

DAFTAR PUSTAKA

- Abe, H., Konishi, H., Arichi, S. 1981. Effect of Saikosaponins on Biological Membrane. 3. Ultrastructure Studies on Effects of Saikosaponin on Cell Surface. *Planta Med* 42. <https://doi.org/10.1055/s-2007-971655>
- Abhishek, S., Vikas, S., Minu, K., Pankaj, M., 2015. Comparative Hypoglycemic Effects of Different Extract of *Clitoria Ternatea* Leaves on Rats. *IOSR Journal of Pharmacy and Biological Sciences* 10, 60–65. <https://doi.org/10.9790/3008-10236065>
- Abiola, T.S., Susan, A.O., Olusegun, B.O., 2020. Tannin-Rich Extract of *Chasmanthera dependens* Stem Potential in Piroxicam-Induced Nephrotoxicity in Adult Male Wistar Rats. *American Journal of Molecular Biology* 10, 29–43. <https://doi.org/10.4236/ajmb.2020.101003>
- Abriyani, E., Yuniarsih, N., Fikayuniar, L., Sulastri, D., Farmasi, F., Buana, U., Karawang, P., Karawang, I., 2022. Skrining Fitokimia Ekstrak Daun *Clitoria ternatea* L. dan Uji Toksisitas terhadap Larva Udang *Artemia salina*. *Journal of Pharmacopolium* 5, 220–225.
- Afrianto, W.F., Tamnge, F., Hasanah, L.N., 2020. Review: A Relation Between Ethnobotany and Bioprospecting of Edible Flower Butterfly Pea (*Clitoria ternatea*) in Indonesia. *Asian Journal of Ethnobiology* 3. <https://doi.org/10.13057/asianjethnobiol/y030202>
- Agidew, M.G., 2022. Phytochemical analysis of some selected traditional medicinal plants in Ethiopia. *Bulletin of National Research Centre* 46. <https://doi.org/10.1186/s42269-022-00770-8>
- Ahmad, F., Anwar, F., Hira, S., 2016. Review on Medicinal Importance of Fabaceae Family. *Pharmacology Online* 3, 151–156.
- Ain, Q.U., Khan, H., Mubarak, M.S., Pervaiz, A., 2016. Plant Alkaloids as Antiplatelet Agent: Drugs of the Future in the Light of Recent Developments. *Front Pharmacol* 7. <https://doi.org/10.3389/fphar.2016.00292>
- Aisyah, S., Rosidah, A., Sri Damayanti, D., 2024. Efek Kombucha Bunga Telang (*Clitoria ternatea*) terhadap Penurunan pH Lambung dan Peningkatan Luas Kerusakan Epitel Mukosa Lambung. *Jurnal Kedokteran Komunitas* 12, 1–11.
- Alechinsky, L., Favreau, F., Cechova, P., Inal, S., Faye, P.A., Ory, C., Thuillier, R., Barrou, B., Trouillas, P., Guillard, J., Hauet, T., 2020. Tannic Acid Improves Renal Function Recovery After Renal Warm Ischemia–reperfusion in a Rat Model. *Biomolecules* 10. <https://doi.org/10.3390/biom10030439>
- Alharbi, K.S., Al-Abbasi, F.A., Alzarea, S.I., Afzal, O., Altamimi, A.S.A., Almalki, W.H., Shahid Nadeem, M., Afzal, M., Sayyed, N., Kazmi, I., 2022. Effects of the Anthocyanin Hirsutidin on Gastric Ulcers: Improved Healing

- through Antioxidant Mechanisms. *Journal of Natural Products* 85, 2406–2412. <https://doi.org/10.1021/acs.jnatprod.2c00620>
- Alsawaf, S., Alnuaimi, F., Afzal, S., Thomas, R.M., Chelakkot, A.L., Ramadan, W.S., Hodeify, R., Matar, R., Merheb, M., Siddiqui, S.S., Vazhappilly, C.G., 2022. Plant Flavonoids on Oxidative Stress-Mediated Kidney Inflammation. *Biology (Basel)*. <https://doi.org/10.3390/biology11121717>
- Al-Shamrani, S.M., Safhi, F.A., Mobasher, M.A., Saleem, R.M., Alharthi, A., Alshaya, D.S., Awad, N.S., 2022. Antiproliferative Effect of *Clitoria ternatea* Ethanolic Extract against Colorectal, Breast, and Medullary Thyroid Cancer Cell Lines. *Separations* 9. <https://doi.org/10.3390/separations9110331>
- Al-Snafi, A.E., 2016. Pharmacological Importance of *Clitoria ternatea*-A Review. *IOSR Journal of Pharmacy* 6, 68–83.
- Altemimi, A., Lakhssassi, N., Baharlouei, A., Watson, D.G., Lightfoot, D.A., 2017. Phytochemicals: Extraction, isolation, and identification of bioactive compounds from plant extracts. *Plants*. <https://doi.org/10.3390/plants6040042>
- Amaya-Montoya, M., Perez-Londono, A., Guatibonza-Garcia, V., Vargas-Villanueva, A., Mendivil, C.O., 2020. Cellular Senescence as a Therapeutic Target for Age-Related Diseases: A Review. *Advances in Therapy* 37, 1407–1424. <https://doi.org/10.6084/m9.figshare.11920182>
- Arifah, Y., Sunarti, S., Prabandari, R., 2022. Efek Bunga Telang (*Clitoria ternatea* L.) Terhadap Kolesterol Total, LDL, HDL Pada Tikus (*Rattus Norvegicus*). *Journal Syifa Sciences and Clinical Research* 4, 18–31. <https://doi.org/10.37311/jsscr.v4i1.13493>
- Arifin, W.N., Zahiruddin, W.M., 2017. Sample Size Calculation in Animal Studies using Resource Equation Approach. *Malaysian Journal of Medical Sciences* 24, 101–105. <https://doi.org/10.21315/mjms2017.24.5.11>
- Arsianti, A., Pasha Mahindra, S., Nur Azizah, N., Megawati Fajrin, A., Dameria Nadapdap, L., 2022. Phytochemical Analysis, Antioxidant and Anticancer Effects of *Clitoria ternatea* Extract on Breast T47D Cancer Cells. *Indonesian Journal of Medical Chemistry and Bioinformatics* 1. <https://doi.org/10.7454/ijmcb.v1i1.1003>
- Aruoma, O.I., Halliwell, B., Hoey, B.M., Butler, J., 1989. The Antioxidant Action of N-acetylcysteine: Its Reaction with Hydrogen Peroxide, Hydroxyl Radical, Superoxide, and Hypochlorous Acid. *Free Radical Biology and Medicine* 6, 593–597. [https://doi.org/10.1016/0891-5849\(89\)90066-X](https://doi.org/10.1016/0891-5849(89)90066-X)
- Asadnejad, S., Nabizadeh, R., Nazarinia, A., Jahed, G.R., Alimohammadi, M., 2018. Data on prevalence of additive colors in local food and beverage

- products, Tehran, Iran. Data Brief 19, 2104–2108. <https://doi.org/10.1016/j.dib.2018.07.001>
- Azwanida, N., 2015. A Review on the Extraction Methods Use in Medicinal Plants, Principle, Strength and Limitation. Med Aromat Plants (Los Angel) 4. <https://doi.org/10.4172/2167-0412.1000196>
- Basten, G., 2010. Introduction to Clinical Biochemistry: Interpreting Blood Results. Ventus Publisher ApS, Denmark.
- Benjamim, J.K.F., Dias da Costa, K.A., Silva Santos, A., 2020. Chemical, Botanical and Pharmacological Aspects of the Leguminosae. Pharmacognosy Reviews 14, 106–120. <https://doi.org/10.5530/phrev.2020.14.15>
- Bhagavan, N.V., Chung-Eun, H., 2015. Essentials of Medical Biochemistry: with Clinical Cases, Second. ed. Academic Press, USA.
- Bishoyi, K.A., 2012. Polymorphism in Flower Colour and Petal Type in Aparajita (*Clitoria ternatea*). Open Access Journal of Medicinal and Aromatic Plants 3, 12–14.
- Blagosklonny, B., 2009. Validation of Anti-Aging Drugs by Treating Age-Related Diseases. Aging 1. <https://doi.org/https://doi.org/10.18632/aging.100034>
- BPOM, 2022. Peraturan Badan Pengawas Obat dan Makanan Nomor 10 Tahun 2022 tentang Pedoman Uji Toksisitas Praklinik secara In Vivo. Badan POM RI, Jakarta.
- BPOM, 2010. Acuan Sediaan Herbal, BPOM. Badan POM RI, Jakarta.
- Brandao-Costa, R., Batistaa, J., Nascimento, T., Porto, A., 2019. Renal function effects of FDS, a saponin isolated from *Filicium decipiens* seeds: Biochemical and Histopathological studies. Journal of Plant Science and Phytopathology 3, 007–010. <https://doi.org/10.29328/journal.jpssp.1001040>
- Broskey, N.T., Marlatt, K.L., Most, J., Erickson, M.L., Irving, B.A., Redman, L.M., 2019. The Panacea of Human Aging: Calorie Restriction Versus Exercise. Exercise and Sport Science Reviews 47, 169–175. <https://doi.org/10.1249/JES.0000000000000193>
- Buddhika, H.D.K., Dharmadasa, R.M., Arawwawala, L.D.A.M., Pakeerathan, K., 2021. Phytochemical Properties of *Clitoria ternatea* L. (Fabaceae)-A Distinct Flower Morphometric Plants Available in Sri Lanka Phytochemical Properties of *Clitoria ternatea* L. (Fabaceae)-A Distinct Flower Morphometric Plants Available in Sri Lanka. Proceedings West Mark Ed Association Conference 68, 3–17. <https://doi.org/10.3390/xxxxx>

