

Mini Review: Extraction Methods, Phytochemical Profile, and Pharmacological Potential of the Marine Sponge *Stylissa carteri*

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Abstract

Stylissa carteri is an Indo-Pacific marine sponge recognized as a prolific source of bioactive secondary metabolites relevant to drug discovery. This mini-review integrates current evidence on extraction strategies, phytochemical diversity, and pharmacological activities reported for this species. Across 12 studies, sample preparation commonly involves freezing, freeze-drying, and pulverization, followed by solvent maceration, predominantly using methanol or ethanol, with polarity-guided fractionation to enrich distinct metabolite classes. Identified constituents include bromopyrrole alkaloids, cyclic peptides, oleanane-type saponins, triterpenes, phenolic diterpenes, fatty acids, ceramides, and cerebrosides, revealing notable geographic and methodological influences on chemical profiles. Biological evaluations demonstrate a broad activity spectrum, including anticancer, antibiofilm, antibacterial, antiviral (anti-HIV), antioxidant, and antiplasmodial effects. Bromopyrrole alkaloids show potent antibiofilm and anti-HIV properties, while cyclic peptides and triterpenes display marked cytotoxicity and antiproliferative action, including effects on drug-resistant cancer cell lines. In addition, metabolites from symbiotic bacteria contribute significant antiplasmodial activity, underscoring the holobiont as a pharmacologically valuable system. Collectively, these findings position *S. carteri* as a versatile reservoir of marine natural products with multi-target therapeutic potential. Nonetheless, heterogeneity in extraction protocols, limited structural standardization, and insufficient mechanistic studies constrain translational progress. Future investigations should prioritize optimized and reproducible extraction workflows, advanced metabolomic characterization, and targeted pharmacological validation to accelerate the development of *S. carteri*-derived lead compounds.

Keywords: *Stylissa carteri*, marine natural products, extraction methods, bromopyrrole alkaloids, pharmacological activity

Introduction

Marine sponges are sessile invertebrates widely distributed across temperate, polar, and tropical regions. They are recognized as one of the most prolific sources of bioactive compounds discovered and isolated from the marine environment (Varijakzhan *et al.*, 2021). The production of these compounds is closely linked to the ecological adaptation of sponges as non-motile organisms, relying heavily on chemical defenses to cope with predation, biofouling, spatial competition, and complex interactions with symbiotic microorganisms (De Caralt *et al.*, 2013; Paul *et al.*, 2019). Numerous studies have reported that more than 5,300 secondary metabolites have been isolated from marine sponges, with hundreds of new structures described annually, several of which have progressed into clinical trials as anticancer and antiviral drug candidates (Naqvi *et al.*, 2022;

Varamogianni-Mamatsi *et al.*, 2023). In Indonesia, marine sponges represent a key biological group within marine biodiscovery programs due to their high biomass availability and ease of access in coral reef ecosystems (Hanif *et al.*, 2019).

Secondary metabolites derived from marine sponges encompass a wide range of chemical classes, including alkaloids, terpenoids, cyclic peptides, polyketides, and glycosides, many of which exhibit anticancer, antiviral, antibacterial, and anti-inflammatory activities (Nadar *et al.*, 2022; Raymond & Rakotondraibe, 2025; Varijakzhan *et al.*, 2021). Among these, bromopyrrole alkaloids constitute a particularly prominent group, with more than 140 derivatives reported from various sponge taxa, demonstrating notable anticancer, anti-HIV, and antibacterial properties (Mahamed *et al.*, 2023). Further investigations on *Stylissa* species from Indonesian waters have identified 27

bromopyrrole alkaloids, including (Z)-hymenialdisine, further underscoring the pharmacological relevance of this metabolite class as a valuable source of bioactive compounds (Nugraha *et al.*, 2023).

Stylissa carteri is a marine sponge belonging to the class Demospongiae and is widely distributed throughout the Indo-Pacific region, particularly in the Red Sea, the Gulf of Aqaba, Southeast Asian waters such as Malaysia, and several locations in Indonesia, including the Seribu Islands and North Sulawesi (Bashari *et al.*, 2019; Giles *et al.*, 2015; Palungan *et al.*, 2022). A growing body of evidence indicates that extracts and fractions of *S. carteri* exhibit a broad spectrum of biological activities, including anticancer, antiviral, antibacterial, antibiofilm, antioxidant, and antiplasmodial effects (Inbaneson & Ravikumar, 2012; Palungan *et al.*, 2022; Rahman *et al.*, 2024). These findings position *S. carteri* as a highly promising subject for further investigation in the context of marine-derived drug discovery, particularly within Indonesia's rich marine biodiversity.

