

Review article

Phytochemical and the Potential of Cocoa (*Theobroma cacao* L.) as an Antibacterial Agent: A Comprehensive Review

Sartika Gunawan Putri^{1*}, Teuku Nanda Saifullah Sulaiman², Bambang Retnoaji¹, Endah Retnaningrum¹¹ Faculty of Biology, Gadjah Mada University² Faculty of Pharmacy, Gadjah Mada University

Abstract

Cocoa (*Theobroma cacao* L.) belongs to the genus *Theobroma* and the family Malvaceae. This plant is one of the leading plantation commodities in Indonesia. This review aims to discuss the potential of *Theobroma cacao* L. as an antibacterial by reviewing its phytochemicals and bioactivity, and to provide scientific evidence for future research. This review was compiled from the results of literature searches via Google Scholar, ResearchGate, Science Direct, and Springer-Link search engines using the keywords "Cocoa Phytochemical and Antibacterial Activity", "Antibacterial activity of cocoa", and other relevant keywords. The articles obtained were selected based on inclusion and exclusion criteria and then discussed narratively. Based on several reviewed research results, the cocoa plant contains phytochemicals, including saponins, flavonoids, polyphenols, tannins, alkaloids, terpenoids, and steroids. These compounds are known to have antibacterial activity by inactivating microbial cell adhesins and enzymes, disrupting the transport of proteins in the inner layers of cells, cell wall polypeptides, so that cell wall formation is less than perfect, damaging bacterial cell membranes, and followed by the release of intracellular compounds until cell lysis occurs.

Keywords: antibacterial, cocoa, phytochemical, *Theobroma cacao*

Received: September 9, 2025 | Revised: November 23, 2025 | Accepted: December 13, 2025

Introduction

Cocoa (*Theobroma cacao* L.) is one of the most economically valuable cultivated plants among the 22 species in the genus *Theobroma* (family Malvaceae). It originates from tropical rainforests characterized by high rainfall, stable temperatures, and relatively high humidity, which are essential condition for optimal growth. In Indonesia, cocoa is typically cultivated at altitudes ranging from 1 to 600 meters above sea level, with ideal temperature conditions between 30°C and 32°C. The botanical classification of *Theobroma cacao* L. is as follows (Tjitrosoepomo, 1988):

Kingdom	: Plantae
Division	: Tracheophyta
Class	: Magnoliopsida
Order	: Malvales
Family	: Malvaceae
Genus	: <i>Theobroma</i>
Species	: <i>Theobroma cacao</i> L.

Morphologically, the cocoa plant comprises roots, stems, leaves, flowers, fruits, and seeds, each of which contributes to cultivation success and the improvement of crop quality and yield (Martono, 2014). As one of Indonesia's leading plantation commodities, cocoa holds

substantial economic importance. Sulawesi Island is the country's primary cocoa-producing region, with Central Sulawesi ranking as the top-producing province, followed by Southeast Sulawesi and South Sulawesi (Directorate General of Plantations, 2021). Beyond its agricultural and economic relevance, cocoa has garnered significant scientific interest due to its rich content of bioactive compounds which have been reported to exhibit antimicrobial activity against a wide range of pathogens. Extensive research has explored the potential applications of various parts of the cocoa plant, including the seeds, pods, seed coats, stem bark, and leaves. In light of the growing prevalence of antibiotic resistance, exploring cocoa as a natural, safe, and effective antibacterial source has become increasingly relevant.

Cocoa seeds and their by-products contain high concentrations of flavonoid (flavanone), phenolic acids, as well as methylxanthines such as theobromine and caffeine (Peláez et al., 2016; Wardana et al., 2024). These phytochemicals are associated with a wide range of biological activities, including antioxidant, anti-inflammatory, cardioprotective, and immunomodulatory effects. Importantly, cocoa-derived compounds have shown antibacterial activity. Several studies have demonstrated that extracts from cocoa pod husks, stem bark, or seeds inhibit the growth of bacteria, including *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, and *Streptococcus mutans* (Hasanuddin et al., 2019; Yahya et al., 2021; Yumas et al., 2022; Rahayu et al., 2023a). For example, analysis of cocoa pod husk extract revealed the presence of flavonoids, tannins, saponins, and triterpenoids, with MIC values of 16 mg/mL for *Porphyromonas gingivalis* and 8 mg/mL for *S. mutans*

* Corresponding Author:

Sartika Gunawan Putri
Faculty of Biology, Gadjah Mada University
Phone: +628525555851
E-mail: sartikagunawanputri@gmail.com

(Rahayu et al., 2023a). Cocoa pod husk extracts, obtained through ultrasonic method with ethanol 70% then formulated into gel, have also shown growth inhibition against *Staphylococcus aureus* (Rahayu et al., 2023b).