- Buoso, E., Attanzio, A., Biundo, F., 2022. Cellular Senescence in Age-Related Diseases: Molecular Bases and Therapeutic Interventions. *Cells*. <https://doi.org/10.3390/cells11132029>
- Cahyaningsih, E., Era Sandhi, P.K., Santoso, P., 2019. Skrining Fitokimia dan Uji Aktivitas Antioksidan Ekstrak Etanol Bunga Telang (*Clitoria ternatea* L.) dengan Metode Spektrofotometri UV-VIS. *Jurnal Ilmiah Medicamento*• 5, 2356–4818.
- Campisi, J., Robert, L., 2014. Cell Senescence: Role in Aging and Age-related Diseases, in: *Aging: Facts and Theories*. S. Karger AG, pp. 45–61. <https://doi.org/10.1159/000358899>
- Chaudhary, P., Janmeda, P., Docea, A.O., Yeskaliyeva, B., Abdull Razis, A.F., Modu, B., Calina, D., Sharifi-Rad, J., 2023. Oxidative Stress, Free Radicals and Antioxidants: Potential Crosstalk in the Pathophysiology of Human Diseases. *Frontiers Chemica and Pharmaceutical Chemistry*. <https://doi.org/10.3389/fchem.2023.1158198>
- Chauhan, N., Rajvaidhya, S., Dubey, B.K., 2012. Antiasthmatic Effect of Roots of *Clitoria ternatea* Linn. *IJPSR* 3, 1076–1079.
- Cheng, L., Shi, L., Wu, J., Zhou, X., Li, X., Sun, X., Zhu, L., Xia, T., Ding, Q. 2018 A Hederagenin Saponin Isolated from *Clematis ganpiniana* Induces apoptosis in Breast Cancer Cells via the Mitochondrial Pathway. *Oncology Letters* 15, <https://doi.org/10.3892/ol.2017.7494>
- Childs, B.G., Durik, M., Baker, D.J., Van Deursen, J.M., 2015. Cellular Senescence in Aging and Age-related Disease: From Mechanisms to Therapy. *Nature Medicine* 21. <https://doi.org/10.1038/nm.4000>
- Chingwaru, C., Bagar, T., Chingwaru, W., 2020. Aqueous Extracts of *Flacourtia indica*, *Swartzia madagascariensis* and *Ximenia caffra* are Strong Antibacterial Agents Against *Shigella* spp., *Salmonella typhi* and *Escherichia coli* O157. *South African Journal of Botany* 128, 119–127. <https://doi.org/10.1016/j.sajb.2019.10.022>
- Civitarese, A.E., Carling, S., Heilbronn, L.K., Hulver, M.H., Ukropcova, B., Deutsch, W., Smith, S., Ravussin, E., 2007. Calorie Restriction Increases Muscle Mitochondrial Biogenesis in Healthy Humans. *PLoS One* 4, 0485–0494. <https://doi.org/10.1371/journal>
- Cohen, M.M., 1987. Role of Endogenous Prostaglandins in Gastric Secretion and Mucosal Defense. *Clin Invest Med* 10, 226–31.
- Cook, D.J., 2003. *Cellular Pathology*. Reed Educational and Professional Publishing Ltd., Oxford.

- Cosan, T.D., Saydam, F., Özbayer, C., Doğaner, F., Soyocak, A., Güneş, H.V., Değirmenci, İ., Kurt, H., Üstüner, M.C., Bal, C., 2015. Impact of Tannic Acid on Blood Pressure, Oxidative Stress and Urinary Parameters in L-NNA-Induced Hypertensive Rats. *Cytotechnology* 67, 97–105. <https://doi.org/10.1007/s10616-013-9661-4>
- Cox, L.S., 2022. Therapeutic Approaches to Treat and Prevent Age-related Diseases through Understanding the Underlying Biological Drivers of Ageing. *Journal of Economics of Ageing* 23. <https://doi.org/10.1016/j.jeoa.2022.100423>
- Cuollo, L., Antonangeli, F., Santoni, A., Soriani, A., 2020. The Senescence-Associated Secretory Phenotype (SASP) in the Challenging Future of Cancer Therapy and Age-related Diseases. *Biology (Basel)* 9, 1–16. <https://doi.org/10.3390/biology9120485>
- Daisy, P., Santosh, K., Rajathi, M., 2009. Antihyperglycemic and Antihyperlipidemic Effects of *Clitoria ternatea* Linn. in Alloxan-induced Diabetic Rats. *African Journal of Microbiology Research* 3, 287–291.
- Daley, S.K., Cordell, G.A., 2021. Alkaloids in Contemporary Drug Discovery to Meet Global Disease Needs. *Molecules* 26. <https://doi.org/10.3390/molecules26133800>
- Dan-Li, H., Li, J.M., Xie, R., Huo, H.R., Xiong, X. jiang, Sui, F., Wang, P. qian, 2023. The Role of Traditional Herbal Medicine for Ischemic Stroke: from Bench to Clinic—A Critical Review. *Phytomedicine*. <https://doi.org/10.1016/j.phymed.2022.154609>
- Das, A.K., Islam, M.N., Faruk, M.O., Ashaduzzaman, M., Dungani, R., 2020. Review on Tannins: Extraction Processes, Applications and Possibilities. *South African Journal of Botany* 135, 58–70. <https://doi.org/10.1016/j.sajb.2020.08.008>
- de Jesus, N.Z.T., de Souza Falcão, H., Gomes, I.F., de Almeida Leite, T.J., de Moraes Lima, G.R., Barbosa-Filho, J.M., Tavares, J.F., da Silva, M.S., de Athayde-Filho, P.F., Batista, L.M., 2012. Tannins, Peptic Ulcers and Related Mechanisms. *International Journal of Molecular Sciences* 13, 3203–3228. <https://doi.org/10.3390/ijms13033203>
- de Oliveira, B.M.M., Serpa, P.Z., da Costa Zanatta, M.E., Aires, B.A., Steffler, A.M., Somensi, L.B., Cury, B.J., dos Santos, A.C., Venzon, L., Boeing, T., Mota da Silva, L., Roman Junior, W.A., 2022. Gastroprotective and Gastric Healing Effects of the Aqueous Extract of *Casearia sylvestris* in Rodents: Ultrasound, Histological and Biochemical Analyzes. *Journal of Ethnopharmacol* 298. <https://doi.org/10.1016/j.jep.2022.115660>
- De Wet, H., Ngubane, S.C., 2014. Traditional Herbal Remedies Used by Women in a Rural Community in Northern Maputaland (South Africa) for the

