunology*, *11*. https://doi.org/10.3389/fimmu.2020.00346

Jaziri, A. A., Shapawi, R., Mokhtar, R. A. M., Noordin, W. N. M., & Huda, N. (2022). Microstructural and Physicochemical Analysis of Collagens from the Skin of Lizardfish (Saurida tumbil Bloch, 1795) Extracted with Different Organic Acids. *Molecules*, *27*(8). https://doi.org/10.3390/molecules27082452

Johnson, T. R., Gómez, B. I., McIntyre, M. K., Dubick, M. A., Christy, R. J., Nicholson, S. E., & Burmeister, D. M. (2018). The Cutaneous Microbiome and Wounds: New Molecular Targets to Promote Wound Healing. *International Journal of Molecular Sciences*, *19*(9), 2699. https://doi.org/10.3390/ijms19092699

Jyothi, S., Mamatha, D. M., Chandra Satapathy, S., Srujan Raju, K., & Favorskaya Editors, M. N. (2019). *Advances in Compytational and Bio-Engineering* (G. A. Tsihrintzis & M. Virvou, Ed.; 1 ed., Vol. 15). Learning and Analytics in Intelligent Systems. https://doi.org/https://doi.org/10.1007/978-3-030-46939-9

Kandhwal, M., Behl, T., Singh, S., Sharma, N., Arora, S., Bhatia, S., Al-Harrasi, A., Sachdeva, M., & Bungau, S. (2022). Role of matrix metalloproteinase in wound healing. Dalam *Am J Transl Res* (Vol. 14, Nomor 7). www.ajtr.org

Keim, K. C., & Horswill, A. R. (2023). Staphylococcus aureus. *Trends in Microbiology*, *31*(12), 1300–1301. https://doi.org/10.1016/j.tim.2023.07.001

Keller, A., & Wallace, T. C. (2021). Tea intake and cardiovascular disease: an umbrella review. *Annals of Medicine*, *53*(1), 929–944. https://doi.org/10.1080/07853890.2021.1933164

Kementrian Kesehatan, B. K. P. K. (2023). *Prevalensi, Dampak, serta Upaya Pengendalian Hipertensi & Diabetes di Indonesia*. www. badankebijakan.kemkes.go.id

Khoiriah, S. F. (2022). *Uji Aktivitas Ekstrak Kolagen Kulit Ikan Salmon (Salmo salar) Sebagai Inhibitro ACE1 Berdasarkan Studi In vitro dan In silico* [Universitas Pendidikan Indonesia]. https://repository.upi.edu/83125/4/S_KIM_1805975_Chapter3.pdf

Kisling, A., Lust, R. M., & Katwa, L. C. (2019). What is the role of peptide fragments of collagen I and IV in health and disease? *Life Sciences*, *228*, 30–34. https://doi.org/10.1016/j.lfs.2019.04.042

Klostermeier, D. (2021). Towards Conformation-Sensitive Inhibition of Gyrase: Implications of Mechanistic Insight for the Identification and Improvement of Inhibitors. *Molecules*, *26*(5), 1234. https://doi.org/10.3390/molecules26051234

Kolimi, P., Narala, S., Nyavanandi, D., Youssef, A. A. A., & Dudhipala, N. (2022). Innovative Treatment Strategies to Accelerate Wound Healing: Trajectory and Recent Advancements. *Cells*, *11*(15), 2439. https://doi.org/10.3390/cells11152439

Kottner, J., Cuddigan, J., Carville, K., Balzer, K., Berlowitz, D., Law, S., Litchford, M., Mitchell, P., Moore, Z., Pittman, J., Sigaudo-Roussel, D., Yee, C. Y., & Haesler, E. (2020). Pressure ulcer/injury classification today: An international perspective. *Journal of Tissue Viability*, *29*(3), 197–203. https://doi.org/https://doi.org/10.1016/j.jtv.2020.04.003

Kumar, Y., Ahmad, T., & Muzaddadi, A. (2021). *Enzymatic method for improving the yield and quality of collagen hydrolysate*. https://doi.org/ICAR-CIPHET/Pub./2021-22/02

Kurniawan, Y. S., Yudha, E., Nugraha, G., Fatmasari, N., Pranowo, H. D., Jumina, J., & Sholikhah, E. N. (2024). Molecular Docking and Molecular Dynamic Investigations of Xanthone-Chalcone Derivatives against Epidermal Growth Factor Receptor for Preliminary Discovery of Novel Anticancer Agent. *Indonesian Journal of Chemistry*, *24*(1), 250. https://doi.org/10.22146/ijc.88449