Despite numerous individual reports describing the secondary metabolites and biological activities of *S. carteri*, a comprehensive synthesis that explicitly integrates extraction methods, resulting phytochemical profiles, and verified pharmacological activities—especially across different Indo-Pacific localities, including Indonesia—remains lacking. Therefore, this mini review aims to: (1) systematically summarize the extraction methods applied to *S. carteri*; (2) map the major classes of secondary metabolites successfully isolated, with particular emphasis on bromopyrrole alkaloids, cyclic peptides, terpenoids, and bioactive lipids; and (3) critically review the reported activity of pharmacological activities. Through this approach, the review seeks to identify existing knowledge gaps and provide a scientific basis for optimizing extraction strategies and advancing the development of new drug candidates derived from *S. carteri* metabolites in the future.

Morphology and Scientific Classification of *Stylissa carteri*

Stylissa carteri (Dendy, 1889) (Figure 1) is a marine sponge belonging to the class

Demospongiae and is morphologically well known under the common name *elephant ear sponge*, reflecting its characteristic leaf-like or ear-shaped body form. The sponge exhibits a robust growth habit and is typically free-standing, with a flabellate (fan-shaped) morphology or blade-like lobed sheets that may form upright “leaf” structures supported by a short stalk. Reported maximum sizes range from approximately 30 to 50 cm in width (George, 2022). Its coloration commonly varies from yellow to yellow-orange, occasionally appearing brownish, while the surface is relatively coarse due to the presence of protruding spicules. The overall consistency is firm to rigid, a trait typical of demosponges.



Figure 1. The marine sponge *Stylissa carteri* (Giles *et al.*, 2015)

The skeletal architecture of *S. carteri* is composed primarily of megascleres of the style or strongyloxea type, arranged in longitudinal bundles that extend toward and often protrude through the surface. This skeletal organization represents a characteristic feature of the family Scopalinidae and serves as an important diagnostic trait distinguishing *Stylissa* from other genera that were previously considered its taxonomic synonyms (Marine Species Traits, 2025). From a taxonomic perspective, *S. carteri* is classified as follows:

- **Kingdom:** Animalia
- **Phylum:** Porifera
- **Class:** Demospongiae
- **Subclass:** Heteroscleromorpha
- **Order:** Scopalinida
- **Family:** Scopalinidae
- **Genus:** *Stylissa*
- **Species:** *Stylissa carteri* (Dendy, 1889)

Global Distribution of *Stylissa carteri*

Geographically, scientific records indicate that *S. carteri* is widely distributed across key regions of the Indo-Pacific. Its occurrence has been documented in the Red Sea, including the Saudi Arabian coast and extending southward to the vicinity of Socotra, as well as along the eastern African coast in the northwestern Indian Ocean. The species is also reported throughout Southeast and East Asia, encompassing Singapore, Malaysia, Thailand, Vietnam, southern China, and Taiwan (Giles *et al.*, 2015; Lim *et al.*, 2016).

Based on sponge inventories conducted in the region spanning the Singapore Strait to the Taiwan Strait, *S. carteri* exhibits a broad geographic range, covering waters from Singapore and the Malay Peninsula to Taiwan (Huang *et al.*, 2016). In Indonesia, the species has been recorded from multiple localities, including the Seribu Islands (Jakarta), North Sulawesi (Manado Bay, Mantehage Island, and Bangka Island), as well as several other sites identified through integrated morphological and molecular approaches (Aisyah *et al.*, 2025; Bashari *et al.*, 2019; Calcinai *et al.*, 2017). Collectively, these records indicate that *S. carteri* represents an important and widespread component of tropical Indo-Pacific sponge fauna.

Extraction Methods of *Stylissa carteri*

Based on a compilation of data from 12 peer-reviewed scientific publications (Table 1), the extraction approaches applied to *S. carteri* can be broadly divided into two main stages: sample preparation and solvent extraction. Among the surveyed studies, maceration emerged as the dominant extraction technique.

Sample Preparation

Sample preparation represents a critical step that substantially influences both the stability of secondary metabolites and overall extraction efficiency. Most studies reported the use of freeze-drying (lyophilization) as the standard preparative method, in which freshly collected sponge material is frozen at low temperatures (−20 to −80 °C) and subsequently dried under vacuum for approximately 48 h. Freeze-drying removes water through the sublimation of ice directly into vapor, bypassing the liquid phase, thereby reducing moisture content to below 5%

while preserving the chemical integrity of thermolabile compounds (Singh *et al.*, 2023), including bromopyrrole alkaloids and cyclic peptides.

Supporting this approach, metabolomic investigations on the sponge *Geodia barretti* demonstrated that samples subjected to immediate flash-freezing in liquid nitrogen yielded the highest metabolite intensities and the lowest inter-replicate variability. These findings indicate that rapid freezing immediately after collection is an optimal strategy for maintaining the native metabolite profile of marine sponges (Erngren *et al.*, 2021). Following freeze-drying, sponge samples are typically ground into a fine powder using a mortar or mechanical grinder to increase the surface area available for solvent contact. From a theoretical perspective, this step enhances diffusion efficiency, facilitating the transfer of bioactive compounds from the tissue matrix into the extraction solvent (Bitwell *et al.*, 2023).

