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Indonesian Medicinal Plants Investigated for Cancer-Related Activity: A Review of Ethnobotanical, Phytochemical, and Preclinical Evidence

Tumbuhan Obat Indonesia yang Diteliti untuk Aktivitas Terkait Kanker: Tinjauan Bukti Etnobotani, Fitokimia, dan Praklinis

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ABSTRACT

Medicinal plants are widely used by Indonesian cancer patients, but the evidence behind this use differs in kind and strength. This review classified 24 studies from Google Scholar, ScienceDirect and PubMed, plus ten further primary studies, by evidence level: traditional use, general toxicity, cancer-cell cytotoxicity, measured mechanism, *in silico* prediction and compound identification. Cancer-cell data existed for 15 of 17 taxa, almost all as crude extracts, and normal-cell controls were rare. The lowest IC_{50} values were 23.7 µg/mL (*Caulerpa racemosa* hexane extract, MCF-7) and 54.48 µg/mL (*Zanthoxylum acanthopodium* fruit ethanol extract, 4T1). The name bajakah covered species of three genera. Mechanisms were measured only for curcumin, *Stenochlaena palustris* and *Ocimum tenuiflorum*, and no *in vivo* efficacy study was found. Botanical authentication, selectivity testing, compound isolation and animal studies should precede therapeutic claims.

Kata kunci:

Etnobotani
Fitokimia
Sitotoksisitas
Tingkat bukti
Tumbuhan obat Indonesia

ABSTRAK

Tumbuhan obat banyak digunakan oleh pasien kanker di Indonesia, tetapi bukti yang mendasari penggunaan tersebut berbeda jenis dan kekuatannya. Tinjauan ini mengelompokkan 24 studi dari Google Scholar, ScienceDirect dan PubMed, ditambah sepuluh studi primer lain, menurut tingkat bukti: penggunaan tradisional, toksisitas umum, sitotoksisitas sel kanker, mekanisme terukur, prediksi *in silico* dan identifikasi senyawa. Data sel kanker tersedia untuk 15 dari 17 takson, hampir seluruhnya berupa ekstrak kasar dan jarang disertai kontrol sel normal. Nilai IC_{50} terendah adalah 23,7 µg/mL (ekstrak heksana *Caulerpa racemosa*, MCF-7) dan 54,48 µg/mL (ekstrak etanol buah *Zanthoxylum acanthopodium*, 4T1). Nama bajakah mencakup spesies dari tiga genus. Mekanisme hanya diukur untuk kurkumin, *Stenochlaena palustris* dan *Ocimum tenuiflorum*, dan tidak ditemukan studi efikasi *in vivo*. Autentikasi botani, uji selektivitas, isolasi senyawa dan studi hewan perlu mendahului klaim terapeutik.

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1. INTRODUCTION

Cancer caused an estimated 9.7 million deaths worldwide in 2022, and breast, lung and colorectal cancers were among the most frequently diagnosed (Bray et al., 2024). In Indonesia the burden is substantial and unevenly distributed across provinces (Santoso et al., 2021), and the treatment of breast, cervical and lung cancer places heavy demands on the national health insurance scheme (Yuliastuti et al., 2023). Surgery, radiotherapy and chemotherapy remain the basis of curative treatment (Mee et al., 2023), but chemotherapy frequently causes adverse effects that patients report late or not at all (Katta et al., 2023; Olver et al., 2018). Traditional and complementary medicine was used by roughly a quarter to a third of Indonesian adults in a national survey (Pengpid & Peltzer, 2018), it is common among cancer patients in Asia (Choi et al., 2024), and studies of Indonesian breast cancer patients describe the personal, cultural and economic reasons behind this choice (Putri et al., 2022; Rahayuwati et al., 2017).

Indonesian herbal medicine, or jamu, draws on a large flora and a long written and oral tradition (Elfahmi et al., 2014). Ethnobotanical records from Dayak communities in Borneo alone document an extensive medicinal flora and its uses (Az-Zahra et al., 2021). Laboratory studies have followed this knowledge, and extracts of bajakah stems and roots, Dayak onion bulbs, kelakai fern, andaliman fruit and the green seaweed *Caulerpa racemosa* (Forssk.) J.Agardh have been tested on breast, colorectal, liver and lung cancer cells (Alamsyah Lubis et al., 2018; Aliviyanti et al., 2021; Rosidah et al., 2019; Sanger et al., 2023; Yanti et al., 2021). Earlier reviews summarised this work as chemopreventive activity against the hallmarks of cancer (Meiyanto & Larasati, 2019), as a bioprospecting inventory of Indonesian plants and their compounds (D. M. Rani et al., 2023), and as a systematic review of *in vitro* studies (Permatasanti & Hidayat, 2023).

Those reviews established that activity has been reported, but they did not grade the kind of evidence that stands behind each claim. In the primary literature, a brine shrimp lethality value, an IC_{50} from a cancer cell line and a docking score are often cited together as anticancer activity, although they answer different questions. Plant identity is a second problem. The local name bajakah is applied to lianas of several genera, and more than 200 plants are said to carry it (Mahfudh et al., 2024), so a result reported for bajakah cannot be assigned to a species unless the material was identified. Selectivity toward cancer cells, which requires parallel testing on non-cancerous cells (Weerapreeyakul et al., 2012), is also rarely addressed, which makes the therapeutic relevance of many reported IC_{50} values difficult to judge.

This review aimed to classify the published evidence on Indonesian medicinal plants investigated for cancer-related activity according to the level of evidence, from traditional use to measured mechanism, and to identify which plants have progressed furthest and which data are still missing. Ethnobotanical, cytotoxic, phytochemical and mechanistic findings were extracted from the included studies, assigned to predefined evidence levels, and compared across taxa.

2. METHODS

2.1. Literature Search

The review used a structured narrative design, which suits a heterogeneous body of ethnobotanical, *in vitro*, and phytochemical studies that cannot be pooled statistically (Munn et al., 2018). Google Scholar, ScienceDirect, and PubMed were searched using the terms “anticancer herbs,” “Indonesian anticancer,” and “anticancer traditional medicine,” with database-specific adaptations where applicable. The exact search strings, search dates, publication-year range and any language or document-type restrictions were not recorded and are therefore not reported. The reference lists of the included articles were subsequently checked to identify additional primary studies concerning the same plants.

2.2. Study Selection

Records were eligible when they reported ethnobotanical, phytochemical, *in vitro*, or *in vivo* findings on a plant or alga that is native to or traditionally used in Indonesia and related the findings to cancer. Review articles, records unrelated to Indonesian medicinal plants or cancer, and records outside the search terms were excluded. The database searches identified 102 records, comprising 16 from Google Scholar, 82 from ScienceDirect, and four from PubMed. After 34 duplicate records were removed, 68 records remained for screening. Of these, 44 records were excluded, resulting in 24 studies included in the review (**Figure 1**). All records were screened independently by one reviewer (the first author), and eligibility decisions were made based on the predefined inclusion and exclusion criteria. As screening was performed by a single reviewer, no inter-reviewer disagreements required resolution.

