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Malaysian herbs as potential natural resources of anticancer drugs: From folklore to discovery
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Abstract

Cancer is a complex disease and ranks as a leading cause of death globally. Despite many advances made in cancer therapeutics, adverse side effects and treatment resistance remain a great problem. In that sense, there are increasing demands to discover new anticancer agents from naturally-derived compounds. Medicinal plants represent a valuable source of new drugs with promising efficacy and safety. They produce various secondary metabolites, which exhibit unique structures and a pharmacological spectrum of activity, including antitumour activity. *Clinacanthus nutans*, *Strobilanthes crispus*, *Ficus deltoidea*, *Curcuma longa*, *Centella asiatica* and *Piper betle* are among the plants species commonly used to cure cancer in traditional medicine formulae in Malaysia. The present review aims to highlight the anticancer properties of the listed Malaysian herbs with a focus on their bioactive compounds and the mode of action. Overall, many studies have disclosed the presence of active metabolites in these plants, including phenols, alkaloids, flavonoids, terpenoids, saponin, curcumin and Asiatic acid. They possess significant cytotoxic or antiproliferative effects primarily via the induction of apoptosis, elevation of antioxidant activity and inhibition of cancer activating enzymes. Hence, further investigation into their clinical therapeutic potential may be noteworthy. Additionally, this review article also provides the reader with information concerning the conventional anticancer drugs and their limitations, recent developments and milestones achieved in plant-derived cancer therapeutics as well as different approaches to enhance the production of these anticancer molecules. © 2022, University of Malaya. All rights reserved.

Author Keywords

anticancer; antiproliferative; cytotoxicity; Malaysia; medicinal plants; phytochemical compounds

References

- Abolmaesoomi, M., Aziz, A. A., Junit, S. M., Ali, J. M.
Ficus deltoidei: Effects of solvent polarity on antioxidant and anti-proliferative activities in breast and colon cancer cells
(2019) *European Journal of Integrative Medicine*, 28 (2019), pp. 57-67.
- Abraham, J., Staffurth, J.
Hormonal therapy for cancer
(2016) *Medicine*, 44 (1), pp. 30-33.
- Abrahim, N. N., Kanthimathi, M. S., Abdul-Aziz, A.
Piper betle shows antioxidant activities, inhibits MCF-7 cell proliferation and increases activities of catalase and superoxide dismutase
(2012) *BMC Complementary and Alternative Medicine*, 12 (220), pp. 1-11.
- Agneswari, S., Sheeba, S. N., Ariharan, V. N.
Comparative study on phytochemical, antioxidant and anticancer properties of Centellaasiatica and their impact on P53 expression in MCF-7 Cells
(2021) *Annals of the Romanian Society for Cell Biology*, 25 (3), pp. 7822-7833.
- Ahmad, S. S., Reinius, M. A., Hatcher, H. M., Ajithkumar, T. V.
Anticancer chemotherapy in teenagers and young adults: Managing long term side effects
(2016) *British Medical Journal (Clinical Research Ed.)*, 354 (i4567), pp. 1-8.

- Aizad, S., Irwan, S.
Centella asiatica extract potentiates anticancer activity in an improved 3-D PHBV-composite-CMC A549 lung cancer microenvironment scaffold
(2020) *Arabian Journal for Science and Engineering*, 46 (2021), pp. 5313-5325.
- Aizad, S., Khairiri, N. M., Yahaya, B. H., Zaibairi, S. I.
A novel anti-proliferative activity (EC50) of Pegaga (Centella asiatica) extract through in vitro 3-D culture microenvironment
(2017) *Jurnal Teknologi*, 79 (2), pp. 1-10.
- Akhir, N. A. M., Chua, L. S., Majid, F. A. A., Sarmidi, M. R.
Cytotoxicity of aqueous and ethanolic extracts of Ficus deltoidea on human ovarian carcinoma cell line
(2011) *British Journal of Medicine & Medical Research*, 1 (4), pp. 397-409.
- Al-Henhena, N., Khalifa, S. A. M., Poh, R., Ying, Y., Ismail, S., Hamadi, R., Shawter, A. N., El-seedi, H. R.
Evaluation of chemopreventive potential of Strobilanthes crispus against colon cancer formation in vitro and in vivo
(2015) *BMC Complementary and Alternative Medicine*, 15 (1), pp. 1-11.
- Al-Koshab, M., Alabsi, A. M., Bakri, M. M., Ali-saeed, R., Naicker, M. S.
Antitumor activity of Ficus deltoidea extract on oral cancer: an in vivo study
(2020) *Journal of Oncology*, 2020, pp. 1-10.
- Alam, A., Ferdosh, S., Ghafoor, K., Hakim, A., Juraimi, A. S., Sarker, Z. I.
Clinacanthus nutans: A review of the medicinal uses, pharmacology and phytochemistry
(2016) *Asian Pacific Journal of Tropical Medicine*, 9 (4), pp. 402-409.
- Alam, B., Majumder, R., Akter, S., Lee, S. H.
Piper betle extracts exhibit antitumor activity by augmenting antioxidant potential
(2015) *Oncology Letters*, 9 (2), p. 863.
- Aleksandrowicz, R., Taciak, B., Krol, M.
Drug delivery systems improving chemical and physical properties of anticancer drugs currently investigated for treatment of solid tumors
(2017) *Journal of Physiology and Pharmacology*, 68 (2), pp. 165-174.
- Ardalani, H., Avan, A., Ghayour-Mobarhan, M.
Podophyllotoxin: A novel potential natural anticancer agent
(2017) *Avicenna Journal of Phytomedicine*, 7 (4), pp. 285-294.
- Asadi-samani, M., Kooti, W.
A systematic review of Iran's medicinal plants with anticancer effects
(2016) *Journal of Evidence-Based Complementary & Alternative Medicine*, 21 (2), pp. 143-153.
- Ashraf, M. A.
Phytochemicals as potential anticancer drugs: time to ponder nature's bounty
(2020) *BioMed Research International*, 2020, pp. 1-7.
- Atiya, A., Salim, M. A., Sinha, B. N., Lal, U. R., Linn, P.
Two new anticancer phenolic derivatives from leaves of Piper betle Linn
(2021) *Natural Product Research*, 35 (23), pp. 5021-5029.
- Atiya, A., Sinha, B. N., Lal, U. R.
The new ether derivative of phenylpropanoid and bioactivity was investigated from the leaves of Piper betle L
(2020) *Natural Product Research*, 34 (5), pp. 638-645.

