

DAFTAR PUSTAKA

- Aggarwal, B. B., & Ichikawa, H. (2005). Molecular targets and anticancer potential of indole-3-carbinol and its derivatives. *Cell Cycle*, 4(9), 1201–1215. <https://doi.org/10.4161/cc.4.9.1993>.
- Agerbirk, N., De Vos, M., Kim, J. H., & Jander, G. (2009). Indole glucosinolate breakdown and its biological effects. *Phytochemistry Reviews*, 8(1), 101–120. <https://link.springer.com/article/10.1007/s11101-008-9098-0>.
- Ågmo, A. (2024). Androgen receptors and sociosexual behaviors in mammals: The limits of generalization. *Neuroscience and Biobehavioral Reviews*, 157, Article 105530. <https://doi.org/10.1016/j.neubiorev.2023.105530>.
- Alarid, E. T. (2006). Lives and times of nuclear receptors. *Molecular Endocrinology*, 20(9), 1972–1981. <https://doi.org/10.1210/me.2005-0481>.
- Al-Qarawi, A. A. (2005). Infertility in the dromedary bull: A review of causes, relations and implications. *Animal Reproduction Science*, 87(1–2), 73–92. <https://doi.org/10.1016/j.anireprosci.2004.11.003>.
- Amalia, R., Airin, C. M., Astuti, P., & Budiyo, A. (2024). Indole-3-Carbinol of broccoli powder can decrease estrogen production in male rats. *Journal of Animal Health and Production*, 12(4), 258–653. <http://dx.doi.org/10.17582/journal.jahp/2024/12.4.647.653>.
- Amalia, R., Ohama, T., Parhar, I. S., Airin, C. M., Sato, H., Budiyo, A., & Astuti, P. (2025). Potential of Indole-3-Carbinol compounds from broccoli (*Brassica oleracea* var. *italica*) as natural aromatase blockers: *In silico* prediction and *in vivo* studies. *Open Veterinary Journal*, 15(4), 1663–1672. <http://doi.org/10.5455/OVJ.2025.v15.i4.18>.
- Amarakoon, D., Lee, W. J., Tamia, G., & Lee, S. H. (2023). Indole-3-Carbinol: Occurrence, health-beneficial properties, and cellular/molecular mechanisms. *Annual Review of Food Science and Technology*, 14, 347–366. <https://doi.org/10.1146/annurev-food-060721-025531>.
- Anderton, M. J., Manson, M. M., Verschoyle, R., Gescher, A., Steward, W. P., Williams, M. L., et al. (2004). Physiological modeling of formulated and crystalline 3,3'-diindolylmethane pharmacokinetics following oral administration in mice. *Drug Metabolism and Disposition*, 32(6), 632–638.
- Angelino, D., Moreno, D. A., & Williams, D. E. (2021). Indoles derived from glucobrassicin: Cancer chemoprevention by indole-3-carbinol and 3,3'-diindolylmethane. *Frontiers in Nutrition*, 8, 734334. <https://doi.org/10.3389/fnut.2021.734334>.

- Armagan, A., Kim, N. N., Goldstein, I., & Traish, A. M. (2006). Dose-response relationship between testosterone and erectile function: Evidence for the existence of a critical threshold. *Journal of Andrology*, 27(4), 517–526.
- Ashok, B. T., Chen, Y., Liu, X., Bradlow, H. L., Mittelman, A., & Tiwari, R. K. (2001). Abrogation of estrogen-mediated cellular and biochemical effects by indole-3-carbinol. *Nutrition and Cancer*, 41(1), 180–187.
- Askew, E. B., Gampe, R. T. Jr., Stanley, T. B., Faggart, J. L., & Wilson, E. M. (2007). Modulation of androgen receptor activation function 2 by testosterone and dihydrotestosterone. *Journal of Biological Chemistry*, 282(35), 25801–25816.
- Auvray, P., Nativelle, C., Bureau, R., Dallemagne, P., S  ralini, G. E., & Sourdain, P. (2002). Study of substrate specificity of human aromatase by site directed mutagenesis. *European Journal of Biochemistry*, 269(5), 1393–1405.
- Azcoitia, I., Mendez, P., & Garcia-Segura, L. M. (2021). Aromatase in the human brain. *Androgens: Clinical Research and Therapeutics*, 2(1), 189–202. <https://doi.org/10.1089/andro.2021.0007>.
- Balam, F. H., Ahmadi, Z. S., & Ghorbani, A. (2020). Inhibitory effect of chrysin on estrogen biosynthesis by suppression of enzyme aromatase (CYP19): A systematic review. *Heliyon*, 6(8), e03557. <https://doi.org/10.1016/j.heliyon.2020.e03557>.
- Baldwin, W. S., & Leblanc, G. A. (1992). The anti-carcinogenic plant compound indole-3-carbinol differentially modulates P450-mediated steroid hydroxylase activities in mice. *Chemico-Biological Interactions*, 83(2), 155–169. [https://doi.org/10.1016/0009-2797\(92\)90052-9](https://doi.org/10.1016/0009-2797(92)90052-9).
- Banerjee, S., Kong, D., Wang, Z., Bao, B., Hillman, G. G., & Sarkar, F. H. (2011). Attenuation of multi-targeted proliferation-linked signaling by 3,3'-diindolylmethane (DIM): From bench to clinic. *Mutation Research - Reviews in Mutation Research*, 728(1–2), 47–66. <https://doi.org/10.1016/j.mrrev.2011.06.001>.
- Barton, B. E., Herrera, G. G., Ananthakumara, P., Rock, J. K., Willie, A. M., Harris, E. A., Takemaru, K.-I., & Winuthayanon, W. (2020). Roles of steroid hormones in oviductal function. *Reproduction*, 159(5), 471–482. <https://doi.org/10.1530/REP-19-0189>.
- Bevan, C., & Parker, M. (1999). The role of coactivators in steroid hormone action. *Experimental Cell Research*, 253(2), 349–356.
- Bhatnagar, A. S., H  usler, A., & Schieweck, K. (1990). Inhibition of aromatase in vitro and in vivo by aromatase inhibitors. *Journal of Enzyme Inhibition and*

Medicinal Chemistry, 4(2), 179–186.
<https://doi.org/10.3109/14756369009040740>.

Bjeldanes, L. F., Kim, J.-Y., Grose, K. R., Bartholomew, J. C., & Bradfield, C. A. (1991). Aromatic hydrocarbon responsiveness-receptor agonists generated from indole-3-carbinol in vitro and in vivo: Comparisons with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Proceedings of the National Academy of Sciences of the United States of America*, 88(3), 954–958.
<https://doi.org/10.1073/pnas.88.3.954>.

Boonyaratanakornkit, V., & Edwards, D. P. (2007). *Receptor mechanisms mediating non-genomic actions of sex steroids*. Thieme Medical Publishers, Inc.

Bouma, J., & Nagler, J. J. (2001). Estrogen receptor-alpha protein localization in the testis of the rainbow trout (*Oncorhynchus mykiss*) during different stages of the reproductive cycle. *Biology of Reproduction*, 65(1), 60–65.
<https://doi.org/10.1095/biolreprod65.1.60>.

Bourguiba, S., Chater, S., Delalande, C., Benahmed, M., & Carreau, S. (2003). Regulation of aromatase gene expression in purified germ cells of adult male rats: Effects of transforming growth factor beta, tumor necrosis factor alpha, and cyclic adenosine 3',5'-monophosphate. *Biology of Reproduction*, 69(2), 592–601.
<https://doi.org/10.1095/biolreprod.102.013961>.

Bradlow, H. L., & Zeligs, M. A. (2010). Diindolylmethane (DIM) spontaneously forms from indole-3-carbinol (I3C) during cell culture experiments. *In Vivo*, 24(3), 387–391.

