

DAFTAR PUSTAKA

- Aas, T., Børresen, A., Geisler, S., Smith-Sørensen, B., Johnsen, H., Varhaug, J., Akslen, L., Lønning, P., 1996, Specific P53 mutations are associated with *de novo* resistance to doxorubicin in breast cancer patients, *Nat. Med.*, 2, 811–814.
- Abd-Elzaher, M.M., Ammar, A., Labib., Hanan, A., Mousa., Samia, A., Moustafa., Mamdouh, M., Ali., Ahmed, A., El-Rashedy., 2016, synthesis, anticancer activity and molecular docking study of schiff base complexes containing thiazole moiety, *Beni-Suef University Journal of Basic and Applied Science*, 5(1), 85-96.
- Abelhady, M.I.S., Motaal, A.A., Beerhucs, L., 2011, Total Phenolic Content and Antioxidant Activity of Standardized Extracts from Leaves and Cell Cultures of Three *Callistemon* Species, *Am. J. Plant Sci.*, 2, 847-850.
- Alam, S., dan Khan, F., 2014, QSAR and docking studies on xanthone derivatives for anticancer activity targeting DNA topoisomerase II α , *Drug Des Devel Ther.*, 8, 183–195.
- Ali, S.S., Kasoju, N., Luthra, A., Singh, A., Shranabasava, H., Sahu A., Bora U., 2008, Indian medicinal herbs as sources of antioxidant, *Food. Res. Int.*, 41, 1-5
- Amanatie, Jumina, Mustofa, Hanafi, M., Armunanto, R., 2010, QSAR study of xanthone derivatives as antiplasmodial agent, *Indones. J. Chem.*, 10, 357 – 362.
- Aminah, H., Hernowo, B.S., Nur, M.I., Yusuf, M., 2011, Korelasi imunoekspresi Her2/Neu dan P53 dengan respon kemoterapi csplatin pada karsinoma paru bukan-sel kecil, *Majalah Patologi*, 20, 27-36.
- Anonim, 2012, New anti-cancer drug developed, <http://www.sciencedaily.com/releases/2012/05/120522115252.html>.
- Azevedo, C.M.B., Afonso, C.M.M., Soares, J.X., Salette, R., Sousa, D., Lima, R.L., Vasconcelos, M.H., Pedro, M., Barbosa, J., Gales, L., Pinto, M.M.M., 2013, Pyranoxanthones: Synthesis, growth inhibitory activity on human tumor cell lines and determination of their lipophilicity in two membrane models, *Eur. J. Med. Chem.*, 69, 798-816.
- Baheshti, A., Poubasheer, E., Nekoei, M., Vahdani, S., 2012, QSAR modeling of antimalarial activity of urea derivatives using alogarithm-multiple linier regressions, *Saudi. Chem. Soc.*, 6, 420-435.

- Bernas, T., dan Dobruchi, J., 2002, Mitochondrial and nonmitochondrial reduction of MTT with TMRE, JC-1, and NAO mitochondrial fluorescent probes, *Cytometry*, 47, 236-242.
- Berenblum, I., 1941, The mechanism of carcinogenesis, *Cancer Res.*, 1, 807–814.
- Barhate, N. B., Gajare, A. S., Wakharkar, R. D., Bedekar, A. V., 1999, Simple and practical halogenation of arenes, alkenes and alkynes with hydrohalic acid/H₂O₂ (or TBHP), *Tetrahedron*, 55, 11127.
- Boulikas, T., 2007, Molecular mechanisms of cisplatin and its liposomally encapsulated form lipoplatin TM as a chemo-therapy and antiangiogenesis drug, *Cancer Ther.*, 5, 351-76.
- Borisa, A., dan Bhatt, H., 2015, 3D-QSAR (CoMFA, CoMFA-RG, CoMSIA) and docking molecule study of thienopyrimidine and thienopyridine derivatives to explore structural requirements for aurora-B kinase inhibition, *Eur. J. Pharm. Sci.*, 79, 1–12.
- Bovonsombat, P., Ali, R., Khan, C., Leykajarakul, J., Pla-on, K., Aphimanchindakul, S., Pungcharoenpong, N., Timsuea, N., Arunrat, A., Punpongjareorn, N., 2010, Facile p-toluenesulfonic acid-promoted paraselective monobromination and chlorination of phenol and analogues, *Tetrahedron*, 66, 6928.
- Brooks B.R., Brooks III C. L., Mackerell A. D., Nilsson L., Petrella R. J., Roux B., Won Y., Archontis G., Bartels C., Boresch S., Caflisch A., Caves L., Cui Q., Dinner A. R., Feig M., Fischer S., Gao J., Hodoseck M., Im W., Kuczera K., Lazaridis T., Ma J., Ovchinnikov V., Paci E., Pastor R. W., Post C. B., Pu J. Z., Schaefer M., Tidor B., Venable R. M., Woodcock H. L., Wu X., Yang W., York D. M., Karplus, M., 2009, CHARMM: The Biomolecular simulation Program, *J. Comp. Chem.*, 30, 1545-1615.
- Brown, W.H., 1988, *Introduction to Organic Chemistry*, Edisi ke-4, International Thomson Books, Books Cole and Nelson, Singapore.
- Bruton, L., Lazo, J. S., Parker, K. L., 2005, *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, Edisi ke-11, McGraw Hill, Lange.
- Castanheiro, R.A.P., Pinto, M.M.M., Silva, A.M.S., Cravo, S.M.M., Gales, L., Damas, A.M., Nazareth, N., Nascimento, M.S.J., Eaton G., 2007, Dihydroxyxanthenes prenylated derivatives: Synthesis, structure elucidation, and growth inhibitory activity on human tumor cell lines with improvement of selectivity for MCF-7, *Bioorg. Med. Chem.*, 15, 6080–6088.