Ten further primary studies were identified outside the database searches to complement the profiles of plants already represented among the 24 included studies. These additional studies were identified through examination of the reference lists of relevant articles and from the authors’ prior research records. They are listed in **Table S1** together with the 24 database-identified studies and were not counted in the database-search flow diagram. The reference list of this article also contains epidemiological, clinical, and methodological sources that support the Introduction and interpretation of the results; these sources were not part of the evidence set.

2.3. Data Extraction and Evidence Classification

From each study the following were extracted: the taxon as named by the authors, the accepted name according to Plants of the World Online (POWO, 2026), the plant part and preparation, the test system, the endpoint, the numerical result, the comparator and any normal-cell control. Each finding was then assigned to one of six evidence levels: (i) traditional use, a documented ethnomedical use against cancer or tumours; (ii) general toxicity, lethality in a

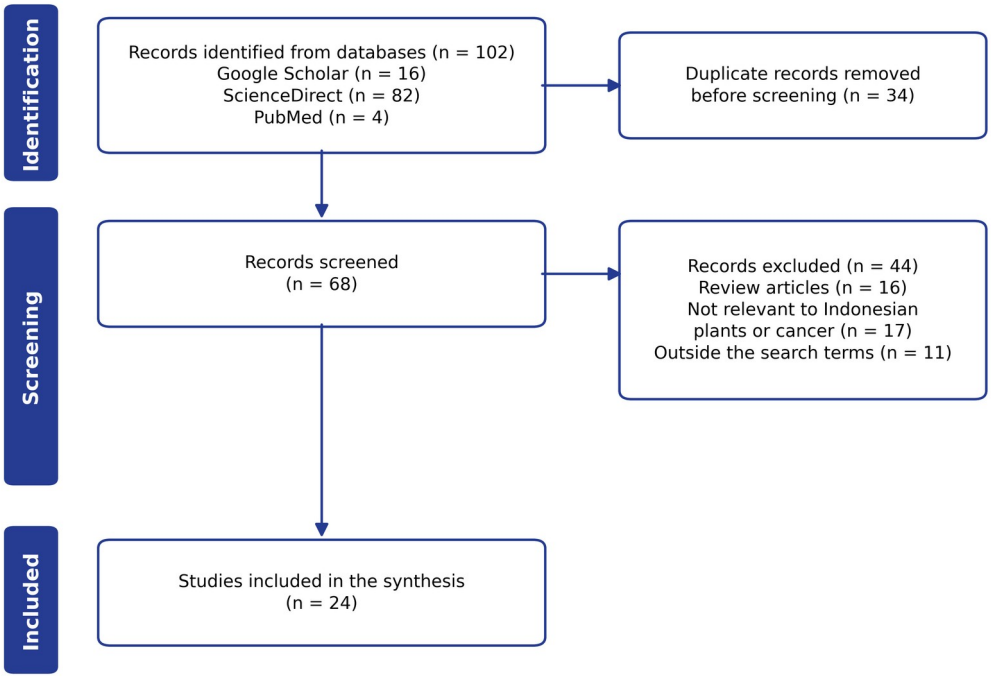

Figure 1. Flow of records through the identification, screening and inclusion stages of the review, drawn in the layout of the PRISMA 2020 flow diagram (Page et al., 2021)

non-cancer organism such as *Artemia* larvae in the brine shrimp lethality test (BSLT); (iii) cancer-cell cytotoxicity, growth inhibition or cell death measured in cancer cell lines; (iv) measured mechanism, a molecular or cellular endpoint such as protein expression, caspase activation or cell-cycle distribution determined experimentally; (v) *in silico* prediction, such as molecular docking; and (vi) compound identification, a constituent isolated and structurally elucidated or identified by chromatography–mass spectrometry. *In vivo* efficacy was recorded as a seventh category.

Concentrations reported in ppm were converted to µg/mL (1 ppm = 1 µg/mL in aqueous media). Where an IC_{50} in normal cells was available, selectivity was expressed as the selectivity index, the IC_{50} in normal cells divided by that in cancer cells, with a value of 3 or more taken to indicate selective activity (Weerapreeyakul et al., 2012). Because test systems, preparations and endpoints differed widely, the findings were compared narratively and no pooled estimate was calculated.

3. RESULTS AND DISCUSSION

3.1. Most Evidence Stops at Cytotoxicity of Crude Extracts

Among the 24 included studies, eleven reported cancer-cell cytotoxicity, two measured a mechanism, one used the brine shrimp test only, nine were phytochemical or analytical studies, and one described medicinal potential without an experimental endpoint (**Table S1**). Together with the ten supplementary studies they covered 17 taxa with experimental or phytochemical data, including one green alga (**Figure 2**). Cancer-cell cytotoxicity (15 taxa) and compound identification (11 taxa) were the most frequent levels, whereas a mechanism had been measured for three taxa, *in silico* predictions were available for two, and no taxon had *in vivo* efficacy data. For most plants the evidence has therefore moved from traditional use to cell-line screening but not beyond it, and the results below should be read with that ceiling in mind.

3.2. Traditional Use Is Well Documented, but Botanical Identity Is Often Uncertain

The plants with a documented cancer-related use or test are listed in **Table 1** with the identity reported in each source and the rank at which the material was identified. Most are used by particular communities, such as the Dayak of Kalimantan for bajakah, kelakai and paku atai merah, the Batak of North Sumatra for andaliman, and communities in North Sulawesi for pinang yaki (Adrian et al., 2023; Aisyah et al., 2020; Az-Zahra et al., 2021; Simbala et al., 2022). The table also shows that identity cannot be taken for granted, even when a scientific name is given.

Bajakah shows the problem most clearly. The name bajakah tampala denotes *Uncaria lanosa* var. *ferrea* (Blume) Ridsdale in the studies of Yusuf et al. (2023, 2026) but *Spatholobus littoralis* Hassk. in the study of Aliviyanti et al. (2021), which also tested roots of *Uncaria gambir* (Hunter) Roxb., *Spatholobus ferrugineus* (Zoll. & Moritzi) Benth. and *Schefflera petiolosa* (Miq.) Harms, all known locally by bajakah names. The stem extract tested in the brine shrimp assay by Zein et al. (2022) was identified only as *Uncaria* sp. Species of three genera in three families are thus reported as bajakah, and their results cannot be combined. A claim that bajakah is an anticancer plant has meaning only when the species,

the plant part and a voucher specimen are stated, as Mahfudh et al. (2024) also argued.

