

Phytochemical Constituents and Anticancer Potential of *Spatholobus littoralis* Hassk. Against Breast Cancer: A Narrative Review

Muhammad Edo Tanayah¹, Dini Aulia Cahya², Louisa Caroline Pramesti³, Amir Putra Firmansyah⁴

^{1,2,3,4}Universitas Negeri Surabaya, Indonesia

Email: edotanayahhits@gmail.com

Abstract

Breast cancer remains one of the leading causes of cancer-related mortality among women worldwide. Despite advances in conventional therapies, treatment resistance and adverse effects continue to limit clinical outcomes, highlighting the need for novel plant-derived therapeutic agents. *Spatholobus littoralis* Hassk. (Bajakah) has attracted increasing attention because of its diverse phytochemical constituents and potential anticancer properties. This study aimed to analyze the phytochemical constituents, biological activities, and molecular mechanisms underlying the anticancer potential of *Spatholobus littoralis* in breast cancer using a narrative review approach. Literature searches were conducted through PubMed, Scopus, ScienceDirect, and Google Scholar using relevant keywords related to *Spatholobus littoralis*, breast cancer, anticancer activity, cytotoxicity, phytochemicals, and molecular mechanisms. Articles published between 2020 and 2025 that met the inclusion criteria were reviewed. A total of 15 studies were included in the final analysis. The findings indicate that *S. littoralis* contains bioactive compounds, particularly flavonoids and phenolic compounds, which exhibit antioxidant, cytotoxic, and potential anticancer activities through the modulation of apoptosis, oxidative stress, and cancer-related signaling pathways. Although current evidence supports its potential as a plant-derived therapeutic candidate for breast cancer, further in vivo studies and clinical investigations are required to confirm its efficacy and safety.

Keywords: *Spatholobus Littoralis*, Breast Cancer, Phytochemicals, Anticancer Activity, Molecular Mechanisms.



A. INTRODUCTION

Breast cancer remains the most commonly diagnosed cancer among women worldwide and represents a major global public health burden. In 2024, approximately 2.4 million new cases were estimated globally, with the burden expected to increase substantially in the coming decades, particularly in low- and middle-income countries where disparities in screening and access to comprehensive cancer care remain substantial (World Health Organization, 2026). Despite advances in early detection and multimodal treatment, breast cancer continues to exhibit considerable biological heterogeneity, and treatment resistance and disease recurrence remain important challenges, particularly in aggressive subtypes such as triple-negative breast cancer (Bianchini et al., 2022; Zhang et al., 2021).

Current breast cancer management includes surgery, chemotherapy, radiotherapy, endocrine therapy, targeted therapy, and immunotherapy, depending on tumor subtype and disease stage. However, treatment-related toxicity, acquired resistance, and limited therapeutic responses in certain patient populations highlight

the continuing need for novel agents with improved efficacy and multitarget mechanisms of action (Loibl et al., 2021). Natural products remain an important source of bioactive compounds for drug discovery, while phytochemicals such as flavonoids, phenolic compounds, alkaloids, and terpenoids have demonstrated diverse anticancer activities through the modulation of apoptosis, proliferation, oxidative stress, inflammation, angiogenesis, and metastasis (Newman & Cragg, 2020; Atanasov et al., 2021).

Indonesia's exceptional biodiversity provides considerable opportunities for the discovery and development of medicinal plants as potential sources of novel therapeutic compounds. One plant that has recently attracted increasing scientific interest is *Spatholobus littoralis* Hassk., commonly known as Bajakah, which has traditionally been used as a medicinal plant in Indonesia (Sianipar et al., 2023). Phytochemical investigations of *S. littoralis* and the broader *Spatholobus* genus have identified diverse bioactive constituents, particularly flavonoids and phenolic compounds, which have been associated with antioxidant, anti-inflammatory, and other pharmacological activities (Afifah & Iskandar, 2023; Liu et al., 2022).

Emerging evidence also suggests that *S. littoralis* may possess anticancer properties relevant to breast cancer. Recent studies have reported cytotoxic effects of *S. littoralis* extracts and isolated compounds against breast cancer cell models, while molecular docking and computational analyses have suggested potential interactions with estrogen receptors and other molecular targets involved in tumor progression (Atun et al., 2025). Furthermore, the integration of metabolomic profiling, network pharmacology, and experimental validation has provided additional insights into potential bioactive compounds and signaling pathways underlying the anti-breast cancer activity of *S. littoralis* (Rustandi et al., 2025).

Nevertheless, the current evidence concerning the anticancer potential of *S. littoralis* remains fragmented and is predominantly derived from phytochemical characterization, *in vitro* cytotoxicity assays, molecular docking, and network pharmacology studies. Evidence from other *Spatholobus* species, such as *Spatholobus suberectus*, has demonstrated broader anticancer effects involving multiple signaling pathways; however, these findings cannot be directly extrapolated to *S. littoralis* without species-specific validation (Liu et al., 2022; Zhang et al., 2022). Therefore, a comprehensive synthesis of the available evidence is needed to clarify the phytochemical basis, biological activities, proposed molecular mechanisms, and translational potential of *S. littoralis* in breast cancer.

