WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 7, 547-603. Review Article ISSN 2277–7105

PHYTOCHEMISTRY AND THERAPEUTIC POTENTIAL OF *AEGLE MARMELOS* LEAVES: A COMPREHENSIVE REVIEW

Vijay Gadhave*[1], Nayana Dhatrak[2], Amardip Borse[4], Dr. Jitendra Nehete[3]

[1,2,4]Final Year B.Pharm Students, Department of Pharmacognosy, MGV Pharmacy College, Nashik, Maharashtra, India.

[3]Assistant Professor, Department of Pharmacognosy, MGV Pharmacy College, Nashik, Maharashtra, India.

Article Received on 04 March 2026,
Article Revised on 24 March 2026,
Article Published on 01 April 2026,

https://doi.org/10.5281/zenodo.19327600

***Corresponding Author**

Vijay Gadhave

Final Year B.Pharm Students, Department of Pharmacognosy, MGV Pharmacy College, Nashik, Maharashtra, India.

How to cite this Article: Vijay Gadhave*[1], Nayana Dhatrak[2], Amardip Borse[4], Dr. Jitendra Nehete[3] (2026). Phytochemistry And Therapeutic Potential Of Aegle Marmelos Leaves: A Comprehensive Review. World Journal of Pharmaceutical Research, 15(7), 547–603.

ABSTRACT

Aegle marmelos (L.) Correa ex Roxb., commonly known as Bael or Bilva, is a culturally revered medicinal tree extensively used in Ayurvedic and folk systems of medicine across the Indian subcontinent for gastrointestinal, metabolic, inflammatory, and infectious disorders. Among its various parts, the leaves constitute the most frequently prescribed component in classical formulations; however, leaf-specific evidence has only recently been systematized using modern phytochemical and pharmacological tools. Contemporary research has revealed that *A. marmelos* leaves are a rich repository of coumarins (imperatorin, marmelosin, and auraptene), alkaloids (aegeline and marmesiline), flavonoids (rutin and quercetin), phenolic acids, terpenoids, and other bioactive secondary metabolites with multi-targeted antioxidant, anti-inflammatory, antidiabetic, antimicrobial, hepatoprotective, gastroprotective, and anticancer properties. This comprehensive review critically synthesises the botanical context, ethnomedicinal uses, detailed phytochemical profiles, pharmacological activities, pharmacokinetic considerations, safety evaluations, and research gaps pertaining specifically to *Bael* leaves. While preclinical evidence is extensive and encouraging, the translational pipeline remains underdeveloped, with a striking paucity of rigorous clinical trials on standardised leaf preparations. The review emphasises that rational standardisation, mechanistic depth, and well-designed human studies are essential to

transform this classical Ayurvedic drug into an evidence-anchored phytopharmaceutical for contemporary noncommunicable and infectious diseases.

KEYWORDS: *Aegle marmelos*, Bael, Bilva, leaves, coumarins, aegeline, flavonoids, antioxidant, antidiabetic, anti-inflammatory, Ayurveda, phytochemistry, standardization

1. INTRODUCTION

Plants have historically served as primary sources of therapeutic agents, and a substantial proportion of modern pharmaceuticals derive directly or indirectly from botanical leads.[1–3] *Aegle marmelos* (L.) Correa ex Roxb., a medium-sized deciduous tree of the Rutaceae family, occupies a unique position at the intersection of ethnomedicine, religious practice, and contemporary phytotherapy.[4– 6] In India, Sri Lanka, Bangladesh, and adjoining regions, the plant is deeply embedded in Hindu ritual traditions, where its trifoliate leaves are sacred offerings to Lord Shiva; simultaneously, it is a cornerstone ingredient in numerous Ayurvedic formulations prescribed for disorders spanning the gastrointestinal, metabolic, immunological, and dermatological systems.[7–10]

Classical Ayurvedic texts describe Bilva as possessing tikta-kashaya (bitter-astringent) rasa, laghu-ruksha (light-dry) guna, ushna (warm) virya, and katu (pungent) vipaka, with predominant actions on Vata and Kapha doshas.[11–13] These pharmacological attributes traditionally rationalize its deployment in conditions such as atisara (diarrhea), grahani (malabsorption/irritable bowel-like syndromes), prameha (diabetes mellitus), and various inflammatory and infectious states.

While early pharmacognostic and pharmacological investigations commonly treated *A. marmelos* as a monolithic entity, subsequent research has revealed substantial organ-specific variation in phytochemical composition and biological activity across the fruit, leaves, bark, and roots.[15–17] Among these plant parts, the leaves stand out for their ready availability, rapid vegetative regeneration, favorable sustainability profile, and distinct phytochemical signature that distinguishes them from fruit pulp and other tissues.[18–20] Given these advantages and the extensive traditional use of leaf preparations, a focused leaf-centric review is scientifically justified and practically valuable.

In parallel, the global burden of chronic diseases driven by oxidative stress and low-grade inflammation—including type 2 diabetes, cardiovascular disease, non-alcoholic fatty liver

disease, and cancer—continues to escalate at alarming rates, particularly in low- and middle-income countries.[21–24] These multifactorial conditions often respond poorly to single-target pharmacological interventions, thereby renewing scientific interest in multi-component phytotherapeutics capable of simultaneously modulating several interconnected pathogenic pathways.[25–27] In this context, polyphenol-, coumarin- and alkaloid-enriched botanicals such as *A. marmelos* leaves, which display convergent antioxidant, anti-inflammatory, and metabolic-modulating effects, have attracted considerable contemporary attention.[28–30]

Several narrative and systematic reviews have previously summarized the pharmacological activities of *A. marmelos* as a whole plant.[31–33] However, these accounts frequently amalgamate data from disparate plant tissues without adequate distinction, thereby obscuring the tissue-specific phytochemistry that ultimately determines pharmacodynamic behavior and safety.[34–36] Moreover, many earlier reviews predate the recent wave of studies employing high-resolution chromatographic techniques, LC–MS/MS, NMR-guided isolation, molecular docking, and in silico pharmacokinetic prediction, which have substantially refined current understanding of leaf-derived metabolites and their structure–activity relationships.[37–40]

Therefore, this review pursues three interrelated objectives. First, it collates and critically appraises contemporary phytochemical data on *A. marmelos* leaves, with an emphasis on modern extraction methodologies, analytical characterisation, identification of key marker compounds, and quantitative variability across geographic and seasonal contexts. Second, it comprehensively evaluates preclinical pharmacological evidence for leaf extracts and isolated leaf constituents across major therapeutic domains—antioxidant, anti-inflammatory, antidiabetic, antimicrobial, hepatoprotective, gastroprotective, and anticancer—highlighting experimental design rigor, translational relevance, mechanistic plausibility, and the quality of supporting evidence. Third, it identifies critical methodological gaps, safety considerations, standardisation imperatives, and future research priorities required for rational phytopharmaceutical development. By maintaining a deliberate leaf-centric focus and integrating both classical Ayurvedic insights and contemporary biomedical data, this review aims to provide a nuanced, evidence-based resource for pharmacognosists, medicinal chemists, phytopharmacologists, and clinicians interested in the translational potential of *A. marmelos* leaves.

Botanical, Ethnomedicinal and Ayurvedic Context

2.1 Botanical description and taxonomy

Aegle marmelos is the sole representative of the genus *Aegle* within the Rutaceae family and is distributed across South Asia, with India as its primary center of diversity.[41–43] The plant is a medium-sized, deciduous tree that typically attains heights of 6–12 m and is characterised by a crooked, often spreading trunk, aculeate (spiny) branches, and a dense, umbrella-like crown. Leaves are alternate, compound, trifoliate (three leaflets), exstipulate, with individual leaflets being ovatelanceolate to oblanceolate, glabrous, acute-tipped, and bearing 1–3 cm petioles. The leaflets display a distinctive aromatic odour due to the presence of aromatic oils housed within specialised secretory cavities (idioblasts) distributed throughout the leaf lamina and the petiole. The flowers are small, greenish-white, fragrant, and borne in terminal or axillary racemes or panicles. The fruit is globose to pyriform, with a hard, woody, yellowish-green pericarp enclosing fibrous, pale-yellow, sweet, mucilaginous pulp interspersed with numerous seeds embedded in locules.

Figure 1: Trifoliate leaf arrangement of Aegle marmelos (Rutaceae) with labelled parts. It shows a single intact leaf with a slender petiole and three elliptic leaflets, each clearly marked as individual units, highlighting the characteristic trifoliate form. Source:

Taxonomically, *A. marmelos* is recognized by the binomial *Aegle marmelos* (L.) Correa ex Roxb., with earlier synonyms including *Crataeva marmelos* L. and *Feronia limonia* (L.) Swingle. The species is native to India and Sri Lanka but now occurs widely across South Asia, Southeast Asia, and has been introduced into parts of Africa and the Caribbean, where it has naturalized and adapted to diverse tropical and subtropical agro-climatic conditions.

2.2 Ethnomedicinal uses of leaves

Ethnobotanical and ethnopharmacological surveys conducted across India, Nepal, Bangladesh, Sri Lanka, and Thailand consistently document extensive traditional use of *A.*

marmelos leaves in household medicine and folk healing systems.[54–57] Fresh, sun-dried, or shade-dried leaves are prepared as decoctions, aqueous infusions, powders, or medicinal pastes and deployed for the management of a wide spectrum of clinical conditions.[58–60]

The most reported ethnomedicinal uses include:

- **Gastrointestinal disorders:** acute and chronic diarrhea, dysentery, bloody stools, and related digestive complaints.
- **Parasitic and helminthic infections:** intestinal worms and other parasitic infestations.
- **Metabolic disorders:** diabetes mellitus, excessive thirst, and poor digestion.
- **Inflammatory conditions:** fever, general inflammation, and pain.
- **Dermatological disorders:** eczema, psoriasis, fungal skin infections, and ulcerative lesions.
- **Ophthalmic conditions:** conjunctivitis, eye inflammations, and vision disturbances.
- **Wound healing:** chronic or non-healing wounds, cuts, and traumatic lesions.

Preparation methods reported in ethnomedicinal contexts include: (i) leaf decoctions consumed orally (typically 50–100 mL of a decoction prepared by boiling 5–10 g dried leaves in water for 5– 10 minutes, taken once or twice daily), (ii) fresh leaf juice administered with honey or buttermilk, (iii) leaf powder mixed with water or butter milk, and (iv) topical application of fresh leaf paste or leaf juice to affected skin areas.

Table 1: Summary of major ethnomedicinal uses of Aegle marmelos leaves across South and Southeast Asian traditional medicine systems.

Region	Preparation	Main Indication(s)	Reference(s)
India	Leaf decoction	Diarrhoea, dysentery	[2]
South India	Leaf juice (fresh)	Indigestion, colic (abdominal pain)	[3]
Nepal	Leaf decoction	Fever, intestinal worms	[4]
Sri Lanka	Leaf paste (topical)	Wounds, skin infections	[4]
Bangladesh	Leaf powder in water or juice	Diabetes, thirst	[6]
Thailand	**(Unclear/Not well documented)**	—	[4]

These traditional applications consistently presage many of the pharmacological activities subsequently demonstrated in experimental and preclinical work, particularly in domains of antidiarrhoeal, antimicrobial, antidiabetic, anti-inflammatory, and wound-healing effects, thereby lending credence to the empirical basis of folk medicine.

2.3 Ayurvedic pharmacology and classical formulations

In Ayurveda, Bilva (Aegle marmelos) is highly valued and appears in numerous classical texts and formulations.[11,65–67] The plant is traditionally categorized as a component of important polyherbal groups and finds particular application in the management of disorders characterized by aggravation of Vata and Kapha doshas.[1] From a classical Ayurvedic pharmacological perspective, the leaves of Bilva are described as follows:

- **Rasa (taste):** tikta (bitter) and kashaya (astringent)
- **Guna (qualities):** laghu (light), ruksha (dry)
- **Virya (potency):** ushna (warm/heating)
- **Vipaka (post-digestive effect):** katu (pungent)
- **Prabhava (specific action):** affinity for gastrointestinal, metabolic, and immune functions
- **Dosha karma:** Primarily Vata-shamaka and Kapha-shamaka (balancing Vata and Kapha)

These properties rationalise the traditional deployment of Bilva leaves in a spectrum of classical conditions:[11,65–67]

- **Atisara (diarrhea/chronic loose stools):** the astringent and antimicrobial properties help bind stools and reduce excessive secretion.
- **Grahani (malabsorption, IBS-like syndrome):** the digestive and anti-fermentative properties aid restoration of healthy intestinal function.
- **Krimi (parasitic/helminthic infestation):** the antimicrobial and anthelmintic actions eliminate unwanted organisms.
- **Prameha (diabetes mellitus):** the metabolic and antioxidant properties help regulate blood glucose and lipids.
- **Jvara (fever):** the cooling (though paradoxically warm) and immune-modulating actions alleviate fever and support recovery.
- **Kushtha (skin diseases):** topical and systemic antimicrobial and anti-inflammatory actions support healing.

Table 2: Representative classical Ayurvedic formulations containing Aegle marmelos leaves.

Formulation (English)	Form	Indication(s)	Dose / Frequency	Reference
Bilvadi Tablet	Gutika	Diarrhoea, Grahani, Fever	1–2 tablets, 2–3×/day after meals	[8]

Bilva Electuary	Paste / Avaleha	Diarrhoea, Grahani, Haemorrhoids, Poor digestion	1–2 tsp (10–15 g) 1–2×/day after food	[9]
Dasamoola Decoction	Decoction	Vata disorders, Fever, Dyspnoea, Cough, Low back pain	40–60 mL 1–2×/day	[10]
Grahani Powder	Powder	Grahani, Diarrhoea, Indigestion, Toxinrelated disorders	3–5 g 2–3×/day with warm water/buttermilk	[11]
Panchamrita Parpati	Parpati	Grahani, Diarrhoea, Diabetes, Abdominal disorders	125–250 mg 1–2×/day with buttermilk/curd rice	[12]
Bilva Oil	Medicated Oil	Joint pain, Osteoarthritis, Low back pain	Apply 1–2×/day; for nasya/abhyanga as prescribed	[13]
Kutaj-Bilvadi Decoction	Decoction	Diarrhoea, Chronic dysentery, Grahani	40–60 mL 1–2×/day before food	[14]
Bilvadi Tonic	Paste / Lehya	Grahani, Chronic diarrhoea, Postinfective weakness	1–2 tsp 1–2×/day after meals	[15]

When contemporary biomedical mechanisms are juxtaposed with these Ayurvedic pharmacological descriptions, a striking degree of empirical concordance emerges. For example, the Ayurvedic emphasis on astringency correlates with modern findings of tannins and polyphenols that reduce intestinal permeability and diarrheal fluid secretion; the ascribed anthelmintic and antimicrobial properties align with contemporary data on coumarin-, alkaloid- and terpenoid-mediated inhibition of pathogenic microorganisms; the metabolic and digestive properties resonate with antidiabetic and enzyme-inhibitory activities documented in modern pharmacology. This alignment between traditional claims and experimental findings strengthens the case for evidence-based development of Bilva leaf therapeutics.

3. Phytochemistry of *Aegle marmelos* Leaves

3.1 Extraction methods and analytical techniques

Phytochemical investigations of *A. marmelos* leaves have employed a diverse portfolio of extraction protocols, spanning both ethnobotanically informed traditional methods (aqueous decoctions, herbal teas) and modern high-efficiency laboratory extraction schemes.[69–72] Systematic investigations typically use sequential extraction with solvents of increasing polarity—for example, hexane, chloroform, ethyl acetate, methanol, ethanol, or aqueous systems—to partition and isolate metabolites according to their chemical properties.[73–75]

Initial characterization of crude extracts typically involves qualitative phytochemical screening to detect the presence or absence of major secondary metabolite classes, including alkaloids (Wagner, Dragendorff, or Mayer reagent tests), flavonoids (Shinoda, Wilstätter, or $FeCl_3$ tests), phenolic compounds and tannins, saponins, terpenoids, and sterols (Salkowski or Liebermann-Burchard tests).[76–78]

For more refined analysis, thin-layer chromatography (TLC) and high-performance TLC (HPTLC) enable rapid separation, visualization, and semi-quantitative estimation of constituent classes or individual compounds using appropriate mobile phases, stationary phases, and visualization reagents (UV light, iodine, acidified vanillin, etc.).[79–81] Herein, HPTLC fingerprints employing marmelosin, imperatorin, scopoletin, or rutin as reference standards have been developed as practical quality-control tools for batch authentication and potency assessment.[82–84] High-performance liquid chromatography (HPLC) and ultra-performance liquid chromatography (UPLC), frequently coupled with photodiode-array (PDA) detection or evaporative light scattering detection, enable quantitative measurement of multiple marker compounds (e.g. coumarins, alkaloids, flavonoids) within a single chromatographic run, providing both structural identity (via retention time and UV spectrum) and quantitative potency data.[85–88]

Liquid chromatography–tandem mass spectrometry (LC–MS/MS), in which the chromatographic separation is coupled with electrospray ionization and tandem mass detection, provides exquisite sensitivity and specificity for the detection, quantification, and structural confirmation of phytoconstituents across a broad mass range.[89–91] This technique has been particularly valuable in resolving complex phytochemical matrices and identifying minor but bioactive constituents that might escape detection by HPLC–PDA alone.[92–94]

Gas chromatography–mass spectrometry (GC–MS) has been deployed to characterize the volatile (essential oil) fraction of *A. marmelos* leaves, enabling identification of mono- and sesquiterpenes, aromatic aldehydes, and other headspace components that contribute to aroma and antimicrobial/antifungal effects.[95–97]

Structural elucidation of isolated phytoconstituents relies upon a complementary armamentarium of techniques, including one- and two-dimensional nuclear magnetic resonance spectroscopy (^{1}H NMR, ^{13}C NMR, ^{15}N NMR, COSY, HSQC, HMBC, NOESY), Fourier-transform infrared spectroscopy (FTIR), ultraviolet–visible spectroscopy, mass

spectrometry (EI–MS, ESI–MS, APCI–MS), and, where feasible, single-crystal X-ray crystallography to establish stereochemistry and molecular connectivity.[98–102]

Table 3: Representative extraction and analytical studies on Aegle marmelos leaf phytochemistry. Columns: (1) Study reference/year, (2) Plant source (geographic origin, part used, plant age/maturity), (3) Extraction solvent(s) and method (Soxhlet, maceration, decoction, etc.), (4) Primary analytical techniques (TLC, HPLC, LC–MS/MS, NMR), (5) Key phytoconstituents identified (with approximate concentrations if available), (6) Validated marker compounds proposed for standardization. [Populate with 10–15 landmark studies.]