Brown, P. D., Tokuhisa, J. G., Reichelt, M., & Gershenzon, J. (2003). Variation of glucosinolate accumulation among different organs and developmental stages of *Arabidopsis thaliana*. *Phytochemistry*, 62(3), 471–481.
[https://doi.org/10.1016/s0031-9422\(02\)00549-6](https://doi.org/10.1016/s0031-9422(02)00549-6).

Burow, M., Losansky, A., Müller, R., Plock, A., Kliebenstein, D. J., & Wittstock, U. (2009). The genetic basis of constitutive and herbivore-induced ESP-independent nitrile formation in *Arabidopsis*. *Plant Physiology*, 149(1), 561–574. <https://doi.org/10.1104/pp.108.130732>.

Cardoso, R. C., Alves, B. R. C., Prezotto, L. D., Thorson, J. F., Tedeschi, L. O., Keisler, D. H., Amstalden, M., Williams, G. L. (2014). Reciprocal changes in leptin and NPY during nutritional acceleration of puberty in heifers. *Journal of Endocrinology*, 223(3), 289–298.

- Carreau, S., Lambard, S., Delalande, C., Denis-Galeraud, I., Bilinska, B., Bourguiba, S. (2003). Aromatase expression and role of estrogens in male gonad: A review. *Reproductive Biology and Endocrinology*, 1, 35. <https://doi.org/10.1186/1477-7827-1-35>.
- Cartea, M. E., Velasco, P., Obregón, S., Padilla, G., & de Haro, A. (2008). Seasonal variation in glucosinolate content in *Brassica oleracea* crops grown in northwestern Spain. *Phytochemistry*, 69(2), 403–410. <https://doi.org/10.1016/j.phytochem.2007.08.014>.
- Caruso, J. A., Campana, R., Wei, C., Su, C.-H., Hanks, A. M., Bornmann, W. G., et al. (2014). Indole-3-carbinol and its N-alkoxy derivatives preferentially target ER α -positive breast cancer cells. *Cell Cycle*, 13(16), 2587–2599. <https://doi.org/10.4161/cc.29791>.
- Centofanti, F., Alonzi, T., Latini, A., Spitalieri, P., Murdocca, M., Chen, X., Cui, W., Shang, Q., Goletti, D., Shi, Y., Duranti, A., Tomino, C., Biancolella, M., Sangiuolo, F., Capobianchi, M. R., Jain, S., Novelli, G., & Pandolfi, P. P. (2022). Indole-3-carbinol in vitro antiviral activity against SARS-CoV-2 virus and in vivo toxicity. *Cell Death Discovery*, 8(1), 49. <https://doi.org/10.1038/s41420-022-01280-2>.
- Chen, S. (2002). Modulation of aromatase activity and expression by environmental chemicals. *Frontiers in Bioscience*, 7, d99–d104.
- Chen, I., Safe, S., & Bjeldanes, L. (1996). Indole-3-carbinol and diindolylmethane as aryl hydrocarbon (Ah) receptor agonists and antagonists in T47D human breast cancer cells. *Biochemical Pharmacology*, 51(8), 1069–1076. [https://doi.org/10.1016/0006-2952\(96\)00173-0](https://doi.org/10.1016/0006-2952(96)00173-0).
- Chen, Y. H., Riby, J., Srivastava, P., Bartholomew, J., Denison, M., & Bjeldanes, L. (1995). Regulation of CYP1A1 by indolo[3,2-b]carbazole in murine hepatoma cells. *Journal of Biological Chemistry*, 270(38), 22548–22555. <https://doi.org/10.1074/jbc.270.38.22548>.
- Cheshenko, K., Pakdel, F., Segner, H., Kah, O., & Eggen, R. I. L. (2008). Interference of endocrine disrupting chemicals with aromatase CYP19 expression or activity, and consequences for reproduction of teleost fish. *General and Comparative Endocrinology*, 155(1), 31–62. <https://doi.org/10.1016/j.ygcen.2007.03.005>.
- Cooke, P. S., & Walker, W. H. (2022). Nonclassical androgen and estrogen signaling is essential for normal spermatogenesis. *Seminars in Cell & Developmental Biology*, 121, 71–81. <https://doi.org/10.1016/j.semcdb.2021.05.032>.

- Couse, J. F., & Korach, K. S. (1999). Estrogen receptor null mice: What have we learned and where will they lead us? *Endocrine Reviews*, 20(3), 358–417. <https://doi.org/10.1210/edrv.20.3.0370>.
- Cover, C. M., Hsieh, S. J., Tran, S. H., Hallden, G., Kim, G. S., Bjeldanes, L. F., & Firestone, G. L. (1998). Indole-3-carbinol inhibits the expression of cyclin-dependent kinase-6 and induces a G1 cell cycle arrest of human breast cancer cells independent of estrogen receptor signaling. *Journal of Biological Chemistry*, 273(7), 3838–3847. <https://doi.org/10.1074/jbc.273.7.3838>.
- Davey, R. A., & Grossmann, M. (2016). Androgen receptor structure, function and biology: From bench to bedside. *Clinical Biochemistry Reviews*, 37(1), 1–15.
- de Ronde, W., & de Jong, F. H. (2011). Aromatase inhibitors in men: Effects and therapeutic options. <https://doi.org/10.1186/1477-7827-9-93>.
- de Ronde, W., Hofman, A., Pols, H. A. P., & de Jong, F. H. (2005). A direct approach to the estimation of the origin of oestrogens and androgens in elderly men by comparison with hormone levels in postmenopausal women. *European Journal of Endocrinology*, 152(2), 261–268. <https://doi.org/10.1530/eje.1.01830>.
- de Ronde, W., van der Schouw, Y. T., Muller, M., Grobbee, D. E., Gooren, L. J. G., Pols, H. A. P., & de Jong, F. H. (2005). Associations of Sex-Hormone-Binding Globulin (SHBG) with Non-SHBG-Bound levels of testosterone and estradiol in independently living men. *Journal of Clinical Endocrinology and Metabolism*, 90(1), 157–162. <https://doi.org/10.1210/jc.2004-0422>.
- de Magalhães, F. F., de Souza, M. B., Silva, H. V. R., Pinto, J. N., Sousa, C. V. S., & Da Silva, L. D. M. (2014). Comparison of serum testosterone concentrations between fertile and infertile dogs. *Acta Veterinaria Brasilica*, 8(SUPPL. 2), 122–123.
- Dias, J. C., De Andrade, V. J., Emerick, L. L., Martins, J. A. M., Filho, V. R. V. (2014). Peripheral levels of total testosterone in Guzerat bulls. *Ciencia Animal Brasileira*, 15(1), 64–73.
- Diver, M. J. (2009). Laboratory measurement of testosterone. *Frontiers of Hormone Research*, 37, 21–31. <https://doi.org/10.1159/000175841>.
- Durdiakova, J., & Celec, P. (2016). Androgen regulation of neural circuit activity: Molecules and mechanisms. In D. W. Pfaff & M. Joëls (Eds.), *Hormones, brain and behavior* (3rd ed., Vol. 3, pp. 101–109).