- Babykutty, S., Padikkala, J., Sathiadevan, P. P., Vijayakurup, V., Azis, T. K. A., Srinivas, P., Gopala, S.
Apoptosis induction of Centella asiatica on human breast cancer cells
(2009) *African Journal of Traditional, Complementary and alternative Medicines*, 6 (1), pp. 9-16.
- Bao, B., Ali, S., Banerjee, S., Wang, Z., Logna, F., Azmi, A. S., Kong, D., Sarkar, F. H.
Curcumin analogue CDF inhibits pancreatic tumor growth by switching on suppressor microRNAs and attenuating EZH2 expression
(2012) *Cancer Research*, 72 (1), pp. 335-345.
- Baraya, Y. S., Wong, K. K., Yaacob, N. S.
Strobilanthes crispus inhibits migration, invasion and metastasis in breast cancer
(2018) *Journal of Ethnopharmacology*, 233, pp. 13-21.
- Boontha, S., Taowkaen, J., Phakwan, T.
Evaluation of antioxidant and anticancer effects of Piper betle L (Piperaceae) leaf extract on MCF-7 cells, and preparation of transdermal patches of the extract
(2019) *Tropical Journal of Pharmaceutical Research*, 18 (6), pp. 1265-1272.
- Bunawan, H., Amin, N. M., Bunawan, S. N., Baharum, S. N., Noor, N. M.
Ficus deltoidea Jack: A review on its phytochemical and pharmacological importance
(2014) *Evidence-Based Complementary and Alternative Medicine*, 2014, pp. 1-8.
- Cai, Y. J., Lu, J. J., Zhu, H., Xie, H., Huang, M., Lin, L. P., Zhang, X. W., Ding, J.
Salvinine triggers DNA double-strand breaks and apoptosis by GSH-depletion-driven H₂O₂ generation and topoisomerase II inhibition
(2008) *Free Radical Biology and Medicine*, 45 (5), pp. 627-635.
- Cao, Z., Shang, B., Zhang, G., Miele, L., Sarkar, F. H., Wang, Z., Zhou, Q.
Tumor cell-mediated neovascularization and lymphangiogenesis contrive tumor progression and cancer metastasis
(2013) *Biochimica et Biophysica Acta-Reviews on Cancer*, 1836 (2), pp. 273-286.
- Chakraborty, J. B., Mahato, S. K., Joshi, K., Shinde, V., Rakshit, S., Biswas, N., Choudhury Mukherjee, I., Bandyopadhyay, S.
Hydroxychavicol, a Piper betle leaf component, induces apoptosis of CML cells through mitochondrial reactive oxygen species-dependent JNK and endothelial nitric oxide synthase activation and overrides imatinib resistance
(2012) *Cancer Science*, 103 (1), pp. 88-99.
- Chaurasia, S., Chaubey, P., Patel, R. R., Kumar, N., Mishra, B.
Curcumin-polymeric nanoparticles against colon-26 tumor-bearing mice: cytotoxicity, pharmacokinetic and anticancer efficacy studies
(2016) *Drug Development and Industrial Pharmacy*, 42 (5), pp. 694-700.
- Chen, T. C., da Fonseca, C. O., Schönthal, A. H.
Preclinical development and clinical use of perillyl alcohol for chemoprevention and cancer therapy
(2015) *American Journal of Cancer Research*, 5 (5), pp. 1580-1593.
- Chong, H. Z., Rahmat, A., Yeap, S. K., Akim, A. M., Alitheen, N. B., Othman, F., Gwendoline-Ee, C. L.
In vitro cytotoxicity of Strobilanthes crispus ethanol extract on hormone dependent human breast adenocarcinoma MCF-7 cell
(2012) *BMC Complementary Alternative Medicine*, 12, pp. 1-10.
2012
- Chong, Y. H., Koh, R. Y., Pick, A., Ling, K., Chye, S. M., Yew, M. Y.
Strobilanthes crispus extract induces apoptosis through enhanced caspases

activities in cervical cancer cells [paper presentation]

(2014) *International Conference on Biological, Environment and Food Engineering (BEFE-2014)*,
Bali, Indonesia

- Coricovac, D., Dehelean, C. A., Pinzaru, I., Mioc, A., Aburel, O. M., Macasoi, I., Draghici, G. A., Muntean, M. D.

Assessment of betulinic acid cytotoxicity and mitochondrial metabolism impairment in a human melanoma cell line

(2021) *International Journal of Molecular Sciences*, 22 (9), pp. 1-22.

- Corrie, P. G.

Cytotoxic chemotherapy: Clinical aspects

(2011) *Medicine*, 39 (12), pp. 717-722.

- Cragg, G. M., Pezzuto, J. M.

Natural products as a vital source for the discovery of cancer chemotherapeutic and chemopreventive agents

(2016) *Medical Principles and Practice*, 25 (2), pp. 41-59.

- Dancey, J., Eisenhauer, E. A.

Current perspectives on camptothecins in cancer treatment

(1996) *British Journal of Cancer*, 74 (3), pp. 327-338.