However, studies on cocoa's antibacterial activity remain fragmented and limited in several aspects. First, considerable variability in extraction methods, including solvent choice and technique, strongly affects the yield and composition of bioactive compounds. Second, many studies rely on crude extracts without fully characterizing the compounds responsible for antibacterial effects. Although total phenolic content has often been measured, detailed profiling (e.g., using HPLC-MS) is rarely performed for each plant part. Third, most antibacterial assays have been conducted *in vitro*, with few addressing bioavailability, stability in biological systems, or potential applications in therapeutics.

Therefore, a systematic synthesis of the existing literature is needed to clarify the antibacterial potential of cocoa and identify critical knowledge gaps. This review aims to summarize the key bioactive compounds present in cocoa and their known biological activities, evaluate and compare findings from antibacterial studies across various plant parts (seeds, pod husks, seed coats, stem bark, and leaves), and discuss the proposed mechanisms underlying the observed antibacterial effects. By integrating and analyzing these findings, this article intends to provide a valuable reference for future research and the development of cocoa-based antibacterial agents.

Methods

Data Collection

The data used in this review article were obtained from scientific journal articles accessed through several academic search engines, including Google Scholar, ResearchGate, ScienceDirect, and SpringerLink. The key-

words used in the search included "Cacao Phytochemical and Antibacterial Activity," "Antibacterial Activity of Cacao Against Acne Bacteria," and other relevant terms. The retrieved articles and books were screened according to predefined inclusion and exclusion criteria, particularly focusing on studies published mostly (80%) within the last ten years to ensure the relevance and timeliness of the reviewed data. The eligible studies were subsequently analyzed and synthesized in a narrative format.

Inclusion and Exclusion Criteria

The selected articles were published in either Indonesian or English, originating from national or international peer-reviewed journals, and were available in Open Access and full text. Eligible studies focused on the phytochemical content of *Theobroma cacao* L. and its antibacterial activity, particularly those involving *in vitro* testing. Textbooks providing botanical descriptions of *Theobroma cacao* L. were also included. Articles or textbooks that focused solely on the geographical distribution of the plant or discussed other pharmacological properties unrelated to antibacterial activity were excluded.

Results

Phytochemical and Antibacterial Potential of Cocoa

Plants produce both primary metabolites, which are essential for cellular metabolism, and secondary metabolites, which serve important ecological functions such as defense against pests and diseases. The chemical composition of a plant is often closely associated with its taxonomy and nomenclature (Pujoarinto, 2001). Based on various phytochemical studies conducted on cocoa plants, the identified chemical compounds are summarized in Table 1. Meanwhile, the antibacterial potential of cocoa leaf extracts is shown in Table 2.

Table 1. Phytochemical compound of cocoa (*Theobroma cacao* L.)

Plant Parts	Solvent	Compounds	References
Stem bark	Ethanol	Alkaloids, Saponins, Phenols, Glycosides, Carboxylic acids, Flavonoids, Tannins	Nwokonkwo & Okeke, 2014
Leaf	Methanol	Flavonoids, Flavanols, Procyanidins, Methylxanthines, Polyphenols, Triterpenes, Steroids, Saponins, Tannins	Singh et al., 2015; Syarifah, 2018; Hartiningsih & Supriyanto, 2023; Nayim et al., 2018
	Ethanol	Flavonoids, Alkaloids, Tannins, Saponins, Steroids, Glycosides	Rani et al., 2022
Seed	Methanol	Alkaloids, Tannins, Flavonoids, Polyphenols, Saponins, Steroids, Triterpenes, Anthraquinones	Singh et al., 2015; Nayim et al., 2018
	Acetic acid & Methanol	Theobromine	Peláez et al., 2016
Pod husk	Methanol	Alkaloids, Phenols, Flavonoids, Saponins, Tannins, Triterpenes	Singh et al., 2015; Rachmawaty et al., 2017
	Ethanol	Alkaloids, Flavonoids, Tannins, Saponins, and Triterpenoids	Rahayu et al., 2023
	Ethyl acetate	Flavonoids, Saponins, Tannins	Singh et al., 2015
	n-Hexane	Terpenoids, Steroids	Mustanir et al., 2020
	Dichloromethane	Steroids (γ -sitosterol and Stigmasterol)	Febrina et al., 2024
Seed coat	Ethanol	Alkaloids, Polyphenols, Flavonoids, Tannins, Terpenoids, Saponins	Yumas, 2017

Table 2. Antibacterial potential of extracts from the cocoa plant (*Theobroma cacao* L.)