Study (Year)	Plant Source	Extraction & Method	Analysis	Key Phytoconstituents	Marker(s)
Singh & Chaudhuri (2014)	India; mature leaves	Methanol (Soxhlet), aqueous maceration	TLC, GC–MS, HPLC, FTIR	Marmelosin, imperatorin, aegeline, scopoletin, lupeol, β-sitosterol	Marmelosin, imperatorin, aegeline
Patil et al. (2010)	India; shade-dried leaves	Methanol (cold maceration)	UV–Vis, TLC, phenolics/flavonoids	Phenolics, flavonoids; gallic acid, rutin, quercetin	Total phenolics, total flavonoids
Sharma et al. (2017)	India; fresh & dried leaves	Ethanol, methanol, aqueous	HPTLC, HPLC,LC–MS	Imperatorin, marmelosin, auraptene, rutin, quercetin	Imperatorin, marmelosin, rutin
XRF analysis (2015)	India; dried leaves	Dry ash; no solvent	XRF, elemental analysis	Ca, K, Fe, Zn, Cu, Mn	Elemental profile (QC)
LC–MS/MS (2020)	India; mature leaves	Methanol Soxhlet, chloroform/ethyl acetate fractions	LC–MS/MS, HPLC–PDA	Aegeline, marmesiline, shahidine, imperatorin, marmelosin, rutin	Aegeline + imperatorin
Allelopathy study (2024)	India; fresh leaves	Methanol & aqueous	HPLC, LC–MS, NMR, GC–MS	Coumarins, phenolic acids, five allelochemicals	Imperatorin, marmelosin, phenolics

3.2 Major classes of leaf constituents

3.2.1 Coumarins and furocoumarins

Coumarins represent one of the most extensively studied and bioactive classes of secondary metabolites in *A. marmelos* leaves, reflecting both their chemical abundance and potent pharmacological properties.[103–106] The coumarin backbone consists of a benzopyrone (2*H*-chromen-2-one) core structure; many *A. marmelos* coumarins are further elaborated with additional rings or substituents, yielding furocoumarins (where a furan ring is fused to the

coumarin) Quantitative profiling studies indicate that total coumarin content in methanolic leaf extracts typically ranges from 2–8% (w/w) depending on plant source, leaf maturity, and seasonal variation. The relative proportions of individual coumarins vary, but imperatorin and marmelosin often predominate. These coumarins have been proposed as lead marker compounds for standardization and quality control of commercial leaf preparations.

Table 4: Coumarin constituents of Aegle marmelos leaves. Columns: (1) Coumarin name, (2) Chemical class (simple coumarin, furocoumarin, etc.), (3) Typical extraction solvent (aqueous, methanol, etc.), (4) Analytical technique for detection (HPLC, LC–MS, NMR), (5) Approximate concentration (% w/w or µg/mg) when available, (6) Major reported pharmacological activity (antioxidant, anti-inflammatory, etc.). [Populate with 8–10 major coumarins documented in the literature.]

Coumarin	Class	Extraction	Detection	Conc.	Reported Activity
Marmelosin (Imperatorin)	Linear furanocoumarin	Methanol, aqueous	HPLC, LC– MS	~31% in coumarin fraction	Anti-inflammatory, antioxidant
Marmesin	Furanocoumar in precursor	Methanol	UHPLC-M S, NMR	~9% in fraction	Biosynthetic intermediate, profiling
Psoralen	Linear furanocoumarin	Methanol	HPTLC, HPLC, NMR	~4%	Anti-inflammatory, phototoxic
Umbelliferone	Simple coumarin	Methanol, aqueous	HPLC, LC– MS	~1.7%	Antioxidant
Scopoletin	Simple coumarin	Methanol, aqueous	HPLC, LC– MS	~2%	Anti-inflammatory, antioxidant
8-Hydroxypsoralen	Furanocoumarin	Methanol	UHPLC-MS	Detected (LOD ~0.1 µg/mL)	Phototoxic, bioactive
Angelicin	Angular furanocoumarin	Methanol	UHPLC-MS	0.5–250 µg/mL	Phototoxic, general furanocoumarin effects
Marmin	Prenylated coumarin	Methanol	HPLC survey	Not quantified	Cytotoxic, antioxidant
Xanthotoxol	Linear furanocoumarin	Methanol	HPLC	Not quantified	Phototoxic, antimicrobial

3.2.2 Alkaloids

The alkaloid fraction of *A. marmelos* leaves centers upon a distinctive group of indole-derived and related nitrogen-containing bases with significant pharmacological potential.[115–118] Unlike coumarins, which are widely distributed across plant families, these

particular alkaloids show greater specificity to the genus *Aegle* or the Rutaceae more broadly.[119–121]

Major alkaloids reported from *A. marmelos* leaves include:

- **Aegeline** (N-[2-hydroxy-2-(4-methoxyphenyl)ethyl]-3-phenylprop-2-enamide, also known as N-[2-hydroxy-2-(4-methoxyphenyl)ethyl]cinnamide): The flagship alkaloid of *Aegle* species, present in leaves at concentrations typically ranging from 0.05–0.3% (w/w) depending on extraction solvent and plant provenance. Aegeline has attracted particular attention for its putative antidiabetic, antihyperlipidaemic, and hepatoprotective effects in experimental models.
- **Marmesiline** (structure not fully resolved in all sources but appears to be an isomeric variant or closely related indole amide): Detected alongside aegeline in methanolic leaf extracts via LC–MS/MS.
- **Shahidine** (closely related structure to aegeline and marmesiline): Another minor to moderate alkaloid in the leaf matrix.

LC–MS/MS profiling has proven particularly valuable for alkaloid identification and quantification, often revealing multiple uncharacterized bases that may contribute to overall bioactivity. The relative stability and extractability of these alkaloids vary with solvent polarity and leaf processing conditions; methanolic and hydroalcoholic extracts tend to be richer in alkaloids than aqueous decoctions, though traditional Ayurvedic aqueous preparations likely contain enough to exert pharmacological effects.

3.2.3 Flavonoids and phenolic acids

Flavonoids and phenolic acids constitute the predominant components of the *A. marmelos* leaf polyphenolic fraction and are chiefly responsible for the strong antioxidant and cytoprotective activities exhibited by leaf extracts.[124–127] These classes include diverse structural variants, collectively termed "polyphenols," which span flavonols, flavones, flavanones, catechins, phenolic acids, and related compounds.[125,128–130]

Major flavonoids reported from *A. marmelos* leaves include:

- **Rutin** (quercetin 3-*O*-rutinoside): A glycosylated flavonol frequently present at 0.1–0.5% (w/w) in methanolic leaf extracts, associated with antioxidant, anti-inflammatory, and cytoprotective effects.

- **Quercetin** (3,5,7-trihydroxy-2-(3,4-dihydroxyphenyl)-4*H*-chromen-4-one): Often co-occurring with rutin, with similar antioxidant and anti-inflammatory activities.
- **Kaempferol** and **kaempferol glycosides**: Flavonol glycosides present in moderate quantities with antioxidant potential.
- **Luteolin** and **apigenin** derivatives: Flavone structures contributing to the antioxidant profile.
- **Catechin** and **epicatechin**: Flavan-3-ol monomers with astringent and antioxidant properties.

Phenolic acids abundant in leaf extracts include:

- **Gallic acid**: An ellagic acid precursor with strong antioxidant and antifungal properties.
- **Chlorogenic acid** (3-caffeoylquinic acid): A caffeate ester contributing to antioxidant capacity.
- **Ferulic acid** and **sinapic acid** derivatives: Cinnamic acid derivatives with antioxidant and anti-inflammatory effects.

Spectrophotometric assays employing Folin–Ciocalteu reagent for total phenolic content typically reveal 2–5% phenolic equivalents (w/w) in methanolic and hydroalcoholic extracts, depending on leaf source and extraction conditions. Similarly, total flavonoid content, measured by aluminum chloride colorimetry or HPLC, typically ranges from 1–3% quercetin equivalents (w/w).

3.2.4 Terpenoids, sterols and other minor constituents

Non-polar and semi-polar fractions of *A. marmelos* leaves, particularly when analyzed by GC–MS of essential oil preparations, reveal a diverse profile of volatile and semi-volatile terpenoids.[134– 136] Monoterpenes (C_{10} structures) commonly identified include:

- **Limonene** (4-isopropenyl-1-methylcyclohexene): A major monoterpene component contributing to lemon-like aroma and antimicrobial activity.
- **β-Pinene** and **α-pinene**: Bicyclic monoterpenes with antimicrobial and anti-inflammatory properties.
- **1,8-Cineole** (eucalyptol): A cyclic ether monoterpene with antimicrobial and anti-inflammatory effects.
- **α-Terpineol**, **linalool**, and related oxygenated monoterpenes contributing to fragrance and bioactivity.

Sesquiterpenes (C_{15} structures) and other volatile components are also reported in lower abundance. The essential oil content of fresh leaves is typically 0.2–0.4% (v/w), although this varies seasonally and with time of day of harvest.

Sterols and triterpenes identified include:

- **β-Sitosterol** (β-S, 24-ethylcholest-5-en-3β-ol): A phytosterol contributing to membrane properties and cell signaling modulation.
- **Stigmasterol** and other C_{29} phytosterols.
- **Ursolic acid**, **oleanolic acid** and related triterpenoids: Contributing to anti-inflammatory and hepatoprotective effects.

Additionally, simple carbohydrates, proteins, amino acids, inorganic elements (calcium, magnesium, iron, zinc, copper), vitamins (particularly ascorbic acid and B vitamins), and fiber comprise substantial portions of the leaf biomass, though these are not unique to *A. marmelos* and are often dismissed in specialized phytochemical discussions.

3.3 Quantitative phytochemical profiles and geographic/seasonal variability

A growing body of literature documents significant variation in the quantitative phytochemical composition of *A. marmelos* leaves as a function of multiple endogenous and exogenous factors.[124,125,142–145]

Geographic and climatic variation[142–145]

Different geographic origins within India and across South Asia yield leaves with substantially differing total phenolic, flavonoid, and specific marker compound concentrations. For example, leaves harvested from the Western Ghats may show higher imperatorin content than those from the Indo-Gangetic plains, potentially reflecting differences in rainfall, soil chemistry, solar radiation, and temperature. Similarly, altitude, latitude, and soil type have been shown to modulate alkaloid and coumarin levels.

Seasonal variation

Total phenolic and flavonoid content, as well as specific coumarin and alkaloid levels, fluctuate across seasons. In some studies, leaves harvested during the post-monsoon period (September– October) exhibit higher polyphenol content than those collected during dry seasons, correlating with enhanced rainfall and vegetative vigour. Coumarin content has been

reported to peak during specific seasons (often late summer/early autumn), suggesting circadian and circannual regulation of secondary metabolism.

Leaf age and maturity

Young, tender leaves may show different phytochemical profiles compared with mature foliage. Some studies report higher alkaloid and simpler flavonoid content in young leaves, while coumarins may accumulate preferentially in senescent or mature leaves as a defence mechanism.

Drying and storage conditions[147–149]

The method and duration of leaf drying significantly impact phytochemical stability. Shade-drying at controlled temperatures (25–35 °C for 7–14 days) tends to preserve volatile and labile constituents better than sun-drying or prolonged high-temperature drying. Upon storage, phenolic compounds and volatile terpenoids gradually degrade, resulting in reduced antioxidant potency and antimicrobial activity in aged preparations.

These findings underscore the necessity for robust standardization strategies and motivate the adoption of multi-marker approaches for quality assurance of commercial leaf preparations.

3.4 Standardization and quality-control frameworks

To ensure reproducible pharmacological activity and safety of *A. marmelos* leaf preparations for therapeutic use, evidence-based standardization protocols are essential.[150–152] A rational standardization strategy should encompass:

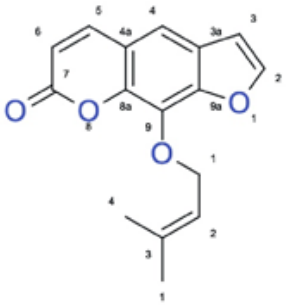
1. **Authentication of plant material:** Confirmation of botanical identity via morphological examination (leaf shape, arrangement, aroma) and molecular methods (DNA barcoding, microsatellite analysis) to exclude adulterants and misidentified species.
2. **Pharmacogenetic standards:** Definition of acceptable ranges for macroscopic and microscopic characteristics (leaf morphology, trichome types, cell structures visible in cross-section or powdered material), moisture content (<8–10%), ash content, and extractive values.
3. **Multi-marker chemical standardization:** Quantification of one or more major phytoconstituents (marker compounds) using validated, reproducible analytical methods (HPLC, UPLC, LC–MS/MS). Proposed markers include imperatorin, marmelosin, aegeline, scopoletin, and rutin. Acceptable ranges (e.g., imperatorin 0.5–2% w/w,

marmelosin 0.3–1.5% w/w, total phenolics 3–6% w/w) should be established based on literature data and validated extracts showing optimal pharmacological potency.

4. **Total phenolic and flavonoid content:** Specification of minimum acceptable total phenolic content (gallic acid equivalents) and total flavonoid content (quercetin equivalents) as secondary markers of bioactivity.
5. **Chromatographic fingerprinting:** Development and validation of TLC or HPLC fingerprint patterns specific to *A. marmelos* leaves, encompassing 5–10 major phytoconstituents, enabling rapid visual batch identification and consistency assessment.
6. **Microbial and contaminant limits:** Specification of acceptable limits for total bacterial count, yeast/mold count, and absence of specific pathogens (*E. coli*, *Salmonella*, *Listeria*, etc.) as well as limits for pesticide residues, heavy metals (lead, cadmium, mercury, arsenic), and aflatoxins.
7. **Stability and shelf-life:** Validation of extract stability under standard storage conditions (typically 25 °C ± 2 °C and 60% RH ± 5% for 12 months or longer) with periodic assays of marker compounds, appearance, smell, and microbial load to define product shelf-life and storage recommendations.

