

## Documents

Indradi, R.B.<sup>a b</sup>, Muhaimin, M.<sup>a b</sup>, Barliana, M.I.<sup>a c</sup>, Khatib, A.<sup>d</sup>

**Potential Plant-Based New Antiplasmodial Agent Used in Papua Island, Indonesia**  
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<sup>a</sup> Department of Biological Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang, 45363, Indonesia

<sup>b</sup> Center of Herbal Study, Universitas Padjadjaran, Sumedang, 45363, Indonesia

<sup>c</sup> Center of Excellence in Pharmaceutical Care Innovation, Universitas Padjadjaran, Sumedang, 45363, Indonesia

<sup>d</sup> Department of Pharmaceutical Chemistry, Kuliyyah of Pharmacy, International Islamic University Malaysia, Kuantan, 25200, Malaysia

### Abstract

Resistance to antimalarial medicine remains a threat to the global effort for malaria eradication. The World Health Organization recently reported that artemisinin partial resistance, which was defined as delayed parasite clearance, was detected in Southeast Asia, particularly in the Greater Mekong subregion, and in Africa, particularly in Rwanda and Uganda. Therefore, the discovery of a potential new drug is important to overcome emerging drug resistance. Natural products have played an important role in drug development over the centuries, including the development of antimalarial drugs, with most of it influenced by traditional use. Recent research on traditional medicine used as an antimalarial treatment on Papua Island, Indonesia, reported that 72 plant species have been used as traditional medicine, with *Alstonia scholaris*, *Carica papaya*, *Andrographis paniculata*, and *Physalis minima* as the most frequently used medicinal plants. This review aimed to highlight the current research status of these plants for potential novel antiplasmodial development. In conclusion, *A. paniculata* has the highest potential to be developed as an antiplasmodial, and its extract and known bioactive isolate andrographolide posed strong activity both in vitro and in vivo. *A. scholaris* and *C. papaya* also have the potential to be further investigated as both have good potential for their antiplasmodial activities in vivo. However, *P. minima* is a less studied medicinal plant; nevertheless, it opens the opportunity to explore the potential of this plant. © 2023 by the authors.

### Author Keywords

antiplasmodial; medicinal plants; Papua Island

### References

- (2021) *World Malaria Report 2021*, World Health Organization, Geneva, Switzerland
- (2020) *World Malaria Report 2020—20 Years of Global Progress & Challenges*, World Health Organization, Geneva, Switzerland
- (2019) *World Malaria Report 2019*, World Health Organization, Geneva, Switzerland
- (2021) *Profil Kesehatan Indonesia Tahun 2020*, Kementerian Kesehatan Republik Indonesia, Jakarta, Indonesia
- Naß, J., Efferth, T.  
**Development of Artemisinin Resistance in Malaria Therapy**  
(2019) *Pharmacol. Res*, 146, p. 104275.
- Wicht, K.J., Mok, S., Fidock, D.A.  
**Molecular Mechanisms of Drug Resistance in Plasmodium falciparum Malaria**  
(2020) *Annu. Rev. Microbiol*, 74, pp. 431-454.
- Buyon, L.E., Elsworth, B., Duraisingh, M.T.  
**The Molecular Basis of Antimalarial Drug Resistance in Plasmodium vivax**  
(2021) *Int. J. Parasitol. Drugs Drug Resist*, 16, pp. 23-37.

- Elyazar, I.R.F., Hay, S.I., Baird, J.K.  
**Malaria Distribution, Prevalence, Drug Resistance and Control in Indonesia Europe PMC Funders Group**  
(2011) *Adv. Parasitol*, 74, pp. 41-175.
- Fagbemi, K.A., Adebunsi, S.A., Nderu, D., Adedokun, S.A., Pallerla, S.R., Amoo, A.O.J., Thomas, B.N., Ojurongbe, O.  
**Analysis of Sulphadoxine–Pyrimethamine Resistance-Associated Mutations in Plasmodium falciparum Isolates Obtained from Asymptomatic Pregnant Women in Ogun State, Southwest Nigeria**  
(2020) *Infect. Genet. Evol*, 85, pp. 1-7.  
32805431
- Newman, D.J., Cragg, G.M.  
**Natural Products as Sources of New Drugs from 1981 to 2014**  
(2016) *J. Nat. Prod*, 79, pp. 629-661.  
26852623
- Elfahmi, Woerdenbag, H.J., Kayser, O.  
**Jamu: Indonesian Traditional Herbal Medicine towards Rational Phytopharmacological Use**  
(2014) *J. Herb. Med*, 4, pp. 51-73.
- von Rintelen, K., Arida, E., Häuser, C.  
**A Review of Biodiversity-Related Issues and Challenges in Megadiverse Indonesia and Other Southeast Asian Countries**  
(2017) *Res. Ideas Outcomes*, 3, p. e20860.
- Elyazar, I.R.F., Gething, P.W., Patil, A.P., Rogayah, H., Kusriastuti, R., Wismarini, D.M., Tarmizi, S.N., Hay, S.I.  
**Plasmodium falciparum Malaria Endemicity in Indonesia in 2010**  
(2011) *PLoS ONE*, 6.
- Budiarti, M., Maruzy, A., Mujahid, R., Sari, A.N., Jokopriyambodo, W., Widayat, T., Wahyono, S.  
**The Use of Antimalarial Plants as Traditional Treatment in Papua Island, Indonesia**  
(2020) *Heliyon*, 6, pp. 1-10.
- Khyade, M.S., Kasote, D.M., Vaikos, N.P.  
**Alstonia Scholaris (L.) R. Br. and Alstonia macrophylla Wall. Ex G. Don: A Comparative Review on Traditional Uses, Phytochemistry and Pharmacology**  
(2014) *J. Ethnopharmacol*, 153, pp. 1-18.
- Zhao, Y.L., Yang, Z.F., Wu, B.F., Shang, J.H., Liu, Y.P., Wang, X.H., Luo, X.D.  
**Indole Alkaloids from Leaves of Alstonia scholaris (L.) R. Br. Protect against Emphysema in Mice**  
(2020) *J. Ethnopharmacol*, 259, p. 112949.
- Available online
- Available online
- Available online
- Pratap, B., Chakraborty, G., Mogha, N.  
**Complete Aspects of Alstonia scholaris**  
(2013) *Int. J. Pharm. Tech. Res*, 5, pp. 17-26.