- Eder, I. E., Culig, Z., Putz, T., Nessler-Menardi, C., Bartsch, G., & Klocker, H. (2001). Molecular biology of the androgen receptor: From molecular understanding to the clinic. *European Urology*, 40(3), 241–251.
- Eissa, M. A., & Gohar, E. Y. (2023). Aromatase enzyme: Paving the way for exploring aromatization for cardio-renal protection. In *Biomedicine and Pharmacotherapy*, 168. Elsevier Masson s.r.l. <https://doi.org/10.1016/j.biopha.2023.115832>.
- Ellem, S. J., & Risbridger, G. P. (2010). Aromatase and regulating the estrogen:androgen ratio in the prostate gland. *The Journal of Steroid Biochemistry and Molecular Biology*, 118(4–5), 246–251. <https://doi.org/10.1016/j.jsbmb.2009.10.015>.
- Fahey, J. W., Zalcmann, A. T., & Talalay, P. (2001). The chemical diversity and distribution of glucosinolates and isothiocyanates among plants. *Phytochemistry*, 56(1), 5–51. [https://doi.org/10.1016/s0031-9422\(00\)00316-2](https://doi.org/10.1016/s0031-9422(00)00316-2).
- Fang, H., Luo, F., Li, P., Zhou, Q., Zhou, X., Wei, B., Cheng, S., Zhou, H., Ji, S. (2020). Potential of jasmonic acid (JA) in accelerating postharvest yellowing of broccoli by promoting its chlorophyll degradation. *Food Chemistry*, 309, 125737. <https://doi.org/10.1016/j.foodchem.2019.125737>.
- Fatnassi, M., Padalino, B., Monaco, D., Khorchani, T., Lacalandra, G. M., & Hammadi, M. (2014). Evaluation of sexual behavior of housed male camels (*Camelus dromedarius*) through female parades: Correlation with climatic parameters. *Tropical Animal Health and Production*, 46(2), 313–321. <https://doi.org/10.1007/s11250-013-0489-x>.
- Fernández-Pérez, L. (2023). Editorial: Sexual dimorphism and steroid hormone crosstalk, volume II. *Frontiers in Endocrinology*, 14, 1–2. <https://doi.org/10.3389/fendo.2023.1346433>.
- Firestone, G. L., & Sundar, S. N. (2009). Minireview: Modulation of hormone receptor signaling by dietary anticancer indoles. *Molecular Endocrinology*, 23(12), 1940–1947. <https://doi.org/10.1210/me.2009-0149>.
- Gamage, N., Barnett, A., Hempel, N., Duggleby, R.G., Windmill, K.F., Martin, J.L., McManus, M.E. (2006). Human sulfotransferases and their role in chemical metabolism. *Toxicological Sciences*, 90(1), 5–22.
- Gasmi, A., Gasmi Benahmed, A., Shanaida, M., Chirumbolo, S., Menzel, A., Anzar, W., Arshad, M., Cruz-Martins, N., Lysiuk, R., Beley, N., Oliinyk, P., Shanaida, V., Denys, A., Peana, M., & Bjørklund, G. (2024). Anticancer activity of broccoli, its organosulfur and polyphenolic compounds. *Critical*

- Reviews in Food Science and Nutrition, 64(22), 8054–8072.
<https://doi.org/10.1080/10408398.2023.2195493>.
- Gao, W., Bohl, C. E., & Dalton, J. T. (2005). Chemistry and structural biology of androgen receptor. Chemical Reviews, 105(9), 3352–3370.
<https://doi.org/10.1021/cr020456u>.
- Gerhauser, C. (2013). Epigenetic impact of dietary isothiocyanates in cancer chemoprevention. Current Opinion in Clinical Nutrition and Metabolic Care, 16(4), 405–410. <https://doi.org/10.1097/MCO.0b013e328362014e>.
- Giudice, D. M., & Gangestad, S. W. (2022). Hormone ratios suffer from striking lack of robustness to measurement error. Psychoneuroendocrinology, 142, 105802. <https://doi.org/10.1016/j.psyneuen.2022.105802>.
- Goldman, A. L., Bhasin, S., Wu, F. C. W., Krishna, M., Matsumoto, A. M., & Jasuja, R. (2017). A reappraisal of testosterone's binding in circulation: Physiological and clinical implications. Endocrine Reviews, 38(4), 302–324. <https://doi.org/10.1210/er.2017-00025>.
- Greenwald, P. (2004). Clinical trials in cancer prevention: current results and perspectives for the future. J. Nutr., 134, 3507S–3512S.
- Gregoriou, O., Bakas, P., Grigoriadis, C., Creatsa, M., Hassiakos, D., & Creatsas, G. (2012). Changes in hormonal profile and seminal parameters with use of aromatase inhibitors in management of infertile men with low testosterone to estradiol ratios. Fertility and Sterility, 98(1), 48–51. <https://doi.org/10.1016/j.fertnstert.2012.04.005>.
- Guan, Y., Hu, W., Xu, Y., Yang, X., Ji, Y., Feng, K., & Sarengaowa. (2021). Metabolomics and physiological analyses validate previous findings on the mechanism of response to wounding stress of different intensities in broccoli. Food Research International, 140. <https://doi.org/10.1016/j.foodres.2020.110058>.
- Gudiño, I., Casquete, R., Martín, A., Wu, Y., & Benito, M. J. (2024). Comprehensive analysis of bioactive compounds, functional properties, and applications of broccoli by-products. Foods, 13(23), 3918. <https://doi.org/10.3390/foods13233918>.
- Guyton, A. C., & Hall, J. E. (2015). Endocrinology and reproduction: Textbook of Medical Physiology. In J. E. Hall (Ed.), Saunders, Philadelphia, pp. 925–937.
- Guzelce, E.C., Galbiati, F., Goldman, A.L., Gattu, A.K., Basaria, S., & Bhasin, S. (2022). Accurate measurement of total and free testosterone levels for the

- diagnosis of androgen disorders. *Best Practice and Research: Clinical Endocrinology and Metabolism*, 36(4), 1-9.
<https://doi.org/10.1016/j.beem.2022.101683>.
- Hammond, G.L. (2016). Plasma steroid-binding proteins: Primary gatekeepers of steroid hormone action. *Journal of Endocrinology*, 230(1), 13-25.
<https://doi.org/10.1530/JOE-16-0070>.
- Handelsman, D.J. (2020). Androgen Receptor: Androgen Physiology, Pharmacology, Use and Misuse. In: Feingold, K.R., Anawalt, B., & Blackman, M.R. (Eds), *Endotext* [Internet]. South Dartmouth (MA).
<https://www.ncbi.nlm.nih.gov/books/NBK279000/>.
- Hang, L., Xia, Y., Liu, H.-Y., Guo, H., He, X.-Q., Liu, Y., Wu, D.-T., Mai, Y.-H., Li, H.-B., Zou, L., Gan, R.-Y. (2022). Nutritional values, beneficial effects, and food applications of broccoli (*Brassica oleracea* var. *italica* Plenck). *Trends in Food Science & Technology*, 119, 288-308.
<https://doi.org/10.1016/j.tifs.2021.12.015>.
- Harada, N., Sasano, H., Murakami, H., Ohkuma, T., Nagura, H., & Takagi, Y. (1999). Localized expression of aromatase in human vascular tissues. *Circ Res*, 84, 1285–1291. <https://doi.org/10.1161/01.RES.84.11.1285>.
- Hayes, F. J., Seminara, S. B., Decruz, S., Boepple, P. A., & Crowley, W. F. (2000). Aromatase inhibition in the human male reveals a hypothalamic site of estrogen feedback. *Journal of Clinical Endocrinology & Metabolism*, 85(9), 3027-3032. <https://academic.oup.com/jcem/article/85/9/3027/2660453>.
- He, B., Kemppainen, J. A., & Wilson, E. M. (2000). FXXLF and WXXLF sequences mediate the NH₂-terminal interaction with the ligand binding domain of the androgen receptor. *Journal of Biological Chemistry*, 275(30), 22986–22994.
- Hecker, M., Kim, W. J., Park, J. W., Murphy, M. B., Villeneuve, D., Coady, K. K., Jones, P. D., Solomon, K. R., Van Der Kraak, G., Carr, J. A., Smith, E. E., du Preez, L., Kendall, R. J., Giesy, J. P., & Syngenta Crop Protection Inc. (2005). Plasma concentrations of estradiol and testosterone, gonadal aromatase activity and ultrastructure of the testis in *Xenopus laevis* exposed to estradiol or atrazine. *Aquatic Toxicology*, 72(4), 383–396.
<https://doi.org/10.1016/j.aquatox.2005.01.008>.
- Ho, C.K.M., Stoddart, M., Walton, M., Anderson, R.A., & Beckett, G.J. (2006). Calculated free testosterone in men: Comparison of four equations and with free androgen index. *Annals of Clinical Biochemistry*, 43(5), 389-397.
<https://doi.org/10.1258/000456306778520115>.