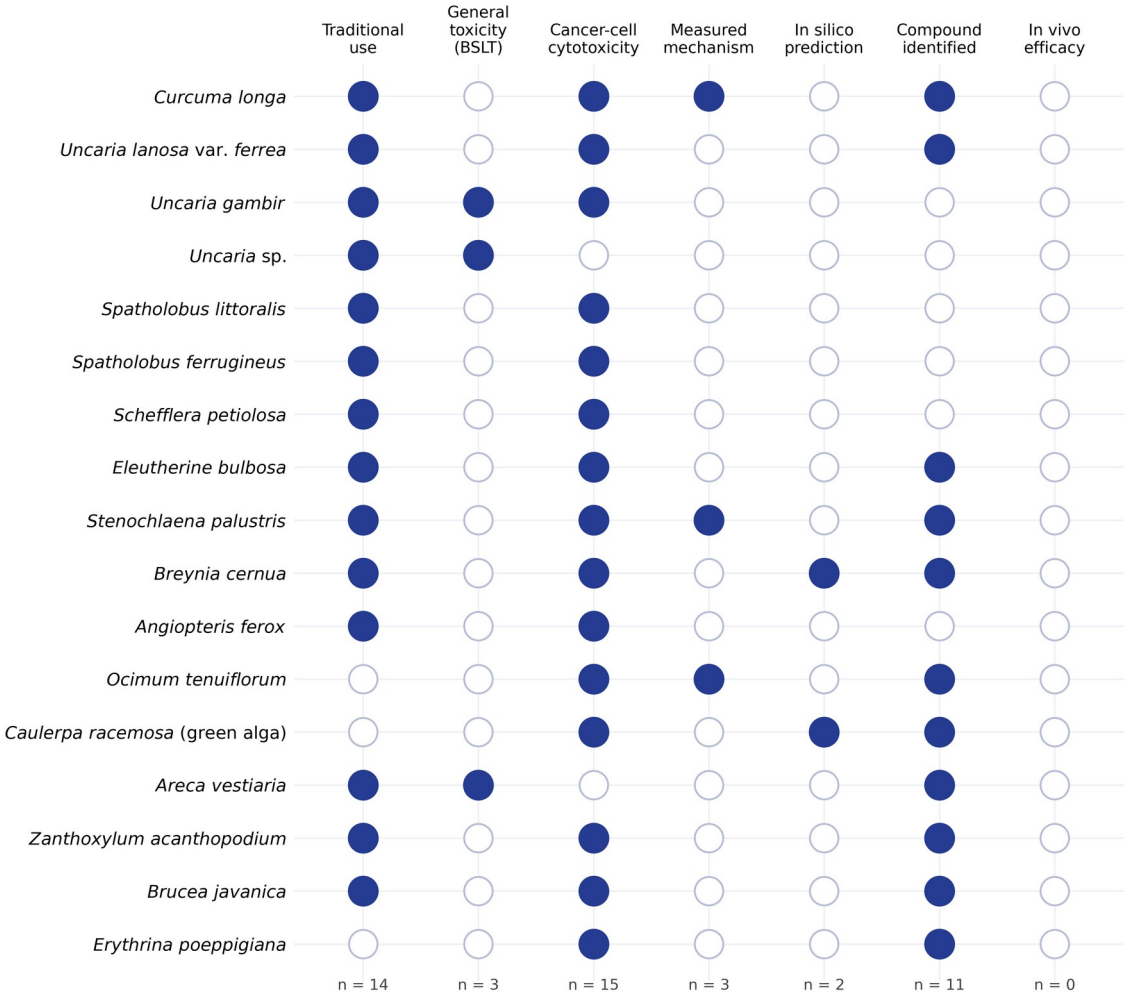

Figure 2. Evidence map of the 17 taxa with experimental or phytochemical data. Filled circles mark the evidence levels reported for each taxon in the included and supplementary studies (Table S1); n is the number of taxa with evidence at each level. BSLT, brine shrimp lethality test

Other local names need the same care. Katuk hutan refers to *Breynia cernua* (Poir.) Müll.Arg. in Papua (Dirgantara et al., 2018) and to *Phyllanthus reticulatus* Poir. in East Kalimantan (Husodo et al., 2021), and only the former has been tested on cancer cells. Dayak onion appears as *Eleutherine palmifolia* (L.) Merr. in one report (Muti'ah et al., 2020) and as *Eleutherine bulbosa* (Mill.) Urb. in others (Alamsyah Lubis et al., 2018; V. S. Rani, 2018); the two names refer to one species, for which *E. bulbosa* is the accepted name, and the part used is a bulb (POWO, 2026). Even for soursop, *Annona muricata* L., the cancer-related study located here tested endophytic fungi isolated from the leaves rather than the leaf itself (Hasan et al., 2022). A list of plants with traditional anticancer use is therefore a starting point for research, not evidence of activity.

Table 1. Indonesian medicinal plants with a documented cancer-related use or test, their identity as reported in the sources, and the rank of identification

Local name (region)	Taxon (accepted name)	Family	Part	Cancer-related use or test	Identified to	Reference(s)
Bajakah tampala (Central Kalimantan)	*Uncaria lanosa* var. *ferrea* (Blume) Ridsdale	Rubiaceae	Stem	MCF-7 cytotoxicity	Variety	Yusuf et al. (2023, 2026)
Bajakah tampala (Kalimantan)	*Spatholobus littoralis* Hassk.	Fabaceae	Root	T47D cytotoxicity	Species	Aliviyanti et al. (2021)
Bajakah kalalawit (Kalimantan)	*Uncaria gambir* (Hunter) Roxb.	Rubiaceae	Root, stem	T47D cytotoxicity; BSLT; total flavonoids	Species	Aliviyanti et al. (2021); Alfani et al. (2023); Permatasari et al. (2023)