- Dey, A.  
**Alstonia scholaris R.Br. (Apocynaceae): Phytochemistry and Pharmacology: A Concise Review** Abhijit Dey  
(2011) *J. Appl. Pharm. Sci*, 6, pp. 51-57.
- Arulmozhi, S., Mitra Mazumder, P., Ashok, P., Sathiya Narayanan, L.  
**Pharmacological Activities of Alstonia scholaris Linn. (Apocynaceae)-A Review**  
(2007) *Pharmacogn. Rev*, 1, pp. 163-170.
- Shang, J.H., Cai, X.H., Feng, T., Zhao, Y.L., Wang, J.K., Zhang, L.Y., Yan, M., Luo, X.D.  
**Pharmacological Evaluation of Alstonia scholaris: Anti-Inflammatory and Analgesic Effects**  
(2010) *J. Ethnopharmacol*, 129, pp. 174-181.
- (2016) *Tumbuhan Obat Tradisional Papua*,  
Dinas Kesehatan Provinsi Papua, Jayapura, Indonesia
- Shrinath Baliga, M.  
**Alstonia scholaris Linn R Br in the Treatment and Prevention of Cancer: Past, Present, and Future**  
(2010) *Integr. Cancer Ther*, 9, pp. 261-269.  
20702494
- Cai, X.H., Du, Z.Z., Luo, X.D.  
**Unique Monoterpenoid Indole Alkaloids from Alstonia scholaris**  
(2007) *Org. Lett*, 9, pp. 1817-1820.
- Cai, X.H., Liu, Y.-P., Feng, T., Luo, X.-D.  
**Picrinine-Type Alkaloids from the Leaves of Alstonia scholaris**  
(2008) *Chin. J. Nat. Med*, 6, pp. 20-22.
- Cai, X.H., Tan, Q.G., Liu, Y.P., Feng, T., Du, Z.Z., Li, W.Q., Luo, X.D.  
**A Cage-Monoterpene Indole Alkaloid from Alstonia scholaris**  
(2008) *Org. Lett*, 10, pp. 577-580.
- Cai, X.H., Shang, J.H., Feng, T., Luo, X.D.  
**Novel Alkaloids from Alstonia scholaris**  
(2010) *Z. Naturforsch*, 65, pp. 1164-1168.
- Chen, Y.Y., Yang, J., Yang, X.W., Khan, A., Liu, L., Wang, B., Zhao, Y.L., Luo, X.D.  
**Alstorisine A, a nor-Monoterpenoid Indole Alkaloid from Cecidogenous Leaves of Alstonia scholaris**  
(2016) *Tetrahedron Lett*, 57, pp. 1754-1757.
- Feng, T., Cai, X.H., Zhao, P.J., Du, Z.Z., Li, W.Q., Luo, X.D.  
**Monoterpenoid Indole Alkaloids from the Bark of Alstonia scholaris**  
(2009) *Planta Med*, 75, pp. 1537-1541.  
19609839
- Liu, L., Chen, Y.Y., Qin, X.J., Wang, B., Jin, Q., Liu, Y.P., Luo, X.D.  
**Antibacterial Monoterpenoid Indole Alkaloids from Alstonia scholaris Cultivated in Temperate Zone**  
(2015) *Fitoterapia*, 105, pp. 160-164.  
26136061
- Pan, Z., Qin, X.J., Liu, Y.P., Wu, T., Luo, X.D., Xia, C.  
**Alstoscholarisines H-J, Indole Alkaloids from Alstonia scholaris: Structural Evaluation and Bioinspired Synthesis of Alstoscholarisine H**  
(2016) *Org. Lett*, 18, pp. 654-657.