Laksmiwati, A. A. I. A. M., Sahara, E., & Ariati, N. K. (2024). Penentuan Kadar Asam Amino Bebas Dan Kadar Protein Terlarut Dari Ekstrak Kecambah Kacang Merah (Phaseolus Vulgaris L.) Dengan Variasi Waktu Perkecambahan. *Jurnal Kimia*, 73. https://doi.org/10.24843/JCHEM.2024.v18.i01.p11

Lara-Juache, H. R., Wong-Paz, J. E., Sanchez-Chino, X. M., Martinez-Salinas, R. I., Barba-Macias, E., Morales-Lopez, J. J., Armas-Tizapantzi, A., & Torres-Dosal, A. (2024). Extraction and characterization of collagen from the skin of Pterygoplichthys spp. (armored catfish) from Chiapas. *Food Science and Technology*, *44*. https://doi.org/10.5327/fst.00287

Le, T. M. T., Nguyen, V. M., Tran, T. T., Takahashi, K., & Osako, K. (2020). Comparison of acid-soluble collagen characteristic from three important freshwater fish skins in Mekong Delta Region, Vietnam. *Journal of Food Biochemistry*, *44*(9). https://doi.org/10.1111/jfbc.13397

Lee, C., Kim, M.-J., Kumar, A., Lee, H.-W., Yang, Y., & Kim, Y. (2025). Vascular endothelial growth factor signaling in health and disease: from molecular mechanisms to therapeutic perspectives. *Signal Transduction and Targeted Therapy*, *10*(1), 170. https://doi.org/10.1038/s41392-025-02249-0

Lee, J., Nguyen, N.-T., Tran, L.-M., Kim, Y.-H., & Min, J. (2023). Targeted Killing of Staphylococcus aureus Using Specific Peptides Displayed on Yeast Vacuoles. *Microbiology Spectrum*, *11*(3). https://doi.org/10.1128/spectrum.00920-23

Li, L., Yu, Y., Wu, W., & Wang, P. (2023). Extraction, Characterization and Osteogenic Activity of a Type I Collagen from Starfish (Asterias amurensis). *Marine Drugs*, *21*(5), 274. https://doi.org/10.3390/md21050274

Lin, H., Zheng, Z., Yuan, J., Zhang, C., Cao, W., & Qin, X. (2021). Collagen peptides derived from Sipunculus nudus accelerate wound healing. *Molecules*, *26*(5). https://doi.org/10.3390/molecules26051385

Lin, S., Zhang, Q., Li, S., Zhang, T., Wang, L., Qin, X., Zhang, M., Shi, S., & Cai, X. (2020). Antioxidative and Angiogenesis-Promoting Effects of Tetrahedral Framework Nucleic Acids in Diabetic Wound Healing with Activation of the Akt/Nrf2/HO-1 Pathway. *ACS Applied Materials & Interfaces*, *12*(10), 11397–11408. https://doi.org/10.1021/acsami.0c00874

Liu, H., & Li, B. (2022). Separation and identification of collagen peptides derived from enzymatic hydrolysate of Salmo salar skin and their anti-inflammatory activity in lipopolysaccharide (LPS)-induced inflammatory model. *Journal of Food Biochemistry*, *46*(7). https://doi.org/10.1111/jfbc.14122

Liu, Y., Yang, X., Liu, Y., Jiang, T., Ren, S., Chen, J., Xiong, H., Yuan, M., Li, W., Machens, H., & Chen, Z. (2021). NRF2 signalling pathway: New insights and progress in the field of wound healing. *Journal of Cellular and Molecular Medicine*, *25*(13), 5857–5868. https://doi.org/10.1111/jcmm.16597

Liza, S. A., & Abdulla-Al-Mamun, Md. (2025). Microbial degradation of tannery chrome-solid waste using Bacillus thuringiensis : optimization of collagen hydrolysate extraction via response surface methodology. *RSC Sustainability*, *3*(7), 3198–3214. https://doi.org/10.1039/D4SU00666F

Malik, F. K., & Guo, J. (2022). Insights into protein–DNA interactions from hydrogen bond energy-based comparative protein–ligand analyses. *Proteins: Structure, Function, and Bioinformatics*, *90*(6), 1303–1314. https://doi.org/10.1002/prot.26313

Mamun, A. Al, Shao, C., Geng, P., Wang, S., & Xiao, J. (2024). Recent advances in molecular mechanisms of skin wound healing and its treatments. *Frontiers in Immunology*, *15*. https://doi.org/10.3389/fimmu.2024.1395479

