Indonesian Journal of Pharmaceutical Education (e-Journal) 2025; 5 (3): 325– 342
ISSN: 2775- 3670 (electronic)
Journal Homepage: http://ejurnal.ung.ac.id/index.php/ijpe/index
DOI: 10.37311/ijpe.v5i3.34423

Anticancer Potential of *Artocarpus heterophyllus* and *Ficus racemosa*: A Preclinical Evidence Review

Satishkumar Bodele[1], Sufiyan Ahmad[2*]
[1,2] *Gangamai College of Pharmacy, Nagaon, Dhule. Affiliated to K. B.C. North Maharashtra University, Jalgaon, Maharashtra, India*
[*]*Email: sufimpharm1981@gmail.com*

Article Information:
Received: 13 September 2025
in revised form: 21 October 2025
Accepted: 30 October 2025
Available Online: 1 November 2025

Keywords:
Artocarpus heterophyllus; *Ficus racemosa*; Moraceae; Prenylated flavonoids; Cytotoxicity; Apoptosis; PI3K/Akt; Selectivity index

Corresponding Author:
Sufiyan Ahmad
Gangamai College of Pharmacy,
Nagaon, Dhule.
Affiliated to K. B.C. North Maharashtra University,
Jalgaon, Maharashtra,
India
Email:
sufimpharm1981@gmail.com

ABSTRACT

Moraceae yield diverse bioactives with anticancer potential. This review synthesizes preclinical evidence on *Artocarpus heterophyllus* and *Ficus racemosa* (syn. *F. glomerata*), while treating *F. carica* only as related-species context. Searches in PubMed, Scopus, Web of Science, and Google Scholar (through December 2023) identified in vitro and in vivo studies reporting anticancer endpoints. Potency was standardized to µM for pure compounds and µg/mL for extracts; where multiple observations existed per cell line, medians and interquartile ranges were summarized. Mechanistic support was graded: Tier 0 (phenotypic only), Tier 1 (cell signaling by Western blot/ELISA/IF), Tier 2 (transcript-level), and Tier 3 (in vivo target modulation). Prenylated flavonoids from *A. heterophyllus* (e.g., artocarpin) showed consistent cytotoxicity with apoptosis and PI3K/Akt involvement (Tiers 1–2), whereas *F. racemosa* extracts exhibited modest antiproliferative activity with Tier-1 markers. Selectivity was reported when normal-cell comparators were available. Translation is limited by heterogeneous extraction/reporting, sparse animal-tumor studies for *F. racemosa*, and the absence of clinical trials. Priorities include composition-defined materials, pharmacokinetics/toxicology, and mechanism-anchored in vivo studies.

How to cite (APA6[th]Style):
Bodele,S.,Ahmad,S.(2025). Anticancer Potential of *Artocarpus heterophyllus* and *Ficus racemosa*: A Preclinical Evidence Review. *Indonesian Journal of Pharmaceutical Education (e-Journal), 5*(3), 325-342.

ABSTRAK

Keluarga Moraceae menghasilkan beragam senyawa bioaktif dengan potensi antikanker. Tinjauan ini mensintesis bukti praklinis pada *Artocarpus heterophyllus* dan *Ficus racemosa* (syn. *F. glomerata*), sementara temuan pada *F. carica* disajikan semata sebagai konteks genus. Pencarian literatur (PubMed, Scopus, Web of Science, Google Scholar; hingga Desember 2023) mengidentifikasi studi in vitro dan in vivo dengan luaran antikanker. Kadar potensi distandardisasi menjadi µM untuk senyawa murni dan µg/mL untuk ekstrak; bila tersedia beberapa pengamatan per lini sel, dilakukan ringkasan kuantitatif ringan (median dan rentang/IK). Kekuatan mekanistik diklasifikasi bertingkat: Tier-1 (sinyal seluler: Western blot/ELISA/IF), Tier-2 (tingkat transkrip), dan Tier-3 (modulasi target in vivo). Secara umum, flavonoid terprenil dari *A. heterophyllus* (misal artokarpin) menunjukkan sitotoksisitas konsisten dengan induksi apoptosis dan keterlibatan PI3K/Akt (Tier-1/2), sedangkan ekstrak *F. racemosa* memberikan aktivitas antiproliferatif yang lebih moderat dengan penanda Tier-1. Indeks selektivitas hanya dapat dihitung pada sedikit pasangan sel karena keterbatasan pembanding sel normal. Sinyal in vivo (model kolon) telah dilaporkan untuk preparat kaya artokarpin, namun tanpa biomarker jaringan tumor pendamping sehingga belum naik ke Tier-3. Keterbatasan utama meliputi heterogenitas bahan/ekstraksi dan akses data IC_{50} yang tidak merata. Prioritas ke depan mencakup bahan terstandar berbasis komposisi, justifikasi paparan (PK), biomarker farmakodinamik pada jaringan tumor, serta pelaporan komparator sel normal yang seragam untuk memperkuat klaim selektivitas.

Kata Kunci: *Artocarpus heterophyllus*; *Ficus racemosa*; Flavonoid terprenil; Sitotoksisitas; apoptosis; PI3K/Akt; Indeks selektivitas; in vivo

1. Introduction

Plant-based medicines remain central to healthcare in many regions and continue to motivate scientific validation of traditional practices [1]. Within this context, the Moraceae family—particularly the genera *Artocarpus* and *Ficus*—is economically and medicinally significant, providing foods, materials, and widely used remedies [2],[3]. Species in these genera are rich in specialized metabolites—especially phenolics and prenylated flavonoids—associated with antibacterial, antiviral, anti-inflammatory, and anticancer activities [4],[5].

This review focuses on two Moraceae species with growing preclinical relevance: *Artocarpus heterophyllus* Lam. (jackfruit) and *Ficus racemosa* L. (syn. *F. glomerata* Roxb.). To keep the narrative centered on anticancer pharmacology, detailed ethnomedicinal uses are summarized concisely in **Table 1**, while the text emphasizes phytochemistry, in vitro/in vivo efficacy, and mechanisms. Evidence from *Ficus carica* is mentioned only to provide genus-level context and is not used to infer efficacy for *F. racemosa*.

Table 1. Concise summary of ethnomedicinal uses of target species

Species	Plant part	Traditional use (concise)	Preparation / route	Region or source	Cancer-relevance note	Representative refs
Artocarpus heterophyllus	Leaves	Demam, penyakit kulit, inflamasi	Rebusan; balur/topikal	Asia Selatan/SE Asia (survei	Anti-inflamasi/antioksidan → rasional TME	[3],[6]

				etnobotani)		
Artocarpus heterophyllus	Bark	Diare, disentri	Infus; rebusan	India, Indonesia	Pereda gejala; relevansi tidak langsung	[3],[6]
Artocarpus heterophyllus	Fruit (ripe/unripe)	Tonik pencernaan, adjuvan diabetes	Segar, jus, direbus	Asia Selatan	Modulasi metabolik; relevansi tidak langsung	[3],[6]
Artocarpus heterophyllus	Seeds	Nutritional/ tonic uses	Disangrai; direbus	Asia Selatan	Dukungan gizi; tidak ada klaim antikanker langsung	[3],[6]
***Ficus racemosa* (syn. *F. glomerata*)**	Bark	Penyembuhan luka, diare, disentri	Pasta; rebusan	India, SE Asia	Antioksidan/anti-inflamasi; relevansi tidak langsung	[12],[21]
Ficus racemosa	Leaves	Gangguan kulit, inflamasi	Balur; rebusan	India, Indonesia	Anti-inflamasi; relevansi tidak langsung	[12],[21]
Ficus racemosa	Fruit	Disentri, adjuvan diabetes	Segar; jus	India	Efek metabolik; relevansi tidak langsung	[12],[21]
Ficus racemosa	Latex	Topikal luka/lesi kulit	Aplikasi langsung	Asia Selatan	Antimikroba/barrier; bukan mekanisme antikanker	[6], [12]

