

## DAFTAR PUSTAKA

- Alfonso-Prieto, M., Biarnés, X., Vidossich, P., & Rovira, C., 2009. The molecular mechanism of the catalase reaction, *Journal of the American Chemical Society*, 131(33), 11751-11761.
- Bae, O. N., Noh, M., Chun, Y. J., & Jeong, T. C., 2015. Keratinocytic vascular endothelial growth factor as a novel biomarker for pathological skin condition, *Biomolecules & therapeutics*, 23(1), 12.
- Angel, P., Szabowski, A. and Schorpp-Kistner, M., 2001. Function and regulation of AP-1 subunits in skin physiology and pathology, *Oncogene*, 20(19), pp.2413-2423.
- Bae, G.S., Kim, M.S., Jung, W.S., Seo, S.W., Yun, S.W., Kim, S.G., Park, R.K., Kim, E.C., Song, H.J. and Park, S.J., 2010. Inhibition of lipopolysaccharide-induced inflammatory responses by piperine, *European journal of pharmacology*, 642(1-3), pp.154-162.
- Bagheri, H., Abdul Manap, M.Y.B., dan Solati, Z., 2014. Antioxidant activity of Piper nigrum L. essential oil extracted by supercritical CO<sub>2</sub> extraction and hydro-distillation, *Talanta*, 121: 220–228.
- Baldi, P., Baldi, P. P., Brunak, S., & Bach, F., 2001. *Bioinformatics: The Machine Learning Approach*. MIT Press.
- Bang, J.S., Choi, H.M., Sur, B.J., Lim, S.J., Kim, J.Y., Yang, H.I., Yoo, M.C., Hahm, D.H. and Kim, K.S., 2009. Anti-inflammatory and antiarthritic effects of piperine in human interleukin 1 $\beta$ -stimulated fibroblast-like synoviocytes and in rat arthritis models, *Arthritis research & therapy*, 11(2), pp.1-9.
- Bao, Q., Pan, J., Qi, H., Wang, L., Qian, H., Jiang, F., & Hu, X., 2014. Aging and age-related diseases—from endocrine therapy to target therapy, *Molecular and cellular endocrinology*, 394(1-2), 115-118
- Bell, S., Degitz, K., Quirling, M., Jilg, N., Page, S. and Brand, K., 2003. Involvement of NF- $\kappa$ B signalling in skin physiology and disease. *Cellular signalling*, 15(1), pp.1-7
- Bocco, A., Cuvelier, M.-E., Richard, H., & Berset, C., 1998. Antioxidant Activity and Phenolic Composition of Citrus Peel and Seed Extracts, *Journal of Agricultural and Food Chemistry*, 46(6), 2123–2129.
- Bottazzi, B., Riboli, E. and Mantovani, A., 2018. December. Aging, inflammation and cancer. In *Seminars in immunology* (Vol. 40, pp. 74-82). Academic Press.
- Calleja, M. A., Vieites, J. M., Montero-Meterdez, T., Torres, M. I., Faus, M. J., Gil, A., & Suárez, A., 2013. The antioxidant effect of  $\beta$ -caryophyllene protects rat liver from carbon tetrachloride-induced fibrosis by inhibiting hepatic stellate cell activation, *British journal of nutrition*, 109(3), 394-401.
- Cancemi, P., Aiello, A., Accardi, G., Caldarella, R., Candore, G., Caruso, C., Ciaccio, M., Cristaldi, L., Di Gaudio, F., Siino, V., & Vasto, S., 2020. *The Role of Matrix Metalloproteinases (MMP-2 and MMP-9) in Ageing and Longevity: Focus on Sicilian Long-Living Individuals (LLIs)*, Mediators of Inflammation; Hindawi.

- Cătană, C. S., Atanasov, A. G., & Berindan-Neagoe, I., 2018. Natural products with anti-aging potential: Affected targets and molecular mechanisms, *Biotechnology advances*, 36(6), 1649-1656.
- Cavinato, M., Waltenberger, B., Baraldo, G., Grade, C. V., Stuppner, H., & Jansen-Dürr, P., 2017. Plant extracts and natural compounds used against UVB-induced photoaging. *Biogerontology*, 18(4), 499-516
- Cela, E.M., Friedrich, A., Paz, M.L., Vanzulli, S.I., Leoni, J. and González Maglio, D.H., 2015. Time-course study of different innate immune mediators produced by UV-irradiated skin: comparative effects of short and daily versus a single harmful UV exposure. *Immunology*, 145(1), pp.82-93.
- Chandrashekar, D. S., Bashel, B., Balasubramanya, S. A. H., Creighton, C. J., Ponce-Rodriguez, I., Chakravarthi, B. V., & Varambally, S., 2017. UALCAN: a portal for facilitating tumor subgroup gene expression and survival analyses, *Neoplasia*, 19(8), 649-658.