Local name (region)	Taxon (accepted name)	Family	Part	Cancer-related use or test	Identified to	Reference(s)
Longkur (Kalimantan)	*Spatholobus ferrugineus* (Zoll. & Moritzi) Benth.	Fabaceae	Root	T47D cytotoxicity	Species	Aliviyanti et al. (2021)
Bajakah jari lima (Kalimantan)	*Schefflera petiolosa* (Miq.) Harms	Araliaceae	Root	T47D cytotoxicity	Species	Aliviyanti et al. (2021)
Bajakah (Kalimantan)	*Uncaria* sp.	Rubiaceae	Stem	BSLT	Genus	Zein et al. (2022)
Bawang Dayak (Kalimantan)	*Eleutherine bulbosa* (Mill.) Urb. (syn. *Eleutherine palmifolia* (L.) Merr.)	Iridaceae	Bulb	WiDr cytotoxicity	Species	Alamsyah Lubis et al. (2018); Muti'ah et al. (2020)
Kelakai (South and Central Kalimantan)	*Stenochlaena palustris* (Burm.f.) Bedd.	Blechnaceae	Herb	HepG2 and T47D cytotoxicity	Species	Yanti et al. (2021); Safitri et al. (2021)
Katuk hutan (Papua)	*Breynia cernua* (Poir.) Müll.Arg.	Phyllanthaceae	Leaf, stem	MCF-7 cytotoxicity	Species	Dirgantara et al. (2018); Wiraswati et al. (2023)
Katuk hutan (East Kalimantan)	*Phyllanthus reticulatus* Poir.	Phyllanthaceae	Leaf	Medicinal use; no cancer test	Species	Husodo et al. (2021)
Paku atai merah (East Kalimantan)	*Angiopteris ferox* Copel.	Marattiaceae	Tuber	T47D cytotoxicity	Species	Aisyah et al. (2020)
Andaliman (North Sumatra)	*Zanthoxylum acanthopodium* DC.	Rutaceae	Fruit	4T1 and HepG2 cytotoxicity	Species	Rosidah et al. (2019); Tala & Siregar (2022)
Buah makasar	*Brucea javanica* (L.) Merr.	Simaroubaceae	Fruit	Bruceine A; T47D antiproliferation	Species	Subeki & Muhartono (2015)
Dadap belendung (West Java)	*Erythrina poeppigiana* (Walp.) O.F.Cook	Fabaceae	Stem bark	α-Erythroidine; MCF-7 cytotoxicity	Species	Ambardhani et al. (2019)
Kunyit (widespread)	*Curcuma longa* L.	Zingiberaceae	Rhizome	Curcumin; MCF-7 and SGC-7901	Species	Elfahmi et al. (2014); Li et al. (2012); Patel et al. (2015)
Sirsak (widespread)	*Annona muricata* L.	Annonaceae	Leaf	Endophytic fungi; HeLa cytotoxicity	Species	Hasan et al. (2022)
Pinang yaki (North Sulawesi)	*Areca vestiaria* Giseke	Arecaceae	Seed, fruit	Flavonoid isolate; BSLT	Species	Rerung et al. (2017); Satolom (2015); Simbala et al. (2022)
Ruku-ruku (Java)	*Ocimum tenuiflorum* L. (syn. *Ocimum sanctum* L.)	Lamiaceae	Leaf	A549 apoptosis	Species	Wihadmadyatami et al. (2019)
Anggur laut (North Sulawesi)	*Caulerpa racemosa* (Forssk.) J.Agardh (green alga)	Caulerpaceae	Thallus	MCF-7 cytotoxicity	Species	Sanger et al. (2023)

Note. Accepted plant names follow Plants of the World Online (POWO, 2026). "Identified to" gives the most specific rank at which each source identified its material. BSLT, brine shrimp lethality test.

3.3. Cytotoxic Potency Varies Widely and Selectivity Is Seldom Tested

The quantitative results are summarised in **Table 2**. Potency spanned almost two orders of magnitude, from an IC_{50} of 23.7 µg/mL for the hexane extract of *C. racemosa* on MCF-7 cells (Sanger et al., 2023) to more than 1000 µg/mL for several bajakah root extracts on T47D cells (Aliviyanti et al., 2021). Only three preparations fell below 60 µg/mL: the *C. racemosa* hexane extract, the ethanol extract of *Zanthoxylum acanthopodium* DC. fruit on 4T1 cells (54.48 µg/mL; Rosidah et al., 2019), and the hexane extract of *E. bulbosa* on WiDr cells (56.15 µg/mL; Alamsyah Lubis et al., 2018). The reference drugs in the same studies were far more potent, for example doxorubicin at 0.80 µg/mL against 4T1 cells, cisplatin at 4.50 µg/mL against MCF-7 cells and tamoxifen at 9 µg/mL against T47D cells (Aliviyanti et al., 2021; Rosidah et al., 2019; Yusuf et al., 2026).

Two points limit how far these numbers can be taken. First, selectivity data were limited. Selectivity indices could be calculated for the n-hexane and ethyl acetate extracts of *E. bulbosa* because corresponding IC_{50} values in Vero normal cells were

reported, yielding SI values of 2.89 and 4.57, respectively (Alamsyah Lubis et al., 2018); only the ethyl acetate extract therefore met the threshold of 3 for selective activity. For the other preparations in **Table 2**, corresponding IC_{50} values in non-cancerous cells were not identified in the cited studies. Thus, the available evidence was insufficient to assess selectivity broadly across the reviewed preparations. Second, the brine shrimp results measure lethality to a crustacean larva. The LC_{50} of 23.84 µg/mL reported for the *Uncaria* sp. stem extract (Zein et al., 2022) is therefore evidence of general toxicity and says nothing about activity against cancer cells, and the same applies to the flavonoid isolate from seeds of *Areca vestiaria* Giseke (Rerung et al., 2017) and to the *U. gambir* stem fractions (Permatasari et al., 2023).

Differences in assay format further restrict comparison between plants. MTT and WST-8 assays, exposure times, solvent systems and cell lines varied between studies, and fractions were compared with crude extracts in several reports. Within single studies, however, the comparisons are informative. Less polar fractions were consistently more active than aqueous ones: the hexane fraction of *U. lanosa* var. *ferrea* was twice as potent as the water fraction on MCF-7 cells (Yusuf et al., 2026), the hexane and ethyl acetate fractions of *Stenochlaena palustris* (Burm.f.) Bedd. inhibited T47D cells whereas the water fraction did not (Safitri et al., 2021), and the ethyl acetate fraction of *Angiopteris ferox* Copel. was six times more potent than the parent ethanol extract (Aisyah et al., 2020). These within-study patterns point to semipolar and nonpolar constituents as the carriers of activity and identify the fractions that most deserve bioassay-guided isolation.

Two plants were tested as isolated compounds rather than extracts. Bruceine A, a quassinoid from the fruit of *Brucea javanica* (L.) Merr., inhibited the proliferation of T47D cells (Subeki & Muhartono, 2015), and α-erythroidine from the stem bark of *Erythrina poeppigiana* (Walp.) O.F.Cook was cytotoxic to MCF-7 cells (Ambardhani et al., 2019). Studies of this kind, in which activity is linked to a defined structure, are the exception in the Indonesian literature but offer the clearest route from traditional use to a candidate molecule.