Mathew-Steiner, S. S., Roy, S., & Sen, C. K. (2021). Collagen in wound healing. Dalam *Bioengineering* (Vol. 8, Nomor 5). MDPI AG. https://doi.org/10.3390/bioengineering8050063

Menezes, M. do L. L. R., Ribeiro, H. L., Abreu, F. de O. M. da S., Feitosa, J. P. de A., & Filho, M. de S. M. de S. (2020). Optimization of the collagen extraction from Nile tilapia skin (Oreochromis niloticus) and its hydrogel with hyaluronic acid. *Colloids and Surfaces B: Biointerfaces*, *189*. https://doi.org/10.1016/j.colsurfb.2020.110852

Mersi, J. K., Kurnia Wulandari, N., Mardiyono, M., & Rahayu, U. M. (2024). Gambaran Kepatuhan Diet dan Gula Darah Puasa pada Pasien Diabetes Tipe II. *Jurnal Keperawatan Mersi*, *13*, 75–85. https://doi.org/10.31983/jkm.v13i2.12277

Milanović, Ž. (2024). Exploring enzyme inhibition and comprehensive mechanisms of antioxidant/prooxidative activity of natural furanocoumarin derivatives: A comparative kinetic DFT study. *Chemico-Biological Interactions*, *396*, 111034. https://doi.org/10.1016/j.cbi.2024.111034

Munahi, A. K., Allban, A. A. H., Farman, R. H., & Towfik, A. I. (2025). Use of Nano-Collagen Creams Extracted from Catfish Skin in Treatment of Second-Degree Skin Burns in Rabbits. *Macedonian Veterinary Review*. https://doi.org/10.2478/macvetrev-2025-0021

Muyonga, J. H., Cole, C. G. B., & Duodu, K. G. (2004). Characterisation of acid soluble collagen from skins of young and adult Nile perch (Lates niloticus). *Food Chemistry*, *85*(1), 81–89. https://doi.org/10.1016/j.foodchem.2003.06.006

Nandi, S. K., Jana, S., Datta, P., Das, H., Jaiswal, S., Ghosh, P., Lahiri, D., & Kundu, B. (2022). Copper and Cobalt Doped Bioactive Glass-Fish Dermal Collagen Electrospun Mat Triggers Key Events of Diabetic Wound Healing in Full-Thickness Skin Defect Model. *SSRN Electronic Journal*. https://doi.org/10.2139/ssrn.4135099

Nugraha, R., Kurniawan, F., Abdullah, A., Lopata, A. L., & Ruethers, T. (2024). Antihypertensive and Antidiabetic Drug Candidates from Milkfish (Chanos chanos)—Identification and Characterization through an Integrated Bioinformatic Approach. *Foods*, *13*(16), 2594. https://doi.org/10.3390/foods13162594

Oliveira, V. de M., Assis, C. R. D., Costa, B. de A. M., Neri, R. C. de A., Monte, F. T. D., Freitas, H. M. S. da C. V., França, R. C. P., Santos, J. F., Bezerra, R. de S., & Porto, A. L. F. (2021a). Physical, biochemical, densitometric and spectroscopic techniques for characterization collagen from alternative sources: A review based on the sustainable valorization of aquatic by-products. *Journal of Molecular Structure*, *1224*, 129023. https://doi.org/10.1016/j.molstruc.2020.129023

Oliveira, V. de M., Assis, C. R. D., Costa, B. de A. M., Neri, R. C. de A., Monte, F. T. D., Freitas, H. M. S. da C. V., França, R. C. P., Santos, J. F., Bezerra, R. de S., & Porto, A. L. F. (2021b). Physical, biochemical, densitometric and spectroscopic techniques for characterization collagen from alternative sources: A review based on the sustainable valorization of aquatic by-products. *Journal of Molecular Structure*, *1224*, 129023. https://doi.org/10.1016/j.molstruc.2020.129023

Olsen, T. H., Yesiltas, B., Marin, F. I., Pertseva, M., García-Moreno, P. J., Gregersen, S., Overgaard, M. T., Jacobsen, C., Lund, O., Hansen, E. B., & Marcatili, P. (2020). AnOxPePred: using deep learning for the prediction of antioxidative properties of peptides. *Scientific Reports*, *10*(1), 21471. https://doi.org/10.1038/s41598-020-78319-w

Ong, K. L., Stafford, L. K., McLaughlin, S. A., Boyko, E. J., Vollset, S. E., Smith, A. E., Dalton, B. E., Duprey, J., Cruz, J. A., Hagins, H., Lindstedt, P. A., Aali, A., Abate, Y. H., Abate, M. D., Abbasian, M., Abbasi-Kangevari, Z., Abbasi-Kangevari, M., Abd ElHafeez, S., Abd-Rabu, R., … Vos, T. (2023). 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*(10397), 203–234. https://doi.org/10.1016/S0140-6736(23)01301-6