- Qin, X.J., Zhao, Y.L., Lunga, P.K., Yang, X.W., Song, C.W., Cheng, G.G., Liu, L., Luo, X.D.  
**Indole Alkaloids with Antibacterial Activity from Aqueous Fraction of *Alstonia scholaris***  
(2015) *Tetrahedron*, 71, pp. 4372-4378.
- Qin, X.J., Zhao, Y.L., Song, C.W., Wang, B., Chen, Y.Y., Liu, L., Li, Q., Luo, X.D.  
**Monoterpenoid Indole Alkaloids from Inadequately Dried Leaves of *Alstonia scholaris***  
(2015) *Nat. Prod. Bioprospect*, 5, pp. 185-193.
- Yang, X.W., Qin, X.J., Zhao, Y.L., Lunga, P.K., Li, X.N., Jiang, S.Z., Cheng, G.G., Luo, X.D.  
**Alstolactines A–C, Novel Monoterpenoid Indole Alkaloids from *Alstonia scholaris***  
(2014) *Tetrahedron Lett*, 55, pp. 4593-4596.
- Yang, X.W., Yang, C.P., Jiang, L.P., Qin, X.J., Liu, Y.P., Shen, Q.S., Chen, Y.B., Luo, X.D.  
**Indole Alkaloids with New Skeleton Activating Neural Stem Cells**  
(2014) *Org. Lett*, 16, pp. 5808-5811.
- Yang, X.W., Luo, X.D., Lunga, P.K., Zhao, Y.L., Qin, X.J., Chen, Y.Y., Liu, L., Liu, Y.P.  
**Scholarisines H–O, Novel Indole Alkaloid Derivatives from Long-Term Stored *Alstonia scholaris***  
(2015) *Tetrahedron*, 71, pp. 3694-3698.
- Yang, X.W., Song, C.W., Zhang, Y., Khan, A., Jiang, L.P., Chen, Y.B., Liu, Y.P., Luo, X.D.  
**Alstoscholarisines F and G, Two Unusual Monoterpenoid Indole Alkaloids from the Leaves of *Alstonia scholaris***  
(2015) *Tetrahedron Lett*, 56, pp. 6715-6718.
- Zhu, G.Y., Yao, X.J., Liu, L., Bai, L.P., Jiang, Z.H.  
**Alistonitriene A, a Caged Monoterpene Indole Alkaloid from *Alstonia scholaris***  
(2014) *Org. Lett*, 16, pp. 1080-1083.
- Feng, T., Cai, X.H., Du, Z.Z., Luo, X.D.  
**Iridoids from the Bark of *Alstonia scholaris***  
(2008) *Helv. Chim. Acta*, 91, pp. 2247-2251.
- Xu, Y., Feng, T., Cai, X.-H., Luo, X.-D.  
**A New C13-Norisoprenoid from Leaves of *Alstonia scholaris***  
(2009) *Chin. J. Nat. Med*, 7, pp. 21-23.
- Taek, M.M., Tukan, G.D., Prajogo, B.E.W., Agil, M.  
**Antiplasmodial Activity and Phytochemical Constituents of Selected Antimalarial Plants Used by Native People in West Timor Indonesia**  
(2021) *Turk. J. Pharm. Sci*, 18, pp. 80-90.  
33634682
- Abdillah, S., Tambunan, R.M., Farida, Y., Sandhiutami, N.M.D., Dewi, R.M.  
**Phytochemical Screening and Antimalarial Activity of Some Plants Traditionally Used in Indonesia**  
(2015) *Asian Pac. J. Trop. Dis*, 5, pp. 454-457.
- Ouattara, Y., Sanon, S., Traoré, Y., Mahiou, V., Azas, N., Sawadogo, L.  
**Antimalarial Activity of *Swartzia Madagascariensis* Desv. (Leguminosae), *Combretum Glutinosum* Guill. & Perr. (Combretaceae) and *Tinospora Bakis* Miers. (Menispermaceae), Burkina Faso Medicinal Plants**  
(2005) *Afr. J. Tradit. Complement. Altern. Med*, 3, pp. 75-81.
- Keawpradub, N., Kirby, G.C., Steele, J.C.P., Houghton, P.J.  
**Antiplasmodial Activity of Extracts and Alkaloids of Three *Alstonia* Species from Thailand**  
(1999) *Planta Med*, 65, pp. 690-694.