Solvent Maceration Extraction

The most frequently applied extraction method for *S. carteri* is organic solvent maceration of dried, powdered sponge material. Methanolic maceration is widely employed for the isolation of bromopyrrole alkaloids and other polar metabolites from samples collected in the Red Sea, Bidong Island, the Gulf of Aqaba, as well as from transplanted specimens originating from Pramuka Island. In contrast, ethanol is more commonly used for Indonesian samples, particularly those from Pramuka Island and Bangka Island. Subsequent stepwise fractionation using solvents of increasing polarity (n-hexane, chloroform or dichloromethane, n-butanol, and ethyl acetate) is primarily applied to samples from the Red Sea and Bangka Island to separate distinct classes of compounds, including saponins, phenolic diterpenes, triterpenes, and peptides. Meanwhile, direct extraction with ethyl acetate has been employed for samples from Manado Bay to preferentially enrich semi-polar constituents associated with antibacterial activity. Overall, the combination of freeze-drying or low-temperature drying, followed by fine grinding and solvent maceration, has proven to be a consistent and effective strategy for preserving secondary metabolite stability while yielding a broad spectrum of biological activities.

The preference for polar solvents such as methanol or ethanol in *S. carteri* extraction

aligns with general practices in marine sponge research, where solvent polarity is a key determinant of metabolite diversity. Studies on other sponge taxa, for example *Xestospongia* spp., have shown that increasing the proportion of ethanol in solvent mixtures enhances the diversity of extracted metabolites and tends to enrich polar compounds such as alkaloids and glycosides. In contrast, the inclusion of dichloromethane preferentially extracts non-polar components, including sterols and fatty acids (Bayona *et al.*, 2018). This pattern is consistent with observations in *S. carteri*, where methanol-based extraction optimizes the recovery of bromopyrrole alkaloids and other polar metabolites associated with antibiofilm and anti-HIV activities, whereas ethanol and ethyl acetate fractions are more frequently linked to broad cytotoxic effects against various cancer cell lines.

In comparison with these studies, current extraction protocols for *S. carteri* are generally appropriate in terms of solvent selection. Nevertheless, there remains considerable potential for optimization, particularly through stricter temperature control or the adoption of modern extraction techniques such as ultrasound-assisted extraction (UAE) or microwave-assisted extraction (MAE), which may enhance metabolite yield without compromising the stability of bioactive compounds.

Phytochemical Constituents of *Stylissa carteri*

The phytochemical profile of *S. carteri* indicates that this sponge is a major producer of bromopyrrole alkaloids and cyclic peptides, which are predominantly reported from samples collected in the Red Sea, the Gulf of Aqaba, Bidong Island, and Bangka Island. Compounds such as debromohymenialdisine, hymenialdisine, 10Z-hymenialdisine, oroidin, manzacidin A, and stylisinone represent the pyrrole-imidazole alkaloid group and are associated with antibiofilm, anti-HIV, and anticancer activities. In parallel, cyclic heptapeptides including carteritins A and B, hakellistatin 13, and hymenamides C and D exhibit strong cytotoxic properties.

In contrast, samples from the Egyptian Red Sea are characterized by the dominance of oleanane-type saponins, phenolic diterpenes,

lupane triterpenes, as well as ceramides (styliissamide A) and cerebrosides (styliissoside A). Meanwhile, specimens from Pramuka Island display a phytochemical profile enriched in fatty acids, such as linoleic acid and its derivatives, along with semi-volatile components detected by GC-MS analysis. These findings highlight pronounced geographic variation in the chemical composition of *S. carteri*.

Such variation appears to be strongly influenced by both geographic origin and solvent fractionation. Red Sea samples tend to yield a combination of bromopyrrole alkaloids and structurally complex terpenoids, whereas Indonesian samples (Pramuka, Bangka, and Manado) are comparatively enriched in cyclic peptides, fatty acids, and phenolic or antioxidant compounds. Similar geographic patterns have been observed in other sponge genera, such as *Petrosia* and *Agelas*, where ecological pressures and habitat conditions play a decisive role in shaping the dominance of specific metabolite classes—for example, polyacetylenes in *Petrosia* from temperate regions versus terpenoids and alkaloids in tropical environments (Lee *et al.*, 2021). Collectively, these observations support the interpretation that the diversity of oleanane saponins, triterpenes, cyclic peptides, and alkaloids identified in *S. carteri* from the Red Sea and Indonesian waters reflects distinct ecological adaptations and biogenetic specializations among geographically separated populations (Rohde *et al.*, 2012).

