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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

DAFTAR PUSTAKA

Adimi, P. (2011). The Prognostic Importance of EGFR and COX-2 Expression in Cervix Cancer Stages IIb-IVa. *J Cancer Ther*. doi:10.4236/jct.2011.21002

Ahmed, D., Eide, P. W., Eilertsen, I. a, Danielsen, S. a, Eknæs, M., Hektoen, M., … Lothe, R. a. (2013). Epigenetic and genetic features of 24 colon cancer cell lines. *Oncogenesis*, *2*(0424), e71. doi:10.1038/oncsis.2013.35

Aisha, A. F. a, Abu-Salah, K. M., Ismail, Z., & Majid, A. M. S. A. (2012). In vitro and in vivo anti-colon cancer effects of Garcinia mangostana xanthones extract. *BMC Complement and Alt Med*, *12*, 104. doi:10.1186/1472-6882-12-104

Al-Salahi, R., Alswaidan, I., & Marzouk, M. (2014). Cytotoxicity Evaluation of a New Set of 2-Aminobenzo[de]iso-quinoline-1,3-diones. *Int J Mol Sci*, *15*, 22483–22491. doi:10.3390/ijms151222483

Andrade, C. H., Pasqualoto, K. F. M., Ferreira, E. I., & Hopfinger, A. J. (2010). 4D-QSAR: Perspectives in drug design. *Molecules*, *15*, 3281–3294. doi:10.3390/molecules15053281

Ashenden, M., van Weverwijk, A., Murugaesu, N., Fearns, A., Campbell, J., Gao, Q., … Isacke, C. M. (2017). An In Vivo Functional Screen Identifies JNK Signaling As a Modulator of Chemotherapeutic Response in Breast Cancer. *Mol Cancer Ther*, *16*, 1967–1978. doi:10.1158/1535-7163.MCT-16-0731

Ashton, K. S., St, D. J., Jr, J., Poon, S. F., Lee, M. R., Allen, J. G., … Hungate, R. (2011). Bioorganic & Medicinal Chemistry Letters Design and synthesis of novel amide AKT1 inhibitors with selectivity over CDK2. *Bioorg Med Chem Lett*, *21*(18), 5191–5196. doi:10.1016/j.bmcl.2011.07.056

Attardi, L. D., Reczek, E. E., Cosmas, C., Demicco, E. G., McCurrach, M. E., Lowe, S. W., & Jacks, T. (2000). PERP, an apoptosis-associated target of p53, in a novel member of the PMP-22/gas3 family. *Genes Dev*, *14*, 704–718. doi:10.1101/gad.14.6.704

Azevedo, C. M. G., Afonso, C. M. M., Sousa, D., Lima, R. T., Helena Vasconcelos, M., Pedro, M., … Pinto, M. M. M. (2013). Multidimensional optimization of promising antitumor xanthone derivatives. *Bioorg and Med Chem*, *21*, 2941–2959. doi:10.1016/j.bmc.2013.03.079

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Baltus, C. B., Jorda, R., Marot, C., Berka, K., Bazgier, V., Kryštof, V., … Viaud-Massuard, M. C. (2016). Synthesis, biological evaluation and molecular modeling of a novel series of 7-azaindole based tri-heterocyclic compounds as potent CDK2/Cyclin E inhibitors. *Eur J Med Chem*, *108*, 701–719. doi:10.1016/j.ejmech.2015.12.023

Beale, G., Haagensen, E., Thomas, H., Lz, W., Revill, C., Payne, S., … Cano, C. (2017). Combined PI3K and CDK2 inhibition induces cell death and enhances in vivo anti-tumour activity in colorecal cancer. *British J Cancer*, (February). doi:DOI: http://dx.doi.org/10.1038/bjc.2016.238

Belaidi, S., Mazri, R., Belaidi, H., Lanez, T., & Bouzidi, D. (2013). Electronic structure and physico-chemical property relationship for thiazole derivatives. *Asian J Chem*, *25*(16), 9241–9245. doi:10.14233/ajchem.2013.15199

Benazzi, C., Al-Dissi, A., Chau, C. H., Figg, W. D., Sarli, G., Oliveira, J. T. De, & Gärtner, F. (2014). Angiogenesis in spontaneous tumors and implications for comparative tumor biology. *The Sci World J*, *2014*. doi:10.1155/2014/919570

BIO-RAD Laboratories. (2006). *Applications Guide table of contents Table of Contents* (pp. 2–4).

Bradley, C. J., Yabroff, K. R., Dahman, B., Feuer, E. J., Mariotto, A., & Brown, M. L. (2008). Productivity costs of cancer mortality in the United States: 2000-2020. *J Nat Cancer Inst*, *100*, 1763–1770. doi:10.1093/jnci/djn384

Bray, F., Jemal, A., Grey, N., Ferlay, J., & Forman, D. (2012). Global cancer transitions according to the Human Development Index (2008 – 2030): a population-based study. *Lancet Oncol*, *13*(August), 790–801. doi:10.1016/S1470-2045(12)70211-5

Bremer, E., Dam, G. Van, Kroesen, B. J., Leij, L. De, & Helfrich, W. (2006). Targeted induction of apoptosis for cancer therapy : current progress and prospects. *Trends in Mol Med*, *12*(8), 382–393. doi:10.1016/j.molmed.2006.06.002

Buseman, C. M., Wright, W. E., & Shay, J. W. (2012). Is telomerase a viable target in cancer? *Mutation Res*. doi:10.1016/j.mrfmmm.2011.07.006

Bustin, S. A. (2000). Absolute quantification of mrna using real-time reverse transcription polymerase chain reaction assays. *J Mol Endocrinol*, *25*, 169–193. doi:10.1677/jme.0.0250169

Bustin, S. A., & Nolan, T. (2009). Analysis of mRNA Expression by Real-Time PCR. In J. Logan, K. Edwards, & N. Saunders (Eds.), *Real-time PCR: Current Technology and Applications*. Norfolk, UK: Caister Academic Press. Retrieved from https://books.google.co.id/books?isbn=1904455395

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Cancer Chemoprevention Research Center [CCRC]. (2009). Prosedur Tetap Uji Kombinasi dengan Agen Kemoterapi. Retrieved from http://ccrc.farmasi.ugm.ac.id/?page_id=240

Cao, W., Chi, W., Wang, J., Tang, J., & Lu, Y. (2005). promotes Doxorubicin-induced cell apoptosis and anti-cancer effect through downregulation of p21 in p53-deficient tumor cells. *Biochem Biophys Res Comm*, *330*, 1034–1040. doi:10.1016/j.bbrc.2005.02.188

Carvalho, C., Santos, R. X., Cardoso, S., Correia, S., Oliveira, P. J., Santos, M. S., & Moreira, P. I. (2009). Doxorubicin : The Good , the Bad and the Ugly Effect. *Curr Med Chem*, *16*, 3267–3285.