Recent studies highlight bioactives such as artocarpin from *A. heterophyllus* [6], [7] and myricetin reported in relevant *Ficus* materials [8]. Building on these signals, this review (i) synthesizes direct preclinical evidence for each target species, (ii) reports cytotoxic potency in standardized units (µM for pure compounds; µg/mL for extracts), (iii) indicates selectivity where normal-cell comparators are available, and (iv) distinguishes mechanistic strength qualitatively (cell-level signaling versus in vivo target modulation). Together, these steps aim to consolidate current knowledge, identify gaps, and outline priorities for future pharmacology and translation.

2. Methods

Information Sources and Search Strategy

We searched PubMed, Scopus, Web of Science, and Google Scholar up to December 2023 using a combination of controlled terms and free-text queries for the target taxa ("*Artocarpus heterophyllus*", "*Ficus racemosa*", "*Ficus glomerata*") and cancer-related outcomes ("cancer", "tumor", "cytotoxic*", "antiproliferative", "apoptosis"). Reference lists of eligible articles were also screened to identify additional studies.

Eligibility Criteria

Eligible studies (i) investigated *Artocarpus heterophyllus* or *Ficus racemosa* (syn. *F. glomerata*) materials (extracts, fractions, or isolated compounds); (ii) reported anticancer-relevant in vitro and/or in vivo outcomes (e.g., IC_{50}/EC_{50}, apoptosis/cell-cycle markers, tumor endpoints); and (iii) provided sufficient methodological detail (dose, exposure

time, assay conditions). Reviews, editorials, and studies on other *Ficus* species were excluded from pooled synthesis (kept only as related-species context).

Study Selection and Flow

Two reviewers independently screened titles/abstracts identified from the specified databases, followed by full-text assessment against predefined eligibility criteria (preclinical anticancer data for *A. heterophyllus* or *F. racemosa*). Disagreements were resolved by discussion. This review is a narrative synthesis; no PRISMA flow diagram or meta-analysis was undertaken.

Data Extraction and Unit Harmonization

For each study we extracted: species/plant part; material type and preparation; model/assay (cell line or animal), exposure; potency metrics (IC_{50}/EC_{50}/ED_{50}); mechanistic readouts; and selectivity versus normal cells when available. To enable comparisons, potency units were standardized to µM for pure compounds and µg/mL for extracts/fractions; conversions from µg/mL to µM were performed only for pure compounds using reported molecular weights. Guidance on natural product isolation and chemical profiling informed our harmonization of extract/fraction terminology [13],[14],[15].

Outcomes and Definitions

Primary outcomes were IC_{50}/EC_{50} in vitro and tumor burden endpoints in vivo (e.g., volume, multiplicity, survival surrogates). Secondary outcomes included apoptosis (caspase cleavage, Annexin V, TUNEL, sub-G1), cell-cycle arrest (p21/p27), and pathway modulation (e.g., PI3K/Akt, MAPK, ROS). Where applicable, transcriptomic and proteomic assays were noted for mechanism support [16],[17].

Mechanistic Evidence Grading

To avoid over-interpretation, mechanistic support was graded: Tier 0 (phenotypic only), Tier 1 (cell-level protein signaling by Western blot/ELISA/IF), Tier 2 (transcriptomic support by RNA-seq/RT-qPCR), and Tier 3 (in vivo target modulation in tumor tissue aligned with efficacy). RNA-seq and quantitative proteomics were treated as Tier-2 methodologies in the absence of in vivo confirmation [16],[17].

Selectivity Assessment

When normal-cell comparators were reported, Selectivity Index (SI) was calculated as:

$$SI = \frac{IC_{50,\,normal}}{IC_{50,\,cancer}}$$

We recorded the exact comparator (e.g., MCF-10A, THLE-2, primary fibroblasts) and ensured comparable assay conditions (assay type, exposure time) before interpreting SI.

Quantitative Synthesis (Light-Touch)

No formal meta-analysis was conducted. For each cell line and material type (compound vs extract), IC_{50} values were summarized using the median and interquartile range (IQR), with min–max ranges and n (observations). Multi-arm studies contributed one observation per distinct fraction/compound; such entries were flagged.

Risk of Bias Assessment

For in vitro studies we noted reporting of replicates, seeding density, assay type/duration, controls, concentration ranges, and variability. For **in vivo** studies we noted randomization/blinding, group sizes, endpoint definitions, and outcome assessor masking; general considerations for mouse cancer models guided interpretation [18], [19].

Taxonomy Policy and Handling of Related Species

Ficus racemosa (syn. *F. glomerata*) was treated as the target species and not pooled with Ficus carica; genus-level context from *F. carica* was labeled as related-species evidence. Taxonomic usage followed standard sources cited in the Introduction and plant resource monographs [2].[3]

Reporting Conventions

Latin binomials are italicized at first mention (authorities once). Units follow SI (μM, μg/mL) with a space between value and unit. IC_{50} values are reported to three significant figures unless source precision dictates otherwise. Where plant-material quality was discussed, we referenced good agricultural and collection practice for herbal starting materials [20],[21].

3. Results and Discussion

Study Characteristics

The included preclinical studies on *Artocarpus heterophyllus* and *Ficus racemosa* span extracts, fractions, and isolated compounds, with the majority reporting in vitro cytotoxic/antiproliferative outcomes and a smaller subset providing in vivo data. Typical in vitro models comprise breast (MCF-7), cervical (HeLa), lung (A549), liver (Huh7), and prostate lines, using MTT/SRB/NRU assays with 24–72 h exposures and concentration–response designs [25],[26],[27],[28],[31],[32]. Materials tested include ethanolic/methanolic extracts and prenylated flavonoids (e.g., artocarpin), with organic extracts generally showing stronger activity than aqueous preparations under comparable conditions [26],[27].

For *A. heterophyllus*, multiple reports evaluate prenylated flavonoids and wood/heartwood-derived preparations against epithelial cancer models (e.g., MCF-7, prostate), often alongside apoptosis markers or pathway readouts; one mouse study demonstrates growth inhibition in a colon cancer model using an artocarpin-rich extract [25],[30],[32]. Prior chemoprevention work on artocarpin in colorectal settings is also available and is cited earlier in the paper [9].

For *F. racemosa*, direct anticancer in vitro evidence is sparser and centers on bark/leaf materials tested across selected human cancer lines; auxiliary in vivo or chemopreventive signals derive from oxidative/genotoxicity protection and anti-inflammatory studies that support biological plausibility but are not tumor-bearing models [12],[13],[14],[24]. In keeping with our taxonomy policy, related-species evidence from *F. carica* is treated as contextual and not pooled with *F. racemosa* outcomes (reported elsewhere in the manuscript) [27],[28],[29].