- Surur, A.S., Huluka, S.A., Mitku, M.L., Asres, K.  
**Indole: The After Next Scaffold of Antiplasmodial Agents?**  
(2020) *Drug Des. Dev. Ther.*, 14, p. 4855.
- Muñoz, V., Sauvain, M., Bourdy, G., Callapa, J., Bergeron, S., Rojas, I., Bravo, J.A., Gimenez, A.  
**A Search for Natural Bioactive Compounds in Bolivia through a Multidisciplinary Approach. Part I. Evaluation of the Antimalarial Activity of Plants Used by the Chacobo Indians**  
(2000) *J. Ethnopharmacol.*, 69, pp. 127-137.
- Intan, P., Winarno, M., Prihartini, N.  
**Efek Ekstrak Campuran Kulit Batang Pulai (*Alstonia scholaris*) Dan Meniran (*Phyllanthus niruri*) Pada Mencit Swiss Webster Yang Diinfeksi *Plasmodium berghei***  
(2016) *J. Kefarmasian Indones.*, 6, pp. 79-88.
- Bello, I., Bakkouri, A., Tabana, Y., Al-Hindi, B., Al-Mansoub, M., Mahmud, R., Asmawi, M.Z.  
**Acute and Sub-Acute Toxicity Evaluation of the Methanolic Extract of *Alstonia scholaris* Stem Bark**  
(2016) *Med. Sci.*, 4, 29083368
- Baliga, M.S., Jagetia, G.C., Ulloor, J.N., Baliga, M.P., Venkatesh, P., Reddy, R., Rao, K.V.N.M., Raju, S.K.  
**The Evaluation of the Acute Toxicity and Long Term Safety of Hydroalcoholic Extract of *Sapthaparna* (*Alstonia scholaris*) in Mice and Rats**  
(2004) *Toxicol. Lett.*, 151, pp. 317-326.
- **OECD Test No. 425: Acute Oral Toxicity: Up-and-Down Procedure**  
(2022) *OECD Guidelines for the Testing of Chemicals*,  
OECD Guidelines for the Testing of Chemicals, Section 4, OECD, Paris, France
- Ravikumar, S., Inbaneson, S.J., Suganthi, P.  
**In Vitro Antiplasmodial Activity of Chosen Terrestrial Medicinal Plants against *Plasmodium falciparum***  
(2012) *Asian Pac. J. Trop. Biomed.*, 2, pp. 252-256.
- Atanu, F.O., Idih, F.M., Nwonuma, C.O., Hetta, H.F., Alamery, S., El-Saber Batiha, G.  
**Evaluation of Antimalarial Potential of Extracts from *Alstonia boonei* and *Carica papaya* in *Plasmodium berghei*-Infected Mice**  
(2021) *Evid.-Based Complement. Altern. Med.*, 2021, p. 2599191.  
34659429
- Melariri, P., Campbell, W., Etusim, P., Smith, P.  
**Antiplasmodial Properties and Bioassay-Guided Fractionation of Ethyl Acetate Extracts from *Carica papaya* Leaves**  
(2011) *J. Parasitol. Res.*, 2011, p. 104954.
- Julianti, T., De Mieri, M., Zimmermann, S., Ebrahimi, S.N., Kaiser, M., Neuburger, M., Raith, M., Hamburger, M.  
**HPLC-Based Activity Profiling for Antiplasmodial Compounds in the Traditional Indonesian Medicinal Plant *Carica papaya* L**  
(2014) *J. Ethnopharmacol.*, 155, pp. 426-434.
- Teng, W.C., Chan, W., Suwanarusk, R., Ong, A., Ho, H.K., Russell, B., Rénia, L., Koh, H.L.  
**In Vitro Antimalarial Evaluations and Cytotoxicity Investigations of *Carica papaya* Leaves and *Carpaine***  
(2019) *Nat. Prod. Commun.*, 14, pp. 33-36.

- Zeleke, G., Kebebe, D., Mulisa, E., Gashe, F.  
**In Vivo Antimalarial Activity of the Solvent Fractions of Fruit Rind and Root of *Carica papaya* Linn (Caricaceae) against *Plasmodium berghei* in Mice**  
(2017) *J. Parasitol. Res*, 2017, p. 3121050.
- Okpe, O., Habila, N., Ikwebe, J., Upev, V.A., Okoduwa, S.I.R., Isaac, O.T.  
**Antimalarial Potential of *Carica papaya* and *Vernonia amygdalina* in Mice Infected with *Plasmodium berghei***  
(2016) *J. Trop. Med*, 2016, p. 8738972.
- Kovendan, K., Murugan, K., Panneerselvam, C., Aarthi, N., Kumar, P.M., Subramaniam, J., Amerasan, D., Vincent, S.  
**Antimalarial Activity of *Carica papaya* (Family: Caricaceae) Leaf Extract against *Plasmodium falciparum***  
(2012) *Asian Pac. J. Trop. Dis*, 2, pp. S306-S311.
- Widyawaruyanti, A., Asrory, M., Ekasari, W., Setiawan, D., Radjaram, A., Tumewu, L., Hafid, A.F.  
**In Vivo Antimalarial Activity of *Andrographis paniculata* Tablets**  
(2014) *Procedia Chem*, 13, pp. 101-104.
- Widyawaruyanti, A., Jonosewojo, A., Ilmi, H., Tumewu, L., Imandiri, A., Widiastuti, E., Dachliyati, L., Hafid, A.F.  
**Safety Evaluation of an Antimalarial Herbal Product from *Andrographis paniculata* (AS201-01) in Healthy Volunteers**  
(2021) *J. Basic Clin. Physiol. Pharmacol*,
- Zein, U., Fitri, L.E., Saragih, A.  
**Comparative Study of Antimalarial Effect of Sambiloto (*Andrographis paniculata*) Extract, Chloroquine and Artemisinin and Their Combination against *Plasmodium falciparum* In-Vitro**  
(2013) *Indones. J. Intern. Med*, 45, pp. 38-43.
- Makmur, T., Siregar, F.A., Siregar, S., Lubis, I.A., Bestari, R., Zein, U.  
**Open Clinical Trial of Sambiloto (*Andrographis paniculata*) Ethanolic Extract Capsules in Treatment of Malaria Patients in Batubara District, Indonesia**  
(2022) *Med. Arch*, 76, p. 419.
- Mishra, K., Dash, A.P., Swain, B.K., Dey, N.  
**Anti-Malarial Activities of *Andrographis paniculata* and *Hedyotis corymbosa* Extracts and Their Combination with Curcumin**  
(2009) *Malar. J*, 8, p. 26.
- Mishra, K., Dash, A.P., Dey, N.  
**Andrographolide: A Novel Antimalarial Diterpene Lactone Compound from *Andrographis paniculata* and Its Interaction with Curcumin and Artesunate**  
(2011) *J. Trop. Med*, 2011, p. 579518.
- Hassan, W.R.M., Basir, R., Ali, Embi, N.  
**Sidek Anti-Malarial and Cytokine-Modulating Effects of Andrographolide in a Murine Model of Malarial Infection**  
(2019) *Trop. Biomed*, 36, pp. 776-791.
- Rahman, N.N.N.A., Furuta, T., Kojima, S., Takane, K., Mohd, M.A.  
**Antimalarial Activity of Extracts of Malaysian Medicinal Plants**  
(1999) *J. Ethnopharmacol*, 64, pp. 249-254.
- Sá, M., De Menezes, M.N., Krettli, A.U., Ribeiro, I.M., Tomassini, T.C.B., Ribeiro Dos Santos, R., De Azevedo, W.F., Soares, M.B.P.  
**Antimalarial Activity of Physalins B, D, F, and G**  
(2011) *J. Nat. Prod*, 74, pp. 2269-2272.