Oslan, S. N. H., Shapawi, R., Mokhtar, R. A. M., Noordin, W. N. Md., & Huda, N. (2022). Characterization of Acid- and Pepsin-Soluble Collagen Extracted from the Skin of Purple-Spotted Bigeye Snapper. *Gels*, *8*(10), 665. https://doi.org/10.3390/gels8100665

Pace, C. N., Fu, H., Lee Fryar, K., Landua, J., Trevino, S. R., Schell, D., Thurlkill, R. L., Imura, S., Scholtz, J. M., Gajiwala, K., Sevcik, J., Urbanikova, L., Myers, J. K., Takano, K., Hebert, E. J., Shirley, B. A., & Grimsley, G. R. (2014). Contribution of hydrogen bonds to protein stability. *Protein Science*, *23*(5), 652–661. https://doi.org/10.1002/pro.2449

Peng, X., Luo, Y., Xu, T., Chen, Z., Chen, P., Hu, C., & Liu, S. (2025). Antibiotic-conjugated antimicrobial peptides for enhanced bacterial inhibition. *RSC Advances*, *15*(25), 19751–19761. https://doi.org/10.1039/D5RA02932E

Porel, P., Kaur, M., Sharma, V., & Aran, K. R. (2025). Understanding molecular mechanism of diabetic wound healing: addressing recent advancements in therapeutic managements. *Journal of Diabetes & Metabolic Disorders*, *24*(1), 76. https://doi.org/10.1007/s40200-025-01588-7

Prajaputra, V., Isnaini, N., Maryam, S., Ernawati, E., Deliana, F., Haridhi, H. A., Fadli, N., Karina, S., Agustina, S., Nurfadillah, N., Arisa, I. I., Desiyana, L. S., & Bakri, T. K. (2024). Exploring marine collagen: Sustainable sourcing, extraction methods, and cosmetic applications. *South African Journal of Chemical Engineering*, *47*, 197–211. https://doi.org/10.1016/j.sajce.2023.11.006

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

Pratap Singh, C., Mathur, M., Dadhich, H., & Ganguly, S. (2018). Molecular Characterization of Staphylococcus aureus of Camel (Camelus dromedarius) Skin Origin. *International Journal of Current Microbiology and Applied Sciences*, *7*(1), 3486–3490. https://doi.org/10.20546/ijcmas.2018.701.410

Rafael, M. J., & Velacso, R. (2023). Characterization of Fish protein Hydrolysate from Tilapia by-products using acid and enzymatic hydrolysis. *International Journal of Biosciences (IJB)*. https://doi.org/10.12692/ijb/22.4.85-95

Rahman, A., Rehmani, R., Pirvu, D. G., Huang, S. M., Puri, S., & Arcos, M. (2024). Unlocking the Therapeutic Potential of Marine Collagen: A Scientific Exploration for Delaying Skin Aging. *Marine Drugs*, *22*(4), 159. https://doi.org/10.3390/md22040159

Rahmawati, C., & Nopitasari, B. L. (2021). A pharmacoeconomic study: Cost-utility analysis of modern wound dressings vs conventional wound dressings in patients with diabetic foot ulcer. *Pharmacy Education*, *21*(2), 71–76. https://doi.org/10.46542/pe.2021.212.7176

Rahmawati, H., Agustini, T. W., Dewi, E. N., & Trianto, A. (2024). Karakteristik hidrolisat kolagen kulit ikan tenggiri kering dengan enzim papain. *Jurnal Pengolahan Hasil Perikanan Indonesia*, *27*(12), 1156–1171. https://doi.org/10.17844/jphpi.v27i12.55831

Rajabimashhadi, Z., Gallo, N., Salvatore, L., & Lionetto, F. (2023). Collagen Derived from Fish Industry Waste: Progresses and Challenges. *Polymers*, *15*(3), 544. https://doi.org/10.3390/polym15030544

Ramlan, R. D., Wan Ismail, W. A., Zamery, M. 'Izzuddin, Ramli, N. A., Effendi, T. J. B., Baharuddin, H., & Hazizul Hasan, M. (2023). Extraction and Characterisation of Suckermouth Catfish Collagen. *Malaysian Journal of Medicine and Health Sciences*, *19*(s18), 60–67. https://doi.org/10.47836/mjmhs19.s18.9