- Carey, F.A., dan Sunberg, R.J., 2007, *Advanced Organic Chemistry, Part A: Structure and Mechanisms*, Edisi ke-5, Springer, New York.
- Cepeda, V., Fuertes, M.A., Castilla, J., Alonso, C., Quevedo, C., Perez, J.M., 2007, Biochemical mechanism of cisplatin cytotoxicity, *Anticancer Agents Med. Chem.*, 7, 3-18.
- Chaube, C., Chhatbar, D., Bhatt, H., 2016, 3D-QSAR, Molecular dynamics simulations and docking molecule studies of benzoxazepine moiety as mTOR inhibitor for the treatment of lung cancer, *Bioorg. Med. Chem. Lett.*, 26, 864-874.
- Champoux, J. J., dan Bullock, P. A., 1988, *In Genetic Recombination*; Kucherlapati, R.; Smith, G. R., Eds.; American Society for Microbiology, Washington, DC., pp 655-666.
- Champoux, J. J., 2001, DNA topoisomerases: Structure, function, and mechanism, *Annu Rev Biochem.*, 70, 369-413.
- Cidade, H., Rocha, V.N., Palmeira, A., Marques, C., Tiritan, M.E., Ferreira, H., Lobo, J.S., Almeida, I.F., Sousa, M.E., Pinto, M., 2017, In silico and in vitro antioxidant and cytotoxicity evaluation of oxygenated xanthone derivatives, *Arabian J. Chem.* Article in press.
- Cheng, J.H., Huang, A.M., Hour, T.C., Yang, S-C., Yeong-Shiau P.U., Chun-Nan L., 2011, Antioxidant xanthone derivatives induce cell cycle arrest and apoptosis and enhance cell death induce by cipstalin in NTUB1 cells associated with ROS, *Eur. J. Med. Chem.*, 46, 1222-1231.
- Chen, R., dan Weng, Z., 2003, ZDOCK: An Initial-stage Protein-Docking Algorithm, *Proteins*, 52, 80-87.
- Chen, H., Lyne, P.D., Giordanetto, F., Lovell, T., Li, J., 2006, On evaluating molecular-docking methods for pose prediction and enrichment factors, *J. Chem. Inf. Model.*, 46(1), 401-15.
- Chen, L.G., Yang, L.L., Wang, C.C., 2008, Anti-inflammatory activity of mangostins from *Garcinia mangostana*, *Food Chem. Toxicol.*, 46, 688-693
- Choi, T., dan Ma, E., 2007, Simple and Regioselective Bromination of 5,6 Disubstitutedindan- 1-ones with Br₂ Under Acidic and Basic Conditions, *Molecules*, 12, 74-85.

- Cramer, C.J., 2004. *Essentials of Computational Chemistry*, Edisi ke-2, John Wiley and Sons Ltd., Chichester.
- Cristiano, R., Ma, K., Pottanat, G., Weiss, R. G., 2009, Tetraalkylphosphonium trihalides. Room temperature ionic liquids as halogenation reagents, *J. Org. Chem.*, 74, 9027.
- Cui, J., Hu, W., Cai, Z., Liu Y, Li, S., Tao, W., Xiang, H., 2010, New medicinal properties of mangostins: analgesic activity and pharmacological characterization of active ingredients from the fruit hull of *Garcinia mangostana* L., *Pharmacol. Biochem. Behav.*, 95, 166–172.
- Dai, M., Yuan, X., Kang, J., Zhi-Jun, Z., Yue, R.C., Yuan, H., Bing-Yang, C., Zhang, W-D., Liu, R.H., Sun, Q.Y., 2013, Synthesis and biological evaluation of phenyl substituted polyoxygenated xanthone derivatives as anti-hepatoma agents, *Eur. J. Med. Chem.*, 69, 159-166.
- Danesi, R., de Braud, F., Fogli, S., de Pas, T.M., Di Paolo, A., Curigliano, G., 2003 Pharma-cogenetics of anticancer drug sensitivity in non-small cell lung cancer, *Pharmacol. Rev.*, 55, 57-103.
- Damia, G., dan D’Incalci, M., 2009, Contemporary pre-clinical development of anticancer agents-what are the optimal preclinical models, *Eur. J. Cancer*, 45, 2768 – 2781.
- Desmurs, J. R., dan Jouve, I., 1989, Chlorination of nitrophenols, U.S. Patent 4,827,047.
- Dodean, R.A., Jane, X., Peyton, K.Y., Gary, L., Gard, M.K., Riscoe, Rolf, W., Winter, 2008, Synthesis and heme-binding correlation with antimalarial activity of 3,6-bis-(x-N,N-diethylaminoamyoxy)-4,5-difluoroxanthone, *Bioorg. Med. Chem.*, 16, 1174–1183.
- Delley, Bi., 1990, An all-electron numerical method for solving the local density functional for polyatom,ic molecules, *J. Chem. Phys.*, 92, 508
- Doyle, A., dan Griffiths, J.B., 2000, *Cell and Tissue for medical research*, John willey and sons, Ltd., New York.
- Diderot, N.T., Silvere, N., Etienne, T., 2006, Xanthone as therapeutic agents: Chemistry and Pharmacology, *Adv. Phytomed.*, 2, 273-298.

