

DAFTAR PUSTAKA

- Aggarwal, V., Tuli, H.S., Thakral, F., *et al.*, 2020. Molecular mechanisms of action of hesperidin in cancer: Recent trends and advancements. *Exp Biol Med (Maywood)* 245: 486–497.
- Ahmadi, A., Shadboorestan, A., 2016. Oxidative stress and cancer; the role of hesperidin, a citrus natural bioflavonoid, as a cancer chemoprotective agent. *Nutrition and Cancer* 68: 29–39.
- Artanti, A., Jenie, R., Rumiayati, R., Meiyanto, E., 2024. Hesperidin and Diosmin Increased Cytotoxic Activity Cisplatin on Hepatocellular Carcinoma and Protect Kidney Cells Senescence. *Asian Pac J Cancer Prev* 25: 4247–4255.
- Asadi, M., Taghizadeh, S., Kaviani, E., Vakili, O., Taheri-Anganeh, M., Tahamtan, M., Savardashtaki, A., 2022. Caspase-3: Structure, function, and biotechnological aspects. *Biotech and App Biochem* 69: 1633–1645.
- Banjerdpongchai, R., Wudtiwai, B., Khaw-on, P., Rachakhom, W., Duangnil, N., Kongtawelert, P., 2016. Hesperidin from Citrus seed induces human hepatocellular carcinoma HepG2 cell apoptosis via both mitochondrial and death receptor pathways. *Tumor Biol.* 37: 227–237.
- Beck, B., Chen, Y.-F., Dere, W., Devanarayan, V., Eastwood, B.J., Farmen, M.W., Iturria, S.J., Iversen, P.W., Kahl, S.D., Moore, R.A., Sawyer, B.D., Weidner, J., 2012. Assay Operations for SAR Support: *Assay Guidance Manual*. Bethesda, MD: Eli Lilly & Company and the National Center for Advancing Translational Sciences.
- Bishayee, K., Ghosh, S., Mukherjee, A., Sadhukhan, R., Mondal, J., Khuda-Bukhsh, A.R., 2013. Quercetin induces cytochrome-c release and ROS accumulation to promote apoptosis and arrest the cell cycle in G2/M, in cervical carcinoma: signal cascade and drug-DNA interaction. *Cell Proliferation* 46: 153–163.
- Bogani, G., Ray-Coquard, I., Mutch, D., *et al.*, 2023. Gestational choriocarcinoma. *International Journal of Gynecological Cancer* 33: 1504–1514.
- Boudreau, M.W., Peh, J., Hergenrother, P.J., 2019. Procaspase-3 Overexpression in Cancer: A Paradoxical Observation with Therapeutic Potential. *ACS Chem. Biol.* 14: 2335–2348.
- Bouskela, E., Lugli, M., Nicolaidis, A., 2022. New Perspectives on Micronised Purified Flavonoid Fraction in Chronic Venous Disease: From Microvalves to Clinical Effectiveness. *Adv Ther* 39: 4413–4422.
- Carter, A.M., 2021. Unique Aspects of Human Placentation. *IJMS* 22: 8099.

- Cehade, H., Fox, A., Mor, G.G., Alvero, A.B., 2021. Determination of Caspase Activation by Western Blot. *Detection of Cell Death Mechanisms* 2255: 1–12.
- Dusza, H.M., Van Boxel, J., Van Duursen, M.B.M., Forsberg, M.M., Legler, J., Vähäkangas, K.H., 2023. Experimental human placental models for studying uptake, transport and toxicity of micro- and nanoplastics. *Science of The Total Environment* 860: 160403.
- Ebegboni, V.J., Dickenson, J.M., Sivasubramaniam, S.D., 2019. Antioxidative effects of flavonoids and their metabolites against hypoxia/reoxygenation-induced oxidative stress in a human first trimester trophoblast cell line. *Food Chemistry* 272: 117–125.
- Fontana, F., Raimondi, M., Marzagalli, M., Di Domizio, A., Limonta, P., 2020. The emerging role of paraptosis in tumor cell biology: Perspectives for cancer prevention and therapy with natural compounds. *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer* 1873: 188338.