- Treatment of Gynaecology and Obstetric Complaints. *South African Journal of Botany* 94, 129–139. <https://doi.org/10.1016/j.sajb.2014.06.009>
- Debela, D.T., Muzazu, S.G.Y., Heraro, K.D., Ndalama, M.T., Mesele, B.W., Haile, D.C., Kitui, S.K., Manyazewal, T., 2021. New Approaches and Procedures for Cancer Treatment: Current Perspectives. *SAGE Open Medicine*. <https://doi.org/10.1177/20503121211034366>
- Del Hierro, N.J., Herrera, T., Fornari, T., Reglero, G., Martin, D., 2018. The Gastrointestinal Behavior of Saponins and its Significance for Their Bioavailability and Bioactivities. *Journal of Functional Foods* 40, 484–497. <https://doi.org/10.1016/j.jff.2017.11.032>
- Dewi, S., Astuti, K.I., Rusida, E.R., 2023. Uji Toksisitas Akut Ekstrak Etanol 70% Bunga Telang (*Clitoria ternatea* L.) terhadap Tikus Betina Galur Wistar dengan Metode OECD 425. *Jurnal Ilmiah Farmasi Farmasyifa* 6, 60–66. <https://doi.org/10.29313/jiff.v6i1.10420>
- Dey, P., Kundu, A., Kumar, A., Gupta, M., Lee, B.M., Bhakta, T., Dash, S., Kim, H.S., 2020. Analysis of Alkaloids (Indole Alkaloids, Isoquinoline Alkaloids, Tropane Alkaloids), in: *Recent Advances in Natural Products Analysis*. Elsevier, pp. 505–567. <https://doi.org/10.1016/B978-0-12-816455-6.00015-9>
- Dias, M.C., Pinto, D.C.G.A., Silva, A.M.S., 2021. Plant Flavonoids: Chemical Characteristics and Biological Activity. *Molecules*. <https://doi.org/10.3390/molecules26175377>
- Dikkala, P.K., Kakarlapudi, J., Rokalla, P., Vedantam, S.K., Kaur, A., Kaur, K., Sharma, M., Sridhar, K., 2023. Computational Screening of Phytochemicals for Anti-diabetic Drug Discovery, in: *Phytochemistry, Computational Tools and Databases in Drug Discovery*. Elsevier, pp. 285–311. <https://doi.org/10.1016/B978-0-323-90593-0.00009-5>
- Diwan, F.H., Abdel-Hassan, A., Mohammed, S.T., 2000. Effect of Saponin on Mortality and Histopathological Changes in Mice. *Eastern Mediterranean Health Journal* 6, 345–351.
- Diwan, V., Brown, L., Gobe, G.C., 2017. The Flavonoid Rutin Improves Kidney and Heart structure and Function in an Adenine-induced Rat Model of Chronic Kidney Disease. *Journal of Functional Foods* 33, 85–93. <https://doi.org/10.1016/j.jff.2017.03.012>
- Du, Y. guang, Wang, L. pei, Qian, J. wen, Zhang, K. na, Chai, K. fu, 2016. Panax notoginseng Saponins Protect Kidney from Diabetes by Up-regulating Silent Information Regulator 1 and Activating Antioxidant Proteins in Rats. *Chinese Journal of Integrative Medicine* 22, 910–917. <https://doi.org/10.1007/s11655-015-2446-1>

- Eguchi, R., Ono, N., Hirai Morita, A., Katsuragi, T., Nakamura, S., Huang, M., Altaf-Ul-Amin, M., Kanaya, S., 2019. Classification of Alkaloids According to the Starting Substances of Their Biosynthetic Pathways Using Graph Convolutional Neural Networks. *BMC Bioinformatics* 20. <https://doi.org/10.1186/s12859-019-2963-6>
- Elfadil, A.G., Sabahelkier, M.K., Rayan, M.Y., Daa M. O., Nagla, A.H., Israa, S.B., 2013. Effect of Tannin and Plant Tannins on some Organs and Physico-Chemical Characters of Diabetic Wistar Rats. *International Journal of Advance Research (Indore)* 1, 165–170.
- Emamiyan, M.Z., Vaezi, G., Tehranipour, M., Shahrohkabadi, K., Shiravi, A., 2018. Preventive Effects of the Aqueous Extract of *Cichorium intybus* L. Flower on Ethylene glycol-induced Renal Calculi in Rats. *Avicenna Journal of Phytomedicine* 8, 170–178.
- Falcão, H.D.S., Leite, J.A., Barbosa-Filho, J.M., De Athayde-Filho, P.F., Chaves, M.C.D.O., Moura, M.D., Ferreira, A.L., De Almeida, A.B.A., Souza-Brito, A.R.M., Diniz, M.D.F.F.M., Batista, L.M., 2008. Gastric and Duodenal Antiulcer Activity of Alkaloids: A Review. *Molecules* 13, 3198–3223. <https://doi.org/10.3390/molecules13123198>
- Fang, J., Zeng, L., He, Y., Liu, X., Zhang, T., Wang, Q., 2022. Effects of Dietary Tannic Acid on Obesity and Gut Microbiota in C57BL/6J Mice Fed with High-Fat Dietary Foods 11, 3325. <https://doi.org/10.3390/foods11213325>
- Faria, J., Ahmed, S., Gerritsen, K.G.F., Mihaila, S.M., Masereeuw, R., 2019. Kidney-based in Vitro Models for Drug-induced Toxicity Testing. *Archives of Toxicology*. <https://doi.org/10.1007/s00204-019-02598-0>
- Fekete, M., Szarvas, Z., Fazekas-Pongor, V., Feher, A., Csipo, T., Forrai, J., Dosa, N., Peterfi, A., Lehoczki, A., Tarantini, S., Varga, J.T., 2023. Nutrition Strategies Promoting Healthy Aging: From Improvement of Cardiovascular and Brain Health to Prevention of Age-Associated Diseases. *Nutrients*. <https://doi.org/10.3390/nu15010047>
- Ferreira, M.L.F., Rius, S.P., Casati, P., 2012. Flavonoids: Biosynthesis, Biological Functions, and Biotechnological Applications. *Frontiers Plant Science* 3. <https://doi.org/10.3389/fpls.2012.00222>
- Fitria, L., Lukitowati, F., Kristiawati, D., 2019. Nilai Rujukan untuk Evaluasi Fungsi Hati dan Ginjal pada Tikus (*Rattus norvegicus* Berkenhout, 1769) Galur Wistar. *Jurnal Pendidikan Matematika dan IPA* 10, 81. <https://doi.org/10.26418/jpmipa.v10i2.34144>
- Flanagan, E.W., Most, J., Mey, J.T., Redman, L.M., 2020. Calorie Restriction and Aging in Humans. *Annual Review of Nutrition* 40. <https://doi.org/10.1146/annurev-nutr-122319-034601>

- Flores, F., Dibona, D.R., Beck, C.H., Leaf, A. 1972. The Role of Cell Swelling in Ischemic Renal Damage and the Protective Effect of Hypertonic Solute. *Journal of Clinical Investigation* 51, 118-26. <https://doi.org/10.1172/jci106781>
- Francis, G., Kerem, Z., Makkar, H.P.S., Becker, K., 2002. The Biological Action of Saponins in Animal Systems: A Review. *British Journal of Nutrition* 88, 587–605. <https://doi.org/10.1079/bjn2002725>
- Fu, X., Wu, Q., Wang, J., Chen, Y., Zhu, G., Zhu, Z., 2021. Spectral Characteristic, Storage Stability and Antioxidant Properties of Anthocyanin Extracts from Flowers of Butterfly Pea (*Clitoria ternatea* L.). *Molecules* 26. <https://doi.org/10.3390/molecules26227000>
- Fuente, M.D. La, Miquel, J., 2009. An Update of the Oxidation-Inflammation Theory of Aging: The Involvement of the Immune System in Oxi-Inflamm-Aging. *Current Pharmacy* 15, 3003–3026.
- Gamage, G.C.V., Lim, Y.Y., Choo, W.S., 2021. Anthocyanins From *Clitoria ternatea* Flower: Biosynthesis, Extraction, Stability, Antioxidant Activity, and Applications. *Frontiers Plant Science*. <https://doi.org/10.3389/fpls.2021.792303>
- Gamage, V., Gayan Chandrajith, Lim, Y.Y., Choo, W.S., 2021. Anthocyanins from *Clitoria ternatea* Flower: Biosynthesis, Extraction, Stability, Antioxidant Activity, and Applications. *Frontiers Plant Science* 12. <https://doi.org/10.3389/fpls.2021.792303>
- Golmohammadi, M.G., Banaei, S., Abedi, A., 2022. Saponin Protects Against Cyclophosphamide-Induced Kidney and Liver Damage via Antioxidant and Anti-Inflammatory Actions. *Physiology International* 110. <https://doi.org/10.21203/rs.3.rs-1398111/v1>
- Gould, K.S., 2004. Nature's Swiss Army Knife: The Diverse Protective Roles of Anthocyanins in Leaves. *Journal of Biomedicine and Biotechnology* 2004, 314–320. <https://doi.org/10.1155/S1110724304406147>
- Gounden, V., Bhatt, H., Jialal, I., 2023. Renal Function Tests. StarPearls Publishing LLC.
- Gowda, S., Desai, P.B., Kulkarni, S.S., Hull, V. V, Math, A.A.K., Vernekar, S.N., 2010. Markers of Renal Function Tests. *Nprth American Journal Medical Sciences* 2, 170–173.
- Guo, J., Huang, X., Dou, L., Yan, M., Shen, T., Tang, W., Li, J., 2022. Aging and Aging-related Diseases: from Molecular Mechanisms to Interventions and Treatments. *Signal Transduction and Targeted Therapy*. <https://doi.org/10.1038/s41392-022-01251-0>