- Chauhan, P., & Shakya, M., 2009. Modeling signaling pathways leading to wrinkle formation: Identification of the skin aging target, *Indian Journal of Dermatology, Venereology and Leprology*, 75(5), 463.
- Chayaratanasin P, Barbieri MA, Suanpairintr N and Adisakwattana S., 2015. Inhibitory effect of *Clitoria ternatea* flower petal extract on fructose-induced protein glycation and oxidation-dependent damages to albumin *in vitro*, *BMC Complement Altern Med* ;15:27
- Chen, B., Li, R., Yan, N., Chen, G., Qian, W., Jiang, H.-L., Ji, C., & Bi, Z.-G., 2015. Astragaloside IV controls collagen reduction in photoaging skin by improving transforming growth factor- $\beta$ /Smad signaling suppression and inhibiting matrix metalloproteinase-1, *Molecular Medicine Reports*, 11(5), 3344–3348.
- Chen, J., Zhao, M., Rao, R., Inoue, H. and Hao, C.M., 2005. C/EBP $\beta$  and its binding element are required for NF $\kappa$ B-induced COX2 expression following hypertonic stress, *Journal of Biological Chemistry*, 280(16), pp.16354-16359
- Choudhuri, S., 2014. *Bioinformatics for beginners: genes, genomes, molecular evolution, databases and analytical tools*, Elsevier.
- Chung, J. H., & Eun, H. C., 2007. Angiogenesis in skin aging and photoaging. *The Journal of dermatology*, 34(9), 593-600.
- Chuchawankul, S., Khorana, N. and Poovorawan, Y., 2012. Piperine inhibits cytokine production by human peripheral blood mononuclear cells, *Genet Mol Res*, 11(1), pp.617-27.
- Chusak, C., Thilavech, T., Henry, C. J., & Adisakwattana, S., 2018. Acute effect of *Clitoria ternatea* flower beverage on glycemic response and antioxidant capacity in healthy subjects: a randomized crossover trial, *BMC complementary and alternative medicine*, 18(1), 1-11.
- Cuadrado, A. and Nebreda, A.R., 2010. Mechanisms and functions of p38 MAPK signalling. *Biochemical Journal*, 429(3), pp.403-417.
- Damanhour, Z. A., & Ahmad, A., 2014. A review on therapeutic potential of *Piper nigrum* L. *Black Pepper*: *The King of Spices, Med. Aromat. Plants*, 3, 161.

- Do, M. T., Kim, H. G., Choi, J. H., Khanal, T., Park, B. H., Tran, T. P., & Jeong, H. G., 2013. Antitumor efficacy of piperine in the treatment of human HER2-overexpressing breast cancer cells, *Food chemistry*, 141(3), 2591-2599
- Doncheva, N. T., Morris, J. H., Gorodkin, J., & Jensen, L. J., 2019. Cytoscape StringApp: Network Analysis and Visualization of Proteomics Data, *Journal of Proteome Research*, 18(2), 623–632
- Eckert, R.L., Efimova, T., Dashti, S.R., Balasubramanian, S., Deucher, A., Crish, J.F., Sturniolo, M. and Bone, F., 2002. Keratinocyte survival, differentiation, and death: many roads lead to mitogen-activated protein kinase, In *Journal of Investigative Dermatology Symposium Proceedings* (Vol. 7, No. 1, pp. 36-40). Elsevier.
- Eckert, R.L., Adhikary, G., Young, C.A., Jans, R., Crish, J.F., Xu, W. and Rorke, E.A., 2013. AP1 transcription factors in epidermal differentiation and skin cancer, *Journal of skin cancer*, 2013.
- Farage, M. A., Miller, K. W., Elsner, P., & Maibach, H. I., 2008. Intrinsic and extrinsic factors in skin ageing: A review, *International Journal of Cosmetic Science*, 30(2), 87–95. <https://doi.org/10.1111/j.1468-2494.2007.00415.x>
- Fisher, G. J., Kang, S., Varani, J., Bata-Csorgo, Z., Wan, Y., Datta, S., & Voorhees, J. J., 2002, Mechanisms of Photoaging and Chronological Skin Aging. *Archives of Dermatology*, 138(11).
- Fisher, G.J., Talwar, H.S., Lin, J. and Voorhees, J.J., 1999. Molecular mechanisms of photoaging in human skin in vivo and their prevention by all-trans retinoic acid, *Photochemistry and photobiology*, 69(2), pp.154-157.
- Francomano, F., Caruso, A., Barbarossa, A., Fazio, A., La Torre, C., Ceramella, J. & Sinicropi, M. S., 2019.  $\beta$ -Caryophyllene: a sesquiterpene with countless biological properties, *Applied Sciences*, 9(24), 5420.