Table 2. Cytotoxicity and general toxicity reported for Indonesian medicinal plants in the included and supplementary studies

Taxon and material	Model	Result (µg/mL)	Reference drug (µg/mL)	Evidence level	Reference
Uncaria sp., stem ethanol extract	*Artemia franciscana* (BSLT)	LC_{50} 23.84	NR	General toxicity	Zein et al. (2022)
A. vestiaria, seed flavonoid isolate	*Artemia* (BSLT)	LC_{50} 583.45	NR	General toxicity	Rerung et al. (2017)
U. lanosa var. *ferrea*, stem ethanol extract	MCF-7	IC_{50} 193.2	NR	Cancer-cell cytotoxicity	Yusuf et al. (2023)
U. lanosa var. *ferrea*, stem hexane, ethyl acetate and water fractions	MCF-7	IC_{50} 105.37, 130.58 and 209.91	Cisplatin 4.50	Cancer-cell cytotoxicity	Yusuf et al. (2026)
U. gambir, *S. littoralis*, *S. ferrugineus* and *S. petiolosa*, root ethanol extracts (reflux)	T47D	IC_{50} 407, 708, 881 and 1096	Tamoxifen 9	Cancer-cell cytotoxicity	Aliviyanti et al. (2021)
E. bulbosa, bulb hexane, ethyl acetate and ethanol extracts	WiDr	IC_{50} 56.15, 70.76 and 364.10	NR	Cancer-cell cytotoxicity	Alamsyah Lubis et al. (2018)
S. palustris, herb extract and most active fraction	HepG2	IC_{50} 865.84 and 224.12; p53 and caspase-3 increased	NR	Cytotoxicity; measured mechanism	Yanti et al. (2021)
S. palustris, herb hexane and ethyl acetate fractions	T47D	IC_{50} 86.99 and 98.43; p53 increased, Bcl-2 decreased	NR	Cytotoxicity; measured mechanism	Safitri et al. (2021)
B. cernua, 96% ethanol extract and *n*-hexane fraction	MCF-7	IC_{50} 246.84 and 165.65	NR	Cancer-cell cytotoxicity	Dirgantara et al. (2018)
A. ferox, tuber ethanol extract and ethyl acetate fraction	T47D	IC_{50} 513.06 and 84.8	NR	Cancer-cell cytotoxicity	Aisyah et al. (2020)
C. racemosa, hexane, ethyl acetate and ethanol extracts	MCF-7	IC_{50} 23.7, 66.7 and 182.7	NR	Cytotoxicity; *in silico*	Sanger et al. (2023)
Z. acanthopodium, fruit ethanol extract	4T1	IC_{50} 54.48	Doxorubicin 0.80	Cancer-cell cytotoxicity	Rosidah et al. (2019)

Taxon and material	Model	Result (µg/mL)	Reference drug (µg/mL)	Evidence level	Reference
Z. acanthopodium, fruit extract	HepG2	IC_{50} 122.66	NR	Cancer-cell cytotoxicity	Tala & Siregar (2022)
O. tenuiflorum, leaf ethanol extract	A549	Viability decreased; ROS and caspase-3 increased; Bcl-2, SOD2 and GPx decreased	NR	Measured mechanism	Wihadmadyatami et al. (2019)

Note. Values are as reported in the sources; ppm was converted to µg/mL (1 ppm = 1 µg/mL). Selectivity index (SI) was calculated as IC_{50} in non-cancerous cells divided by IC_{50} in cancer cells when both values were available from the same study. For *Eleutherine bulbosa*, IC_{50} values in Vero cells were reported by Alamsyah Lubis et al. (2018) for the n-hexane and ethyl acetate extracts, giving SI values of 2.89 and 4.57, respectively; the ethanol extract was not evaluated against Vero cells. For the other preparations in **Table 2**, no corresponding non-cancerous-cell IC_{50} value was identified in the cited study.

3.4. Phytochemical Evidence Rarely Links a Compound to the Activity Measured

The phytochemical evidence is summarised in **Table 3**, which separates constituents that were isolated and structurally elucidated from those identified by chromatography–mass spectrometry and from class-level screening. Isolated and elucidated compounds were reported for *B. javanica*, *E. poeppigiana*, *E. bulbosa, A. vestiaria* and *C. racemosa* (Ambardhani et al., 2019; V. S. Rani, 2018; Satolom, 2015; Subeki & Muhartono, 2015; Yang et al., 2015). For *E. bulbosa*, a naphthoquinone-type compound was isolated from the bulbs and characterised by UV, IR, LC–MS and ^{1}H-NMR spectroscopy (V. S. Rani, 2018), and afzelechin was identified in *A. vestiaria* seeds from its ^{1}H-NMR spectrum, in which two doublets at δ 7.22 and 6.79 ppm (J = 8.4 Hz) indicated a para-substituted B-ring (Satolom, 2015).

Most other entries in **Table 3** rest on chromatographic profiles or colour-reaction screening. Profiles of *S. palustris*, *B. cernua* and *U. lanosa* var. *ferrea* list tens of constituents (Fatmawati et al., 2022; Wiraswati et al., 2023; Yusuf et al., 2026), and screening of *A. ferox*, *U. gambir* and *U. lanosa* var. *ferrea* detected flavonoids, terpenoids, steroids, alkaloids and tannins (Aisyah et al., 2020; Alfani et al., 2023; Yusuf et al., 2023). Such data show what an extract contains but not which constituent is active, because none of these compounds was tested on its own. The identified constituents of *Ocimum tenuiflorum* L. were characterised in material from outside Indonesia (Domlur Thyagaraj et al., 2013; Utispan et al., 2023), so their relevance to Indonesian samples also needs confirmation. Closing the gap between chemical profile and activity requires bioassay-guided fractionation, in which each fraction is tested and the active one is resolved into its constituents.

Table 3. Phytochemical evidence reported for the plants reviewed, by type of identification

Taxon	Constituent(s) or class	Chemical class	Type of identification	Tested for cancer-related activity	Reference
C. longa	Curcumin, demethoxycurcumin, bisdemethoxycurcumin	Curcuminoids (diarylheptanoids)	Isolated, structure established	Yes (curcumin)	Sharma et al. (2005)
B. javanica	Bruceine A	Quassinoid	Isolated, structure elucidated	Yes, T47D	Subeki & Muhartono (2015)
E. poeppigiana	α-Erythroidine	*Erythrina* alkaloid	Isolated, structure elucidated	Yes, MCF-7	Ambardhani et al. (2019)
E. bulbosa	Naphthoquinone derivative	Naphthoquinone	Isolated; UV, IR, LC–MS, ^{1}H-NMR	No	V. S. Rani (2018)
A. vestiaria	Afzelechin; flavonoid isolate	Flavan-3-ol; flavonoid	Isolated; UV, ^{1}H-NMR	BSLT only (isolate)	Rerung et al. (2017); Satolom (2015)
C. racemosa	Racemobutenolids A and B; 4′,5′-dehydrodiodictyonema A; cacospongionolide C; trans-phytol; trans-phytyl acetate; α-tocospira A; α-tocoxylenoxy; α-tocopherol quinone; α-tocospirone; (23E)-3β-hydroxy-stigmasta-5,23-dien-28-one; (3β,24R)-stigmasta-5,28-diene-3,24-diol;	Various	Isolated, structure elucidated	Yes, A-549 and HL-60	Yang et al. (2015)