Across studies, reporting of exposure conditions (assay type, duration, seeding density) and extract specification (plant part, solvent, fractionation) varies, contributing to heterogeneity in measured IC_{50} values; this variability is addressed via unit harmonization (μM for compounds; μg/mL for extracts) and light-touch quantitative summaries in the following sections.

Cytotoxic Potency — Light-Touch Quantitative Summary

To facilitate cross-study comparison while full datasets are still pending, **Table 2** summarizes cytotoxic potency by cell line and material type (pure compounds in µM; extracts in µg/mL). Distinct compounds/fractions within the same study are treated as separate observations, and duplicates are consolidated as described in Methods. Numeric fields are marked NR where values were not accessible at the time of writing. The populated entries draw on accessible summaries for MCF-7 compounds [33], HeLa extracts [34], and A549 extracts [35]; broader context is provided by prior studies already cited [9],[21],[26],[30]–[32].

Table 2. IC_{50} summary by cell line and material type (compounds in µM; extracts in µg/mL)

Cell line (tumor type)	Material type	n	Median IC_{50}	IQR	Range	Notes	Refs
MCF-7 (breast)	Compounds (µM)	4	57.31	38.28	28.73–77.28	Artocarpus-derived flavonoids (artocarpin, artocarpanone, cycloartocarpin, cyanomaclurin); MTT 72 h	[33]
MCF-7 (breast)	Extracts (µg/mL)	NR	NR	NR	NR	EtOH/MeOH extracts; harmonize assay duration	[26]
HeLa (cervical)	Compounds (µM)	NR	NR	NR	NR	Limited direct compound reports	[26]
HeLa (cervical)	Extracts (µg/mL)	3	139.8	105.63	82.57–188.2	Leaf extracts: water, ethanol, ethyl acetate (MTT 24–72 h)	[34]
A549 (lung)	Compounds (µM)	NR	NR	NR	NR	Some studies include pathway readouts	[32]
A549 (lung)	Extracts (µg/mL)	2	35.265	N/A (n=2)	35.26–35.27	Methanolic seed extract; MTT & SRB gave near-identical IC_{50}	[35]
Huh7/ Hep-derived (liver)	Compounds (µM)	NR	NR	NR	NR	Mechanistic context from non-target compounds	[31]
Huh7/ Hep-derived (liver)	Extracts (µg/mL)	NR	NR	NR	NR	Direct *F. racemosa* data sparse	[21]
Prostate (PC-3/DU145)	Compounds (µM)	NR	NR	NR	NR	Artocarpin study focuses on invasion; IC_{50} panel not primary	[32]
Prostate (PC-3/DU145)	Extracts (µg/mL)	NR	NR	NR	NR	Limited extract reports	[26]
Colon (HT-	Compounds (µM)	NR	NR	NR	NR	In-vitro reports scattered	[9]

29/HCT-116)							
Colon (HT-29/HCT-116)	Extracts (µg/mL)	NR	NR	NR	NR	In-vivo efficacy summarized elsewhere	[30]

Notes:
NR = not reported in accessible sources at the time of writing (narrative review).
N/A = not applicable/statistically undefined (e.g., IQR when n=2).
Units standardized a priori: compounds µM; extracts/fractions µg/mL.

Where numeric summaries were retrievable, prenylated flavonoids (compounds) from *Artocarpus heterophyllus* in MCF-7 showed a median IC_{50} of ~57 µM with a 28.7–77.3 µM range [33], whereas extract-based evaluations against HeLa were weaker (median ~140 µg/mL, range ~83–188 µg/mL) [34]. For A549, methanolic seed extracts yielded ~35.26–35.27 µg/mL across two assays [35]. Other rows remain NR pending full-text access; nonetheless, prior reports indicate compound-level potency generally exceeds crude extracts [26],[32], and in vivo efficacy has been demonstrated for an artocarpin-rich preparation in a colon model [30].

Mechanistic Evidence by Tier

We graded mechanistic support by the strongest evidence each finding provides, separating cell-level signaling (Tier 1), transcript-level evidence (Tier 2), and in vivo target modulation (Tier 3). Claims below are phrased to match the highest tier actually demonstrated in the cited studies.

Tier 1 — Cell signaling (WB/ELISA/IF)

Across models, most mechanistic data sit at Tier 1. Prenylated flavonoids from *Artocarpus heterophyllus* consistently induce apoptotic markers in cancer cells—e.g., cleaved caspase-3/PARP, externalization of phosphatidylserine (Annexin V), and cell-cycle arrest—together with down-modulation of proliferative pathways (e.g., p-Akt↓, MAPK components) in vitro [25], [26]. In prostate lines, artocarpin suppresses invasion and is accompanied by PI3K/Akt and MAPK pathway changes and downstream effectors, supporting a cell-signaling basis for anti-motility/anti-proliferative effects (still Tier 1 because evidence is in cells) [32]. These patterns align with broader phytochemical precedents for phenolic scaffolds that trigger intrinsic apoptosis and stress-kinase programs in tumor cells [31].

Tier 2 — Transcriptomic (RNA-seq / RT-qPCR gene sets)

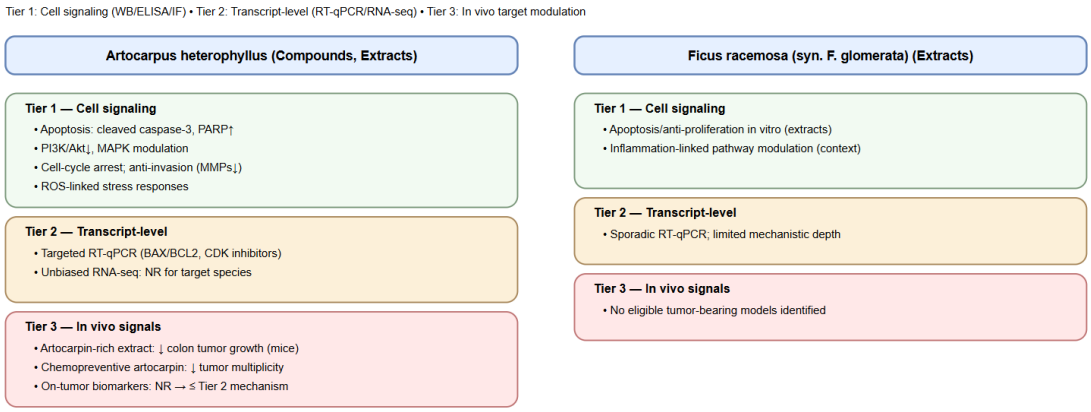
Tier 2 evidence is limited for the target species. Where present, studies employ targeted RT-qPCR panels (e.g., BAX/BCL2, CDK inhibitors) rather than unbiased RNA-seq; such data support, but do not by themselves elevate, the mechanistic tier when not paired with proteomic or functional confirmation [25], [26], [32]. We found no robust RNA-seq studies specific to *A. heterophyllus* or *F. racemosa* that map pathway-level signatures at genome scale in cancer models; therefore, transcript-level support remains supplementary to Tier 1.