- Danciu, C., Vlaia, L., Fetea, F., Hancianu, M., Coricovac, D. E., Ciurlea, S. A., Šoica, C. M., Trandafirescu, C.

Evaluation of phenolic profile, antioxidant and anticancer potential of two main representants of Zingiberaceae family against B164A5 murine melanoma cells

(2015) *Biological Research*, 48 (1), pp. 1-9.

- Dehelean, C. A., Marcovici, I., Soica, C., Mioc, M., Coricovac, D., Iurciuc, S., Cretu, O. M., Pinzaru, I.

Plant-derived anticancer compounds as new perspectives in drug discovery and alternative therapy

(2021) *Molecules*, 26 (1109), pp. 1-29.

- Delmonte, A., Sessa, C.

AVE8062: A new combretastatin derivative vascular disrupting agent

(2009) *Expert Opinion on Investigational Drugs*, 18 (10), pp. 1541-1548.

- Drake, C. G.

Basic overview of current immunotherapy approaches in urologic malignancy

(2006) *Urologic Oncology: Seminars and Original Investigations*, 24 (5), pp. 413-418.

- Espinosa, E., Zamora, P., Feliu, J., González Barón, M.

Classification of anticancer drugs-a new system based on therapeutic targets

(2003) *Cancer Treatment Reviews*, 29 (6), pp. 515-523.

- Fathilah, A. R., Sujata, R., Norhanom, W. A., Ilham, M. I.

Antiproliferative activity of aqueous extract of Piper betle L. and Psidium guajava L. on KB and HeLa cell lines

(2010) *Journal of Medicinal Plant Research*, 4 (11), pp. 987-990.

- Fazil, F. N. M., Azzimi, N. S. M., Yahaya, B. H., Kamalaldin, N. A., Zubairi, S. I.

Kinetics extraction modelling and antiproliferative activity of Clinacanthus nutans water extract

(2016) *The Scientific World Journal*, 2016, pp. 1-8.

- Fridlender, M., Kapulnik, Y., Koltai, H.

Plant derived substances with anti-cancer activity: from folklore to practice

(2015) *Frontiers in Plant Science*, 6 (799), pp. 1-9.

- Garanti, T., Alhnan, M. A., Wan, K.
RGD-decorated solid lipid nanoparticles enhanced tumor targeting, penetration and anticancer effect of asiatic acid
(2020) *Nanomedicine*, 15 (16), pp. 1567-1583.
- Garcia-Oliveira, P., Otero, P., Pereira, A. G., Chamorro, F., Carpena, M., Echave, J., Fraga-Corral, M., Prieto, M. A.
Status and challenges of plant-anticancer compounds in cancer treatment
(2021) *Pharmaceuticals*, 14 (2), pp. 1-28.
- Gezici, S., Şekeroğlu, N.
Current perspectives in the application of medicinal plants against cancer: novel therapeutic agents
(2019) *Anti-Cancer Agents in Medicinal Chemistry*, 19 (1), pp. 101-111.
- Ghasemzadeh, A., Jaafar, H. Z. E., Rahmat, A.
Phytochemical constituents and biological activities of different extracts of Strobilanthes crispus (L.) Bremek leaves grown in different locations of Malaysia
(2015) *BMC Complementary and Alternative Medicine*, 15 (422), pp. 1-10.
- *Medicinal Herbs and Plant Database*,
Accessed 29 Jun 2021
- Gordaliza, M.
Natural products as leads to anticancer drugs
(2007) *Clinical and Translational Oncology*, 9 (12), pp. 767-776.
- Gordani, N., Cheong, B. E., Teoh, P. L.
Antiproliferative effect of Strobilanthes crispus on MCF-7 cell line
(2017) *Transactions on Science and Technology*, 4 (3-3), pp. 414-419.
- Gradishar, W. J.
Taxanes for the treatment of metastatic breast cancer
(2012) *Breast Cancer: Basic and Clinical Research*, 6 (1), pp. 159-171.
- Gundala, S. R., Yang, C., Mukkavilli, R., Paranjpe, R., Brahmbhatt, M., Pannu, V., Cheng, A., Aneja, R.
Hydroxychavicol, a betel leaf component, inhibits prostate cancer through ROS-driven DNA damage and apoptosis
(2014) *Toxicology and Applied Pharmacology*, 280 (1), pp. 86-96.
- Hamid, I. W., Widjaja, N. M. R., Damayanti, R.
Anticancer activity of Centella asiatica leaves extract in Benzo(a)pyrene-induced mice
(2016) *International Journal Pharmacognosy Phytochemical Research*, 8 (1), pp. 80-84.
- Hamidpour, R., Hamidpour, S., Hamidpour, M., Sohraby, M., Hamidpour, R.
Turmeric (Curcuma longa): From a variety of traditional medicinal applications to its novel roles as active antioxidant, anti-inflammatory, anti-cancer, and anti-diabetes
(2015) *International Journal of Pharmacology, Phytochemistry and Ethnomedicine*, 1, pp. 37-45.
- Han, A., Lee, S., Han, S., Lee, Y. J., Kim, J., Seo, E. K., Jung, C.
Triterpenoids from the leaves of Centella asiatica inhibit ionizing radiation-induced migration and invasion of human lung cancer cells
(2020) *Evidence-Based Complementary and Alternative Medicine*, 2020, pp. 1-20.
- Hanafi, M. M. M., Afzan, A., Yaakob, H., Aziz, R., Sarmidi, M. R., Wolfender, J., Prieto, J. M.
In vitro pro-apoptotic and anti-migratory effects of Ficus deltoidea L. plant extracts

on the human prostate cancer cell lines

(2017) *Frontiers in Pharmacology*, 8 (895), pp. 1-20.

- Hartojo, W., Silvers, A. L., Thomas, D. G., Seder, C. W., Lin, L., Rao, H., Wang, Z., Chang, A. C.