Pharmacological Activities

The pharmacological activity of *S. carteri* encompasses a broad range of anti-infective, antioxidant, and anticancer activities. Debromohymenialdisine isolated from Bidong Island exhibits strong antibiofilm activity against *Pseudomonas aeruginosa* through a non-microbicidal mechanism, making it particularly relevant for biofilm control strategies that minimize selective pressure for antimicrobial resistance. Bromopyrrole alkaloids from Red Sea specimens, including debromohymenialdisine, hymenialdisine, oroidin, and manzacidin A, display not only cytotoxic effects but also potent inhibition of HIV-1 replication. These effects are mediated through the suppression of reverse transcriptase and integrase activities, as well as modulation of kinase signaling pathways. Moreover, their

combination with silver nanoparticles has been shown to further expand their antibacterial activity against clinically relevant pathogens.

In Indonesia, ethanol and ethyl acetate extracts of *S. carteri* from Pramuka Island, Bangka Island, and Manado demonstrate consistent anticancer activity against breast, cervical, and colon cancer cell lines, including trastuzumab- and paclitaxel-resistant variants. These extracts also exhibit antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*, alongside strong antioxidant capacity, indicating their potential utility both as lead compounds for drug development and as adjuvants in chemotherapy.

Beyond sponge-derived metabolites, symbiotic bacteria associated with *S. carteri* from the Thondi coast further expand its pharmacological profile by exhibiting significant antiparasitic activity against *Plasmodium falciparum*. This finding supports the view of the *S. carteri* holobiont as an integrated source of novel antimalarial metabolites. Overall, the combined presence of bromopyrrole alkaloids, highly cytotoxic cyclic peptides (carteritins and hymenamides), oleanane-type saponins, triterpenes, and symbiont-derived metabolites generates a diverse bioactivity portfolio encompassing antibiofilm, anti-HIV,

antibacterial, antiparasitic, antioxidant, and multi-target cytotoxic effects. These features position *S. carteri* as one of the most pharmacologically comprehensive Indo-Pacific marine sponges documented to date.

The pharmacological activities reported for *S. carteri* are consistent with general trends observed in marine sponge metabolites. Several reviews indicate that sponges such as *Spongia*, *Neopetrosia*, *Callyspongia*, and *Melophlus* typically exhibit prominence in only a limited number of activities—for example, anticancer and antibacterial, or anti-inflammatory and antioxidant effects—while specific antibiofilm and anti-HIV activities remain relatively underreported (Fristiody et al., 2024; Yang & Liang, 2024). In comparison, the concurrent presence of antibiofilm and anti-HIV bromopyrrole alkaloids, strongly cytotoxic cyclic peptides, and cytotoxic saponins and terpenoids in *S. carteri* highlights an exceptional breadth of bioactivity. Furthermore, the identification of symbiont-derived metabolites with antiparasitic activity reinforces its classification as a “multi-target” marine sponge species, capable of producing a portfolio of bioactive compounds that simultaneously address cancer pathways as well as viral, bacterial, and parasitic infections.

Table 1. Summary of extraction Methods, Chemical Constituents, and Pharmacological Activities of *Stylissa carteri*

Geographic distribution	Sample preparation	Extraction Method	Major Phytochemical Compound	Pharmacological Activities	Reference
Bidong Island, Terengganu, Malaysia	The sponges were collected, cleaned, frozen, and freeze-dried, then ground into a fine powder prior to extraction.	The dried powder was subjected to methanolic maceration, followed by solvent partitioning and chromatographic purification.	Debromohymenialdisine, a bromopyrrole alkaloid, was identified as the main antibiofilm compound.	The extract exhibited antibiofilm activity against <i>Pseudomonas aeruginosa</i> and other bacteria through a non-microbicidal antibacterial mechanism.	(Rahman et al., 2024)
Pramuka Island, Kepulauan Seribu, Jakarta, Indonesia	Fresh sponge specimens were carefully cleaned, dried (either air-dried or in a low-temperature oven), and then ground into a fine powder.	The powder was macerated with ethanol and the extract was concentrated; in several studies, this was followed by stepwise fractionation using solvents such as n-hexane and ethyl acetate.	GC-MS analysis revealed the presence of 1,2-benzenediol, dibutyl phthalate, and 9,12-octadecadienoic acid (ethyl ester/linoleic acid), while other constituents were not fully identified.	The extract showed anticancer properties, displaying cytotoxicity against various breast cancer cell lines (MCF-7, T47D, MDA-MB-231, HCC-1954), including trastuzumab-resistant cells, with antiproliferative effects and induction of apoptosis.	(Bashari et al., 2019)