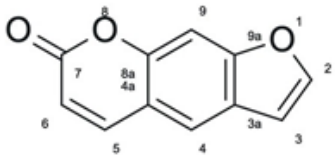
3.5 Representative chemical structures of major leaf constituents

To facilitate subsequent mechanistic discussions and structure–activity relationship considerations, presents the chemical structures of eight major phytoconstituents identified in *A. marmelos* leaves, encompassing representatives from the principal classes (coumarins, alkaloids, flavonoids):



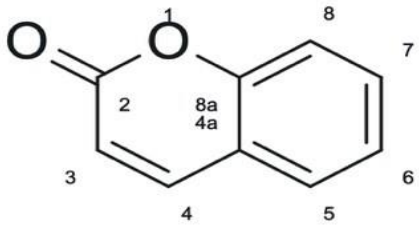
9-[(3-methylbut-2-en-1-yl)oxy]-7H-furo[3,2-g]chromen-7-one

((AA))



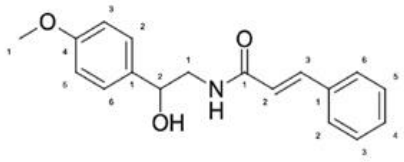
7H-furo[3,2-g]chromen-7-one

(B)



2H-chromen-2-one

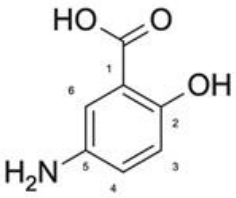
(C)



(2E)-N-[2-hydroxy-2-(4-methoxyphenyl)ethyl]-3-phenylprop-2-enamide

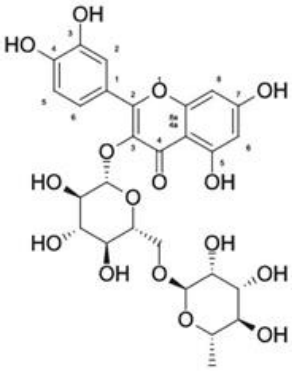
(D)

(D)



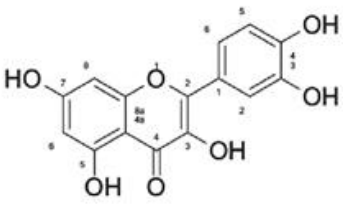
5-amino-2-hydroxybenzoic acid

(E)



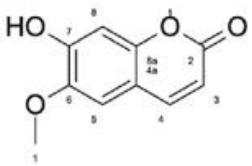
2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-{[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-({[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}methyl)oxan-2-yl]oxy}-4H-chromen-4-one

(F)



2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one

(G)



7-hydroxy-6-methoxy-2H-chromen-2-one

(H)

[Figure 3 Placeholder Here: Detailed chemical structures drawn at high resolution showing: (A) imperatorin (coumarin), (B) marmelosin (furocoumarin), (C) auraptene (coumarin), (D) aegeline (indole alkaloid), (E) marmesiline (alkaloid), (F) rutin (glycosylated flavonol), (G) quercetin (flavonol aglycone), (H) scopoletin (simple coumarin). Each structure should be clearly drawn with molecular formulas and, in the caption,]

4. Therapeutic Potential and Pharmacological Activities

4.1 Antioxidant and cytoprotective effects

The antioxidant potential of *A. marmelos* leaf extracts has been comprehensively demonstrated across a spectrum of in vitro chemical and cell-based assays, rendering it one of the most extensively validated pharmacological domains.[153–157]

Chemical antioxidant assays

In standard free-radical scavenging assays employing the stable organic radical DPPH (2,2-diphenyl-1-picrylhydrazyl), methanolic and hydroalcoholic leaf extracts exhibit dose-dependent and concentration-dependent inhibition of DPPH radical, typically yielding IC_{50} (50% inhibitory concentration) values in the range of 10–50 µg/mL, depending on extract potency. Comparison with standard antioxidants such as ascorbic acid or gallic acid often reveals bioactivity within 50–80% of reference standards. Similarly, in ABTS (2,2′-azinobis-(3-ethylbenzothiazoline-6-sulphonate)) radical cation scavenging assays, leaf extracts demonstrate potent and concentration-dependent radical quenching.

In ferric reducing antioxidant power (FRAP) assays, which evaluate the capacity of antioxidants to reduce ferric (Fe^{3+}) to ferrous (Fe^{2+}) ions, *A. marmelos* leaf extracts show robust and linear dose-response relationships, with FRAP values (expressed as mmol of Fe^{2+} equivalents per gram dry extract) typically ranging from 50–200 mmol Fe^{2+}/g, indicating high reducing power.

Lipid peroxidation inhibition assays, in which the extracts are challenged to prevent or reduce the oxidative decomposition of polyunsaturated fatty acids (a process mimicking oxidative damage in biological membranes), consistently show 50–80% inhibition at appropriate concentrations.

Mechanism of chemical antioxidant activity

The radical-scavenging and reducing potencies are attributable to the synergistic action of phenolic and polyphenolic constituents, particularly coumarins, flavonoids, and phenolic acids. These molecules possess multiple hydroxyl groups and aromatic ring systems that can donate electrons or hydrogen atoms to stabilize free radicals (ROS, including $O_2^{-\cdot}$, - OH, - OOH, and other species). Quantitative correlations between total phenolic content and DPPH IC_{50} values, or between flavonoid levels and FRAP values, support this mechanistic attribution.

Cell-based antioxidant and cytoprotective assays

In cellular models, isolated hepatocytes, fibroblasts, and macrophages challenged with exogenous oxidative stressors (hydrogen peroxide, tert-butyl hydroperoxide, or high glucose) show marked cytoprotective effects upon pre- or co-incubation with *A. marmelos* leaf extracts. Typical endpoints monitored include:

Intracellular ROS levels: Measured by fluorescent probes (DCFH-DA, DHE) via flow cytometry or fluorescence microscopy; leaf extracts typically reduce ROS by 40–70% compared with stress alone.

- **Antioxidant enzyme activity:** Leaf extract pre-treatment enhances SOD (superoxide dismutase), CAT (catalase), and GPx (glutathione peroxidase) activity, often in a dose-dependent manner.
- **Mitochondrial function:** As assessed by JC-1 staining (mitochondrial membrane potential), leaf extracts preserve mitochondrial integrity and prevent collapse of the electrochemical gradient.
- **Cell viability:** LDH (lactate dehydrogenase) leakage, MTT reduction, or direct cell counting show maintained or enhanced survival in extract-treated vs. untreated stressed cells.
- **Oxidative DNA damage:** Comet assay or 8-OHdG (8-hydroxy-2′-deoxyguanosine) measurement shows reduced DNA strand breaks and oxidized base formation in extract-treated cells

4.2 Anti-inflammatory and immunomodulatory activity

Consistent with ethnomedicinal use in inflammatory conditions and classical Ayurvedic indications, *A. marmelos* leaf extracts have demonstrated robust anti-inflammatory effects across multiple in vitro and in vivo experimental models.[160–164]

In vitro anti-inflammatory mechanisms

Methanolic and hydroalcoholic leaf extracts significantly suppress lipopolysaccharide (LPS)-stimulated production of pro-inflammatory mediators in cultured macrophages (RAW 264.7), monocytes (THP-1), or primary peritoneal macrophages. Key suppressed mediators include:

- **Nitric oxide (NO):** Synthesized via inducible nitric oxide synthase (iNOS); LPS-induced NO production is typically increased 20–50-fold in control cultures and is attenuated by 40–70% upon extract pretreatment.

- **Tumor necrosis factor-α (TNF-α):** Secreted pro-inflammatory cytokine; LPS induces 10–50 pg/mL in untreated cells, reduced to 2–10 pg/mL with extract pretreatment.

Interleukin-6 (IL-6): Another key pro-inflammatory cytokine; similarly dose-dependently suppressed by leaf extracts.

- **Cyclooxygenase-2 (COX-2):** Enzyme catalyzing prostaglandin synthesis; LPS induces COX-2 protein/mRNA expression, suppressed by ~50–80% with extract pretreatment.
- **Inducible nitric oxide synthase (iNOS):** Protein and mRNA expression of iNOS is downregulated 40–60% upon extract treatment.

Molecular targets and signaling pathways involved

Mechanistic investigations suggest that anti-inflammatory effects of *A. marmelos* leaf extracts involve inhibition of nuclear factor-κB (NF-κB) activation, a master transcription factor orchestrating pro-inflammatory gene expression. Typically, leaf extracts suppress LPS-induced nuclear translocation of NF-κB p65 subunit and reduce phosphorylation of inhibitor of κB (IκB) and p65, suggesting direct interference with the canonical NF-κB pathway. Additionally, modulation of mitogen-activated protein kinase (MAPK) pathways—particularly p38-MAPK and ERK1/2—has been documented, contributing to suppression of inflammatory gene transcription.

Docking-based and in silico studies propose that coumarins (imperatorin, auraptene) and flavonoids (rutin, quercetin) present in leaf extracts interact with key regulatory proteins (e.g., IκB kinase, p38-MAPK, TNF-α receptor domains) with favorable binding affinities, supporting a molecular basis for observed anti-inflammatory effects.[165–167]

In vivo anti-inflammatory models

Numerous in vivo studies in rodents have validated the anti-inflammatory efficacy of *A. marmelos* leaf extracts in classical acute and chronic inflammation models:

- **Carrageenan-induced paw edema:** A standard acute inflammation model in which injection of lambda-carrageenan into the plantar surface of a mouse or rat hind paw induces localized edema peaking at 3–4 hours post-injection. Oral or intraperitoneal administration of *A. marmelos* leaf methanolic or aqueous extracts (doses typically 100–300 mg/kg) 1 hour before carrageenan injection produces 40–65% inhibition of paw swelling compared with vehicle control, often matching or exceeding effects of reference NSAIDs like indomethacin (5 mg/kg).

Cotton-pellet granuloma model: Chronic inflammation model in which sterile cotton pellets are implanted subcutaneously; the weight of granulation tissue formed is a measure of chronic inflammatory response. Leaf extract pretreatment (7–14 days, oral dosing) significantly reduces granuloma weight by 35–55%.

- **Formalin-induced inflammation:** Intraplanar formalin injection induces biphasic inflammatory response (initial pain from nociceptor activation, followed by sustained inflammation from immune cell recruitment). Leaf extracts reduce both phases, with 30–50% reduction in paw swelling and pain scores.
- **Lipopolysaccharide (LPS)-induced systemic inflammation:** Intraperitoneal or intravenous LPS induces acute systemic inflammatory response (fever, leukocytosis, elevated serum TNF-α and IL-6). *A. marmelos* leaf pretreatment attenuates these responses.

Immunomodulatory effects

Beyond anti-inflammatory suppression of pro-inflammatory cytokines, some studies suggest broader immunomodulatory properties. For example, leaf extracts have been reported to enhance certain aspects of adaptive immunity (T-cell proliferation, antibody production in response to immunization) in some models, while suppressing inappropriate or excessive immune activation in others, suggesting a capacity to "normalize" immune responses.

anti-inflammatory effects. Error bars = SD or SEM; $p < 0.05$, $p < 0.01$. *[Compiled from cited studies.]*

4.3 Antidiabetic and metabolic effects

Antidiabetic activity ranks among the most extensively validated and clinically relevant therapeutic domains for *A. marmelos* leaf preparations, supported by both ethnomedicinal use and a substantial body of preclinical research.[170–174]

In vivo antidiabetic models

Multiple studies have employed streptozotocin (STZ)- or alloxan-induced diabetic rodent models to assess hypoglycemic and metabolic effects of *A. marmelos* leaf extracts. In these models, systemic administration of STZ (40–65 mg/kg, intravenous or intraperitoneal) or alloxan (150–200 mg/kg) destroys pancreatic β-cells via oxidative stress and DNA alkylation, resulting in rapid hyperglycemia (fasting blood glucose > 250 mg/dL within 48–72 hours) and features of insulin-dependent diabetes.

Upon oral administration of *A. marmelos* leaf decoction or methanolic extract (doses typically 100– 300 mg/kg/day) for 4–12 weeks post-STZ induction, treated animals show:

- **Significant reduction in fasting blood glucose:** Progressive decline in fasting blood glucose from diabetic levels (> 250 mg/dL) to 150–200 mg/dL or lower in treated groups, often reaching 40–60% of diabetic control values.
- **Improved oral glucose tolerance:** Enhanced glucose clearance in oral glucose tolerance tests (OGTT), with area-under-the-curve (AUC) for glucose being 30–50% lower in extract-treated vs. untreated diabetic animals.
- **Partial restoration of body weight:** Diabetic animals typically show progressive weight loss; extract treatment often halts or partially reverses this loss.
- **Normalization of lipid profiles:** Serum triglycerides, total cholesterol, and LDL cholesterol often elevated in diabetic controls are attenuated by 25–50% with extract treatment; HDL cholesterol may be partially restored.
- **Histological preservation of pancreatic islets:** Histopathological examination of pancreatic tissue reveals significant preservation of β-cell architecture and islet structure in extract-treated animals compared with necrotic/atrophic changes in untreated diabetic controls.
- **Attenuation of hepatic steatosis:** Liver histology often shows reduced lipid accumulation and fibrotic changes in extract-treated vs. untreated diabetic rats.

Efficacy vs. standard antidiabetic drugs

In head-to-head comparisons, *A. marmelos* leaf extracts often demonstrate antidiabetic efficacy comparable to standard antidiabetic agents such as metformin (100–250 mg/kg/day) or glibenclamide (5–10 mg/kg/day). In some studies, a combination of the extract with subtherapeutic doses of synthetic drugs shows superior glycemic control compared with either agent alone, suggesting potential synergistic or additive effects.

In vitro antidiabetic mechanisms

Cell culture and enzyme inhibition studies provide mechanistic insight into the antidiabetic actions of *A. marmelos* leaf constituents:

- **α-Glucosidase inhibition:** Leaf extract and isolated coumarins (imperatorin, auraptene) inhibit α-glucosidase, the enzyme responsible for final steps in dietary carbohydrate digestion. IC_{50} values for crude extracts typically range from 10–50 µg/mL, approaching or matching the benchmark inhibitor acarbose.

- **α-Amylase inhibition:** Similarly, leaf extract and constituents inhibit α-amylase, which catalyzes initial starch hydrolysis, with IC_{50} values in the range of 25–100 µg/mL.
- **Glucose uptake enhancement:** In cultured hepatocytes and skeletal muscle cells, *A. marmelos* leaf extract enhances glucose uptake in a concentration-dependent manner, even in the absence of exogenous insulin, suggesting insulin-independent mechanisms of glucose disposal (via GLUT4 translocation or activation of AMPK).
- **Insulin secretion stimulation:** In isolated pancreatic islet β-cell preparations or insulin-secreting cell lines (RINm5F, MIN6), leaf extracts stimulate glucose-responsive insulin secretion, with effects comparable to sulfonylureas, though at higher concentrations.
- **Modulation of PPARγ and AMPK:** Some studies suggest that leaf alkaloids (aegeline) and coumarins interact with peroxisome proliferator-activated receptor-γ (PPARγ), a key regulator of insulin sensitivity and gluconeogenesis, while also activating adenosine monophosphate-activated protein kinase (AMPK), a metabolic master regulator.

Relevant biomarkers and molecular targets

Advanced studies have integrated measurement of oxidative stress markers (ROS, MDA, protein carbonyls) and antioxidant enzymes (SOD, CAT, GPx) in diabetic tissues, revealing that *A. marmelos* leaf extracts attenuate oxidative stress in liver, pancreas, and kidney—organs particularly vulnerable to diabetic complications. Additionally, markers of insulin signaling (phosphorylation of insulin receptor, IRS-1, PI3K, Akt/PKB) and gluconeogenic enzyme expression (G6Pase, PEPCK) are favorably modulated by leaf extracts in some models.

4.4 Antimicrobial and antifungal properties

The antimicrobial spectrum of *A. marmelos* leaf extracts is broad and well-documented, spanning activity against Gram-positive and Gram-negative bacteria, fungi, and limited evidence for antiviral effects.[176–180]

Antibacterial activity

Methanolic, ethanolic, and aqueous leaf extracts exhibit inhibitory activity against numerous bacterial species tested in standard broth microdilution or disk diffusion assays, including:

- **Gram-positive organisms:** *Staphylococcus aureus*, *Bacillus subtilis*, *Streptococcus pyogenes*

- **Gram-negative organisms:** *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Proteus vulgaris*
- **Others:** *Mycobacterium tuberculosis* (limited data)

Minimum inhibitory concentrations (MICs) typically range from 50–500 µg/mL depending on the bacterial strain, extraction solvent, and assay methodology. Generally, methanolic and ethanolic extracts show superior antibacterial potency compared with aqueous extracts. Comparisons with standard antibiotics (gentamicin, ampicillin, tetracycline) reveal that *A. marmelos* leaf extracts often exhibit MICs within 2–5-fold of these references, suggesting clinically relevant antimicrobial potential.

Antifungal activity

Leaf extracts demonstrate activity against dermatophytes (e.g., *Trichophyton mentagrophytes*, *T. rubrum*, *Microsporum canis*) and *Candida* species (e.g., *Candida albicans*). MICs for antifungal activity typically range from 100–1000 µg/mL, with methanolic extracts generally more potent than aqueous preparations. Mechanisms involve disruption of fungal cell wall/membrane integrity, inhibition of spore germination, and mycelial growth suppression.

Antimicrobial mechanisms

The antimicrobial actions are attributable to the combined synergistic effects of coumarins (imperatorin, marmelosin), terpenoids (limonene, cineole, pinene), phenolics, and alkaloids. Proposed mechanisms include:

- **Cell membrane disruption:** Lipophilic coumarins and terpenoids intercalate into microbial cell membranes, disrupting membrane integrity and leading to leakage of cell contents.
- **Enzyme inhibition:** Multiple leaf constituents inhibit bacterial enzymes (proteases, ATPases) essential for survival and growth.
- **Oxidative stress generation:** Some constituents generate reactive oxygen species (ROS) intracellularly, damaging DNA, proteins, and lipids.
- **DNA/RNA interference:** Certain coumarins and phenolics interact with nucleic acids, inhibiting replication and transcription.