Plant Parts	Bacteria	References
Leaf	<i>Klebsiella pneumoniae</i> , <i>Shigella dysenteriae</i> , <i>Staphylococcus aureus</i> , and <i>Enterobacter aerogenes</i>	Singh et al., 2015; Nayim et al., 2018
	<i>Staphylococcus aureus</i>	Mandhaki et al., 2021
	<i>Cutibacterium acnes</i> and <i>Staphylococcus epidermidis</i>	Putri & Kaliu, 2022
Seed	<i>Staphylococcus aureus</i> , <i>Salmonella</i> sp., <i>Pseudomonas aeruginosa</i> , <i>Klebsiella pneumoniae</i> , and <i>Escherichia coli</i>	Singh et al., 2015; Nayim et al., 2018
	<i>Streptococcus mutans</i>	Yumas et al., 2022
	<i>Fusobacterium nucleatum</i>	Lagha et al., 2021
Stem bark	<i>Klebsiella pneumoniae</i> , <i>Shigella dysenteriae</i> , <i>Staphylococcus aureus</i> , <i>Salmonella</i> sp., and <i>Serratia marcescens</i> ;	Singh et al., 2015
	<i>Staphylococcus epidermidis</i> , <i>Pseudomonas aeruginosa</i> , and <i>Salmonella choleraesuis</i>	Santos et al., 2014
	<i>Staphylococcus aureus</i> , <i>Salmonella</i> sp., and <i>Escherichia coli</i>	Hasanuddin et al., 2019
	<i>Staphylococcus aureus</i> and <i>Escherichia coli</i>	Yahya et al., 2021
	<i>Phorphyromonas gingivalis</i> and <i>Streptococcus mutans</i>	Rahayu et al., 2023(a)
	<i>Staphylococcus aureus</i>	Indrianingsih et al., 2021
Pod husk	<i>Propionibacterium acnes</i>	Adha et al., 2021
	<i>Staphylococcus aureus</i>	Rahayu et al., 2023(b)

Discussion

Cocoa leaf, pod husk, seed, and stem bark extracts have potential as an antibacterial agent because it contains phytochemicals such as saponins, flavonoids, tannins, alkaloids, terpenoids, and steroids (Singh et al., 2015; Syarifah, 2018; Hartiningsih & Supriyanto, 2023; Rani et al., 2022; Nayim et al., 2018; Rachmawaty et al., 2017; Rahayu et al., 2023; Nwokonkwo & Okeke, 2014).

Saponins

Saponins are natural compounds typically composed of a sugar moiety (glycone) and a non-sugar moiety (aglycone) linked through a glycosidic bond. These compounds can be classified as either triterpenoid saponins (C-30) or steroid saponins (C-27). In *Theobroma cacao* L., saponin compounds belong to the glycoside group, specifically anthraquinones (Nwokonkwo & Okeke, 2014; Nayim et al., 2018).

Saponins damage bacterial cells by degrading the cell wall, followed by disruption of membrane proteins and the cytoplasmic membrane, leading to leakage of cellular contents (Dong et al., 2020). Saponins bind to lipopolysaccharides in the bacterial cell wall, thereby increasing its permeability. This destabilizes the bacterial cell wall membrane and reduces its surface tension in both Gram-positive (Hassan, 2008) and Gram-negative bacteria (Lawal et al., 2014), leading to cell wall lysis.

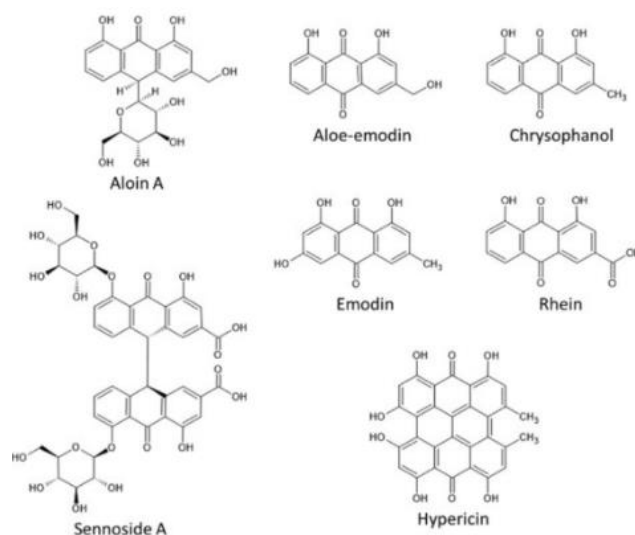


Fig. 1. Structure of the glycoside group (anthraquinones) compounds (Soto-Blanco, 2022)

Flavonoids

The type of flavonoid compound found in the cocoa plant is procyanidin (Syarifah, 2018). Several studies have reported that procyanidin exhibits antibacterial activity (Bi et al., 2021; Huang et al., 2022; Ares et al., 2023). Procyanidin belongs to the class of phenolic compounds, which also includes flavonols, phenolic acids, and anthocyanins. Cocoa seed extract, rich in polyphenols (30.93%) mainly as procyanidins (96.82%, 75%

pathogen infections, not necessarily in “normal” healthy tissue, and the studies did not link arjunolic acid in cacao to antibacterial or bacterial growth inhibition.