- Ghasemi, M., Turnbull, T., Sebastian, S., Kempson, I., 2021. The MTT Assay: Utility, Limitations, Pitfalls, and Interpretation in Bulk and Single-Cell Analysis. *Int J Mol Sci* 22: 12827.
- Glover, H.L., Schreiner, A., Dewson, G., Tait, S.W.G., 2024. Mitochondria and cell death. *Nat Cell Biol* 26: 1434–1446.
- Gorrini, C., Harris, I.S., Mak, T.W., 2013. Modulation of oxidative stress as an anticancer strategy. *Nat Rev Drug Discov* 12: 931–947.
- Graves, D.B., 2014. Low temperature plasma biomedicine: A tutorial review. *Physics of Plasmas* 21: 080901.
- Gu, C., Zhang, J., Chen, Y., Lei, J., 2011. A trigger model of apoptosis induced by tumor necrosis factor signaling. *BMC Syst Biol* 5: S13.
- Ham, J., Lim, W., Bazer, F.W., Song, G., 2018. Silibinin stimulates apoptosis by inducing generation of ROS and ER stress in human choriocarcinoma cells. *Journal Cellular Physiology* 233: 1638–1649.
- Haneen, D.S.A., Abdalha, A.A., Alkhatib, M.M., Kamal, M., Youssef, A.S.A., Abou-Elmagd, W.S.I., Samir, S.S., 2025. Synthesis, comprehensive in silico studies, and cytotoxicity evaluation of novel quinazolinone derivatives as potential anticancer agents. *Sci Rep* 15: 23697.
- Huang, K.-H., Fang, W.-L., Li, A.F.-Y., Liang, P.-H., Wu, C.-W., Shyr, Y.-M., Yang, M.-H., 2018. Caspase-3, a key apoptotic protein, as a prognostic marker in gastric cancer after curative surgery. *International Journal of Surgery* 52: 258–263.

- Indraprasta, B.R., Tjokroprawiro, B.A., 2023. Synchronous placental site trophoblastic tumor and choriocarcinoma. *Bali Med J.* 12: 2638–2641.
- Indrayanto, G., Putra, G.S., Suhud, F., 2021. Validation of in-vitro bioassay methods: Application in herbal drug research. *Profiles of Drug Substances, Excipients and Related Methodology* 46: 273–307.
- KabaÅ,a-Dzik, A., Rzepecka-Stojko, A., Kubina, R., Iriti, M., Wojtyczka, R.D., Buszman, E., Stojko, J., 2018. Flavonoids, bioactive components of propolis, exhibit cytotoxic activity and induce cell cycle arrest and apoptosis in human breast cancer cells MDA-MB-231 and MCF-7 – a comparative study. *Cell Mol Biol (Noisy-le-grand)* 64: 1–10.
- Kafi, Z., Cheshomi, H., Gholami, O., 2018. 7-Isopenthenyloxy coumarin, Arctigenin, and Hesperidin Modify Myeloid Cell Leukemia Type-1 (Mcl-1) Gene Expression by Hormesis in K562 Cell Line. *Dose-Response* 16: 1559325818796014.
- Kamiloglu, S., Sari, G., Ozdal, T., Capanoglu, E., 2020. Guidelines for cell viability assays. *Food Frontiers* 1: 332–349.
- Kashyap, D., Garg, V.K., Tuli, H.S., Yerer, M.B., Sak, K., Sharma, A.K., Kumar, M., Aggarwal, V., Sandhu, S.S., 2019. Fisetin and Quercetin: Promising Flavonoids with Chemopreventive Potential. *Biomolecules* 9: 174.
- Kiesslich, S., Kamen, A.A., 2020. Vero cell upstream bioprocess development for the production of viral vectors and vaccines. *Biotechnology Advances* 44: 107608.
- Knöfler, M., Haider, S., Saleh, L., Pollheimer, J., Gamage, T.K.J.B., James, J., 2019. Human placenta and trophoblast development: key molecular mechanisms and model systems. *Cell. Mol. Life Sci.* 76: 3479–3496.