This narrative review aims to comprehensively synthesize and critically evaluate current evidence regarding the phytochemical constituents, pharmacological activities, and anticancer potential of *Spatholobus littoralis* Hassk. against breast cancer. In addition, this review discusses the proposed molecular mechanisms, identifies limitations in the current evidence, and highlights future research priorities required to support the development of evidence-based phytopharmaceuticals derived from this Indonesian medicinal plant.

B. METHOD

This study was conducted as a narrative literature review using a structured literature search to synthesize evidence regarding the phytochemical composition, biological activities, and potential anticancer properties of *Spatholobus littoralis* Hassk., with particular emphasis on its potential application in breast cancer. Literature searches were conducted in PubMed, Scopus, and Google Scholar using combinations of keywords related to *S. littoralis*, breast cancer, phytochemicals, cytotoxicity, anticancer activity, and molecular mechanisms. The search primarily included publications from 2020 to 2025, while relevant earlier studies were considered when necessary to provide foundational evidence. Reference lists of relevant publications were also screened to identify additional potentially eligible studies.

Studies were considered eligible if they directly investigated *S. littoralis* using *in vitro*, *in vivo*, or *in silico* approaches and evaluated its phytochemical constituents, biological activities, cytotoxicity, anticancer potential, or associated molecular mechanisms. Studies that were not relevant to *S. littoralis* and/or breast cancer, used ineligible study designs, were published as opinion articles or in non-indexed journals, or did not assess relevant molecular pathways or cytotoxic effects were excluded. The literature selection process was documented using a PRISMA 2020-based flow diagram to transparently report the identification, screening, eligibility assessment, and inclusion of relevant literature. A total of 495 records were initially identified, of which 340 remained after duplicate removal. Following title and abstract screening, full-text assessment, and application of the eligibility criteria, 15 studies were included in the final narrative synthesis.

Data were extracted from the included studies regarding publication year, study design, plant part, extraction or fractionation method, phytochemical constituents, experimental models, cancer cell lines, outcome measures, molecular targets, and principal findings. The evidence was synthesized narratively and organized into four major themes: (1) phytochemical composition of *S. littoralis*, (2) antioxidant and other biological activities, (3) direct evidence of anticancer activity, and (4) potential molecular mechanisms underlying its anticancer effects. Particular attention was given to evidence from breast cancer models and molecular pathways associated with cancer cell proliferation, survival, apoptosis, angiogenesis, and metastasis. Due to the heterogeneity of study designs, plant materials, extraction methods, experimental models, and outcome measures, the findings were qualitatively synthesized rather than quantitatively pooled.

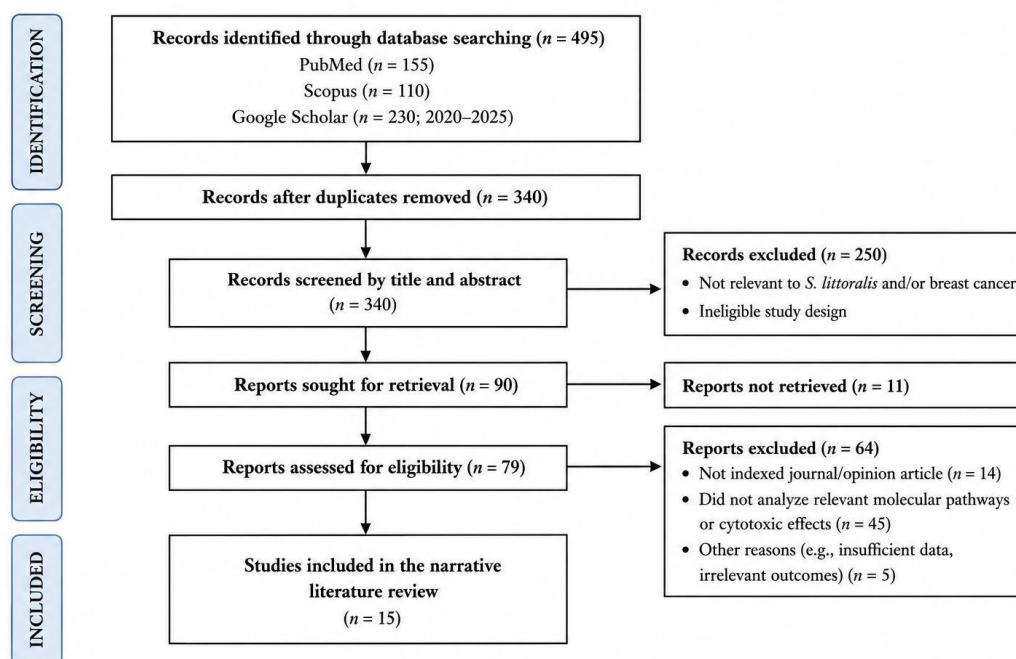


Figure 1. PRISMA Flow Diagram of the Literature Selection Process for the Narrative Review of *Spatholobus littoralis* and Its Potential Anticancer Activity in Breast Cancer

