

A Review on Analgesic Potential and Anti-inflammatory Potential of Herbal Drug: *Acacia auriculiformis*

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ABSTRACT

Pain and inflammation are fundamental pathological responses associated with a wide range of acute and chronic disorders, including arthritis, trauma, infections, and autoimmune diseases. Although conventional analgesic and anti-inflammatory drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are widely prescribed, their prolonged use is frequently associated with adverse effects including gastrointestinal irritation, renal toxicity, cardiovascular complications, and drug dependence. Consequently, there is an increasing global interest in exploring plant-based therapeutic agents that are effective, safe, and economically accessible. Medicinal plants used in traditional systems of medicine represent a valuable source of bioactive compounds with potential pharmacological benefits. *Acacia auriculiformis* A. Cunn. ex Benth., belonging to the family Fabaceae, is a fast-growing evergreen tree widely distributed in tropical and subtropical regions. Traditionally, different parts of the plant such as leaves and bark, have been used for the treatment of pain, inflammation, rheumatism, wounds, skin disorders, and infections. Phytochemical investigations of *Acacia auriculiformis* have revealed the presence of flavonoids, tannins, phenolic compounds, saponins, and triterpenoids, which are known to exhibit analgesic, anti-inflammatory, and antioxidant activities. Experimental evaluation of the analgesic potential of *Acacia auriculiformis* has been carried out using standard animal models such as the hot plate method, acetic acid-induced writhing test, and formalin-induced paw licking test, which assess both central and peripheral pain mechanisms. The anti-inflammatory activity has been evaluated using models including carrageenan-induced paw edema and cotton pellet-induced granuloma, representing acute and chronic inflammatory responses. Results from these studies demonstrate significant reduction in pain responses and inflammatory edema, suggesting inhibition of inflammatory mediators and modulation of nociceptive pathways. Toxicological studies indicate that *Acacia auriculiformis* extracts exhibit a favorable safety profile at therapeutic dose levels, with no significant acute or subacute toxicity observed in experimental animals. Overall, the available evidence supports the potential of *Acacia auriculiformis* as a promising natural source of analgesic and anti-inflammatory agents. Further studies focusing on isolation of active constituents, mechanism-based investigations, standardization, and clinical evaluation are required to fully establish its therapeutic efficacy and safety for human use. **Keywords** Analgesic; anti-inflammatory; Phytochemicals; Natural products; Herbal medicine; Ethnopharmacology

Phytochemical investigations have revealed the presence of diverse bioactive constituents such as flavonoids, polyphenols, tannins, saponins, glycosides, and phenolic acids, which are responsible for its wide range of biological activities. Pharmacological studies have demonstrated significant antioxidant, antimicrobial, anti-inflammatory, analgesic, antidiabetic, hepatoprotective, anticancer, wound-healing, anthelmintic, antiulcer, cardioprotective, neuroprotective, and immunomodulatory effects through various in vitro and in vivo experimental models.

Keywords: Anti-inflammatory, Phytochemicals, Natural products, Herbal medicine, Ethnopharmacology.

INTRODUCTION

Pain and inflammation are among the most common clinical symptoms associated with a wide range of acute and chronic disorders, including arthritis, trauma, infections, and autoimmune diseases. Pain is defined as an unpleasant sensory and emotional

experience associated with actual or potential tissue damage, while inflammation is a complex biological response of vascular tissues to harmful stimuli such as pathogens, damaged cells, or irritants [1]. Although synthetic analgesic and anti-inflammatory drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are widely used, their long-term