Cavas, M., Beltrán, D., & Navarro, J. F. (2005). Behavioural effects of dimethyl sulfoxide (DMSO): Changes in sleep architecture in rats. *Toxicol Lett*, *157*, 221–232. doi:10.1016/j.toxlet.2005.02.003

Cerimele, F., Battle, T., Lynch, R., Frank, D. A., Murad, E., Cohen, C., … Arbiser, J. L. (2005). Reactive oxygen signaling and MAPK activation distinguish Epstein-Barr Virus (EBV)-positive versus EBV-negative Burkitt's lymphoma. *Proc Nat Acad Sci United States of America*, *102*(1), 175–9. doi:10.1073/pnas.0408381102

Chan, K. M., Hamzah, R., Rahaman, A. A., Jong, V. Y. M., Khong, H. Y., Rajab, N. F., … Inayat-Hussain, S. H. (2012). The pyranoxanthone inophyllin A induces oxidative stress mediated-apoptosis in Jurkat T lymphoblastic leukemia cells. *Food and Chem Toxicol*, *50*, 2916–2922. doi:10.1016/j.fct.2012.04.048

Chang, H. F., Huang, W. T., Chen, H. J., & Yang, L. L. (2010). Apoptotic effects of??-mangostin from the fruit hull of garcinia mangostana on human malignant glioma cells. *Molecules*, *15*(3), 8953–8966. doi:10.3390/molecules15128953

Chattopadhyay, M., Kodela, R., Nath, N., & Barsegian, A. (2012). Hydrogen sulfide-releasing aspirin suppresses NF- k B signaling in estrogen receptor negative breast cancer cells in vitro and in vivo. *Biochem Pharmacol*, *83*(6), 723–732. doi:10.1016/j.bcp.2011.12.019

Chen, T. R., Drabkowski, D., Hay, R. J., Macy, M., & Peterson, W. (1987). WiDr is a derivative of another colon adenocarcinoma cell line, HT-29. *Cancer Genet Cytogenet*, *27*, 125–134. doi:10.1016/0165-4608(87)90267-6

Cheng, J. H., Huang, A.-M., Hour, T. C., Yang, S. C., Pu, Y. S., & Lin, C. N. (2011). Antioxidant xanthone derivatives induce cell cycle arrest and apoptosis and enhance cell death induced by cisplatin in NTUB1 cells associated with ROS. *Eur J Med Chem*, *46*, 1222–1231. doi:10.1016/j.ejmech.2011.01.043

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Chiaradonna, F., Moresco, R. M., Airoldi, C., Gaglio, D., Palorini, R., Nicotra, F., … Alberghina, L. (2012). From cancer metabolism to new biomarkers and drug targets. *Biotechnol Adv*. doi:10.1016/j.biotechadv.2011.07.006

Chou, T. (2006). Theoretical Basis, Experimental Design, and Computerized Simulation of Synergism and Antagonism in Drug Combination Studies. *Pharmacol Rev*, *58*(3), 621–681. doi:10.1124/pr.58.3.10.

Chou, T. (2010). Drug combination studies and their synergy quantification using the chou-talalay method. *Cancer Research*, *70*(2), 440–446. doi:10.1158/0008-5472.CAN-09-1947

Costa, E. (2014). *Design , Synthesis and Biochemical Evaluation of Novel Ck2 and Cdk2 Inhibitors*. Universita degli Studi di Padova.

Coxon, C. R., Anscombe, E., Harnor, S. J., Martin, M. P., Carbain, B., Golding, B. T., … Cano, C. (2017). Cyclin-Dependent Kinase (CDK) Inhibitors: Structure-Activity Relationships and Insights into the CDK-2 Selectivity of 6-Substituted 2-Arylaminopurines. *J Med Chem*, *60*, 1746–1767. doi:10.1021/acs.jmedchem.6b01254

Dachineni, R., Ai, G., Kumar, D. R., Sadhu, S. S., Tummala, H., & Bhat, G. J. (2016). Cyclin A2 and CDK2 as Novel Targets of Aspirin and Salicylic Acid: A Potential Role in Cancer Prevention. *Mol Cancer Res*, *14*, 241–252. doi:10.1158/1541-7786.MCR-15-0360

Dai, M., Yuan, X., Kang, J., Zhu, Z., Yue, R., & Yuan, H. (2013). Synthesis and biological evaluation of phenyl substituted polyoxygenated xanthone derivatives as anti-hepatoma agents. *Eur J Med Chem*, *69*, 159–166.

Dang, B. C. T., Shapiro, C. L., Hudis, C. A., & Effects, I. (2002). Potential Role of Selective COX-2 Inhibitors in Cancer Management Mechanisms of Prostaglandins in Carcinogenesis Mechanisms of Cyclooxygenase in Carcinogenesis. *Cancer Network*, 1–10.

Davis, J. M., Navolanic, P. M., Weinstein-oppenheimer, C. R., Steelman, L. S., Hu, W., Konopleva, M., & Blagosklonny, M. V. (2003). Raf-1 and Bcl-2 Induce Distinct and Common Pathways That Contribute to Breast Cancer Drug Resistance 1. *Clin Cancer Res*, *9*(March), 1161–1170.

De Abreu Costa, L., Ottoni, M. H. F., Dos Santos, M. G., Meireles, A. B., De Almeida, V. G., De Fátima Pereira, W., … Brito-Melo, G. E. A. (2017). Dimethyl sulfoxide (DMSO) decreases cell proliferation and TNF-α, IFN-, and IL-2 cytokines production in cultures of peripheral blood lymphocytes. *Molecules*, *22*, 1–10. doi:10.3390/molecules22111789

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

De Oliveira, D., & Gaudio, A. (2001). BuildQSAR: a new computer program for QSAR analysis. *Quant. Struct-Activ. Relat.*, *19*(6), 599–601.

De Oliveira, P. F., Alves, J. M., Damasceno, J. L., Oliveira, R. A. M., Júnior Dias, H., Crotti, A. E. M., & Tavares, D. C. (2015). Cytotoxicity screening of essential oils in cancer cell lines. *Brazilian J Pharmacognosy*, *25*(2), 183–188. doi:10.1016/j.bjp.2015.02.009

De Ruiter, J. (2005). Principles of Drug Action 1: Resonace and Induction Tutorial, 1–19. Retrieved from https://www.auburn.edu/~deruija/pdareson.pdf

Deng, Y., Shipps, G. W., Zhao, L., Siddiqui, M. A., Popovici-muller, J., Curran, P. J., … Windsor, W. T. (2015). Bioorganic & Medicinal Chemistry Letters Modulating the interaction between CDK2 and cyclin A with a quinoline-based inhibitor. *Bioorg Med Chem Lett*, *24*(1), 199–203. doi:10.1016/j.bmcl.2013.11.041

Diaz-moralli, S., Tarrado-castellarnau, M., Miranda, A., & Cascante, M. (2013). Targeting cell cycle regulation in cancer therapy. *Pharmacol & Ther*, *138*, 255–271.