- Freitas-Rodriguez, S., Folgueras, A.R. and Lopez-Otin, C., 2017. The role of matrix metalloproteinases in aging: Tissue remodeling and beyond, *Biochimica et Biophysica Acta (BBA)-Molecular Cell Research*, 1864(11), pp.2015-2025.
- Ganceviciene, R., Liakou, A.I., Theodoridis, A., Makrantonaki, E. and Zouboulis, C.C., 2012. Skin anti-aging strategies, *Dermato-endocrinology*, 4(3), pp.308-319.
- Gao, M., Zhu, S.Y., Tan, C.B., Xu, B., Zhang, W.C. and Du, G.H., 2010. Pinocembrin protects the neurovascular unit by reducing inflammation and extracellular proteolysis in MCAO rats, *Journal of Asian Natural Products Research*, 12(5), pp.407-418
- Ginzburg, S., Golovine, K.V., Makhov, P.B., Uzzo, R.G., Kutikov, A. and Kolenko, V.M., 2014. Piperlongumine inhibits NF- $\kappa$ B activity and attenuates aggressive growth characteristics of prostate cancer cells, *The Prostate*, 74(2), pp.177-186
- Godic, A., Poljšak, B., Adamic, M., & Dahmane, R., 2014, The role of antioxidants in skin cancer prevention and treatment, *Oxidative medicine and cellular longevity*, 2014.
- Goldsmith, T. C., 2013. Arguments against non-programmed aging theories, *Biochemistry (Moscow)*, 78(9), 971–978.

- Gollen B, M. J., 2018, *Clitoria ternatea* Linn: A Herb with Potential Pharmacological Activities: Future Prospects as Therapeutic Herbal Medicine. 3(1), 9.
- Gong, F., Cui, L., Zhang, X., Zhan, X., Gong, X. and Wen, Y., 2018. Piperine ameliorates collagenase-induced Achilles tendon injury in the rat. *Connective tissue research*, 59(1), pp.21-29
- Green, J. A., Dholakia, S., Janczar, K., Ong, C. W., Moores, R., Fry, J., Elkington, P. T., Roncaroli, F., & Friedland, J. S., 2011. Mycobacterium tuberculosis-infected human monocytes down-regulate microglial MMP-2 secretion in CNS tuberculosis via TNF $\alpha$ , NF $\kappa$ B, p38 and caspase 8 dependent pathways, *Journal of Neuroinflammation*, 8(1), 46.
- Gu, F., Wu, G., Fang, Y., & Zhu, H., 2018. Nontargeted metabolomics for phenolic and polyhydroxy compounds profile of pepper (*Piper nigrum* L.) products based on LC-MS/MS analysis, *Molecules*, 23(8), 1985.
- Gülçin, İ., 2005. The antioxidant and radical scavenging activities of black pepper (*Piper nigrum*) seeds. *International Journal of Food Sciences and Nutrition*, 56: 491–499
- Huang, J.S., Guh, J.Y., Chen, H.C., Hung, W.C., Lai, Y.H. and Chuang, L.Y., 2001. Role of receptor for advanced glycation end-product (RAGE) and the JAK/STAT-signaling pathway in AGE-induced collagen production in NRK-49F cells. *Journal of cellular biochemistry*, 81(1), pp.102-113.
- Kojima, H., Inoue, T., Kunitomo, H., & Nakajima, K., 2013. IL-6-STAT3 signaling and premature senescence, *Jak-stat*, 2(4), e25763.
- Kim, Y. M., & Cho, M., 2014. Activation of NADPH oxidase subunit NCF4 induces ROS-mediated EMT signaling in HeLa cells. *Cellular signalling*, 26(4), 784-796.
- Kim, S.H. and Lee, Y.C., 2009. Piperine inhibits eosinophil infiltration and airway hyperresponsiveness by suppressing T cell activity and Th2 cytokine production in the ovalbumin-induced asthma model, *Journal of Pharmacy and Pharmacology*, 61(3), pp.353-359.
- Ham, Sun Ah, Yoo, T., Hwang, J. S., Kang, E. S., Paek, K. S., Park, C., Kim, J.-H., Do, J. T., & Seo, H. G., 2014. Peroxisome proliferator-activated receptor  $\delta$  modulates MMP-2 secretion and elastin expression in human dermal fibroblasts exposed to ultraviolet B radiation, *Journal of Dermatological Science*, 76(1), 44–50.
- Huang, D. W., Sherman, B. T., Tan, Q., Kir, J., Liu, D., Bryant, D & Lempicki, R. A., 2007. DAVID Bioinformatics Resources: expanded annotation database and novel algorithms to better extract biology from large gene lists, *Nucleic acids research*, 35(suppl\_2), W169-W175
- Jacob, L., & Latha, M. S., 2013. In vitro antioxidant activity of *Clitoria ternatea* Linn, *International Journal of Research in Phytochemistry and Pharmacology*, 3(1), 35-39.