C. RESULT AND DISCUSSION

To synthesize the current evidence regarding the phytochemical composition, biological activities, and potential anticancer properties of *Spatholobus littoralis* Hassk., a structured review of relevant literature was conducted. The included studies investigated various aspects of *S. littoralis*, including its phytochemical constituents, antioxidant properties, cytotoxic effects, anticancer potential, and possible molecular mechanisms associated with cancer-related pathways. Understanding these biological properties is important because *S. littoralis* has been traditionally used as a medicinal plant in Indonesia, while recent experimental studies have begun to investigate its potential as a source of bioactive compounds for breast cancer research.

The literature analysis presented in Table 1 summarizes the key characteristics of the included studies, including the study design, plant material or extract investigated, experimental models, major findings, and the relevance of each study to the potential anticancer activity of *S. littoralis*. The evidence was categorized according to its primary contribution, including phytochemical characterization, antioxidant activity, direct cytotoxic or anticancer effects, and molecular mechanism investigation.

Table 1. Literature Analysis of Phytochemical Composition, Biological Activities, and Potential Anticancer Effects of *Spatholobus littoralis* Hassk.

No.	Author(s) and Year	Study Design	Plant Material/ Preparation	Experimental Model/Analysis	Main Findings
1.	Atun et al. (2025)	In vitro and in silico	Wood extract and fractions of <i>S. littoralis</i>	T47D and 4T1 breast cancer cells; molecular docking with ER- α and ER- β	Ethanol extract showed weak activity against 4T1 and no cytotoxicity against T47D, whereas several fractions demonstrated stronger cytotoxic activity; phenolic compounds showed predicted interactions with ER- α and ER- β
2.	Rustandi et al. (2025)	Analytical, in silico, and experimental validation	Stem fractions of <i>S. littoralis</i>	UHPLC-Q-Exactive Orbitrap HRMS, network pharmacology, molecular docking, and experimental validation	Identified candidate bioactive compounds and potential molecular targets associated with anti-breast cancer activity
3.	Atun et al. (2025)	Isolation, in vitro, and in silico	Wood of <i>S. littoralis</i>	T47D and 4T1 breast cancer cells; molecular docking	Two isolated carbamic acid ester compounds demonstrated cytotoxic activity against breast cancer cells and showed predicted interactions with a breast cancer-related receptor
4.	Iskandar et al. (2022)	In vitro	Wood fractions of <i>S. littoralis</i>	4T1 breast cancer cells and Vero normal cells	Evaluated phenolic content, antioxidant activity, cytotoxicity, and selectivity of different fractions
5.	Hadanu et al. (2023)	Phytochemical and in vitro	Ethanol extract of <i>S. littoralis</i>	FT-IR, LC-MS/MS, and antioxidant assay	Identified several chemical constituents and demonstrated

					antioxidant activity
6.	Mahfudh et al. (2024)	Phytochemical and in vitro	Ethanol extract of <i>S. littoralis</i>	Total phenolic, total flavonoid, and DPPH assays	Reported phenolic and flavonoid contents associated with antioxidant activity
7.	Bagiman et al. (2025)	Phytochemical and in vitro	Ethanol extract of <i>S. littoralis</i> stem	Total phenolic content and DPPH assay	Demonstrated phenolic content and antioxidant activity in stem extract
8.	Amanda et al. (2025)	Phytochemical and in vitro	Fractions of <i>S. littoralis</i>	Phytochemical screening and DPPH assay	Ethyl acetate fraction demonstrated antioxidant activity and contained several secondary metabolite classes
9.	Ariesanti et al. (2023)	Experimental in vitro	Roots, stems, and leaves	Antioxidant activity assay	Compared antioxidant activity among different plant parts
10.	Natasa et al. (2021)	Phytochemical analysis	Ethanol extract of <i>S. littoralis</i> root	Flavonoid identification	Identified flavonoid constituents in <i>S. littoralis</i> root extract
11.	Iskandar et al.	Experimental, phytochemical, and molecular analysis	Ethyl acetate fraction of <i>S. littoralis</i> stems	LC-MS/MS, FTIR, NMR, MTT, and molecular structure prediction	Isolated compounds demonstrated cytotoxic activity and were structurally characterized
12.	Ervina et al. (2026)	In silico	Compounds from <i>S. littoralis</i> wood	Molecular docking involving p38 MAPK-related target	Predicted potential interactions between <i>S. littoralis</i> compounds and cancer-associated signaling targets
13.	Sianipar et al. (2025)	In vitro and in silico	<i>S. littoralis</i> combined with <i>Sauropus androgynus</i>	Antioxidant and anti-inflammatory assays and computational analysis	Demonstrated potential antioxidant and anti-inflammatory effects

14.	Atun et al. (2025)	In vitro and in silico	<i>S. littoralis</i> wood extract and fractions	TPC, DPPH, FRAP, and molecular docking against ROS1 kinase	Extract and fractions showed antioxidant activity; phenolic compounds demonstrated predicted interactions with ROS1 kinase.
15.	Afifah & Iskandar (2024)	Narrative literature review	<i>S. littoralis</i> root (bajakah root)	Literature synthesis of phytochemical and pharmacological studies	Reported diverse secondary metabolites and pharmacological activities, including antioxidant and potential anticancer effects.