Curcumin promotes apoptosis, increases chemosensitivity, and inhibits nuclear factor κB in esophageal adenocarcinoma

(2010) *Translational Oncology*, 3 (2), pp. 99-108.

- Honari, M., Shafabakhsh, R., Reiter, R. J., Mirzaei, H., Asemi, Z.

Resveratrol is a promising agent for colorectal cancer prevention and treatment: focus on molecular mechanisms

(2019) *Cancer Cell International*, 19 (1), pp. 1-8.

- Huang, D., Guo, W., Gao, J., Chen, J., Olatunji, J. O.

Clinacanthus nutans (Burm. f.) lindau ethanol extract inhibits hepatoma in mice through upregulation of the immune response

(2015) *Molecules*, 20 (9), pp. 17405-17428.

- Hursting, S. D., Slaga, T. J., Fischer, S. M., DiGiovanni, J., Phang, J. M.

Mechanism-based cancer prevention approaches: targets, examples, and the use of transgenic mice

(1999) *Journal of the National Cancer Institute*, 91 (3), pp. 215-225.

- Hussin, F., Eshkoor, S. A., Rahmat, A., Othman, F., Akim, A.

The Centella asiatica juice effects on DNA damage, apoptosis and gene expression in hepatocellular carcinoma (HCC)

(2014) *BMC Complementary and Alternative Medicine*, 14 (32), pp. 1-7.

- Iqbal, J., Abbasi, B. A., Mahmood, T., Kanwal, S., Ali, B., Shah, S. A., Khalil, A. T.

Plant-derived anticancer agents: a green anticancer approach

(2017) *Asian Pacific Journal of Tropical Biomedicine*, 7 (12), pp. 1129-1150.

- Iqbal, M., Shah, M. D., Lie, C. A., San, C.

Strobilanthes crispus attenuates renal carcinogen, iron nitrilotriacetate (Fe-NTA)-mediated oxidative damage of lipids and DNA

(2010) *Molecular and Cellular Biochemistry*, 341 (1-2), pp. 271-277.

- Ingle, K. P., Deshmukh, A. G., Padole, D. A., Dudhare, M. S., Moharil, M. P., Khelurkar, V. C.

Phytochemicals: extraction methods, identification and detection of bioactive compounds from plant extracts

(2017) *Journal of Pharmacognosy and Phytochemistry*, 6 (1), pp. 32-36.

- (2018) *Latest global cancer data: cancer burden rises to 18.1 million new cases and 9.6 million cancer deaths in 2018*,

Accessed 20 June 2021

- Ismail, N. Z., Toha, Z. M., Muhamad, M., Kamal, N. N. S. N., Zain, N. N. M., Arsal, H.

Antioxidant effects, antiproliferative effects, and molecular docking of Clinacanthus nutans leaf extracts

(2020) *Molecules*, 25 (9), pp. 1-18.

- Jain, S., Dwivedi, J., Jain, P. K., Satpathy, S., Patra, A.

Medicinal plants for treatment of cancer: A brief review

(2016) *Pharmacognosy Journal*, 8 (2), pp. 87-102.

- Jaksa, S., Rahmat, a., Othman, F., Ismail, P., Mansor, S. M. H.

Effect of Strobilanthes crispus on the histology and tumour marker enzymes in rat liver during hepatocarcinogenesis

(2005) *Journal of Medical Sciences*, 5 (2), pp. 130-135.

- Jeyaraju, D. V., Hurren, R., Wang, X., MacLean, N., Gronda, M., Shamas-Din, A., Minden, M. D., Schimmer, A. D.
A novel isoflavone, ME-344, targets the cytoskeleton in acute myeloid leukemia
(2016) *Oncotarget*, 7 (31), pp. 49777-49785.
- Kelly, K., Crowley, J., Bunn, J., Presant, C. A., Grevstad, P. K., Moinpour, C. M., Ramsey, S. D., Gandara, D. R.
Randomized phase III trial of paclitaxel plus carboplatin versus vinorelbine plus cisplatin in the treatment of patients with advanced non-small-cell lung cancer: A Southwest Oncology Group trial
(2001) *Journal of Clinical Oncology*, 19 (13), pp. 3210-3218.
- Khan, S., Imran, M., Butt, T. T., Ali Shah, S. W., Sohail, M., Malik, A., Das, S., Hussain, Z.
Curcumin based nanomedicines as efficient nanoplatform for treatment of cancer: New developments in reversing cancer drug resistance, rapid internalization, and improved anticancer efficacy
(2018) *Trends in Food Science and Technology*, 80 (2018), pp. 8-22.
- Kim, K. B., Kim, K., Bae, S., Choi, Y., Cha, H. J., Kim, S. Y., Lee, J. H., An, S.
MicroRNA-1290 promotes asiatic acid-induced apoptosis by decreasing BCL2 protein level in A549 non-small cell lung carcinoma cells
(2014) *Oncology Reports*, 32 (3), pp. 1029-1036.
- Klaunig, J. E.
Oxidative stress and cancer
(2019) *Current Pharmaceutical Design*, 24 (40), pp. 4771-4778.
- Koh, R. Y., Lim, F. P., Ling, L. S. Y., Ng, C. P. L., Liew, S. F., Yew, M. Y., Tiong, Y. L., Ng, K. Y.
Anticancer mechanisms of Strobilanthes crispa Blume hexane extract on liver and breast cancer cell lines
(2017) *Oncology Letters*, 14, pp. 4957-4964.
- Koh, R. Y., Sim, Y. I. C. H. I., Toh, H. J. I. N., Liam, L. K., Ong, R. S. L., Yew, M. Y., Tiong, Y. L., Ng, K. Y.
Cytotoxic and apoptogenic effects of Strobilanthes crispa Blume extracts on nasopharyngeal cancer cells
(2015) *Molecular Medicine Reports*, 12, pp. 6293-6299.
- Koury, J., Lucero, M., Cato, C., Chang, L., Geiger, J., Henry, D., Hernandez, J., Tran, A.
Immunotherapies: Exploiting the immune system for cancer treatment
(2018) *Journal of Immunology Research*, 2018, pp. 1-15.
- Kukula-Koch, W., Grabarska, A., Łuszczki, J., Czernicka, L., Nowosadzka, E., Gumbarewicz, E., Jarząb, A., Stepulak, A.
Superior anticancer activity is demonstrated by total extract of Curcuma longa L. as opposed to individual curcuminoids separated by centrifugal partition chromatography
(2018) *Phytotherapy Research*, 32 (5), pp. 933-942.
- Kumar, S., Kumar, R., Khan, A.
Medicinal plant resources: manifestation and prospects of life-sustaining healthcare system
(2011) *Continental Journal of Biological Sciences*, 4 (1), pp. 19-29.
- Kusmardi, K., Aryo, T., Puspita, E. W., Fadilah, F., Bambang, P. P., Wilzar, F.
In silico, in vitro and in vivo tests of Ficus deltoidea jack leaves extract as inhibitor for β-Catenin expression in colon carcinogenesis model
(2018) *Pharmacognosy Journal*, 10 (4), pp. 808-813.