- Jayakar B and Suresh B., 2011. Hepatoprotective potential of *Clitoria ternatea* leaf extract against paracetamol induced damage in mice. *Molecules*, 16: 10134-10145.

- Jeena, K., Liju, V.B., Umadevi, N.P., dan Kuttan, R., 2014. Antioxidant, Anti-inflammatory and Antinociceptive Properties of Black Pepper Essential Oil (*Piper nigrum* Linn), *Journal of Essential Oil Bearing Plants*, **17**: 1–12.
- Jurkiewicz BA, Buettner GR., 1996. EPR detection of free radicals in UV-irradiated skin: mouse versus human, *Photochem Photobiol* ;64:918–22.
- Kähäri, V.M. and Saarialho-Kere, U., 1997. Matrix metalloproteinases in skin, *Experimental dermatology*, 6(5), pp.199-213.
- Kalmankar, N. V., Venkatesan, R., Balaram, P., & Sowdhamini, R., 2020. Transcriptomic profiling of the medicinal plant *Clitoria ternatea*: identification of potential genes in cyclotide biosynthesis, *Scientific reports*, 10(1), 1-20.
- Kanehisa M, Goto S, Furumichi M, Tanabe M, Hirakawa M, 2010. KEGG for representation and analysis of molecular networks involving diseases and drugs, *Nucleic Acids Res*, 38: D355–D360
- Kamkaem N, Wilkinson J.M., 2009. The antioxidant activity of *Clitoria ternatea* flower petal and eye gel, *Phytother Res* 23: 1624-1625
- Kementrian Kesehatan Republik Indonesia, 2010. *Suplemen I Farmakope Herbal Indonesia*. Kementrian Kesehatan Republik Indonesia.
- Kim, J., Lee, C.-W., Kim, E. K., Lee, S.-J., Park, N.-H., Kim, H.-S., Kim, H.-K., Char, K., Jang, Y. P., & Kim, J.-W., 2011. Inhibition effect of *Gynura procumbens* extract on UV-B-induced matrix-metalloproteinase expression in human dermal fibroblasts, *Journal of Ethnopharmacology*, 137(1), 427–433.
- Kong, R., Cui, Y., Fisher, G.J., Wang, X., Chen, Y., Schneider, L.M. and Majmudar, G., 2016. A comparative study of the effects of retinol and retinoic acid on histological, molecular, and clinical properties of human skin. *Journal of cosmetic dermatology*, 15(1), pp.49-57.
- Krieg, T., Aumailley, M., Koch, M., Chu, M.-L., & Uitto, J., 2012, Chapter 63. Collagens, Elastic Fibers, and Other Extracellular Matrix Proteins of the Dermis. In L. A. Goldsmith, S. I. Katz, B. A. Gilchrest, A. S. Paller, D. J. Leffell, & K. Wolff (Eds.), *Fitzpatrick's Dermatology in General Medicine* (8th ed.). The McGraw-Hill Companies.
- Kirtikar K.R, Basu B.D., 1966. *Indian Medicinal Plants*, 2nd edn.
- Koivukangas, V., Kallioinen, M., Autio-Harmainen, H., & Oikarinen, A., 1994. UV irradiation induces the expression of gelatinases in human skin in vivo, *Acta dermato-venereologica*, 74(4), 279-282
- Kostyuk, V., Potapovich, A., Albuhaydar, A. R., Mayer, W., De Luca, C., & Korkina, L., 2018. Natural substances for prevention of skin photoaging: screening systems in the development of sunscreen and rejuvenation cosmetics, *Rejuvenation Research*, 21(2), 91-101
- Kulka, M., 2013. Mechanisms and treatment of photoaging and photodamage. *Using Old Solutions to New Problems—Natural Drug Discovery in the 21st Century*, Kulka M (Ed.). InTech, Croatia, pp.255-276.
- Kusindarta, D. L., & Wihadmadyatami, H., 2018. The role of extracellular matrix in tissue regeneration, *Tissue regeneration*, 75728, 6.



- Kwon, M. J., Kim, B., Lee, Y. S., & Kim, T. Y., 2012. Role of superoxide dismutase 3 in skin inflammation. *Journal of dermatological science*, 67(2), 81-87.
- Lai, L.H., Fu, Q.H., Liu, Y., Jiang, K., Guo, Q.M., Chen, Q.Y., Yan, B., Wang, Q.Q. and Shen, J.G., 2012. Piperine suppresses tumor growth and metastasis in vitro and in vivo in a 4T1 murine breast cancer model. *Acta Pharmacologica Sinica*, 33(4), pp.523-530.