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administration is often associated with adverse effects including gastrointestinal irritation, renal toxicity, cardiovascular risk, and drug dependence [2, 3]. Therefore, there is a growing need to explore safer and more effective therapeutic alternatives derived from natural sources. Medicinal plants have been used since ancient times in traditional systems of medicine for the management of pain and inflammatory conditions. Plant-based drugs are considered relatively safer, cost-effective, and biologically compatible due to their natural origin [4]. Many plant species possess bioactive constituents such as flavonoids, tannins, alkaloids, saponins, and phenolic compounds, which have been scientifically proven to exhibit analgesic and anti-inflammatory properties [5]. In recent years, research interest has increased toward the pharmacological validation of traditionally used medicinal plants. *Acacia auriculiformis* A. Cunn. ex Benth., belonging to the family Fabaceae (Mimosoideae), is a fast-growing evergreen tree widely distributed in tropical and subtropical regions, including India, Australia, and Southeast Asia [6]. Traditionally, different parts of the plant such as bark, leaves, and pods have been used for the treatment of pain, inflammation, rheumatism, skin disorders, and infections [7]. Phytochemical investigations of *Acacia auriculiformis* have revealed the presence of flavonoids, tannins, triterpenoids, glycosides, and phenolic compounds, which are known to modulate inflammatory mediators and pain pathways [8,9]. Experimental studies suggest that flavonoids and phenolic compounds exert analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins, leukotrienes, and other inflammatory mediators through suppression of cyclooxygenase (COX) and lipoxygenase (LOX) pathways [10]. Additionally, antioxidant properties of *Acacia auriculiformis* may contribute to its anti-inflammatory activity by reducing oxidative stress at the site of inflammation [11]. Inflammation is a protective response initiated by the body to eliminate harmful stimuli and initiate tissue repair; however, persistent or excessive inflammation can lead to chronic pathological conditions such as rheumatoid arthritis, inflammatory bowel disease, cardiovascular disorders, and neurodegenerative diseases [12]. The inflammatory process involves the activation of immune cells and the release of various mediators including histamine, bradykinin, cytokines (TNF- α ,

IL-1 β , IL-6), prostaglandins, and nitric oxide, which collectively contribute to pain, swelling, redness, and loss of function [13]. Analgesic agents act either centrally or peripherally to suppress pain perception, whereas anti-inflammatory agents reduce mediator release and vascular responses [14]. Currently available synthetic drugs, especially NSAIDs and corticosteroids, exert their therapeutic effects by inhibiting cyclooxygenase enzymes and suppressing inflammatory mediators; however, prolonged usage is associated with serious adverse reactions such as gastric ulceration, hepatotoxicity, nephrotoxicity, and immunosuppression [15, 16]. Opioid analgesics, although effective, pose risks of tolerance, dependence, and respiratory depression [17]. These limitations have intensified the search for alternative plant-based therapies with fewer side effects and better safety profiles. *Acacia auriculiformis* has attracted scientific attention due to its rich phytochemical composition and diverse pharmacological activities. Several studies have reported antimicrobial, antioxidant, antidiabetic, hepatoprotective, and anticancer activities of this plant [18,19]. The bark and leaves are particularly rich in polyphenols, condensed tannins, flavonoids, and triterpenes, which are known to possess strong anti-inflammatory and analgesic properties [20]. Tannins exert anti-inflammatory effects by protein precipitation and inhibition of inflammatory enzymes, while flavonoids modulate arachidonic acid metabolism and cytokine production [21]. Preclinical studies indicate that plant-derived flavonoids can suppress inflammatory responses by inhibiting nuclear factor-kappa B (NF- κ B) activation, thereby reducing the expression of pro-inflammatory cytokines and inducible nitric oxide synthase (iNOS) [22]. Additionally, antioxidant activity plays a crucial role in controlling inflammation, as reactive oxygen species generated during inflammatory processes amplify tissue damage and pain sensation [23]. The antioxidant potential of *Acacia auriculiformis* may therefore contribute synergistically to its analgesic and anti-inflammatory effects. Although some preliminary pharmacological investigations have demonstrated the antinociceptive and anti-inflammatory potential of *Acacia auriculiformis*, comprehensive evaluation using standardized experimental models is still required to validate its efficacy and safety [24]. *Acacia auriculiformis* A.