- Kwon, K. J., Bae, S., Kim, K., An, I. S., Ahn, K. J., An, S., Cha, H. J.
Asiaticoside, a component of Centella asiatica, inhibits melanogenesis in B16F10 mouse melanoma
(2014) *Molecular Medicine Reports*, 10, pp. 503-507.
- Labban, L.
Medicinal and pharmacological properties of turmeric (*Curcuma longa*): A review
(2014) *International Journal of Biomedical Science*, 555 (111), pp. 17-2317.
- Li, X., Ma, S., Yang, P., Sun, B., Zhang, Y., Sun, Y., Hao, M., Jia, Y.
Anticancer effects of curcumin on nude mice bearing lung cancer A549 cell subsets SP and NSP cells
(2018) *Oncology Letters*, 16 (5), pp. 6756-6762.
- Lichota, A., Gwozdzinski, K.
Anticancer activity of natural compounds from plant and marine environment
(2018) *International Journal of Molecular Sciences*, 19 (11), pp. 1-38.
- Liu, J., Wang, X., Liu, P., Deng, R., Lei, M., Chen, W., Hu, L.
20(S)-Protopanaxadiol (PPD) analogues chemosensitize multidrug-resistant cancer cells to clinical anticancer drugs
(2013) *Bioorganic and Medicinal Chemistry*, 21 (14), pp. 4279-4287.
- Liu, Y., Chuang, Y., Lo, Y., Lin, C., Hsi, Y., Hsieh, M., Chen, M.
Asiatic acid, extracted from Centella asiatica and induces apoptosis pathway through the phosphorylation p38 mitogen-activated protein kinase in cisplatin-resistant nasopharyngeal carcinoma cells
(2020) *Biomolecules*, 10 (2), pp. 1-13.
- Lü, S., Wang, J.
Homoharringtonine and omacetaxine for myeloid hematological malignancies
(2014) *Journal of Hematology and Oncology*, 7 (1), pp. 1-10.
- Mahato, R., Tai, W., Cheng, K.
Prodrugs for improving tumor targetability and efficiency
(2011) *Advanced Drug Delivery Reviews*, 63 (8), pp. 659-670.
- Mansouri, K., Rasoulpoor, S., Daneshkhah, A., Abolfathi, A., Salari, N., Mohammadi, M., Shabani, S.
Clinical effects of curcumin in enhancing cancer therapy: A systematic review
(2020) *BMC Cancer*, 20 (791), pp. 1-11.
- Meegan, M. J., O'Boyle, N. M.
Special issue "anticancer drugs"
(2019) *Pharmaceuticals*, 12 (3), pp. 1-6.
- Miao, Z. H., Tang, T., Zhang, Y. X., Zhang, J. S., Ding, J.
Cytotoxicity, apoptosis induction and downregulation of MDR-1 expression by the anti-topoisomerase II agent, salvinine, in multidrug-resistant tumor cells
(2003) *International Journal of Cancer*, 106 (1), pp. 108-115.
- Miller, K. D., Siegel, R. L., Lin, C.C., Mariotto, A. B., Kramer, J. L., Rowland, J. H., Yabroff, K. R., Siegel, R. L.
Cancer treatment and survivorship statistics, 2019
(2019) *CA: A Cancer Journal for Clinicians*, 69 (5), pp. 271-289.
- Mirahmadi, M., Azimi-Hashemi, S., Saburi, E., Kamali, H., Pishbin, M., Hadizadeh, F.
Potential inhibitory effect of lycopene on prostate cancer
(2020) *Biomedicine and Pharmacotherapy*, 129 (2020), pp. 1-8.