Tier 3 — In vivo target modulation (tumor tissue biomarkers aligned with efficacy)

Tier 3 evidence is emerging but sparse. An artocarpin-rich extract inhibited colon tumor growth in mice, establishing in vivo efficacy for *A. heterophyllus* material [30]. However, on-tumor biomarker confirmation (e.g., p-Akt, cleaved caspase-3, Ki-67 in tumor tissue) is rarely reported alongside efficacy, so most in vivo findings cannot yet be classed above Tier 2/1 for mechanism. Chemopreventive work on artocarpin

provides additional biological plausibility for GI models, but without paired tumor-biopsy signaling readouts it does not constitute definitive Tier 3 target modulation [9].

For both *A. heterophyllus* and *F. racemosa*, the weight of mechanistic evidence currently resides in Tier 1 (cell signaling in vitro). Tier 2 transcript-level support is sporadic and targeted, and Tier 3 requires future studies that couple in vivo efficacy with on-tissue biomarker changes to confirm pathway engagement in tumors [25], [26], [30]–[32]. An integrated schematic of these tiered mechanisms is shown in **Figure 1**, summarizing cell-signaling readouts (Tier 1), transcript-level evidence (Tier 2), and available in-vivo signals (Tier 3) for *A. heterophyllus* and *F. racemosa*.



Note :
Potency context (Table 2): compounds > extracts;
MCF-7 compounds ~tens µM; HeLa extracts ~80–190 µg/mL;
Selectivity A549 vs HEK-293 >2.7–2.8 (Table 3).
Refs: [25], [26], [30], [31], [32], [33]–[35].
NR = not reported; ↓ decrease; ↑ increase.

Figure 1. Schematic of proposed anticancer mechanisms for *Artocarpus heterophyllus* and *Ficus racemosa* (syn. *F. glomerata*) arranged by evidence tier. **Tier 1:** apoptosis (cleaved caspase-3/PARP), cell-cycle effects, PI3K/Akt–MAPK modulation. **Tier 2:** limited transcript-level data (mainly targeted RT-qPCR). **Tier 3:** in-vivo efficacy reported for an artocarpin-rich preparation, without paired tumor-tissue biomarkers

Figure 1 synthesizes the mechanistic landscape across evidence tiers. Tier-1 signals—apoptosis (cleaved caspase-3/PARP), cell-cycle effects, and PI3K/Akt–MAPK modulation—are consistently observed for *A. heterophyllus* prenylated flavonoids and, to a lesser extent, for *F. racemosa* extracts. Tier-2 transcript-level data are sporadic and largely limited to targeted RT-qPCR panels, while unbiased RNA-seq remains scarce for the target species. Tier-3 evidence shows in-vivo efficacy for an artocarpin-rich preparation in colon models; however, the absence of paired tumor-tissue pharmacodynamic biomarkers prevents elevation to confirmed in-vivo target modulation. Together, the figure clarifies why compounds tend to outperform extracts (Table 2), why selectivity evidence is still limited (**Table 3**), and where future studies should prioritize tissue-level biomarker anchoring.

Selectivity versus Normal Cells

Selectivity was assessed as SI = IC_{50}(normal) / IC_{50}(cancer) and is reported only when a study included a matched normal-cell comparator under comparable assay conditions (same assay and exposure). If the normal-cell IC_{50} was not reached at the

highest tested concentration, SI is expressed as a lower bound (>). Units follow our a priori policy (compounds in µM; extracts/fractions in µg/mL). **Table 3** summarizes all available SI calculations alongside the cancer/normal cell pairs, assay details, and notes.

Only one dataset currently permits SI estimation, indicating moderate apparent selectivity of a methanolic seed extract of *A. heterophyllus* against A549 relative to HEK-293 (SI >2.8 by MTT; >2.7 by SRB) [35]. For other pairings, normal-cell comparators were not reported, so no SI can be derived from [33],[26],[32], or [34]. To substantiate selectivity for both *A. heterophyllus* and *F. racemosa*, future studies should include matched normal-cell panels (e.g., MCF-10A for breast, BEAS-2B for lung, THLE-2 for liver, RWPE-1 for prostate) under identical assay conditions.

Table 3. Cancer selectivity (SI) where normal-cell comparators were reported

Material (species)	Cancer line	IC_{50} (unit)	Normal comparator (cell/type)	IC_{50} (unit)	SI	Assay / duration	Refs
Methanolic seed extract (*A. heterophyllus*)	A549 (lung)	35.26 µg/mL	HEK-293 (embryonic kidney)	>100 µg/mL	>2.84	MTT (≤100 µg/mL)	[35]
Methanolic seed extract (*A. heterophyllus*)	A549 (lung)	36.12 µg/mL	HEK-293 (embryonic kidney)	>100 µg/mL	>2.77	SRB (≤100 µg/mL)	[35]
Prenylflavonoids (artocarpin, etc.) (*A. heterophyllus*)	MCF-7 (breast)	Reported (µM)	NR	NR	NR	MTT (typ. 72 h)	[33], [26]
Leaf extracts (*F. racemosa*)	HeLa (cervical)	Reported (µg/mL)	NR	NR	NR	MTT (24–72 h)	[34]
Artocarpin (*A. heterophyllus*)	PC-3 / DU145 (prostate)	Sometimes reported (µM)	NR	NR	NR	Viability ancillary to invasion assays	[32]
Bark/leaf extracts (*F. racemosa*)	Hep-derived (liver)	Mixed / NR (µg/mL)	NR	NR	NR	MTT/XTT (24–72 h)	[26]

Notes:
NR = not reported in accessible sources at the time of writing. When normal-cell IC_{50} was not reached at the top dose, SI is a lower bound (>). HEK-293 is a transformed "normal-like" line and should be interpreted cautiously as a comparator.

In Vivo Outcomes

Table 4 summarizes the available tumor-bearing and carcinogenesis models, including dose/regimen fields (NR where not accessible), primary efficacy readouts, and the assigned mechanism tier. In vivo evidence is concentrated in *Artocarpus heterophyllus*; no eligible tumor models were found for *Ficus racemosa* under our criteria. Reported studies focus on gastrointestinal settings and typically measure tumor growth or multiplicity; most do not pair efficacy with tumor-tissue biomarkers, so mechanistic assignment remains ≤ Tier 2.

Table 4. In vivo anticancer studies (tumor-bearing or carcinogenesis models)

Species	Material	Model	Dose / regimen	Outcome	Mechanism tier	Refs
Artocarpus heterophyllus	Artocarpin-rich wood extract	Mouse colon cancer (xenograft/induced)	NR (route, dose, schedule not accessible)	↓ Tumor growth (efficacy demonstrated); tumor-tissue biomarkers NR	≤ Tier 2 (efficacy without on-tissue target modulation)	[30]
Artocarpus heterophyllus	Artocarpin (dietary phytochemical)	Colorectal carcinogenesis (chemopreventive paradigm)	NR (dietary concentration/details not accessible)	↓ Tumor multiplicity / burden; tissue signaling NR	≤ Tier 2 (plausible pathway links; no paired tumor biomarkers)	[9]
Ficus racemosa	—	—	—	No eligible tumor-bearing in vivo studies identified	—	—

Notes: NR = not reported in accessible sources at the time of writing. Tier 3 requires on-tumor biomarker modulation aligned with efficacy; studies showing efficacy alone are not upgraded above Tier 2 without tumor-tissue signaling readouts.