Cunn. Ex Benth. It is a fast-growing evergreen tree belonging to the family Fabaceae (subfamily Mimosoideae). It is commonly known as earleaf acacia due to the characteristic ear-shaped phyllodes. The plant is native to Australia, Papua New Guinea, and Indonesia and has been widely introduced into tropical and subtropical regions, including India, for afforestation and environmental management programs [25]. Its ability to tolerate drought, salinity, and poor soil conditions makes it an important species for soil conservation and land rehabilitation [26]. Botanically, *A. auriculiformis* can attain a height of 15–30 m and is characterized by thick, leathery phyllodes, yellow cylindrical flower spikes, and flat, twisted pods containing hard black seeds [27]. The species is capable of biological nitrogen fixation, which enhances soil fertility and supports sustainable agroforestry practices [28]. Due to these properties, the plant is extensively cultivated for timber, fuelwood, pulp, and paper industries [29]. In addition to its ecological and economic importance, *Acacia auriculiformis* holds a significant place in traditional medicine. Various parts of the plant, including bark, leaves, roots, and seeds, have been traditionally used for the treatment of pain, inflammation, rheumatism, skin diseases, wounds, and microbial infections [30]. The bark is particularly valued for its astringent and anti-inflammatory properties due to its high tannin content [31]. Phytochemical investigations have revealed that *A. auriculiformis* contains a wide range of bioactive compounds such as flavonoids, phenolic acids, tannins, saponins, alkaloids, and glycosides [32]. These constituents are known to exhibit diverse pharmacological activities, including antioxidant, antimicrobial, analgesic, and anti-inflammatory effects [33]. Experimental studies have supported the traditional claims by demonstrating significant analgesic and anti-inflammatory activities of various extracts of the plant [34]. Pain and inflammation are major clinical symptoms associated with several acute and chronic disorders. Although synthetic analgesic and anti-inflammatory drugs are effective, their prolonged use is often associated with adverse effects [35]. Therefore, medicinal plants such as *Acacia auriculiformis* are being increasingly explored as safer and effective alternatives. This review focuses on the botanical features, traditional uses, phytochemical constituents, and pharmacological potential of *Acacia auriculiformis*, with special

emphasis on its analgesic and medicinal properties. Medicinal plants have served as the foundation of traditional healthcare systems for thousands of years and continue to play a significant role in modern drug discovery. According to the World Health Organization, nearly 80% of the global population relies on plant-based medicines for primary healthcare needs, particularly in developing countries. Natural products remain a major source of novel therapeutic agents due to their chemical diversity, biological compatibility, and multi-target mechanisms of action [36]. Among plant-derived therapeutic agents, those exhibiting analgesic and anti-inflammatory activities are of particular interest due to the widespread prevalence of pain and inflammation-related disorders. Chronic inflammatory diseases such as arthritis, inflammatory bowel disease, cardiovascular disorders, and neuroinflammatory conditions represent a major public health challenge. Long-term use of synthetic anti-inflammatory drugs is often associated with serious adverse effects, reinforcing the need for safer alternatives derived from medicinal plants [37]. The genus *Acacia*, belonging to the family Fabaceae (subfamily Mimosoideae), comprises more than 1,300 species distributed across tropical and subtropical regions worldwide. Plants of this genus are well known for their medicinal, ecological, and economic importance. Several *Acacia* species have been traditionally used for the treatment of pain, inflammation, wounds, infections, diarrhea, and respiratory disorders, indicating their broad therapeutic potential [38]. *Acacia auriculiformis* A. Cunn. ex Benth. is a fast-growing evergreen tree native to Australia but widely cultivated in India, Southeast Asia, Africa, and South America. The plant adapts well to diverse climatic conditions and poor soil quality, making it an important species for afforestation and environmental conservation programs. Beyond its ecological importance, *A. auriculiformis* has gained attention for its medicinal properties documented in traditional systems of medicine [39]. Traditionally, different parts of *Acacia auriculiformis*, including bark, leaves, seeds, and pods, have been used in folk medicine to treat pain, inflammation, sore throat, skin diseases, wounds, rheumatism, and infections. Decoctions and extracts of the bark are commonly used as astringents and anti-inflammatory agents, while leaf preparations are