Geographic distribution	Sample preparation	Extraction Method	Major Phytochemical Compound	Pharmacological Activities	Reference
Red Sea, Saudi Arabia	Sponge specimens were collected by SCUBA diving from coral reefs in the Saudi Red Sea, then carefully cleaned, dried (either air-dried or in a low-temperature oven), and ground to a coarse powder.	The material was macerated with methanol, followed by solvent partitioning and chromatographic separation (open-column and HPLC) to isolate individual alkaloids.	Debromohymenialdisine, hymenialdisine, 10Z-hymenialdisine, and oroidin—bromopyrrole alkaloids—were identified as key scaffolds with inhibitory activity against HIV-1 and several kinases.	These compounds exhibited anti-HIV-1 effects by blocking viral replication and targeting reverse transcriptase/integrase, alongside demonstrable in vitro anticancer activity.	(O’rourke <i>et al.</i> , 2016)
Red Sea, Hurghada, Egypt	Sponge specimens were collected from the Sharm El Sheikh/Hurghada area, then cleaned, dried, and ground into a powder.	The powdered material was extracted by methanol maceration, followed by stepwise fractionation with n-hexane, chloroform, and n-butanol, and subsequent chromatographic purification.	This work led to the isolation of oleanane-type saponins, phenolic diterpenes, lupane triterpenes, as well as a ceramide (stylissamide A) and a cerebroside (stylissoside A).	These compounds showed cytotoxic effects against several cancer cell lines (MCF-7, HepG2, HCT-116), with some exhibiting IC ₅₀ values in the low tens of micromolar range.	(Abdelhameed <i>et al.</i> , 2020)
Gulf of Aqaba, Yordania	Sponge samples were frozen, freeze-dried for 48 hours, then ground to powder.	Extracted with methanol and dichloromethane, followed by fractionation and chemical characterization.	Identified bromopyrrole alkaloids (manzacidine A, debromohymenialdisine, hymenialdisine) and formulated them with silver nanoparticles.	The formulation showed anticancer activity across several cell lines and antibacterial effects against pathogenic bacteria.	(Alqaraleh <i>et al.</i> , 2025)
Red Sea, Saudi Arabia	Sample details not fully described	Methanol extraction	New pyrrole alkaloid, stylisinone	Exhibits anticancer activity against A549 lung adenocarcinoma cells; mechanism still under study.	(Hawas & Abou El-Kassem, 2025)
Bangka Island, North Sulawesi, Indonesia	Sponge specimens were collected, then cleaned, dried, and ground into a powder.	Extracted by methanol maceration, followed by fractionation (n-hexane, chloroform, n-butanol) and chromatographic purification.	Isolated oleanane saponins, phenolic diterpenes, lupane triterpenes, a ceramide (stylissamide A), and a cerebroside (stylissoside A).	Compounds showed cytotoxicity against MCF-7, HepG2, and HCT 116 cells, with several IC ₅₀ values in the low micromolar range.	(Afifi <i>et al.</i> , 2016)
Manado Bay, North Sulawesi, Indonesia	Sponge samples were collected, then cleaned, dried, and ground	Powder macerated with ethyl acetate; the crude extract was assessed	Phytochemical constituents not detailed; emphasis placed on biological	In antibacterial tests, the extract produced clear inhibition zones against	(Palungan <i>et al.</i> , 2022)

Geographic distribution	Sample preparation	Extraction Method	Major Phytochemical Compound	Pharmacological Activities	Reference
	into a powder.	mainly for biological activity rather than full chemical characterization.	activity.	<i>Staphylococcus aureus</i> and <i>Escherichia coli</i> , showing promising antibacterial activity.	
Pramuka Island, Kepulauan Seribu, Indonesia	Transplanted sponge was dried and ground to powder, then macerated with methanol	Macerated with methanol	Specific compounds were not detailed; effects were attributed to phenolic and antioxidant constituents.	The methanol extract showed fairly strong antioxidant activity (DPPH, FRAP)	(Adewali <i>et al.</i> , 2025)
Pramuka Island, Kepulauan Seribu, Indonesia	Sponge collected at Pramuka Island, dried and ground (details not specified).	Macerated with ethanol	Compounds not detailed; focus on the biological effects of the total extract.	Cytotoxic to cervical cancer HeLa cells, both parental and paclitaxel-resistant; induces cell death.	(Hardani <i>et al.</i> , 2018)
Thondi coast, Palk Strait, Tamil Nadu, India	Not direct sponge tissue; symbiotic bacteria from <i>S. carteri</i> were isolated on agar media, then cultured and extracted.	Bacterial metabolites extracted from liquid cultures with organic solvents (e.g., ethyl acetate), followed by antiplasmodial bioassays.	Symbiotic bacterial metabolites (strain code THB17); chemical structures not detailed, focus placed on biological activity.	In vitro antiplasmodial activity against <i>Plasmodium falciparum</i> with high inhibition, indicating the antimalarial potential of <i>S. carteri</i> symbiont metabolites.	(Inbaneson & Ravikumar, 2012)
Pramuka Island, Kepulauan Seribu, Indonesia	<i>S. carteri</i> sponge collected at Pramuka Island, cleaned, dried, and ground into powder; used as raw material for ethanol extract.	Macerated with ethanol, solvent evaporated to obtain a concentrated extract, then tested on HCT 116 colon cancer cells.	Specific compounds not identified (crude extract); focus on cytotoxic and antiproliferative effects.	Cytotoxic and antiproliferative against HCT 116 colon cancer cells, significantly reducing cell viability and inducing cell death.	(Dwiwina <i>et al.</i> , 2023)