Duffy, R., Wade, C., & Chang, R. (2012). Discovery of anticancer drugs from antimalarial natural products: A MEDLINE literature review. *Drug Discov Today*, *17*(17-18), 942–953. doi:10.1016/j.drudis.2012.03.013

Eichhorn, M. E., Kleespies, a., Angele, M. K., Jauch, K. W., & Bruns, C. J. (2007). Angiogenesis in cancer: Molecular mechanisms, clinical impact. *Langenbeck's Archives of Surgery*, *392*, 371–379. doi:10.1007/s00423-007-0150-0

Eisinger, A. L., Prescott, S. M., Jones, D. a., & Stafforini, D. M. (2007). The role of cyclooxygenase-2 and prostaglandins in colon cancer. *Prostaglandins and Other Lipid Mediators*, *82*, 147–154. doi:10.1016/j.prostaglandins.2006.05.026

Fernandes, C., Masawang, K., Tiritan, M. E., Sousa, E., De Lima, V., Afonso, C., … Pinto, M. M. (2014). New chiral derivatives of xanthones: Synthesis and investigation of enantioselectivity as inhibitors of growth of human tumor cell lines. *Bioorg and Med Chem*, *22*, 1049–1062. doi:10.1016/j.bmc.2013.12.042

Ferrara, N. (2004). O ncologist Vascular Endothelial Growth Factor as a Target for Anticancer Therapy. *The Oncologist*, *9*(suppl 1), 2–10.

Ferreira, L. G., Dos Santos, R. N., Oliva, G., & Andricopulo, A. D. (2015). Molecular docking and structure-based drug design strategies. *Molecules*, *20*, 13384–13421. doi:10.3390/molecules200713384

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Fessenden, R. J., & Fessenden, J. S. (2010). Senyawa Aromatik. In Syarifudin & Y. Wulandari (Eds.), *Dasar-dasar Kimia Organik* (pp. 203–245). Tangerang: Binarupa Aksara.

Fouche, G., Cragg, G. M., Pillay, P., Kolesnikova, N., Maharaj, V. J., & Senabe, J. (2008). In vitro anticancer screening of South African plants. *J Ethnopharm*, *119*, 455–461. doi:10.1016/j.jep.2008.07.005

Franca, H. S., Rocha, L., Fernande, C. P., Ruiz, A. L. T., & Carvalho, J. E. de. (2013). Antiproliferative activity of the hexanic extract and phloroglucinols from Hypericum brasiliense. *Brazilian J Pharmacognosy*, *23*, 844–847.

Fuggetta, M. P., Lanzilli, G., Tricarico, M., Cottarelli, A., Falchetti, R., Ravagnan, G., & Bonmassar, E. (2006). Effect of resveratrol on proliferation and telomerase activity of human colon cancer cells in vitro. *J Exper Clin Cancer Res*, *25*(July), 189–93. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16918129

Futcher, B., Latter, G. I., Monardo, P., McLaughlin, C. S., & Garrels, J. I. (1999). A Sampling of the Yeast Proteome. *Mol Cell Biol*, *19*(11), 7357–7368. doi:10.1128/MCB.19.11.7357

Gallego, G. A., Díaz Prado, S., Jiménez Fonseca, P., García Campelo, R., Cassinello Espinosa, J., & Antón Aparicio, L. M. (2007). Cyclooxygenase-2 (COX-2): A molecular target in prostate cancer. *Clin and Translational Oncol*, *9*, 694–702. doi:10.1007/s12094-007-0126-0

Garibyan, L., & Avashia, N. (2013). Polymerase Chain Reaction. *J Invest Dermatol*, *133*, e6. doi:10.1038/jid.2013.1

Ghanbari, M., & Asadi, A. (2016). Study of the Cytotoxicity Effect of Doxorubicin-loaded/Folic acid-Targeted Super Paramagnetic Iron Oxide Nanoparticles on AGS Cancer Cell Line. *J Nanomed Nanotechnol*, *7*(2). doi:10.4172/2157-7439.1000368

Greenbaum, D., Colangelo, C., Williams, K., & Gerstein, M. (2003). Comparing protein abundance and mRNA expression levels on a genomic scale. *Genome Biol*, *4*. doi:10.1186/gb-2003-4-9-117

Gunasekaran, S., Anita, B., & Seshadri, S. (2010). Vibrational spectroscopy study of diethyl carbamazine using semi-empirical calculations. *Indian J Pure Appl Phys*, *48*(March), 183–191.

Guo, M., & Hay, B. A. (1999). Cell proliferation and apoptosis. *Curr Opin Cell Biol*, *11*, 745–752.

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Hajrezaie, M., Paydar, M., Looi, C. Y., Maghadamtousi, S. Z., Hassandarvish, P., Salga, M. S., … Abdulla, M. A. (2015). Apoptotic effect of novel Schiff Based. *Scientific Reports*, *5*, 1–11. doi:10.1038/srep09097

Hamad Elgazwy, A. S. S., Ismail, N. S. M., & Elzahabi, H. S. A. (2010). A convenient synthesis and molecular modeling study of novel purine and pyrimidine derivatives as CDK2/cyclin A3 inhibitors. *Bioorg Med Chem*, *18*, 7639–7650. doi:10.1016/j.bmc.2010.08.033

Han, A. R., Kim, J. A., Lantvit, D. D., Kardono, L. B. S., Riswan, S., Chai, H., … Kinghorn, a. D. (2009). Cytotoxic xanthone constituents of the stem bark of Garcinia mangostana (mangosteen). *J Nat Prod*, *72*, 2028–2031. doi:10.1021/np900517h

Hanahan, D., & Weinberg, R. A. (2011). Review Hallmarks of Cancer : The Next Generation. *Cell*, *144*, 646–674. doi:10.1016/j.cell.2011.02.013

Harrington, K. J. (2011). Biology of cancer. *Medicine*, *39*, 689–692.

Harris, R. E., Alshafie, G. a, Abou-Issa, H., & Seibert, K. (2000). Chemoprevention of breast cancer in rats by celecoxib, a cyclooxygenase 2 inhibitor. *Cancer Res*, *60*, 2101–3. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10786667

Houzé, S., Hoang, N., Lozach, O., Bras, J., Meijer, L., Galons, H., & Demange, L. (2014). Several Human Cyclin-Dependent Kinase Inhibitors, Structurally Related to Roscovitine, Are New Anti-Malarial Agents. *Molecules*, *19*, 15237–15257. doi:10.3390/molecules190915237

Hu, B., Mitra, J., Heuvel, S. Van Den, & Enders, H. (2001). S and G 2 Phase Roles for Cdk2 Revealed by Inducible Expression of a Dominant-Negative Mutant in Human Cells S and G 2 Phase Roles for Cdk2 Revealed by Inducible Expression of a Dominant-Negative Mutant in Human Cells. *Mol Cell Biol*, *21*(8), 2755–2766. doi:10.1128/MCB.21.8.2755

Huang, S. Y., & Zou, X. (2010). Advances and challenges in Protein-ligand docking. *Intern J Mol Sci*. doi:10.3390/ijms11083016

Huang, S., & Zou, X. (2007). Efficient molecular docking of NMR structures : Application to HIV-1 protease. *Protein Sci*, *16*, 43–51. doi:10.1110/ps.062501507.a

International Agency for Research on Cancer [IARC] (2013). Latest world cancer statistics Global cancer burden rises to 14 . 1 million new cases in 2012 : Marked increase in breast cancers must be addressed. *IARC*, (December 2013). Retrieved from http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223_E.pdf

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Ibrahim, D. A., & Ismail, N. S. M. (2011). Design, synthesis and biological study of novel pyrido[2,3-d]pyrimidine as anti-proliferative CDK2 inhibitors. *Eur J Med Chem*, *46*, 5825–5832. doi:10.1016/j.ejmech.2011.09.041