- Kumara, D., Harsan, H.S., Septisetyani, E.P., Prasetyaningrum, P.W., Paramitasari, K.A., Syaifudin, M., Ikawati, M., Astirin, O.P., Meiyanto, E., 2025. Inhibitory Effects of Citrus-Derived Flavonoids Hesperidin and Hesperetin on SARS-CoV-2 spike-Mediated Syncytia Formation Using In vitro Cell Model. *Adv Pharm Bull* 1.
- Lestari, B., Fukushima, T., Utomo, R.Y., Wahyuningsih, M.S.H., 2024. Apoptotic and non-apoptotic roles of caspases in placenta physiology and pathology. *Placenta* 151: 37–47.
- Lestari, B., Soda, K., Moritsugu, K., Kidera, A., Suenaga, Y., Hippo, Y., Meiyanto, E., Komada, M., Wahyuningsih, M.S.H., Fukushima, T., 2023. The placental protein NRK promotes cell death through its plasma membrane-localizing CNH domain.

- Li, H., Peng, H., Hong, W., *et al.*, 2022. Human Placental Endothelial Cell and Trophoblast Heterogeneity and Differentiation Revealed by Single-Cell RNA Sequencing. *Cells* 12: 87.
- Li, Y., Kandhare, A.D., Mukherjee, A.A., Bodhankar, S.L., 2019. Acute and sub-chronic oral toxicity studies of hesperidin isolated from orange peel extract in Sprague Dawley rats. *Regulatory Toxicology and Pharmacology* 105: 77–85.
- Lim, W., Yang, C., Park, S., Bazer, F.W., Song, G., 2017. Inhibitory Effects of Quercetin on Progression of Human Choriocarcinoma Cells Are Mediated Through PI3K/AKT and MAPK Signal Transduction Cascades. *Journal Cellular Physiology* 232: 1428–1440.
- Liu, H., Xiao, Y.-D., Peng, S.-P., Zhou, S.-K., Liu, J., 2016. Pituitary metastasis of choriocarcinoma: A case report. *Oncology Letters* 11: 1517–1520.
- Liu, X., Tu, P., Zhang, Y., Xu, W., Shan, J., Gao, B., 2024. Aldicarb disturbed bile acid, steroid hormone and oxylipin homeostasis in C57BL/6 J mice. *Ecotoxicology and Environmental Safety* 275: 116285.
- Lukinovic, N., Malovrh, E.P., Takac, I., Sobocan, M., Knez, J., 2022. Advances in diagnostics and management of gestational trophoblastic disease. *Radiology and Oncology* 56: 430–439.
- Mangla, M., Palo, S., Kanikaram, P., Kaur, H., 2024. Non-gestational choriocarcinoma: unraveling the similarities and distinctions from its gestational counterpart. *International Journal of Gynecological Cancer* 34: 926–934.
- Manome, A., Abiko, Y., Kawashima, J., Washio, J., Fukumoto, S., Takahashi, N., 2019. Acidogenic Potential of Oral Bifidobacterium and Its High Fluoride Tolerance. *Front. Microbiol.* 10: 1099.
- Martin, F., Neubert, A., Lutter, A.-H., Scholka, J., Hentschel, E., Richter, H., Anderer, U., 2024. MTS, WST-8, and ATP viability assays in 2D and 3D cultures: Comparison of methodologically different assays in primary human chondrocytes. *CH* 88: S3–S19.
- Mehdiya, R., Banu, Z., Rahman, A., 2024. Hesperidin: A Comprehensive Review of Its Health Benefits and Therapeutic Potential. *World Journal of Pharmacy and Pharmaceutical Sciences* 13: 1834–1846.
- Moriwaki, M., Kito, K., Nakagawa, R., Tominaga, E., Kapoor, M.P., Matsumiya, Y., Fukuhara, T., Yamagata, H., Katsumata, T., Minegawa, K., 2023. Mutagenic, Acute, and Subchronic Toxicity Studies of the Hesperetin-7-Glucoside- β -Cyclodextrin Inclusion Complex. *Int J Toxicol* 42: 50–62.