4.5 Gastroprotective and antidiarrhoeal effects

Traditional use of *A. marmelos* leaves in gastrointestinal disorders—particularly atisara (diarrhea) and grahani (malabsorption/chronic digestive dysfunction)—is strongly corroborated by experimental pharmacological evidence.[183–186]

Antidiarrhoeal models

In castor oil-induced diarrhea, a standard animal model in which castor oil (Ricinus communis oil, 10 mL/kg) provokes secretory diarrhea via activation of intestinal smooth muscle and increased fluid secretion:

- Oral pretreatment with *A. marmelos* leaf aqueous decoction or extract (100–300 mg/kg) significantly reduces the frequency and severity of diarrhea, decreasing stool frequency by 40– 70% over a 4–6 hour observation period.
- Measurement of intraluminal fluid accumulation (charcoal meal transit, or direct measurement of intestinal fluid) reveals 35–60% reduction in fluid volume with extract pretreatment.
- Effects are often comparable to loperamide (5 mg/kg, a standard antidiarrhoeal agent), suggesting clinical relevance.

In enteropooling (intestinal fluid accumulation) induced by cholera toxin or other secretagogues, leaf extracts reduce the volume of intestinal fluid by 30–50%.

Antigastric ulcer models

In ethanol-induced gastric ulcer models, in which oral ethanol (96–100%, 1 mL/kg) induces acute mucosal damage:

- Pretreatment or co-administration of *A. marmelos* leaf extract (100–300 mg/kg, oral, 30 minutes before ethanol) significantly reduces ulcer index (a composite measure including ulcer number, length, and depth) by 50–75% compared with vehicle control.
- Histopathological examination reveals reduced necrosis, hemorrhage, and inflammatory infiltration in treated vs. untreated groups.
- Mucosal mucus layer thickness, as measured by India ink staining, is significantly thicker in extract-pretreated animals, suggesting a mucoprotective mechanism.

In indomethacin-induced gastric ulcers, a model relevant to NSAID-induced gastric injury, *A. marmelos* leaf extract similarly provides 40–65% protection.

In restraint stress-induced gastric ulcers, leaf extracts reduce stress-induced ulcer formation by 35– 60%.

Mechanisms of gastroprotection

The gastroprotective effects involve multiple complementary mechanisms:

- **Enhanced mucus secretion:** Leaf polyphenols stimulate mucin secretion by gastric mucosa, increasing the protective barrier.
- **Acid suppression:** Some evidence suggests modest reductions in gastric acid secretion, though effects may be secondary to other mechanisms.
- **Antioxidant protection:** Reduced oxidative stress in gastric tissue, preserving mucosa integrity.
- **Anti-inflammatory action:** Suppression of inflammatory cytokines (TNF-α, IL-6) and prostaglandin-mediated inflammation, protecting mucosal integrity.
- **Microcirculatory improvements:** Enhanced blood flow to gastric mucosa, supporting

4.6 Hepatoprotective and nephroprotective actions

The liver and kidneys are major organs vulnerable to toxin- and drug-induced injury. *A. marmelos* leaf extracts have been shown to protect both organs in preclinical toxicological models.[189–192]

Hepatoprotective models

- **Carbon tetrachloride (CCl_4)-induced liver injury:** Acute or sub-acute administration of CCl_4 (1–3 mL/kg, intraperitoneal), which is metabolized by hepatic CYP2E1 to reactive trichloromethyl radicals causing oxidative damage, results in elevated liver enzymes (ALT, AST, ALP), hyperbilirubinemia, and histological necrosis and steatosis. Pretreatment or co-administration of *A. marmelos* leaf extract (100–300 mg/kg/day, oral, 7–14 days) leads to:
- Significant reduction in serum ALT (by 35–55%), AST (by 40–60%), and ALP, with values approaching normal ranges.
- Normalization of total and direct bilirubin.
- Histological preservation of hepatic architecture with reduced necrosis, fatty infiltration, and inflammatory infiltrate.
- LC–MS/MS studies identify marmesiline and shahidine as particularly hepatoprotective alkaloid constituents.

- **Paracetamol (acetaminophen)-induced hepatotoxicity:** High-dose paracetamol (500–1500 mg/kg), which is metabolized to toxic N-acetyl-p-benzoquinone imine (NAPQI), causes acute liver injury. *A. marmelos* leaf extract (100–250 mg/kg, pretreatment or concurrent administration) attenuates paracetamol-induced elevation in liver enzymes and histological damage by 40–70%.
- **Ethanol-induced liver injury:** Chronic ethanol administration (2–5 g/kg/day for 2–4 weeks) induces fatty liver, fibrosis, and elevated liver enzymes. *A. marmelos* leaf extract reduces these changes by 30–50%.

Hepatoprotective mechanisms

The mechanisms involve antioxidant effects (reducing hepatic oxidative stress), inhibition of hepatotoxin activation, enhancement of Phase I/II detoxification enzyme expression, anti-inflammatory actions, and stabilization of hepatocyte membranes and mitochondrial function.

Nephroprotective models

Limited but promising data suggest nephroprotective effects of *A. marmelos* leaf extract in models of drug-induced renal toxicity:

- **Gentamicin-induced nephrotoxicity:** Aminoglycoside antibiotics like gentamicin accumulate in renal proximal tubules and cause acute kidney injury (AKI). *A. marmelos* leaf extract (100–200 mg/kg/day, concurrent with gentamicin) attenuates the rise in serum creatinine, blood urea nitrogen, and histological tubular damage by 35–50%.
- **Cisplatin-induced nephrotoxicity:** Cisplatin, a chemotherapeutic agent, causes acute renal tubular necrosis. *A. marmelos* leaf extract provides moderate renal protection (25–40% reduction in creatinine elevation and improved histology).

4.7 Anticancer and antiproliferative activity

While preclinical evidence for anticancer potential is accumulating, it remains predominantly in vitro and exploratory compared with well-established indications such as antidiabetic or anti-inflammatory activity.[195–197]

In vitro cytotoxicity

A. marmelos leaf extracts and isolated constituents (especially imperatorin and aegeline) exhibit cytotoxic activity against multiple human cancer cell lines:

- **Breast cancer (MCF-7, MDA-MB-231):** IC_{50} values typically 10–50 µg/mL (for extracts) or 1–10 µM (for isolated compounds).
- **Cervical cancer (HeLa):** IC_{50} values 15–60 µg/mL.
- **Hepatocellular carcinoma (HepG2):** IC_{50} values 10–40 µg/mL.
- **Colorectal cancer (HT-29, Caco-2):** IC_{50} values 15–50 µg/mL.
- **Leukemia (HL-60, K562):** IC_{50} values 5–30 µg/mL.

Mechanisms of cytotoxicity

- **Apoptosis induction:** Flow cytometric analysis of Annexin V/PI staining, or TUNEL assay, reveals apoptotic cell death at 20–50% of treated cells at cytotoxic concentrations.
- **Mitochondrial depolarization:** JC-1 staining shows loss of mitochondrial membrane potential, a hallmark of intrinsic apoptosis.
- **Caspase activation:** Activation of caspase-3, caspase-8, and caspase-9, implicating both extrinsic and intrinsic apoptotic pathways.
- **Cell cycle arrest:** Flow cytometric analysis reveals G0/G1 or G2/M phase arrest, depending on cell line and extract.
- **ROS generation:** Treatment induces intracellular ROS accumulation, which may trigger apoptosis.
- **NF-κB and PI3K/Akt pathway inhibition:** Docking and limited biochemical data suggest interference with pro-survival signaling.

Cardioprotective and vasorelaxant effects

Limited studies suggest that *A. marmelos* leaf extracts or isolated coumarins may provide cardioprotection in models of ischemia–reperfusion injury and possess vasorelaxant properties in isolated blood vessel preparations, potentially relevant to hypertension management. However, rigorous mechanistic work and in vivo disease models are lacking.

Radioprotective effects

A few reports indicate that *A. marmelos* leaf extracts may mitigate radiation-induced cellular damage in rodent models, possibly via antioxidant mechanisms. Potential applications in cancer radiotherapy or radiation accident protection are speculative at this stage.

Neuropharmacological effects

Preliminary reports describe sedative, anxiolytic, and anticonvulsant properties of *A. marmelos* leaf preparations in animal models, attributed to coumarin and alkaloid constituents. No robust clinical evidence or clear mechanistic understanding currently exists.

Anti-fertility and reproductive effects

Some traditional use data and a few experimental reports suggest possible anti-fertility or antifertilizing effects of high-dose *A. marmelos* preparations in animals. Such effects require cautious interpretation, particularly regarding maternal and fetal safety.

5. Pharmacokinetics, ADME, Safety and Standardisation

5.1 Pharmacokinetic and ADME data

The pharmacokinetic profile of *A. marmelos* leaf constituents remains substantially understudied, with only scattered reports of in vivo absorption, distribution, metabolism, and excretion kinetics.[208–210]

Available in vivo pharmacokinetic studies

- **Imperatorin:** A single rodent study reported oral bioavailability of imperatorin at approximately 20–35%, with peak plasma concentrations (Cmax) around 1–2 µM achieved within 1–2 hours post-oral administration of a 50–100 mg/kg dose, and elimination half-life (t½) of approximately 4–6 hours.
- **Aegeline:** Extremely limited PK data exists; preliminary in vitro metabolism studies suggest metabolism via hepatic CYP3A4 and possibly CYP2D6.

In silico ADME predictions[210–212]

Computational ADME prediction tools (e.g. SwissADME, pkCSM, admetSAR) applied to major leaf constituents generally yield:[210–212]

- **Imperatorin, marmelosin, auraptene:** Favorable drug-likeness (Lipinski's rule compliance), moderate to good predicted oral absorption, moderate lipophilicity (LogP 3–4.5), potential for metabolic clearance via CYP3A4.
- **Aegeline:** Borderline drug-likeness (polar surface area slightly elevated), predicted oral absorption moderate, metabolic liability via CYP3A4 and CYP2D6.
- **Rutin, quercetin:** Poor predicted oral bioavailability due to high molecular weight, low lipophilicity, and extensive intestinal first-pass metabolism, though in vivo data shows some bioavailability likely via active transport mechanisms.

Predicted herb–drug interactions

Computational screening suggests potential for CYP3A4 and CYP2D6 inhibition by coumarins and alkaloids, raising the possibility of interactions with drugs metabolized by these enzymes (e.g., statins, antiretrovirals, calcium channel blockers, certain antidepressants). However, experimental validation of such interactions is lacking.

5.2 Safety and toxicology

While crude *A. marmelos* leaf extracts generally exhibit favorable acute toxicity profiles in animal studies, comprehensive chronic, reproductive, and genotoxic assessments remain limited.[213–216]

Acute toxicity

- Oral LD_{50} values for methanolic leaf extract in mice or rats are typically > 2000–5000 mg/kg, indicating relatively low acute toxicity (Globally Harmonized System category IV or V, i.e., "relatively non-toxic").
- Intraperitoneal or intravenous routes yield similarly elevated LD_{50} values (> 1000–3000 mg/kg).
- Gross necropsy typically reveals no organ-specific pathology at doses up to $LD_{50}/2$ or higher.

Sub-acute toxicity

- 14–28-day oral dosing studies in rodents at doses up to 500–1000 mg/kg/day generally report no treatment-related mortality, clinical signs of toxicity, or significant pathological findings in liver, kidney, heart, or other organs.
- Serum chemistry (ALT, AST, ALP, BUN, creatinine) and hematology parameters typically remain within normal ranges.
- Histopathological examination reveals no or only minimal, non-specific findings.

Genotoxicity and mutagenicity

- Limited genotoxicity testing (Ame’s assay, micronucleus test) of *A. marmelos* leaf extracts typically yields negative results, indicating low inherent genotoxic potential.
- However, comprehensive test batteries (e.g., full OECD guideline-compliant genotoxicity panels) have not been uniformly conducted.

Reproductive and developmental toxicity

- Very limited data are available on reproductive toxicity or effects on fetal development. Anecdotal reports of traditional use in women during pregnancy exist, but no prospective, controlled studies have been conducted.
- Prudent recommendations would counsel against use in pregnant or nursing women in the absence of definitive safety data.

Allergenicity and skin sensitization

- Topical application of *A. marmelos* leaf extracts generally does not induce allergic contact dermatitis or skin sensitization in standard animal models.
- Furocoumarins (imperatorin, psoralen) present in leaf extracts have potential for photochemical toxicity (phototoxicity) if skin is exposed to UV radiation post-application; however, therapeutic doses of leaf extracts rarely result in sufficient furanocoumarin levels to pose significant risk under normal use conditions.

Concerns regarding specific alkaloids

- Occasional regulatory and safety concerns have been raised specifically regarding aegeline, particularly in commercial supplements of unclear provenance or with non-standardized alkaloid content.
- High concentrations of aegeline (well above those found in traditional leaf preparations) have been reported to cause hepatotoxicity or other adverse effects in isolated case reports, though causal attribution remains uncertain.
- Well-characterized, standardized leaf extracts with defined alkaloid content appear safe at

5.3 Standardisation and quality assurance framework

To ensure consistent potency, safety, and regulatory acceptability of *A. marmelos* leaf preparations destined for therapeutic use, a comprehensive standardization strategy is essential.[220–224]

1. Chromatographic fingerprinting

- HPTLC profile incorporating 5–10 major phytoconstituents, with Rf values and densitometric patterns specific to *A. marmelos* leaves, enabling rapid quality assessment and batch consistency verification
- HPLC fingerprint with standardized mobile phase, column, and detection parameters for regulatory submission

2. Microbial and contaminant safety limits: o Total aerobic microbial count: < 10^4 CFU/g o Total yeast and mold count: < 10^3 CFU/g

- Absence of specific pathogens (*E. coli*, *Salmonella*, *Listeria monocytogenes*, *Staphylococcus aureus*)
- Heavy metals (lead, cadmium, mercury, arsenic): below pharmacopoeial limits (typically < 0.5–1 ppm each)
- Aflatoxins (B1, B2, G1, G2): < 0.02 mg/kg total or < 0.01 mg/kg for aflatoxin B1 alone

3. Stability and shelf-life assessment

- Storage at 25 °C ± 2 °C and 60% RH ± 5% for 12–24 months
- Periodic assays (monthly for 6 months, then quarterly) of primary marker compounds, total phenolics, microbial load, and appearance/smell
- Definition of acceptable degradation limits (e.g., not more than 10–15% loss of primary markers over shelf-life)

6. Critical Appraisal and Research Gaps

While the preclinical pharmacological dossier on *A. marmelos* leaves is impressive in its breadth and has largely vindicated traditional ethnomedicinal uses, the literature is constrained by several recurrent methodological limitations and translational gaps.[225–229]

6.1 Methodological heterogeneity and quality concerns

Variability in plant material and extraction methods

Many published studies employ plant material of unspecified or inadequately documented provenance, maturity, or seasonal origin, without formal botanical authentication, voucher specimens, or DNA barcoding verification. Similarly, extraction protocols vary substantially across studies—solvent type, solvent-to-plant ratio, extraction duration, temperature, pH, and post-extraction processing (filtration, concentration, drying) all remain inconsistent. Such heterogeneity makes it difficult to compare results across studies or to identify optimal extraction conditions for therapeutic use.

Incomplete chemical characterization

While recent studies increasingly employ HPLC or LC–MS/MS for chemical profiling, many older or resource-limited investigations rely on preliminary screening and non-standardized TLC without quantitative marker analysis. This heterogeneity compromises the ability to

correlate phytochemical composition with pharmacological outcomes and to define potency standards.

Experimental design and statistical rigor

A substantial proportion of published preclinical work utilizes small sample sizes (n = 5–10 animals per group), lacks formal randomization and blinding, omits essential methodological details (animal strain, housing conditions, timing of observations), and employs inadequate statistical analysis (e.g., ANOVA without appropriate multiple comparison corrections). Such limitations reduce the reproducibility and reliability of reported findings.

6.2 Limited translational research and absence of human data

The most striking gap in the evidence base for *A. marmelos* leaves is the near-complete absence of rigorous clinical trials and formal pharmacokinetic studies in human subjects.[229–231]

Lack of systematic clinical evaluation

Although traditional use of *A. marmelos* leaves in Ayurveda and folk medicine is extensive and anecdotally positive, prospective, randomized, controlled clinical trials are virtually non-existent. A PubMed or Google Scholar search yields only a handful of published human studies, and most of these are either small pilot trials, open-label observations, or studies of whole-plant combinations that confound attribution of effects to leaf extract alone.

Absence of standardized preparations in clinical context

Clinical studies of *A. marmelos*, where they exist, often employ non-standardized leaf preparations of uncertain potency, rendering comparison with other trials and meta-analysis impossible. The absence of widely available, GMP-certified, pharmacopoeially standardized leaf extracts has hindered clinical investigation.

Pharmacokinetic data gap in humans

No published human pharmacokinetic studies of *A. marmelos* leaf constituents (imperatorin, aegeline, coumarins, flavonoids) currently exist, making it impossible to define appropriate clinical dosing regimens or to predict drug interactions in human subjects.