Invitrogen. (2010). Cell Culture Basics Handbook. *ThermoFisher Scientific Inc.*, 1–61. Retrieved from papers3://publication/uuid/514B97BF-B151-40A6-9721-B0B41B2B4E3A

Iwamoto, K., Shinomiya, N., & Mochizuki, H. (1999). Different cell cycle mechanisms between UV-induced and X-ray-induced apoptosis in WiDr colorectal carcinoma cells. *Apoptosis*, *4*(1), 59–66. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14634296

Jemal, A., Center, M. M., DeSantis, C., & Ward, E. M. (2010). Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol, Biomarkers & Prev*, *19*(8), 1893–907. doi:10.1158/1055-9965.EPI-10-0437

Jia, B., Li, S., Hu, X., Zhu, G., & Chen, W. (2015). Recent Research on Bioactive Xanthones from Natural Medicine: Garcinia hanburyi. *AAPS PharmSciTech*, *16*(4), 742–58. doi:10.1208/s12249-015-0339-4

Kadowaki, I., Ichinohasama, R., Harigae, H., Ishizawa, K., Okitsu, Y., Kameoka, J., & Sasaki, T. (2005). Accelerated lymphangiogenesis in malignant lymphoma: possible role of VEGF-A and VEGF-C. *British J Haematol*, *130*, 869–877. doi:10.1111/j.1365-2141.2005.05695.x

Kamal, A., Mallareddy, A., & Suresh, P. (2012). Heterocyclics as Inducers of Apoptosis. In *Novel Apoptotic Regulators in Carcinogenesis* (pp. 45–92). doi:10.1007/978-94-007-4917-7

Karelson, M., & Lobanov, V. (1996). Quantum-chemical descriptors in QSAR / QSPR studies. *Chemical Rev*, *96*, 1027–1043. doi:10.1021/cr950202r

Karpova, M., Schoumans, J., Berg, I. E., Henter, J., Nordenskjold, M., & Fadeel, B. (2005). Raji revisited : cytogenetics of the original Burkitt ' s lymphoma cell line. *Leukemia*, *19*, 159–161. doi:10.1038/sj.leu.2403534

Kashif, M., Andersson, C., Hassan, S., Karlsson, H., Senkowski, W., Fryknäs, M., … Gustafsson, M. G. (2015). In vitro discovery of promising anti-cancer drug combinations using iterative maximisation of a therapeutic index. *Scientific Reports*, *5*(August), 14118. doi:10.1038/srep14118

Kementerian Kesehatan Republik Indonesia. (2013). *Peraturan Menteri Kesehatan Republik Indonesia Nomor 87 tahun 2013*. *Kementerian Kesehatan republik Indonesia*. doi:10.1017/CBO9781107415324.004

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Kerbel, R. S. (2008). Tumor angiogenesis. *NEJM*. doi:10.1056/NEJMc081278

Kim, J. H., Kang, M. J., Park, C. U., Kwak, H. J., Hwang, Y., & Koh, G. Y. (1999). Amplified CDK2 and cdc2 activities in primary colorectal carcinoma. *Cancer*, *85*, 546–553. doi:10.1002/(SICI)1097-0142(19990201)85:3<546::AID-CNCR5>3.0.CO;2-0

Kim, K. K., Kawar, N. M., Singh, R. K., Lange, T. S., Brard, L., & Moore, R. G. (2011). Tetrathiomolybdate induces doxorubicin sensitivity in resistant tumor cell lines. *Gynecol Oncol*, *122*, 183–189. doi:10.1016/j.ygyno.2011.03.035

Kopparapu, P. K., Boorjian, S. a, Robinson, B. D., Downes, M., Gudas, L. J., Mongan, N. P., & Persson, J. L. (2013). Expression of VEGF and Its receptors VEGFR1 / VEGFR2 Is Associated with Invasiveness of Bladder Cancer. *Anticancer Res*, *33*, 2381–2390. doi:33/6/2381 [pii]

Korb, O., Stutzle, T., & Exner, T. E. (2009). Empirical scoring functions for advanced Protein-Ligand docking with PLANTS. *J Chem Inf Model*, *49*, 84–96. doi:10.1021/ci800298z

Kroemer, R. T. (2007). Structure-Based Drug Design: Docking and Scoring. *Curr Protein Peptide Sci*, *8*, 312–328. doi:10.2174/138920307781369382

Kuete, V., Sandjo, L. P., Nantchouang, J. L., Fouotsa, H., Wiench, B., & Efferth, T. (2014). Cytotoxicity and modes of action of three naturally occurring xanthones (8-hydroxycudraxanthone G , morusignin I and cudraxanthone I) against sensitive and multidrug-resistant cancer cell lines. *Phytomed*, *21*, 315–322.

Kumar, V., Gupta, G. K., Kaur, K., & Singh, R. (2013). 4-Fluorophenylhydrazones as potential COX-2 inhibitors: A novel, efficient, one pot solid phase synthesis, docking study and pharmacological evaluation. *Med Chem Res*, *22*, 5890–5900. doi:10.1007/s00044-013-0566-8

Kummalue, T., Suntiparpluacha, M., & Jiratchariyakul, W. (2012). Antiproliferative activity of combination of Thai herbal remedy and chemotherapeutic agents on human cancer cell lines. *J Med Plants Res*, *6*(2), 200–205. doi:10.5897/JMPR11.573

Kurumbail, W., & A.M. Stevens, J.K Gierse, J.J McDonald, R.A. Stegeman, J. Y. Pak, D. Gildehaus, J. M iyashiro, T.D Penning, K. Seibert, P. C. Isakson, W. C. S. (1996). "Structural basis for selective inhibition of cyclooxigenase-2 by anti-inflammatory agents." *Nature*, *384(6610):*(December), 400–402.

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Kuwai, T., Kitadai, Y., Tanaka, S., Onogawa, S., Matsutani, N., Kaio, E., … Chayama, K. (2003). Expression of hypoxia-inducible factor-1α is associated with tumor vascularization in human colorectal carcinoma. *Intern J Cancer*, *105*, 176–181. doi:10.1002/ijc.11068

Larson, S. M., Mariani, G., & Strauss, H. W. (2013). Tumor biology as a basis for molecular targeting in cancer. *Clin Trans Imaging*, *1*, 397–406. doi:10.1007/s40336-013-0044-9

Lavecchia, A., & Giovanni, C. D. (2013). Virtual screening strategies in drug discovery: A critical review. *Curr Med Chem*, *20*, 2839–2860. doi:10.2174/09298673113209990001

Leahy, K. M., Ornberg, R. L., Wang, Y., Zweifel, B. S., Koki, A. T., & Masferrer, J. L. (2002). Cyclooxygenase-2 Inhibition by Celecoxib Reduces Proliferation and Induces Apoptosis in Angiogenic Endothelial Cells in Vivo Advances in Brief Cyclooxygenase-2 Inhibition by Celecoxib Reduces Proliferation and Induces Apoptosis in Angiogenic Endothelial C. *Cancer Res*, *62*(23), 625–631.