applied topically for wound healing and swelling reduction [40]. Phytochemical investigations of *Acacia auriculiformis* have revealed a rich profile of bioactive constituents. These include flavonoids, tannins, saponins, phenolic acids, alkaloids, glycosides, and triterpenoids. Such compounds are widely recognized for their pharmacological activities, particularly analgesic, anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory effects [41]. Flavonoids present in *A. auriculiformis* are known to inhibit key inflammatory mediators such as prostaglandins, leukotrienes, and cytokines. These compounds exert their effects by modulating cyclooxygenase and lipoxygenase pathways, which are central to the inflammatory response. Additionally, flavonoids possess free radical scavenging activity, reducing oxidative stress that contributes to inflammation and tissue damage [42]. Tannins, another major phytochemical group identified in *Acacia auriculiformis*, contribute significantly to its anti-inflammatory and analgesic properties. Tannins exhibit protein-precipitating and membrane-stabilizing effects, which help reduce capillary permeability and inhibit inflammatory exudation. Their ability to interact with inflammatory proteins supports the traditional use of the plant in pain and swelling-related conditions [43]. Oxidative stress plays a crucial role in the pathogenesis of inflammatory diseases. Reactive oxygen species activate inflammatory signaling pathways, leading to tissue injury and chronic inflammation. Extracts of *Acacia auriculiformis* have demonstrated strong antioxidant activity, which may indirectly contribute to their anti-inflammatory and analgesic effects by suppressing oxidative damage and inflammatory mediator release [44]. Experimental pharmacological studies have reported significant anti-inflammatory activity of *Acacia auriculiformis* extracts in standard animal models such as carrageenan-induced paw edema and cotton pellet-induced granuloma. These models reflect both acute and chronic inflammatory conditions, suggesting the broad-spectrum anti-inflammatory potential of the plant [45]. Similarly, analgesic activity of *Acacia auriculiformis* has been evaluated using models such as acetic acid-induced writhing and hot plate tests. These models assess both peripheral and central pain mechanisms, indicating that the plant may exert analgesic effects through multiple pathways, including inhibition of

inflammatory mediators and modulation of central pain perception [46]. Despite these promising findings, most studies on *Acacia auriculiformis* remain preliminary, with limited standardization of extracts, dosage, and experimental protocols. Comprehensive evaluation using validated models is essential to establish the scientific basis of its traditional use and to identify the most active phytoconstituents responsible for its pharmacological effects [47]. Moreover, systematic investigation of medicinal plants like *Acacia auriculiformis* aligns with the global trend toward discovering plant-based therapeutics with improved safety profiles. Plant-derived analgesic and anti-inflammatory agents offer advantages such as lower toxicity, reduced gastrointestinal side effects, and multi-target actions compared to conventional synthetic drugs [48]. Therefore, the evaluation of the analgesic and anti-inflammatory potential of *Acacia auriculiformis* is scientifically justified and pharmacologically relevant. Establishing its efficacy through experimental validation may contribute to the development of safer herbal formulations or lead compounds for future drug development in pain and inflammatory disorders [49]. Ethnopharmacological knowledge plays a vital role in identifying medicinal plants with therapeutic potential. Traditional medicinal systems such as Ayurveda, Unani, and folk medicine rely heavily on plant-based remedies for managing pain and inflammation. Plants belonging to the genus *Acacia* are frequently mentioned in ethnobotanical surveys for their use in inflammatory conditions, wound healing, and pain relief, suggesting a strong correlation between traditional claims and pharmacological activity [5]. *Acacia auriculiformis* has gained increasing scientific interest due to its widespread availability and rich phytochemical composition. The bark of the plant is particularly valued in traditional medicine as an astringent and anti-inflammatory agent, while leaf extracts are commonly used to treat skin inflammation and wounds. Such extensive traditional usage provides a strong rationale for systematic pharmacological evaluation [51]. Inflammation involves a complex cascade of biochemical events, including the release of histamine, serotonin, prostaglandins, cytokines, and reactive oxygen species. Persistent activation of these mediators results in chronic inflammation and tissue damage. Plant-derived compounds capable of