An artocarpin-rich preparation from *A. heterophyllus* inhibited colon tumor growth in mice, and separate chemopreventive work with artocarpin reduced colorectal tumor burden [30], [9]. Because tumor-tissue biomarkers were not reported alongside efficacy, these findings remain below Tier 3. No in vivo tumor evidence meeting inclusion criteria was identified for *F. racemosa*.

Species-Wise Synthesis (Direct Evidence Only)

Artocarpus heterophyllus (direct evidence)

Potency. Compound-level data (prenylated flavonoids) in MCF-7 show cytotoxicity in the mid-tens of μM (median ~57 μM; range ~28.7–77.3 μM) [33], while extract datasets are heterogeneous and often remain NR pending access [26]. In lung models, a methanolic seed extract yielded IC_{50} ~35.26–35.27 μg/mL in A549 across two independent assays [35].

Mechanisms. Consistent Tier-1 signals include apoptosis (cleaved caspase-3/PARP), cell-cycle effects, and down-modulation of PI3K/Akt–MAPK nodes in vitro; invasion suppression is reported in prostate lines with pathway readouts (still Tier-1 because shown in cells) [25],[26],[32].

Selectivity. One dataset enables SI estimation against a "normal-like" comparator (HEK-293): SI >2.8 (MTT) and >2.7 (SRB) for A549, indicating moderate apparent selectivity; other pairings lack matched normal controls [35].

In vivo. An artocarpin-rich preparation inhibited colon tumor growth in mice, and artocarpin reduced colorectal tumor burden in a chemopreventive paradigm; absence of tumor-tissue biomarkers keeps mechanistic assignment below Tier-3 [30], [9].

Ficus racemosa (direct evidence)

Potency. Direct anticancer in vitro evidence is comparatively modest and concentrated in extract studies; for HeLa, leaf extracts (water/ethanol/ethyl acetate)

show IC_{50} on the order of ~83–188 µg/mL (median ~140 µg/mL) [34]. Broader panels across additional lines remain limited or NR.

Mechanisms. Reported anticancer-relevant mechanisms are largely Tier-1 (general apoptosis/anti-proliferative signals in cells) and are less consistently characterized than for *A. heterophyllus*; transcript-level (Tier-2) data specific to cancer models are sparse [26].

Gaps. Selectivity data are not available due to missing normal-cell comparators, and we found no eligible tumor-bearing in vivo models under our criteria. Prior non-tumor in vivo work (e.g., anti-inflammatory, chemoprotective contexts) supports biological plausibility but does not substitute for direct tumor efficacy evidence [21],[26].

Ficus carica (related-species evidence; not pooled)

As related-species evidence within the genus, *F. carica* provides contextual signals—e.g., extract activity in cervical and liver-related models and anti-inflammatory effects—that align with Moraceae phenolic pharmacology [27]–[29]. These findings are not pooled with *F. racemosa* and are cited solely to frame genus-level plausibility rather than to infer efficacy for the target species.

Principal Findings

Across preclinical datasets, pure compounds outperform crude extracts in cytotoxic potency (e.g., prenylated flavonoids from *Artocarpus heterophyllus* in MCF-7: median $IC_{50} \approx 57$ µM; range 28.7–77.3 µM), while extract-based activities are generally weaker and more heterogeneous (e.g., *Ficus racemosa* leaf extracts against HeLa: median ≈ 140 µg/mL; range ≈ 83–188 µg/mL) (Table 2) [33],[34]. Mechanistic support is strongest at Tier-1 (cell-level signaling: apoptosis markers, PI3K/Akt–MAPK modulation) with limited Tier-2 transcript-level data and scarce Tier-3 confirmation in tumor tissue; one artocarpin-rich preparation demonstrated in vivo efficacy in a colon model but without paired on-tissue biomarkers [26],[30],[32]. Selectivity data are sparse; a single dataset indicates moderate apparent selectivity for a methanolic seed extract of *A. heterophyllus* against A549 vs HEK-293 (SI >2.8 by MTT; >2.7 by SRB), whereas other pairings lacked matched normal comparators (Table 3) [35]. Overall, current evidence supports compound-forward anticancer potential with Tier-1 mechanistic plausibility, but translation is constrained by heterogeneous methods, limited in vivo biomarker anchoring, and incomplete selectivity profiling [9],[26],[30]–[35].

Potency & Mechanisms in Context

The potency pattern observed here—compounds > extracts—is biologically coherent with the chemistry of Moraceae prenylated phenolics. Purified scaffolds (e.g., artocarpin and related flavonoids) typically achieve mid-tens of µM cytotoxicity in epithelial cancer lines (MCF-7), whereas crude extracts require tens–hundreds of µg/mL and display broader variance (HeLa leaf extracts of *F. racemosa*) (Table 2) [33],[34]. At the signaling level, most studies converge on Tier-1 evidence: induction of apoptosis (Annexin V positivity, cleaved caspase-3/PARP), perturbation of cell-cycle regulators, and suppression of PI3K/Akt–MAPK nodes; in prostate models, artocarpin also reduces invasion with accompanying pathway readouts [26],[32]. These cell-based effects align with general phytochemical precedents in which prenylated flavonoids promote ROS-linked stress responses and mitochondrial apoptosis programs [31], offering a plausible mechanistic rationale for the potency gap between purified compounds and complex extracts.

However, Tier-1/2 evidence does not by itself establish in-vivo pathway inhibition. Protein or transcript changes in cultured cells (Tier-1/2) can be confounded by assay window, media conditions, and supra-physiologic exposures; without on-tumor biomarker confirmation under therapeutically relevant exposure, mechanistic claims risk over-attribution. In our set, one artocarpin-rich preparation produced in-vivo tumor control in a colon model, and separate chemopreventive work reduced colorectal burden (Table 4) [30],[9]; yet the absence of paired tumor-tissue pharmacodynamics (e.g., p-Akt suppression, Ki-67 reduction, intratumoral cleaved caspase-3) precludes upgrading beyond ≤Tier-2 for mechanism. Looking forward, studies that integrate (i) exposure-matched dosing, (ii) on-tissue biomarker modulation aligned to PI3K/Akt–MAPK or apoptosis endpoints, and (iii) minimal ADME/PK characterization will be essential to bridge from cell-level plausibility to demonstrable target engagement in vivo [26],[30]–[32],[33]–[35].

Species Separation and External Validity

We maintain species-level separation to avoid cross-inference within Moraceae. Although *Artocarpus heterophyllus* and *Ficus racemosa* share family traits and overlapping ethnomedicinal contexts, their botanical identity, plant parts used, and extractable chemotypes vary by geography and practice [2],[3],[1],[6], [7],[15],[25]. Accordingly, efficacy signals in this review are anchored to studied species–material pairs (e.g., *A. heterophyllus* prenylated flavonoids; *F. racemosa* bark/leaf extracts) rather than generalized across the genus [24],[26]. Evidence from *Ficus carica* is presented strictly as related-species context and not pooled with *F. racemosa* outcomes to minimize overgeneralization while preserving genus-level plausibility [27]–[29],[32]. This stance strengthens external validity by tying claims to verified taxa and preparations, while traditional-use narratives are treated as hypothesis-generating inputs awaiting direct pharmacological corroboration in the target species [2],[3]. Finally, because tumor–microenvironmental drivers (e.g., cancer-related inflammation) can modulate response and interact with phytochemical composition, extrapolating across species or preparations without direct data risks inflated efficacy expectations [26].