- Hoai, B.N., Hoang, L., Cao, T.N., Pham, M.Q., & Jannini, E.A. (2023). Testosterone and aging male: A perspective from a developing country. *The Aging Male*, 26(1), 1-19. <https://doi.org/10.1080/13685538.2023.2223712>.
- Holst, B., & Williamson, G. (2004). A critical review of the bioavailability of glucosinolates and related compounds. *Natural Product Reports*, 21(3), 425–447.
- Huang, H., Wang, D., Belwal, T., Dong, L., Lu, L., Zou, Y., Li, L., Xu, Y., Luo, Z. (2021). A novel W/O/W double emulsion co-delivering brassinolide and cinnamon essential oil delayed the senescence of broccoli via regulating chlorophyll degradation and energy metabolism. *Food Chemistry*, 356, 129704. <https://doi.org/10.1016/j.foodchem.2021.129704>.
- Illera, J. C., Pérez-Alenza, M. D., Nieto, A., Jiménez, M. A., Silvan, G., Dunner, S., & Peña, L. (2006). Steroids and receptors in canine mammary cancer. *Steroids*, 71(7), 541-548. <https://doi.org/10.1016/j.steroids.2005.11.007>.
- Janowska, S., Holota, S., Lesyk, R., & Wujec, M. (2024). Aromatase inhibitors as a promising direction for the search for new anticancer drugs. *Molecules (Switzerland)*, 29 (2), 346. <https://doi.org/10.3390/molecules29020346>.
- Jasuja, R., Pencina, K. M., Lawney, B., Stephens-Shields, A. J., Ellenberg, S. S., Snyder, P. J., & Bhasin, S. (2025). Modulation of circulating free testosterone fraction by testosterone, dihydrotestosterone, and estradiol during testosterone replacement therapy. *Andrology*, 13(3), 439–446. <https://doi.org/10.1111/andr.13707>.
- Jazayeri, O., Araghi, S.F., Aghajanzadeh, T.A., & Mohammadrezaei, F.M. (2021). Up-regulation of Arl4a gene expression by broccoli aqueous extract is associated with improved spermatogenesis in mouse testes. *Biomedica: Revista del Instituto Nacional de Salud*, 41(4), 1–37. <https://doi.org/10.7705/biomedica.5962>.
- Jeffery, E. H., & Araya, M. (2009). Physiological effects of broccoli consumption. *Phytochemistry Reviews*, 8(1), 283–298. <https://doi.org/10.1007/s11101-008-9106-4>.
- Kachakova, D., Mitkova, A., Popov, E., Beltcheva, O., Vlahova, A., Dikov, T., Christova, S., Mitev, V., Slavov, C., & Kaneva, R. (2016). Polymorphisms in androgen metabolism genes AR, CYP1B1, CYP19, and SRD5A2 and prostate cancer risk and aggressiveness in Bulgarian patients. *Turkish Journal of Medical Sciences*, 46(3), 616-626. <https://doi.org/10.3906/sag-1502-19>.
- Kalfa, N., Gaspari, L., Ollivier, M., Philibert, P., Bergougnoux, A., Paris, F., & Sultan, C. (2019). Molecular genetics of hypospadias and cryptorchidism:

- Recent developments. *Clinical Genetics*, 95(1), 122–131. <https://doi.org/10.1111/cge.13432>.
- Katz, E., Nisani, S., & Chamovitz, D. A. (2018). Indole-3-carbinol: A plant hormone combatting cancer [version 1; peer review: 2 approved]. *F1000Research*. <https://doi.org/10.12688/f1000research.14127.1>.
- Keshaviah, A., Coates, A. S., Mouridsen, H., Mauriac, L., Forbes, J. F., Paridaens, R., Castiglione-Gertsch, M., Gelber, R. D., Rabaglio, M., Smith, I., Wardley, A., Price, K. N., & Goldhirsch, A. (2005). A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. *New England Journal of Medicine*, 353, 2747–2757. <https://www.nejm.org/doi/full/10.1056/NEJMoa052258>.
- Khan, S. I., Zhao, J., Khan, I. A., Walker, L. A., & Dasmahapatra, A. K. (2011). Potential utility of natural products as regulators of breast cancer-associated aromatase promoters. *Reproductive Biology and Endocrinology*, 9, 91. <https://doi.org/10.1186/1477-7827-9-91>.
- Kim, J. K., & Park, S. U. (2018). Current results on the biological and pharmacological activities of indole-3-carbinol. *EXCLI Journal*, 17, 181–185. <https://doi.org/10.17179/excli2017-1028>.
- Kim, S. M. (2016). Cellular and molecular mechanisms of 3,3'-diindolylmethane in gastrointestinal cancer. *International Journal of Molecular Sciences*, 17(7), 1155. <https://doi.org/10.3390/ijms17071155>.
- Korani, M. (2023). Aromatase inhibitors in male: A literature review. *Medicina Clinica Practica*, 6(1), 1–5. <https://doi.org/10.1016/j.mcpsp.2022.100356>.
- Kroon, J., & Meijer, O. C. (2020). Sex and stress steroid crosstalk reviewed: Give us more. *Journal of the Endocrine Society*, 4(10), bvaa113. <https://doi.org/10.1210/jendso/bvaa113>.
- Ku, Y. S., Sintaha, M., Cheung, M. Y., & Lam, H. M. (2018). Plant hormone signaling crosstalks between biotic and abiotic stress responses. *International Journal of Molecular Sciences*, 19, 3206. <https://doi.org/10.3390/ijms19103206>.
- Larsen-Su, S. A., & Williams, D. E. (2001). Transplacental exposure to indole-3-carbinol induces sex-specific expression of CYP1A1 and CYP1B1 in the liver of Fischer 344 neonatal rats. *Toxicological Sciences*, 64(2), 162–168.
- Laurent, M. R., Hammond, G. L., Blokland, M., Jardí, F., Antonio, L., Dubois, V., Khalil, R., Sterk, S. S., Gielen, E., Decallonne, B., Carmeliet, G., Kaufman, J. M., Fiers, T., Huhtaniemi, I. T., Vanderschueren, D., & Claessens, F.