Taxon	Constituent(s) or class	Chemical class	Type of identification	Tested for cancer-related activity	Reference
	(3β,24S)-stigmasta-5,28-diene-3,24-diol; (22E)-3β-hydroxy-cholesta-5,22-dien-24-one; fucosterol; 24R,28S-epoxyfucosterol; and 24S,28R-epoxyfucosterol				
U. lanosa var. *ferrea*	Ten metabolites in the hexane fraction	Various	UHPLC–HRMS, tentative	Fraction tested, MCF-7	Yusuf et al. (2026)
S. palustris	Volatile and semivolatile constituents	Various	GC–MS profile	No	Fatmawati et al. (2022); Nurmilatina (2017)
B. cernua	45 compounds in the stem methanol extract	Various	GC–MS profile; docking	Extract tested, MCF-7	Wiraswati et al. (2023)
O. tenuiflorum	Rosmarinic acid and eugenol	Phenolic acid; phenylpropanoid	HPLC quantification against standards	No	Domlur Thyagaraj et al. (2013)
O. tenuiflorum	Rosmarinic acid and apigenin	Phenolic acid; flavone	HPLC–ESI–TOF–MS	Extract tested, head and neck cancer cells	Utispan et al. (2023)
Z. acanthopodium	Quercetin and other extract constituents	Flavonol and other constituents	Quercetin quantification; UHPLC–HRMS profiling	No (immunomodulatory study)	Hutapea et al. (2025)
U. lanosa var. *ferrea*; *A. ferox*; *U. gambir*	Flavonoids, terpenoids, steroids, alkaloids, tannins, saponins	Class level	Colour-reaction screening; total flavonoid assay	Extracts tested	Aisyah et al. (2020); Alfani et al. (2023); Yusuf et al. (2023)

Note. "Isolated" denotes a pure compound whose structure was established spectroscopically; chromatographic profiles identify constituents in a mixture without isolating them; class-level screening detects groups of metabolites by colour reactions. BSLT, brine shrimp lethality test; ESI–TOF–MS, electrospray ionisation time-of-flight mass spectrometry; GC–MS, gas chromatography–mass spectrometry; HPLC, high-performance liquid chromatography; LC–MS, liquid chromatography–mass spectrometry; ^{1}H-NMR, proton nuclear magnetic resonance; UHPLC–HRMS, ultra-high-performance liquid chromatography–high-resolution mass spectrometry.

3.5. Mechanistic Evidence Is Concentrated on Curcumin

Curcumin from *Curcuma longa* L., a staple of jamu (Elfahmi et al., 2014), has the most detailed mechanistic evidence of any compound in this review and serves here as a reference for what pathway-level evidence looks like (**Figure 3**). In MCF-7 cells, curcumin arrested the cell cycle in G1, reduced cyclin D, cyclin E and cyclin-dependent kinases 2, 4 and 6, raised the CDK inhibitors p21 and p27, and increased caspase-3 and caspase-9 activity (Li et al., 2012). In SGC-7901 gastric cancer cells it lowered Bcl-2 and raised Bax, dissipated the mitochondrial membrane potential, released cytochrome c into the cytosol and led to cleavage of caspase-3 and PARP (Xue et al., 2014). Combined with citral, curcumin generated reactive oxygen species, activated p53- and PARP-1-mediated apoptosis and arrested MCF-7 cells in G0/G1 without harming normal breast epithelial cells (Patel et al., 2015). These effects were measured in cell lines, and the poor oral bioavailability of curcumin has long been recognised as a barrier to turning them into clinical benefit (Sharma et al., 2005).

For the other plants, mechanistic evidence is thin. Measured markers were available for *S. palustris*, whose extract and fractions raised p53 and caspase-3 in HepG2 cells and raised p53 while lowering Bcl-2 in T47D cells (Safitri et al., 2021; Yanti et al., 2021), and for *O. tenuiflorum*, whose leaf extract increased reactive oxygen species and caspase-3 and lowered Bcl-2, SOD2 and glutathione peroxidase in A549 lung cancer cells (Wihadmadyatami et al., 2019). The mechanistic statements for *C. racemosa* and *B. cernua* come from docking of extract constituents against cancer-related proteins (Sanger et al., 2023; Wiraswati et al., 2023), which predicts binding but does not show that the compounds act on these targets in cells. For the remaining plants the mechanism has not been studied, so descriptions of them as acting through apoptosis or cell-cycle arrest should be confined to the species for which such effects were measured.

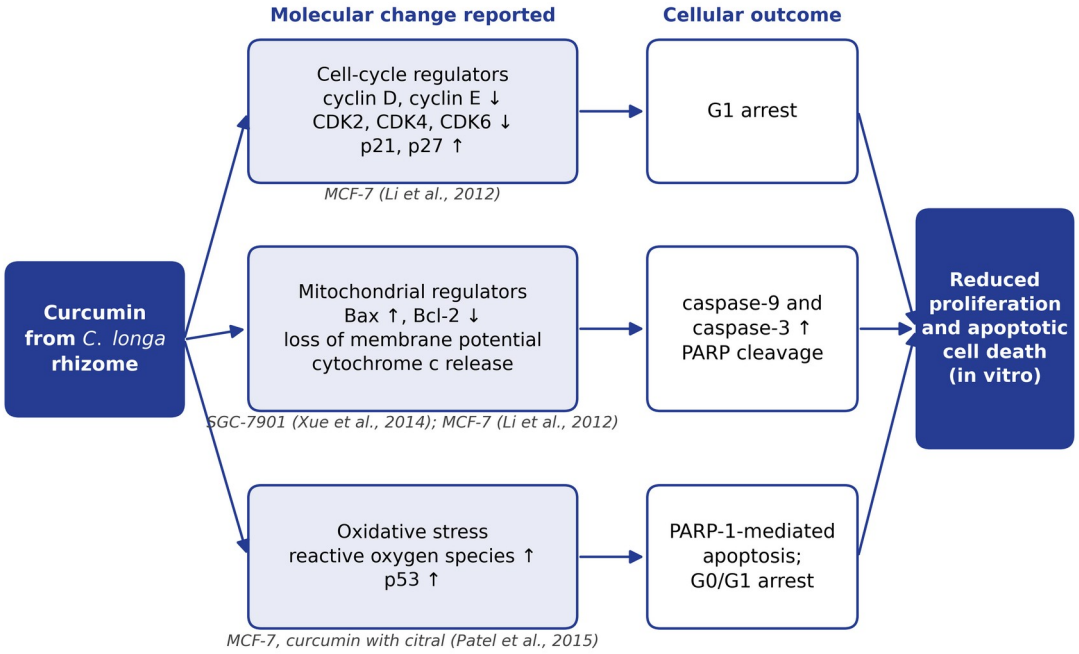

Figure 3. Molecular and cellular effects of curcumin reported in the cited cell-line studies. Arrows indicate an increase (↑) or decrease (↓) in the level or activity of the marker. Bax and Bcl-2, pro- and anti-apoptotic Bcl-2 family proteins; CDK, cyclin-dependent kinase; p21 and p27, CDK inhibitors; PARP, poly(ADP-ribose) polymerase