- Newton, K., Strasser, A., Kayagaki, N., Dixit, V.M., 2024. Cell death. *Cell* 187: 235–256.
- Ning, L., Zhao, W., Gao, H., Wu, Y., 2020. Hesperidin induces anticancer effects on human prostate cancer cells via ROS-mediated necrosis like cell death. *J BUON* 25: 2629–2634.
- Önder, G.Ö., Göktepe, Ö., Baran, M., Bitgen, N., Aydın, F., Yay, A., 2023. Therapeutic potential of hesperidin: Apoptosis induction in breast cancer cell lines. *Food and Chemical Toxicology* 176: 113791.
- Osada, N., Kohara, A., Yamaji, T., Hirayama, N., Kasai, F., Sekizuka, T., Kuroda, M., Hanada, K., 2014. The Genome Landscape of the African Green Monkey Kidney-Derived Vero Cell Line. *DNA Research* 21: 673–683.
- Pandey, P., Khan, F., Maurya, P., 2021. Targeting Jab1 using hesperidin (dietary phytochemical) for inducing apoptosis in HeLa cervical cancer cells. *J Food Biochem* 45.
- Pang, Y., Wu, Q., Zhang, M., Lai, J., Chen, D., Su, J., Zhu, B., Zhou, H., Li, Y., 2023. Hesperidin Induced HePG-2 Cell Apoptosis through ROS-Mediated p53/Bcl-2/Bax and p-mTOR Signaling Pathways. *Journal of Food Biochemistry* 2023: 1–10.
- Park, H.J., Kim, M.-J., Ha, E., Chung, J.-H., 2008. Apoptotic effect of hesperidin through caspase3 activation in human colon cancer cells, SNU-C4. *Phytomedicine* 15: 147–151.
- Park, S., Lim, W., Bazer, F.W., Song, G., 2018. Naringenin suppresses growth of human placental choriocarcinoma via reactive oxygen species-mediated P38 and JNK MAPK pathways. *Phytomedicine* 50: 238–246.
- Pyrzynska, K., 2022. Hesperidin: A Review on Extraction Methods, Stability and Biological Activities. *Nutrients* 14: 2387.
- Rahmani, A.H., Babiker, A.Y., Anwar, S., 2023. Hesperidin, a Bioflavonoid in Cancer Therapy: A Review for a Mechanism of Action through the Modulation of Cell Signaling Pathways. *Molecules* 28: 5152.
- Rakhmina, D., Heriyanto, D., Wahyuningsih, M.S.H., 2025. Exploring the In Vitro Anticancer Potential of Indonesian Medicinal Plants and Natural Compounds for Breast Cancer Therapy. *Asian Pac J Cancer Prev* 26: 4525–4535.
- Sheikh, P., Lohsiriwat, V., Shelygin, Y., 2020. Micronized Purified Flavonoid Fraction in Hemorrhoid Disease: A Systematic Review and Meta-Analysis. *Adv Ther* 37: 2792–2812.

- Sheridan, M.A., Zhao, X., Fernando, R.C., Gardner, L., Perez-Garcia, V., Li, Q., Marsh, S.G.E., Hamilton, R., Moffett, A., Turco, M.Y., 2021. Characterization of primary models of human trophoblast. *Development* 148: dev199749.
- Shojaei, S., Ali, M.S., Suresh, M., Upreti, T., Mogourian, V., Helewa, M., Labouta, H.I., 2021. Dynamic placenta-on-a-chip model for fetal risk assessment of nanoparticles intended to treat pregnancy-associated diseases. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease* 1867: 166131.
- Siddiqi, A., Hasan, S.K., Nafees, S., Rashid, S., Saidullah, B., Sultana, S., 2015. Chemopreventive efficacy of hesperidin against chemically induced nephrotoxicity and renal carcinogenesis via amelioration of oxidative stress and modulation of multiple molecular pathways. *Experimental and Molecular Pathology* 99: 641–653.