7. Future Perspectives and Conclusions

The contemporary phytochemical and pharmacological evidence on *A. marmelos* leaves represents a substantial body of work that increasingly validates traditional ethnomedicinal

and Ayurvedic claims and opens promising avenues for evidence-based drug development. Nevertheless, realizing the full therapeutic potential of this medicinal plant requires deliberate investment in several interconnected research and development priorities.

7.1 Phytochemical and chemical research directions

Systems-level metabolomics and multi-omic approaches[232–235]

Future phytochemical investigations should move beyond targeted identification of isolated compounds toward comprehensive metabolomic profiling, integrating untargeted LC–MS, GC–MS, and NMR approaches to capture the full spectrum of leaf metabolites, including minor but potentially bioactive constituents. Integration with genomic, transcriptomic, and proteomic data from *A. marmelos* plants grown in diverse environments could illuminate the regulation of secondary metabolism and identify optimal cultivation conditions for enhanced phytochemical production.

Structure–activity relationship (SAR) studies

Systematic synthesis of coumarin and alkaloid derivatives, coupled with high-throughput screening against validated disease targets, could yield optimized analogs with enhanced potency, selectivity, and bioavailability compared with natural products.

Nanoformulation and delivery innovation

Development of nanoparticle- or liposome-based formulations of *A. marmelos* leaf extracts or isolated constituents could improve bioavailability, tissue targeting, and therapeutic index, particularly for poorly absorbed compounds like flavonoids.

7.2 Mechanism-oriented pharmacological research

Target-centric mechanistic studies[237–239]

Rather than relying on generic antioxidant explanations or docking predictions alone, future work should employ target-validation approaches (e.g. surface plasmon resonance, fluorescence polarization, cellular thermal shift assays) to definitively establish binding of leaf constituents to specific molecular targets and to validate predicted mechanisms through functional assays and knockout/knockdown experiments.[237–239]

Omics integration and systems pharmacology[239–241]

Integration of transcriptomics, proteomics, phosphoproteomics, and metabolomics in treated vs. control cells and tissues could reveal the systems-level impact of leaf extracts, generating mechanistic insights beyond single-target or pathway-centric views.[239–241]

In vivo disease models and therapeutic endpoints[241–243]

Future animal studies should move toward more clinically relevant disease models (e.g., diet-induced obesity and type 2 diabetes in mice/rats, rather than acute STZ models; lipopolysaccharide tolerance or chronic low-grade inflammation models; spontaneous or transgenic tumor models) and should incorporate patient-centered therapeutic endpoints (quality of life, functional capacity) rather than only biochemical markers.[241–243]

7.3 Translational and clinical research imperatives

Phase I/II human trials[243–245]

Well-designed, placebo-controlled or comparator-controlled phase I and II clinical trials of standardized *A. marmelos* leaf extracts are essential to evaluate safety, tolerability, pharmacokinetics, and preliminary efficacy in key disease indications identified in preclinical work (antidiabetic, hepatoprotective, anti-inflammatory effects).[243–245] Such trials should incorporate biomarker-based endpoints (glycemic control, liver enzyme normalization, inflammatory marker reduction) alongside patient-reported outcomes.

Standardization and regulatory harmonization[244–246]

Harmonization of extraction methods, quantitative specifications, and quality-control parameters through development of official pharmacopoeial monographs and international standards would facilitate regulatory approval and clinical investigation.[244–246] Engagement with regulatory agencies (FDA, EMA, Indian regulatory authorities) early in the development pipeline is essential.

Long-term safety surveillance and pharmacovigilance

Post-marketing surveillance systems and pharmacovigilance programs should be established to monitor long-term safety, adverse event profiles, and herb–drug interactions in large populations using standardized leaf preparations.

7.4 CONCLUSION

Aegle marmelos leaves represent a chemically diverse, pharmacologically multi-targeted botanical resource whose traditional uses across centuries are increasingly supported by contemporary preclinical pharmacology. The leaves are enriched in bioactive coumarins (imperatorin, marmelosin, auraptene), indole alkaloids (aegeline, marmesiline), flavonoids (rutin, quercetin), phenolic acids, and terpenoids that collectively exert potent antioxidant, anti-inflammatory, antidiabetic, antimicrobial, hepatoprotective, gastroprotective, and antiproliferative effects in cellular and animal models.[248–250]

While methodological heterogeneity and incomplete mechanistic depth constrain the current literature, the cumulative evidence base is sufficiently robust to justify investment in rigorous standardization, phytochemical optimization, mechanistically driven experimentation, and clinical validation.[248–250] Strategic pursuit of these objectives—particularly the conduct of well-designed phase I/II human trials of standardized leaf preparations in disease indications with strong preclinical support (type 2 diabetes, non-alcoholic fatty liver disease, inflammatory bowel disease)—has realistic potential to transform *A. marmelos* leaves from a traditionally used herbal remedy into a globally recognized, evidence-anchored phytopharmaceutical.

The integration of Ayurvedic wisdom with contemporary biomedical science, coupled with rigorous analytical, preclinical, and clinical investigation, positions *A. marmelos* leaves as a valuable model for rational phytopharmaceutical development in the 21st century.

REFERENCES

1. Swarbrick, J. T., & Mercado, B. L. (1987). *Weed science and weed control in Southeast Asia: An introductory text for students of agriculture in Southeast Asia* (FAO plant production and protection paper 81). Food and Agriculture Organization.
2. Oerke, E. C., & Dehne, H. W. (1997). Global crop production and the efficacy of crop protection: Current situation and future trends. *European Journal of Plant Pathology, 103*(3): 203–215. https://doi.org/10.1023/A:1008602111248
3. Karim, S. M. R. (1998). Relative yields of crops and crop losses due to weed competition in Bangladesh. *Pakistan Journal of Science and Industrial Research, 41:* 318–324.
4. Mamun, A. A. (1990). Agro-ecological studies of weeds and weed control in a flood prone village of Bangladesh. *JSARD Publications, 17*: 28–29.

5. Samson, J. (2006, May 4–5). *Roundup Ready corn: A newly approved agbiotech product for Filipino corn farmers*. 4th Philippine National Corn Congress, Pangasinan, Philippines.
6. Aktar, W., Sengupta, D., & Chowdhury, A. (2009). Impact of pesticides use in agriculture: Their benefits and hazards. *Interdisciplinary Toxicology, 2*(1): 1–12. https://doi.org/10.2478/v10102-009-0001-7
7. Wilson, C., & Tisdell, C. (2001). Why farmers continue to use pesticides despite environmental, health and sustainability costs. *Ecological Economics, 39*(3): 449–462. https://doi.org/10.1016/S0921-8009(01)00238-5
8. Pell, M., Stenberg, B., & Torstensson, L. (1998). Potential denitrification and nitrification tests for evaluation of pesticide effects in soil. *Ambio, 27*(1): 24–28.
9. Heap, I. (2018). *International survey of herbicide resistant weeds*. WeedScience.org. http://www.weedscience.org/
10. International Allelopathy Society. (2018). *International Allelopathy Society*. http://allelopathysociety.osupytheas.fr/about/
11. Rice, E. L. (1984). *Allelopathy* (2nd ed.). Academic Press.
12. Weir, T. L., Park, S. W., & Vivanco, J. M. (2004). Biochemical and physiological mechanisms mediated by allelochemicals. *Current Opinion in Plant Biology, 7*(4): 472–479. https://doi.org/10.1016/j.pbi.2004.05.007
13. Yu, J. Q., Ye, S. F., Zhang, M. F., & Hu, W. H. (2003). Effects of root exudates and aqueous root extracts of cucumber (*Cucumis sativus*) and allelochemicals on photosynthesis and antioxidant enzymes in cucumber. *Biochemical Systematics and Ecology, 31*(2): 129–139. https://doi.org/10.1016/S0305-1978(02)00150-3
14. Meier, C. L., & Bowman, W. D. (2008). Phenolic-rich leaf carbon fractions differentially influence microbial respiration and plant growth. *Oecologia, 158*(1): 95–107. https://doi.org/10.1007/s00442-008-1124-9
15. Yu, X., Yu, D., Lu, Z., & Ma, K. (2005). A new mechanism of invader success: Exotic plant inhibits natural vegetation restoration by changing soil microbe community. *Chinese Science Bulletin, 50*(11): 1105–1112. https://doi.org/10.1360/04WC0280
16. Zhou, B., Kong, C. H., Li, Y. H., Wang, P., & Xu, X. H. (2013). Crabgrass (*Digitaria sanguinalis*) allelochemicals that interfere with crop growth and the soil microbial community. *Journal of Agricultural and Food Chemistry, 61*(23): 5310–5317. https://doi.org/10.1021/jf401605g

17. Smith, A. E., & Martin, L. D. (1994). Allelopathic characteristics of three cool-season grass species in the forage ecosystem. *Agronomy Journal, 86*(2), 243–246. https://doi.org/10.2134/agronj1994.00021962008600020006x
18. Vyvyan, J. R. (2002). Allelochemicals as leads for new herbicides and agrochemicals. *Tetrahedron, 58*(9): 1631–1646. https://doi.org/10.1016/S0040-4020(02)00052-2
19. Duke, S. O., Dayan, F. E., Romagni, J. G., & Rimando, A. M. (2000). Natural products as sources of herbicides: Current status and future trends. *Weed Research, 40*(1): 99–111. https://doi.org/10.1046/j.13653180.2000.00161.x
20. Kamboj, V. P. (2000). Herbal medicine. *Current Science, 78*(1): 35–39.
21. Verma, S., & Singh, S. P. (2008). Current and future status of herbal medicines. *Veterinary World, 1*(11): 347–350. https://doi.org/10.5455/vetworld.2008.347-350
22. Mukherjee, P. K., Ponnusankar, S., & Venkatesh, M. (2010). Ethnomedicine in complementary therapeutics. In D. Chattopadhyay (Ed.), *Ethnomedicine: A source of complementary therapeutics* (pp. 29–52). Research Signpost.
23. Wakdikar, S. (2004). Global health care challenge: Indian experiences and new prescriptions. *Electronic Journal of Biotechnology, 7*(3): 214–220.
24. Verpoorte, R. (2000). Pharmacognosy in the new millennium: Leadfinding and biotechnology. *Journal of Pharmacy and Pharmacology, 52*(3): 253–262. https://doi.org/10.1211/0022357001773931
25. Appiah, K. S., Mardani, H. K., Osivand, A., Kpabitey, S., Amoatey, C. A., Oikawa, Y., & Fujii, Y. (2017). Exploring alternative use of medicinal plants for sustainable weed management. *Sustainability, 9*(8): 1468. https://doi.org/10.3390/su9081468
26. Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. *Environmental Health Perspectives, 109*(Suppl. 1): 69–75.
27. Swain, T. (1977). Secondary compounds as protective agents. *Annual Review of Plant Physiology, 28*(1), 479– 501. https://doi.org/10.1146/annurev.pp.28.060177.002403
28. Einhellig, F. A., & Leather, G. R. (1988). Potentials for exploiting allelopathy to enhance crop production. *Journal of Chemical Ecology, 14*(10): 1829–1844. https://doi.org/10.1007/BF01013480
29. Chevallier, A. (1996). *The encyclopedia of medicinal plants: A practical reference guide to over 550 key herbs and their medicinal uses*. Dorling Kindersley.
30. Wink, M. (1999). Introduction: Biochemistry, role and biotechnology of secondary metabolites. In M. Wink (Ed.), *Biochemistry of plant secondary metabolism* (pp. 1–16). Sheffield Academic Press.

31. Qasem, J. R. (2002). Allelopathic effects of selected medicinal plants on *Amaranthus retroflexus* and *Chenopodium murale*. *Allelopathy Journal, 10*(2): 105–122.
32. Azizi, M., & Fujii, Y. (2006). Allelopathic effect of some medicinal plant substances on seed germination of *Amaranthus retroflexus* and *Portulaca oleracea*. *Acta Horticulturae, 699*, 61–67. https://doi.org/10.17660/ActaHortic.2006.699.5
33. Lin, D., Tsuzuki, E., Sugimoto, Y., Dong, Y., Matsuo, M., & Terao, H. (2003). Assessment of dwarf lilyturf (*Ophiopogon japonicus* K.) dried powders for weed control in transplanted rice. *Crop Protection, 22*(3): 431– 435. https://doi.org/10.1016/S0261-2194(02)00190-4
34. Lin, D., Tsuzuki, E., Sugimoto, Y., Dong, Y., Matsuo, M., & Terao, H. (2004). Elementary identification and biological activities of phenolic allelochemicals from dwarf lilyturf plant (*Ophiopogon japonicus* K.) against two weeds of paddy rice field. *Plant Production Science, 7*(3): 260–265. https://doi.org/10.1626/pps.7.260
35. Han, C. M., Pan, K. W., Wu, N., Wang, J. C., & Li, W. (2008). Allelopathic effect of ginger on seed germination and seedling growth of soybean and chive. *Scientia Horticulturae, 116*(3): 330–336. https://doi.org/10.1016/j.scienta.2008.01.005
36. Li, H., Pan, K., Liu, Q., & Wang, J. (2009). Effect of enhanced ultraviolet-B on allelopathic potential of *Zanthoxylum bungeanum*. *Scientia Horticulturae, 119*(3): 310–314. https://doi.org/10.1016/j.scienta.2008.08.010
37. Sodaeizadeh, H., Rafieiolhossaini, M., Havlík, J., & van Damme, P. (2009). Allelopathic activity of different plant parts of *Peganum harmala* L. and identification of their growth inhibitors substances. *Plant Growth Regulation, 59*(3): 227–236. https://doi.org/10.1007/s10725-009-9408-6
38. Islam, A. K. M. M., & Kato-Noguchi, H. (2014). Phytotoxic activity of *Ocimum tenuiflorum* extracts on germination and seedling growth of different plant species. *The Scientific World Journal, 2014*; Article 676242. https://doi.org/10.1155/2014/676242
39. Fujii, Y., Parvez, S. S., Parvez, M. M., Ohmae, Y., & Uda, N. (2003). Screening of 239 medicinal plant species for allelopathic activity using the sandwich method. *Weed Biology and Management, 3*(4): 233–241. https://doi.org/10.1046/j.1444-6162.2003.00111.x
40. Fujii, Y., Shibuya, T., & Yasuda, T. (1990). Survey of Japanese weeds and crops for the detection of waterextractable allelopathic chemicals using Richards' function fitted to lettuce germination test. *Weed Research (Japan), 35*: 362–370.

41. Fujii, Y., Furukawa, M., Hayakawa, Y., Sugawara, K., & Shibuya, T. (1991). Survey of Japanese medicinal plants for the detection of allelopathic properties. *Journal of Weed Science and Technology, 36:* 36–42.
42. Azizi, M., Amini, S., Joharchi, M. R., Oroojalian, F., & Baghestani, Z. (2009). Genetic resources for allelopathic and medicinal plants from traditional Persian experience. In *Challenges for agro-environmental research in monsoon Asia* (MARCO symposium). Tsukuba, Japan.
43. Gilani, S. A., Fujii, Y., Shinwari, Z. K., Adnan, M., Kikuchi, A., & Watanabe, K. N. (2010). Phytotoxic studies of medicinal plant species of Pakistan. *Pakistan Journal of Botany, 42*(2): 987–996.
44. Mardani, H., Azizi, M., Osivand, A., & Fujii, Y. (2014). Evaluation of allelopathic activity of Iranian medicinal plants by sandwich method. *Journal of Weed Science and Technology, 53*(Suppl.): 85.
45. Amini, S., Azizi, M., Joharchi, M. R., & Moradinezhad, F. (2016). Evaluation of allelopathic activity of 68 medicinal and wild plant species of Iran by sandwich method. *International Journal of Horticultural Science and Technology, 3*(2): 243–253.
46. Islam, A. K. M. M., Hasan, M., Hasan, M. M., Uddin, M. K., Juraimi, A. S., & Anwar, M. P. (2018). Exploring 55 tropical medicinal plant species available in Bangladesh for their possible allelopathic potentiality. *Annals of Agricultural Sciences, 63*(1): 99–107. https://doi.org/10.1016/j.aoas.2018.05.005
47. Piyatida, P., & Kato-Noguchi, H. (2010). Screening of allelopathic activity of eleven Thai medicinal plants on seedling growth of five test plant species. *Asian Journal of Plant Sciences, 9*(8): 486–491. https://doi.org/10.3923/ajps.2010.486.491
48. Suwitchayanon, P., Kunasakdakul, K., & Kato-Noguchi, H. (2017). Screening the allelopathic activity of 14 medicinal plants from northern Thailand. *Environmental Control in Biology, 55*(4): 143–145.
49. Khanh, T. D., Hong, N. H., Xuan, T. D., & Chung, I. M. (2005). Paddy weed control by medicinal and leguminous plants from Southeast Asia. *Crop Protection, 24*(5): 421–431. https://doi.org/10.1016/j.cropro.2004.09.020
50. Khan, A. L., Hamayun, M., Hussain, J., Khan, H., Gilani, S. A., Kikuchi, A., Watanabe, K. N., Jung, E. H., & Lee, I. J. (2009). Assessment of allelopathic potential of selected medicinal plants of Pakistan. *African Journal of Biotechnology, 8*(6): 1024–1029.