3.6. Priorities for Moving Indonesian Plants beyond Cell-Line Screening

The evidence map in **Figure 2** points to four steps that would add most value. The first is botanical authentication: every study should state the accepted name, the plant part, the collection site and a voucher number, which is essential for plants known by shared names such as bajakah and katuk hutan (Mahfudh et al., 2024). The second is the routine inclusion of a non-cancerous cell line, so that a selectivity index can be reported alongside each IC_{50} (Weerapreeyakul et al., 2012). The third is bioassay-guided isolation from the most active fractions, particularly the hexane fraction of *U. lanosa* var. *ferrea*, the hexane and ethyl acetate fractions of *S. palustris*, the ethyl acetate fraction of *A. ferox* and the hexane extract of *C. racemosa*. The fourth is *in vivo* testing of standardised preparations, which no study in this review had reached, together with toxicity data that would allow traditional preparations to be judged for safety.

This synthesis draws on a modest set of database records and on values as reported rather than re-analysed, and formal risk-of-bias tools were not applied because they are not designed for this mix of ethnobotanical and *in vitro* work. Its contribution is the explicit separation of evidence levels, which shows that most Indonesian plants investigated for cancer-related activity remain at the stage of crude-extract cytotoxicity and that the few with mechanistic data are those also studied as defined compounds or fractions.

4. CONCLUSION

Indonesian medicinal plants investigated for cancer-related activity are supported mainly by traditional use and by the cytotoxicity of crude extracts in cancer cell lines. Of 17 taxa with experimental or phytochemical data, 15 had cancer-cell cytotoxicity data, three had measured mechanisms, none had *in vivo* efficacy data, and selectivity toward cancer cells was shown only for the ethyl acetate extract of *E. bulbosa* and for curcumin combined with citral. The most potent preparations were the hexane extract of *C. racemosa* (IC_{50} 23.7 µg/mL, MCF-7), the ethanol extract of *Z. acanthopodium* fruit (54.48 µg/mL, 4T1) and the hexane extract of *E. bulbosa* (56.15 µg/mL, WiDr), whereas the brine shrimp results for bajakah indicate general toxicity only. Because the local name bajakah covered species of three genera, results must be reported by species. Authenticated material, selectivity indices, isolation of the active constituents and *in vivo* studies of standardised preparations are needed before any of these plants can be considered a candidate for cancer therapy.

AUTHOR CONTRIBUTIONS

Conceptualization, M.Y. and M.M.; methodology, M.Y. and M.M.; validation, M.Y., M.M., R.A., Y.I. and S.; writing—original draft preparation, M.Y., M.M., R.A., Y.I. and S.; writing—review and editing, M.M., R.A. and Y.I. All authors have read and agreed to the published version of the manuscript.

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DATA AVAILABILITY STATEMENT

The data extracted from the included and supplementary studies are provided in Table S1 (Supplementary Materials). No new data were created.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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DECLARATION OF GENERATIVE ARTIFICIAL INTELLIGENCE (AI) USE

During the preparation of this manuscript, the authors used Claude (Anthropic) to assist in improving the clarity, structure, or readability of the text. After using this tool, the authors thoroughly reviewed, edited, and verified the entire content to ensure it accurately represents their own ideas and interpretations. The authors take full responsibility for the integrity and originality of the published work.

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Supplementary Materials

Table S1. Data extracted from the studies included in the review (I01–I24, database search) and from the additional studies (A01–A10) used to complete the plant profiles

ID	Reference	Taxon / taxa	Plant material / preparation	Test system	Extracted result / finding	Evidence level	Normal cells / SI
I01	Yusuf et al. (2023)	*Uncaria lanosa* var. *ferrea* (Blume) Ridsdale; plus class-level screening of *U. lanosa* var. *ferrea*, *Angiopteris ferox* and *Uncaria gambir*	Stem; ethanol extract / class-level phytochemical screening	MCF-7; phytochemical screening	IC_{50} 193.2 µg/mL; flavonoids, terpenoids, steroids, alkaloids, tannins and saponins reported at class level	Cancer-cell cytotoxicity; compound identification	NR
I02	Aliviyanti et al. (2021)	*Spatholobus littoralis*; *Uncaria gambir*; *Spatholobus ferrugineus*; *Schefflera petiolosa*	Roots; ethanol extracts (reflux)	T47D	IC_{50} 407, 708, 881 and 1096 µg/mL, respectively; tamoxifen 9 µg/mL	Cancer-cell cytotoxicity	NR
I03	Zein et al. (2022)	*Uncaria sp.*	Stem; ethanol extract	*Artemia franciscana* (BSLT)	LC_{50} 23.84 µg/mL	General toxicity	NR
I04	Alamsyah Lubis et al. (2018)	*Eleutherine bulbosa* (Mill.) Urb.	Bulb; hexane, ethyl acetate and ethanol extracts	WiDr	IC_{50} 56.15, 70.76 and 364.10 µg/mL; Vero-cell IC_{50} available for hexane and ethyl acetate	Cancer-cell cytotoxicity	SI 2.89 (hexane); 4.57 (ethyl acetate)
I05	Muti'ah et al. (2020)	*Eleutherine bulbosa* (Mill.) Urb.	Bulb extract	WiDr	Cytotoxicity; apoptosis/cell-cycle effects reported in the cited study	Cancer-cell cytotoxicity / mechanism	NR
I06	Yanti et al. (2021)	*Stenochlaena palustris* (Burm.f.) Bedd.	Herb extract and most active fraction	HepG2	IC_{50} 865.84 and 224.12 µg/mL; p53 and caspase-3 increased	Cancer-cell cytotoxicity / measured mechanism	NR
I07	Safitri et al. (2021)	*Stenochlaena palustris* (Burm.f.) Bedd.	Herb; hexane and ethyl acetate fractions	T47D	IC_{50} 86.99 and 98.43 µg/mL; p53 increased and Bcl-2 decreased	Cancer-cell cytotoxicity / measured mechanism	NR
I08	Dirgantara et al. (2018)	*Breynia cernua* (Poir.) Müll.Arg.	Leaf/stem; 96% ethanol extract and n-hexane fraction	MCF-7	IC_{50} 246.84 and 165.65 µg/mL	Cancer-cell cytotoxicity	NR
I09	Wiraswati et al. (2023)	*Breynia cernua* (Poir.) Müll.Arg.	Stem methanol extract	MCF-7; GC–MS/docking	45 compounds; GC–MS profile and docking reported	Compound identification / *in silico* prediction	NR
I10	Husodo et al. (2021)	*Phyllanthus reticulatus* Poir.	Leaf	No cancer test	Medicinal use; no experimental cancer endpoint	Traditional/ medicinal use	NR
I11	Aisyah et al.	*Angiopteris ferox*	Tuber; ethanol	T47D	IC_{50} 513.06 and 84.8	Cancer-cell	NR