- DiPaola, R.S., 2002, To arrest or not to G(2)-M Cell-cycle arrest : commentary re: A. K. Tyagi et al., Silibinin strongly synergizes human prostate carcinoma DU145 cells to doxorubicin-induced growth inhibition, G(2)-M arrest, and apoptosis, *Clin. Cancer Res.*, 8, 3512 – 3519.
- Eswar, N., Marti-Renom, M.A., Webb, B., Madhusudhan, M.S., Eramian, D., Shen, M., Pieper, U., Sali, A., 2006, Comparative Protein Structure Modeling With MODELLER. *Current Protocols in Bioinformatics*, John Wiley & Sons, Inc., Supplement, 15, 5.6.1-5.6.30.
- Fei, X., Jo, M., Lee, B., Han, S.B., Lee, K., Jung, J.K., Seo, S.Y., Kwak, Y.S., 2014, Synthesis of xanthone derivatives based on a-mangostin and their biological evaluation for anti-cancer agents, *Bioorg. Med. Chem. Lett.*, 24, 2062 -2065.
- Feig, M., Onufriev, A., Lee, M.S., Im, W., Case, D.A., Brooks, C.L., 2004, Performance comparison of generalized born and Poisson methods in the calculation of electrostatic solvation energies for protein structures, *J. Comput. Chem.*, 25(2): 265–284.
- Fessenden, R.J., dan Fessenden, J.S., 1982, *Kimia Organik*, Jilid 1, Edisi Ketiga, (diterjemahkan oleh: Pudjaatmaka, A.H.), Penerbit Erlangga, Jakarta.
- Fessenden, R.J., dan Fessenden, J.S., 1986, *Kimia Organik*, Jilid 2, (diterjemahkan oleh: Pudjaatmaka, A.H.), Penerbit Erlangga, Jakarta.
- Finnegan, R.A., dan Merkel, K.E., 1972, The synthesis of 2,5- and 4,5-dihydroxyxanthone, *J. Org. Chem.*, 37, 2986.
- Frimayanti, N., Yam, M.L., Lee, H.B., Othman, R., 2011, Validation of quantitative structure activity relationship (QSAR) model for photosensitizer activity prediction, *Int. J. Mol. Sci.*, 12, 8626–8644.
- Ghalal, S.A., Abdelsamie, A.S., Tokuda, H., Suzuki, N., Lida, A., El Hefnawid, M.M., Ramadan, R.A., Atta, M.H.E., El Diwani, H., 2011, Part I : Synthesis, cancer chemopreventive activity and docking molecule study of novel quinoxaline derivatives, *Eur. J. Med. Chem.*, 46, 327-340.
- Golbraikh, A., Shen, M., Xiao, Z., Xiao, Y., Lee, K., 2003, Rational selection of training and test sets for the development of validated QSAR models, *J. Comp.-Aid. Mol. Des.*, 17, 241–253.
- Giallombardo, D., Nevin, A.C., Lewis, W., Nawrat, C.C., Kitson, R.R.A., Moody, C.J., 2014, Synthesis of toxyloxanthone B, *Tetrahedron*, 70, 1283-1288.

- Grover P.K., Shah G.D. dan Shah R.C., 1955, Xanthones. Part IV, *J. Chem. Soc.*, 3982.
- Han Ah-Reum, Kim, Jeong-Ah, Lantvit D.D., Kardono, L.B.S., Riswan, S., Chai H., de Blanco, E.C.J., Farnsworth, N.R., Swanson, S.M., Kinghorn, A.D., 2009, Cytotoxic xanthone constituents of the stem bark of *Garcinia mangostana* (Mangosteen), *J. Nat. Prod.*, 72, 2028–2031.
- Halliwell, B., dan Gutteridge, J.M.S., 1999, *Free Radicals In Biology and Medecine*, 3th Ed., Oxford University Press. Inc., New York.
- Heffeter, P., Jakupec, M.A., Karner, W., Chiba, P., Pirker, C., Dornetshuber, R., Elbling, L., Sutterluty, H., Micklsche, M., Keppler, B.K., Berger, W., 2007, Multidrug-resistant cancer cells are preferential targets of the new antineoplastic lanthanum compound KP772 (FFC24), *Biochem. Pharmacol.*, 73, 1873-1886.
- Hemmateenejad, B., Javidnia, K., Nematollahi, M., Elyasi, M., 2009, QSAR studies on the antiviral compounds of natural origin, *J. Iran. Chem. Soc.*, 6, 420-435.
- Hoffman, R.V., Weiner, W.S., Maslouh, N., 2001, Highly stereoselective synthesis of anti-n-protected- α -amino epoxides, *J. Org. Chem.*, 66, 5790.
- Hossain, M.A., dan Asada, K., 1985, Monodehydro ascorbate reductase from cucumber is a Flavin adenine dinucleotida enzyme, *J. Biol. Chem.*, 260, 12920-12926.
- Iranshahi, M., Sahebkar, A., Hosseini, S.T., Takasaki, M., Konoshima, T., Tokuda, H., 2010, Cancer chemopreventive activity of divers in from *Ferula diversivitta* *in vitro* and *in vivo*, *Phytomedicine*, 17, 269–273.
- Itharat, A., dan Ooraikul, B., 2007, Research on thai medicinal plants for cancer treatment, *Advances Med. Plant Res.*, 13, 287 – 317.
- Jacquesy, J., Jouannetaud, M., Makani, S., 1980, meta-Bromination of phenols in superacids, *J. Chem. Soc. Commun.*, 110–111.
- Jayashree, B.S., Gurushyam, S., Pai, A., 2016, Synthesis, characterization, antioxidant and anticancer evaluation of some novel flavone-4-oximes, *Asian J. Pharm. Sci.*, 185 – 186.
- Jerzy, G., dan Slawomir, Z., 1997, Oxidative chlorination of acetanilides by metal chlorides Hydrogen peroxide in acid–aqueous medium systems, *Synth. Commun.*, 27, 3291.