- Guo, R., Shang, J.-H., Ye, R.-H., Zhao, Y.-L., Luo, X.-D., 2023. Pharmacological Investigation of Indole Alkaloids from *Alstonia scholaris* Against Chronic Glomerulonephritis. *Phytomedicine* 118, 154958. <https://doi.org/10.1016/j.phymed.2023.154958>
- Guo, Y., Tan, K., 2007. Research on Tripterygium Toxicity. *Journal of Chinese Medical Materials* 1, 112–117.
- Gupta, G.K., Chahal, J., Bhatia, M., 2010. *Clitoria ternatea* (L.): Old and New Aspects. *Journal of Pharmacy Research* 3, 2610–2614.
- Gupta, G.K., Kumar Gupta, G., 2010. *Clitoria ternatea* (L.): Old and new aspects. Jagbir Chahal *et al.* / *Journal of Pharmacy Research* 3, 2610–2614.
- Hage-Sleiman, R., Mroueh, M., Daher, C.F., 2011. Pharmacological Evaluation of Aqueous Extract of (*Althaea officinalis*) Flower Grown in Lebanon. *Pharm Biol* 49, 327–333. <https://doi.org/10.3109/13880209.2010.516754>
- Hammad, F.T., Al-Salam, S., Hammad, W.F., Yasin, J., Lubbad, L., 2020. Despite Initial Recovery of GFR, Long-term Renal Functions Deteriorate Following Short Periods of Unilateral Ureteral Obstruction. *American Journal of Physiology-Renal Physiology* 319, F523–F533. <https://doi.org/10.1152/ajprenal.00096.2020>
- Hanum, G.R., Ardiansyah, S., 2018. Deteksi Dini Penyakit Degeneratif pada Remaja Anggota Karang Taruna. *Abadimas Adi Buana* 2.
- Heilbronn, L.K., De Jonge, L., Frisard, M.I., DeLany, J.P., Larson-Meyer, D.E., Rood, J., Nguyen, T., Martin, C.K., Volaufova, J., Most, M.M., Greenway, F.L., Smith, S.R., Deutsch, W.A., Williamson, D.A., Ravussin, E., 2006. Effect of 6-month Calorie Restriction on Biomarkers of Longevity, Metabolic Adaptation, and Oxidative Stress in Overweight Individuals: A Randomized Controlled Trial. *JAMA* 295, 1539–1548. <https://doi.org/10.1001/jama.295.13.1539>
- Hidayati, N.S., Rijai, H.R., Narsa, A.C., 2023. Optimasi Basis Sediaan Masker Gel Peel off dan Skrining Fitokimia Ekstrak Etanol Bunga Telang (*Clitoria ternatea* L.) Optimization of Gel Mask Preparation Base Peel off and Phytochemical Screening of Telang Flower Ethanol Extract (*Clitoria ternatea* L.), in: *Proceeding of Mulawarman Pharmaceuticals Conferences*. pp. 13–20. <https://doi.org/10.25026/mpc.v17i1.684>
- Hosseinzadeh, E., Banaee, N., Nedaie, H.A., 2017. Cancer and Treatment Modalities. *Current Cancer Therapy Reviews* 13. <https://doi.org/10.2174/1573394713666170531081818>
- Hu, Q., Qu, C., Xiao, X., Zhang, W., Jiang, Y., Wu, Z., Song, D., Peng, X., Ma, X., Zhao, Y.L., 2021. Flavonoids on diabetic nephropathy: advances and

- therapeutic opportunities. Chinese Medicine (United Kingdom). <https://doi.org/10.1186/s13020-021-00485-4>
- Humason, G., 1962. Animal Tissue Techniques. W.H. Freeman and Company, United States of America.
- Iamsaard, S., Burawat, J., Kanla, P., Arun, S., Sukhorum, W., Sripanidkulchai, B., Uabun-Dit, N., Wattathorn, J., Hipkaeo, W., Fongmoon, D., Kondo, H., 2014. Antioxidant Activity and Protective Effect of *Clitoria ternatea* Flower Extract on Testicular Damage induced by Ketoconazole in Rats. J Zhejiang Univ Sci B 15, 548–555. <https://doi.org/10.1631/jzus.B1300299>
- Ino, Y., Yamazaki-Itoh, R., Shimada, K., Iwasaki, M., Kosuge, T., Kanai, Y., Hiraoka, N., 2013. Immune Cell Infiltration as an Indicator of the Immune Microenvironment of Pancreatic Cancer. British Journal of Cancer 108, 914–923. <https://doi.org/10.1038/bjc.2013.32>
- Isobe, T., Saitoh, S., Takagi, S., Takeuchi, H., Chiba, Y., Katoh, N., Shimamoto, K., 2005. Influence of Gender, Age and Renal Function on Plasma Adiponectin Level: the Tanno and Sobetsu Study. Europe Journal of Endocrinology 153, 91–98. <https://doi.org/10.1530/eje.1.01930>
- ITIS, 2023. *Clitoria ternatea* L. URL <https://www.gbif.org/species/102287322> (accessed 2.8.24).
- Jain, N.N., Ohal, C.C., Shroff, S.K., Bhutada, R.H., Somani, R.S., Kasture, V.S., Kasture, S.B., 2003. *Clitoria ternatea* and the CNS. Pharmacology Biochemistry and Behavior 75, 529–536. [https://doi.org/10.1016/S0091-3057\(03\)00130-8](https://doi.org/10.1016/S0091-3057(03)00130-8)
- Jamil, N., Mohd Zairi, M.N., Mohd Nasim, N.A., Pa’ee, F., 2018. Influences of Environmental Conditions to Phytoconstituents in *Clitoria ternatea* (Butterfly Pea Flower) – A Review. Journal of Science and Technology 10. <https://doi.org/10.30880/jst.2018.10.02.029>
- Jaul, E., Barron, J., 2017. Age-Related Diseases and Clinical and Public Health Implications for the 85 Years Old and Over Population. Frontiers Public Health. <https://doi.org/10.3389/fpubh.2017.00335>
- Jedidi, S., Selmi, H., Aloui, F., Rtibi, K., Sammari, H., Abbes, C., Sebai, H., 2022. Antioxidant Properties, Phytoactive Compounds and Potential Protective Action of *Salvia officinalis* Flowers Against Combined Gastro-Intestinal Ulcer and Diarrhea Experimentally Induced in Rat. Dose-Response 20. <https://doi.org/10.1177/15593258221102313>
- Jeyaraj, E.J., Lim, Y.Y., Choo, W.S., 2021. Extraction methods of butterfly pea (*Clitoria ternatea*) flower and biological activities of its phytochemicals. Journal of Food Science and Technology. <https://doi.org/10.1007/s13197-020-04745-3>

- Jitäreanu, A., Trifan, A., Vieriu, M., Caba, I.C., Mârțu, I., Agoroaei, L., 2023. Current Trends in Toxicity Assessment of Herbal Medicines: A Narrative Review. *Processes*. <https://doi.org/10.3390/pr11010083>
- Juliastuti, J., Miko, A., Ramli, N., Emilda, E., Lajuna, L., Yuniwati, C., Fithriany, F., Anita, A., Sari, Y., Veri, N., 2017. The Effect of Ethanol Extract of Ylang-ylang Flower (*Cananga odorata*) on Vascular and Kidney Histology in Menopausal Mice. *Clinical Nutrition Experimental* 15, 1–8. <https://doi.org/10.1016/j.yclnex.2017.08.001>
- Kanagasundaram, N.S., 2015. Pathophysiology of Ischaemic Acute Kidney Injury. *Annals of Clinical Biochemistry* 52, 193–205. <https://doi.org/10.1177/0004563214556820>
- Karel, A., Kumar, H., Chowdhary, B., 2018a. *Clitoria ternatea* L. A Miraculous Plant. *International Journal of Current Microbiology and Applied Science* 7, 672–674. <https://doi.org/10.20546/ijcmas.2018.709.079>
- Karel, A., Kumar, H., Chowdhary, B., 2018b. *Clitoria ternatea* L. A Miraculous Plant. . *International Journal of Current Microbiology and Applied Science* 7, 672–674. <https://doi.org/10.20546/ijcmas.2018.709.079>
- Karimi, A., Majlesi, M., Rafieian-Kopaei, M., 2015. Herbal Versus Synthetic Drugs: Beliefs and Facts. *Journal of Nephropharmacol* 4, 27–30.
- Karta, J., Pandjaitan, M., Rahminiwati, M., 2013. Evaluation of Acute Oral Toxicity of Butterfly Pea Root Extract on Experimental Mice, in: 3rd International Conference on Instrumentation, Communications, Information Technology, and Biomedical Engineering (ICICI-BME). pp. 317–323.
- Katzir, I., Adler, M., Karin, O., Mendelsohn-Cohen, N., Mayo, A., Alon, U., 2021. Senescent Cells and the Incidence of Age-related Diseases. *Aging Cell* 20. <https://doi.org/10.1111/ace1.13314>
- Kelemu, S., Cardona, C., Segura, G., 2004. Antimicrobial and Insecticidal Protein Isolated from Seeds of *Clitoria ternatea*, a Tropical Forage Legume. *Plant Physiology and Biochemistry* 42, 867–873. <https://doi.org/10.1016/j.plaphy.2004.10.013>
- Kern, J.C., Kehrer, J.P., 2005. Free Radicals and Apoptosis: Relationships with Glutathione, Thioredoxin, and the BCL Family Proteins. *Frontiers in Bioscience* 10, 1727–1738.
- Khan, K.N.M., Hard, G.C., Alden, C.L., 2013. Kidney, in: Haschek and Rousseaux's Handbook of Toxicologic Pathology. Elsevier, pp. 1667–1773. <https://doi.org/10.1016/B978-0-12-415759-0.00047-9>