- Lee, Y.-R., Noh, E.-M., Han, J.-H., Kim, J.-M., Hwang, J.-K., Hwang, B.-M., Chung, E.-Y., Kim, B.-S., Lee, S.-H., Lee, S. J., & Kim, J.-S., 2012. Brazilin inhibits UVB-induced MMP-1/3 expressions and secretions by suppressing the NF- $\kappa$ B pathway in human dermal fibroblasts. *European Journal of Pharmacology*, 674(2), 80–86.
- Levin, N., Salek, R. M., & Steinbeck, C., 2016. From Databases to Big Data. Dalam *Metabolic Phenotyping in Personalized and Public Healthcare* (hlm. 317–331). Elsevier.
- Liu, Y., Chang, Y., Yang, C., Sang, Z., Yang, T., Ang, W., Ye, W., Wei, Y., Gong, C. and Luo, Y., 2014. Biodegradable nanoassemblies of piperlongumine display enhanced anti-angiogenesis and anti-tumor activities. *Nanoscale*, 6(8), pp.4325-4337.
- Luscombe, N. M., Greenbaum, D., & Gerstein, M., 2001, What is bioinformatics? An introduction and overview. *Yearbook of Medical Informatics*, 10(01), 83–100.
- Loo, T.G., 1987. *Ikhtisar Ringkas Dari Dasar-Dasar Farmakognosi*, 6. PT Kinta-PT Bunda Karya
- Manayi, A., Saeidnia, S., Gohari, A. R., & Abdollahi, M., 2014. Methods for the discovery of new anti-aging products–targeted approaches. *Expert Opinion on Drug Discovery*, 9(4), 383-405.
- Masaki H, Atsumi T, Sakurai H., 1995. Detection of hydrogen peroxide and hydroxylradicals in murine skin fibroblasts under UVB irradiation. *Biochem BiophysRes Commun*, 206:474–9
- Masaki H, Okano Y, Sakurai H, 1999. Generation of active oxygen species from advanced glycation end-products (AGEs) during ultraviolet light A (UVA) irradiation and a possible mechanism for cell damaging. *Biochim BiophysActa*, 1428:45–56.
- Mondal, S., Adhikari, N., Banerjee, S., Amin, S.A. and Jha, T., 2020. Matrix metalloproteinase-9 (MMP-9) and its inhibitors in cancer: A minireview. *European journal of medicinal chemistry*, 194, p.112260.
- Muegge, K., Williams, T.M., Kant, J., Karin, M., Chiu, R., Schmidt, A., Siebenlist, U., Young, H.A. and Durum, S.K., 1989. Interleukin-1 costimulatory activity on the interleukin-2 promoter via AP-1. *Science*, 246(4927), pp.249-251.
- Muthusamy, V., & Piva, T. J., 2010. The UV response of the skin: a review of the MAPK, NF $\kappa$ B and TNF $\alpha$  signal transduction pathways, *Archives of dermatological research*, 302(1), 5-17.

- Nahak, G., & Sahu, R. K., 2011. Phytochemical evaluation and antioxidant activity of *Piper cubeba* and *Piper nigrum*. *Journal of Applied Pharmaceutical Science*, 1(8), 153.
- Nilforoushzadeh, M. A., Ahmadi Ashtiani, H. R., Jaffary, F., Jahangiri, F., Nikkhah, N., Mahmoudbeyk, M., Fard, M., Ansari, Z., & Zare, S., 2017. Dermal Fibroblast Cells: Biology and Function in Skin Regeneration. *Journal of Skin and Stem Cell*, *In Press*.
- Nithianantham K, Shyamala M, Chen Y., 2011. Hepatoprotective potential of *Clitoria ternatea* leaf extract against paracetamol-induced damage in mice, *Molecules*.; 16(12):10134-45.
- Pal, S. K., Bandyopadhyay, S., & Ray, S. S., 2006. Evolutionary computation in bioinformatics: A review. *IEEE Transactions on Systems, Man, and Cybernetics, Part C (Applications and Reviews)*, 36(5), 601–615.
- Pant, A., Saikia, S. K., Shukla, V., Asthana, J., Akhoun, B. A., & Pandey, R., 2014. Beta-caryophyllene modulates expression of stress response genes and mediates longevity in *Caenorhabditis elegans*, *Experimental Gerontology*, 57, 81-95.
- Petruk G, Del Giudice R, Rigano M. M., & Monti D. M., 2018. Antioxidants from plants protect against skin photoaging, *Oxidative medicine and cellular longevity*.
- Phan, S. H., 2008. Biology of Fibroblasts and Myofibroblasts, *Proceedings of the American Thoracic Society*, 5(3), 334–337.
- Piska, K., Gunia-Krzyżak, A., Koczurkiewicz, P., Wójcik-Pszczola, K., & Pękala, E., 2018. Piperlongumine (piplartine) as a lead compound for anticancer agents—Synthesis and properties of analogues: A mini-review. *European journal of medicinal chemistry*, 156, 13-20.