- Jun, K-Y., Lee, E-Y., Jung, M-J., Lee, O-H., Lee, E-S., Choo., Na, Y., Kwon, Y., 2011, Synthesis, biological evaluation, and molecular docking study of 3-(30-heteroatom substituted-20-hydroxy-10-propyloxy) xanthone analogues as novel topoisomerase IIa catalytic inhibitor, *Eur. J. Med. Chem.*, 46, 1964-1971.
- Jung, H. A., Su, B. N., Keller, W. J., Mehta, R. G., Kinghorn, A. D., 2006, Antioxidant xanthenes from the pericarp of *Garcinia mangostana* (Mangosteen), *J. Agric. Food Chem.*, 54, 2077.
- Kaomongkolgit, R., Jamdee, K., Chaisomboon, N., 2009, Antifungal activity of alphamangostin against *Candida albicans*, *J. Oral Sci.*, 51, 401-406.
- Kastan, M.B., dan Bartek, J., 2004, Cell-cycle checkpoints and cancer, *Nature*, 432, 316 -323.
- Katritzky, A.R., Kuanar, M., Slavov, S., Hall, C.D., Karelson, M., Kahn, I., Dobchev, D.A., 2010, Quantitative correlation of physical and chemical properties with chemical structure: utility for prediction, *Chem. Rev.*, 110, 5714-5789.
- Kovačević, S.Z., Podunavac-Kuzmanović, S.O., Jevrić, L.R., Vukić, V.R., Savić, M.P., Djurendić, R.A., 2016, reselection of A- and B- modified D-homo lactone and D-seco androstane derivatives as potent compounds with antiproliferative activity against breast and prostate cancer cells QSAR approach and docking molekulanalysis, *Euro. J. Pharm. Sci.*, 93, 107-113.
- Kovalenko, M., Gazit, A., Böhmer, A., Rorsman, C., Rönstrand, L., Heldin C-H., Waltenberger, J., Böhmer, F-D., Levitzki, A., 1994, Selective Platelet-derived Growth Factor Receptor Kinase Blockers Reverse *sis*-Transformation, *Cancer Res.*, 54, 6106 -6114.
- Kuete, V., Sandjo, L.P., Ouete, J.L.N., Fouotsa, H., Wiench, B., Efferth, T., 2014, Cytotoxicity and modes of action of three naturally occurring xanthenes (8-hydroxycudraxanthone *G. morusignin* I and cudraxanthone I) against sensitive and multidrug-resistant cancer, *Phytomedicine*, 21, 315-22.
- Khonkarn R., Mankhetkorn S., Talelli M., Hennink E.W., Okonogi S., 2012, Cytostatic effect of xanthone-loaded mPEG-b-p(HPMAm-Lac2) micelles towards doxorubicin sensitive and resistant cancer cells, *Colloids and Surfaces B: Biointerfaces*, 94, 266- 273.
- Lapenna, S., dan Giordano, A., 2009, Cell cycle kinases as therapeutic targets for cancer, *Nat. Rev. Drug Discov.*, 8, 547 - 566.

- Lawrence, J.L., Patterson, R.P., Ooi Li-Ling, Cook D., Ducki S., 2006, Effects of a-substitutions on structure and biological activity of anticancer chalcones, *Bioorg. Med. Chem. Lett.*, 16, 5844–5848.
- Lee, B.W., Lee, J.H., Lee, S-T., Lee, H.S., Lee, W.S., Jeong, T-S., Park, K.H., 2005, Antioxidant and cytotoxic activities of xanthenes, *Bioorg. Med. Chem. Lett.*, 15, 5548–5552.
- Le, T., Epa, V. C., Burden, F. R., Winkler, D. A., 2012, Quantitative structure-property relationship modeling of diverse materials properties, *Chem. Rev.*, 112, 2889–919.
- Lengauer, T., dan Rarey, M., 1996, Computational method for biomolecular docking, *Current Opinion in Structural Biology*, 6(3), 402 – 406.
- Lennartsson, J., Jelacic, T., Linnekin, D., Shivakrupa, R., 2005, Normal and oncogenic forms of the receptor tyrosine kinase kit, *Stem. Cells*, 23, 16–43.
- Levine, I.N., 2000, *Quantum Chemistry*, Edisi ke-5, Prentice Hall Upper Saddle River, New Jersey.
- Lieberman, M.M., Patterson, G.M.L., Moore, R.E., 2011, In vitro for anticancer drug screening: affect of concentration and assay parameters on growth inhibitory activity, *Cancer Lett.*, 173, 21 -29.
- Likhitwitayawuid, K., Angerhofer, C.K., Cordell, G.A., Pezzuto, J.M., Ruangrunsi, N., 1993, Cytotoxic and antimalarial bisbenzylisoquinoline alkaloids from *Stephania erecta*, *J. Nat. Prod.*, 56(1), 30-38.
- Lim, C.K., Tho, L.Y., Lim L.M., Shah S.A.A., Weber, J-F.F., 2012, Synthesis of 1,3,6-Trioxxygenated Prenylated Xanthone Derivatives as Potential Antitumor Agents, *Lett Org Chem.*, 9(8), 549-555.
- Ling, C.S., 2013, Synthesis and antioxidant activity of prenylated xanthenes derived from 1,3,6-trihydroxyxanthone, *B.Sc Degree*, Faculty of Science Universiti Tunku Abdul Rahman.
- Liu, Y., Ma, L., Chen, W.H., Wang, B., Xu Z-L., 2007, Synthesis of xanthone derivatives with extended p-systems as a-glucosidase inhibitors: Insight into the probable binding mode, *Bioorg. Med. Chem.*, 15, 2810–2814.