The mechanism of action of terpenoids involves binding to transmembrane proteins in the outer membrane of the bacterial cell wall, forming strong polymeric bonds that cause damage and thereby inhibit bacterial growth or induce cell death. The broad mechanism for both terpenoids and triterpenoids seems to overlap, as membrane disruption appears common to both general terpenoids and triterpenoids. However, because triterpenoids are larger and more lipophilic, they might have a greater ability to interact with lipid membranes (especially in bacteria) and possibly penetrate deeper into the cell or interfere with intracellular targets (protein synthesis, DNA repair) more than smaller terpenoids (Cowan, 1999; Ibrahim et al., 2019; Yamaguchi, 2022). Some research suggest that triterpenoids often show synergy with conventional antibiotics (e.g., the pentacyclic triterpenoids + antibiotics paper), indicating perhaps additional modes of action (or at least beneficial combinations) (Hamza et al., 2016). The specificity of mode of action studies for terpenoids or triterpenoids is still somewhat limited.

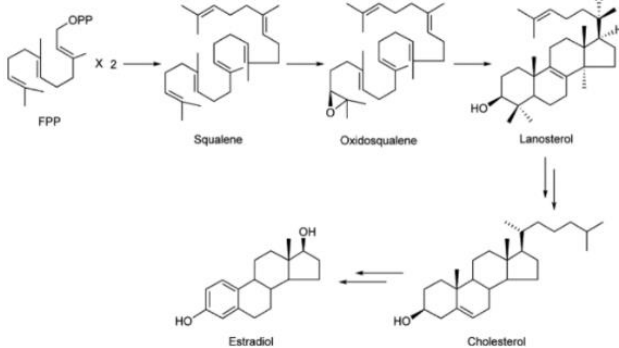


Fig. 5. Structure of the triterpenoid compound group (Kushiro & Ebizuka, 2010)

Steroids

Steroid compounds found in the cocoa plant include stigmasterol and γ -sitosterol (Febrina et al., 2024). Several studies have demonstrated that stigmasterol (Alawode et al., 2021; Yusuf et al., 2018) and γ -sitosterol exhibit antibacterial activity (Ríos-Chávez et al., 2019). Steroids act as antibacterial agents by inhibiting bacterial growth through interactions with lipid membranes and by altering the sensitivity of bacterial liposomes to steroid components, leading to leakage (Madduluri et al., 2013).

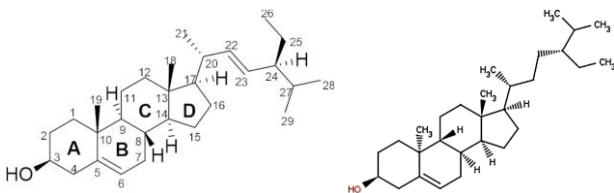


Fig. 6. Structures of stigmasterol (a) and γ -sitosterol (b) compounds (Dube et al., 2023; Balamurugan et al., 2015)

Conclusion

Extracts of the cocoa plant (*Theobroma cacao* L.) have demonstrated potential as natural antibacterial agents against both Gram-negative and Gram-positive bacteria, as evidenced by several *in vitro* studies. The phytochemical constituents identified in *T. cacao*, such as saponins, flavonoids, tannins, alkaloids, terpenoids, and steroids, are widely recognized for their antibacterial properties through various mechanisms, including disruption of bacterial cell membranes, inhibition of metabolic enzymes, and interference with nucleic acid synthesis.

Nevertheless, current research on the antibacterial activity of *T. cacao* remains predominantly qualitative and descriptive. Most studies have focused on the mere presence of phytochemical groups rather than comprehensive quantitative analyses or structural elucidation of the active compounds. Consequently, the specific bioactive molecules responsible for antibacterial activity in most parts of the cocoa plant have not been clearly identified. This limitation makes it difficult to establish clear relationships between phytochemical composition and antibacterial potency.

Comparative findings from different plant parts indicate varying antibacterial potential. Extracts from cocoa leaves are generally reported to exhibit stronger inhibition against Gram-positive bacteria, which is often attributed to a higher content of flavonoids and phenolic compounds. In contrast, extracts from seeds and pods tend to show moderate activity. These differences may be influenced by variations in phytochemical distribution, extraction techniques, solvent polarity, and the bacterial strains tested. Therefore, standardization of extraction and assay methods is necessary to enable more accurate comparisons and reproducibility across studies.

In addition, limited attention has been given to possible synergistic or antagonistic interactions among phytochemicals in cocoa extracts. Considering that antibacterial efficacy may result from complex interactions rather than single compounds, further investigation into these interactions is essential. Another significant research gap lies in the scarcity of *in vivo* studies, as most existing reports rely solely on *in vitro* assays. Mechanistic studies at the molecular and cellular levels are also lacking. To date, few studies have examined how specific phytochemicals from various cocoa plant parts affect bacterial cell structures or functions. The potential cellular targets such as the bacterial cell wall, cytoplasmic membrane, protein synthesis machinery, or genetic material have not been clearly identified.