- Pittayapruek, P., Meephansan, J., Prapapan, O., Komine, M., & Ohtsuki, M., 2016. Role of Matrix Metalloproteinases in Photoaging and Photocarcinogenesis. *International Journal of Molecular Sciences*, 17(6), 868.
- Poon, F., Kang, S. and Chien, A.L., 2015. Mechanisms and treatments of photoaging, *Photodermatology, photoimmunology & photomedicine*, 31(2), pp.65-74.
- Preisach, C., Burkhardt, H., Schmidt-Thieme, L. and Decker, R. eds., 2008. Data Analysis, Machine Learning and Applications: Proceedings of the 31st Annual Conference of the Gesellschaft Für Klassifikation EV, *Albert-Ludwigs-Universität Freiburg, March 7-9, 2007*, Springer Science & Business Media.
- Purohit T, He T, Qin Z, Li T, Fisher G. J, Yan Y, Voorhees J. J, & Quan T, 2016. Smad3-dependent regulation of type I collagen in human dermal fibroblasts: Impact on human skin connective tissue aging, *Journal of Dermatological Science*, 83(1), 80–83.
- Qi, Y.B., Yang, W., Si, M. and Nie, L., 2020. Wnt/ $\beta$ -catenin signaling modulates piperine-mediated antitumor effects on human osteosarcoma cells, *Molecular medicine reports*, 21(5), pp.2202-2208.
- Quan T, & Fisher G. J, 2015. Role of Age-Associated Alterations of the Dermal Extracellular Matrix Microenvironment in Human Skin Aging: A Mini-Review, *Gerontology*, 61(5), 427–434.

- Rabe, J. H., Mamelak, A. J., McElgunn, P. J., Morison, W. L., & Sauder, D. N., 2006. Photoaging: mechanisms and repair. *Journal of the American Academy of Dermatology*, 55(1), 1-19.
- Raj, L., Ide, T., Gurkar, A.U., Foley, M., Schenone, M., Li, X., Tolliday, N.J., Golub, T.R., Carr, S.A., Shamji, A.F. and Stern, A.M., 2011. Selective killing of cancer cells by a small molecule targeting the stress response to ROS, *Nature*, 475(7355), pp.231-234.
- Rasul, A., Millimouno, F. M., Ali Eltayb, W., Ali, M., Li, J., & Li, X., 2013. Pinocembrin: a novel natural compound with versatile pharmacological and biological activities, *BioMed research international*.
- Ravindran, P. N., dan J. A. Kallapurackal, 2012. Black Pepper, Sawston, Inggris: Woodhead Publishing Limited.
- Rinnerthaler, M., Bischof, J., Streubel, M. K., Trost, A., & Richter, K., 2015. Oxidative stress in aging human skin. *Biomolecules*, 5(2), 545-589.
- Rozario T, & De Simone D. W, 2010. The extracellular matrix in development and morphogenesis: A dynamic view, *Developmental Biology*, 341(1), 126–140.
- Saewan N and Jimtaisong A, 2015. Natural products as photo-protection, *Journal of Cosmetic Dermatology*, vol. 14, no. 1, pp. 47–63.
- Safran, M., Dalah, I., Alexander, J., Rosen, N., Iny Stein, T., Shmoish, M., Nativ, N., Bahir, I., Doniger, T., Krug, H. and Sirota-Madi, A., 2010. GeneCards Version 3: the human gene integrator. *Database*, 2010.
- Saha, S. dan Verma, R.J., 2015. In vitro and in silico study of Piper nigrum on cyclooxygenase-2, inducible nitric oxide synthase and antioxidant enzymes, *Journal of Herbal Medicine*, 5: 86–98.
- Sbardella, D., Fasciglione, G. F., Gioia, M., Ciaccio, C., Tundo, G. R., Marini, S., & Coletta, M., 2012. Human matrix metalloproteinases: an ubiquitarian class of enzymes involved in several pathological processes, *Molecular aspects of medicine*, 33(2), 119-208
- Sharmila G, Nikitha V. S, Ilaiyarasi S, Dhivya K, Rajasekar V, Kumar N. M, & Muthukumaran, C., 2016. Ultrasound assisted extraction of total phenolics from *Cassia auriculata* leaves and evaluation of its antioxidant activities, *Industrial Crops and Products*, 84, 13-21.
- Sherman, B. T., Huang, D., Tan, Q., Guo, Y., Bour, S., Liu, D., Stephens, R., Baseler, M. W., Lane, H. C., & Lempicki, R. A., 2007. DAVID Knowledgebase: A gene-centered database integrating heterogeneous gene annotation resources to facilitate high-throughput gene functional analysis, *BMC Bioinformatics*, 8(1), 426.