- Liu, Y., Zhuofeng, K., Cui, J., Chen, W.H., Ma, L., Wang, B., 2008, Synthesis, inhibitory activities, and QSAR study of xanthone derivatives as α -glucosidase inhibitors, *Bioorg. Med. Chem.*, 16, 7185-7192.
- Luo, C-T., Mao, S-S., Liu, F-L., Yang, M-X., Chen, H., Kurihara, H., Li Y., 2013, Antioxidant xanthenes from *Swertiamussotii*, a high altitude plant, *Fitoterapia*, 91, 140-147.
- Luo, L., Qin, J.K., Dai, Z.K., and Gou, S-H., 2013, Synthesis and biological evaluation of novel benzo[b]xanthone derivatives as potential antitumor agents, *J. Serb. Chem. Soc.*, 78, 1301-1308.
- Lu, J.M., Lin, P.H., Yao, Q., Chen, C., 2010, Chemical and molecular mechanism of antioxidant: experimental approaches and model systems, *J. Cell. Mol. Med.*, 14(4), 840 - 860.
- Mahavorasirikul, W., Viyanant, V., Chaijaroenkul, W., Itharat A., Na-Bangchang, K., 2010, Cytotoxic activity of Thai Medicinal Plants against human cholangiocarcinoma, laryngeal and Hepatocarcinoma cell in vitro, *BMC Compl. Alt. Med.*, 10, 55.
- Mahendran, G., Manoj, M., Muruges, E., Sathish Kumar, R., Shanmughavel, P., Rajendra Prasad, K.J., Narmatha Bai, V., 2014, In vivo anti-diabetic, antioxidant and docking molekul studies of 1,2, 8-trihydroxy-6-methoxy xanthone and 1,2-dihydroxy-6-methoxyxanthone-8-O-d-xylopyranosyl isolated from *Swertia corymbosa*, *Phytomedicine*, 21, 1237-1248.
- Mahajan, T., Kumar, L., Dwivedi, K., and Agarwal, D.D., 2012, Efficient and facile chlorination of industrially-important aromatic compounds using NaCl/p-TsOH/NCS in aqueous media, *Ind. Eng. Chem. Res.*, 51, 3881-3886.
- Majetich, G., Hicks, R., Reister, S., 1997, Electrophilic aromatic bromination using bromodimethyl-sulfonium bromide generated in situ, *J. Org. Chem.*, 62, 4321-4326.
- Martinez, J.D., Parker, M.T., Fultz, K.E., Ignatenko, N.A., Gerner, E.W., 2003, *Molecular Biology of Cancer*, 6th, Vol.5, John Willey and Sons Inc.
- Masters, K.Y., dan Brase S., 2012, Xanthenes from fungi, lichens, and bacteria: the natural products and their synthesis, *Chem. Rev.*, 112, 3717-3776.

- Matsumoto, K., Akao, Y., Kobayashi, E., Ohguchi, K., Ito, T., Tanaka, T., Iinuma, M., Nozawa, Y., 2003, Induction of apoptosis by xanthenes from mangosteen in human leukemia cell lines, *J. Nat. Prod.*, 66, 1124–1127.
- Matsuzawa, N., Seto, J., Dixon, D.A., 1997, Density Functional Theory Predictions of Second-Order Hyperpolarizabilities of Metallocenes, *J. Phys. Chem. A*, 101, 9391-9398.
- Meshram, H. M., Reddy, P. N., Sadashiv, K., Yadav, J. S., 2005, Amberlyst-15-promoted efficient 2-halogenation of 1,3-keto-esters and cyclic ketones using N-halosuccinimides, *Tetrahedron Lett.*, 46, 623.
- Moreau, S., Varache-Lembege, M., Larrouture, S., Fall, D., Neveu, A., Deffieux, G., Vercauteren, J., Nuhrich, A., 2002, (2-Arylhyaazonomethyl)-substituted xanthenes as antimycotics: synthesis and fungistatic activity against *Candida* species, *Eur. J. Med. Chem.*, 37, 237-253.
- Meislich, R., Sharefkin, Nechamkin H., Hademenos G.J., 1999, *Schaum's Outlines of Theory and Problems of Organic Chemistry*, Edisi ke-3, McGraw-Hills.
- Micheal S., dan Kostanecki Y., 1892, Xanthone in synthesis: reactivity via polyphenol and salicylic acid, *Tetrahedron*, 20, 1082-1195.
- Mishra, M., Mishra, V. K., Senger, P., Pathak, A. K., Kashaw, S. K., 2014, Exploring QSAR studies on 4-substituted quinazoline derivatives as antimalarial compounds for the development of predictive models, *Med.Chem. Res.*, 23, 1397 – 1405.
- Michielan, L. dan Moro, S., 2010, Pharmaceutical perspectives of nonlinear QSAR strategies, *J. Chem. Inf. Model.*, 50, 961–978.
- Min-Yang, Z.M., Huang, J., Qin, J.K., Dai, Z.K., Lan, W.L., Su, G.F., Tang, H., Yang, F., 2014, Design, synthesis and biological evaluation of novel 1-hydroxyl-3-aminoalkoxy xanthone derivatives as potent anticancer agents, *Eur. J. Med. Chem.*, 85, 487-497.
- Mohan, K.V.V.K., Narender, N., Srinivasu, P., Kulkarni, S.J., Ragavan, K.V., 2004, Novel bromination method for aniline and anisole using $\text{NH}_4\text{Br}/\text{H}_2\text{O}_2$ in CH_3COOH , *Synth. Commun.*, 34, 2143–2152.
- Molyneux, P., 2004, The Use of Stable Free Radical Diphenylpicrylhydrazin (DPPH) for Estimating Antioxidant Activity, *J. Sci. Tech.*, 2, 211-219.

- Morris, G.M., dan Lim-Wilby, M., 2008, Molecular Docking, *Methods Mol. Biol.*, 443, 365-382
- Mosmann, T., 1983, Rapid colorimetric assay for cellular growth and survival application to proliferation and cytotoxicity assays, *J. Immunol. Methods*, 65, 55 – 63.
- Motta, L.F. dan Almeida, W.P., 2011, Quantitative structure-activity relationships (QSAR) of a series of ketone derivatives as anti-*Candida albicans*, *Int. J. Dru. Disc.*, 3, 100–117.
- Muathen, H. A., 1996, Mild chlorination of aromatic compounds with tin (IV) chloride and lead tetraacetate, *Tetrahedron*, 52, 8863.
- Murahari, M., Kharkar, P.S., Lonikar, N., Mayur, C.Y., 2017, Design, synthesis, biological evaluation, docking molecule and QSAR studies of 2,4-dimethylacridones as anticancer agents, *Eur. J. Med. Chem.*, 130, 154-170.
- Nakatani, K., Atsumi, M., Arakawa, T., Oosawa, K., Shimura, S., Nakahata, N., Ohizumi, Y., 2002, Inhibitions of histamine release and prostaglandin E2 synthesis by mangosteen, a Thai medicinal plant, *Biol. Pharm. Bull.*, 25, 1137–1141.
- Nantasenamat, C., Isarankura-na-ayudhya, C., Naenna, T., 2009, Review article: A practical overview of quantitative structure-activity relationship, *EXCLI Journal*, 8, 74–88.
- Narender, N., Srinivasu, P., Kulkarni, S. J., Raghavan, K. V., 2002, Highly efficient, para-selective oxychlorination of aromatic compounds using potassium chloride and oxone, *Synth. Commun.*, 32, 279.
- Núñez, M.B., F.P. Maguna, N.B., Okulik, E.A., Castro, QSAR modeling of the MAO inhibitory activity of xanthenes derivatives, *Bioorg. Med. Chem. Lett.*, 14, 5611–5617.
- Oliver L., Cordel S., Barbieux I., LeCabellec M.T., Mefflah K., Grégoire M., Vallette F.M., 2002, Resistance to apoptosis is increased during metastatic dissemination of colon cancer, *Clin. Exp. Metastasis*, 19, 175-180.
- Osheroff, N., 1989, Biochemical Basic for The interactions of Type I and Type II Topoisomerases with DNA, *Pharmacol. Ther.*, 41, 223-241.