Understanding these mechanisms is not only essential for elucidating the biological role of cocoa-derived compounds but also crucial for guiding the development of targeted antibacterial agents or natural-based antibiotics. Knowledge of how these phytochemicals interact with bacterial cells will enable the design of more effective and specific antimicrobial formulations, reduce the risk of bacterial resistance, and enhance the utilization of cocoa plant derivatives in pharmaceutical or food preservation applications.

This review synthesizes the available literature and emphasizes the need for more comprehensive, integrative, and standardized research on the phytochemical composition and antibacterial activity of all parts of the cocoa plant. A deeper understanding of the distribution, concentration, and mechanisms of these bioactive compounds will strengthen the scientific foundation for the development of cocoa-based antibacterial agents.

Acknowledgment

The authors gratefully acknowledge the financial support provided by the Indonesian Education Scholarship, Center for Higher Education Funding and Assessment, and Indonesian Endowment Fund for Education.

References

- Adha, S., Dwi, & Ibrahim, M. (2021). Aktivitas antibakteri ekstrak kulit buah kakao (*Theobroma cacao* L.) terhadap bakteri *Propionibacterium acnes*. *LenteraBio : Berkala Ilmiah Biologi*, 10(2), 140-145. <https://doi.org/10.26740/lenterabio.v10n2.p140-145>
- Alawode, T. T., Lajide, L., Olaleye, M. & Owolabi, B. (2021). Stigmasterol and β -sitosterol: antimicrobial compounds in the leaves of *Icacina trichantha* identified by GC-MS. *Beni-Suef Univ J Basic and Appl Sci*, 10(80), 1-8. <https://doi.org/10.1186/s43088-021-00170-3>
- Ares, P.S., Gaur, G., Willing, B.P., Weber, F., Schieber, A., Ganzle, G. M. (2023). Antibacterial and enzyme inhibitory activities of flavan-3-ol monomers and procyanidin-rich grape seed fractions. *Journal of Functional Foods*, 107, 105643. <https://doi.org/10.1016/j.jff.2023.105643>
- Balamurugan, R., Stalin, A., Aravinthan, A., & Kim, J. (2015). γ -sitosterol a potent hypolipidemic agent: in silico docking analysis. *Med Chem Res*, 24, 124-130. <https://doi.org/10.1007/s00044-014-1075-0>
- Bi, J., Tian, C., Zhang, G.L., Hao, H., Hou, H.M. (2021). Novel procyanidins-loaded chitosan-graft-polyvinyl alcohol film with sustained antibacterial activity for food packaging. *Food Chemistry*, 365, 130534. <https://doi.org/10.1016/j.foodchem.2021.130534>
- Campos-Vega, R., Nieto-Figueroa, K. H., & Oomah, B. D. (2018). Cocoa (*Theobroma cacao* L.) Pod husk: renewable source of bioactive compounds. *Trends in Food Science and Technology*, 81, 172-184. <https://doi.org/10.1016/j.tifs.2018.09.022>
- Chen, F., Tang, Q., Ma, H., Bian, K., Seeram, N. P., Li, D. (2019). Hydrolyzable tannins are iron chelators that inhibit dna repair enzyme ALKBH2. *Chem Res Toxicol*, 32(6), 1082-1086. <https://doi.org/10.1021/acs.chemrestox.8b00398>
- Cowan, M. (1999). Plant Product as Antimicrobial Agent. *Clinical Microbiology Reviews*, 12(4), 564-582. <https://doi.org/10.1128/cmr.12.4.564>
- Directorate General of Plantations. (2021). *Statistical of national leading estate crops commodity 2020-2022*. Secretariat of the Directorate General of Plantations, Ministry of Agriculture, Jakarta.
- Dewi, A. M., Priantari I., Munandar, K. (2021). Antibacterial inhibitory test of hand washing soap products made from cocoa husk extract (*Theobroma cacao* L.) On pathogenic bacteria. *Bioscientist: Jurnal Ilmiah Biologi*, 13(2), 1256-1267. <https://doi.org/10.33394/bioscientist.v13i2.15237>
- Dong, S., Yang, X., Zhao, L., Zhanga, F., Houd, Z., Xue, P. (2020). Antibacterial activity and mechanism of action saponins from *Chenopodium quinoa* wildl. Husks against foodborne pathogenic bacteria. *Industrial Crop & Products*, 149, 112350. <https://doi.org/10.1016/j.indcrop.2020.112350>
- Dube, N. P., Tembu, V. J., Nyemba, G. R., Davison, C., Rakodi, G. H., Kemboi, D., Mare, J., Siwe-Noundou, X. & Manicung, A. E. (2023). In vitro cytotoxic effect of stigmasterol derivatives against breast cancer cells. *BMC Complementary Med Ther*, 23(316), 1-12. <https://doi.org/10.1186/s12906-023-04137-y>