Raval, K., & Ganatra, T. (2022). Basics, types and applications of molecular docking: A review. *IP International Journal of Comprehensive and Advanced Pharmacology*, *7*(1), 12–16. https://doi.org/10.18231/j.ijcaap.2022.003

Reátegui-Pinedo, N., Salirrosas, D., Sánchez-Tuesta, L., Quiñones, C., Jáuregui-Rosas, S. R., Barraza, G., Cabrera, A., Ayala-Jara, C., Martinez, R. M., Baby, A. R., & Prieto, Z. A. (2022). Characterization of Collagen from Three Genetic Lines (Gray, Red and F1) of Oreochromis niloticus (Tilapia) Skin in Young and Old Adults. *Molecules*, *27*(3), 1123. https://doi.org/10.3390/molecules27031123

Rodrigues, C. V., Sousa, R. O., Carvalho, A. C., Alves, A. L., Marques, C. F., Cerqueira, M. T., Reis, R. L., & Silva, T. H. (2023a). Potential of Atlantic Codfish (Gadus morhua) Skin Collagen for Skincare Biomaterials. *Molecules*, *28*(8). https://doi.org/10.3390/molecules28083394

Rodrigues, C. V., Sousa, R. O., Carvalho, A. C., Alves, A. L., Marques, C. F., Cerqueira, M. T., Reis, R. L., & Silva, T. H. (2023b). Potential of Atlantic Codfish (Gadus morhua) Skin Collagen for Skincare Biomaterials. *Molecules*, *28*(8). https://doi.org/10.3390/molecules28083394

Rusdiana Puspa Dewi, S., Sinulingga, S., Natasya, M., Devita Utami, S., & Ramadhan Algiffary Irianto Dunda, P. (2023). Determination of Secondary Compounds in Extracts from Catfish (Pangasius sp). *JURNAL KIMIA MULAWARMAN*, *21*(1), 67–72. https://jurnal.kimia.fmipa.unmul.ac.id/index.php/JKM

Sahiba, N., Joshi, D., Agarwal, L. K., Manhas, A., Teli, P., & Agarwal, S. (2024). Screening of synthesized perimidine compounds for the assessment of antimicrobial potential: in-vitro and in-silico molecular docking and molecular dynamics simulation studies. *Discover Chemistry*, *1*(1), 30. https://doi.org/10.1007/s44371-024-00021-x

Schillinger, J., Koci, M., Bravo-Rodriguez, K., Heilmann, G., Kaschani, F., Kaiser, M., Beuck, C., Luecke, H., Huber, R., Hellerschmied, D., Burston, S. G., & Ehrmann, M. (2024). High resolution analysis of proteolytic substrate processing. *Journal of Biological Chemistry*, *300*(11), 107812. https://doi.org/10.1016/j.jbc.2024.107812

Senger, D. R., & Davis, G. E. (2011). Angiogenesis. *Cold Spring Harbor Perspectives in Biology*, *3*(8), a005090–a005090. https://doi.org/10.1101/cshperspect.a005090

Shah, F. H., Nam, Y. S., Bang, J. Y., Hwang, I. S., Kim, D. H., Ki, M., & Lee, H.-W. (2025). Targeting vascular endothelial growth receptor-2 (VEGFR-2): structural biology, functional insights, and therapeutic resistance. *Archives of*

Pharmacal Research, *48*(5), 404–425. https://doi.org/10.1007/s12272-025-01545-1

Shaik, F., Cuthbert, G., Homer-Vanniasinkam, S., Muench, S., Ponnambalam, S., & Harrison, M. (2020). Structural Basis for Vascular Endothelial Growth Factor Receptor Activation and Implications for Disease Therapy. *Biomolecules*, *10*(12), 1673. https://doi.org/10.3390/biom10121673

Shams, F., Moravvej, H., Hosseinzadeh, S., Mostafavi, E., Bayat, H., Kazemi, B., Bandehpour, M., Rostami, E., Rahimpour, A., & Moosavian, H. (2022). Overexpression of VEGF in dermal fibroblast cells accelerates the angiogenesis and wound healing function: in vitro and in vivo studies. *Scientific Reports*, *12*(1), 18529. https://doi.org/10.1038/s41598-022-23304-8

Sharifiaghdam, M., Shaabani, E., Faridi-Majidi, R., De Smedt, S. C., Braeckmans, K., & Fraire, J. C. (2022). Macrophages as a therapeutic target to promote diabetic wound healing. *Molecular Therapy*, *30*(9), 2891–2908. https://doi.org/10.1016/j.ymthe.2022.07.016