- Pai, A, Kumar, D.V, Jayashree, B.S., 2016, Synthesis, characterization, antibacterial and anticancer evaluation of some novel flavone-3-ols, *Asian J. Pharm. Sci.*, 187-188.
- Park, M.T., dan Lee, S.J., 2003, Cell cycle and cancer, *J.Bio. Mol. Biol.*, 36(1), 60 -65.
- Pisoni, D. S., Gamba, D., Fonseca, C. V., de Costa, J. S., Petzhold, C. L., de Oliveria, E. R., Ceschi, M. A., 2006, InCl₃/NaClO: A reagent for allylic chlorination of terminal olefins, *J. Braz. Chem. Soc.*, 17, 321.
- Pranowo, H.D., 2011, *Pengantar kimia komputasi*, Lubuk Agung, Bandung.
- Prasad, K.N., Hao, J., Yi, C., Zhang, D., Qiu, S., Jiang Y., Zhang, M., Chen, F., 2009, Antioxidant and anticancer activity of wampee (*Clausena lansium* (Lour.) Skeel) Pell, *J. Biomed. Biotech.*, 1, 1-6.
- Prayong, P., Barusrux, S., Weeraapreeyakul, N., 2008, Cytotoxic activity screening of some indigenous Thai Plants, *Fitoterapia*, 79, 598-601.
- Prior, R.L., Wu, X., Schaich, K., 2005, Standardizes method for the determination of antioxidant capacity and phenolic in food and dietary supplements, *J. Agric. Food Chem.*, 53, 4920 -4302.
- Puzyn, T., Leszczyński, J., Cronin, M.T., 2010, *Recent advances in QSAR studies: Methods and applications*, Springer. USA.
- Paliwal, S., Sharma, J., Paliwal, Shailendra, 2012, Quantitative structure activity relationship analysis of bisbenzofuran cations as antimalarial agents employing multivariate statistical approach, *Indian J. Chem. Sect. B-Org.*, 51, 617-630.
- Podunavac-kuzmanovic, S.O., Cvetkovi, D.D., Barna, D.J., 2009, QSAR analysis of 2-amino or 2-methyl-1-substituted benzimidazoles against *Pseudomonas aeruginosa*, *Int. J. Mol. Sci.*, 10, 1670-1682.
- Qi-meng, R., dan Jia-you, S., 2004, *Fries Rearrangement: A new practical synthesis of 4,4'-dihydroxybenzophenine (I)*, Wuhai University, Hubei.
- Quillian, A.J., dan Scheinmann, F., 1973, Studies in the xanthone series. Part XII. A general synthesis of polyoxygenated xanthenes from benzophenone precursors, *J. Chem. Soc. Perkin Trans I.*, 2, 1329.
- Rajski, S.R., dan Williams, R.M., 1998, DNA cross-linking agents as antitumor drugs, *Chem. Rev.*, 98(8), 2723-279.

- Radisky, D.C., Radisky, E.S., Barrows, E.L., Copp, B.R., Kramer, R., A.Irealnd, C.M., 1993, Novel cytotoxic topoisomerase II inhibiting Pyrroloiminoquinones from Fijian sponge of the genus *Zyssia*, *J. American. Chem. Soc.*, 115, 1632 – 1638.
- Robards, K., Antolovich, M., Prenzler, P.P., Patsalides, L., and McDonald, S., 2002, Methods for Testing Antioxidant Activity, *Analyst.*, 127, 183-198.
- Rocchia, W., Alexov, E., and Honig, B., 2001, Extending the Applicability of the Nonlinear Poisson-Boltzmann Equation: Multiple Dielectric Constants and Multivalent Ions. *J. Phys. Chem. B*, 105, 6507-6514.
- Rode, H.J., 2008, (Ed).Adopsi, *Cytotoxicity and Cell Proliferation*, 4thEd., Roche Dagnostic GmbH, 124 -126.
- Rarey, M., Kramer, B., Lengauer, T., Klebe, G., 1996, A fast flexible docking method using an incremental construction algorithm, *J. Mol. Biol.*, 261, 470–489.
- Roy, K., dan Roy, P.P., 2009, Comparative chemometric modeling of cytochrome 3A4 inhibitory activity of structurally diverse compounds using stepwise MLR , FA-MLR , PLS , GFA , G/PLS and ANN techniques, *Eur. J. Med. Chem.*, 44, 2913–2922.
- Ruske, W., 1964, In *Friedel-Crafts and Related Reactions*; Olah, G. A., Ed.; Interscience Publishers, John Wiley and Sons, New York, 383.
- Saragi, R.T., 2014, Sintesis 3,6-dihidroksixanton dan 3,4,6-trihidroksixanton serta uji aktivitasnya pada penghambatan polimerisasi hem, *Skripsi*, Fakultas MIPA, UGM, Yogyakarta.
- Sakagami, Y., Iinuma, M., Piyasena, K.G., Dharmaratne, H.R., 2005, Antibacterial activity of alpha-mangostin against vancomycin resistant enterococci (VRE) and synergism with antibiotics, *Phytomedicine*, 12, 203–208.
- Saleh, A.M., Taha, O.M., Azis, M.A, Al-Qudah A.M., Abu tayeh R.F., Rizvi, S.A., 2016, Novel anticancer compound [trifluoromethyl-substituted pyrazole N-nucleoside] inhibits FLT3 activity to induce differentiation in acute myeloid leukemia cells, *Cancer Lett.*, 375, 199–208
- Sampath, D., Cortes, J., Estrov, Z., Du, M., Shi, Z., Andreeff, M., Gandhi, V., Plunkett, W., 2006, Pharmacodynamics of cytarabine alone and in combination with 7-hydroxystaurosporine (UCN-01) in AML blasts *in vitro* and during a clinical trial, *Blood.*, 107, 2517–2574.