- Khatib, A., Tofrizal, Arsanty, D., 2024. Toxicity Effect of *Clitoria ternatea* L. Extract in Liver and Kidney Histopathological Examination in *Mus musculus*. *IIUM Medical Journal Malaysia* 23, 133–142.
- Khenouf, S., Benabdallah, H., Gharzouli, K., Amira, S., Ito, H., Kim, T.H., Yoshida, T., Gharzouli, A., 2003. Effect of Tannins from *Quercus suber* and *Quercus coccifera* Leaves on Ethanol-induced Gastric Lesions in Mice. *Journal of Agricultural and Food Chemistry* 51, 1469–1473. <https://doi.org/10.1021/jf020808y>
- Khoo, H.E., Azlan, A., Tang, S.T., Lim, S.M., 2017. Anthocyanidins and Anthocyanins: Colored Pigments as Food, Pharmaceutical Ingredients, and the Potential Health Benefits. *Food Nutr Res* 61, 1361779. <https://doi.org/10.1080/16546628.2017.1361779>
- King-Thom, C., Wei, C.-I., Johnson, M.G., 1998. Are Tannins a Double-edged Sword in Biology and Health? *Trends Food Sci Technol* 9, 168–175. [https://doi.org/10.1016/S0924-2244\(98\)00028-4](https://doi.org/10.1016/S0924-2244(98)00028-4)
- Kiran, T.R., Otlu, O., Karabulut, A.B., 2023. Oxidative Stress and Antioxidants in Health and Disease. *Journal of Laboratory Medicine*. <https://doi.org/10.1515/labmed-2022-0108>
- Kumar, Ashutosh, Kumar, B., Kumar, R., Kumar, Ajay, Singh, M., Tiwari, V., Trigunayat, A., Paul, P., Singh, P., 2022. Acute and Subacute Toxicity Study of Ethanolic Extract of *Calotropis procera* (Aiton) Dryand Flower in Swiss Albino Mice. *Phytomedicine Plus* 2. <https://doi.org/10.1016/j.phyplu.2022.100224>
- Kumar, K.V., Shifow, A.A., Naidu, M.U.R., Ratnakar, K.S., 2000. Carvedilol: A beta Blocker with Antioxidant Property Protects against Gentamicin-Induces Nephrotoxicity in Rats. *Life Science* 66, 2603–261. [https://doi.org/https://doi.org/10.1016/s0024-3205\(00\)00594-4](https://doi.org/https://doi.org/10.1016/s0024-3205(00)00594-4)
- Kumar, P.K., Krishna Ch, G., Kumar kola, P., Professor, A., Sudeepthi, lakshmi N., 2014. Gastroprotective Effect of Flower Extracts of *Hibiscus rosa sinensis* Against Acute Gastric Lesion Models in Rodents. *Journal Pharmacognosy and Phytochemistry* 3, 137–145.
- Kuna, L., Jakab, J., Smolic, R., Raguz-Lucic, N., Vcev, A., Smolic, M., 2019. Peptic Ulcer Disease: A Brief Review of Conventional Therapy and Herbal Treatment Options. *Journal of Clinal Medicine*. <https://doi.org/10.3390/jcm8020179>
- Kupradinun, P., Tepsuwan, A., Tanthasri, N., Meesiripan, N., Tunsakul, S., Tompat, W., Jarratwisarutporn, Kusamran, W.R., 2010. Toxicity Testing of Flowers of Neem Tree (*Azadirachta indica* A. Juss). *Thai Journal of Veterinary Medicine* 40, 47–55.

- Lal, N., Sahu, N., Shirale, A.O., Gurav, P., Rani, K., Meena, B.P., Diwan, G., Biswas, A.K., 2023. Plant Secondary Metabolites and Their Impact on Human Health. pp. 295–321. https://doi.org/10.1007/978-3-031-35147-1_15
- Lavecchia, T., Rea, G., Antonacci, A., Giardi, M.T., 2013. Healthy and Adverse Effects of Plant-Derived Functional Metabolites: The Need of Revealing their Content and Bioactivity in a Complex Food Matrix. *Critical Reviews in Food Science and Nutrition* 53, 198–213. <https://doi.org/10.1080/10408398.2010.520829>
- Lepidi, H., Durack, D.T., Raoult, D., 2002. Diagnostic Methods: Current Best Practices and Guidelines for Histologic Evaluation in Infectives Endocarditis. *Infectious Disease Clinical of North America* 16, 339–361. [https://doi.org/10.1016/S0891-5520\(02\)00005-3](https://doi.org/10.1016/S0891-5520(02)00005-3)
- Li, H.-J., Shen, H.-R., Shao, G.-F., Shi, B.-M., 2017. Tannins from Pomegranate Seeds Ameliorate Renal Injury in streptozotocin-induced Diabetic Rat through the activation of microRNA-495 via Regulating SMAD7, *International Journal of Clinical and Experimental Medicine*.
- Li, Y.X., Lu, Y.P., Tang, D., Hu, B., Zhang, Z.Y., Wu, H.W., Fan, L.J., Cai, K.W., Tang, C., Zhang, Y.Q., Hong, L., Dong, J. jing, Guan, B. zhang, Yin, L.H., Dai, Y., Bai, W. bin, Zheng, Z.H., Zhu, T., 2022. Anthocyanin Improves Kidney Function in Diabetic Kidney Disease by Regulating Amino Acid Metabolism. *Journal of Translational Medicine* 20. <https://doi.org/10.1186/s12967-022-03717-9>
- Li, Z., Zhang, Z., Ren, Y., Wang, Y., Fang, J., Yue, H., Ma, S., Guan, F., 2021. Aging and Age-related Diseases: from Mechanisms to Therapeutic Strategies. *Biogerontology*. <https://doi.org/10.1007/s10522-021-09910-5>
- Lieberman, M., Peet, A., 2018. *Basic Medical Biochemistry: A Clinical Approach*, 5th ed. Wolters Kluwer, Philadelphia.
- Liga, S., Paul, C., Péter, F., 2023. Flavonoids: Overview of Biosynthesis, Biological Activity, and Current Extraction Techniques. *Plants*. <https://doi.org/10.3390/plants12142732>
- Liguori, I., Russo, G., Aran, L., Bulli, G., Curcio, F., Della-Morte, D., Gargiulo, G., Testa, G., Cacciatore, F., Bonaduce, D., Abete, P., 2018. Sarcopenia: Assessment of disease burden and strategies to improve outcomes. *Clin Interv Aging*. <https://doi.org/10.2147/CIA.S149232>
- Lijon, M.B., Meghla, N.S., Jahedi, E., Rahman, M.A., Hossain, I., 2017. Phytochemistry and Pharmacological Activities of *Clitoria ternatea*. *International Journal of Natural and Social Sciences* 4, 1–10.
- Lin, K., Deng, T., Qu, H., Ou, H., Huang, Q., Gao, B., Li, X., Wei, N., 2023. Gastric Protective Effect of *Alpinia officinarum* Flavonoids: Mediating

TLR4/NF- κ B and TRPV1 Signalling Pathways and Gastric Mucosal Healing. *Pharm Biol* 61, 50–60. <https://doi.org/10.1080/13880209.2022.2152058>

Liu, Yanfei, Weng, W., Gao, R., Liu, Yue, Monacelli, F., 2019. New Insights for Cellular and Molecular Mechanisms of Aging and Aging-Related Diseases: Herbal Medicine as Potential Therapeutic Approach. *Oxid Med Cell Longev*. <https://doi.org/10.1155/2019/4598167>

Lobo, V., Patil, A., Phatak, A., Chandra, N., 2010. Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacogn Rev*. <https://doi.org/10.4103/0973-7847.70902>

Luo, J., Mills, K., le Cessie, S., Noordam, R., van Heemst, D., 2020. Ageing, Age-related Diseases and Oxidative Stress: What to do next? *Ageing Res Rev*. <https://doi.org/10.1016/j.arr.2019.100982>

Majeed, S.F., Hamza, N.M., Obeid, A.K., 2023. Study of the Toxicological Effects of Flower of Hibiscus sabdariffa Aqueous Extract on Some Histological Parameters of the Kidneys in Albino Rat, in: *AIP Conf. Proc*. <https://doi.org/10.1063/5.0116050>

Mandal, M., Sarkar, M., Khan, A., Biswas, M., Masi, A., Rakwal, R., Agrawal, G.K., Srivastava, A., Sarkar, A., 2022. Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) in plants– maintenance of structural individuality and functional blend. *Advances in Redox Research* 5, 100039. <https://doi.org/10.1016/j.arres.2022.100039>

Manisha, Hasan, W., Rajak, R., Jat, D., 2017. Oxidative Stress and Antioksidan: An Overview. *IJARR* 2, 110–119.