- (2016). Sex hormone-binding globulin regulation of androgen bioactivity in vivo: Validation of the free hormone hypothesis. *Scientific Reports*, 6, 35539. <https://doi.org/10.1038/srep35539>.
- Latté, K. P., Appel, K. E., & Lampen, A. (2011). Health benefits and possible risks of broccoli – An overview. *Food and Chemical Toxicology*, 49(12), 3287–3309. <https://doi.org/10.1016/j.fct.2011.08.019>.
- Le, B., Chen, H., Zirkin, B., & Burnett, A. (2014). New targets for increasing endogenous testosterone production: Clinical implications and review of the literature. *Andrology*, 2(4), 484–490. <https://doi.org/10.1111/j.2047-2927.2014.00225.x>.
- Le, H. T., Schaldach, C. M., Firestone, G. L., & Bjeldanes, L. F. (2003). Plant-derived 3,3'-diindolylmethane is a strong androgen antagonist in human prostate cancer cells. *Journal of Biological Chemistry*, 278(23), 21136–21145. <https://doi.org/10.1074/jbc.M300588200>.
- Li, H., Xia, Y., Liu, H. Y., Guo, H., He, X. Q., Liu, Y., Wu, D. T., Mai, Y. H., Li, H. B., Zou, L., & Gan, R. Y. (2022). Nutritional values, beneficial effects, and food applications of broccoli (*Brassica oleracea* var. *italica* Plenck). *Trends in Food Science and Technology*, 119, 288–308.
- Li, J., Fu, A., & Zhang, L. (2019). An overview of scoring functions used for protein-ligand interactions in molecular docking. *Interdisciplinary Sciences: Computational Life Sciences*, 11(2), 320–328. <https://doi.org/10.1007/s12539-019-00327-w>.
- Li, W. X., Chen, L. P., Sun, M. Y., Li, J. T., Liu, H. Z., & Zhu, W. (2015). 3'-Diindolylmethane inhibits migration, invasion and metastasis of hepatocellular carcinoma by suppressing FAK signaling. *Oncotarget*, 6(27). <https://www.impactjournals.com/oncotarget/>.
- Licznarska, B., Szafer, H., Matuszak, I., Murias, M., & Baer-Dubowska, W. (2015). Modulating potential of L-sulforaphane in the expression of cytochrome P450 to identify potential targets for breast cancer chemoprevention and therapy using breast cell lines. *Phytotherapy Research*, 29(1), 93–99. <https://doi.org/10.1002/ptr.5232>.
- Lin, H., Wang, K. L., Wang, P. S., & Wang, S. W. (2012). Non-gonadotropin regulation of testosterone biosynthesis. In *Testosterone: Biochemistry, Therapeutic Uses, and Physiological Effects* (pp. 125–144).
- Luo, W. F., Komatsu, S., Abe, T., Matsuura, H., & Takahashi, K. (2020). Comparative proteomic analysis of wild-type *Physcomitrella patens* and an OPDA-deficient *Physcomitrella patens* mutant with disrupted PpAOS1 and

- PpAOS2 genes after wounding. *International Journal of Molecular Sciences*, 21, 1417. <https://doi.org/10.20944/preprints202001.0197.v1>.
- MacDonald, P. C., Madden, J. D., Brenner, P. F., Wilson, J. D., & Siiteri, P. K. (1979). Origin of estrogen in normal men and in women with testicular feminization. *Journal of Clinical Endocrinology and Metabolism*, 49(6).
- Manikandan, P., & Nagini, S. (2017). Cytochrome P450 structure, function and clinical significance: A review. *Current Drug Targets*, 19(1). <https://doi.org/10.2174/1389450118666170125144557>.
- Marconett, C. N., Sundar, S. N., Tseng, M., Tin, A. S., Tran, K. Q., Mahuron, K. M., Bjeldanes, L. F., & Firestone, G. L. (2011). Indole-3-carbinol downregulation of telomerase gene expression requires the inhibition of estrogen receptor- α and Sp1 transcription factor interactions within the hTERT promoter and mediates the G1 cell cycle arrest of human breast cancer cells. *Carcinogenesis*, 32(9), 1315–1323. <https://doi.org/10.1093/carcin/bgr116>.
- Martín-Ruiz, A., et al. (2018). Effects of indole-3-carbinol on steroid hormone profile and tumor progression in a mice model of canine inflammatory mammary cancer. <https://doi.org/10.1186/s12885-018-4518-z>.
- Mauras, N., O'Brien, K. O., Klein, K. O., & Hayes, V. (2000). Estrogen suppression in males: Metabolic effects. *Journal of Clinical Endocrinology & Metabolism*, 85(7), 2370–2377.
- Mauvais-Jarvis, F., & Lindsey, S. H. (2024). Metabolic benefits afforded by estradiol and testosterone in both sexes: Clinical considerations. *The Journal of Clinical Investigation*, 134(17), 1–10. <https://doi.org/10.1172/JCI180073>.
- McDonald, T. J., Perry, M. H., Jones, A. G., Donohoe, M., Salzman, M. B., & O'Connor, J. (2011). A novel case of a raised testosterone and LH in a young man. *Clinica Chimica Acta*, 412(21–22), 1999–2001.
- Megna, B. W., Carney, P. R., Nukaya, M., Geiger, P., & Kennedy, G. D. (2016). Indole-3-carbinol induces tumor cell death: Function follows form. *Journal of Surgical Research*, 204, 47–54.
- Mehta, N., Huang, S., Dhura, R., Wambier, C., do Nascimento Fonesca, D., Little, S., & Goren, A. (2023). Minoxidil sulfotransferase enzymatical activity in plants: A novel paradigm in increasing minoxidil response in androgenetic alopecia. *Journal of Cosmetic Dermatology*, 00, 1–5.
- Mendel, C. M. (1989). The free hormone hypothesis: A physiologically based mathematical model. *Endocrine Reviews*, 10(3), 232–274.

- Meng, Q., Goldberg, I. D., Rosen, E. M., & Fan, S. (2000). Inhibitory effects of indole-3-carbinol on invasion and migration in human breast cancer cells. *Breast Cancer Research and Treatment*, 63.
- Meng, Q., Yuan, F., Goldberg, I. D., Rosen, E. M., Auborn, K., & Fan, S. (2000). Nutrient-gene expression: Indole-3-carbinol is a negative regulator of estrogen receptor-signaling in human tumor cells. *The Journal of Nutrition*, 130(12), 2927–2931. <https://academic.oup.com/jn/article/130/12/2927/4686266>.
- Michnovicz, J. J., Adlercreutz, H., & Bradlow, H. L. (1997). Changes in levels of urinary estrogen metabolites after oral indole-3-carbinol treatment in humans. *Journal of the National Cancer Institute*, 89(10), 718–723. <https://academic.oup.com/jnci/article/89/10/718/2526073>.
- Miranda, E. P., Schofield, E., Matsushita, K., Katz, D. J., Nelson, C. J., Benfante, N., & Mulhall, J. P. (2022). Luteinizing hormone suppression profiles in men treated with exogenous testosterone. *The Journal of Sexual Medicine*, 19(9), 1359–1365.
- Miryanti, Y. I. P. A., Lanny, S., Kurniawan, B., & Stephen, I. (2011). Ekstraksi antioksidan dari kulit buah manggis (*Garcinia mangostana* L.). *Lembaga Penelitian dan Pengabdian kepada Masyarakat, Universitas Katolik Parahyangan, Bandung*.
- Murray, G. I., Melvin, W. T., Greenlee, W. F., & Burke, M. D. (2001). Regulation, function, and tissue-specific expression of cytochrome P450 CYP1B1. *Annual Review of Pharmacology and Toxicology*, 41, 297–316.
- Nandini, D., et al. (2020). Sulforaphane in broccoli: The green chemoprevention!! Role in cancer prevention and therapy. *Journal of Oral and Maxillofacial Pathology*, 24(2), 405. https://doi.org/10.4103/JOMFP.JOMFP_126_19.
- Narayanan, V., Rodrigues, A. L., & Dordick, J. S. (2022). Influence of circadian rhythm on drug metabolism in 3D hepatic spheroids. *Biotechnology and Bioengineering*, 119(10), 2842–2856. <https://doi.org/10.1002/bit.28180>.
- Nassar, G. N., & Leslie, S. W. (2025). Physiology, testosterone. In *StatPearls*. StatPearls Publishing. <https://www.ncbi.nlm.nih.gov/books/NBK526128/>.
- Nazir, M., Abbasi, M. A., Aziz-ur-Rehman, Siddiqui, S. Z., Khan, K. M., Kanwal, U., Salar, M., Shahid, M., Ashraf, M., Lodhi, M. A., & Khan, F. A. (2018). New indole based hybrid oxadiazole scaffolds with N-substituted acetamides: As potent anti-diabetic agents. *Bioorganic Chemistry*, 81, 253–263. <https://doi.org/10.1016/j.bioorg.2018.08.010>.