Conclusions

The evidence compiled in this review shows that *S. carteri* is a significant Indo-Pacific source of structurally diverse secondary metabolites with broad pharmacological promise. Conventional preparation and solvent-based maceration consistently yield metabolite classes such as bromopyrrole alkaloids, cyclic peptides, saponins, triterpenes, and lipids, which together underpin anticancer, antibiofilm, antibacterial, antiviral, antioxidant, and antiplasmodial activities. Variations in geographic origin and extraction approaches clearly influence chemical profiles and bioactivity outcomes, highlighting the need for standardized methodologies and deeper mechanistic studies. Continued integration of optimized extraction techniques,

metabolomic tools, and targeted biological evaluation is likely to accelerate the discovery of clinically relevant lead compounds from *S. carteri*, while clarifying its role as a strategically important marine resource for future drug development.

Conflict of Interest

I have nothing to declare.

Declaration of generative AI

During the preparation of this work the author(s) used Perplexity in order to assist with language editing and clarification of wording. After using

this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

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Author contribution

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References

- Abdelhameed, R. F. A., Habib, E. S., Eltahawy, N. A., Hassanean, H. A., Ibrahim, A. K., Mohammed, A. F., Fayez, S., Hayallah, A. M., Yamada, K., Behery, F. A., Al-Sanea, M. M., Alzarea, S. I., Bringmann, G., Ahmed, S. A., & Abdelmohsen, U. R. (2020). New cytotoxic natural products from the Red Sea sponge *Stylissa carteri*. *Marine Drugs*, 18(5), 241. <https://doi.org/10.3390/md18050241>.
- Adewal, M. A. K., Abdullah, A., Zamani, N. P., Arafat, D., Ayu, I. P., & Subhan, B. (2025). Potential antioxidant activity of sea sponge *Stylissa carteri* extract. *Jurnal Pengolahan Hasil Perikanan Indonesia*, 28(3), 245–253. <https://doi.org/10.17844/jphpi.v28i3.60270>.
- Afifi, A. H., El-Desoky, A. H., Kato, H., Mangindaan, R. E. P., De Voogd, N. J., Ammar, N. M., Hifnawy, M. S., & Tsukamoto, S. (2016). Carteritins A and B, cyclic heptapeptides from the marine sponge *Stylissa carteri*. *Tetrahedron Letters*, 57(11), 1285–1288. <https://doi.org/10.1016/j.tetlet.2016.02.031>.
- Aisyah, S. Z., Zamani, N. P., Cahyani, N. K. D., Elfahmi, Syafrizayanti, Andriani, Y., Arafat, D., Bashari, M. H., Hanif, N., Sani, L. M. I., Ayu, I. P., Akbar, N., & Subhan, B. (2025). Challenges in molecular and morphological identification of sponge species in Raja Ampat. *Journal of the Indonesian Tropical Animal Agriculture*, 30(1), 115–125. <https://doi.org/10.14710/ik.ijms.30.1.115-125>.
- Alqaraleh, M., Khleifat, K. M., Al-Samydai, A., Al-Najjar, B. O., Saqallah, F. G., Al Qaisi, Y. T., Alsarayreh, A. Z., Alqudah, D. A., & Fararjeh, A. S. (2025). Bioactive potency of extracts from *Stylissa carteri* and *Amphimedon chloros* with silver nanoparticles against cancer cell lines and pathogenic bacteria. *Biomedical Reports*, 22(2), Article 19. <https://doi.org/10.3892/br.2024.1912>.
- Bashari, M. H., Huda, F., Tartila, T. S., Shabrina, S., Putri, T., Qomarilla, N., Atmaja, H., Subhan, B., Sudji, I. R., & Meiyanto, E. (2019). Bioactive compounds in the ethanol extract of marine sponge *Stylissa carteri* demonstrate potential anti-cancer activity in breast cancer cells. *Asian Pacific Journal of Cancer Prevention*, 20(4), 1199–1206. <https://doi.org/10.31557/apjcp.2019.20.4.1199>.
- Bayona, L. M., Videnova, M., & Choi, Y. H. (2018). Increasing metabolic diversity in marine sponge extracts by controlling extraction parameters. *Marine Drugs*, 16(10), 393. <https://doi.org/10.3390/md16100393>.
- Bitwell, C., Sen, S. I., Luke, C., & Kakoma, M. K. (2023). A review of modern and conventional extraction techniques and their applications for extracting phytochemicals from plants. *Scientific African*, 19, e01585. <https://doi.org/10.1016/j.sciaf.2023.e01585>.
- Calcinai, B., Bastari, A., Bavestrello, G., Bertolino, M., Horcajadas, S. B., Pansini, M., Makapedua, D. M., & Cerrano, C. (2017). Demosponge diversity from North Sulawesi, with the description of six new species. *ZooKeys*, 680, 105–150. <https://doi.org/10.3897/zookeys.680.12135>.
- De Caralt, S., Bry, D., Bontemps, N., Turon, X., Uriz, M. J., & Banaigs, B. (2013). Sources of secondary metabolite variation in *Dysidea avara* (Porifera: Demospongiae): The importance of having good neighbors. *Marine Drugs*, 11(2), 489–503. <https://doi.org/10.3390/md11020489>.
- Dwiwina, R. G., Sabrina, S., Pratiwi, Y. S., Halleyana, P., Rahman, A., & Bashari, M. H. (2023). Cytotoxic and anti-proliferative effects of ethanol extract of marine sponge *Stylissa carteri* on colon cancer HCT-116 cell line. *Indonesian Journal of Cancer Chemoprevention*, 14(1), 33–38. <https://doi.org/10.14499/indonesianjcanchemoprev.14iss1pp33-38>.
- Erngren, I., Smit, E., Pettersson, C., Cárdenas, P., & Hedeland, M. (2021). The effects of sampling and storage conditions on the metabolite profile of the marine sponge *Geodia barretti*. *Frontiers in Chemistry*, 9, 662659. <https://doi.org/10.3389/fchem.2021.662659>.