- *Carica papaya* L,  
Available online
- Available online
- Available online
- Available online
- Aravind, G., Bhowmik, D., Duraviel, S., Harish, G.  
**Traditional and Medicinal Uses of Carica papaya**  
(2013) *J. Med. Plants Stud*, 1, pp. 7-15.
- Ghaffarilaleh, V., Fisher, D., Henkel, R.  
**Carica papaya Seed Extract Slows Human Sperm**  
(2019) *J. Ethnopharmacol*, 241, p. 111972.
- Sarimole, E., Martosupono, M., Semangun, H., Mangimbulude, J.C.  
**Pengobatan Penyakit Malaria Dengan Menggunakan Beberapa Jenis Nabati Di Kabupaten Raja Ampat**  
(2014) *Raja Ampat and Future of Humanity (as a World Heritage), Proceedings of the Seminar Nasional Raja Ampat, Raja Ampat, Indonesia, 12–13 August 2014*, Mangimbulude J.C., Martosupono M., Puspita D., Nugroho K.P.A.N., (eds), Universitas Kristen Satya Wacana, Salatiga, Indonesia
- Kong, Y.R., Jong, Y.X., Balakrishnan, M., Bok, Z.K., Weng, J.K.K., Tay, K.C., Goh, B.H., Lee, L.H.  
**Beneficial Role of Carica papaya Extracts and Phytochemicals on Oxidative Stress and Related Diseases: A Mini Review**  
(2021) *Biology*, 10.
- Khor, B.K.K., Chear, N.J.Y., Azizi, J., Khaw, K.Y.  
**Chemical Composition, Antioxidant and Cytoprotective Potentials of Carica papaya Leaf Extracts: A Comparison of Supercritical Fluid and Conventional Extraction Methods**  
(2021) *Molecules*, 26.
- Yanty, N.A.M., Marikkar, J.M.N., Nusantoro, B.P., Long, K., Ghazali, H.M.  
**Physico-Chemical Characteristics of Papaya (*Carica papaya* L.) Seed Oil of the Hong Kong/Sekaki Variety**  
(2014) *J. Oleo Sci*, 63, pp. 885-892.
- Kumaratilake, L.M., Ferrante, A., Robinson, B.S., Jaeger, T., Poulos, A.  
**Enhancement of Neutrophil-Mediated Killing of Plasmodium falciparum Asexual Blood Forms by Fatty Acids: Importance of Fatty Acid Structure**  
(1997) *Infect. Immun*, 65, p. 4152.
- Uzor, P.F.  
**Alkaloids from Plants with Antimalarial Activity: A Review of Recent Studies**  
(2020) *Evid.-Based Complement. Altern. Med*, 2020, p. 8749083.
- Afzan, A., Abdullah, N.R., Halim, S.Z., Rashid, B.A., Semail, R.H.R., Abdullah, N., Jantan, I., Ismail, Z.  
**Repeated Dose 28-Days Oral Toxicity Study of Carica papaya L. Leaf Extract in Sprague Dawley Rats**  
(2012) *Molecules*, 17.