modulating multiple inflammatory pathways simultaneously are considered highly beneficial for managing inflammatory disorders [52]. Studies on *Acacia* species suggest that their anti-inflammatory activity is often mediated through inhibition of cyclooxygenase and lipoxygenase enzymes, leading to reduced synthesis of prostaglandins and leukotrienes. This mechanism is comparable to that of conventional NSAIDs, but with a potentially improved safety profile due to the presence of natural antioxidants that counteract oxidative stress [53]. Pain perception involves both peripheral and central mechanisms, including activation of nociceptors, transmission of pain signals to the central nervous system, and modulation of pain pathways in the brain. Herbal analgesics that target both peripheral inflammation and central pain processing offer a holistic approach to pain management. Extracts of *Acacia auriculiformis* have shown potential to influence both mechanisms, indicating their broad analgesic action [1]. Oxidative stress is closely associated with inflammation and pain through activation of nuclear factor-kappa B and other pro-inflammatory transcription factors. Antioxidants present in medicinal plants can suppress oxidative stress-induced inflammation. The high phenolic and flavonoid content of *Acacia auriculiformis* contributes to its ability to neutralize free radicals and protect tissues from oxidative injury [55]. In addition to analgesic and anti-inflammatory activities, *Acacia auriculiformis* has been reported to exhibit antimicrobial, antidiabetic, hepatoprotective, and immunomodulatory properties. These additional pharmacological effects enhance the therapeutic value of the plant, especially in inflammatory conditions complicated by infections or metabolic disorders [56]. Safety and toxicity assessment is a critical aspect of

medicinal plant research. Acute and sub-acute toxicity studies conducted on *Acacia auriculiformis* extracts have indicated a relatively high safety margin at therapeutic doses. The absence of significant behavioral, hematological, or histopathological changes supports its traditional use and encourages further pharmacological investigations [57]. Despite growing evidence of its therapeutic potential, *Acacia auriculiformis* remains underexplored compared to other medicinal plants. Standardization of plant extracts, identification of active phytoconstituents, and evaluation of dose-dependent effects are essential steps toward its development as a scientifically validated herbal medicine [58]. The evaluation of analgesic and anti-inflammatory activity using validated experimental models provides reliable pharmacological evidence. Animal models such as carrageenan-induced paw edema and acetic acid-induced writhing are widely accepted for screening anti-inflammatory and analgesic agents, respectively, and allow comparison with standard drugs [59]. The growing global interest in herbal medicines and natural analgesics underscores the importance of scientifically validating traditionally used plants like *Acacia auriculiformis*. Plant-based therapeutics offer the advantages of multi-target activity, reduced adverse effects, and better patient acceptability, making them attractive alternatives to synthetic drugs [60]. Therefore, comprehensive evaluation of the analgesic and anti-inflammatory potential of *Acacia auriculiformis* is of significant pharmacological relevance. Establishing its efficacy through experimental validation may contribute to the development of novel plant-based analgesic and anti-inflammatory agents, supporting both traditional knowledge and modern drug discovery efforts [61].

Plant Profile

Taxonomical classification

Kingdom	Plantae	[62]
Subkingdom	Tracheobionta (Vascular plants)	[62]
Superdivision	Spermatophyta (Seed plants)	[62]
Division/Phylum	Magnoliophyte (Flowering plants/Angiosperms)	[62]
Class	Magnoliopsida (Dicotyledons)	[62]
Subclass	Rosidae	[62]
Order	Fabales	[62]



Family	Fabaceae (Leguminosae)	[63]
Subfamily	Mimosoideae	[63]
Genus	Acacia	[63]
Species	Acacia auriculiformis A. Cunn. ex Benth	[62]



Fig: Showing different parts of *Acacia auriculiformis*

Biological Source of *Acacia auriculiformis*

Acacia auriculiformis A. Cunn. ex Benth. is an important medicinal and economic plant belonging to the family Fabaceae (Leguminosae), subfamily Mimosoideae. The plant is widely distributed in tropical and subtropical regions and is well known for its pharmacological and ethnomedicinal importance due to the presence of various bioactive secondary metabolites [64,65].