51. Anjum, A., Hussain, U., Yousaf, Z., Khan, F., & Umer, A. (2010). Evaluation of allelopathic action of some selected medicinal plant on lettuce seeds by using sandwich method. *Journal of Medicinal Plants Research, 4*(6): 536–541.
52. Laosinwattana, C., Teerarak, M., & Charoenying, P. (2012). Effects of *Aglaia odorata* granules on the seedling growth of major maize weeds and the influence of soil type on the granule residue's efficacy. *Weed Biology and Management, 12*(3): 117–122. https://doi.org/10.1111/j.1445-6664.2012.00444.x
53. Islam, A. K. M. M., & Kato-Noguchi, H. (2012). Allelopathic potentiality of medicinal plant *Leucas aspera*. *International Journal of Sustainable Agriculture, 4*(1): 1–7.
54. Islam, A. K. M. M., & Kato-Noguchi, H. (2013). *Mentha sylvestris*: A potential allelopathic medicinal plant. *International Journal of Agriculture and Biology, 15*(6), 1313–1318.
55. Khan, M. S. I., Islam, A. K. M. M., & Kato-Noguchi, H. (2013). Evaluation of allelopathic activity of three mango (*Mangifera indica*) cultivars. *Asian Journal of Plant Sciences, 12*(5): 252–261. https://doi.org/10.3923/ajps.2013.252.261
56. Islam, A. K. M. M., & Kato-Noguchi, H. (2013). Plant growth inhibitory activity of medicinal plant *Hyptis suaveolens*: Could allelopathy be a cause? *Emirates Journal of Food and Agriculture, 25*(9): 692–701.https://doi.org/10.9755/ejfa.v25i9.16073
57. Islam, A. K. M. M., Khan, M. S. I., & Kato-Noguchi, H. (2013). Allelopathic activity of *Litchi chinensis* Sonn. *Acta Agriculturae Scandinavica, Section B—Soil & Plant Science, 63*(8): 669–675.
58. Islam, A. K. M. M., & Kato-Noguchi, H. (2013). Allelopathic potential of five Labiatae plant species on barnyard grass (*Echinochloa crus-galli*). *Australian Journal of Crop Science, 7*(9): 1369–1374.
59. Itani, T., Nakahata, Y., & Kato-Noguchi, H. (2013). Allelopathic activity of some herb plant species. *International Journal of Agriculture and Biology, 15*(6): 1359–1362.
60. Baličević, R., Ravlić, M., & Ravlić, I. (2015). Allelopathic effect of aromatic and medicinal plants on *Tripleurospermum inodorum* (L.) C. H. Schultz. *Herbologia, 15*(2): 41–53.
61. Qasem, J. R. (2017). A survey on the phytotoxicity of common weeds, wild grown species and medicinal plants on wheat. *Allelopathy Journal, 42*(2): 179–194. https://doi.org/10.26651/allelo.j./2017-42-2-1115

62. Algandaby, M. M., & El-Darier, S. M. (2016). Management of the noxious weed *Medicago polymorpha* L. via allelopathy of some medicinal plants from Taif region, Saudi Arabia. *Saudi Journal of Biological Sciences, 25*(7): 1339–1347.
63. Pachlatko, J. P. (1998). Natural products in crop protection. *Chimia, 52*(1–2): 29–47.
64. Duke, S. O., Dayan, F. E., Rimando, A. M., Schrader, K. K., Aliotta, G., Oliva, A., & Romagni, J. G. (2002).

Chemicals from nature for weed management. *Weed Science, 50*(2): 138–151. https://doi.org/10.1614/00431745(2002)050[0138:IPCFNF]2.0.CO;2

65. Fujii, Y. (2001). Screening and future exploitation of allelopathic plants as alternative herbicides with special reference to hairy vetch. *Journal of Crop Production, 4*(2): 257–275. https://doi.org/10.1300/J144v04n02_09
66. Singh, H. P., Batish, D. R., & Kohli, R. K. (2003). Allelopathic interactions and allelochemicals: New possibilities for sustainable weed management. *Critical Reviews in Plant Sciences, 22*(3–4): 239–311. https://doi.org/10.1080/713610858
67. Hong, N. H., Xuan, T. D., Eiji, T., Hiroyuki, T., Mitsuhiro, M., & Khanh, T. D. (2003). Screening for allelopathic potential of higher plants from Southeast Asia. *Crop Protection, 22*(6): 829–836. https://doi.org/10.1016/S0261-2194(03)00051-6
68. Yang, R. Z., & Tang, C. S. (1988). Plants used for pest control in China: A literature review. *Economic Botany, 42*(3): 376–406. https://doi.org/10.1007/BF02860162
69. Netzly, D. H., & Butler, L. G. (1986). Roots of sorghum exude hydrophobic droplets containing biologically active components. *Crop Science, 26*(4): 775–778. https://doi.org/10.2135/cropsci1986.0011183X002600040031x
70. Rimando, A. M., Dayan, F. E., Czarnota, M. A., Weston, L. A., & Duke, S. O. (1998). A new photosystem II electron transfer inhibitor from *Sorghum bicolor*. *Journal of Natural Products, 61*(7): 927–930. https://doi.org/10.1021/np9800708
71. Tellez, M. R., Canel, C., Rimando, A. M., & Duke, S. O. (1999). Differential accumulation of isoprenoids in glanded and glandless *Artemisia annua* L. *Phytochemistry, 52*(6), 1035–1040. https://doi.org/10.1016/S00319422(99)00308-8
72. Kohli, R. K., Batish, D., & Singh, H. P. (1997). Allelopathy and its implications in agroecosystems. *Journal of Crop Production, 1*(1): 169–202. https://doi.org/10.1300/J144v01n01_08
73. Macías, F. A., Molinillo, J. M. G., Varela, R. M., & Galindo, J. C. G. (2007). Allelopathy: A natural alternative for weed control. *Pest Management Science, 63*(4): 327–348. https://doi.org/10.1002/ps.1342

74. Caamal-Maldonado, J. A., Jiménez-Osornio, J. J., Torres-Barragán, A., & Anaya, A. L. (2001). The use of allelopathic legume cover and mulch species for weed control in cropping systems. *Agronomy Journal, 93*(1): 27–36. https://doi.org/10.2134/agronj2001.93127x
75. Milchunas, D. G., Vandever, M. W., Ball, L. O., & Hyberg, S. (2011). Allelopathic cover crop prior to seeding is more important than subsequent grazing/mowing in grassland establishment. *Rangeland Ecology & Management, 64*(3): 291–300. https://doi.org/10.2111/REM-D-10-00117.1
76. Urbano, B., González-Andrés, F., & Ballesteros, A. (2006). Allelopathic potential of cover crops to control weeds in barley. *Allelopathy Journal, 17*(1): 53–64.
77. Putnam, A. R., & Duke, W. B. (1978). Allelopathy in agroecosystems. *Annual Review of Phytopathology, 16*(1), 431–451. https://doi.org/10.1146/annurev.py.16.090178.002243
78. Habib, S. A., & Rahman, A. A. A. (1988). Evaluation of some weed extracts against field dodder on alfalfa (*Medicago sativa*). *Journal of Chemical Ecology, 14*(2): 443–452. https://doi.org/10.1007/BF01013896
79. Khaliq, A., Aslam, Z., & Cheema, Z. A. (2002). Efficacy of different weed management strategies in mungbean (*Vigna radiata* L.). *International Journal of Agriculture and Biology, 4*(2): 237–239.
80. Iqbal, J., & Cheema, Z. A. (2007). Effect of allelopathic crops water extracts on glyphosate dose for weed control in cotton (*Gossypium hirsutum*). *Allelopathy Journal, 19*(2): 403–410.
81. Jabran, K., Farooq, M., Hussain, M., Rehman, H., & Ali, M. A. (2010). Wild oat (*Avena fatua* L.) and canary grass (*Phalaris minor* Retz.) management through allelopathy. *Journal of Plant Protection Research, 50*(1): 41–44. https://doi.org/10.2478/v10045-010-0007-3
82. Putnam, A. R. (1988). Allelochemicals from plants as herbicides. *Weed Technology, 2*(4): 510–518. https://doi.org/10.1017/S0890037X00032371
83. Barnes, J. P., & Putnam, A. R. (1983). Rye residues contribute weed suppression in no-tillage cropping systems. *Journal of Chemical Ecology, 9*(8): 1045–1057. https://doi.org/10.1007/BF00982210
84. Cheema, Z. A., Rakha, A., & Khaliq, A. (2000). Use of sorgaab and sorghum mulch for weed management in mungbean. *Pakistan Journal of Agricultural Sciences, 37*(3–4); 140–144.

85. Lovett, J. V. (1990). Chemicals in plant protection: Is there a natural alternative? In C. Bassett, L. J. Whitehouse, & J. A. Zabkiewicz (Eds.), *Alternatives to the chemical control of weeds* (pp. 57–67). Forest Research Institute.
86. Iqbal, J., & Cheema, Z. A. (2008). Purple nutsedge (*Cyperus rotundus* L.) management in cotton with combined application of sorgaab and S-metolachlor. *Pakistan Journal of Botany, 40*(5): 2383–2391.
87. Razzaq, A., Cheema, Z. A., Jabran, K., Farooq, M., Khaliq, A., Haider, G., & Basra, S. M. A. (2010). Weed management in wheat through combination of allelopathic water extract with reduced doses of herbicides. *Pakistan Journal of Weed Science Research, 16*(3): 247–256.
88. Dilday, R. H., Frans, R. E., Semidey, N., Smith, R. J., & Oliver, L. R. (1992). Weed control with crop allelopathy. *Arkansas Farm Research, 41*(5): 14–15.
89. Wu, H., Pratley, J., Lemerle, D., & Haig, T. (1999). Crop cultivars with allelopathic capability. *Weed Research, 39*(3): 171–180. https://doi.org/10.1046/j.1365-3180.1999.00136.x
90. Mushtaq, M. N., Cheema, Z. A., Khaliq, A., & Naveed, M. R. (2010). A 75% reduction in herbicide use through integration with sorghum + sunflower extracts for weed management in wheat. *Journal of the Science of Food and Agriculture, 90*(11): 1897–1904. https://doi.org/10.1002/jsfa.4159
91. Xuan, T. D., Tsuzuki, E., Uematsu, H., & Terao, H. (2001). Weed control with alfalfa pellets in transplanting rice. *Weed Biology and Management, 1*(4): 231–235. https://doi.org/10.1046/j.1445-6664.2001.00034.x
92. Hong, N. H., Xuan, T. D., Eiji, T., & Khanh, T. D. (2004). Paddy weed control by higher plants from Southeast Asia. *Crop Protection, 23*(3), 255–261. https://doi.org/10.1016/j.cropro.2003.08.008
93. Laosinwattana, C., Huypao, J., Charoenying, P., Lertdetdecha, K., & Teerarak, M. (2013). Herbicidal activity of PORGANIC™, application and its potential use as natural post-emergence herbicide in paddy rice. In *Proceedings of the 24th Asian-Pacific Weed Science Society Conference* (pp. 376–382).
94. Xuan, T. D., Shinkichi, T., Khanh, T. D., & Chung, I. M. (2005). Biological control of weeds and plant pathogens in paddy rice by exploiting plant allelopathy: An overview. *Crop Protection, 24*(3): 197–206. https://doi.org/10.1016/j.cropro.2004.08.004

95. Einhellig, F. A., & Souza, I. F. (1992). Phytotoxicity of sorgoleone found in grain sorghum root exudates. *Journal of Chemical Ecology, 18*(1): 1–11. https://doi.org/10.1007/BF00997160
96. Nimbal, C. I., Pedersen, J. F., Yerkes, C. N., Weston, L. A., & Weller, S. C. (1996). Phytotoxicity and distribution of sorgoleone in grain sorghum germplasm. *Journal of Agricultural and Food Chemistry, 44*(5): 1343–1347. https://doi.org/10.1021/jf950561n
97. Czarnota, M. A., Paul, R. N., Dayan, F. E., Nimbal, C. I., & Weston, L. A. (2001). Mode of action, localization of production, chemical nature, and activity of sorgoleone: A potent PSII inhibitor in *Sorghum* spp. Root exudates. *Weed Technology, 15*(4): 813–825. https://doi.org/10.1614/0890-037X(2001)015[0813:MOALOP]2.0.CO;2
98. Weston, L. A., & Czarnota, M. A. (2001). Activity and persistence of sorgoleone, a long-chain hydroquinone produced by *Sorghum bicolor*. *Journal of Crop Production, 4*(2): 363–377. https://doi.org/10.1300/J144v04n02_17
99. Hoagland, R. E. (2009). Toxicity of tomatine and tomatidine on weeds, crops and phytopathogenetic fungi. *Allelopathy Journal, 23*(2): 425–436.
100. Dayan, F. E., Romagni, J. G., Tellez, M. R., Rimando, A. M., & Duke, S. O. (1999). Managing weeds with natural products. *Pesticide Outlook, 10*(5): 185–188.
101. Xuan, T. D., Elzaawely, A. A., Deba, F., Fukuta, M., & Tawata, S. (2006). Mimosine in *Leucaena* as a potent bio-herbicide. *Agronomy for Sustainable Development, 26*(2): 89–97. https://doi.org/10.1051/agro:2006001
102. Cornes, D. (2005). Callisto: A very successful maize herbicide inspired by allelochemistry. In *Proceedings of the 4th World Congress on Allelopathy*. Wagga Wagga, NSW, Australia. http://www.regional.org.au/au/allelopathy/2005/2/7/2636_cornesd.htm
103. Kato-Noguchi, H., Suzuki, M., Noguchi, K., Ohno, O., Suenaga, K., & Laosinwattana, C. (2016). A potent phytotoxic substance in *Aglaia odorata* Lour. *Chemistry & Biodiversity, 13*(4): 549–554. https://doi.org/10.1002/cbdv.201500175
104. Dayan, F. E., Cantrell, C. L., & Duke, S. O. (2009). Natural products in crop protection. *Bioorganic & Medicinal Chemistry, 17*(12), 4022–4034. https://doi.org/10.1016/j.bmc.2009.01.046
105. Bayer CropScience. (2011). *Material safety data sheet*. https://www.cropscience.bayer.com/en
106. Kato-Noguchi, H., Tanaka, Y., Murakami, T., Yamamura, S., & Fujihara, S. (2002). Isolation and identification of an allelopathic substance from peel of *Citrus junos*. *Phytochemistry, 61*(8): 849–853. https://doi.org/10.1016/S0031-9422(02)00382-5

107. Suwitchayanon, P., Pukclai, P., Ohno, O., Suenaga, K., & Kato-Noguchi, H. (2015). Isolation and identification of an allelopathic substance from *Hibiscus sabdariffa*. *Natural Product Communications, 10*(5): 765–766.
108. Heisey, R. M. (1996). Identification of an allelopathic compound from *Ailanthus altissima* (Simaroubaceae) and characterization of its herbicidal activity. *American Journal of Botany, 83*(2), 192–200. https://doi.org/10.1002/j.1537-2197.1996.tb12697.x
109. Islam, A. K. M. M., Ohno, O., Suenaga, K., & Kato-Noguchi, H. (2014). Two novel phytotoxic substances from *Leucas aspera*. *Journal of Plant Physiology, 171*(10): 877–883. https://doi.org/10.1016/j.jplph.2014.03.003
110. Islam, A. K. M. M., Ohno, O., Suenaga, K., & Kato-Noguchi, H. (2014). Suaveolic acid: A potent phytotoxic substance of *Hyptis suaveolens*. *The Scientific World Journal, 2014*, Article 425942. https://doi.org/10.1155/2014/425942
111. Suzuki, M., Khan, M. S. I., Iwasaki, A., Suenaga, K., & Kato-Noguchi, H. (2017). Allelopathic potential and an allelopathic substance in mango leaves. *Acta Agriculturae Scandinavica, Section B—Soil & Plant Science, 67*(1): 37–42. https://doi.org/10.1080/09064710.2016.1215517
112. Tuyen, P. T., Xuan, T. D., Anh, T. T. T., Van, T. M., Ahmad, A., Elzaawely, A. A., & Khanh, T. D. (2018). Weed suppressing potential and isolation of potent plant growth inhibitors from *Castanea crenata* Sieb. et Zucc. *Molecules, 23*(2): 345. https://doi.org/10.3390/molecules23020345
113. Shao, H., Huang, X., Zhang, Y., & Zhang, C. (2013). Main alkaloids of *Peganum harmala* L. and their different effects on dicot and monocot crops. *Molecules, 18*(3): 2623–2634. https://doi.org/10.3390/molecules18032623
114. Kato-Noguchi, H., Salam, M. A., Ohno, O., & Suenaga, K. (2014). Nimbolide B and nimbic acid B, phytotoxic substances in neem leaves with allelopathic activity. *Molecules, 19*(6): 6929–6940. https://doi.org/10.3390/molecules19066929
115. Charoenying, P., Teerarak, M., & Laosinwattana, C. (2010). An allelopathic substance isolated from *Zanthoxylum limonella* Alston fruit. *Scientia Horticulturae, 125*(3): 411–416. https://doi.org/10.1016/j.scienta.2010.04.045
116. Teerarak, M., Charoenying, P., & Laosinwattana, C. (2012). Physiological and cellular mechanisms of natural herbicide resource from *Aglaia odorata* Lour. on bioassay plants. *Acta Physiologiae Plantarum, 34*(4): 1277–1285. https://doi.org/10.1007/s11738-011-0923-5