The articles included in this narrative review were derived from various scientific publications investigating the phytochemical composition, antioxidant properties, cytotoxicity, and potential anticancer activity of *S. littoralis*. Most of the primary studies employed experimental approaches, including *in vitro* cytotoxicity assays, antioxidant assays, phytochemical characterization, molecular docking, network pharmacology, and high-resolution mass spectrometry. Studies directly investigating breast cancer models included T47D and 4T1 cell lines, while other studies provided supporting evidence through the identification of bioactive constituents and evaluation of antioxidant or computational molecular activity.

The findings summarized in Table 1 indicate that the available evidence on *S. littoralis* can be broadly organized into several interconnected themes, namely phytochemical composition and bioactive constituents, antioxidant activity, direct cytotoxic and anticancer effects, and potential molecular mechanisms. The following sections discuss these findings in greater detail while considering the strength and limitations of the available evidence.

1. Phytochemical Composition and Bioactive Constituents

The reviewed studies demonstrate that *S. littoralis* contains diverse secondary metabolites, particularly phenolic and flavonoid compounds, which may contribute to its biological activities. The presence of these compounds provides a plausible biochemical basis for the antioxidant and potential anticancer properties reported in several experimental investigations (Hadanu et al., 2023; Mahfudh et al., 2024).

Hadanu et al. (2023) identified eight chemical constituents in the ethanol extract of *S. littoralis* roots using FT-IR and LC-MS/MS analysis, including apocynoside I, quercetin, hexosylphingosine, 3-hydroxy-7-methoxybaicalein, momor-cerebroside I, ambronal, stigmastan-3,6-dione, and trilaurin. The identification of these compounds demonstrates the chemical diversity of *S. littoralis*.

and provides a basis for further investigation of specific constituents that may contribute to its biological effects (Hadanu et al., 2023).

The chemical composition of *S. littoralis* may vary according to the plant part, extraction solvent, and preparation method. Such variability is important because differences in extraction procedures can influence the concentration and profile of bioactive compounds and may consequently affect the antioxidant or cytotoxic activity observed between studies (Hadanu et al., 2023; Atun et al., 2025).

High-resolution analytical approaches have further expanded the characterization of *S. littoralis* constituents. Rustandi et al. (2025) investigated the stem extract using multiple solvent systems and combined antioxidant assays with computational approaches involving SwissADME, Deep-PK, ProTox 3.0, STITCH, and AutoDock Vina to explore the potential biological activities of its bioactive compounds (Rustandi et al., 2025). However, the identification of phytochemical constituents does not by itself establish their anticancer efficacy. The biological relevance of individual compounds requires further investigation of their bioavailability, pharmacokinetics, target engagement, and functional effects using appropriate experimental models.

2. Antioxidant Activity and Its Biological Relevance

Antioxidant activity represents one of the most frequently investigated biological properties of *S. littoralis*. Several studies have evaluated extracts or fractions using assays such as DPPH and FRAP, with phenolic-rich preparations generally demonstrating measurable antioxidant activity (Hadanu et al., 2023; Atun et al., 2025).

Mahfudh et al. (2024) reported strong antioxidant activity of *S. littoralis* ethanol extract, with a DPPH IC₅₀ value of 54.19 ± 8.15 µg/mL, alongside total phenolic and flavonoid contents of $0.649 \pm 0.026\%$ GAE and $1.084 \pm 0.043\%$ QE, respectively. These findings suggest a possible association between the phenolic and flavonoid content of the extract and its radical-scavenging activity (Mahfudh et al., 2024). Similarly, Bagiman et al. (2025) reported a total phenolic content of 148.1415 mg TAE/g sample and a DPPH IC₅₀ value of 7.4954 ± 0.286 ppm for ethanol extract of *S. littoralis* stem. The variation in antioxidant values between studies highlights the potential influence of plant origin, extraction conditions, and analytical methods on the measured biological activity (Bagiman et al., 2025).

Atun et al. (2025) also reported that the ethanol extract and chloroform and ethyl acetate fractions of *S. littoralis* wood contained phenolic compounds and demonstrated antioxidant activity based on DPPH and FRAP assays. These findings further support the contribution of phenolic constituents to the antioxidant properties of *S. littoralis* (Atun et al., 2025).

From a cancer biology perspective, antioxidant activity may be biologically relevant because oxidative stress is associated with DNA damage, inflammation, and dysregulation of signaling pathways involved in carcinogenesis. Nevertheless, chemical radical-scavenging assays should be interpreted as supporting evidence

rather than direct evidence of anticancer efficacy (Hadanu et al., 2023; Mahfudh et al., 2024).