Lee, C. S., Kim, H., Yu, J., Yu, S. H., Ban, S., Oh, S., … Kim, T. H. (2017). Doxorubicin-loaded oligonucleotide conjugated gold nanoparticles: A promising in vivo drug delivery system for colorectal cancer therapy. *Eur J Med Chem*. doi:10.1016/j.ejmech.2017.08.063

Lee, E., Jeong, K.-W., Jnawali, H. N., Shin, A., Heo, Y.-S., & Kim, Y. (2014). Cytotoxic activity of 3,6-dihydroxyflavone in human cervical cancer cells and its therapeutic effect on c-Jun N-terminal kinase inhibition. *Molecules*, *19*, 13200–11. doi:10.3390/molecules190913200

Lee, L. T., Tsai, H. P., Wang, C. C., Chang, C. N., Liu, W. C., Hsu, H. C., … Iinuma, M. (2013). Guttiferone F from the fruit of Garcinia multiflora and its anti-hepatocellular carcinoma activity. *Biomed and Prev Nutr*, *3*, 247–252. doi:10.1016/j.bionut.2012.10.007

Legan, M., Luzar, B., Marolt, V. F., & Cör, A. (2006). Expression of cyclooxygenase-2 is associated with p53 accumulation in premalignant and malignant gallbladder lesions. *World J Gastroenterol*, *12*(21), 3425–3429.

Legraverend, M., Tunnah, P., Noble, M., Ducrot, P., Ludwig, O., Grierson, D. S., … Endicott, J. (2000). Cyclin-dependent kinase inhibition by new C-2 alkynylated purine derivatives and molecular structure of a CDK2-inhibitor complex. *J Med Chem*, *43*, 1282–1292. doi:10.1021/jm9911130

Levine, A. J. (2011). Introduction: The Changing Directions of p53 Research. *Genes & Cancer*, *2*, 382–384. doi:10.1177/1947601911413463

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Li, B., Gao, Y., Rankin, G. O., Rojanasakul, Y., Cutler, S. J., Tu, Y., … Edwards, J. C. (2015). Chaetoglobosin K induces apoptosis and G2 cell cycle arrest through p53-dependent pathway in cisplatin-resistant ovarian cancer cells. *Cancer Lett*, *356*, 418–433.

Li, W. W., Li, V. W., Hutnik, M., & Chiou, A. S. (2012). Tumor angiogenesis as a target for dietary cancer prevention. *J Oncol*, *2012*. doi:10.1155/2012/879623

Liu, J., & Lin, A. (2005). Role of JNK activation in apoptosis: a double-edged sword. *Cell Res*, *15*(1), 36–42. Retrieved from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15686625

Liu, L. L., He, L. S., Xu, Y., Han, Z., Li, Y. X., Zhong, J. L., … Qian, P. Y. (2013). Caspase-3-dependent apoptosis of citreamicin ε-induced heLa iells Is associated with reactive oxygen species generation. *Chem Res in Toxicol*, *26*, 1055–1063. doi:10.1021/tx4000304

Livak, K. J., & Schmittgen, T. D. (2001). Analysis of Relative Gene Expression Data Using Real- Time Quantitative PCR and the 2 ⌧ ⌬⌬ C T Method. *Methods*, *25*, 402–408. doi:10.1006/meth.2001.1262

Low, K. C., & Tergaonkar, V. (2013). Telomerase: Central regulator of all of the hallmarks of cancer. *Trends in Biochem Sci*. doi:10.1016/j.tibs.2013.07.001

Lu, F., Luo, G., Qiao, L., Jiang, L., Li, G., & Zhang, Y. (2016). Virtual screening for potential allosteric inhibitors of cyclin-dependent kinase 2 from traditional chinese medicine. *Molecules*, *21*, 1–14. doi:10.3390/molecules21091259

MacConaill, L. E., & Garraway, L. a. (2010). Clinical implications of the cancer genome. *J Clin Oncol*, *28*(35), 5219–5228. doi:10.1200/JCO.2009.27.4944

Malek, S. N. A., Phang, C. W., Ibrahim, H., Wahab, N. A., & Sim, K. S. (2011). Phytochemical and cytotoxic investigations of Alpinia mutica rhizomes. *Molecules*, *16*, 583–589. doi:10.3390/molecules16010583

Masters, K. S., & Bräse, S. (2012). Xanthones from fungi, lichens, and bacteria: The natural products and their synthesis. *Chem Rev*. doi:10.1021/cr100446h

McDonald, O., Lackey, K., Davis-Ward, R., Wood, E., Samano, V., Maloney, P., … Hunter, R. (2006). Aza-stilbenes as potent and selective c-RAF inhibitors. *Bioorg Med Chem Lett*, *16*(April 2015), 5378–5383. doi:10.1016/j.bmcl.2006.07.063

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

McGrath, C. F., Pattabiraman, N., Kellogg, G. E., Lemcke, T., Kunick, C., Sausville, E. a, … Gussio, R. (2005). Homology model of the CDK1/cyclin B complex. *J Biomol Struct Dynamics*, *22*, 493–502. doi:10.1080/07391102.2005.10531227

Meenambiga, S. S., Rajagopal, K., & Durga, R. (2015). In silico docking studies on the components of inonotus sp., a medicinal mushroom against cyclooxygenase-2 enzyme. *Asian J Pharmaceutic Clin Res Res*, *8*(3), 142–145.

Meng, X.-Y., Zhang, H.-X., Mezei, M., & Cui, M. (2011). Molecular Docking: A Powerful approach for structure-basde drug discoveryNIH Public Access. *Curr Comput Aided Drug Des*, *7*, 146–157. doi:10.1016/j.surg.2006.10.010.Use

Mikhail, S., Albanese, C., & Pishvaian, M. J. (2015). Cyclin-dependent kinase inhibitors and the treatment of gastrointestinal cancers. *Am J Pathol*, *185*(5), 1185–1197. doi:10.1016/j.ajpath.2015.01.008

Miladiyah, I., Jumina, J., Haryana, S. M., & Mustofa, M. (2017). In silico molecular docking of xanthone derivatives as cyclooxygenase-2 inhibitor agents. *Int J Pharm Pharm Sci*, *9*(3), 98–104.

Miladiyah, I., Jumina, J., Haryana, S. M., & Mustofa, M. (2018). Biological activity, quantitative structure – activity relationship analysis , and molecular docking of xanthone derivatives as anticancer drugs. *Drug Des Dev Ther*, *12*, 149–158.

Miladiyah, I., Tahir, I., Jumina, Mubarika, S., & Mustofa. (2016). Quantitative structure-activity relationship analysis of xanthone derivates as cytotoxic agents in liver cancer cell line HepG2. *Jurnal Molekul*, *11*(1), 143–157.

Mohan, S., Ibrahim, S., Kamalidehghan, B., Syam, S., Sue, K., Saad, N., … Zajmi, A. (2012). Involvement of NF-κB and Bcl2/Bax signaling pathways in the apoptosis of MCF7 cells induced by a xanthone compound Pyranocycloartobiloxanthone A. *Phytomed*, *19*, 1007–1015.

Moorthy, N. S. H. N., Ramos, M. J., & Fernandes, P. A. (2011). Topological , hydrophobicity , and other descriptors on α -glucosidase inhibition : a QSAR study on xanthone derivatives. *J Enzyme Inhib Med Chem*, *26*(May 2010), 755–766. doi:10.3109/14756366.2011.549089

Moossavi, S., & Bishehsari, F. (2012). Inflammation in sporadic colorectal cancer. *Arch Iranian Med*. doi:012153/AIM.0012

Mosmann, T. (1983). Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. *J Immunol Methods*, *65*, 55–63. doi:10.1016/0022-1759(83)90303-4

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Mukesh, B., & Rakesh, K. (2011). MOLECULAR DOCKING : A REVIEW. *IntJ Res in Ayurveda & Pharm*, *2*(6), 1746–1751.