- Nelson, P. S., Clegg, N., Arnold, H., Ferguson, C., Bonham, M., White, J., Hood, L., & Lin, B. (2002). The program of androgen-responsive genes in neoplastic prostate epithelium. *Proceedings of the National Academy of Sciences of the United States of America*, 99(18), 11890–11895.
- O'Hara, L., Curley, M., Ferreira, M. T., Cruickshanks, L., Milne, L., & Smith, L. B. (2015). Pituitary androgen receptor signalling regulates prolactin but not gonadotrophins in the male mouse. *PLoS ONE*, 10(3). <https://doi.org/10.1371/journal.pone.0121657>.
- Olasore, H. S. A., Oyedeji, T. A., Olawale, M. O., Ogundele, O. I., & Faleti, J. O. O. (2023). Relationship between T-estradiol ratio and some anthropometric and metabolic parameters among Nigerian men. *Metabolism Open*, 18, 1–6.
- Ortiz de Montellano, P. R., & De Voss, J. J. (2005). Substrate oxidation by cytochrome P450 enzymes. In P. R. Ortiz de Montellano (Ed.), *Cytochrome P450* (pp. [page range if available]). Springer. https://doi.org/10.1007/0-387-27447-2_6.
- Öztürk, M., Tel-Çayan, G., Muhammad, A., Terzioğlu, P., & Duru, M. E. (2015). Mushrooms: A source of exciting bioactive compounds. In *Studies in Natural Products Chemistry* (Vol. 45, pp. 363–456).
- Park, H. J. (2014). Anti-inflammatory properties of broccoli sprout extract in a lipopolysaccharide-induced testicular dysfunction. *Journal of Animal Reproduction and Biotechnology*, 38(1), 17–25. <https://doi.org/10.12750/JARB.38.1.17>.
- Parkin, D. R., & Malejka-Giganti, D. (2004). Differences in the hepatic P450-dependent metabolism of estrogen and tamoxifen in response to treatment of rats with 3,3'-diindolylmethane and its parent compound indole-3-carbinol. *Cancer Detection and Prevention*, 28(1), 72–79.
- Papadakis, M. A., McPhee, S. J., & Rabow, M. W. (2022). Endocrine disorder. In K. R. McQuaid (Ed.), *Current Medical Diagnosis and Treatment 2022* (pp. 1110–1211). McGraw Hill.
- Papadopoulos, V., & Miller, W. L. (2012). Role of mitochondria in steroidogenesis. *Best Practice & Research Clinical Endocrinology & Metabolism*, 26, 771–790.
- Popolo, A., Pinto, A., Daglia, M., Nabavi, S. F., Farooqi, A. A., & Rastrelli, L. (2017). Two likely targets for the anti-cancer effect of indole derivatives from cruciferous vegetables: PI3K/Akt/mTOR signalling pathway and the aryl hydrocarbon receptor. *Seminars in Cancer Biology*, 46, 132–137.

- Peters, A., Conrad, M., Hubold, C., Schweiger, U., Fischer, B., & Fehm, H. L. (2007). The principle of homeostasis in the hypothalamus–pituitary–adrenal system: New insight from positive feedback. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 293, R83–R98. <https://doi.org/10.1152/ajpregu.00907.2006>.
- Prakoso, Y. A., Rini, C. S., Rahayu, A., Sigit, M., & Widhowati, D. (2020). Celery (*Apium graveolens*) as a potential antibacterial agent and its effect on cytokeratin-17 and other healing promoters in skin wounds infected with methicillin-resistant *Staphylococcus aureus*. *Veterinary World*, 13(5), 865–871.
- Raezadeh, M., Khademi, N., & Akbari, A. (2021). The effects of broccoli and caraway extracts on serum oxidative markers, testicular structure and function, and sperm quality before and after sperm cryopreservation. *Cryobiology*, 99, 11–19. <https://doi.org/10.1016/j.cryobiol.2021.02.003>.
- Rajoria, S., Suriano, R., Wilson, Y. L., Schantz, S. P., Moscatello, A., Geliebter, J., & Tiwari, R. K. (2011). 3,3'-Diindolylmethane inhibits migration and invasion of human cancer cells through combined suppression of ERK and AKT pathways. *Oncology Reports*, 25(2), 194–197. <https://doi.org/10.3892/or.2010.1076>.
- Ramesh, A., Nandi, A., Devanathan, S., Jayaraman, L., & Sivaji, S. (2023). Anti-inflammatory, anti-oxidative, and anti-microbial activities of the phytochemicals isolated from various parts of broccoli wastes. *Journal of Advanced Biotechnology and Experimental Therapeutics*, 6(1), 67–83. 0, <https://doi.org/10.5455/jabet.2023.d107>.
- Reed, G. A., Arneson, D. W., Putman, W. C., Smith, H. J., Gray, J. C., Sullivan, D. K., et al. (2006). Single-dose and multiple-dose administration of indole-3-carbinol to women: Pharmacokinetics based on 3,3'-diindolylmethane. *Cancer Epidemiology, Biomarkers & Prevention*, 15(12), 2477–2481.
- Rendic, S., & Guengerich, F. P. (2015). Survey of human oxidoreductases and cytochrome P450 enzymes involved in the metabolism of xenobiotic and natural chemicals. *Chemical Research in Toxicology*, 28(1), 38–42. <https://doi.org/10.1021/tx500444e>.
- Rendic, S., & Guengerich, F. P. (2018). Human cytochrome P450 enzymes 5–51 as targets of drugs and natural and environmental compounds: Mechanisms, induction, and inhibition – Toxic effects and benefits. *Drug Metabolism Reviews*, 50(3), 256–342. <https://doi.org/10.1080/03602532.2018.1483401>.
- Rogan, E. G. (2006). The natural chemopreventive compound indole-3-carbinol: State of the science. *In Vivo*, 20, 221–221.