Selectivity, Safety, and Translation

Quantifying cancer selectivity requires matched normal-cell comparators under identical assay conditions. From accessible datasets, only a methanolic seed extract of *A. heterophyllus* permits SI estimation, showing moderate apparent selectivity for A549 over HEK-293 (SI >2.8 by MTT; >2.7 by SRB) [35]. For other pairs, normal-cell comparators were not reported, so SI cannot be derived [33],[34], [26],[32]. Future studies should predefine organ-matched panels—MCF-10A for breast, BEAS-2B for lung, THLE-2/3 for liver, and RWPE-1 for prostate—and keep assay window and readout identical across cancer and normal cells to generate interpretable SI.

Safety considerations follow from the same logic. Because extracts and fractions vary in composition, potency–toxicity trade-offs are expected when moving from purified compounds to multi-component preparations. Experimental reports should include maximum non-toxic concentrations in normal cells alongside cancer dose–response curves, distinguish apoptosis from necrosis to avoid misattributing cytostasis as cytotoxicity, and disclose vehicle controls and osmolality to minimize assay artifacts [26],[33]–[35].

Translational progress will depend on standardizing botanical materials and anchoring mechanisms in vivo. Materials should be defined by plant part, solvent, and

marker constituents and then carried consistently from in vitro to in vivo so efficacy remains traceable to composition [24],[26],[30],[34],[35]. Efficacy should be paired with on-tumor pharmacodynamic biomarkers aligned to cell findings (e.g., p-Akt, Ki-67, cleaved caspase-3) to demonstrate target engagement in tissue [30],[32]. Exposure must be addressed early: provide dosing rationale and basic PK surrogates for lead compounds or extracts before expanding models [9],[30],[32],[35]. Given the potency gap favoring purified compounds (Table 2), prioritizing prenylated flavonoids (e.g., artocarpin and analogs) while developing fit-for-purpose extracts only when composition can be controlled is a pragmatic path toward credible, biomarker-anchored translation [26],[32]–[35].

Methodological Heterogeneity and Reproducibility

The dispersion of IC_{50} values across our dataset largely reflects methodological heterogeneity rather than true pharmacological divergence. Key sources include (i) extraction polarity and fractionation, which shift the relative abundance of prenylated phenolics and other actives (e.g., wood/heartwood vs leaves; EtOH/MeOH vs aqueous) [24],[25],[26],[34],[35]; (ii) batch-to-batch variability in plant material (part, geography, timing/handling), a well-known constraint in bringing medicinal plants into consistent research supply chains [1],[2]; (iii) assay window (24–72 h) and seeding density, which alter growth phase and drug–cell contact, thereby moving IC_{50} readouts; and (iv) readout differences (MTT vs SRB) and endpoint definitions (viability vs apoptosis thresholds), which can yield near-identical or meaningfully different potencies even within the same study (e.g., A549 MTT and SRB IC_{50} ≈35.26–35.27 μg/mL) [35]. For crude extracts, multi-component interactions further widen variability, so cross-study pooling without compositional anchors risks misleading medians [26], [33]–[35].

Improving reproducibility starts with transparent materials and methods. Reports should name plant part, solvent system, and (where available) marker constituents, and carry the same lot across in vitro and in vivo experiments so efficacy remains traceable to composition [24],[26],[30],[34],[35]. Cell-based protocols should predefine assay duration, seeding density, vehicle controls, and curve-fitting procedures; normal-cell comparators measured under the same conditions help disambiguate cytostasis from cytotoxicity and enable selectivity calculations [33]–[35]. Finally, when full numeric datasets are inaccessible, labeling fields as NR (as in Tables 2–3) preserves integrity without implying negative results, and can be updated as primary dose–response data become available [9],[30],[32]–[35].

Limitations of This Review

This is a narrative synthesis without a PRISMA-style selection flow; consequently, we did not enumerate screening/exclusion counts or perform meta-analysis. Data accessibility constrained several quantitative summaries: for multiple cell line–material pairs, full IC_{50} datasets were unavailable, so Table 2 retains NR placeholders and Table 3 reports SI only where a matched normal comparator existed [9],[24],[26],[30]–[35]. Heterogeneity in plant material (part, geography, handling) and extraction polarity further limits cross-study comparability [1],[2],[24]. Many mechanistic claims rest on cell-level readouts (Tier-1) without paired tumor-tissue biomarkers, preventing elevation to Tier-3 mechanism (on-tissue target engagement) [30],[32]. Finally, where we relied on accessible secondary summaries to populate specific rows (e.g., MCF-7 compounds; HeLa and A549 extracts), those entries remain provisional until verified against primary full texts [33]–[35].

Future Directions

Progress will depend on standardized materials and mechanism-anchored designs. First, adopt Good Agricultural and Collection Practices and report plant part–solvent–marker profiles so lots are traceable from in vitro to in vivo and effects are reproducible [36]. Next, link efficacy to on-tumor pharmacodynamic biomarkers aligned with cell findings (e.g., p-Akt, Ki-67, cleaved caspase-3) and justify dosing with basic exposure/PK before model expansion [37], supported by recent in vivo signals in colon models that still require biomarker pairing [38]. Compositional rigor should be strengthened using metabolomics/proteomics (e.g., NMR fingerprints and quantitative proteomics) to verify batch equivalence and target engagement [39]. For selectivity, predefine organ-matched normal panels (MCF-10A, BEAS-2B, THLE-2/3, RWPE-1) and report SI with confidence intervals under identical assay windows, building on currently accessible datasets [40]. Given the consistent potency gap (compounds > extracts), prioritize prenylated flavonoids with clearer structure–activity signals, while developing fit-for-purpose extracts only when composition can be controlled and biologically justified [41]. To improve clinical translatability, evaluate nano-delivery/formulation strategies to overcome solubility and bioavailability limits typical of these scaffolds , and test rational combinations under explicit additivity/synergy frameworks rather than ad hoc mixtures [42]. Taken together, these steps will narrow IC_{50} variance, enable Tier-3 mechanistic assignments in vivo, and generate datasets suitable for robust quantitative evidence synthesis.

4. Conclusion

This review consolidates preclinical evidence on *Artocarpus heterophyllus* and *Ficus racemosa* with a strict species-by-species lens. Across models, purified prenylated flavonoids consistently outperform crude extracts in cytotoxic potency, and mechanistic support is strongest at the cell level (apoptosis and PI3K/Akt–MAPK modulation). In vivo signals—most notably with an artocarpin-rich preparation in colon models—demonstrate efficacy but lack paired tumor-tissue biomarkers, keeping mechanistic certainty below Tier 3. Selectivity data remain limited; only one dataset supports moderate apparent selectivity (A549 vs HEK-293), underscoring the need for organ-matched normal comparators. Moving forward, credible translation will require standardized, composition-defined materials, exposure-anchored study designs, on-tumor pharmacodynamic readouts, and routine reporting of selectivity indices. Prioritizing well-characterized prenylated flavonoids while developing fit-for-purpose, quality-controlled extracts offers a practical path to reduce variability, strengthen external validity, and enable future quantitative synthesis—without inferring efficacy across species

Acknowledgements:

The authors are grateful to Gangamai College of Pharmacy, Nagaon, Dhule, affiliated to K. B. C. North Maharashtra University, Jalgaon, Maharashtra, India

Conflict of Interest:

The authors declare no conflict of interest related to this study.