ID	Reference	Taxon / taxa	Plant material / preparation	Test system	Extracted result / finding	Evidence level	Normal cells / SI
	(2020)	Copel.	extract and ethyl acetate fraction		µg/mL	cytotoxicity; class-level phytochemistry	
I12	Rosidah et al. (2019)	*Zanthoxylum acanthopodium* DC.	Fruit; ethanol extract	4T1	IC_{50} 54.48 µg/mL; doxorubicin 0.80 µg/mL	Cancer-cell cytotoxicity	NR
I13	Tala & Siregar (2022)	*Zanthoxylum acanthopodium* DC.	Fruit extract	HepG2	IC_{50} 122.66 µg/mL	Cancer-cell cytotoxicity	NR
I14	Subeki & Muhartono (2015)	*Brucea javanica* (L.) Merr.	Fruit; isolated bruceine A	T47D	Antiproliferative activity reported; quantitative value not reproduced in current main tables	Cancer-cell cytotoxicity / compound identification	NR
I15	Ambardhani et al. (2019)	*Erythrina poeppigiana* (Walp.) O.F.Cook	Stem bark; isolated α-erythroidine	MCF-7	Cytotoxicity reported; quantitative value not reproduced in current main tables	Cancer-cell cytotoxicity / compound identification	NR
I16	Elfahmi et al. (2014)	*Curcuma longa* L.	Rhizome; curcuminoid-related evidence	Cancer-related literature	Curcumin, demethoxycurcumin and bisdemethoxycurcumin discussed	Compound identification / background evidence	NR
I17	Li et al. (2012)	*Curcuma longa* L.	Curcumin	MCF-7; SGC-7901	Cell-cycle arrest and apoptosis-related molecular changes reported	Measured mechanism	NR
I18	Patel et al. (2015)	*Curcuma longa* L.	Curcumin + citral	MCF-7	ROS generation; p53/PARP-1-mediated apoptosis; G0/G1 arrest; normal breast epithelial cells assessed	Measured mechanism	Normal breast epithelial cells
I19	Hasan et al. (2022)	*Annona muricata* L.	Endophytic fungi isolated from leaves	HeLa	Cytotoxicity of endophytic fungi	Cancer-cell cytotoxicity	NR
I20	Rerung et al. (2017)	*Areca vestiaria* Giseke	Seed/fruit; flavonoid isolate	*Artemia* (BSLT)	LC_{50} 583.45 µg/mL	General toxicity / compound identification	NR
I21	Satolom (2015)	*Areca vestiaria* Giseke	Seed; afzelechin/isolate	Phytochemical characterization	Afzelechin identified from 1H-NMR data	Compound identification	NR
I22	Simbala et al. (2022)	*Areca vestiaria* Giseke	Seed/fruit	Ethnobotanical context	Traditional/cancer-related use context	Traditional use	NR
I23	Wihadmadyatami et al. (2019)	*Ocimum tenuiflorum* L.	Leaf ethanol extract	A549	Viability decreased; ROS and caspase-3 increased; Bcl-2, SOD2 and GPx decreased	Measured mechanism	NR
I24	Sanger et al. (2023)	*Caulerpa racemosa* (Forssk.) J.Agardh	Thallus; hexane, ethyl acetate and ethanol extracts	MCF-7	IC_{50} 23.7, 66.7 and 182.7 µg/mL; *in silico* prediction also reported	Cancer-cell cytotoxicity / *in silico* prediction	NR

ID	Reference	Taxon / taxa	Plant material / preparation	Test system	Extracted result / finding	Evidence level	Normal cells / SI
A01	Yusuf et al. (2026)	*Uncaria lanosa* var. *ferrea* (Blume) Ridsdale	Stem; hexane, ethyl acetate and water fractions	MCF-7; UHPLC–HRMS	IC_{50} 105.37, 130.58 and 209.91 µg/mL; ten metabolites tentatively profiled in hexane fraction	Cancer-cell cytotoxicity / compound identification	NR
A02	Alfani et al. (2023)	*Uncaria gambir* (Hunter) Roxb.	Root/stem extract	Phytochemical screening	Total flavonoids and metabolite classes reported	Compound identification / class-level screening	NR
A03	Permatasari et al. (2023)	*Uncaria gambir* (Hunter) Roxb.	Stem fractions	Brine shrimp lethality test	General toxicity reported; exact LC_{50} not reproduced in current main tables	General toxicity	NR
A04	V. S. Rani (2018)	*Eleutherine bulbosa* (Mill.) Urb.	Bulb; isolated compound	Phytochemical characterization	naphthoquinone derivative; isolated and characterized by UV, IR, LC–MS and 1H-NMR	Compound identification	NR
A05	Yang et al. (2015)	*Caulerpa racemosa* (Forssk.) J.Agardh	Thallus; isolated compounds	Phytochemical characterization	17 compounds isolated and structurally elucidated	Compound identification	NR
A06	Fatmawati et al. (2022)	*Stenochlaena palustris* (Burm.f.) Bedd.	Herb	Phytochemical characterization	Volatile and semivolatile constituents; GC–MS profile	Compound identification	NR
A07	Nurmilatina (2017)	*Stenochlaena palustris* (Burm.f.) Bedd.	Herb	Phytochemical characterization	Volatile and semivolatile constituents; GC–MS profile	Compound identification	NR
A08	Domlur Thyagaraj et al. (2013)	*Ocimum tenuiflorum* L.	Plant material; rosmarinic acid and eugenol	Phytochemical characterization	HPLC quantification against standards	Compound identification	NR
A09	Utispan et al. (2023)	*Ocimum tenuiflorum* L.	Plant extract; rosmarinic acid and apigenin	Head and neck cancer cells	HPLC–ESI–TOF–MS; extract tested against head and neck cancer cells	Compound identification / cancer-related test	NR
A10	Hutapea et al. (2025)	*Zanthoxylum acanthopodium* DC.	Fruit; ethanolic extract	Immunomodulatory study	Quercetin and other extract constituents; quercetin quantification and UHPLC–HRMS profiling	Compound identification	NR

Note. Values are as reported in the sources; ppm was converted to µg/mL (1 ppm = 1 µg/mL). Study IDs I01–I24 denote the studies retrieved by the database search (Figure 1) and A01–A10 the additional studies; full references are given in the reference list. BSLT, brine shrimp lethality test; GC–MS, gas chromatography–mass spectrometry; HPLC, high-performance liquid chromatography; NR, not reported; ROS, reactive oxygen species; SI, selectivity index; UHPLC–HRMS, ultra-high-performance liquid chromatography–high-resolution mass spectrometry.