- Fristiohady, A., Sahidin, I., Sadarun, B., Purnama, L. O. M. J., Rahmatika, N. S., Tien, T., Haruna, L. A., Yodha, A. W. M., & Wahyuni, W. (2024). Anti-inflammatory activity of ethanolic extract of *Melophlus* sp. and *Callyspongia* sp. from Southeast Sulawesi. *Indonesian Journal of Pharmaceutical Science and Technology*, 11(1), 26–34. <https://doi.org/10.24198/ijpst.v11i1.28809>.
- George, A. M. (2022). Tale of two species of *Stylissa* (Porifera: Demospongiae: Scopalinida) from the west and east coasts of India. *Zootaxa*, 5178(1), 72–80. <https://doi.org/10.11646/zootaxa.5178.1.4>.
- Giles, E. C., Saenz-Agudelo, P., Hussey, N. E., Ravasi, T., & Berumen, M. L. (2015). Exploring seascape genetics and kinship in the reef sponge *Stylissa carteri* in the Red Sea. *Ecology and Evolution*, 5(13), 2487–2502. <https://doi.org/10.1002/ece3.1511>.
- Hanif, N., Murni, A., Tanaka, C., & Tanaka, J. (2019). Marine natural products from Indonesian waters. *Marine Drugs*, 17(6), 364. <https://doi.org/10.3390/md17060364>.
- Hardani, I. N., Damara, F. A., Nugrahani, A. D., & Bashari, M. H. (2018). Ethanol extract of *Stylissa carteri* induces cell death in parental and paclitaxel-resistant cervical cancer cells. *International Journal of Integrated Health Sciences*, 6(2), 91–96.
- Hawas, U. W., & Abou El-Kassem, L. T. (2025). New bioactive pyrrole alkaloid isolated from the Saudi Red Sea sponge *Stylissa carteri* with potential anticancer activity against human lung adenocarcinoma cells. *Natural Product Research*. <https://doi.org/10.1080/14786419.2025.2479252>.
- Huang, Y. M., De Voogd, N. J., Cleary, D. F. R., Li, T. H., Mok, H. K., & Ueng, J. P. (2016). Biodiversity pattern of subtidal sponges (Porifera: Demospongiae) in the Penghu Archipelago, Taiwan. *Journal of the Marine Biological Association of the United Kingdom*, 96(2), 417–427. <https://doi.org/10.1017/S002531541500017X>.
- Inbaneson, S. J., & Ravikumar, S. (2012). In vitro antiplasmodial activity of marine sponge *Stylissa carteri*-associated bacteria against *Plasmodium falciparum*. *Asian Pacific Journal of Tropical Disease*, 2(5), 370–374. [https://doi.org/10.1016/S2222-1808\(12\)60081-4](https://doi.org/10.1016/S2222-1808(12)60081-4).
- Lee, Y. J., Cho, Y., & Tran, H. N. K. (2021). Secondary metabolites from the marine sponges of the genus *Petrosia*: A literature review of 43 years of research. *Marine Drugs*, 19(3), 122. <https://doi.org/10.3390/md19030122>.
- Lim, S.-C., Putschakarn, S., Thai, M.-Q., Wang, D., & Huang, Y. M. (2016). Inventory of sponge fauna from the Singapore Strait to the Taiwan Strait along the western coastline of the South China Sea. *Raffles Bulletin of Zoology*, Supplement No. 34, 1–90.
- Mahamed, S., Motal, R., Govender, T., Dlamini, N., Khuboni, K., Hadeb, Z., Shaik, B. B., Moodley, K., Mohite, S. B., & Karpoormath, R. (2023). A concise review on marine bromopyrrole alkaloids as anticancer agents. *Bioorganic & Medicinal Chemistry Letters*, 80, 129102. <https://doi.org/10.1016/j.bmcl.2022.129102>.
- Marine Species Traits. (2025). *Stylissa carteri* (Dendy, 1889). *Marine Species Traits*. <https://marinespecies.org/traits/aphia.php?p=taxdetails&id=165705>.
- Nadar, V. M., Manivannan, S., Chinnaiyan, R., Govarthan, M., & Ponnuchamy, K. (2022). Review on marine sponge alkaloid aaptamine: A potential antibacterial and anticancer drug. *Chemical Biology & Drug Design*, 99(1), 103–110. <https://doi.org/10.1111/cbdd.13932>.
- Naqvi, S. A. R., Sherazi, T. A., Hassan, S. U., Shahzad, S. A., & Faheem, Z. (2022). Anti-inflammatory, anti-infectious, and anticancer potential of marine algae and sponges: A review. *European Journal of Inflammation*, 20, 1–14. <https://doi.org/10.1177/20587392221075514>.
- Nugraha, A. S., Firli, L. N., Rani, D. M., Hidayatiningsih, A., Lestari, N. D., Wongso, H., Tarman, K., Rahaweman, A. C., Manurung, J., Ariantari, N. P., Papu, A., Putra, M. Y., Pratama, A. N. W., Wessjohann, L. A., & Keller, P. A. (2023). Indonesian marine and its medicinal contribution. *Natural Products and Bioprospecting*, 13(1), Article 38. <https://doi.org/10.1007/s13659-023-00403-1>.
- O'Rourke, A., Kremb, S., Bader, T. M., Helfer, M., Schmitt-Kopplin, P., Gerwick, W. H., Brack-Werner, R., & Voolstra, C. R. (2016). Alkaloids from the sponge *Stylissa carteri* present prospective scaffolds for the inhibition of human immunodeficiency virus 1 (HIV-1) (Supplementary material). *Marine Drugs*, 14(8), Article 152.
- Palungan, I., Bara, R. A., Mangindaan, R. E., Kemer, K., Wullur, S., & Rembet, U. N. (2022). Antibacterial activity of *Stylissa carteri* sponge extract from Manado Bay, North Sulawesi. *Jurnal Ilmiah PLATAX*, 10(1), 9–18. <https://doi.org/10.35800/jip.v10i1.36020>.
- Paul, V. J., Freeman, C. J., & Agarwal, V. (2019). Chemical ecology of marine sponges: New opportunities through “-omics”. *Integrative and Comparative Biology*, 59(4), 765–776. <https://doi.org/10.1093/icb/icz014>.
- Rahman, N. I. A., Ramzi, M. M., Rawi, N. N., Siong, J. Y. F., Bakar, K., Bhubalan, K., Ariffin, F., Saidin, J., Azemi, A. K., & Ismail, N. (2024). Characterization of antibiofilm compound from marine sponge *Stylissa carteri*. *Environmental Science and Pollution Research*, 31(25), 37552–37563. <https://doi.org/10.1007/s11356-024-33704-0>.
- Raymond, M. J. F., & Rakotondraibe, H. L. (2025). Recent updates on terpenoids and other bioactive constituents of marine sponges. *Molecules*, 30(5),