Therefore, the antioxidant findings provide a biological rationale for further anticancer investigation but cannot independently establish therapeutic efficacy. Direct evidence of anticancer activity requires validation through cellular, animal, and ultimately clinical studies.

3. Direct Cytotoxic and Anticancer Activity

The most direct evidence of the potential anticancer activity of *S. littoralis* is derived from studies investigating its extracts, fractions, or isolated compounds using cancer cell models. Among the reviewed evidence, breast cancer models such as T47D and 4T1 provide particular relevance to the potential application of *S. littoralis* in breast cancer research (Atun et al., 2025).

Atun et al. (2025) evaluated *S. littoralis* wood extract and fractions against T47D and 4T1 breast cancer cells using an MTT assay. The study demonstrated differences in cytotoxic activity among the tested preparations, suggesting that fractionation may influence the concentration of compounds responsible for the observed biological effects (Atun et al., 2025).

The same study further investigated potential interactions between phytochemical constituents and estrogen receptors ER- α and ER- β through molecular docking. These findings provide a possible mechanistic hypothesis linking selected *S. littoralis* constituents with estrogen-related breast cancer signaling, although the predicted interactions require experimental validation (Atun et al., 2025).

Rustandi et al. (2025) investigated the antioxidant and potential anticancer properties of *S. littoralis* stem extracts using *in vitro* antioxidant assays and *in silico* computational analyses. Their findings indicated that the 70% ethanol extract demonstrated a favorable antioxidant profile, while several bioactive compounds showed predicted interactions with CDK-2 and ROCK1, two molecular targets relevant to cancer biology (Rustandi et al., 2025).

The computational analysis performed by Rustandi et al. (2025) further identified daidzein as one of the compounds with favorable predicted binding affinities toward the investigated targets. However, because these findings are primarily based on molecular docking and computational prediction, they should be interpreted as hypothesis-generating evidence rather than confirmation of anticancer efficacy (Rustandi et al., 2025).

Overall, the direct anticancer evidence remains limited and heterogeneous. Differences in plant material, extraction procedures, cell lines, concentrations, and experimental conditions may contribute to variations in biological responses, emphasizing the need for standardized experimental protocols in future studies.

4. Potential Molecular Mechanisms

The potential anticancer effects of *S. littoralis* appear to involve multiple molecular mechanisms rather than a single signaling pathway. The reviewed studies

have explored molecular targets associated with estrogen receptor signaling, cell-cycle regulation, cytoskeletal dynamics, oxidative stress, and kinase-mediated signaling (Atun et al., 2025; Rustandi et al., 2025).

Estrogen receptor signaling is particularly relevant to breast cancer because ER-positive tumors may depend on estrogen-mediated pathways for proliferation and survival. The predicted interactions of selected *S. littoralis* compounds with ER- α and ER- β therefore suggest a potential mechanism that warrants further investigation in breast cancer models (Atun et al., 2025).

Cell-cycle regulation represents another potential mechanism of interest. Rustandi et al. (2025) investigated CDK-2 as one of the molecular targets of *S. littoralis* bioactive compounds, suggesting that modulation of cell-cycle-associated proteins may contribute to the potential anticancer activity of the plant (Rustandi et al., 2025). ROCK1 was also investigated as a potential molecular target in the same computational study. Because ROCK1 is involved in cytoskeletal regulation and cellular processes related to migration and invasion, its predicted interaction with bioactive compounds may provide a basis for future research into the potential effects of *S. littoralis* on cancer progression (Rustandi et al., 2025).

Another molecular pathway explored in the reviewed literature involves ROS1 kinase. Atun et al. (2025) evaluated the potential interactions of phenolic compounds from *S. littoralis* and related *Spatholobus* species with ROS1 kinase receptors using molecular docking, identifying favorable predicted interactions that may be relevant to future anticancer drug discovery (Atun et al., 2025). The available evidence suggests that the anticancer activity of *Spatholobus littoralis* is mediated through multiple interconnected molecular mechanisms rather than a single signaling pathway. Based on the findings synthesized from the included studies, a proposed mechanistic framework is presented in Figure 2 to illustrate the potential interactions between its bioactive phytochemicals, cellular processes, and cancer-related signaling pathways.