Manzoor, F., Nisa, M.U., Hussain, H.A., Khan, M.K., Ahmad, R.S., Ahmad, N., Imran, M., Umbreen, H., 2021. Effect of Hydrolysable Tannin on Nutrient Intake Obesity and Other Associated Metabolic Risk Factors in Polycystic Rats. *Transl Med Commun* 6, 10. <https://doi.org/10.1186/s41231-021-00089-y>

Maroyi, A., 2023. Medicinal Uses of the Fabaceae Family in Zimbabwe: A Review. *Plants*. <https://doi.org/10.3390/plants12061255>

Martemucci, G., Costagliola, C., Mariano, M., D'andrea, L., Napolitano, P., D'Alessandro, A.G., 2022. Free Radical Properties, Source and Targets, Antioxidant Consumption and Health. *Oxygen* 2, 48–78. <https://doi.org/10.3390/oxygen2020006>

Mathur, S., Hoskins, C., 2017. Drug Development: Lessons from Nature. *Biomed Rep* 6, 612–614. <https://doi.org/10.3892/br.2017.909>

Matsui, H., Shimokawa, O., Kaneko, T., Nagano, Y., Rai, K., Hyodo, I., 2011. The Pathophysiology of Nonsteroidal Antiinflammatory Drug (NSAID)

- Induced Mucosal Injuries in Stomach and Small Intestine. *J. Clin. Biochem. Nutr* 48, 107–111. <https://doi.org/10.3164/jcbn.10079>
- Maynard, R.L., Downes, N., 2019. *Anatomy and Histology of the Laboratory Rat in Toxicology and Biomedical Research*. Academic Press, United Kingdom.
- McInnes, E., 2017. *Pathology for Toxicologists: Principles and Practice of Laboratory Animal Pathology for Study Personnel*. John Wiley & Sons Ltd., United Kingdom.
- Melzig, M.F., Bader, G., Loose, R. 2001. Investigations of the Mechanism of Membrane Activity of Selected Triterpenoid Saponins. *Planta Med* 67. <https://doi.org/10.1055/s-2001-10632>
- Merry, T.L., Ristow, M., 2016. Do Antioxidant Supplements Interfere with Skeletal Muscle Adaptation to Exercise Training? *Journal of Physiology* 594, 5135–5147. <https://doi.org/10.1113/JP270654>
- Moore, K.L., Dalley, A.F., Agur, A.M.R., 2013. *Clinically Oriented Anatomy*, 7th ed. Lippincott Williams & Wilkins, Philadelphia.
- Morris, J.B., 2009. Characterization of Butterfly Pea (*Clitoria ternatea* L.) Accessions for Morphology, Phenology, Reproduction and Potential Nutraceutical, Pharmaceutical Trait Utilization. *Genet Resour Crop Evol* 56, 421–427. <https://doi.org/10.1007/s10722-008-9376-0>
- Motamedi, F., Nematbakhsh, M., Monajemi, R., Pezeshki, Z., Talebi, A., Zolfaghari, B., Mansoori, A., Saberi, S., Dehghani, A., Ashrafi, F., 2014. Effect of Pomegranate Flower Extract on Cisplatin-induced Nephrotoxicity in Rats. *J Nephropathol* 3, 133–8. <https://doi.org/10.12860/jnp.2014.26>
- Mothibe, M., Sibanda, M., 2019. African Traditional Medicine: South African Perspective, in: *Traditional and Complementary Medicine*. IntechOpen. <https://doi.org/10.5772/intechopen.83790>
- Naik, P., 2017. *Essential of Biochemistry*, Second Edition. ed. Jaypee Brothers Medical Publisher (P) Ltd., New Delhi.
- Nair, V., Bang, W.Y., Schreckinger, E., Andarwulan, N., Cisneros-Zevallos, L., 2015. Protective Role of Ternatin Anthocyanins and Quercetin Glycosides from Butterfly Pea (*Clitoria ternatea* Leguminosae) Blue Flower Petals against Lipopolysaccharide (LPS)-Induced Inflammation in Macrophage Cells. *J Agric Food Chem* 63, 6355–6365. <https://doi.org/10.1021/acs.jafc.5b00928>
- Nikijuluw, C., Andarwulan, N., 2013. *Color Characteristic of Butterfly Pea (*Clitoria ternatea* L.) Anthocyanin Extracts and Brilliant Blue*. Bogor Agriculture University, Bogor.

- Nithianantham, K., Ping, K.Y., Latha, L.Y., Jothy, S.L., Darah, I., Chen, Y., Chew, A.-L., Sasidharan, S., 2013. Evaluation of Hepatoprotective Effect of Methanolic Extract of *Clitoria ternatea* (Linn.) Flower Against Acetaminophen-induced Liver Damage. *Asian Pac J Trop Dis* 3, 314–319. [https://doi.org/10.1016/S2222-1808\(13\)60075-4](https://doi.org/10.1016/S2222-1808(13)60075-4)
- Nor, A.M., Azmi, N.A., Noordin, L., Bakar, A., Nizam, W.A., Ahmad, W., 2019. Aqueous Extract of *Etlingera elatior* Flower Improved Blood Glucose Control, Kidney Function and Histology of Streptozotocin-Induced Diabetic Rat. *J Sustain Sci Manag* 14, 80–91.
- OECD, 2018. Test No. 452: Chronic Toxicity Studies [WWW Document]. URL https://read.oecd-ilibrary.org/environment/test-no-452-chronic-toxicity-studies_9789264071209-en#page1 (accessed 10.1.23).
- OECD, 2001. Test No. 423: Acute Oral Toxicity - Acute Toxic Class Method [WWW Document]. URL https://read.oecd-ilibrary.org/environment/test-no-423-acute-oral-toxicity-acute-toxic-class-method_9789264071001-en#page1 (accessed 10.1.23).
- Oguis, G.K., Gilding, E.K., Jackson, M.A., Craik, D.J., 2019. Butterfly Pea (*Clitoria ternatea*), a Cyclotide-Bearing Plant with Applications in Agriculture and Medicine. *Front Plant Sci.* <https://doi.org/10.3389/fpls.2019.00645>
- Olaya, M.D.P., Lozano, M.C., Botero, L., Rincón, J., Guerrero, M.F., 2010. Evaluation of the Acute and Subchronic Oral Toxicity of Ethanol Extract from *Valeriana pavonii* Species in Wistar rats*. *Colombia Media* 41, 256–266.
- Omodei, D., Fontana, L., 2011. Calorie Restriction and Prevention of Age-associated Chronic Disease. *FEBS Lett.* <https://doi.org/10.1016/j.febslet.2011.03.015>
- Ovaditya, S.Z., Brilliantika, S.P., Chodidjah, Sumarawati, T., 2022. The effect of *Curcuma longa* on Fasting Blood Glucose, MMP-9 and IFN- γ in Diabetes Mellitus: an Experimental Study. *Bali Medical Journal* 11, 1996–2002. <https://doi.org/10.15562/bmj.v11i3.3648>
- Pagana, K.D., Pagana, T.J., 2010. *Mosby's Manual of Diagnostic and Laboratory Tests*, 4th ed. ed. Mosby Elsevier, Philadelphia.
- Panche, A.N., Diwan, A.D., Chandra, S.R., 2016. Flavonoids: An Overview. *J Nutr Sci.* <https://doi.org/10.1017/jns.2016.41>
- Parker, G.A., Picut, C.A., 2016. *Atlas of Histology of the Juvenile Rat*. Academic Publisher, London.