Shi, L.-W., Zhuang, Q.-Q., Wang, T.-Q., Jiang, X.-D., Liu, Y., Deng, J.-W., Sun, H.-H., Li, Y., Li, H.-H., Liu, T.-B., & Liu, J.-Z. (2023). Synthetic Antibacterial Quaternary Phosphorus Salts Promote Methicillin-Resistant Staphylococcus aureus-Infected Wound Healing. *International Journal of Nanomedicine*, *Volume 18*, 1145–1158. https://doi.org/10.2147/IJN.S398748

Siddik, M. A. B., Howieson, J., Fotedar, R., & Partridge, G. J. (2021). Enzymatic fish protein hydrolysates in finfish aquaculture: a review. Dalam *Reviews in Aquaculture* (Vol. 13, Nomor 1, hlm. 406–430). Wiley-Blackwell. https://doi.org/10.1111/raq.12481

Soundrarajan, N., Somasundaram, P., Kim, D., Cho, H.-S., Jeon, H., Ahn, B., Kang, M., Song, H., & Park, C. (2023). Effective Healing of Staphylococcus aureus-Infected Wounds in Pig Cathelicidin Protegrin-1-Overexpressing Transgenic Mice. *International Journal of Molecular Sciences*, *24*(14), 11658. https://doi.org/10.3390/ijms241411658

Sousa, R. O., Alves, A. L., Carvalho, D. N., Martins, E., Oliveira, C., Silva, T. H., & Reis, R. L. (2020). Acid and enzymatic extraction of collagen from Atlantic cod (Gadus Morhua) swim bladders envisaging health-related applications. *Journal of Biomaterials Science, Polymer Edition*, *31*(1), 20–37. https://doi.org/10.1080/09205063.2019.1669313

Spampinato, S. F., Caruso, G. I., De Pasquale, R., Sortino, M. A., & Merlo, S. (2020). The Treatment of Impaired Wound Healing in Diabetes: Looking among Old Drugs. *Pharmaceuticals*, *13*(4), 60. https://doi.org/10.3390/ph13040060

Stani, C., Vaccari, L., Mitri, E., & Birarda, G. (2020). FTIR investigation of the secondary structure of type I collagen: New insight into the amide III band. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *229*, 118006. https://doi.org/10.1016/j.saa.2019.118006

Stanzione, F., Giangreco, I., & Cole, J. C. (2021). Use of molecular docking computational tools in drug discovery. Dalam *Progress in Medicinal Chemistry* (Vol. 60, hlm. 273–343). Elsevier B.V. https://doi.org/10.1016/bs.pmch.2021.01.004

Tadesse, S. A., Emire, S. A., Barea, P., Illera, A. E., Melgosa, R., Beltrán, S., & Sanz, M. T. (2023). Valorisation of low-valued ray-finned fish (Labeobarbus nedgia) by enzymatic hydrolysis to obtain fish-discarded protein hydrolysates as functional foods. *Food and Bioproducts Processing*, *141*, 167–184. https://doi.org/10.1016/j.fbp.2023.08.003

Tan, B., Zhang, B., & Chen, H. (2024). Gastroenteropancreatic neuroendocrine neoplasms: epidemiology, genetics, and treatment. *Frontiers in Endocrinology*, *15*. https://doi.org/10.3389/fendo.2024.1424839

Tigabu, A., & Getaneh, A. (2021). Staphylococcus aureus, ESKAPE Bacteria Challenging Current Health Care and Community Settings: a Literature Review. *Clinical Laboratory*, *67*(07/2021). https://doi.org/10.7754/Clin.Lab.2020.200930

Utami, R., Trilaksani, W., & Hardiningtyas, S. D. (2024). Karakteristik papain soluble collagen gelembung renang ikan manyung dengan variasi praperlakuan alkali dan rasio ekstraktan. *Jurnal Pengolahan Hasil Perikanan Indonesia*, *27*(3), 223–241. https://doi.org/10.17844/jphpi.v27i3.49968

Victor, P., Sarada, D., & Ramkumar, K. M. (2020). Pharmacological activation of Nrf2 promotes wound healing. *European Journal of Pharmacology*, *886*, 173395. https://doi.org/10.1016/j.ejphar.2020.173395

Vidal, A. R., Cansian, R. L., Mello, R. de O., Demiate, I. M., Kempka, A. P., Dornelles, R. C. P., Rodriguez, J. M. L., & Campagnol, P. C. B. (2022). Production of Collagens and Protein Hydrolysates with Antimicrobial and Antioxidant Activity from Sheep Slaughter By-Products. *Antioxidants*, *11*(6), 1173. https://doi.org/10.3390/antiox11061173