Mukhopadhyay, P., Ali, M. A., Nandi, A., Carreon, P., Choy, H., & Saha, D. (2006). The Cyclin-Dependent Kinase 2 Inhibitor Down-regulates Interleukin-1 B - Mediated Induction of Cyclooxygenase-2 Expression in Human Lung Carcinoma Cells. *Cancer Res*, (3), 1758–1767. doi:10.1158/0008-5472.CAN-05-3317

Naci, D., El Azreq, M. A., Chetoui, N., Lauden, L., Sigaux, F., Charron, D., … Aoudjit, F. (2012). α2β1 integrin promotes chemoresistance against doxorubicin in cancer cells through extracellular signal-regulated kinase (ERK). *J Biol Chem*, *287*(21), 17065–17076. doi:10.1074/jbc.M112.349365

Nakagawa, Y., Iinuma, M., Naoe, T., Nozawa, Y., & Akao, Y. (2007). Characterized mechanism of α-mangostin-induced cell death: Caspase-independent apoptosis with release of endonuclease-G from mitochondria and increased miR-143 expression in human colorectal cancer DLD-1 cells. *Bioorg Med Chem*, *15*, 5620–5628. doi:10.1016/j.bmc.2007.04.071

Nussenbaum, F., & Herman, I. M. (2010). Tumor angiogenesis: Insights and innovations. *J Oncol*. doi:10.1155/2010/132641

Osman, A.-M. M., Bayoumi, H. M., Al-Harthi, S. E., Damanhouri, Z. a, & ElShal, M. F. (2012). Modulation of doxorubicin cytotoxicity by resveratrol in a human breast cancer cell line. *Cancer Cell Int*, *12*, 47. doi:10.1186/1475-2867-12-47

Ottewell, P. D., Woodward, J. K., Lefley, D. V, Evans, C. A., Coleman, R. E., & Holen, I. (2009). Anticancer mechanisms of doxorubicin and zoledronic acid in breast cancer tumor growth in bone. *Mol Cancer Ther*, *8*, 2821–2833. doi:10.1158/1535-7163.MCT-09-0462

Ozdowy, P. J. (2008). *Small-molecule inhibitors of cyclin-dependent kinase 2 (CDK2) and the p53-Mdm2 interaction*. University Muenchen. Retrieved from https://mediatum.ub.tum.de/doc/656378/656378.pdf

Palozza, P., Serini, S., Maggiano, N., Tringali, G., Navarra, P., Ranelletti, F. O., & Calviello, G. (2005). beta-Carotene downregulates the steady-state and heregulin-alpha-induced COX-2 pathways in colon cancer cells. *J Nutr*, *135*(August 2004), 129–36. doi:135/1/129 [pii]

Parekh, B. (2015). QSAR Modeling for Drug Discovery and Development : Applications and Methodology Bhagavati Parekh Category Methods for regres-sion problems Methods 1 . Multiple Linear Regression 2 . Partial Least Squares 3 . Feedforward backpropagation neural network 4 . *Intern J Sci Res*, *4*, 329–331.

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Park, D., & Dilda, P. J. (2010). Mitochondria as targets in angiogenesis inhibition. *Mol Aspects Med*, *31*, 113–131. doi:10.1016/j.mam.2009.12.005

Pinto, M. M. M., Sousa, M. E., & Nascimento, M. S. J. (2005). Xanthone derivatives: new insights in biological activities. *Curr Med Chem*, *12*, 2517–2538.

Poljaková, J., Eckschlager, T., Hřebačková, J., Hraběta, J., & Stiborová, M. (2008). The comparison of cytotoxicity of the anticancer drugs doxorubicin and ellipticine to human neuroblastoma cells. *Interdisciplinary Toxicology*, *1*(2), 186–189. doi:10.2478/v10102-010-0036-9

Prayong, P., Barusrux, S., & Weerapreeyakul, N. (2008). Cytotoxic activity screening of some indigenous Thai plants. *Fitoterapia*, *79*, 598–601. doi:10.1016/j.fitote.2008.06.007

Pugazhendhi, D., & Umamaheswari, T. (2013). In silico methods in Drug Discovery - A Review. *IJARCSSE*, *3*(5), 402–405.

Purnomo, H. (2011). *Molecular Docking PLANTS Penambatan Molekul PLANTS [Protein-Ligand-Ant-System]* (Pertama., pp. 13–21). Yogyakarta: Pustaka Pelajar.

Purnomo, H. (2017). *Desain Molekul Antiiflamasi dan Antikanker Menggunakan HKSA* (Pertama., pp. 60–73). Yogyakarta: Grafika Indah.

Rajasekaran, D., Manoharan, S., Silvan, S., Vasudevan, K., Baskaran, N., & Palanimuthu, D. (2013). Propapoptotic, Anti-Cell Proliferative,Anti-Inflammatory and Anti-Angiogenic Potential of Carnosic Acid during 7, 12-Dimethylbenz[a]anthracene-induced Hamster Buccal Pouch Carcinogenesis. *Afr J Tradit Complement Altern Med*, *10*, 102–111. doi:10.1073/pnas.0703993104

Rapisarda, A., & Melillo, G. (2012). Role of the VEGF/VEGFR Axis in Cancer Biology and Therapy. *Adv Cancer Res*, *114*, 237–267. doi:10.1016/B978-0-12-386503-8.00006-5

Rebouças, E. D. L., Costa, J. J. D. N., Passos, M. J., Passos, J. R. D. S., Hurk, R. Van Den, & Silva, J. R. V. (2013). Real time PCR and importance of housekeepings genes for normalization and quantification of mRNA expression in different tissues. *Brazilian Arch Biol Technol*, *56*(February), 143–154. doi:10.1590/S1516-89132013000100019

Richly, H., Henning, B. F., Kupsch, P., Passarge, K., Grubert, M., Hilger, R. a., … Strumberg, D. (2006). Results of a Phase I trial of sorafenib (BAY 43-9006) in combination with doxorubicin in patients with refractory solid tumors. *Annals Oncol*, *17*(February 2006), 866–873. doi:10.1093/annonc/mdl017

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Rizvi, S. M. D., Shakil, S., & Haneef, M. (2013). A simple click by click protocol to perform docking: Autodock 4.2 made easy for non-bioinformaticians. *EXCLI Journal*, *12*, 830–857.

Robb, C. M., Kour, S., Contreras, J. I., Agarwal, E., Barger, C. J., Rana, S., … Brattain, M. G. (2017). for colorectal cancer therapy. *Oncotarget*, *9*(4). doi:DOI10.18632/oncotarget.23749

Rode, H.-J. (2008). Apoptosis , Cytotoxicity and Cell Proliferation 4th Ed. *Roche Diagnostics GmbH*, 1–178. doi:05242134001

Sadeghi-Aliabadi, H., Minaiyan, M., & Dabestan, A. (2010). Cytotoxic evaluation of doxorubicin in combination with simvastatin against human cancer cells. *Res Pharm Sci*, *5*, 127–133.