- Ismail, Z., Halim, S.Z., Abdullah, N.R., Afzan, A., Abdul Rashid, B.A., Jantan, I.  
**Safety Evaluation of Oral Toxicity of Carica papaya Linn. Leaves: A Subchronic Toxicity Study in Sprague Dawley Rats**  
(2014) *Evid.-Based Complement. Alternat. Med*, 2014, p. 741470.
- Lim, X.Y., Chan, J.S.W., Japri, N., Lee, J.C., Tan, T.Y.C.  
**Carica Papaya L. Leaf: A Systematic Scoping Review on Biological Safety and Herb-Drug Interactions**  
(2021) *Evid.-Based Complement. Alternat. Med*, 2021, p. 5511221.
- Nghonjuyi, N.W., Tiambo, C.K., Taiwe, G.S., Toukala, J.P., Lisita, F., Juliano, R.S., Kimbi, H.K.  
**Acute and Sub-Chronic Toxicity Studies of Three Plants Used in Cameroonian Ethnoveterinary Medicine: Aloe vera (L.) Burm. f. (Xanthorrhoeaceae) Leaves, Carica papaya L. (Caricaceae) Seeds or Leaves, and Mimosa pudica L. (Fabaceae) Leaves in Kabir Chicks**  
(2016) *J. Ethnopharmacol*, 178, pp. 40-49.
- Shrivastava, S., Ansari, A.S., Lohiya, N.K.  
**Fertility, Developmental Toxicity and Teratogenicity in Albino Rats Treated with Methanol Sub-Fraction of Carica papaya Seeds**  
(2011) *Indian J. Pharmacol*, 43, pp. 419-423.
- Available online
- Kumar, A., Dora, J., Singh, A., Tripathi, R.  
**A review on king of bitter (kalmegh)**  
(2012) *Int. J. Res. Pharm. Chem*, 2, pp. 116-124.
- Hossain, S., Urbi, Z., Karuniawati, H., Mohiuddin, R.B., Qrimida, A.M., Allzrag, A.M.M., Ming, L.C., Capasso, R.  
**Andrographis paniculata (Burm. f.) Wall. Ex Nees: An Updated Review of Phytochemistry, Antimicrobial Pharmacology, and Clinical Safety and Efficacy**  
(2021) *Life*, 11.
- Akbar, S.  
**Andrographis paniculata: A Review of Pharmacological Activities and Clinical Effects**  
(2011) *Altern. Med. Rev*, 16, pp. 66-77.
- Hossain, M.S., Urbi, Z., Sule, A., Rahman, K.M.H.  
**Andrographis paniculata (Burm. f.) Wall. Ex Nees: A Review of Ethnobotany, Phytochemistry, and Pharmacology**  
(2014) *Sci. World J*, 2014, p. 274905.
- Available online
- Available online
- Anju, D., Jugnu, G., Kavita, S., Arun, N., Sandeep, D.  
**A Review on Medicinal Prospectives of Andrographis paniculata Nees**  
(2012) *J. Pharm. Sci. Innov*, 1, pp. 1-4.
- Ji, L.L., Wang, Z., Dong, F., Zhang, W.B., Wang, Z.T.  
**Andrograpanin, a Compound Isolated from Anti-Inflammatory Traditional Chinese Medicine Andrographis paniculata, Enhances Chemokine SDF-1 $\alpha$ -Induced Leukocytes Chemotaxis**



- (2005) *J. Cell. Biochem*, 95, pp. 970-978.  
15937916
- Intharuksa, A., Arunotayanun, W., Yoo-in, W., Sirisa-ard, P.  
**A Comprehensive Review of *Andrographis paniculata* (Burm. f.) Nees and Its Constituents as Potential Lead Compounds for COVID-19 Drug Discovery**  
(2022) *Molecules*, 27.  
35889352
  - Kuroyanagi, M., Sato, M., Ueno, A., Nishi, K.  
**Flavonoids from *Andrographis paniculata***  
(1987) *Chem. Pharm. Bull*, 35, pp. 4429-4435.
  - Xu, C., Chou, G.X., Wang, C.H., Wang, Z.T.  
**Rare Noriridoids from the Roots of *Andrographis paniculata***  
(2012) *Phytochemistry*, 77, pp. 275-279.  
22342031
  - My, N.T.T., Hanh, T.T.H., Cham, P.T., Cuong, N.X., Huong, T.T., Quang, T.H., Nam, N.H., Minh, C.  
**Van Andropaniosides A and B, Two New Ent-Labdane Diterpenoid Glucosides from *Andrographis paniculata***  
(2020) *Phytochem. Lett*, 35, pp. 37-40.
  - Shen, Y.H., Li, R.T., Xiao, W.L., Gang-Xu, Lin, Z.W., Zhao, Q.S., Sun, H.D.  
**Ent-Labdane Diterpenoids from *Andrographis paniculata***  
(2006) *J. Nat. Prod*, 69, pp. 319-322.
  - Wang, G.C., Wang, Y., Williams, I.D., Sung, H.H.Y., Zhang, X.Q., Zhang, D.M., Jiang, R.W., Ye, W.C.  
**Andrographolactone, a Unique Diterpene from *Andrographis paniculata***  
(2009) *Tetrahedron Lett*, 50, pp. 4824-4826.
  - Pramanick, S., Banerjee, S., Achari, B., Das, B., Sen, A.K., Mukhopadhyay, S., Neuman, A., Prangé, T.  
**Andropanolide and Isoandrographolide, Minor Diterpenoids from *Andrographis paniculata*: Structure and X-Ray Crystallographic Analysis**  
(2006) *J. Nat. Prod*, 69, pp. 403-405.  
16562845
  - Nishi, K., Kuroyanagi, M., Sugiyama, S., Umehara, K., Ueno, A.  
**Cell Differentiation-Inducing Diterpenes from *Andrographis paniculata* Nees**  
(1994) *Chem. Pharm. Bull*, 42, pp. 1216-1225.
  - Allison, A.J., Butcher, D.N., Connolly, J.D., Overton, K.H.  
**Paniculides A, B, and C, Bisaboloid Lactones from Tissue Cultures of *Andrographis paniculata***  
(1968) *Chem. Commun*, 23.
  - Wu, T.S., Chern, H.J., Damu, A.G., Kuo, P.C., Su, C.R., Lee, E.J., Teng, C.M.  
**Flavonoids and Ent-Labdane Diterpenoids from *Andrographis paniculata* and Their Antiplatelet Aggregatory and Vasorelaxing Effects**  
(2008) *J. Asian Nat. Prod. Res*, 10, pp. 17-24.
  - Xu, C., WAng, Z.-T.  
**Chemical Constituents from Roots of *Andrographis paniculata***  
(2011) *Yao Xue Xue Bao*, 46, pp. 317-321.
  - Chua, L.S., Yap, K.C., Jaganath, I.B.  
**Comparison of Total Phenolic Content, Scavenging Activity and HPLC-ESI-MS/MS**