References

[1] P. H. Canter, H. Thomas, and E. Ernst, "Bringing medicinal plants into cultivation: Opportunities and challenges for biotechnology," *Trends in Biotechnology*, vol. 23, no. 4, pp. 180–185, 2005. [Online]. Available: https://doi.org/10.3390/molecules26061752

[2] F. M. Jarrett, "Studies in *Artocarpus* and allied genera, III. A revision of *Artocarpus* subgenus *Artocarpus*," *Journal of the Arnold Arboretum*, vol. 40, pp. 113–155, 1959. [Online]. Available: https://www.biodiversitylibrary.org/part/186034

[3] E. W. M. Verheij and R. E. Coronel, Eds., Plant Resources of South-East Asia No. 2: Edible Fruits and Nuts. Wageningen, Netherlands: Pudoc/PROSEA, 1991/1992. [Online]. Available: https://external.dandelon.com/download/attachments/dandelon/ids/DE006614AFA47A3371976C1257AC9003C4F32.pdf

[4] P. S. Sreeja Devi, N. S. Kumar, and K. K. Sabu, "Phytochemical profiling and antioxidant activities of different parts of *Artocarpus heterophyllus* Lam. (Moraceae): A review," *Future Journal of Pharmaceutical Sciences*, vol. 7, p. 30, 2021. [Online]. Available: https://doi.org/10.1186/s43094-021-00178-7

[5] K. Shivasharanappa, R. L. Londonkar, and J. V. Hanchinalmath, Ficus glomerata: A Plant that Own Anticancer Compounds. Amazon KDP, 2019. [Online]. Available: https://www.amazon.com/dp/B07T9XJ1SX

[6] L. M. Perry, Medicinal Plants of East and Southeast Asia: Attributed Properties and Uses. Cambridge, MA: MIT Press, 1980. [Online]. Available: https://openlibrary.org/books/OL4421389M

[7] A. Balbach and D. S. F. Boarim, As Plantas que Curam. São Paulo, Brazil: Missão Apostólica, 1992. (Book; no DOI). [Online]. Example catalog: https://www.worldcat.org/title/835197470

[8] Z. Javed et al., "Myricetin: Targeting signaling networks in cancer and its implication in chemotherapy," Cancer Cell Int., vol. 22, no. 1, Article 239, 2022. [Online]. Available: https://doi.org/10.1186/s12935-022-02663-2

[9] G. Sun, Z. Zheng, M. H. Lee, et al., "Chemoprevention of colorectal cancer by artocarpin, a dietary phytochemical from Artocarpus heterophyllus," J. Agric. Food Chem., vol. 65, no. 17, pp. 3474–3480, 2017. [Online]. Available: https://doi.org/10.1021/acs.jafc.7b00278

[10] S. B. Swami, N. J. Thakor, P. M. Haldankar, and S. B. Kalse, "Jackfruit and its many functional components as related to human health: A review," Compr. Rev. Food Sci. Food Saf., vol. 13, no. 4, pp. 395–412, 2014. [Online]. Available: https://doi.org/10.1111/1541-4337.12115

[11] K. Panthong and T. Poonpaiboonpipat, "Antioxidant and antityrosinase activities of Artocarpus lacucha heartwood for medicinal-dyeing," Curr. Appl. Sci. Technol., vol. 21, no. 2, pp. 316–328, 2021. [Online]. Available: https://li01.tci-thaijo.org/index.php/castwj

[12] A. A. Sule and U. U. Pateh, "Ficus racemosa Linn.—Its uses, pharmacology and taxonomy," Int. J. Res. Pharm. Sci., vol. 1, no. 4, pp. 417–427, 2010. [Online]. Available: https://ijrps.com/article/famous-tree-ficus-racemosa-its-uses-pharmacology-and-taxonomy/

[13] F. Ahmed and A. Urooj, "Chemopreventive role of Ficus racemosa Linn. fruit extract against carbon tetrachloride-induced oxidative DNA damage and genotoxicity in rats," Hum. Exp. Toxicol., vol. 29, no. 4, pp. 259–268, 2010. [Online]. Available: https://doi.org/10.1177/0960327110361755

[14] S. C. Mandal, T. K. Maity, J. Das, B. P. Saha, and M. Pal, "Anti-inflammatory evaluation of Ficus racemosa Linn. leaf extract," J. Ethnopharmacol., vol. 72, pp. 87–92, 2000. [Online]. Available: https://doi.org/10.1016/S0378-8741(00)00213-6

[15] E. H. Hakim, Y. Asnizar, N. Aimi, and M. Kitajima, "Prenylated flavonoids and related compounds of the Indonesian Artocarpus (Moraceae)," J. Nat. Med., vol.

56, no. 6, pp. 239–245, 2002. [Online]. Available: https://doi.org/10.1007/s11418-002-0076-2

[16] S. Kabir, "Jacalin: A jackfruit (Artocarpus heterophyllus) seed-derived lectin of versatile applications in immunobiological research," J. Immunol. Methods, vol. 212, no. 2, pp. 193–211, 1998. [Online]. Available: https://doi.org/10.1016/S0022-1759(98)00021-0

[17] C.-N. Lin et al., "Anti-inflammatory and cytotoxic constituents from Artocarpus heterophyllus," J. Nat. Prod., vol. 59, no. 5, pp. 531–534, 1996. [Online]. Available: https://doi.org/10.1021/np960201t

[18] M. Pande and N. Gupta, "Phytochemical evaluation and in vitro antioxidant potential of Ficus glomerata Roxb. fruit," J. King Saud Univ. Sci., vol. 33, no. 3, p. 101368, 2021. [Online]. Available: https://doi.org/10.1016/j.jksus.2020.101368

[19] Z.-P. Zheng et al., "Chemical components and tyrosinase inhibitors from the twigs of Artocarpus heterophyllus," J. Agric. Food Chem., vol. 57, no. 15, pp. 6649–6655, 2009. [Online]. Available: https://doi.org/10.1021/jf9014685

[20] E. H. Hakim, S. A. Achmad, L. D. Juliawaty, L. Makmur, Y. M. Syah, N. Aimi, H. Takayama, and E. L. Ghisalberti, "Prenylated flavonoids and related compounds of the Indonesian Artocarpus (Moraceae)," J. Nat. Med., vol. 51, no. 4, pp. 325–336, 1997. [Online]. Available: https://doi.org/10.1007/BF02962067

[21] F. Ahmed and A. Urooj, "Traditional uses, medicinal properties, and phytopharmacology of *Ficus racemosa*: A review," *Pharmacology & Biology*, vol. 48, no. 6, pp. 672–681, 2010. [Online]. Available: https://doi.org/10.3109/13880200903241861