Saeki, T., Takashima, S., Tachibana, M., Koga, M., Hiyama, E., Salomon, D. S., … Ohnuma, T. (1999). Inhibitory effect of telomere-mimic phosphorothioate oligodeoxy nucleotides (S-ODNS) on human tumor cell lines. *Oncology*, *57 Suppl 2*(January 2016), 27–36. doi:55272 [pii]\n55272

Schefe, J. H., Lehmann, K. E., Buschmann, I. R., Unger, T., & Funke-Kaiser, H. (2006). Quantitative real-time RT-PCR data analysis: current concepts and the novel "gene expression's C T difference" formula. *J Mol Med*, *84*, 901–910. doi:10.1007/s00109-006-0097-6

Schepetkin, I. A., Kirpotina, L. N., Hammaker, D., Kochetkova, I., Khlebnikov, A. I., Lyakhov, S. A., … Quinn, M. T. (2015). Anti-Inflammatory Effects and Joint Protection in Collagen-Induced Arthritis after Treatment with IQ-1S, a Selective c-Jun N-Terminal Kinase Inhibitor. *J Pharmacol Exp Ther*, *353*(June), 505–516. doi:10.1124/jpet.114.220251

Semenza, G. L. (2008). Hypoxia-inducible factor 1 and cancer pathogenesis. *IUBMB Life*. doi:10.1002/iub.93

Shaaban, S., Gaffer, H. E., Alshahd, M., & Elmorsy, S. S. (2015). Cytotoxic symmetrical thiazolediselenides with increased selectivity against MCF-7 breast cancer cells. *Int J Res Dev Pharm Life Sci*, *4*(4), 1654–1668.

Shibuya, M. (2011). Vascular Endothelial Growth Factor (VEGF) and Its Receptor (VEGFR) Signaling in Angiogenesis: A Crucial Target for Anti- and Pro-Angiogenic Therapies. *Genes & Cancer*, *2*, 1097–1105. doi:10.1177/1947601911423031

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Sholikhah, E. N., Mustofa, Miladiyah, I., Hadanu, R., Tahir, I., Jumina, … Supargiyono. (2007). Cytotoxic activity of N-alkyl and N-benzyl 1,10-phenanthroline derivatives in human cancer cell lines. *Berkala Ilmu Kedokteran*, *39*, 1–6.

Silva, S. R., Bowen, K. a., Rychahou, P. G., Jackson, L. N., Weiss, H. L., Lee, E. Y., … Evers, B. M. (2011). VEGFR-2 expression in carcinoid cancer cells and its role in tumor growth and metastasis. *Int J Cancer*, *128*, 1045–1056. doi:10.1002/ijc.25441

Singh, M., Mckenzie, K., & Ma, X. (2017). Effect of dimethyl sulfoxide on in vitro proliferation of skin fibroblast cells. *J Biotech Res*, *8*, 78–82.

Sobolewski, C., Cerella, C., Dicato, M., & Diederich, M. (2011). Cox-2 inhibitors induce early c-Myc downregulation and lead to expression of differentiation markers in leukemia cells. *Cell Cycle*, *10*(January), 2978–2993. doi:10.4161/cc.10.17.16460

Sobolewski, C., Cerella, C., Dicato, M., Ghibelli, L., & Diederich, M. (2010). The Role of Cyclooxygenase-2 in Cell Proliferation and Cell Death in Human Malignancies. *Intern J Cell Biol*, *2010*, 1–21. doi:10.1155/2010/215158

Su, Q., Liu, Y., Cai, Y., Sun, Y., Wang, B., & Xian, L. (2011). Anti-tumour effects of xanthone derivatives and the possible mechanisms of action. *Invest New Drugs*, *29*, 1230–1240. doi:10.1007/s10637-010-9468-5

Susidarti, R. A., Jenie, R. I., Ikawati, M., Putri, D. D. P., & Meiyanto, E. (2014). Cytotoxic activity and apoptosis induction of 8-hydroxyisocapnolactone-2',3'-diol and its combination with Doxorubicin on MCF-7 and T47D cells. *J Appl Pharmaceutic Sci*, *4*(06), 089–097. doi:10.7324/JAPS.2014.40614

Syahri, J., Yuanita, E., Nurohmah, B., Wathon, M., Syafri, R., Armunanto, R., & Purwono, B. (2017). Xanthone as Antimalarial : QSAR Analysis , Synthesis , Molecular Docking and In-vitro Antimalarial Evaluation. *Oriental J Chem*, *33*, 29–40.

Syam, S., Bustamam, A., Abdullah, R., Sukari, M. A., Hashim, N. M., Ghaderian, M., … Ali, H. M. (2014). β-Mangostin induces p53-dependent G2/M cell cycle arrest and apoptosis through ROS mediated mitochondrial pathway and NfkB suppression in MCF-7 cells. *J Funct Foods*, *6*, 290–304. doi:10.1016/j.jff.2013.10.018

Tacar, O., Sriamornsak, P., & Dass, C. R. (2013). Doxorubicin : an update on anticancer molecular action ,. *J Pharm Pharmacol*, 157–170. doi:10.1111/j.2042-7158.2012.01567.x

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Tang, H., & Chen, C. Y. (2014). Drug Design of Cyclin-Dependent Kinase 2 Inhibitor for Melanoma from Traditional Chinese Medicine. *BioMed Res Int*, *2014*. doi:Article ID 798742, 17 pages, 2014. doi:10.1155/2014/798742

Tantengco, G. A., Limbo, a C., Marco, E., Montaño, N., & Jacinto, D. S. (2015). Cytotoxic activity of crude extract and fractions from Sargassum siliquosum (JG Agardh) and other seaweeds against selected human cancer cell lines. *Int J Biosci*, *7*(August), 207–215. doi:10.12692/ijb/7.2.207-215

Tao, L. Y., Zhang, J. Y., Liang, Y. J., Chen, L. M., Zheng, L. S., Wang, F., … Fu, L. W. (2010). Anticancer effect and structure-activity analysis of marine products isolated from metabolites of mangrove fungi in the South China Sea. *Marine Drugs*, *8*, 1094–1105. doi:10.3390/md8041094

Thaimattam, R., Daga, P., Rajjak, S. A., Banerjee, R., & Iqbal, J. (2004). 3D-QSAR CoMFA, CoMSIA studies on substituted ureas as Raf-1 kinase inhibitors and its confirmation with structure-based studies. *Bioorg Med Chem*, *12*(January 2005), 6415–6425. doi:10.1016/j.bmc.2004.09.029

Tresnasari, K., Takakuwa, T., Ham, M. F., Rahadiani, N., Nakajima, H., & Aozasa, K. (2007). Telomere dysfunction and inactivation of the p16(INK4a)/Rb pathway in pyothorax-associated lymphoma. *Cancer Sci*, *98*, 978–984. doi:10.1111/j.1349-7006.2007.00482.x

Trinchieri, G. (2011). Innate inflammation and cancer: Is it time for cancer prevention? *F1000 Medicine Reports*, *3*(June), 11. doi:10.3410/M3-11

Tsakalozou, E., Eckman, A. M., & Bae, Y. (2012). Combination effects of docetaxel and doxorubicin in hormone-refractory prostate cancer cells. *Biochem Res Intern*, *2012*. doi:10.1155/2012/832059