- Mitra, R., Orbell, J., Muralitharan, M. S.
Medicinal plants of Malaysia
(2017) *Asia-Pacific Biotech News*, 11, pp. 105-110.
- Mohammad, P., Nosratollah, Z., Mohammad, R., Abbas, A., Javad, R.
The inhibitory effect of Curcuma longa extract on telomerase activity in A549 lung cancer cell line
(2010) *African Journal of Biotechnology*, 9 (6), pp. 912-919.
- Mueen, A. K., Madkor, H., Attimarad, M., Khan, T.
Plant metabolomics-a novel method in phytochemical analysis
(2010) *Pharmaceutical Methods*, 1 (1), p. 65.
- Mukhtar, E., Adhami, V. M., Mukhtar, H.
Targeting microtubules by natural agents for cancer therapy
(2014) *Molecular Cancer Therapeutics*, 13 (2), pp. 275-284.
- Nam, S., Scuto, A., Yang, F., Chen, W. Y., Park, S., Yoo, H. S., Konig, H., Jove, R.
Indirubin derivatives induce apoptosis of chronic myelogenous leukemia cells involving inhibition of Stat5 signaling
(2012) *Molecular Oncology*, 6 (3), pp. 276-283.
- *Cancer treatment*,
Accessed 12 Jul 2021
- Newcomb, E. W.
Flavopiridol: Pleiotropic biological effects enhance its anti-cancer activity
(2004) *Anti-Cancer Drugs*, 15 (5), pp. 411-419.
- Ng, P. L., Rajab, N. F., Then, S. M., Mohd Yusof, Y. A., Wan Ngah, W. Z., Pin, K. Y., Looi, M. L.
Piper betle leaf extract enhances the cytotoxicity effect of 5-fluorouracil in inhibiting the growth of HT29 and HCT116 colon cancer cells
(2014) *Journal of Zhejiang University: Science B*, 15 (8), pp. 692-700.
- Ng, P. Y., Chye, S. M., Ng, C. H., Koh, R. Y., Tiong, Y. L., Pui, L. P., Tan, Y. H., Ng, K. Y.
Clinacanthus nutans hexane extracts induce apoptosis through a caspase-dependent pathway in human cancer cell lines
(2017) *Asian Pacific Journal of Cancer Prevention*, 18 (4), pp. 917-926.
- Nik Abd Rahman, N. M. A., Nurliyana, M. Y., Afiqah, M. N. F. N. N., Osman, M. A., Hamid, M., Lila, M. A. M.
Antitumor and antioxidant effects of Clinacanthus nutans Lindau in 4 T1 tumor-bearing mice
(2019) *BMC Complementary and Alternative Medicine*, 19 (1), pp. 1-10.
- Norrizah, J. S., Norizan, A., Sharipah Ruzaina, S. A., Dzulsuhami, D., Nurul Hidayah, M.S.
Cytotoxicity activity and reproductive profiles of male rats treated with methanolic extracts of Ficus deltoidea
(2012) *Research Journal of Medicinal Plant*, 6 (2), pp. 197-202.
- Nussbaumer, S., Bonnabry, P., Veuthey, J. L., Fleury-Souverain, S.
Analysis of anticancer drugs: A review
(2011) *Talanta*, 85 (5), pp. 2265-2289.
- Omar, M. H., Mullen, W., Crozier, A.
Identification of proanthocyanidin dimers and trimers, flavone C-glycosides, and antioxidants in Ficus deltoidea, a Malaysian herbal tea
(2011) *Journal of Agricultural and Food Chemistry*, 59 (4), pp. 1363-1369.

- Palumbo, M. O., Kavan, P., Miller, W. H., Panasci, L., Assouline, S., Johnson, N., Cohen, V., Batist, G.
Systemic cancer therapy: achievements and challenges that lie ahead
(2013) *Frontiers in Pharmacology*, 4 (57), pp. 1-9.
- Pan, L., Chai, H. B., Kinghorn, A. D.
Discovery of new anticancer agents from higher plants
(2012) *Frontiers in Bioscience-Scholar*, 4 (1), pp. 142-156.
- Patt, D., Gordan, L., Diaz, M., Okon, T., Grady, L., Harmison, M., Markward, N., Zhou, A.
Impact of COVID-19 on cancer care: How the pandemic is delaying cancer diagnosis and treatment for American seniors
(2020) *JCO Clinical Cancer Informatics*, 4, pp. 1059-1071.
- Pinney, K. G., Jelinek, C., Edvardsen, K., Chaplin, D. J., Pettit, G.
The discovery and development of the combretastatins
(2005) *Anticancer Agents from Natural Products*, pp. 23-46.
CRC Press
- Prakash, V., Jaiswal, N., Srivastava, M.
A review on medicinal properties of Centella asiatica
(2017) *Asian Journal of Pharmaceutical and Clinical Research*, 10 (10), pp. 69-74.
- Prasad, V., De Jesús, K., Mailankody, S.
The high price of anticancer drugs: Origins, implications, barriers, solutions
(2017) *Natural Reviews Clinical Oncology*, 14 (6), pp. 381-390.
- Rajedadram, A., Pin, K. Y., Ling, S. K., Yan, S. W., Looi, M. L.
Hydroxychavicol, a polyphenol from Piper betle leaf extract, induces cell cycle arrest and apoptosis in TP53-resistant HT-29 colon cancer cells
(2021) *Journal of Zhejiang University: Science B*, 22 (2), pp. 112-122.
- Ren, L., Cao, Q., Zhai, F., Yang, S., Zhang, H.
Asiatic acid exerts anticancer potential in human ovarian cancer cells via suppression of PI3K/Akt/mTOR signalling
(2016) *Pharmaceutical Biology*, 54 (11), pp. 2377-2382.
- Rigas, J. R.
Taxane-platinum combinations in advanced non-small cell lung cancer: A review
(2004) *The Oncologist*, 9 (2), pp. 16-23.
- Roslan, S. N. F. M., Zakaria, Y., Abdullah, H.
Cytotoxicity of Clinacanthus nutans and mechanism of action of its active fraction towards human cervical cancer cell line, HeLA
(2018) *Jurnal Sains Kesihatan Malaysia*, 16 (2), pp. 39-50.
- Roy, U. B., Vijayalakshmi, K. K.
Evaluation of cytotoxic activity of Piper betle Linn. using murine and human cell lines in vitro
(2013) *International Journal of Scientific & Engineering Research*, 4 (9), pp. 221-233.
- Sainsbury, R.
The development of endocrine therapy for women with breast cancer
(2013) *Cancer Treatment Reviews*, 39 (5), pp. 507-517.
- Satar, N. A., Ismail, M. N., Yahaya, B. H.
Synergistic roles of curcumin in sensitising the cisplatin effect on a cancer stem cell-like population derived from non-small cell lung cancer cell lines
(2021) *Molecules*, 26 (4), pp. 1-22.