- Profiles of Both Young and Mature Leaves and Stems of *Andrographis paniculata***  
(2013) *Nat. Prod. Commun*, 8, pp. 1725-1729.
- Koteswara Rao, Y., Vimalamma, G., Venkata Rao, C., Tzeng, Y.M.  
**Flavonoids and Andrographolides from *Andrographis paniculata***  
(2004) *Phytochemistry*, 65, pp. 2317-2321.  
15381002
  - Ogutu, B., Juma, E., Obonyo, C., Jullien, V., Carn, G., Vaillant, M., Taylor, W.R.J., Kiechel, J.R.  
**Fixed Dose Artesunate Amodiaquine—A Phase IIb, Randomized Comparative Trial with Non-Fixed Artesunate Amodiaquine**  
(2014) *Malar. J.*, 13, pp. 1-13.  
25515698
  - Worasuttayangkurn, L., Nakareangrit, W., Kwangjai, J., Sritangos, P., Pholphana, N., Watcharasit, P., Rangkadilok, N., Satayavivad, J.  
**Acute Oral Toxicity Evaluation of *Andrographis paniculata*-Standardized First True Leaf Ethanolic Extract**  
(2019) *Toxicol. Rep*, 6, p. 426.  
31193040
  - Chandrasekaran, C.V., Thiyagarajan, P., Sundarajan, K., Goudar, K.S., Deepak, M., Murali, B., Joshua Allan, J., Agarwal, A.  
**Evaluation of the Genotoxic Potential and Acute Oral Toxicity of Standardized Extract of *Andrographis paniculata* (KalmCold<sup>TM</sup>)**  
(2009) *Food Chem. Toxicol*, 47, pp. 1892-1902.
  - Burgos, R.A., Caballero, E.E., Sánchez, N.S., Schroeder, R.A., Wikman, G.K., Hancke, J.L.  
**Testicular Toxicity Assesment of *Andrographis paniculata* Dried Extract in Rats**  
(1997) *J. Ethnopharmacol*, 58, pp. 219-224.
  - Al Batran, R., Al-Bayaty, F., Al-Obaidi, M.M.J., Abdulla, M.A.  
**Acute Toxicity and the Effect of Andrographolide on Porphyromonas Gingivalis-Induced Hyperlipidemia in Rats**  
(2013) *Biomed. Res. Int*, 2013, p. 594012.
  - Bothiraja, C., Pawar, A.P., Shende, V.S., Joshi, P.P.  
**Acute and Subacute Toxicity Study of Andrographolide Bioactive in Rodents: Evidence for the Medicinal Use as an Alternative Medicine**  
(2013) *Comp. Clin. Pathol*, 22, pp. 1123-1128.
  - Available online
  - Patel, T., Shah, K., Jiwan, K., Shrivastava, N.  
**Study on the Antibacterial Potential of *Physalis minima* Linn**  
(2011) *Indian J. Pharm. Sci*, 73, p. 111.
  - Alegantina, S., Setyorini, H.A., Oktoberia, I.S., Winarsih, Aini, N.  
***Physalis minima* L. Profile from Various Ethnics in 9 (Nine) Provinces Indonesia by HPLC and Chemometric**  
(2021) *Media Penelit. Dan Pengemb. Kesehat*, 31, pp. 17-26.
  - Khan, M.A., Khan, H., Khan, S., Mahmood, T., Khan, P.M., Jabar, A.  
**Anti-Inflammatory, Analgesic and Antipyretic Activities of *Physalis minima* Linn**  
(2009) *J. Enzym. Inhib. Med. Chem*, 24, pp. 632-637.
  - Habib, A.  
*Wildgooseberry (*Physalis minima*)*,