Vidal, A. R., Duarte, L. P., Schmidt, M. M., Cansian, R. L., Fernandes, I. A., de Oliveira Mello, R., Demiate, I. M., & Dornelles, R. C. P. (2020). Extraction and characterization of collagen from sheep slaughter by-products. *Waste Management*, *102*, 838–846. https://doi.org/10.1016/j.wasman.2019.12.004

Wang, J., Pei, X., Liu, H., & Zhou, D. (2018). Extraction and characterization of acid-soluble and pepsin-soluble collagen from skin of loach (Misgurnus anguillicaudatus). *International Journal of Biological Macromolecules*, *106*, 544–550. https://doi.org/10.1016/j.ijbiomac.2017.08.046

Wang, X., Bove, A. M., Simone, G., & Ma, B. (2020). Molecular Bases of VEGFR-2-Mediated Physiological Function and Pathological Role. *Frontiers in Cell and Developmental Biology*, *8*. https://doi.org/10.3389/fcell.2020.599281

Wijaya, S. P., Rahayu, P., Suhartono, M. T., & Tjandrawinata, R. (2022). Molecular studies of bioactive peptides of Nile tilapia (Oreochromis niloticus) skin protein hydrolysate DLBS3D33 as MMP-2 inhibitor. *Journal of Applied Pharmaceutical Science*. https://doi.org/10.7324/JAPS.2023.53543

Wirayudha, R. H., Herawati, D., Kusnandar, F., & Nurhayati, T. (2022). The Antioxidant Capacity and Physicochemical Properties of Yellowfin Tuna Skin Collagen Hydrolysate Using Ultrasound-Assisted Enzymatic Hydrolysis. *Jurnal Pengolahan Hasil Perikanan Indonesia*, *25*(3), 393–404. https://doi.org/10.17844/jphpi.v25i3.43325

Wise, L. M., Stuart, G. S., Real, N. C., Fleming, S. B., & Mercer, A. A. (2018). VEGF Receptor-2 Activation Mediated by VEGF-E Limits Scar Tissue Formation Following Cutaneous Injury. *Advances in Wound Care*, *7*(8), 283–297. https://doi.org/10.1089/wound.2016.0721

Wolosowicz, M., Prokopiuk, S., & Kaminski, T. W. (2024). The Complex Role of Matrix Metalloproteinase-2 (MMP-2) in Health and Disease. *International Journal of Molecular Sciences*, *25*(24), 13691. https://doi.org/10.3390/ijms252413691

Wu, J., Kong, L., Zhang, J., & Chen, W. (2019). Extraction and Properties of Acid-Soluble Collagen and Pepsin-Soluble Collagen from Silver Carp (Hypophthalmichthys molitrix) Scales: Prerequisite Information for Fishery Processing Waste Reuse. *Polish Journal of Environmental Studies*, *28*(4), 2923–2930. https://doi.org/10.15244/pjoes/93742

Wu, R., Zhang, H., Zhao, M., Li, J., Hu, Y., Fu, J., Pi, J., Wang, H., & Xu, Y. (2020). Nrf2 in keratinocytes protects against skin fibrosis via regulating epidermal lesion and inflammatory response. *Biochemical Pharmacology*, *174*, 113846. https://doi.org/10.1016/j.bcp.2020.113846

Xiao, L., Lv, J., Liang, Y., Zhang, H., Zheng, J., Lin, F., & Wen, X. (2023). Structural, physicochemical properties and function of swim bladder collagen in promoting fibroblasts viability and collagen synthesis. *LWT*, *173*, 114294. https://doi.org/10.1016/j.lwt.2022.114294

Yadav, J. P., Singh, A. K., Grishina, M., Pathak, P., Verma, A., Kumar, V., Kumar, P., & Patel, D. K. (2024). Insights into the mechanisms of diabetic wounds: pathophysiology, molecular targets, and treatment strategies through conventional and alternative therapies. *Inflammopharmacology*, *32*(1), 149–228. https://doi.org/10.1007/s10787-023-01407-6

Yan, L., Fan, D., Yang, J., Wang, J., Hu, X., Zhang, X., Huang, Y., Wang, H., Yin, W., Cai, X., Shang, R., Huang, C., Luo, G., & He, W. (2025). Fibroblast Exosomes Promote Wound Healing and Improve the Quality of Healed Skin via miR-29a-3p-Mediated KEAP1/Nrf2 Pathway Activation. *Burns & Trauma*. https://doi.org/10.1093/burnst/tkaf035