- Febrina, R. V., Yahya, M., Ginting, B., Saidi, N. (2024). DPPH-based antioxidant activity of dichloromethane extract from cocoa pod husk (*Theobroma cacao* L.). *Jurnal Natural*, 24(2), 82-86. <https://doi.org/10.24815/jn.v24i2.36174>
- Francisco, V.P., Cerny, M., Valentin, R., Delacourt, F.M., Paillard, A., Alignan, M. (2024). Development of gc-ms coupled to gc-fid method for the quantification of *cannabis* terpenes and terpenoids: application to the analysis of five commercial varieties of medicinal *Cannabis*. *Journal of Chromatography B*, 1247, 124316. <https://doi.org/10.1016/j.jchromb.2024.124316>
- Frešer, F., Bren, U., Hostnik, G. (2024). Chelation of iron(ii) ions by ellagitannins—effects of hexahydroxydiphenoyl and nonahydroxytriphenoyl groups. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 313 (124079), 1-14. <https://doi.org/10.1016/j.saa.2024.124079>
- Gold, V. (2019). *The IUPAC compendium of chemical terminology: the gold book* (4th Ed). NC: International Union of Pure and Applied Chemistry (IUPAC), Research Triangle Park.
- Govindarajan, R. K., Revathi, S., Rameshkumar, N., Krishnan, M. & Kayalvizhi, N. (2016). Review microbial tannase: current perspectives and biotechnological advances. *Bio-catalysis and Agricultural Biotechnology*, 6, 168-175. <https://doi.org/10.1016/j.cbab.2016.03.011>
- Guefack, M.G.F., Messina, N.D.M. Mbayeng, A.T., Nayim, P., Kuete, J.R.N., Matieta, V.Y., Chi, G. F., Ngadjui, B.T., Kuete, V. (2022). Antibacterial and antibiotic-potentiating activities of the hydro-ethanolic extract and protoberberine alkaloids from the stem bark of *Enantia chlorantha* against multidrug-resistant bacteria expressing active efflux pumps. *J Ethnopharmacol*, 296, 115518. <https://doi.org/10.1016/j.jep.2022.115518>
- Hamza, M., Nadir, M., Mehmood, N., Farooq, A. (2016). In vitro effectiveness of triterpenoids and their synergistic effect with antibiotics against *Staphylococcus aureus* strains. *Indian Journal Pharmacol*, 4(6), 710-714. <https://doi.org/10.4103/0253-7613.194851>
- Hartiningih, S. & Supriyanto. (2023). Extraction of phenolic total compound and determination of antioxidant activity of cocoa leaves extracted using various solvents. *Journal of Agricultural Engineering Lampung*, 12(1), 129-138. <https://doi.org/10.23960/jtep-l.v12i1.129-138>
- Hasanuddin, A., Anwar, K., Mappatoba, M., & Hafisah. (2019). Antibacterial and antioxidant activities of ethanol extracts of cocoa husk (*Theobroma cacao* L.) with Maltodextrine in various concentration. *IOP Conference Series: Earth and Environmental Science*, 255, 1-10. <https://doi.org/10.1088/1755-1315/255/1/012017>
- Hassan, S. (2008). *Gram-positive and Gram-negative bacteria: morphology, physiology, and pathogenicity*. Pustaka: Cendekia Publisher, Surabaya.
- Huang, L., Yang, K.P., Zhao, Q., Lia, H.J., Wang, J.Y., Wu, Y.C.. (2022). Corrosion resistance and antibacterial activity of procyanidin B2 as a novel environment-friendly inhibitor for Q235 steel in 1 M HCl solution. *Bioelectrochemistry*, 143, 107969. <https://doi.org/10.1016/j.bioelechem.2021.107969>
- Ibrahim, H. A., Elgindi, M. R., Ibrahim, R. R., & El-Hosari, D. G. (2019). Antibacterial activities of triterpenoidal compounds isolated from *Calothamnus quadrifidus* leaves. *BMC Complementary Altern Med*, 19(1), 102-107. <https://doi.org/10.1186/s12906-019-2512-x>
- Indrianingsih, A. W., Wulanjati, M. P., Windarsih, A., Bhattacharjya, D. K., Suzuki, T., Katayama, T. (2021). In vitro studies of antioxidant, antidiabetic, and antibacterial activities of *Theobroma cacao*, *Annona muricata* and *Clitoria ternatea*. *Bio-catalysis and Agricultural Biotechnology*, 33, 101995. <https://doi.org/10.1016/j.BCAB.2021.101995>
- Kushiro, T. & Ebizuka, Y. (2010). *Comprehensive natural products ii: chapter triterpenes* (1st ed.). Elsevier Science.
- Lagha, A. B., Huacho, P. M., Grenier, D. (2021). A cocoa (*Theobroma cacao* L.) extract impairs the growth, virulence properties,