- Article 1112.
<https://doi.org/10.3390/molecules30051112>.
- Rohde, S., Gochfeld, D. J., Ankisetty, S., Avula, B., Schupp, P. J., & Slattery, M. (2012). Spatial variability in secondary metabolites of the Indo-Pacific sponge *Stylissa massa*. *Journal of Chemical Ecology*, 38(5), 463–475. <https://doi.org/10.1007/s10886-012-0124-8>.
- Singh, P., Pandey, V. K., Singh, R., & Dar, A. H. (2023). Spray-freeze-drying as an emerging and substantial quality enhancement technique in the food industry. *Food Science and Biotechnology*, 33(2), 231–244. <https://doi.org/10.1007/s10068-023-01409-8>.
- Varamogianni-Mamatsi, D., Nunes, M. J., Marques, V., Anastasiou, T. I., Kagiampaki, E., Vernadou, E., Dailianis, T., Kalogerakis, N., Branco, L. C., Rodrigues, C. M. P., Sobral, R. G., Gaudêncio, S. P., & Mandalakis, M. (2023). Comparative chemical profiling and antimicrobial/anticancer evaluation of extracts from farmed versus wild *Agelas oroides* and *Sarcotragus foetidus* sponges. *Marine Drugs*, 21(12), Article 612. <https://doi.org/10.3390/md21120612>.
- Varijakzhan, D., Loh, J. Y., Yap, W. S., Yusoff, K., Seboussi, R., Lim, S. H. E., Lai, K. S., & Chong, C. M. (2021). Bioactive compounds from marine sponges: Fundamentals and applications. *Marine Drugs*, 19(5), Article 246. <https://doi.org/10.3390/md19050246>.
- Yang, Q. B., & Liang, L. F. (2024). *Spongia* sponges: Unabated sources of novel secondary metabolites. *Marine Drugs*, 22(5), Article 213. <https://doi.org/10.3390/md22050213>.