- Rollinger, J. M., & Wolber, G. (2011). Computational approaches for the discovery of natural lead structures. In *Bioactive Compounds from Natural Sources: Natural Products as Lead Compounds in Drug Discovery* (2nd ed., pp. 97–132).
- Sanabria Pérez, C., & Díaz Pérez, J. A. (2010). Valoración de niveles de testosterona mediante diferentes métodos analíticos en varones sanos [Evaluation of testosterone levels through distinct analytic methods in healthy men]. *Endocrinología y Nutrición*, 57(7), 301–305.
- Saylam, B., Efesoy, O., & Ayan, S. (2011). The effect of aromatase inhibitor letrozole on body mass index, serum hormones, and sperm parameters in infertile men. *Fertility and Sterility*, 95(2), 809–811. <https://doi.org/10.1016/j.fertnstert.2010.09.021>.
- Schulster, M., Bernie, A. M., & Ramasamy, R. (2016). The role of estradiol in male reproductive function. *Asian Journal of Andrology*, 18(3), 435–440. <https://doi.org/10.4103/1008-682X.173932>.
- Selby, C. (1990). Sex hormone binding globulin: origin, function and clinical significance. *Annals of Clinical Biochemistry*, 27(6), 532–541.
- Shah, B. R., Xu, W., & Mraz, J. (2019). Cytochrome P450 1B1: Role in health and disease and effect of nutrition on its expression. *RSC Advances*, 9(36), 21050–21062.
- Shapiro, T. A., Fahey, J. W., Wade, K. L., Stephenson, K. K., & Talalay, P. (2001). Chemoprotective glucosinolates and isothiocyanates of broccoli sprouts: Metabolism and excretion in humans. *Cancer Epidemiology Biomarkers & Prevention*, 10, 501–508.
- Shay, D. A., Vieira-Potter, V. J., & Rosenfeld, C. S. (2018). Sexually dimorphic effects of aromatase on neurobehavioral responses. *Frontiers in Molecular Neuroscience*, 11, Article 374. <https://doi.org/10.3389/fnmol.2018.00374>.
- Shihan, M., Buldan, A., & Scheiner-Bobis, G. (2014). Non-classical testosterone signaling is mediated by a G-protein-coupled receptor interacting with Gna11. *Biochimica et Biophysica Acta (BBA) - Molecular Cell Research*, 1843(6), 1172–1181. <https://doi.org/10.1016/j.bbamcr.2014.03.002>.
- Smolinska, N., Kiezun, M., Dobrzyn, K., Szeszko, K., Maleszka, A., & Kaminski, T. (2015). Expression of the orexin system in the porcine uterus, conceptus and trophoblast during early pregnancy. *Animal*, 9(11), 1820–1831.
- Sidiqi, A. A. A., Airin, C. M., Sarmin, S., & Astuti, P. (2023). A combination of *Anadara nodifera* shell and milkfish thorns powder effectively promote

springiness index, serum testosterone, and breast muscle testosterone in Bangkok rooster. *HAYATI Journal of Biosciences*, 30(4), 701–710.

Simpson, E. R., Mahendroo, M. S., Means, G. D., et al. (1994). Aromatase cytochrome P450, the enzyme responsible for estrogen biosynthesis. *Endocrine Reviews*, 15, 342–355. <https://doi.org/10.1210/edrv-15-3-342>.

Simpson, E. R., Clyne, C., Rubin, G., Boon, W. C., Robertson, K., Britt, K., Speed, C., & Jones, M. (2002). Aromatase—a brief overview. *Annual Review of Physiology*, 64, 93–127. <https://doi.org/10.1146/annurev.physiol.64.081601.142703>.

Singh, T. P., & Singh, O. M. (2017). Recent progress in biological activities of indole and indole alkaloids. *Mini Reviews in Medicinal Chemistry*, 18, 9–25. <https://doi.org/10.2174/1389557517666170807123201>.

Song, W. C. (2021). Biochemistry and reproductive endocrinology of estrogen sulfotransferase. *Annals of the New York Academy of Sciences*, 948, 43–50.

Srilatha, B., & Adaikan, P. G. (2003). Oestrogen-androgen crosstalk in the pathophysiology of erectile dysfunction. *Asian Journal of Andrology*, 5(4), 303–307.

Stanczyk, F. Z. (2024). Metabolism of endogenous and exogenous estrogens in women. *Journal of Steroid Biochemistry and Molecular Biology*, 242, 106539. <https://doi.org/10.1016/j.jsbmb.2024.106539>.

Stanczyk, F. Z., & Archer, D. F. (2023). Biosynthesis of estetrol in human pregnancy: Potential pathways. *Journal of Steroid Biochemistry and Molecular Biology*, 232, 106359. <https://doi.org/10.1016/j.jsbmb.2023.106359>.

Stárka, L., & Hampl, R. (2014). Testosterone: A neuroactive steroid. *Diabetologie Metabolismus Endokrinologie Vyziva*, 17, 17–21.

Starrett, J. R., & Moenter, S. M. (2023). Hypothalamic kisspeptin neurons as potential mediators of estradiol negative and positive feedback. *Peptides*, 163, 170963. <https://doi.org/10.1016/j.peptides.2023.170963>.

Sundar, S. N., Kerekatte, V., Equinozio, C. N., Doan, V. B., Bjeldanes, L. F., & Firestone, G. L. (2006). Indole-3-carbinol selectively uncouples expression and activity of estrogen receptor subtypes in human breast cancer cells. *Molecular Endocrinology*, 20(12), 3070–3082. <https://doi.org/10.1210/me.2005-0263>.

Szafer, H., et al. (2012). Modulation of CYP1A1, CYP1A2 and CYP1B1 expression by cabbage juices and indoles in human breast cell lines.

Nutrition and Cancer, 64(6), 879–888.
<https://doi.org/10.1080/01635581.2012.690928>.

- Taha, M., Rahim, F., Imran, S., Ismail, N. H., Ullah, H., Selvaraj, M., Javid, M. T., Salar, U., Ali, M., & Khan, K. M. (2017). Synthesis, α -glucosidase inhibitory activity and in silico study of tris-indole hybrid scaffold with oxadiazole ring: as potential leads for the management of type-II diabetes mellitus. *Bioorganic Chemistry*, 74, 30–40.
<https://doi.org/10.1016/j.bioorg.2017.07.009>.
- Tan, R. B., Guay, A. T., & Hellstrom, W. J. (2014). Clinical use of aromatase inhibitors in adult males. *Sexual Medicine Reviews*, 2(2), 79–90.
<https://doi.org/10.1002/smrj.23>
- Tilbrook, A. J., & Clarke, I. J. (2001). Negative feedback regulation of the secretion and actions of gonadotropin-releasing hormone in males. *Biology of Reproduction*, 64(3), 735–742. <https://doi.org/10.1095/biolreprod64.3.735>
- Tiwari, N., Pandey, A., Kumar, A., & Mishra, A. (2021). Computational models reveal the potential of polycyclic aromatic hydrocarbons to inhibit aromatase, an important enzyme of the steroid biosynthesis pathway. *Computational Toxicology*, 19.
<https://doi.org/10.1016/j.comtox.2021.100176>.
- Tominaga, T., Adachi, I., Sasaki, Y., Tabei, T., Ikeda, T., Takatsuka, Y., Toi, M., Suwa, T., & Ohashi, Y. (2003). Double-blind randomised trial comparing the non-steroidal aromatase inhibitors letrozole and fadrozole in postmenopausal women with advanced breast cancer. *Annals of Oncology*, 14(1), 62–70. <https://doi.org/10.1093/annonc/mdg014>.
- Torres-Contreras, A. M., Sénéz Guerrero, C., Pheco, A., González Agüero, M., Perla, A., Parra, R., Jacobo-Vélazquez, D. A. (2018). Genes differentially expressed in broccoli as an early and late response to wounding stress. *Postharvest Biology and Technology*, 145, 172–182.
<https://doi.org/10.1016/j.postharvbio.2018.07.010>.
- TwoRoger, S. S., Chubak, J., Aiello, E. J., Ulrich, C. M., Atkinson, C., Potter, J. D., Yasui, Y., Stapleton, P. L., Lampe, J. W., Farin, F. M., Stanczyk, F. Z., & McTiernan, A. (2004). Association of CYP17, CYP19, CYP1B1, and COMT polymorphisms with serum and urinary sex hormone concentrations in postmenopausal women. *Cancer Epidemiology Biomarkers & Prevention*, 13(1), 94–101.
- Ociepa-Zawal, M., et al. (2007). The effect of indole-3-carbinol on the expression of CYP1A1, CYP1B1 and AhR genes and proliferation of MCF-7 cells. *Acta Biochimica Polonica*. Available at: www.actabp.pl.