- Santos, C.M.M., Freitas, M., Ribeiro, D., Gomes, A., Silva, A.M.S., Cavaleiro, J.A.S., Fernandes, E., 2010, 2,3 Diaryl-xanthenes as strong scavengers of reactive oxygen and nitrogen species: A structure-activity relationship study, *Bioorg. Med. Chem.*, 18, 6776-6784
- Schwartz, G.K., dan Shah, M.A., 2005, Targeting the cell cycle: A new approach to cancer therapy, *J. Clin Oncol.*, 2, 9408 – 9421.
- Shchemelinin, I., Sefc, L., Necas, E., 2006, Protein kinase inhibitors, *Folia Biol. (Praha)*, 52, 137–148.
- Sepehri, B., dan Ghavami, R., Design new P-glycoprotein modulators based on docking molekuland CoMFA study of α,β -unsaturated carbonyl-based compounds and oxime analogs as anticancer agents, *J. Mol. Struct.*, 1130, 922-928.
- Setha, B., Gaspersz, F., Fidors, A.P.S., Rahman, S., Mailda, M.N., 2013, Potential of Seweed *Padina sp.* as a Source of Antioxidant, *Int. J. Sci. Tech. Res.*, 26, 221-224.
- Shahlaei, M., 2013, Descriptor selection methods in quantitative structure –activity relationship studies: A review study, *Chem. Rev.*, 113, 8093–8103.
- Shaffer, B.C., Gillet, J.P., Patel, C., Baer, M.R., Bates, S.E., Gottesman, M.M., 2012, Drug resistance: still a daunting challenge to successful treatments of AML, *Drug Resist. Update*, 15, 62 -69.
- Shrestha^a, A.R., Ali, H.I., Ashida, N., Nagamatsu, T., 2008, Antitumor studies. Part 5: Synthesis, antitumor activity, and docking molekulstudy of 5-(monosubstituted amino)-2-deoxo-2-phenyl-5-deazaflavins, *Bioorg. Med. Chem.*, 16, 9161 – 9170.
- Shrestha^b, A.R., Shindo, T., Ashida N, Nagamatsu, T., 2008, Synthesis, biological active molecular design, and molecular docking study of novel deazaflavin–cholestane hybrid compounds, *Bioorg. Med. Chem.*, 15, 8685-8696.
- Suphavanich, K., Maitarad, P., Hannongbua, S., Sutda, P., Suksamrarmn, S., Limtrakul, T., 2009, CoMFA ang CoMSIA studies on a new series of xanthone derivatives agains the oral human epidomoid carcinoma (KB) cancer cell line, *Monatash Chem.*, 140, 273 – 280.

- Suksamrarn, S., Suwannapoch, N., Phakhodee, W., Thanuhiranlert, J., Ratananukul, P., Chimnoi, N., Suksamrarn, A., 2003, Antimycobacterial activity of prenylated xanthenes from the fruits of *Garcinia mangostana*, *Chem. Pharm. Bull. (Tokyo)*, 51, 857–859.
- Susanti, D., Sirat, H.M., Ahmad, F., Ali, R.M., Aimi, N., Hayasaki, Y., Kitajima, M., 2007, Antioxidant and cytotoxic flavonoids from the flower of *Melastoma malabathricum L.*, *Food Chem.*, 103, 710 -716.
- Sousa, E., Paiva, A., Nazareth, N., Gales, L., Damas, A.M., Nascimento, M.S.J., Pinto M., 2009, Bromoalkoxyxanthenes as promising antitumor agents: Synthesis, crystal structure and effect on human tumor cell lines, *Eur. J. Med. Chem.*, 44, 3830–383.
- Sousa, M.E., dan Pinto, M.M.M., 2005, Synthesis of xanthenes: An overview, *Curr. Med. Chem.*, 12, 2447-2479.
- Su, Q.G., Liu, Y., Cai, C.Y., Sun, Y.L., Wang, B., Xian, L.J., 2011, Anti-tumour effects of xanthone derivatives and the possible mechanisms of action, *Invest New Drugs*, 29, 1230–1240.
- Sykes, P., 1985, *A Guidebook to Mechanism in Organic Chemistry*, Edisi ke-6, Longman Scientific Technical, John Wiley and Sons, New York.
- Szkaradek, N., Rapacz, A., Pytka, K., Filipek, B., Siwek, A., Cegla, M., Marona, H., 2013, Synthesis and preliminary evaluation of pharmacological properties of some piperazine derivatives of xanthone, *Bioorg. Med. Chem.*, 21, 514–522.
- Tan, G., Gyllenhaal, C., Soejarto, D.D., 2006, Biodiversity as a source of anticancer drugs, *Curr. Drug Targets.*, 7, 265 – 277.
- Thomas, G., 2007, *Medicinal Chemistry: An Introduction*, Edisi ke-2, John Wiley & Sons Ltd., Chichester.
- Topcu, Z., 2001, DNA topoisomerases as targets for anticancer drugs, *J. Clin. Pharm. Ther.*, 26(6), 405-16.
- Tjahjani, S., dan Widowati, W., 2013, The potency of xanthenes as antioxidant and antimalarial and their synergism with artemisinin *in vitro*, *J. Indian Med. Assoc.*, 63, 95 -99.
- Tsuruo, T., 2003, Molecular cancer therapeutics: recent progress and targets in drug resistance, *Intern. Med.*, 42, 237 – 243.