117. Kato-Noguchi, H., Hamada, N., Morita, M., & Suenaga, K. (2013). A novel allelopathic substance, 13epi-orthosiphol N, in *Orthosiphon stamineus*. *Journal of Plant Physiology, 170*(1): 1–5. https://doi.org/10.1016/j.jplph.2012.08.011
118. Akbar, S. (2020). *Aegle marmelos* (L.) Correa (Rutaceae). In S. Akbar (Ed.), *Handbook of 200 medicinal plants* (pp. 109–122). Springer.
119. Anh, L. H., Quan, N. V., Nghia, L. T., & Xuan, T. D. (2021). Phenolic allelochemicals: Achievements, limitations, and prospective approaches in weed management. *Weed Biology and Management, 21*(1): 37–67.
120. Baliga, M. S., Bhat, H. P., Joseph, N., & Fazal, F. (2011). Phytochemistry and medicinal uses of the bael fruit (*Aegle marmelos* Correa): A concise review. *Food Research International, 44*(7): 1768–1775.
121. Bari, I. N., & Kato-Noguchi, H. (2017). Phytotoxic effects of *Cerbera manghas* L. leaf extracts on seedling elongation of four monocot and four dicot test species. *Acta Agrobotanica, 70*(1): 1–7.
122. Baziramakenga, R., Simard, R. R., & Leroux, G. D. (1994). Effects of benzoic and cinnamic acids on growth, mineral composition, and chlorophyll content of soybean. *Journal of Chemical Ecology, 20*(11): 2821–2833.
123. Bhar, K., Mondal, S., & Suresh, P. (2019). An eye-catching review of *Aegle marmelos* L. (golden apple). *Pharmacognosy Journal, 11*(1): 207–224.
124. Chafer, A., Tiziana, F., Stateva, R. P., & Angel, B. (2009). Trans-cinnamic acid solubility enhancement in the presence of ethanol as a supercritical CO_2 co-solvent. *Journal of Chemical & Engineering Data, 54*(8): 2263–2268.
125. Chandra, S., Roy, A., Jana, M., & Pahan, K. (2019). Cinnamic acid activates PPARα to stimulate lysosomal biogenesis and lower amyloid plaque pathology in an Alzheimer's disease mouse model. *Neurobiology of Disease, 124*: 379–395.
126. Chhabra, R., Sharma, R., & Kaur, T. (2021). Phyto-allelopathic effect of different trees leaves' aqueous extracts on seed germination and seedling growth of *Echinochloa crus-galli* (L.) Beauv. *Indian Journal of Weed Science, 53*(3): 318–323.
127. Chon, S. U., Choi, S. K., Jung, S., Jang, H. G., Pyo, B. S., & Kim, S. M. (2002). Effects of alfalfa leaf extracts and phenolic allelochemicals on early seedling growth and root morphology of alfalfa and barnyard grass. *Crop Protection, 21*(10): 1077–1082.
128. Clifford, M. N. (1999). Chlorogenic acids and other cinnamates—Nature, occurrence and dietary burden. *Journal of the Science of Food and Agriculture, 79*(3): 362–372.

129. Da Cunha, F. M., Duma, D., Assreuy, J., Buzzi, F. C., Niero, R., Campos, M. M., & Calixto, J. B. (2004). Caffeic acid derivatives: In vitro and in vivo anti-inflammatory properties. *Free Radical Research, 38*(11): 1241–1253.
130. DellaGreca, M., Previtera, L., Purcaro, R., & Zarrelli, A. (2007). Cinnamic ester derivatives from *Oxalis pes-caprae* (Bermuda buttercup). *Journal of Natural Products, 70*(10): 1664–1667.
131. Di Fabio, G., Ladhari, A., Romanucci, V., De Marco, A., & Zarrelli, A. (2018). Phytotoxic effects of Mediterranean plants extract on lettuce, tomato and onion as possible additive in irrigation drips. *Allelopathy Journal, 44*(2): 233–244.
132. Doblinski, P. M. F., Ferrarese, M. L. L., Huber, D. A., Scapim, C. A., Braccini, A. L., & Ferrarese-Filho, O. (2003). Peroxidase and lipid peroxidation of soybean roots in response to p-coumaric and phydroxybenzoic acids. *Brazilian Archives of Biology and Technology, 46*(2): 193–198.
133. El-Raouf, O. M. A., El-Sayed, M., & Manie, M. F. (2015). Cinnamic acid and cinnamaldehyde ameliorate cisplatin-induced splenotoxicity in rats. *Journal of Biochemical and Molecular Toxicology, 29*(9): 426–431.
134. Facenda, G., Real, M., Galán-Pérez, J. A., Gámiz, B., & Celis, R. (2023). Soil effects on the bioactivity of hydroxycoumarins as plant allelochemicals. *Plants, 12*(6): 1278.
135. Francisco, A. M., Molinillo, J. M. G., Rosa, M. V., & Galindo, J. C. G. (2007). Allelopathy—A natural alternative for weed control. *Pest Management Science, 63*(4): 327–348.
136. Fu, Y. H., Quan, W. X., Li, C. C., Qian, C. Y., Tang, F. H., & Chen, X. J. (2019). Allelopathic effects of phenolic acids on seedling growth and photosynthesis in *Rhododendron delavayi* Franch. *Photosynthetica, 57*(2): 377–387.
137. Fujii, Y., & Hiradate, S. (2007). *Allelopathy: New concepts and methodology*. Science Publishers.
138. Friesen, L. F., Jones, T. L., Van Acker, R. C., & Morrison, I. N. (2000). Identification of *Avena fatua* populations resistant to imazamethabenz, flamprop and fenoxaprop-P. *Weed Science, 48*(4): 532–540.
139. Fuentes, M., Navarro-García, V. M., Rojas, G., Avilés, M., & Zepeda, G. (2011). In vitro antifungal activity of coumarin extracted from *Loeselia mexicana* Brand. *Mycoses, 54*(6): 569–571.
140. Glass, A. D. M., & Dunlop, J. (1974). Influence of phenolic acids on ion uptake. *Plant Physiology, 54*(6): 855–858.

141. Hoult, J. R. S., & Payá, M. (1996). Pharmacological and biochemical actions of simple coumarins: Natural products with therapeutic potential. *General Pharmacology: The Vascular System, 27*(4): 713–722.
142. Ito, C., & Furukawa, H. (1987). Constituents of *Murraya exotica* L. Structure elucidation of new coumarins. *Chemical and Pharmaceutical Bulletin, 35*(11): 4277–4285.
143. Jakobek, L., Seruga, M., Novak, I., & Medvidović-Kosanović, M. (2007). Flavonols, phenolic acids and antioxidant activity of some red fruits. *Deutsche Lebensmittel-Rundschau, 103*(8): 369–378.
144. John, J., & Sarada, S. (2012). Role of phenolics in allelopathic interactions. *Allelopathy Journal, 29*(2): 215–230.
145. Jose, C. M., Torres, L. M. B., Torres, M. A. M. G., Shirasuna, R. T., Farias, D. A., dos Santos, N. A., Jr., & Grombone-Guaratini, M. T. (2016). Phytotoxic effects of phenolic acids from *Merostachys riedeliana*, a native and over abundant Brazilian bamboo. *Chemoecology, 26*(5): 235–246.
146. Ju, D., Sun, Y., Xiao, C. L., Shi, K., Zhou, Y. H., & Yu, J. Q. (2007). Physiological basis of different allelopathic reactions of cucumber and figleaf gourd plants to cinnamic acid. *Journal of Experimental Botany, 58*(14): 3765–3773.
147. Kato-Noguchi, H., Matsumoto, K., Sakamoto, C., Tojo, S., & Teruya, T. (2023). Allelopathy and allelopathic substances in the leaves of *Metasequoia glyptostroboides* from pruned branches for weed management. *Agronomy, 13*(4): 1017.
148. Kintzios, S. E. (2006). Terrestrial plant-derived anticancer agents and plant species used in anticancer research. *Critical Reviews in Plant Sciences, 25*(2): 79–113.
149. Kumar, J. I. N., Amb, M. K., & Bora, A. (2010). Chronic response of *Anabaena fertilissima* on growth, metabolites and enzymatic activities by chlorophenoxy herbicide. *Pesticide Biochemistry and Physiology, 98*(2): 168–174.
150. Lambole, V. B., Murti, K., Kumar, U., Sandipkumar, B. P., & Gajera, V. (2010). Phytopharmacological properties of *Aegle marmelos* as a potential medicinal tree: An overview. *International Journal of Pharmaceutical Sciences Review and Research, 5*(2): 67–72.
151. Lee, Y. G., Cho, J. Y., Kim, C. M., Lee, S. H., Kim, W. S., Jeon, T. I., Park, K. H., & Moon, J. H. (2013). Coumaroyl quinic acid derivatives and flavonoids from immature pear (*Pyrus pyrifolia* Nakai) fruit. *Food Science and Biotechnology, 22*(3): 803–810.
152. Li, Z., Wang, Q., Ruan, X., Pan, C., & Jiang, D. (2010). Phenolics and plant allelopathy. *Molecules, 15*(12): 8933–8952.

153. Mahomoodally, M. F., Mollica, A., Stefanucci, A., Aumeeruddy, M. Z., Poorneeka, R., & Zengin, G. (2018). Volatile components, pharmacological profile, and computational studies of essential oil from *Aegle marmelos* (Bael) leaves: A functional approach. *Industrial Crops and Products*, *126*: 13–21.
154. Mamidi, N., & Manna, D. (2013). $Zn(OTf)_2$-promoted chemoselective esterification of hydroxyl group bearing carboxylic acids. *Journal of Organic Chemistry*, *78*(5): 2386–2396.
155. Medvedeva, M., Barinova, K., Melnikova, A., Semenyuk, P., Kolmogorov, V., Gorelkin, P., Erofeev, A., & Muronetz, V. (2020). Naturally occurring cinnamic acid derivatives prevent amyloid transformation of alpha-synuclein. *Biochimie, 170:* 128–139.
156. Moździeń, K., Barabasz-Krasny, B., Stachurska-Swakoń, A., Turisová, I., & Zandi, P. (2021). Germination and growth of radish under influence of nipplewort aqueous extracts. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*, *49*(1): 12195.
157. Mujeeb, F., Bajpai, P., & Pathak, N. (2014). Phytochemical evaluation, antimicrobial activity, and determination of bioactive components from leaves of *Aegle marmelos*. *BioMed Research International, 2014;* Article 497606.
158. Navarro-García, V. M., Rojas, G., Avilés, M., Fuentes, M., & Zepeda, G. (2011). In vitro antifungal activity of coumarin extracted from *Loeselia mexicana* Brand. *Mycoses*, *54*(6): 569–571.
159. Panh, K., Rezaeiroshan, A., Saeedi, M., Morteza-Semnani, K., Akbari, J., Hedayatizadeh-Omran, A., Goli, H., & Nokhodchi, A. (2022). Vesicular formation of trans-ferulic acid: An efficient approach to improve the radical scavenging and antimicrobial properties. *Journal of Pharmaceutical Investigation*, *52*(4): 652–661.
160. Patterson, D. T. (1981). Effects of allelopathic chemicals on growth and physiological response of soybean (*Glycine max*). *Weed Science*, *29*(1): 53–58.
161. Papetti, A., Daglia, M., Aceti, C., Sordelli, B., Spini, V., Carazzone, C., & Gazzani, G. (2008). Hydroxycinnamic acid derivatives occurring in *Cichorium endivia* vegetables. *Journal of Pharmaceutical and Biomedical Analysis*, *48*(2): 472–476.
162. Pinho, I. A., Lopes, D. V., Martins, R. C., & Quina, M. J. (2017). Phytotoxicity assessment of olive mill solid wastes and the influence of phenolic compounds. *Chemosphere*, *185*: 258–267.
163. Prachayasittikul, S., Suphapong, S., Worachartcheewan, A., Lawung, R., Ruchirawat, S., & Prachayasittikul, V. (2009). Bioactive metabolites from *Spilanthes acmella* Murr. *Molecules*, *14*(2): 850–867.

164. Radha, G. V., Sadhana, B., Sastri, K. T., & Ganapaty, S. (2019). Bioactive umbelliferone and its derivatives: An update. *Journal of Pharmacognosy and Phytochemistry, 8*(1): 59–66.
165. Rawat, L. S., Maikhuri, R. K., Bahuguna, Y. M., Jha, N. K., & Phondani, P. C. (2017). Sunflower allelopathy for weed control in agriculture systems. *Journal of Crop Science and Biotechnology, 20*(1): 45–46.
166. Rezaeiroshan, A., Saeedi, M., Morteza-Semnani, K., Akbari, J., Hedayatizadeh-Omran, A., Goli, H., & Nokhodchi, A. (2022). Vesicular formation of trans-ferulic acid: An efficient approach to improve the radical scavenging and antimicrobial properties. *Journal of Pharmaceutical Investigation, 52*(4): 652–661.
167. Rob, M. M., Hossen, K., Ozaki, K., Teruya, T., & Kato-Noguchi, H. (2023). Phytotoxicity and phytotoxic substances in *Calamus tenuis* Roxb. *Toxins, 15*(10): 595.
168. Scarabel, L., Varotto, S., & Sattin, M. (2007). A European biotype of *Amaranthus retroflexus* crossresistant to ALS inhibitors and response to alternative herbicides. *Weed Research, 47*(6): 527–533.
169. Scavo, A., Abbate, C., & Mauromicale, G. (2019). Plant allelochemicals: Agronomic, nutritional and ecological relevance in the soil system. *Plant and Soil, 442*(1–2), 23–48.
170. Seigler, D. S. (1996). Chemistry and mechanisms of allelopathic interactions. *Agronomy Journal, 88*(6): 876–885.
171. Sharma, P. C., Bhatia, V., Bansal, N., & Sharma, A. (2007). A review on bael tree. *Indian Journal of Natural Products and Resources, 6*(2): 171–178.
172. Sim, M. O., Ham, J. R., Lee, H. I., Seo, K. I., & Lee, M. K. (2014). Long-term supplementation of umbelliferone and 4-methylumbelliferone alleviates high-fat diet induced hypertriglyceridemia and hyperglycemia in mice. *Chemico-Biological Interactions, 216*: 9–16.
173. Singh, H. P., Kaur, S., Batish, D. R., & Kohli, R. K. (2014). Ferulic acid impairs rhizogenesis and root growth, and alters associated biochemical changes in mung bean (*Vigna radiata*) hypocotyls. *Journal of Plant Interactions, 9*(1): 267–274.
174. Singh, H. P., Kohli, R. K., & Batish, D. R. (2001). Allelopathy in agroecosystems: An overview. *Journal of Crop Production, 4*(2): 1–41.
175. Siqueira, J. O., Nair, M. G., Hammerschmidt, R., Safir, G. R., & Putnam, A. R. (1991). Significance of phenolic compounds in plant–soil–microbial systems. *Critical Reviews in Plant Sciences, 10*(1): 63–121.