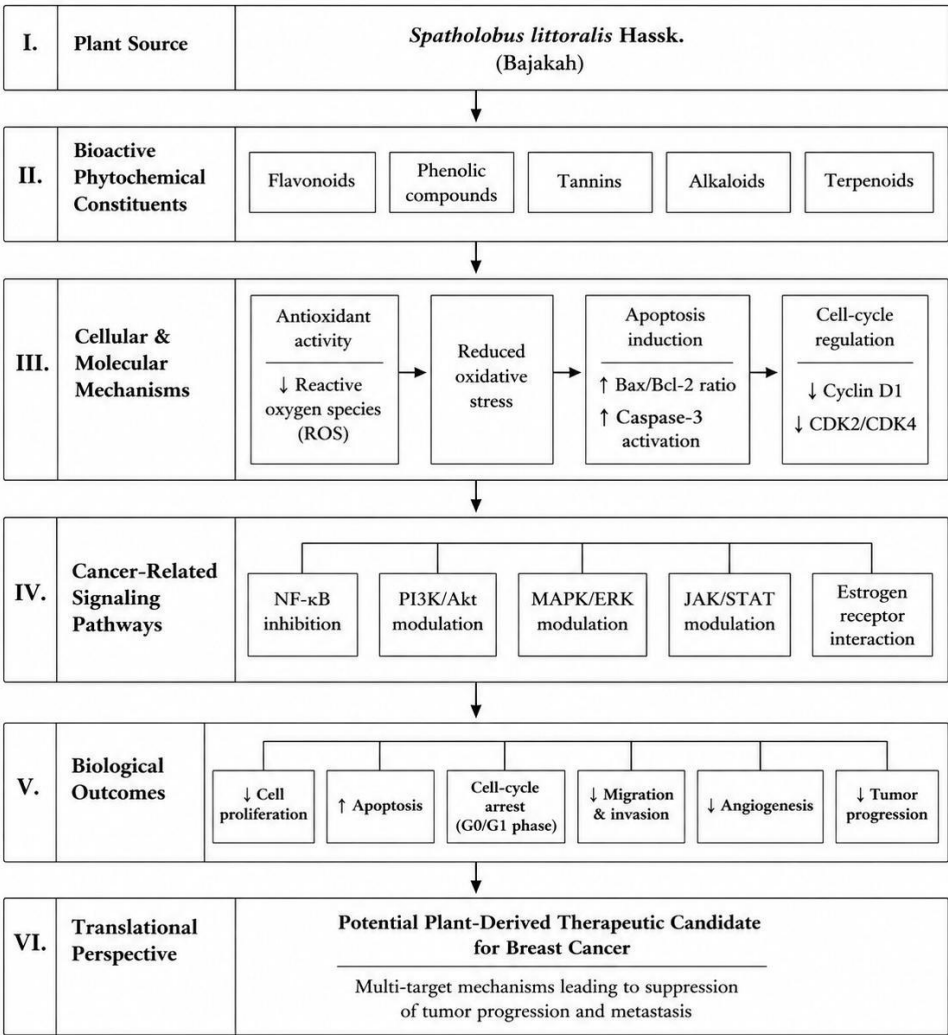


Figure 2. Proposed Molecular Mechanisms Underlying the Anticancer Activity of *Spatholobus littoralis* Hassk. in Breast Cancer.

Taken together, these findings support a potential multi-target mechanism involving hormone receptor signaling, cell-cycle regulation, cytoskeletal pathways, and kinase-associated signaling. However, most mechanistic evidence remains preliminary because molecular docking predictions require confirmation through biochemical assays, cellular experiments, and *in vivo* studies.

5. Critical Appraisal of the Evidence

The overall evidence indicates that *S. littoralis* possesses diverse phytochemical constituents and measurable antioxidant activity, while selected extracts and compounds demonstrate preliminary potential for anticancer research. However, the strength of evidence varies considerably across studies, with a substantial proportion of the literature focusing on phytochemical characterization and antioxidant activity rather than direct evaluation of anticancer outcomes (Hadanu et al., 2023; Mahfudh et al., 2024; Atun et al., 2025).

The most relevant evidence for breast cancer research is derived from studies involving T47D and 4T1 cell models. Nevertheless, these findings remain at the

preclinical stage and cannot be directly extrapolated to clinical efficacy in humans (Atun et al., 2025).

Computational approaches provide additional insights into potential molecular mechanisms by identifying candidate interactions between phytochemicals and cancer-associated targets. However, molecular docking and related computational methods are primarily hypothesis-generating tools and require subsequent biochemical and biological validation (Atun et al., 2025; Rustandi et al., 2025).

A major limitation across the literature is the variability in plant material and extraction procedures. Differences in plant part, geographical origin, solvent, extraction method, and fractionation may influence the phytochemical profile and consequently affect the biological activity of the resulting preparations (Hadanu et al., 2023; Atun et al., 2025).

6. Research Gaps and Future Perspectives

The principal research gap identified in this review is the limited number of studies directly connecting specific *S. littoralis* compounds with experimentally validated anticancer mechanisms in breast cancer. Although existing studies have identified candidate compounds and potential molecular targets, further research is required to establish causal relationships between specific compounds, molecular pathways, and biological outcomes (Atun et al., 2025; Rustandi et al., 2025).

Future investigations should prioritize the isolation and characterization of active compounds followed by mechanistic validation using apoptosis, cell-cycle, estrogen receptor, oxidative stress, and other relevant molecular assays. Such approaches would help determine whether the observed biological effects are mediated by specific and reproducible molecular mechanisms.