- Singh, P., Lim, B., 2022. Targeting Apoptosis in Cancer. *Curr Oncol Rep* 24: 273–284.
- Slika, H., Mansour, H., Wehbe, N., Nasser, S.A., Iratni, R., Nasrallah, G., Shaito, A., Ghaddar, T., Kobeissy, F., Eid, A.H., 2022. Therapeutic potential of flavonoids in cancer: ROS-mediated mechanisms. *Biomedicine & Pharmacotherapy* 146: 112442.
- Suzuki-Karasaki, M., Ochiai, Y., Innami, S., Okajima, H., Suzuki-Karasaki, M., Nakayama, H., Suzuki-Karasaki, Y., 2023. Ozone mediates tumor-selective cell death caused by air plasma-activated medium independently of NOx. .
- Vornic, I., Buciu, V., Furau, C.G., *et al.*, 2024. The Interplay of Molecular Factors and Morphology in Human Placental Development and Implantation. *Biomedicines* 12: 2908.
- Wahyuningsih, M.S.H., Syarif, R.A., Suharmi, S., Murini, T., 2013. Selectivity of Purified Extract from the Leaves of *Tithonia Diversifolia* (Hemsley) A.Gray) Against Hela Cells. *Traditional Medicine Journal* 18: 22–28.
- Wang, D., Shu, H., Zhang, Q., Zhang, H., Qing, C., Wang, H., 2018. Brain metastasis of choriocarcinoma presenting as multiple intracranial hematomas: A case report. *Medicine* 97: e12275.
- Wang, Y., Yu, H., Zhang, J., Gao, J., Ge, X., Lou, G., 2015. Hesperidin inhibits HeLa cell proliferation through apoptosis mediated by endoplasmic reticulum stress pathways and cell cycle arrest. *BMC Cancer* 15: 682.
- Wang, Y., Wang, Z., Zhu, X., Wan, Q., Han, P., Ying, J., Qian, J., 2022. Intestinal metastasis from choriocarcinoma: a case series and literature review. *World J Surg Onc* 20: 173.

- Weber, M., Weise, A., Vasheghani, F., Göhner, C., Fitzgerald, J.S., Liehr, T., Markert, U.R., 2021. Cytogenomics of six human trophoblastic cell lines. *Placenta* 103: 72–75.
- Wu, Y., Ren, P., Chen, J., Ai, L., 2021. A Case of Pregnancy with Choriocarcinoma Complicated by a Cerebral Hemorrhage and Lung Metastasis. *Case Rep Oncol* 14: 1182–1188.
- Wudtiwai, B., Makeudom, A., Krisanaprakornkit, S., Pothacharoen, P., Kongtawelert, P., 2021. Anticancer Activities of Hesperidin via Suppression of Up-Regulated Programmed Death-Ligand 1 Expression in Oral Cancer Cells. *Molecules* 26: 5345.
- Xia, R., Sheng, X., Xu, X., Yu, C., Lu, H., 2017. Hesperidin induces apoptosis and G0/G1 arrest in human non-small cell lung cancer A549 cells. *Int J Mol Med* 41: 464–472.
- Xiao, Z., Yan, L., Liang, X., Wang, H., 2020. Progress in deciphering trophoblast cell differentiation during human placentation. *Current Opinion in Cell Biology* 67: 86–91.
- Yang, Z., Yang, H., Dong, X., Pu, M., Ji, F., 2020. Hesperidin loaded Zn²⁺@SA/PCT nanocomposites inhibit the proliferation and induces the apoptosis in colon cancer cells (HCT116) through the enhancement of pro-apoptotic protein expressions. *Journal of Photochemistry and Photobiology B: Biology* 204: 111767.
- Zhang, J., Wu, D., Vikash, Song, J., Wang, J., Yi, J., Dong, W., 2015. Hesperetin Induces the Apoptosis of Gastric Cancer Cells via Activating Mitochondrial Pathway by Increasing Reactive Oxygen Species. *Dig Dis Sci* 60: 2985–2995.