176. Stokstad, E., & Grullon, G. (2013). Infographic: Pesticide planet. *Science, 341*(6147): 730–731.
177. Sun, W., & Shahrajabian, M. H. (2023). Therapeutic potential of phenolic compounds in medicinal plants—Natural health products for human health. *Molecules, 28*(5): 1845.
178. Tang, Y. Q., Chu, C. Y., Zhu, L., Qian, B., & Shao, L. X. (2011). N-Heterocyclic carbene-Pd(II) complex derived from proline for the Mizoroki–Heck reaction in water. *Tetrahedron, 67*(45): 9479–9483.
179. Trombino, S., Cassano, R., Ferrarelli, T., Barone, E., Picci, N., & Mancuso, C. (2013). Trans-ferulic acidbased solid lipid nanoparticles and their antioxidant effect in rat brain microsomes. *Colloids and Surfaces B: Biointerfaces, 109:* 273–279.
180. Xuan, T. D., Tsuzuki, E., Tawata, S., & Khanh, T. D. (2004). Methods to determine allelopathic potential of crop plants for weed control. *Allelopathy Journal, 13*(2): 149–164.
181. Yu, J. Q., & Matsui, Y. (1994). Phytotoxic substances in the root exudates of cucumber (*Cucumis sativus* L.). *Journal of Chemical Ecology, 20*(1): 21–31.
182. Abenavoli, M. R., Lupini, A., Oliva, S., & Sorgonà, A. (2010). Allelochemical effects on net nitrate uptake and plasma membrane H^+-ATPase activity in maize seedlings. *Biologia Plantarum, 54*(1): 149–153. https://doi.org/10.1007/s10535-010-0024-0
183. Ahmed, R., Uddin, M. B., Khan, M. A. S. A., Mukul, S. A., & Hossain, M. K. (2007). Allelopathic effects of *Lantana camara* on germination and growth behavior of some agricultural crops in Bangladesh. *Journal of Forestry Research, 18:* 301–304. https://doi.org/10.1007/s11676-007-0060-6
184. Alam, S. M. (1990). Effect of wild plant extracts on germination and seedling growth of wheat. pp. 12–13.
185. Ambika, S. R., Poornima, S., Palaniraj, R., Sati, S. C., & Narwal, S. S. (2003). Allelopathic plants. 10. *Lantana camara* L.12: 147–162.
186. Arioli, T., Mattner, S. W., & Winberg, P. C. (2015). Applications of seaweed extracts in Australian agriculture: Past, present and future. *Journal of Applied Phycology, 27*; 2007–2015. https://doi.org/10.1007/s10811-015-0574-9
187. Bashar, H. K., Juraimi, A. S., Ahmad-Hamdani, M. S., Uddin, M. K., Asib, N., Anwar, M. P.,... & Hossain, A. (2023). Evaluation of allelopathic effects of *Parthenium hysterophorus* L. methanolic extracts on some selected plants and weeds. *PLoS ONE, 18*(1): e0280159. https://doi.org/10.1371/journal.pone.0280159

188. Belz, R. G., Reinhardt, C. F., Foxcroft, L. C., & Hurle, K. (2007). Residue allelopathy in *Parthenium hysterophorus* L.—Does parthenin play a leading role? *Crop Protection, 26*(3): 237–245. https://doi.org/10.1016/j.cropro.2005.06.009
189. Bhagwat, S. A., Breman, E., Thekaekara, T., Thornton, T. F., & Willis, K. J. (2012). A battle lost? Report on two centuries of invasion and management of *Lantana camara* L. in Australia, India and South Africa. *PLoS ONE, 7*(3): e32407. https://doi.org/10.1371/journal.pone.0032407
190. Biswas, B., Timsina, J., Garai, S., Mondal, M., Banerjee, H., Adhikary, S., & Kanthal, S. (2023). Weed control in transplanted rice with post-emergence herbicides and their effects on subsequent rapeseed in Eastern India. *International Journal of Pest Management 69*(1): 89–101. https://doi.org/10.1080/09670874.2020.1853276
191. Cai, S. L., & Mu, X. Q. (2012). Allelopathic potential of aqueous leaf extracts of *Datura stramonium* L. on seed germination, seedling growth and root anatomy of *Glycine max* (L.) Merrill. *Allelopathy Journal, 30*(2): 235–245.
192. Cheng, F., & Cheng, Z. (2015). Research progress on the use of plant allelopathy in agriculture and the physiological and ecological mechanisms of allelopathy. *Frontiers in Plant Science, 6:* 1020. https://doi.org/10.3389/fpls.2015.01020
193. Chopra, N., Tewari, G., Tewari, L. M., Upreti, B., & Pandey, N. (2017). Allelopathic effect of *Echinochloa colona* L. and *Cyperus iria* L. weed extracts on the seed germination and seedling growth of rice and soyabean. *Advances in Agriculture, 2017*(1): 5748524. https://doi.org/10.1155/2017/5748524
194. Davis, M. A., Chew, M. K., Hobbs, R. J., Lugo, A. E., Ewel, J. J., Vermeij, G. J., ... & Briggs, J. C. (2011). Don't judge species on their origins. *Nature, 474*(7350): 153–154. https://doi.org/10.1038/474153a
195. de Albuquerque, M. B., dos Santos, R. C., Lima, L. M., Melo Filho, P. D. A., Nogueira, R. J. M. C., Da Câmara, C. A. G., & de Rezende Ramos, A. (2011). Allelopathy, an alternative tool to improve cropping systems. A review. *Agronomy for Sustainable Development, 31:* 379–395. https://doi.org/10.1051/agro/2010031
196. El Sherif, F. (2017). *Aloe vera* leaf extract as a potential growth enhancer for *Populus* trees grown under in vitro conditions. *American Journal of Plant Biology, 2*(4): 101–105. https://doi.org/10.9755/ejfa.v25i9.16073
197. Khalaj, M. A., Amiri, M., & Azimi, M. H. (2013). Allelopathy: Physiological and sustainable agriculture important aspects, 950–962.

198. Kohli, R. K., Batish, D. R., Singh, H. P., & Dogra, K. S. (2006). Status, invasiveness and environmental threats of three tropical American invasive weeds (*Parthenium hysterophorus* L., *Ageratum conyzoides* L., *Lantana camara* L.) in India. *Biological Invasions, 8:* 1501–1510. https://doi.org/10.1007/s10530-005-58421
199. Laizer, H. C., Chacha, M. N., & Ndakidemi, P. A. (2021). Allelopathic effects of *Sphaeranthus suaveolens* on seed germination and seedling growth of *Phaseolus vulgaris* and *Oryza sativa*. *Advances in Agriculture, 2021*(1): 8882824. https://doi.org/10.1155/2021/8882824
200. Lerdau, M., & Wickham, J. D. (2011). Non-natives: Four risk factors. *Nature, 475*(7354): 36–37. https://doi.org/10.1038/475036d
201. Moh, S. M., Tojo, S., Teruya, T., & Kato-Noguchi, H. (2024). Allelopathy and identification of five allelochemicals in the leaves of the aromatic medicinal tree *Aegle marmelos* (L.) Correa. *Plants, 13*(4): 559. https://doi.org/10.3390/plants13040559
202. Molisch, H. (1937). *The effects of plants on each other*. Fischer Jena, 31: 12–16.
203. Ngondya, I. B., Munishi, L., Treydte, A. C., & Ndakidemi, P. A. (2016). Demonstrative effects of crude extracts of *Desmodium* spp. to fight against the invasive weed species *Tagetes minuta*. *Acta Ecologica Sinica, 36*(2): 113–118. https://doi.org/10.1016/j.chnaes.2016.03.001
204. R Development Core Team. (2019). *R: A language and environment for statistical computing* (Version 3.6.2). R Foundation for Statistical Computing. https://cloud.r-project.org/
205. Richardson, D. M., & Rejmánek, M. (2011). Trees and shrubs as invasive alien species—A global review. *Diversity and Distributions, 17*(5): 788–809. https://doi.org/10.1111/j.1472-4642.2011.00782.x
206. Rusdy, M., & Ako, A. (2017). Allelopathic effect of *Lantana camara* and *Chromolaena odorata* on germination and seedling growth of *Centrosema pubescens*. *International Journal of Applied Environmental Sciences, 12*: 1769–1776.
207. Sarma, D., Basumatary, P., & Datta, B. K. (2019). Allelopathic impact of *Melastoma malabathricum* L. on the seed germination and seedling growth of three agricultural crops. *The Journal of Indian Botanical Society, 98*(3–4): 183–193. https://doi.org/10.5958/2455-7218.2019.00021.4
208. Shaanker, R. U., Joseph, G., Aravind, N. A., Kannan, R., & Ganeshaiah, K. N. (2010). Invasive plants in tropical human-dominated landscapes: Need for an inclusive

management strategy. *Bioinvasions and globalization: Ecology, Economics, Management and Policy*, 202–219. https://doi.org/10.1093/acprof:oso/9780199560158.003.0014

209. Singh, A. A., Rajeswari, G., Nirmal, L. A., & Jacob, S. (2021). Synthesis and extraction routes of allelochemicals from plants and microbes: A review. *Reviews in Analytical Chemistry, 40*(1): 293–311. https://doi.org/10.1515/revac-2021-0139
210. Singh, H. P., Batish, D. R., Kaur, S., & Kohli, R. K. (2003). Phytotoxic interference of *Ageratum conyzoides* with wheat (*Triticum aestivum*). *Journal of Agronomy and Crop Science, 189*(5): 341–346. https://doi.org/10.1046/j.1439-037X.2003.00054.x
211. Wise, K., Gill, H., & Selby-Pham, J. (2020). Willow bark extract and the biostimulant complex Root Nectar® increase propagation efficiency in *Chrysanthemum* and lavender cuttings. *Scientia Horticulturae, 263:* 109108. https://doi.org/10.1016/j.scienta.2019.109108
212. Zhao, J., Yang, Z., Zou, J., & Li, Q. (2022). Allelopathic effects of sesame extracts on seed germination of moso bamboo and identification of potential allelochemicals. *Scientific Reports, 12*(1): 6661. https://doi.org/10.1038/s41598-022-10695-x
213. Abenavoli, M. R., Cacco, G., Sorgonà, A., Marabottini, R., Paolacci, A. R., Ciaffi, M., & Badiani, M. (2006). The inhibitory effects of coumarin on the germination of durum wheat (*Triticum turgidum* ssp. *durum* Desf.) seeds. *Journal of Chemical Ecology, 32*(2): 489–506.
214. Anaya, A. L., Cruz-Ortega, R., & Waller, G. R. (2006). Metabolism and ecology of purine alkaloids. In G. R. Waller (Ed.), *Allelochemicals: Role in agriculture and forestry* (pp. 396–417). American Chemical Society.
215. Batish, D. R., Singh, H. P., Kohli, R. K., & Kaur, S. (2008). Eucalyptus essential oil as a natural pesticide. *Forest Ecology and Management, 256*(12): 2166–2174.
216. Bertin, C., Yang, X., & Weston, L. A. (2003). The role of root exudates and allelochemicals in the rhizosphere. *Plant and Soil, 256*(1): 67–83.
217. Bhowmik, P. C., & Doll, J. D. (1982). Corn and soybean response to allelopathic effects of weed and crop residues. *Agronomy Journal, 74*(4): 601–606.
218. Blum, U. (1999). Designing laboratory plant debris-soil bioassays: Some reflections. In *Principles and practices in plant ecology: Allelochemical interactions* (pp. 17–23). CRC Press.
219. Bogatek, R., Gniazdowska, A., Zakrzewska, W., Oracz, K., & Gawronski, S. W. (2006). Allelopathic effects of sunflower extracts on mustard seed germination and seedling growth. *Biologia Plantarum, 50*(1): 156–158.

220. Callaway, R. M., & Aschehoug, E. T. (2000). Invasive plants versus their new and old neighbors: A mechanism for exotic invasion. *Science, 290*(5491): 521–523.
221. Cheng, F., & Cheng, Z. (2016). Allelopathic effects and identification of allelochemicals from root exudates of *Camellia oleifera*. *Allelopathy Journal, 38*(2): 225–238.
222. Choesin, D. N., & Boerner, R. E. J. (1991). Allyl isothiocyanate release and the allelopathic potential of *Brassica napus* (Brassicaceae). *American Journal of Botany, 78*(8): 1083–1090.
223. Colpas, F. T., Cintra, A. C. O., Vanzela, A. L. L., Fonseca, I. C. B., & Santos, O. J. A. P. (2013). Effects of *Artemisia annua* aqueous extract on growth and photosynthetic activity of weed species. *Allelopathy Journal, 31*(1): 199–210.
224. Chou, C. H., & Waller, G. R. (1980). Possible allelopathic constituents of *Coffea arabica*. *Journal of Chemical Ecology, 6*(3): 643–654.
225. Cruz-Ortega, R., Anaya, A. L., Gavilanes-Ruíz, M., & Sánchez-Nieto, S. (2002). Isolation and identification of allelochemicals from the aqueous extract of *Sicyos deppei*. *Journal of Chemical Ecology, 28*(11): 2335–2347.
226. Dann, E. K., Diers, B. W., Byrum, J. R., & Hammerschmidt, R. (1998). Effect of treating soybean with 2,6-dichloroisonicotinic acid (INA) and benzothiadiazole (BTH) on seed yields and the level of disease caused by *Sclerotinia sclerotiorum* in field and greenhouse studies. *European Journal of Plant Pathology, 104*(3): 271–278.
227. Del Fabbro, C., & Prati, D. (2015). Invasive plant species and the restoration of degraded land: A review. *Biodiversity and Conservation, 24*(6): 1291–1309.
228. Dornbos, D. L., Jr., & Spencer, G. F. (1990). Natural products phytotoxicity: A bioassay suitable for small quantities of slightly water-soluble compounds. *Journal of Chemical Ecology, 16*(2): 339–352.
229. Einhellig, F. A. (1996). Interactions involving allelopathy in cropping systems. *Agronomy Journal, 88*(6): 886–893.
230. Fitter, A. (2003). Making allelopathy respectable. *Science, 301*(5638): 1337–1338.
231. Fuerst, E. P., & Putnam, A. R. (1983). Separating the competitive and allelopathic components of interference: Theoretical principles. *Journal of Chemical Ecology, 9*(8): 937–944.
232. Gniazdowska, A., & Bogatek, R. (2005). Allelopathic interactions between plants: Multi site action of allelochemicals. *Acta Physiologiae Plantarum, 27*(3): 395–407.

233. Graña, E., Díaz-Tielas, C., Reigosa, M. J., & Sánchez-Moreiras, A. M. (2013). The plant secondary metabolite citral alters water status and prevents seed germination of competitor plants. *Weed Research, 53*(5): 361–369.
234. Hao, Z. P., Wang, Q., Christie, P., & Li, X. L. (2007). Allelopathic potential of watermelon tissues and root exudates. *Scientia Horticulturae, 112*(3): 315–320.
235. Harper, J. R., & Balke, N. E. (1981). Characterization of the inhibition of K^+ absorption in oat roots by salicylic acid. *Plant Physiology, 68*(6): 1349–1353.
236. Hierro, J. L., & Callaway, R. M. (2003). Allelopathy and exotic plant invasion. *Plant and Soil, 256*(1): 29–39.
237. Inderjit, & Duke, S. O. (2003). Ecophysiological aspects of allelopathy. *Planta, 217*(4): 529–539.
238. Inderjit, & Weston, L. A. (2003). Root exudation: An overview. In H. de Kroon & E. J. W. Visser (Eds.), *Root ecology* (pp. 235–255). Springer.
239. Inoue, M., Nishimura, H., Li, H. H., & Mizutani, J. (1992). Allelochemicals from *Polygonum sachalinense* Fr. Schm. (Polygonaceae). *Journal of Chemical Ecology, 18*(10): 1833–1840.
240. Kalinova, J., Vrchotova, N., & Triska, J. (2007). Exudation of allelopathic substances in buckwheat (*Fagopyrum esculentum* Moench). *Journal of Agricultural and Food Chemistry, 55*(16): 6453–6459.
241. Kobayashi, K. (2004). Factors affecting phytotoxic activity of allelochemicals in soil. *Weed Biology and Management, 4*(1): 1–7.
242. Kruse, M., Strandberg, M., & Strandberg, B. (2000). Ecological effects of allelopathic plants—A review. NERI Technical Report No. 315. National Environmental Research Institute, Denmark.
243. Leather, G. R., & Einhellig, F. A. (1988). Bioassays in the study of allelopathy. In G. R. Waller (Ed.), *Allelochemicals: Role in agriculture and forestry* (pp. 133–145). American Chemical Society.
244. Li, H. H., Inoue, M., Nishimura, H., Mizutani, J., & Tsuzuki, E. (1993). Interactions of trans-cinnamic acid, its related phenolic allelochemicals, and abscisic acid in seedling growth and seed germination of lettuce. *Journal of Chemical Ecology, 19*(9): 1833–1845.
245. Macias, F. A., Galindo, J. C. G., Molinillo, J. M. G., & Cutler, H. G. (Eds.). (2003). *Allelopathy: Chemistry and mode of action of allelochemicals*. CRC Press.

246. Macias, F. A., Marin, D., Oliveros-Bastidas, A., & Molinillo, J. M. G. (2009). Rediscovering the bioactivity and ecological role of 1,4-benzoxazinones. *Natural Product Reports*, *26*(4): 478–489.
247. Mallik, A. U., & Newton, P. F. (1988). Inhibition of black spruce seedling growth by forest-floor substrates of central Newfoundland. *Forest Ecology and Management*, *23*(4): 273–283.
248. Newman, E. I., & Rovira, A. D. (1975). Allelopathy among some British grassland species. *Journal of Ecology*, *63*(3): 727–737.
249. Nimbal, C. I., Yerkes, C. N., Weston, L. A., & Weller, S. C. (1996). Herbicidal activity and site of action of the natural product sorgoleone. *Pesticide Biochemistry and Physiology*, *54*(1): 73–83.
250. Olofsdotter, M., Navarez, D., Rebulanan, M., & Streibig, J. C. (1999). Weed-suppressing rice cultivars— Does allelopathy play a role? *Weed Research*, *39*(6): 441–454.