- and inflammatory potential of *Fusobacterium nucleatum* and improves oral epithelial barrier function. *PLoS One*, 16(5), 1-17. <https://doi.org/10.1371/journal.pone.0252029>
- Liu M., Feng, M., Yang, K., Cao, Y., Zhang, J., Xu, J., Hernández, S. H., Wei, X. & Fan, M. (2020). Transcriptomic and metabolomic analyses reveal antibacterial mechanism of astringent persimmon tannin against methicillin-resistant *Staphylococcus aureus* isolated from pork. *Food Chemistry*, 309, 125692. <https://doi.org/10.1016/j.foodchem.2019.125692>
- Madduluri S., Rao, K.B. & Sitaram, B. (2013). In vitro evaluation of antibacterial activity of five indigenous plants extract against five bacterial pathogens of human. *Intl J Pharm Pharm Sci*, 5(4), 679-684. <https://api.semanticscholar.org/CorpusID:55481382>
- Mandhaki, N., Huda, C. & Putri, A.E. In vitro antibacterial activity of cocoa leaf (*Theobroma cacao* L.) fractions against *Staphylococcus aureus*. (2021). *J Sains Kes*, 3(2), 188-193. <https://doi.org/10.25026/jsk.v3i2.269>
- Martono, B. (2014). *Morphological characteristics and germplasm activities of cocoa plants*. Research Center for Industrial and Beverage Crops, Sukabumi.
- Nayim, P., Mbayeng, A.T., Wamba, B. E., Fanka, A.G., Dzatam, M.J.K. & Kuete, V. (2018). Antibacterial and antibiotic potentiating activities of thirteen cameroonian edible plants against gram-negative resistant phenotypes. *Scientific World Journal*, 11, 1-14. <https://doi.org/10.1155/2018/4020294>
- Nwokonkwo, D., & Okeke, G. (2014). The chemical constituents and biological activities of stem bark extract of *Theobroma cacao* L. *Global Journal of Science Frontier Research : E Interdisciplinary*, 14(4), 35-40. https://globaljournals.org/GJSFR_Volume14/4-The-Chemical-Constituents.pdf
- Osonga, F.J., Akgul, A., Miller, R.M., Eshun, G.B., Yazgan, I., Akgul, A., Sadik, O.A. (2019). Antimicrobial activity of a new class of phosphorylated and modified flavonoids. *ACS Omega*, 4(7), 12865-12871. <https://doi.org/10.1021/acsomega.9b00077>
- Peláez, P. P., Guerra, S., & Contrera, D. (2016). Changes in physical and chemical characteristics of fermented cocoa (*Theobroma cacao*) seeds with manual and semi-mechanized transfer, between fermentation boxes. *Scientia Agropecuaria*, 7(2), 111-119. <https://doi.org/10.17268/sci.agropecu.2016.02.04>
- Pujoarinto, A. (2001). *Taxonomy of Higher Plants*. Open University Publishing Center, Jakarta.
- Putri, S. G. & Kaliu, S. (2022). Antibacterial activity of cocoa leaf extract *Theobroma cacao* L. against acne-causing bacteria *Cutibacterium acnes* and *Staphylococcus epidermidis*. *BI-EDUSCIENCE*, 6(2), 288-293. <https://doi.org/10.22236/jbes/6310267>
- Rahayu, Y. C., Setiawatie, E. M., Rahayu, R. P., Ramaand, D. E. (2023a). Analysis of antioxidant and antibacterial activity of cocoa pod husk extract (*Theobroma cacao* L.). *Dental Journal (Journal of Dental Medicine)*, 56(4), 220-225. <https://doi.org/10.20473/j.djmk.v56.i4.p220-225>
- Rahayu, Y. C., Prihanti, A. M., Salsabila, T. P. (2023b). Inhibition of cocoa pod husk (*Theobroma cacao* L.) extract gel against *Staphylococcus aureus*. *Journal of Dentomaxillofacial Science*, 8(1), 201-204. <https://doi.org/10.15562/jdmfs.v8i1.1188>
- Rani, Z., Ridwanto, Miswanda, D., Yuniarti, R., Sutiani, A., Syahputra, R.A. & Irma, R. (2022). Cytotoxicity test of cocoa leaf ethanol extract (*Theobroma cacao* L.) with Brine Shrimp Lethality Test (BSLT) method. *Indonesian Journal of Chemical Science and Technology (IJCST) Universitas Negeri Medan*, 5(2), 80-87. <https://doi.org/10.24114/ijcst.v5i2.37452>
- Resende, M. L. V., Flood, J., Ramsden, J. D., Rowan, M. G., Beale, M. H., Cooper, R. M. (1996). Novel phytoalexins including elemental sulphur in the resistance of cocoa (*Theobroma cacao* L.) to *Verticillium wilt* (*Verticillium dahlia* Kleb.). *Physiological and Molecular Plant Pathology Journal*, 48(5), 347-359. <https://doi.org/10.1006/pmpp.1996.0028>