Tsujii, M., Kawano, S., & DuBois, R. N. (1997). Cyclooxygenase-2 expression in human colon cancer cells increases metastatic potential. *Proc Natl Acad Sci USA*, *94*(April), 3336–3340. doi:10.1073/pnas.94.7.3336

Tuller, T., Kupiec, M., & Ruppin, E. (2007). Determinants of protein abundance and translation efficiency in S. cerevisiae. *PLoS Comput Biol*, *3*(12), 2510–2519. doi:10.1371/journal.pcbi.0030248

United Nations [UN]. (2015). *Transforming Our World: The 2030 Agenda for Sustainable Development*. doi:10.1017/CBO9781107415324.004

Vasudev, N. S., & Reynolds, A. R. (2014). Anti-angiogenic therapy for cancer: Current progress, unresolved questions and future directions. *Angiogenesis*, *17*, 471–494. doi:10.1007/s10456-014-9420-y

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Vogelstein, B., Papadopoulos, N., Velculescu, V. E., Zhou, S., Diaz, L. a, & Kinzler, K. W. (2013). Cancer genome landscapes. *Science*, *339*(March), 1546–58. doi:10.1126/science.1235122

Wahab, R., Gopalan, V., Islam, F., Mamoori, A., Lee, K. T. W., Lu, C. T., & Lam, A. K. Y. (2018). Expression of GAEC1 mRNA and protein and its association with clinical and pathological parameters of patients with colorectal adenocarcinoma. *Exp Mol Pathol*, *104*(October 2017), 71–75. doi:10.1016/j.yexmp.2018.01.004

Wang, L., Zhang, Q., Zhu, G., Zhang, Z., Zhi, Y., Zhang, L., … Tang, W. (2017). Design, synthesis and evaluation of derivatives based on pyrimidine scaffold as potent Pan-Raf inhibitors to overcome resistance. *Eur J Med Chem*, *130*, 86–106. doi:10.1016/j.ejmech.2017.02.041

Weinstein-oppenheimer, C. R., Henríquez-roldán, C. F., Davis, J. M., Henrı, C. F., Navolanic, P. M., Saleh, O. a, … Mccubrey, J. a. (2001). Role of the Raf Signal Transduction Cascade in the in Vitro Resistance to the Anticancer Drug Doxorubicin Role of the Raf Signal Transduction Cascade in the in Vitro Resistance to the Anticancer Drug Doxorubicin 1. *Clin Cancer Res*, *7*(September), 2898–2907.

Weyermann, J., Lochmann, D., & Zimmer, A. (2005). A practical note on the use of cytotoxicity assays. *Intern J Pharmaceutic*, *288*, 369–376. doi:10.1016/j.ijpharm.2004.09.018

Wong, M. L., & Medrano, J. F. (2005). One-Step Versus Two-Step Real- Time PCR. *BioTechniques*, *39*, 75–85. doi:10.2144/05391RV01

Workman, P., Al-lazikani, B., & Clarke, P. A. (2013). Genome-based cancer therapeutics : targets , kinase drug resistance and future strategies for precision oncology. *Curr Opinion in Pharmacol*, *13*, 486–496.

Wun, T., McKnight, H., & Tuscano, J. M. (2004). Increased cyclooxygenase-2 (COX-2): a potential role in the pathogenesis of lymphoma. *Leuk Res*, *28*, 179–190. doi:10.1016/S0145-2126(03)00183-8

Xu, Y., He, K., & Goldkorn, A. (2011). Telomerase Targeted Therapy in Cancer and Cancer Stem Cells. *Clin Adv Hematol Oncol*, *9*(6), 442–455.

Yamaguchi, T., Kurita, T., Nishio, K., Tsukada, J., Hachisuga, T., Morimoto, Y., … Izumi, H. (2015). Expression of BAF57 in ovarian cancer cells and drug sensitivity. *Cancer Sci*, *106*(4), 359–366. doi:10.1111/cas.12612

Yang, C., Ma, L., Wei, Z., Han, F., & Gao, J. (2012). Advances in Isolation and Synthesis of Xanthone Derivatives. *Chinese Herbal Med*, *4*(308), 87–102. doi:10.3969/j.issn.1674-6384.2012.02.003

UNIVERSITAS GADJAH MADA
UJI SITOTOKSISITAS DAN KOMBINASI, KAJIAN QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR) SENYAWA TURUNAN XANTON TERHADAP SEL KANKER KOLOREKTAL (WiDR) dan LIMFOMA (Raji) SERTA MEKANISME AKSINYA SECARA MOLECULAR DOCKING Kajian Ekspresi mRNA COX-2, VEGF, dan Telomerase
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Universitas Gadjah Mada, 2018 | Diunduh dari http://etd.repository.ugm.ac.id/

Yang, Z.M., Huang, J., Qin, J.K., Dai, Z.K., Lan, W.L., Su, G.F., … 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. doi:10.1016/j.ejmech.2014.07.076

Yao, L., Liu, F., Hong, L., Sun, L., Liang, S., Wu, K., & Fan, D. (2011). The function and mechanism of COX-2 in angiogenesis of gastric cancer cells. *J Exp Clin Cancer Res*, *30*, 13. doi:10.1186/1756-9966-30-13

Yi, T., Yi, Z., Cho, S.G., Luo, J., Pandey, M. K., Agarwal, B. B., & Liu, M. (2008). Gambogic acid inhibits angiogenesis and prostate tumor growth by supressing VEGFR2 signaling. *Cancer Res*, *68*(6), 1843–1850. doi:10.1158/0008-5472.CAN-07-5944.Gambogic

Yousefi, B., Rahmati, M., & Ahmadi, Y. (2014). The roles of p53R2 in cancer progression based on the new function of mutant p53 and cytoplasmic p21. *Life Sci*, *99*, 14–17. doi:10.1016/j.lfs.2014.01.063

Yu, Y., Zhang, Y., Shen, N., Zhang, R., & Lu, X. (2014). Effect of VEGF , P53 and telomerase on angiogenesis of gastric carcinoma tissue. *Asian Pacific J Trop Med*, 293–296. doi:10.1016/S1995-7645(14)60041-9

Yuanita, E. (2017). *QSAR, Docking Molekul, dan Sintesis Senyawa Turunan Hidroksixanton sebagai Antikanker dan Antioksidan*. Disertasi. Fakultas Matematika dan Ilmu Pengetahuan Alam (FMIPA), Universitas Gadjah Mada.

Yuanita, E., Pranowo, H. D., Jumina, J., & Mustofa, M. (2016). Design of Hydroxy Xanthones Derivatives As Anticancer Using Quantitative Structure-Activity Relationship. *Asian J Pharmaceutic Clin Res*, *9*(2), 3–8.

Zhang, N., Fu, J. N., & Chou, T. C. (2016). Synergistic combination of microtubule targeting anticancer fludelone with cytoprotective panaxytriol derived from panax ginseng against MX-1 cells in vitro: Experimental design and data analysis using the combination index method. *Am J Cancer Res*, *6*(1), 97–104. doi:10.1124/pr.58.3.10

Zingde, S. M. (2001). Cancer genes. *Curr Sci*, *81*, 509–514.