- Pebiansyah, A., Rahayuningsih, N., Yeni Aprilia, A., Nuryadin Zain, D., 2022. Aktivitas Hepatoprotektif Ekstrak Etanol Bunga Telang (*Clitoria ternatea* L.) pada Tikus Putih yang Diinduksi Parasetamol. *Jurnal Ilmiah Manuntung* 8, 100–105.
- Peternej, T.-T., Coombes, J.S., 2021. Antioxidant Supplementation during Exercise Training Beneficial or Detrimental? *Sport Med* 41, 1043–1069.
- Pham-Huy, L.A., He, H., Pham-Huy, C., 2008. Free Radicals, Antioxidants in Disease and Health. *International Journal of Biomedical Science* 4, 89–96.
- Phaniendra, A., Jestadi, D.B., Periyasamy, L., 2015. Free Radicals: Properties, Sources, Targets, and Their Implication in Various Diseases. *Indian Journal of Clinical Biochemistry*. <https://doi.org/10.1007/s12291-014-0446-0>
- Pizzi, A., 2019. Tannins: Prospectives and Actual Industrial Applications. *Biomolecules* 9, 344. <https://doi.org/10.3390/biom9080344>
- Pole, A., Dimri, M., P. Dimri, G., 2016. Oxidative Stress, Cellular Senescence and Ageing. *AIMS Mol Sci* 3, 300–324. <https://doi.org/10.3934/molsci.2016.3.300>
- Purwanto, U.M.S., Aprilia, K., Sulistiyani, 2022. Antioxidant Activity of Telang (*Clitoria ternatea* L.) Extract in Inhibiting Lipid Peroxidation. *Current Biochemistry* 9, 26–37.
- Radi, Z.A., 2019. Kidney Pathophysiology, Toxicology, and Drug-Induced Injury in Drug Development. *Int J Toxicol* 38, 215–227. <https://doi.org/10.1177/1091581819831701>
- Rahmatudina, F., Harjanti, R., Widyasti, J.H. 2023. Uji Toksisitas Subkronis Ekstrak Etanol Daun Mengkudu (*Morinda citrifolia* L.) dengan Penetapan Kadar Kreatinin dan BUN Tikus Putih. *As-Syifaa Jurnal Farmasi* 15, 112–119.
- Rai, S.S., Banik, A., Singh, A., Singh, M., 2015. Evaluation of Anti-Ulcer Activity of Aqueous and Ethanolic Extract of Whole Plant of *Clitoria ternatea* in Albino Wistar Rats. *International Journal of Pharmaceutical Sciences and Drug Research* 7, 33–39.
- Raihan, Gabena, I.D., 2022. Uji Sitotoksitas Ekstrak Etanol Bunga Telang (*Clitoria ternatea* L.) Dengan Metode Brine Shrimp Lethality Test (BSLT). *Journal of Health and Medical Science* 1, 187–202.
- Ramirez, R.O., Roa, C.C., 2003. The Gastroprotective Effect of Tannins Extracted from Duhat (*Syzygium cumini* Skeels) Bark on HCl/Ethanol induced Gastric Mucosal Injury in Sprague-Dawley Rats. *Clin Hemorheol Microcirc* 29, 253–61.

- Ranjitha, D., Sudha, K., 2015. Alkaloids in Foods. *IJPCBS* 5, 896–906.
- Rawdkuen, S., Faseha, A., Benjakul, S., Kaewprachu, P., 2020. Application of Anthocyanin as a Color Indicator in Gelatin Films. *Food Biosci* 36. <https://doi.org/10.1016/j.fbio.2020.100603>
- Remi-Martin, L., Awad, P., Campisi, J., Desprez, P.Y., 2012. Epithelial-Mesenchymal Transition Induced by Senescent Fibroblasts. *Cancer Microenvironment*. <https://doi.org/10.1007/s12307-011-0069-4>
- Roopashree, K.M., Naik, D., 2019. Advanced method of secondary metabolite extraction and quality analysis. Article in *International Journal of Pharmacognosy and Phytochemical Research* 8, 1829–1842.
- Roy, A., 2017. A Review on the Alkaloids an Important Therapeutic Compound from Plants. *International Journal of Plant Biotechnology* 3.
- Rui, Y., Li, S., Luan, F., Li, D., Liu, R., Zeng, N., 2022. Several Alkaloids in Chinese Herbal Medicine Exert Protection in Acute Kidney Injury: Focus on Mechanism and Target Analysis. *Oxid Med Cell Longev* 2022, 1–16. <https://doi.org/10.1155/2022/2427802>
- Rusu, M.E., Fizeşan, I., Vlase, L., Popa, D.S., 2022. Antioxidants in Age-Related Diseases and Anti-Aging Strategies. *Antioxidants*. <https://doi.org/10.3390/antiox11101868>
- Sadeghi, F., Nematbakhsh, M., Noori-Diziche, A., Esbarghi-Jazi, F., Talebi, A., Nasri, H., Mansouri, A., Dehghani, A., Saberi, S., Shirdavan, S., Ashrafi, F., 2015. Protective Effect of Pomegranate Flower Extract Against Gentamicin-induced Renal Toxicity in Male Rats. *J Renal Prev* 4, 45–50. <https://doi.org/10.12861/jrip.2015.10>
- Saito, N., Abe, K., Honda, T., Timberlake, C.F., Bridle, P., 1985. Acylated Delphinidin Glucosides and Flavonols from *Clitoria ternatea*. *Phytochemistry* 24, 1583–1586.
- Santos-Buelga, C., Mateus, N., De Freitas, V., 2014. Anthocyanins. *Plant Pigments and Beyond*. *J Agric Food Chem* 62, 6879–6884. <https://doi.org/10.1021/jf501950s>
- Sari, F., Nurkhasanah, Saiful Bachri, M., 2016. Acute Toxicity Test of Rosella (*Hibiscus sabdariffa* L.) Calyx Ethanolic Extract on Sprague Dawley Rats. *Traditional Medicine Journal* 21, 12–18.
- Sarma, A.S., Mallick, A.R., Ghosh, A.K., 2010. Free Radicals and Their Role in Different Clinical Conditions: An Overview. *International Journal of Pharma Sciences and Research (IJPSR)* 1, 185–192.

- Schelling, J.R., 2016. Tubular Atrophy in the Pathogenesis of Chronic Kidney Disease Progression. *Pediatric nephrology* 31, 693–706. <https://doi.org/10.1007/s00467-015-3169-4>
- Sharifi-Rad, M., Anil Kumar, N. V., Zucca, P., Varoni, E.M., Dini, L., Panzarini, E., Rajkovic, J., Tsouh Fokou, P.V., Azzini, E., Peluso, I., Prakash Mishra, A., Nigam, M., El Rayess, Y., Beyrouthy, M. El, Polito, L., Iriti, M., Martins, N., Martorell, M., Docea, A.O., Setzer, W.N., Calina, D., Cho, W.C., Sharifi-Rad, J., 2020. Lifestyle, Oxidative Stress, and Antioxidants: Back and Forth in the Pathophysiology of Chronic Diseases. *Front Physiol.* <https://doi.org/10.3389/fphys.2020.00694>
- Sharp, P., Villano, J., 2012. *The Laboratory Rat*, Second Edition. ed. CRC Press, Boca Raton.
- Shi, J., Arunasalam, K., Yeung, D., Kakuda, Y., Mittal, G., Jiang, Y., 2004. Saponins from Edible Legumes: Chemistry, Processing, and Health Benefits. *J Med Food* 7, 67–78. <https://doi.org/10.1089/109662004322984734>
- Shi, Z., Long, X., Li, Y., Jin, J., Li, J., Yuan, C., Jin, R., 2022. Protective Effect of Tea Saponins on Alcohol-Induced Gastric Mucosal Injury in Mice. *ACS Omega*. <https://doi.org/10.1021/acsomega.2c05880>
- Simangunsong, E.M.V., Febriani, Y., Saputri, M., Arisa, D., Afifah, G.Z., 2023. Effectiveness of Butterfly Pea Ethanol Extract on Decreasing Blood Glucose Levels of Male Mice. *Journal of Health Science and Research* 5, 707–721.
- Singh, N., Singh, P., Shrivastva, S., Mishra, S.K., Lakshmi, V., Sharma, R., Palit, G., 2012. Gastroprotective Effect of Anti-cancer Compound Rohitukine: Possible Role of Gastrin Antagonism and H + K +-ATPase Inhibition. *Naunyn Schmiedebergs Arch Pharmacol* 385, 277–286. <https://doi.org/10.1007/s00210-011-0711-1>
- Sparg, S.G., Light, M.E., Van Staden, J., 2004. Biological Activities and Distribution of Plant Saponins. *J Ethnopharmacol.* <https://doi.org/10.1016/j.jep.2004.05.016>
- Suckow, M.A., Hankenson, F.C., Wilson, R.P., Foley, P.L., 2020. *The Laboratory Rat*. Academic Press, United States.
- Swathi, K.P., Jayaram, S., Sugumar, D., Rymbai, E., 2021. Evaluation of anti-inflammatory and anti-arthritic property of ethanolic extract of *Clitoria ternatea*. *Chin Herb Med* 13, 243–249. <https://doi.org/10.1016/j.chmed.2020.11.004>
- Szczurek, A., 2021. Perspectives on Tannins. *Biomolecules* 11, 442. <https://doi.org/10.3390/biom11030442>