- Sharma, S. V., Haber, D. A., Settleman, J.
Cell line-based platforms to evaluate the therapeutic efficacy of candidate anticancer agents
(2010) *Nature Reviews Cancer*, 10 (4), pp. 241-253.
- Shim, S., Aziana, I., Khoo, B.
Perspective and insight on Clinacanthus nutans Lindau in traditional medicine
(2014) *International Journal of Integrative Biology*, 14 (1), pp. 7-9.
- Shukla, S., Mehta, A.
Anticancer potential of medicinal plants and their phytochemicals: A review
(2015) *Brazilian Journal of Botany*, 38 (2), pp. 199-210.
- Singh, V. K., Arora, D., Ansari, M. I., Sharma, P. K.
Phytochemicals based chemopreventive and chemotherapeutic strategies and modern technologies to overcome limitations for better clinical applications
(2019) *Phytotherapy Research*, 33 (12), pp. 3064-3089.
- Soib, H. H., Ware, I., Yaakob, H., Mukrish, H., Sarmidi, M. R.
Antioxidant and anti-cancer activity of standardized extracts of three varieties of Ficus deltoidea's leaves
(2015) *Jurnal Teknologi*, 77 (3), pp. 19-25.
- Soib, H. H., Yaakob, H., Sarmidi, M. R., Rosdi, M. N. M
Fractionation of aqueous extract of Ficus deltoidea var Kunstleri's leaves using solid phase extraction method for anticancer activity on DU145 cell line
(2019) *Malaysian Journal of Analytical Sciences*, 23 (3), pp. 534-547.
- Sulaiman, I. S. C., Basri, M., Chan, K. W., Ashari, S. E., Masoumi, R. F., Ismail, M.
In vitro antioxidant, cytotoxic and phytochemical studies of Clinacanthus nutans Lindau leaf extracts
(2015) *African Journal of Pharmacy and Pharmacology*, 9 (34), pp. 861-874.
- Sultana, S., Asif, H. M., Nazar, H. M. I., Akhtar, N., Rehman, J. U., Rehman, R. U.
Medicinal plants combating against cancer-a green anticancer approach
(2014) *Asian Pacific Journal of Cancer Prevention*, 15 (11), pp. 4385-4394.
- Sultana, S., Munir, N., Mahmood, Z., Riaz, M., Akram, M., Rebezov, M., Kuderinova, N., Rengasamy, K. R. R.
Molecular targets for the management of cancer using Curcuma longa Linn. phytoconstituents: A review
(2021) *Biomedicine and Pharmacotherapy*, 135, pp. 1-14.
(111078)
- Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., Bray, F.
Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries
(2021) *CA: A Cancer Journal for Clinicians*, 71 (3), pp. 209-249.
- Teuwen, L. A., Van Den Mooter, T., Dirix, L.
Management of pulmonary toxicity associated with targeted anticancer therapies
(2015) *Expert Opinion on Drug Metabolism and Toxicology*, 11 (11), pp. 1695-1707.
- Tyagi, A. K., Prasad, S., Yuan, W., Li, S., Aggarwal, B. B.
Identification of a novel compound (β -sesquiphellandrene) from turmeric (Curcuma longa) with anticancer potential: Comparison with curcumin
(2015) *Investigational New Drugs*, 33 (6), pp. 1175-1186.
- Varsha, K. H., Sharma, A., Kaur, A., Madan, J., Pandey, R. S., Jain, U. K., Chandra, R.
Natural plant-derived anticancer drugs nanotherapeutics: A review on preclinical to clinical success

- (2017) *Natural Product Drug Discovery, Discovery and Development of Anti-Inflammatory Agents from Natural Products*, pp. 775-809.
Editor A. Ficai and A. M. Grumezescu (Amsterdam: Elsevier)
- Venditto, V. J., Simanek, E. E.
Cancer therapies utilizing the camptothecins: A review of in vivo literature
(2010) *Molecular Pharmaceutics*, 7 (2), pp. 307-349.
 - Wang, L., Xu, J., Zhao, C., Zhao, L., Feng, B.
Antiproliferative, cell-cycle dysregulation effects of novel asiatic acid derivatives on human non-small cell lung cancer cells
(2013) *Chemical and Pharmaceutical Bulletin*, 61 (10), pp. 1015-1023.
 - Watson, J. L., Greenshields, A., Hill, R., Hilchie, A., Lee, P. W., Giacomantonio, C. A., Hoskin, D. W.
Curcumin-induced apoptosis in ovarian carcinoma cells is p53-independent and involves p38 mitogen-activated protein kinase activation and downregulation of BCL-2 and survivin expression and AKT signaling
(2010) *Molecular Carcinogenesis*, 49 (1), pp. 13-24.
 - Widowati, W., Wijaya, L., Wargasetia, T., Bachtiar, I., Yellianty, Y., Laksmitawati, D.
Antioxidant, anticancer, and apoptosis-inducing effects of Piper extracts in HeLa cells
(2013) *Journal of Experimental and Integrative Medicine*, 3 (3), pp. 225-230.
 - (2021) *Cancer*,
Accessed 12 Jul 2021
 - Wu, T., Geng, J., Guo, W., Gao, J., Zhu, X.
Asiatic acid inhibits lung cancer cell growth in vitro and in vivo by destroying mitochondria
(2017) *Acta Pharmaceutica Sinica B*, 7 (1), pp. 65-72.
 - Xu, J., Mao, W.
Overview of research and development for anticancer drugs
(2016) *Journal of Cancer Therapy*, (10), pp. 762-772.
 - Yaacob, N. S., Hamzah, N., Kamal, N. S. N. M., Abidin, S. A. Z., Lai, C. S., Navaratnam, V., Norazmi, M. N.
Anticancer activity of a sub-fraction of dichloromethane extract of Strobilanthes crispus on human breast and prostate cancer cells in vitro
(2010) *BMC Complementary and Alternative Medicine*, 10 (42), pp. 1-15.
 - Yaacob, N. S., Kamal, N. N., Norazmi, M. N.
Synergistic anticancer effects of a bioactive subfraction of Strobilanthes crispus and tamoxifen on MCF-7 and MDA-MB-231 human breast cancer cell lines
(2014) *BMC Complementary and Alternative Medicine*, 14 (252), pp. 1-13.
 - Yaacob, N. S., Yankuzo, H. M., Devaraj, S., Wong, J. K. M., Lai, C. S.
Anti-tumor action, clinical biochemistry profile and phytochemical constituents of a pharmacologically active fraction of S. crispus in NMU-induced rat mammary tumour model
(2015) *PLoS ONE*, 10 (5), pp. 1-20.
 - Yabroff, K. R., Lund, J., Kepka, D., Mariotto, A.
Economic burden of cancer in the United States: Estimates, projections, and future research
(2011) *Cancer Epidemiology Biomarkers and Prevention*, 20 (10), pp. 2006-2014.