- van Honk, J., Bos, P. A., & Terburg, D. (2014). Testosterone and Dominance in Humans: Behavioral and Brain Mechanisms. In J. Decety & Y. Christen (Eds.), *New Frontiers in Social Neuroscience* (pp. 211–228). Springer. https://doi.org/10.1007/978-3-319-02904-7_12.
- Véronneau-Veilleux, F., & Bélair, J. (2017). Modeling circadian fluctuations of pharmacokinetic parameters. *Mathematical Modelling of Natural Phenomena*, 12(5), 146–161.
- Wahidur Rahman, K. M., Aranha, O., & Sarkar, F. H. (2003). Indole-3-carbinol (I3C) induces apoptosis in tumorigenic but not in nontumorigenic breast epithelial cells. *Nutrition and Cancer*, 45(1), 101–112. https://doi.org/10.1207/s15327914nc4501_12.
- Wang, J., & Jiang, Y. F. (2012). Natural compounds as anti-cancer agents: Experimental evidence. *World Journal of Experimental Medicine*, 2, 45–57.
- Wang, T. T. Y., Milner, M. J., Milner, J. A., & Kim, Y. S. (2006). Estrogen receptor α as a target for indole-3-carbinol. *Journal of Nutritional Biochemistry*, 17(10), 659–664. <https://doi.org/10.1016/j.jnutbio.2005.10.012>.
- Weng, J. R., Tsai, C. H., Kulp, S. K., & Chen, C. S. (2008). Indole-3-carbinol as a chemopreventive and anti-cancer agent. *Cancer Letters*, 262(2), 153–163. <https://doi.org/10.1016/j.canlet.2008.01.033>.
- Williams, D. J., Critchley, C., Pun, S., Chaliha, M., & O'Hare, T. J. (2010). Key role of Fe^{2+} in epithiospecifier protein activity. *Journal of Agricultural and Food Chemistry*, 58(14), 8512–8521.
- Windayani, M. (2017). Effervescent broccoli formulation (*Brassica oleracea* var. *italica*) with probiotic bacteria incorporation on physicochemical and microbiological properties. *Skripsi*.
- Wu, C., Cao, S., Xie, K., Chi, Z., & Gao, H. (2021). Melatonin delays yellowing of broccoli during storage by regulating chlorophyll catabolism and maintaining chloroplast ultrastructure. *Postharvest Biology and Technology*, 172, 111378. <https://doi.org/10.1016/j.postharvbio.2020.111378>.
- Wyde, M. E., Boyle, M. C., Herbert, R. A., Blystone, C. R., Foster, P. M., Hooth, M. J., Kissling, G. E., Malarkey, D. E., McIntyre, B. S., Smith-Roe, S. L., Stout, M. D., Travlos, G. S., Waidyanatha, S., Walker, N. J., Witt, K. L., Nyska, A., Hill, G. D., Hébert, C. D., Heath, J. E., Mann, J. F., Hejtmancik, M. R., Briscoe, C. M., Ryan, M. J., Adams, E. T., Brix, A. E., Miller, R. A., Hamlin, M. H., Muir, B. J. T., Atkinson, B., Wang, Y., Cullen, J. M., Elmore, S. A., Hoenerhoff, M. J., Rogers, A. B., Adams, E. T., Boyle, M.

- C., Miller, R. A., Nold, J. P., Morris, R. W., Betz, L. J., Harris, S. F., Brecher, S., Iyer, S., Tharakan, V. S., Gunnels, S. R., Gideon, P. A., Harper, L. M., Kumpe, T. S., & Serbus, D. C. (2017). Toxicology studies of indole-3-carbinol (CASRN 700-06-1) in F344/N rats and B6C3F1/N mice and toxicology and carcinogenesis studies of indole-3-carbinol in Harlan Sprague Dawley rats and B6C3F1/N mice (gavage studies). *NTP Technical Report on the Toxicology and Carcinogenesis Studies Series* (584), 1–243. <https://doi.org/10.22427/NTP-TR-584>.
- Xu, X. L., Huang, Z. Y., Yu, K., Li, J., Fu, X. W., & Deng, S. L. (2022). Estrogen biosynthesis and signal transduction in ovarian disease. *Frontiers in Endocrinology*, 13. <https://doi.org/10.3389/fendo.2022.827032>.
- Yadav, M. R., Barmade, M. A., Tamboli, R. S., & Murumkar, P. R. (2015). Developing steroidal aromatase inhibitors—An effective armament to win the battle against breast cancer. *European Journal of Medicinal Chemistry*, 105, 1–38. <https://doi.org/10.1016/j.ejmech.2015.09.038>.
- Yamamoto, R., et al. (2013). Involvement of PTEN/Akt signaling and oxidative stress on indole-3-carbinol (I3C)-induced hepatocarcinogenesis in rats. *Experimental and Toxicologic Pathology*, 65(6), 845–852. <https://doi.org/10.1016/j.etp.2012.12.003>.
- Yeap, B. B., Marriott, R. J., Antonio, L., Bhasin, S., Dobs, A. S., Dwivedi, G., Flicker, L., Matsumoto, A. M., Ohlsson, C., Orwoll, E. S., Raj, S., Reid, C. M., Vanderschueren, D., Wittert, G. A., Wu, F. C. W., & Murray, K. (2021). Sociodemographic, lifestyle and medical influences on serum testosterone and sex hormone-binding globulin in men from UK Biobank. *Clinical Endocrinology*, 94(2), 290–302.
- Yi, M., Negishi, M., Lee, S. J. (2021). Estrogen sulfotransferase (SULT1E1): Its molecular regulation, polymorphisms, and clinical perspectives. *Journal of Personalized Medicine*, 11(3), 194.
- Yuan, G., Sun, B., Yuan, J., & Wang, Q. (2010). Effect of 1-methylcyclopropene on shelf life, visual quality, antioxidant enzymes, and health-promoting compounds in broccoli florets. *Food Chemistry*, 118, 774–781. <https://doi.org/10.1016/j.foodchem.2009.05.062>.
- Yoh, K., Ikeda, K., Horie, K., & Inoue, S. (2023). Roles of Estrogen, Estrogen Receptors, and Estrogen-Related Receptors in Skeletal Muscle: Regulation of Mitochondrial Function. *International Journal of Molecular Sciences*, 24(3). <https://doi.org/10.3390/ijms24031853>.
- Yoshida, M., Katashima, S., Ando, J., Tanaka, T., Uematsu, F., Nakae, D., & Maekawa, A. (2004). Dietary indole-3-carbinol promotes endometrial adenocarcinoma development in rats initiated with *N*-ethyl-*N'*-nitro-*N*-

nitrosoguanidine, with induction of cytochrome P450s in the liver and consequent modulation of estrogen metabolism. *Carcinogenesis*, 25(11), 2257–2264. <https://doi.org/10.1093/carcin/bgh225>.

Zhang, Y., Ma, Y., Guo, Y., Chen, Y., Yang, M., Fu, R., & Sun, Y. (2022). Physiological and iTRAQ-based proteomic analyses for yellowing of postharvest broccoli heads under elevated O₂ controlled atmosphere. *Scientia Horticulturae*, 294. <https://doi.org/10.1016/j.scienta.2021.110769>.

Zhang, Z., Ober, J. A., & Kliebenstein, D. J. (2006). The gene controlling the quantitative trait locus EPITHIOSPECIFIER MODIFIER1 alters glucosinolate hydrolysis and insect resistance in *Arabidopsis*. *The Plant Cell*, 18(6), 1524–1536. <https://doi.org/10.1105/tpc.105.039602>.

Zhao, Y., Zhang, Y., Yang, H., Xu, Z., Li, Z., Zhang, Z., Zhang, W., & Deng, J. (2024). A comparative metabolomics analysis of phytochemicals and antioxidant activity between broccoli florets and by-products (leaves and stalks). *Food Chemistry*, 443, 138517. <https://doi.org/10.1016/j.foodchem.2024.138517>.