- Tan, B.L., Norhaizan, M.E., Liew, W.P.P., Rahman, H.S., 2018. Antioxidant and Oxidative Stress: A Mutual Interplay in Age-related Diseases. *Front Pharmacol.* <https://doi.org/10.3389/fphar.2018.01162>
- Tang, Y., Gao, R., Lee, H.H., Xu, Z., Savoie, B. V., Bao, S., Huo, Y., Fogo, A.B., Harris, R., de Caestecker, M.P., Spraggins, J.M., Landman, B.A., 2021. Renal Cortex, Medulla and Pelviccaliceal System Segmentation on Arterial Phase CT Images with Random Patch-based Networks, in: Landman, B.A., Išgum, I. (Eds.), *Medical Imaging 2021: Image Processing*. SPIE, p. 42. <https://doi.org/10.1117/12.2581101>
- Teoh, E.S., 2016. Secondary Metabolites of Plants, in: *Medicinal Orchids of Asia*. Springer International Publishing, Cham, pp. 59–73. https://doi.org/10.1007/978-3-319-24274-3_5
- Thongprayoon, C., Cheungpasitporn, W., Kashani, K., 2016. Serum Creatinine Level, a Surrogate of Muscle Mass, Predicts Mortality in Critically Ill Patients. *J Thorac Dis* 8, 305–311. <https://doi.org/10.21037/jtd.2016.03.62>
- Toma, W., Trigo, J.R., De Paula, A.C.B., Brito, A.R.M.S., 2004. Preventive Activity of Pyrrolizidine Alkaloids from *Senecio brasiliensis* (Asteraceae) on Gastric and Duodenal Induced Ulcer on Mice and Rats. *J Ethnopharmacol* 95, 345–351. <https://doi.org/10.1016/j.jep.2004.08.017>
- Tong, Z., He, W., Fan, X., Guo, A., 2022a. Biological Function of Plant Tannin and Its Application in Animal Health. *Front Vet Sci.* <https://doi.org/10.3389/fvets.2021.803657>
- Tong, Z., He, W., Fan, X., Guo, A., 2022b. Biological Function of Plant Tannin and Its Application in Animal Health. *Front Vet Sci.* <https://doi.org/10.3389/fvets.2021.803657>
- Tortora, G.J., Derrickson, B., 2011. *Principles of Anatomy & Physiology*, 13th Edition. ed. John Wiley & Sons, Inc., United State.
- Treuting, P.M., Dintzis, S.M., Montine, K.S., 2018. *Comparative Anatomy and Histology A Mouse, Rat, and Human Atlas*, Second Edition. ed. Academic Press, United States.
- Twaij, B.M., Hasan, Md.N., 2022. Bioactive Secondary Metabolites from Plant Sources: Types, Synthesis, and Their Therapeutic Uses. *International Journal of Plant Biology* 13, 4–14. <https://doi.org/10.3390/ijpb13010003>
- Ukoha, U.U., Mbagwu, S.I., Ndukwe, G.U., Obiagboso, C., 2015. Histological and Biochemical Evaluation of the Kidney following Chronic Consumption of (*Hibiscus sabdariffa*). *Adv Biol* 2015, 1–5. <https://doi.org/10.1155/2015/486510>

- Umashankar, D.D., 2020. Plant Secondary Metabolites as Regenerative Medicine. *The Journal of Phytopharmacology* 9, 270–273. <https://doi.org/10.31254/phyto.2020.9410>
- University of Iowa, I., 2024. Anesthesia (Guidline) [WWW Document]. URL <https://animal.research.uiowa.edu/iacuc-guidelines-anesthesia> (accessed 4.16.24).
- Valko, M., Rhodes, C.J., Moncol, J., Izakovic, M., Mazur, M., 2006. Free Radicals, Metals and Antioxidants in Oxidative Stress-induced Cancer. *Chem Biol Interact* 160, 1–40. <https://doi.org/10.1016/j.cbi.2005.12.009>
- Vane, J.R., 1971. Inhibition of Prostaglandin Synthesis as a Mechanism of Action for Aspirin-like Drugs. *Nat New Biol* 231, 232–235. <https://doi.org/10.1038/newbio231232a0>
- Vargas, F., Romecín, P., García-Guillén, A.I., Wangesteen, R., Vargas-Tendero, P., Paredes, M.D., Atucha, N.M., García-Estañ, J., 2018. Flavonoids in Kidney Health and Disease. *Front Physiol.* <https://doi.org/10.3389/fphys.2018.00394>
- Vona, R., Pallotta, L., Cappelletti, M., Severi, C., Matarrese, P., 2021. The Impact of Oxidative Stress in Human Pathology: Focus on Gastrointestinal Disorders. *Antioxidants*. <https://doi.org/10.3390/antiox10020201>
- Wallace, J.L., 2008. Prostaglandins, NSAIDs, and Gastric Mucosal Protection: Why Doesn't the Stomach Digest Itself? *Physiol Rev* 88, 1547–1565. <https://doi.org/10.1152/physrev.00004.2008>
- Wei, J., Wu, H., Zhang, H., Li, F., Chen, S., Hou, B., Shi, Y., Zhao, L., Duan, H., 2018. Anthocyanins Inhibit High Glucose-induced Renal Tubular Cell Apoptosis Caused by Oxidative Stress in db/db Mice. *Int J Mol Med* 41, 1608–1618. <https://doi.org/10.3892/ijmm.2018.3378>
- Wen, L., Xia, N., Tang, P., Hong, Y., Wang, Z., Liu, Yajie, Liu, Yanju, Liu, J., Li, X., 2015. The Gastrointestinal Irritation of Polygala Saponins and its Potential Mechanism In Vitro and In Vivo. *Biomed Res Int* 2015. <https://doi.org/10.1155/2015/918048>
- WHO, 2022. WHO Establishes the Global Centre for Traditional Medicine in India [WWW Document].
- Widowati, W., Darsono, L., Lucianus, J., Setiabudi, E., Susang Obeng, S., Stefani, S., Wahyudianingsih, R., Reynaldo Tandibua, K., Gunawan, R., Riski Wijayanti, C., Novianto, A., Sari Widya Kusuma, H., Rizal, R., 2023. Butterfly pea flower (*Clitoria ternatea* L.) extract displayed antidiabetic effect through antioxidant, anti-inflammatory, lower hepatic GSK-3 β , and pancreatic glycogen on Diabetes Mellitus and dyslipidemia rat. *J King Saud Univ Sci* 35. <https://doi.org/10.1016/j.jksus.2023.102579>

- Widyastuti, D.A., Ristianti, M.A., Sari, I.M., 2018. Efek Subkronis Natrium Nitrit terhadap Struktur Mikroanatomis Ginjal Tikus Putih (*Rattus norvegicus*) Galur Wistar, Jurnal Gizi KH, Desember.
- Yang, W.B., Wang, P., 2014. Research Progress in Chemical Components, Pharmacological Effectiveness, and Toxicity of Aconitine. *Lishizhen Medicine and Materia Medica Research* 25, 427–429.
- Yoshikawa, T., Naito, Y., 2002. What Is Oxidative Stress?, *JMAJ*.
- Yulina, I.K., 2017. Back To Nature: Kemajuan atau Kemunduran. *Mangifera Edu* 2, 20–31.
- Yuniarti, Rousdy, D.W., Rahmawati, 2015. Uji Antiinflamasi Infusa Bunga Seroja (*Nelumbo nucifera* Gaertn) pada Struktur Mikroanatomis Ginjal Mencit (*Mus musculus*) yang Mengalami Stres. *Protobiont* 4, 242–247.
- Zain, D.N., Pebiansyah, A., Aprilia, Y., 2021. Aktivitas Nefroprotektif Ekstrak Etanol Bunga Telang (*Clitoria ternatea* L.) terhadap Tikus yang Diinduksi Paracetamol. *Pharmacoscript* 4, 173–180.
- Zhang, W., Lian, Y., Li, Q., Sun, L., Chen, R., Lai, X., Lai, Z., Yuan, E., Sun, S., 2020. Preventative and Therapeutic Potential of Flavonoids in Peptic Ulcers. *Molecules*. <https://doi.org/10.3390/molecules25204626>
- Zhao, Y., Wang, M., Xu, B., 2021. A Comprehensive Review on Secondary Metabolites and Health-promoting Effects of Edible Lichen. *J Funct Foods* 80, 104283. <https://doi.org/10.1016/j.jff.2020.104283>
- Zhou, Y., Tong, X., Ren, S., Wang, X., Chen, J., Mu, Y., Sun, M., Chen, G., Zhang, H., Liu, P., 2016. Synergistic Anti-liver Fibrosis Actions of Total Astragalus Saponins and Glycyrrhizic Acid via TGF- β 1/Smads Signaling Pathway Modulation. *J Ethnopharmacol* 190, 83–90. <https://doi.org/10.1016/j.jep.2016.06.011>