- Varache-Lembe`ge, M., Moreau, S., Larrouture, S., Montaudon, D., Robert, J., Nuhrich, A., 2008, Synthesis and antiproliferative activity of aryl- and heteroaryl hydrazones derived from xanthone carbaldehydes, *Eur. J. Med. Chem.*, 43, 1336-1343.
- Ventura, C., Latino, D.A.R.S., Martins, F., 2013, Comparison of multiple linear regressions and neural networks based QSAR models for the design of new antitubercular compounds, *Eur. J. Med. Chem.*, 70, 831–845.
- Verma, R.P., Mekapati, S.B., Kuru, A., Hansch, C., 2005, A HKSA review on melanoma toxicity, *Bioorg. Med. Chem.*, 13, 5508–5526.
- Vaqué, M., Arola, A., Aliagas, C., Pujadas, G., 2006, BDT: an easy-to-use front-end application for automation of massive docking tasks and complex docking strategies with AutoDock, *Bioinformatics*, 22, 1803–1804.
- Violette, S., Poulain, L., Dussaulx, E., Pepin, D., Faussat, A.M., Chambaz, J., Lacorte, J.M., Staedel, C., Lesuffleur, T., 2002, Resistance of colon cancer cells to long-term 5-fluorouracil exposure is correlated to the relative level of Bcl-and Bcl-X(L) in addition to Bax and p53 status, *Int. J. Cancer*, 98, 498-504.
- Vyas, P.V., Bhatt, A. K., Ramachandraiah, G., Bedekar, A. V., 2003, Environmentally benign chlorination and bromination of aromatic amines, hydrocarbons and naphthols, *Tetrahedron Lett.*, 44, 4085.
- Vo, T.H., Ngayen, T.N-T., Do, K.Q., Connolly, J.D., Maas, G., Heilmann, J., Werz, U.R., Pham, W.D., Nguyen, D, L-H., 2012, Cytotoxic tetraoxygenated xanthenes from the bark of *Garcinia schomburgkiana*, *Phytochem. Lett.*, 5, 553 - 557.
- Wang, R., Lu, Y., Wang, S., 2003, Comparative evaluation of 11 scoring functions for molecular docking, *J. Med Chem.*, 46, 2287-2303.
- Wei, B.Q., Weaverm, L.H., Ferrari, A.M, Matthews, B.W., Shoichet, B.K., 2004, testing a flexible-receptor docking alogarithm in a model binding site, *J. Mol. Biol.*, 337(5),1161-1182.
- Woo, S., Jung, J., Lee, C., Kwon, Y., Na, Y., 2007, Synthesis of new xanthone analogues and their biological activity testdcytotoxicity, topoisomerase II inhibition, and DNA cross-linking study, *Bioorg. Med. Chem. Lett.*, 17(5), 1163-1166.

- Wu, C., 1998, Structuran and synthetic studies of potential antitumor natural products, *dissertation*, Polytechnic of Virginia Institution and State University, Blacksburg, Virginia.
- Wu, X., Zeng, H., Zhu, X., Ma, Q., Hou, Y., Wu, X., 2013, Novel pyrrolopyridinone derivatives as anticancer inhibitors towards Cdc7: QSAR studies based on dockings by solvation score approach, *Eur. J. Pharm. Sci.*, 50, 323–334.
- Weber, G.F., 2007, *Molecular Mechanisms of Cancer*, Springer, New York.
- Yang, C-H., Ma, L., Zhen-ping, W., Feng, H., Jing, G., 2012, Advances in isolation and synthesis of xanthone derivatives, *Chin. Herb. Med.*, 4, 87-102.
- Yee, B.J., 2011, Chemical synthesis of 1,6 dioxygenated xanthenes and their cytotoxic activities, *B.Sc Degree*, Faculty of Science Universiti Tunku Abdul Rahman.
- Yu, G., Mason, H. J., Wu, X., Endo, M., Douglas, J., Macor, J. E., 2001, A mild and efficient method for aromatic chlorination of electron-rich arylalkyl amines, *Tetrahedron Lett.*, 42, 3247.
- Yu, L., 2001, Free radical scavenging properties of conjugated linolic acids, *J. Agric. Food. Chem.*, 49, 3452 -3456.
- World Health Organization, 2015, <http://www.who.int/cancer/en/>
- Xu, Y., Zhou, J., Zhang, C., Chen, K., Zhang, T., Du, Z., 2014, Synthesis of xanthenes through the palladium-catalyzed carbonylation/C–H activation sequence, *Tetrahedron Lett.*, 55, 6432–6434.
- Zhang, J., Yang, P.L., Gray, N.S., 2009, Targeting cancer with small molecule kinase inhibitors, *Nat. Rev. Cancer*, 9, 28-39.
- Zhang, N., Yin, Y., Xu, S.J., Chen, W.S., 2008, 5-Fluorouracil: Mechanisms of resistance and reversal strategies, *Molecules*, 13, 1551–1569.
- Zhang, Y., 2007, Lewis acid mediated selective halogenation of carbonyl and aromatic compound, *Disertation*, the Faculty of the Division of the Physical Science, The University of Chichago, chichago, Illinois.
- Zhurko, G.A., 2012, Chemcraft Version 1.7 (build 365), Bluesnap Inc., USA.

Zou, Y., Zhao, Q., Hu, H., Hu, L., Yu, S., Xu, M., Wu, Q., 2012, Synthesis and *In Vitro* Antitumor Activities of Xanthone Derivatives Containing 1,4-Disubstituted-1,2,3-triazole Moiety, *Arch. Pharm. Res.*, 35 (12), 2093-2104.

Zare, S., Fereidoonzehad, M., Afshar, D., Ramezani, Z., 2017, A comparative QSAR analysis and molecular docking studies of phenyl piperidine derivatives as potent dual NK1R antagonists/serotonin transporter (SERT) inhibitors, *Comput. Biol. Chem.*, 67, 22–37.