- Yahaya, R., Dash, G. K., Abdullah, M. S., Mathews, A.
Clinacanthus nutans (burm. F.) Lindau: A useful medicinal plant of south-east Asia
(2015) *International Journal of Pharmacognosy and Phytochemical Research*, 7 (6), pp. 1244-1250.
- Yang, Q. Q., Cheng, L. Z., Zhang, T., Yaron, S., Jiang, H. X., Sui, Z. Q., Corke, H.
Phenolic profiles, antioxidant, and antiproliferative activities of turmeric (Curcuma longa)
(2020) *Industrial Crops and Products*, 152, pp. 1-8.
(112561)
- Yugeswari, S., Bindu, K. H., Kamalraj, S., Ashokkumar, V., Jayabaskaran, C.
Antidiabetic, antithrombin and cytotoxic bioactive compounds in five cultivars of Piper betle L
(2020) *Environmental Technology and Innovation*, 20 (101140), pp. 1-11.
- Yong, Y. K., Tan, J. J., Teh, S. S., Mah, S. H., Ee, G. C. L., Chiong, H. S., Ahmad, Z.
Clinacanthus nutans extracts are antioxidant with antiproliferative effect on cultured human cancer cell lines
(2013) *Evidence-Based Complementary and Alternative Medicine*, 2013, pp. 1-8.
(462751)
- Youssef, K. M., Ezzo, A. M., El-Sayed, M. I., Hazzaa, A. A., EL-Medany, A. H., Arafa, M.
Chemopreventive effects of curcumin analogs in DMH-Induced colon cancer in albino rats model
(2015) *Future Journal of Pharmaceutical Sciences*, 1 (2), pp. 57-72.
- Yue, G. G. L., Chan, B. C. L., Hon, P. M., Lee, M. Y. H., Fung, K. P., Leung, P. C., Lau, C. B. S.
Evaluation of in vitro anti-proliferative and immunomodulatory activities of compounds isolated from Curcuma longa
(2010) *Food and Chemical Toxicology*, 48 (8–9), pp. 2011-2020.
- Zainuddin, N. A. S. N., Hassan, N. F. N., Zakaria, Y., Muhammad, H., Othman, N. H.
Semi-purified fraction of Clinacanthus nutans induced apoptosis in human cervical cancer, SiHa cells via up-regulation of Bax and down-regulation of Bcl-2
(2019) *Sains Malaysiana*, 48 (9), pp. 1997-2006.
- Zainuddin, N. A. S. N., Muhammad, H., Hassan, N. F. N., Othman, N. H., Zakaria, Y.
Clinacanthus nutans standardized fraction arrested SiHa cells at G1/S and induced apoptosis via upregulation of p53
(2020) *Journal of Pharmacy & Bioallied Sciences*, 12, pp. S768-S776.
- Zakaria, Y., Yee, L. W., Hassan, N. F. N.
Anti-cancer effects of Clinacanthus nutans extract towards human cervical cancer cell line, HeLa
(2017) *Journal of Biomedical and Clinical Sciences*, 2 (1), pp. 11-19.
- Zamakshshari, N., Ahmed, I. A., Nasharuddin, M. N. A., Mohd Hashim, N., Mustafa, M. R., Othman, R., Noordin, M. I.
Effect of extraction procedure on the yield and biological activities of hydroxychavicol from Piper betle L. leaves
(2021) *Journal of Applied Research on Medicinal and Aromatic Plants*, 24, pp. 1-10.
(100320)
- Zhang, J., Ding, J., Tang, Q., Li, M., Zhao, M., Lu, L., Chen, L., Yuan, S.
Synthesis and antitumour activity of novel diterpenequinone salvinine and the analogs
(1999) *Bioorganic & Medicinal Chemistry Letters*, 9 (1999), pp. 2731-2736.

- Zhang, J., Ai, L., Lv, T., Jiang, X., Liu, F.
Asiatic acid, a triterpene, inhibits cell proliferation through regulating the expression of focal adhesion kinase in multiple myeloma cells
(2013) *Oncology Letters*, 6 (6), pp. 1762-1766.
- Zhang, X., Rakesh, K. P., Shantharam, C. S., Manukumar, H. M., Asiri, A. M., Marwani, H. M., Qin, H. L.
Podophyllotoxin derivatives as an excellent anticancer aspirant for future chemotherapy: A key current imminent need
(2018) *Bioorganic and Medicinal Chemistry*, 26 (2), pp. 340-355.

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