The selectivity of *S. littoralis* compounds toward cancer cells compared with normal cells should also be systematically evaluated. This is essential for distinguishing potentially therapeutic anticancer activity from nonspecific cytotoxicity and for establishing an appropriate therapeutic window.

Further progression toward *in vivo* models is necessary to evaluate antitumor efficacy, pharmacokinetics, biodistribution, and systemic toxicity. The transition from *in vitro* and *in silico* findings to validated animal models will be critical for determining whether the promising biological properties of *S. littoralis* can be translated into clinically relevant therapeutic strategies.

Overall, the current evidence supports *S. littoralis* as a promising source of candidate bioactive compounds for breast cancer drug discovery, but the evidence remains predominantly preclinical and exploratory. Further standardized and mechanistically focused research is required before the potential anticancer properties of *S. littoralis* can be translated into evidence-based therapeutic applications.

D. CONCLUSIONS

Spatholobus littoralis Hassk. demonstrates promising potential as a source of bioactive compounds with antioxidant and preliminary anticancer properties relevant to breast cancer. The available evidence suggests that its biological effects may involve multiple mechanisms, including modulation of estrogen receptor signaling, cell-cycle regulation, and other cancer-associated molecular targets. However, the current evidence remains predominantly based on *in vitro* and *in silico* studies, while robust *in vivo* and clinical validation is still limited. Therefore, further standardized research is needed to identify the active compounds, validate their molecular mechanisms, and evaluate their efficacy, selectivity, pharmacokinetics, and safety before potential translation into breast cancer therapeutic applications.

REFERENCES

1. Iskandar, D., Widodo, N., Warsito, Masruri, Rollando, & Antang, Y. P. P. (2022). Phenolic content, antioxidant, cytotoxic of fractions of *Spatholobus littoralis* Hassk from Kalimantan, Indonesia. *Journal of Hunan University Natural Sciences*, 49(3), 14–23. <https://doi.org/10.55463/issn.1674-2974.49.3.2>
2. Hadanu, R., Irwansyah, S. G. P., & Wahyuningrum, R. (2023). Compound characterization and evaluation of antioxidant potential of ethanol extract *Spatholobus littoralis* Hassk in Kolaka, Southeast Sulawesi, Indonesia. *Journal of Pharmaceutical Research International*, 35(28), 59–70. <https://doi.org/10.9734/jpri/2023/v35i287450>
3. Mahfudh, N., Murdi, H. B., Utami, D., Ahda, M., Nashihah, S., & Andika, A. (2024). Antioxidant activity, total phenolics, and total flavonoids content of Bajakah Tampala (*Spatholobus littoralis*): The indigenous herbal medicine from Kalimantan. *Borneo Journal of Pharmacy*, 7(3), 247–253. <https://doi.org/10.33084/bjop.v7i3.6609>
4. Rustandi, T., Yumassik, A. M., Nugraha, E. J. E. P., Nugroho, M. R., Yasir, M., & Kamalia. (2025). Antioxidant and anticancer activities of *Spatholobus littoralis* stem extract: An *in vitro* and *in silico* computational investigation. *Journal of Food and Pharmaceutical Sciences*, 13(1), 10–24. <https://doi.org/10.22146/jfps.16727>
5. Atun, S., Aznam, N., Rasningtyaswati, R., Cahyani, P. V. D., Izah, L. Q., Danarjati, W. D., & Sangal, A. S. (2025). The potential of the *Spatholobus littoralis* Hassk plant as an antioxidant and prediction of the mechanism of activity against ROS1 kinase receptor *in silico*. *Malaysian Journal of Science*. <https://doi.org/10.22452/mjs.vol44no2.4>
6. Atun S, Aznam N, Arianingrum R, Rasningtyaswati, Sangal A. (2025). Cytotoxic effect of *Spatholobus littoralis* extract on breast cancer cells by *in vitro* and prediction of the mechanism of activity against estrogen receptors (ER- α and ER- β) by *in silico*. *J Herbmmed Pharmacol*, 14(1):19-28. <https://doi.org/10.34172/jhp.2025.49379>
7. Bagiman, N. A., Hasan, T., & Arifin, A. (2025). Penetapan kadar fenolik total dan uji aktivitas antioksidan ekstrak etanol batang bajakah (*Spatholobus littoralis* Hassk.) asal Kabupaten Morowali. *Jurnal Farmasi dan Bahan Alam: FARBAL*, 12(1), 29–36.