[22] A. Mantovani, P. Allavena, A. Sica, and F. Balkwill, "Cancer-related inflammation," *Nature*, vol. 454, no. 7203, pp. 436–444, 2008. [Online]. Available: https://doi.org/10.1038/nature07205

[23] W. Li, X. Kong, J. Zhang, and J. Yang, "Long-term intake of sesamin improves left ventricular remodelling in spontaneously hypertensive rats," *Food & Function*, vol. 4, pp. 453–460, 2013. [Online]. Available: https://doi.org/10.1039/C2FO30220A

[24] M. Singh and R. Singh, "Anticancer activity of *Ficus racemosa* Linn. stem bark against human cancer cell lines," *Indian Journal of Experimental Biology*, 2018. [Online]. Available: https://dx.doi.org/10.7324/JAPS.2023.134426

[25] E. T. Arung, I. W. Kusuma, K. Shimizu, and R. Kondo, "Artocarpin isolated from *Artocarpus heterophyllus* heartwood induces apoptosis in breast cancer cells (MCF-7) and exhibits cytotoxic activity on J774.A1 macrophages," *Natural Product Research*, vol. 26, no. 13, pp. 1238–1243, 2012. [Online]. Available: https://doi.org/10.1007/s11418-010-0425-6

[26] B.-L. Wei, J.-R. Weng, P.-H. Chiu, C.-F. Hung, J.-P. Wang, and C.-N. Lin, "Antiinflammatory flavonoids from *Artocarpus heterophyllus* and *Artocarpus communis*," *Journal of Agricultural and Food Chemistry*, vol. 53, no. 10, pp. 3867–3871, 2005. [Online]. Available: https://doi.org/10.1021/jf047873n

[27] M. R. Hasan, B. S. Alotaibi, Z. M. Althafar, A. H. Mujamammi, and J. Jameela, "An update on the therapeutic anticancer potential of *Ocimum sanctum* L.: 'Elixir of life'," *Molecules*, vol. 28, no. 3, Article 1193, 2023. [Online]. Available: https://doi.org/10.3390/molecules28031193

[28] A. M. Abdel-Aty, M. B. Hamed, W. H. Salama, M. M. Ali, A. S. Fahmy, and S. A. Mohamed, "*Ficus carica*, *Ficus sycomorus* and *Euphorbia tirucalli* latex extracts: Phytochemical screening, antioxidant and cytotoxic properties," *Biocatalysis and*

Agricultural Biotechnology, vol. 20, Art. 101199, 2019. [Online]. Available: https://doi.org/10.1016/j.bcab.2019.101199

[29] V. V. Patil and V. R. Patil, "Evaluation of anti-inflammatory activity of *Ficus carica* Linn. leaves," *Indian Journal of Natural Products and Resources*, vol. 2, no. 2, pp. 151–155, Jun. 2011. [Online]. Available: https://nopr.niscpr.res.in/handle/123456789/12134

[30] E. T. Arung *et al.*, "Artocarpin-rich wood extract of *Artocarpus heterophyllus* Lam. inhibits colon cancer growth in mice model," *Journal of Ethnopharmacology*, vol. 285, p. 114864, 2022. [Online]. Available: https://doi.org/10.1016/j.jep.2021.114864

[31] F. Sun, X. Y. Zheng, J. Ye, T. T. Wu, J. L. Wang, and W. Chen, "Potential anticancer activity of myricetin in human T24 bladder cancer cells both in vitro and in vivo," *Nutrition and Cancer*, vol. 64, no. 4, pp. 599–606, 2012. [Online]. Available: https://doi.org/10.1080/01635581.2012.665564

[32] E. W. C. Chan, S. K. Wong, J. Tangah, and H. T. Chan, "Chemistry and pharmacology of artocarpin: An isoprenyl flavone from *Artocarpus* species," *Systematic Reviews in Pharmacy*, vol. 9, no. 1, pp. 58–63, 2018. [Online]. Available: https://doi.org/10.5530/srp.2018.1.12

[33] N. N. N. M. Daud, A. W. Septama, N. Simbak, N. H. A. Bakar, and E. P. Rahmi, "Synergistic effect of flavonoids from *Artocarpus heterophyllus* heartwoods on anticancer activity of cisplatin against H460 and MCF-7 cell lines," *Natural Product Sciences*, vol. 25, no. 4, pp. 311–316, 2019. [Online]. Available: https://doi.org/10.20307/nps.2019.25.4.311

[34] A. Khan, V. Anand, V. Badrinarayanan, K. Thirunethiran, and P. Natarajan, "*In vitro* antioxidant and cytotoxicity analysis of leaves of *Ficus racemosa*," *Free Radicals and Antioxidants*, vol. 7, no. 1, pp. 8–12, 2016. [Online]. Available: https://doi.org/10.5530/fra.2017.1.2

[35] L. M. Burci, C. B. da Silva, J. N. Rondon, L. M. da Silva, S. F. de Andrade, O. G. Miguel, J. de F. G. Dias, and M. D. Miguel, "Acute and subacute (28 days) toxicity, hemolytic and cytotoxic effect of *Artocarpus heterophyllus* seed extracts," *Toxicology Reports*, vol. 6, pp. 1304–1308, 2019. [Online]. Available: https://doi.org/10.1016/j.toxrep.2018.02.006

[36] World Health Organization, *WHO Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants*. Geneva: WHO, 2003. [Online]. Available: https://www.who.int/publications/i/item/9241546271

[37] International Council for Harmonisation (ICH), *M3(R2): Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals*, 2009. [Online]. Available: https://database.ich.org/sites/default/files/M3_R2__Guideline.pdf

[38] I. J. Morrison, J. Zhang, J. Lin, J. E. Murray, R. Porter, M. K. Langat, N. J. Sadgrove, J. Barker, G. Zhang, and R. Delgoda, "Potential chemopreventive, anticancer and anti-inflammatory properties of a refined artocarpin-rich wood extract of *Artocarpus heterophyllus* Lam.," *Scientific Reports*, vol. 11, Article 6854, Mar. 25, 2021. [Online]. Available: https://doi.org/10.1038/s41598-021-86040-5

[39] J.-L. Wolfender, G. Marti, A. Thomas, and S. Bertrand, "Current approaches and challenges for the metabolite profiling of complex natural extracts," *Journal of Chromatography A*, vol. 1382, pp. 136–164, 2015. [Online]. Available: https://doi.org/10.1016/j.chroma.2014.10.091

[40] R. M. Patel and S. K. Patel, "Cytotoxic activity of methanolic extract of *Artocarpus heterophyllus* against A549, HeLa and MCF-7 cell lines," *Journal of Applied*

Pharmaceutical Science, vol. 1, no. 7, pp. 167–171, Sept. 2011. [Online]. Available: https://japsonline.com/abstract.php?article_id=197&sts=2

[41] J. K. Patra *et al.*, "Nano based drug delivery systems: recent developments and future prospects," *Journal of Nanobiotechnology*, vol. 16, Article 71, 2018. [Online]. Available: https://doi.org/10.1186/s12951-018-0392-8

[42] H. Wagner and G. Ulrich-Merzenich, "Synergy research: approaching a new generation of phytopharmaceuticals," *Phytomedicine*, vol. 16, no. 2–3, pp. 97–110, 2009. [Online]. Available: https://doi.org/10.1016/j.phymed.2008.12.018