Yanti, F., Dharmayanti, N., & Suryanti. (2022). Antioxidant Activity of Collagen from the Skin of Pangas Catfish (Pangasius sp) with Crude Bromelain Enzyme of Pineapple Peel. *Jurnal Pengolahan Hasil Perikanan Indonesia*, *25*(1), 88–96. https://doi.org/10.17844/jphpi.v25i1.36731

Yin, W., Gan, S., & Chao, H. (2023). Negative pressure wound therapy (NPWT) is superior to conventional moist dressings in wound bed preparation for diabetic foot ulcers. *Saudi Medical Journal*, *44*(10), 1020–1029. https://doi.org/10.15537/smj.2023.44.20230386

Yuda, B. N., Fauzana, N. A., Fatmawati, & Biyatmoko, D. (2023). State of Water Quality and Management of Patin Fish Cultivation in Cindai Alus, Banjar District, Indonesia. *Asian Journal of Environment & Ecology*, *21*(3), 52–62. https://doi.org/10.9734/ajee/2023/v21i3464

Zatorski, J. M., Montalbine, A. N., Ortiz-Cárdenas, J. E., & Pompano, R. R. (2020). Quantification of fractional and absolute functionalization of gelatin hydrogels by optimized ninhydrin assay and 1H NMR. *Analytical and Bioanalytical Chemistry*, *412*(24), 6211–6220. https://doi.org/10.1007/s00216-020-02792-5

Zhang, N., Guo, S., Zheng, Y., & Li, W. (2025). Isolation and Characterisation of Acid Soluble Collagens and Pepsin Soluble Collagens from Eel (Anguilla japonica Temminck et Schlegel) Skin and Bone. *Foods*, *14*(3), 502. https://doi.org/10.3390/foods14030502

Zhang, Q., Hou, S., Liu, Y., Du, J., Jia, Y., Yang, Q., Xu, T., Takagi, Y., Li, D., & Zhang, X. (2024). Properties of Skin Collagen from Southern Catfish (Silurus meridionalis) Fed with Raw and Cooked Food. *Foods*, *13*(18). https://doi.org/10.3390/foods13182901

Zhang, W., Chen, L., Xiong, Y., Panayi, A. C., Abududilibaier, A., Hu, Y., Yu, C., Zhou, W., Sun, Y., Liu, M., Xue, H., Hu, L., Yan, C., Xie, X., Lin, Z., Cao, F., Mi, B., & Liu, G. (2021). Antioxidant Therapy and Antioxidant-Related Bionanomaterials in Diabetic Wound Healing. *Frontiers in Bioengineering and Biotechnology*, *9*. https://doi.org/10.3389/fbioe.2021.707479

Zhang, W.-Q., Tang, W., Hu, S.-Q., Fu, X.-L., Wu, H., Shen, W.-Q., & Chen, H.-L. (2023). Effect of matrix metalloproteinases on the healing of diabetic foot ulcer: A systematic review. *Journal of Tissue Viability*, *32*(1), 51–58. https://doi.org/10.1016/j.jtv.2022.12.001

Zhao, Y., Wang, Z., Zhang, J., & Su, T. (2018). Extraction and characterization of collagen hydrolysates from the skin of Rana chensinensis. *3 Biotech*, *8*(3), 181. https://doi.org/10.1007/s13205-018-1198-y

Zheng, S.-Y., Wan, X.-X., Kambey, P. A., Luo, Y., Hu, X.-M., Liu, Y.-F., Shan, J.-Q., Chen, Y.-W., & Xiong, K. (2023). Therapeutic role of growth factors in treating diabetic wound. *World Journal of Diabetes*, *14*(4), 364–395. https://doi.org/10.4239/wjd.v14.i4.364

Zhou, X., Yu, D., Sun, X., Huang, W., Xu, Y., Li, C., & Zhang, Y. (2023). Hypoxia-inducible Factor-1α in Diabetic Foot Ulcers: Plain but Not Simple. *Gene Expression*, *22*(4), 306–320. https://doi.org/10.14218/GE.2023.00051

Zhu, N., Liu, R., Xu, M., & Li, Y. (2024). The Potential of Bioactive Fish Collagen Oligopeptides against Hydrogen Peroxide-Induced NIH/3T3 and HUVEC Damage: The Involvement of the Mitochondria. *Nutrients*, *16*(7). https://doi.org/10.3390/nu16071004

Zhu, Y., Wang, Y., Jia, Y., Xu, J., & Chai, Y. (2019). Roxadustat promotes angiogenesis through HIF-1α/VEGF/VEGFR2 signaling and accelerates cutaneous wound healing in diabetic rats. *Wound Repair and Regeneration*, *27*(4), 324–334. https://doi.org/10.1111/wrr.12708