- Rijayanti, R. P. (2014). In vitro antibacterial activity test of ethanol extract of bacang mango leaves (*Mangifera foetida* L.) Against *Staphylococcus aureus*. *Student Publication Journal PSPD FK Universitas Tanjungpura*, 1(1), 1-17. <https://jurnal.untan.ac.id/index.php/jfk/article/view/6330>
- Ríos-Cháves, P., Perez-Gonzalez, J., Salgado-Garciglia, R., Ramirez-Chávez, E., Molina-Torres, J., Martinez-Trujillo, M., & Carreon-Abud, Y. (2019). Antibacterial and cytotoxicity activities and phytochemical analysis of three ornamental plants grown in Mexico. *An Acad Bras Cienc* 91(2), e20180468. <https://doi.org/10.1590/0001-3765201920180468>
- Russo, E.B. & Marcu, J. D. Kendall, S.P.H. Alexander. (2017). *Chapter Three-Cannabis Pharmacology: The Usual Suspects and A Few Promising Leads*. Academic Press, Advances in Pharmacology.
- Santos, R. X., Oliveira, D. A., Sodre, G. A., Gosmann, G., Brendel, M. & Pungartnik, C. (2014). Antimicrobial activity of fermented *Theobroma cacao* pod husk extract. *Genetics and Molecular Research*, 13(3), 7725-7735. <https://doi.org/10.4238/2014.september.26.10>
- Soto-Blanco, B. (2022). *Herbal biomolecules in healthcare applications chapter 12 : herbal glycosides in healthcare*. Academic Press, United States of America.
- Syarifah, A. N. (2018). Extraction and identification of antioxidant compounds in crude cocoa leaf extract (*Theobroma cacao*) [Thesis]. Yogyakarta. Universitas Gadjah Mada.
- Singh, N., Datta, S., Dey, A., Chowdhury, A. R., & Abraham, J. (2015). Antimicrobial activity and cytotoxicity of *Theobroma cacao* Extracts. *Der Pharmacia Lettre*, 7(7), 287-294. <http://scholarsresearchlibrary.com/archive.html>
- Tjitrosopomo, G. (1988). *Plant taxonomy (Spermathopyta)*. Gajah Mada University Press, Yogyakarta.
- Wardana, I. M. W., Pramitha, D. A. I., Wibawa, A. A. C., Sanjiwani, N. M. S. (2024). Identification of flavonoid compounds in cocoa seed (*Theobroma cacao* L.) isolates from the n-butanol fraction with the highest antioxidant activity using UV-Vis spectrophotometry. *Chimica et Natura Acta*, 12(2), 98-105. <https://doi.org/10.24198/cna.v12.n2.48577>
- Yahya, M., Saidi, N., Ginting, B., Purnama, A. (2020). Chemical composition and cytotoxic activities of n-hexane extract from cacao pod husk (*Theobroma cacao* L.). *Chemical Data Collections*, 30, 2405-8300. <https://doi.org/10.1016/j.cdc.2020.100553>
- Yahya, M., Ginting, B., Saidi, N. (2021). In-vitro screenings for biological and antioxidant activities of water extract from *Theobroma cacao* L. pod husk: potential utilization in foods. *Molecules*, 26(22), 6915. <https://doi.org/10.3390/molecules26226915>
- Yamaguchi, T. (2022). Antibacterial effect of the combination of terpenoids. *Arch Microbiol*, 204, 520. <https://doi.org/10.1007/s00203-022-03142-y>
- Yan, Y., Li, X., Zhang, C., Lv, L., Gao, B., Li, M. (2021). Research progress on antibacterial activities and mechanisms of natural alkaloids: a review. *Antibiotics*, 10(3), 318. <https://doi.org/10.3390/antibiotics10030318>
- Yanti, B. & Rasmin, M. (2016). The role of xanthine in obstructive pulmonary disease. *J Respir Indo*, 36(4), 267-273. <https://arsip.jurnalrespirologi.org/wp-content/uploads/2017/06/JRI-2016-36-4-267.pdf>
- Yumas, M., Loppies, J. E., Khaerunnisa, Ramlah, S., Rosniati & Lullung, A. (2022). Characterization of toothpaste made with unfermented cocoa powder (*Theobroma cacao* L.) against bacteria *Streptococcus mutans*. *E3S Web of Conferences EDP Science*, 344: 1-9. <https://doi.org/10.1051/e3sconf/202234401002>
- Yusuf, A. J., Abdullahi, M. I., Aleku, G. A., Ibrahim, I.A.A., Alebiosu, C. O., Yahya, M., Adamu, H.W., Sanusi, A., Mailafiya, M. M., & Abubakar, H. (2018). Antimicrobial activity of stigmasterol from the stem bark of *Neocarya macrophylla*. *Journal of Medicinal Plants For Economic Development*, 2(1), a38. <https://doi.org/10.4102/jomped.v2i1.38>
- Zhu, F., Du, B., & Li, J. (2015). Recent advance on the antitumor and antioxidant activity of grape seed extracts. *International Journal of Wine Research*, 7, 63-67. <https://doi.org/10.2147/IJWR.S76162>