- Shin, J. W., Kwon, S. H., Choi, J. Y., Na, J. I., Huh, C. H., Choi, H. R., & Park, K. C. 2019. Molecular mechanisms of dermal aging and antiaging approaches, *International journal of molecular sciences*, 20(9), 2126.
- Shi, L.L., Chen, B.N., Gao, M., Zhang, H.A., Li, Y.J., Wang, L. and Du, G.H., 2011. The characteristics of therapeutic effect of pinocembrin in transient global brain ischemia/reperfusion rats, *Life sciences*, 88(11-12), pp.521-528.



- Sala, A., Recio, M. C., Schinella, G. R., Máñez, S., Giner, R. M., Cerdá-Nicolás, M., & Ríos, J. L., 2003, Assessment of the anti-inflammatory activity and free radical scavenger activity of tiliroside, *European Journal of Pharmacology*, 461(1), 53-61.
- Singh, G., P. Marimuthu, C. Catalan, and M. deLampasona. 2004. Chemical, antioxidant and antifungal activities of volatile oil of black pepper and its acetone extract, *Journal of the Science of Food and Agriculture* 84 (14):1878–84.
- Singh, S., I. P. S. Kapoor, G. Singh, C. Schuff, M. P. De Lampasona, and C. A. N. Catalan, 2013. Chemistry, antioxidant and antimicrobial potentials of white pepper (*Piper nigrum* L.) essential oil and oleoresins, *Proceedings of the National Academy of Sciences*, India Section B: Biological Sciences 83 (3):357–66.
- Singh, A.K., Fechtner, S., Chourasia, M., Sicalo, J. and Ahmed, S., 2019. Critical role of IL-1 $\alpha$  in IL-1 $\beta$ -induced inflammatory responses: cooperation with NF- $\kappa$ Bp65 in transcriptional regulation, *The FASEB Journal*, 33(2), pp.2526-2536
- Soromou, L.W., Chu, X., Jiang, L., Wei, M., Huo, M., Chen, N., Guan, S., Yang, X., Chen, C., Feng, H. and Deng, X., 2012. In vitro and in vivo protection provided by pinocembrin against lipopolysaccharide-induced inflammatory responses, *International immunopharmacology*, 14(1), pp.66-74.
- Sparavigna A., 2020. Role of the extracellular matrix in skin aging and dedicated treatment—State of the art, *Plastic and Aesthetic Research*, 7.
- Srinivasan K, 2007. Black pepper and its pungent principle-piperine: a review of diverse physiological effects. *Critical reviews in food science and nutrition*, 47(8), 735-748.
- Sudjarwo, S.A., Eraiko, K. and Giftania Wardani Sudjarwo, K., 2017. Protective effects of piperine on lead acetate induced-nephrotoxicity in rats. *Iranian journal of basic medical sciences*, 20(11), p.1227.
- Surendiran, A., Pradhan, S. C., & Adithan, C., 2008. Role of pharmacogenomics in drug discovery and development. *Indian Journal of Pharmacology*, 40(4), 137–143.
- Stojanović-Radić, Z., Pejčić, M., Dimitrijević, M., Aleksić, A., V Anil Kumar, N., Salehi, B., & Sharifi-Rad, J., 2019. Piperine-a major principle of black pepper: a review of its bioactivity and studies. *Applied Sciences*, 9(20), 4270.
- Svobodová, A., & Vostálová, J., 2010. Solar radiation induced skin damage: review of protective and preventive options, *International journal of radiation biology*, 86(12), 999-1030
- Szklarczyk, D., Morris, J. H., Cook, H., Kuhn, M., Wyder, S., Simonovic, M., Santos, A., Doncheva, N. T., Roth, A., Bork, P., Jensen, L. J., & von Mering, C., 2017. The STRING database in 2017: Quality-controlled protein–protein association networks, made broadly accessible. *Nucleic Acids Research*, 45(D1), D362–D368

- Tanaka, K., Asamitsu, K., Uranishi, H., Iddamalghoda, A., Ito, K., Kojima, H. and Okamoto, T., 2010. Protecting skin photoaging by NF- $\kappa$ B inhibitor, *Current drug metabolism*, 11(5), pp.431-435.
- Tewari A., Grys K., Kollet J., Sarkany R., & Young A. R., 2014. Upregulation of MMP12 and Its Activity by UVA1 in Human Skin: Potential Implications for Photoaging. *Journal of Investigative Dermatology*, 134(10), 2598–2609.
- Thul, P. J., & Lindskog, C., 2018. The human protein atlas: a spatial map of the human proteome. *Protein Science*, 27(1), 233-244
- Toutfaire M., Bauwens E, & Debacq-Chainiaux F, 2017. The impact of cellular senescence in skin ageing: A notion of mosaic and therapeutic strategies. *Biochemical Pharmacology*, 142, 1–12.