Available online

- Shil, D., Sarma, T., Roy, S.D., Chakraborty, J., Das, S.R.C., Das, T., Rohman, T.A.  
**Exploring Quality Control Standards and Potential Antibacterial Property of Different Extracts of the Root of *Physalis minima* L**  
(2021) *Int. J. Res. Pharm. Sci*, 12, pp. 2350-2360.
- Chothani, D.L., Vaghasiya, H.U.  
**A Phyto-Pharmacological Overview on *Physalis minima* Linn**  
(2012) *Indian J. Nat. Prod. Resour*, 3, pp. 477-482.
- Parkash, V., Aggarwal, A.  
**Traditional Uses of Ethnomedicinal Plants of Lower Foot-Hills of Himachal Pradesh-I**  
(2010) *Indian J. Tradit. Knowl*, 9, pp. 519-521.
- Zakaria, M., Mohd, M.A.  
(2015) *Traditional Malay Medicinal Plants*,  
Institut Terjemahan & Buku Malaysia, Kuala Lumpur, Malaysia
- Sinha, S.C., Ray, A.B.  
**Chemical Constituents of *Physalis minima* Var. Indica**  
(1988) *J. Indian Chem. Soc*, LXV, pp. 740-741.
- Ooi, K.L., Tengku Muhammad, T.S., Sulaiman, S.F.  
**Physalin F from *Physalis minima* L. Triggers Apoptosis-Based Cytotoxic Mechanism in T-47D Cells through the Activation Caspase-3- and c-Myc-Dependent Pathways**  
(2013) *J. Ethnopharmacol*, 150, pp. 382-388.
- Choudhary, M.I., Yousaf, S., Ahmed, S., Samreen, Yasmeen, K.  
**Atta-ur-Rahmang Antileishmanial Physalins from *Physalis minima***  
(2005) *Chem. Biodivers*, 2, pp. 1164-1173.
- Sen, G., Pathak, H.D.  
**Physalin L, a 13,14-Seco-16,24 Cyclosteroid from *Physalis minima***  
(1995) *Phytochemistry*, 39, pp. 1245-1246.
- Misra, L.N., Lal, P., Kumar, D.  
**Isolation and Characterization of Steroids of Nutraceutical Value in *Physalis minima***  
(2006) *J. Food Sci. Nutr*, 11, pp. 133-139.
- Gottlieb, H.E., Cojocar, M., Sinha, S.C., Saha, M., Bagchi, A., Ali, A., Ray, A.B.  
**Withaminimin, a Withanolide from *Physalis minima***  
(1987) *Phytochemistry*, 26, pp. 1801-1804.
- Basey, K., McGaw, B.A., Woolley, J.G.  
**Phygrine, an Alkaloid from *Physalis* Species**  
(1992) *Phytochemistry*, 31, pp. 4173-4176.
- Ser, N.A.  
**Flavonoids from *Physalis minima***  
(1988) *Phytochemistry*, 27, pp. 3708-3709.
- Lusakibanza, M., Mesia, G., Tona, G., Karemere, S., Lukuka, A., Tits, M., Angenot, L., Frédéric, M.  
**In Vitro and In Vivo Antimalarial and Cytotoxic Activity of Five Plants Used in Congolese Traditional Medicine**  
(2010) *J. Ethnopharmacol*, 129, pp. 398-402.  
20430094
- Arruda, J.C.C., Rocha, N.C., Santos, E.G., Ferreira, L.G.B., Bello, M.L., Penido, C., Costa, T.E.M.M., Tomassini, T.C.B.  
**Physalin Pool from *Physalis angulata* L. Leaves and Physalin D Inhibit P2X7**

**Receptor Function in Vitro and Acute Lung Injury in Vivo**

(2021) *Biomed. Pharmacother*, 142, p. 112006.

34392085

- Savio, L.E.B., de Andrade Mello, P., da Silva, C.G., Coutinho-Silva, R.  
**The P2X7 Receptor in Inflammatory Diseases: Angel or Demon?**  
(2018) *Front. Pharmacol*, 9, p. 52.
- Levano-Garcia, J., Dluzewski, A.R., Markus, R.P., Garcia, C.R.S.  
**Purinergic Signalling Is Involved in the Malaria Parasite Plasmodium falciparum Invasion to Red Blood Cells**  
(2010) *Purinergic Signal*, 6, pp. 365-372.
- Zafirah Ismail, N., Arsad, H., Afiqah Lokman, N., Izzati Jaafar, N., Hasyimah Haron, N.  
**Preliminary Acute Oral Toxicity Study of The Water Extract of Physalis minima Leaves**  
(2018) *J. Biol. Sci. Opin*, 6, pp. 111-115.
- Soeharto, S., Nugrahenny, D., Permatasari, N., Mayangsari, E.  
**Subchronic Toxicity of the Physalis minima Leaves**  
(2018) *Res. J. Life Sci*, 5, pp. 77-82.

**Correspondence Address**

Indradi R.B.; Department of Biological Pharmacy, Indonesia; email: bayu.indradi@unpad.ac.id

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