8. Ariesanti, Y., Wahyudina, S. P., Poedjiastoeti, W., & Angraini, Y. (2023). Antioxidant activity of roots, stems, and leaves *Spatholobus littoralis* Hassk.: An experimental study. *Padjadjaran Journal of Dentistry*, 35(3), 206–210. <https://doi.org/10.24198/pjd.vol35no3.50423>
9. Marsuki, N. A. F., Wijaya, M., & Muharram. (2024). Identifikasi dan uji bioaktivitas senyawa metabolit sekunder dari batang bajakah tampala (*Spatholobus littoralis* Hassk.). *Chemica: Jurnal Ilmiah Kimia dan Pendidikan Kimia*, 25(1). <https://doi.org/10.35580/chemica.v25i1.58556>
10. Nura, A. D. F., Zakiah, M., & Asseggaf, S. N. Y. R. S. (2024). Potensi antioksidan dari akar tanaman bajakah (*Spatholobus littoralis* Hassk.) asal Kubu Raya Kalimantan Barat. *Ibnu Sina: Jurnal Kedokteran dan Kesehatan*, 23(2), 129–137. <https://doi.org/10.30743/ibnusina.v23i2.622>
11. Rahminiwati, M., Sianipar, R. N. R., Sutriah, K., Iswantini, D., Trivadila, Achmadi, S. S., & Sulistyawan, I. H. (2023). Optimization of xanthine oxidase activity, phytochemical screening, toxicity assay, and antigout activity of *Spatholobus littoralis* Hassk. extract. *Pharmacognosy Journal*, 15(3), 258–269. <https://doi.org/10.5530/pj.2023.15.72>
12. Werdiningsih, S., & Saragih, B. (2024). Rendemen ekstrak, total flavonoid, dan aktivitas antioksidan kombinasi simplisia bajakah (*Spatholobus littoralis* Hassk) dan kayu manis (*Cinnamomum verum*). *Journal of Tropical AgriFood*, 6(2). <http://dx.doi.org/10.35941/jtaf.6.2.2024.11774.92-96>
13. Amanda, N. G., Fadma Sari, G. N., Novita, M., & Marlina, D. (2025). Antioxidant activity profiling of red Bajakah Tampala (*Spatholobus littoralis* Hassk) fractions using the DPPH radical scavenging method. *Berita Biologi*, 24(3). https://doi.org/10.55981/berita_biologi.2025.11322
14. Rustandi, T., Nugroho, M. R., Yasir, M., Kamalia, Nugraha, E. J. E. P., Fawwazi, M. H. A. F., Amalia, S. P., Yumassik, A. M., Hayati, F., Mahal, A., & Obaidullah, A. J. (2025). Untargeted UHPLC-Q Exactive Orbitrap HRMS-based network pharmacology for the discovery of anti-breast cancer compounds from *Spatholobus littoralis* stem fractions and experimental validation. *Natural Product Research*. <https://doi.org/10.1080/14786419.2025.2511158>
15. Sianipar, R. N. R., Suryanegara, L., Fatriasari, W., Arung, E. T., Kusuma, I. W., Achmadi, S. S., et al. (2023). The role of selected flavonoids from bajakah tampala (*Spatholobus littoralis* Hassk.) stem on cosmetic properties: A review. *Saudi Pharmaceutical Journal*, 31(3), 382–400. <https://doi.org/10.1016/j.jsps.2023.01.006>
16. Atanasov, A. G., Zotchev, S. B., Dirsch, V. M., & Supuran, C. T. (2021). Natural products in drug discovery: Advances and opportunities. *Nature Reviews Drug Discovery*, 20, 200–216. <https://doi.org/10.1038/s41573-020-00114-z>
17. Bianchini, G., De Angelis, C., Licata, L., & Gianni, L. (2022). Treatment landscape of triple-negative breast cancer—Expanded options, evolving needs. *Nature Reviews Clinical Oncology*, 19, 91–113. <https://doi.org/10.1038/s41571-021-00565-2>
18. Liu, Y., Xiang, Q., Liang, Q., Shi, J., & He, J. (2022). Genus *Spatholobus*: A comprehensive review on ethnopharmacology, phytochemistry, pharmacology,

- and toxicology. *Food & Function*, 13(14), 7448–7472. <https://doi.org/10.1039/D2FO00895E>
19. Loibl, S., Poortmans, P., Morrow, M., Denkert, C., & Curigliano, G. (2021). Breast cancer. *The Lancet*, 397(10286), 1750–1769. [https://doi.org/10.1016/S0140-6736\(20\)32381-3](https://doi.org/10.1016/S0140-6736(20)32381-3)
 20. Newman, D. J., & Cragg, G. M. (2020). Natural products as sources of new drugs over the nearly four decades from 1981 to 2019. *Journal of Natural Products*, 83(3), 770–803. <https://doi.org/10.1021/acs.jnatprod.9b01285>
 21. Zhang, F., Ganesan, K., Liu, Q., & Chen, J. (2022). A review of the pharmacological potential of *Spatholobus suberectus* Dunn on cancer. *Cells*, 11(18), 2885. <https://doi.org/10.3390/cells11182885>
 22. Zhang, F., Liu, Q., Ganesan, K., & Chen, J. (2021). The antitriple negative breast cancer efficacy of *Spatholobus suberectus* Dunn on ROS-induced noncanonical inflammasome pyroptotic pathway. *Oxidative Medicine and Cellular Longevity*, 5187569. <https://doi.org/10.1155/2021/5187569>
 23. World Health Organization. (2026). *Breast cancer*. [WHO Breast Cancer Fact Sheet](#)