- Toyama B. H., & Hetzer M. W, 2013. Protein homeostasis: Live long, won't prosper. *Nature Reviews Molecular Cell Biology*, 14(1), 55–61.
- Valencia A, Kochevar IE, 2008. Nox1-based NADPH oxidase is the major source of UVA-induced reactive oxygen species in human keratinocytes, *J Invest Dermatol*, 128:214–22.
- Varani, J., Warner, R.L., Gharaee-Kermani, M., Phan, S.H., Kang, S., Chung, J., Wang, Z., Datta, S.C., Fisher, G.J. and Voorhees, J.J., 2000. Vitamin A antagonizes decreased cell growth and elevated collagen-degrading matrix metalloproteinases and stimulates collagen accumulation in naturally aged human skin1. *Journal of Investigative Dermatology*, 114(3), pp.480-486.
- Varani J, Dame M. K, Rittie L, Fligiel S. E. G, Kang S, Fisher G. J, & Voorhees J. J, 2006. Decreased Collagen Production in Chronologically Aged Skin, *The American Journal of Pathology*, 168(6), 1861–1868.
- Vijayakumar, R. S., & Nalini, N, 2006. Efficacy of piperine, an alkaloidal constituent from *Piper nigrum* on erythrocyte antioxidant status in high fat diet and antithyroid drug induced hyperlipidemic rats, *Cell Biochemistry and Function: Cellular biochemistry and its modulation by active agents or disease*, 24(6), 491-498
- Vijayakumar, R.S., Surya, D., dan Nalini, N., 2004. Antioxidant efficacy of black pepper ( *Piper nigrum* L.) and piperine in rats with high fat diet induced oxidative stress, *Redox Report*, 9: 105–110.
- Visse R., and Nagase H., 2003. Matrix metalloproteinases and tissue inhibitors of metalloproteinases structure, function, and biochemistry, *Circulation research*, 92: 827-839.
- Wlaschek M., Tantcheva-Poor I., Naderi L., Ma W., Schneider L. A., Razi-Wolf Z., Schuller J., & Scharffetter-Kochanek K., 2001. *Solar UV irradiation and dermal photoaging*.
- Wongpa, S., Himakoun, L., Soontornchai, S., dan Temcharoen, P., 2007, Antimutagenic effects of piperine on cyclophosphamide-induced chromosome aberrations in rat bone marrow cells, *Asian Pac J Cancer Prev*, 8: 623–627
- Woo C.-H., Lim J.-H., & Kim J.-H., 2004. Lipopolysaccharide Induces Matrix Metalloproteinase-9 Expression via a Mitochondrial Reactive Oxygen Species-

- p38 Kinase-Activator Protein-1 Pathway in Raw 264.7 Cells, *The Journal of Immunology*, 173(11), 6973–6980.
- Yano K, Kajiya K, Ishiwata M, Hong YK, Miyakawa T, Detmar M., 2004. Ultraviolet B-induced skin angiogenesis is associated with a switch in the balance of vascular endothelial growth factor and thrombospondin-1 expression, *J Invest Dermatol*, 122: 201–208.
- Yeung, N., Cline, M. S., Kuchinsky, A., Smoot, M. E., & Bader, G. D., 2008, Exploring Biological Networks with Cytoscape Software, *Current Protocols in Bioinformatics*, 23(1).
- Ying, J., Jiang, Y.D., Chen, Y., Samuel, S. and Du, G.H., 2011. Electrophysiological effects of pinocembrin on *Aplysia* SN/L7 co-cultures, *Chinese Pharmacological Bulletin*.
- Ying, X., Yu, K., Chen, X., Chen, H., Hong, J., Cheng, S. and Peng, L., 2013. Piperine inhibits LPS induced expression of inflammatory mediators in RAW 264.7 cells, *Cellular immunology*, 285(1-2), pp.49-54.
- Zarai, Z., E. Boujelbene, N. Ben Salem, Y. Gargouri, and A. Sayari. 2013. Antioxidant and antimicrobial activities of various solvent extracts, Piperine and Piperic acid from *Piper nigrum*. *LWT - Food Science and Technology* 50 (2):634–41.
- Zeng, X., Zhang, P., Wang, Y., Qin, C., Chen, S., He, W., ... & Chen, Y. Z., 2019. CMAUP: a database of collective molecular activities of useful plants, *Nucleic acids research*, 47(D1), D1118-D1127
- Zhang S., & Duan E., 2018. Fighting against Skin Aging, *Cell Transplantation*, 27(5), 729–738.
- Zhang, J., Zhu, X., Li, H., Li, B., Sun, L., Xie, T., Zhu, T., Zhou, H. and Ye, Z., 2015. Piperine inhibits proliferation of human osteosarcoma cells via G2/M phase arrest and metastasis by suppressing MMP-2/-9 expression, *International immunopharmacology*, 24(1), pp.50-58