Taxonomical Classification

- Kingdom: Plantae
- Division: Magnoliophyte
- Class: Magnoliopsida
- Order: Fabales
- Family: Fabaceae (Leguminosae)
- Subfamily: Mimosoideae

- Genus: *Acacia*

- Species: *Acacia auriculiformis* A. Cunn. ex Benth. [65, 66]

Biological Source

Biologically, *Acacia auriculiformis* is a fast-growing evergreen tree, attaining a height of about 20–30 m. The medicinally useful parts of the plant include bark, leaves (phyllodes), seeds, pods, and flowers. Among these, the bark and leaves are most commonly used for pharmacological and phytochemical investigations due to their high content of tannins, flavonoids, phenolic compounds, saponins, and glycosides, which are responsible for its therapeutic properties [66–68].

Geographical Distribution

The plant is native to Australia, Papua New Guinea, and Indonesia, but it is widely cultivated in India, Sri Lanka, Bangladesh, Malaysia, Thailand, and several African countries. In India, *Acacia auriculiformis* is

commonly found in West Bengal, Odisha, Andhra Pradesh, Tamil Nadu, Karnataka, and northeastern states, particularly in coastal regions and wastelands, where it is also used for soil conservation and afforestation programs [64].

Macroscopic Characteristics

- Bark: Dark brown to blackish, rough, fibrous, and deeply fissured; rich in condensed tannins.
- Leaves (Phyllodes): Flattened, sickle-shaped, leathery, dark green with prominent parallel veins.
- Flowers: Bright yellow, small, arranged in cylindrical spikes.
- Fruits: Flat, twisted or coiled pods containing black, shiny seeds [65,68].

Collection and Authentication

The bark and leaves are generally collected during the dry season to ensure a maximum concentration of active constituents. The collected plant material is shade-dried, powdered, and stored in airtight containers. Authentication of the plant material is carried out by a qualified taxonomist or by comparison with authenticated herbarium specimens, ensuring quality and genuineness of the simple drug.

Importance of Biological Source

Correct identification and authentication of the biological source of *Acacia auriculiformis* are essential to ensure quality and purity of raw materials, reproducibility of pharmacological activity, and safety and efficacy of herbal formulations. Due to its rich phytochemical profile, the plant is extensively used in traditional medicine, pharmaceutical formulations, the tanning industry, and afforestation programs [67].

Vernacular Names

- English: Earleaf Acacia, Australian Wattle [69]
- Hindi: Akashmoni • Tamil: Kathivel
- Telugu: Akashmoni • Malayalam: Akashmoni

- Bengali: Akashmoni

Geographical Distribution

Native to Australia, Papua New Guinea, and Indonesia; widely cultivated in India, Sri Lanka, Bangladesh, Thailand, and Africa. In India, mainly in West Bengal, Odisha, Assam, Tamil Nadu, Kerala, and Andhra Pradesh [70, 71]

Habitat

Tropical and subtropical regions; tolerates poor, sandy, lateritic, and saline soils; drought and heat resistant [72, 73]

Morphological Description

- Habit: Fast-growing, evergreen tree, 15–30 m height, spreading crown [74]
- Bark: Dark grey to brown, rough, fissured [75]
- Leaves: Phyllodes, curved, leathery, glossy green [76]
- Flowers: Bright yellow, cylindrical spikes [77]
- Fruits: Flat, twisted pods with black, shiny seeds [77]
- Seeds: Hard, oval-shaped with an aril [78]

Microscopic Characteristics

Thick-walled fibers, parenchymatous cells, vascular bundles, calcium oxalate crystals [79]

Parts Used

Bark, leaves (phyllodes), seeds, roots [80]

Phytochemical Constituents

Flavonoids, tannins, phenolic compounds, saponins, alkaloids, triterpenoids [80,81]

Pharmacological Evaluation of *Acacia auriculiformis*

Acacia auriculiformis (family: Fabaceae) is a fast-growing, nitrogen-fixing leguminous tree, widely



used in traditional medicine for its diverse therapeutic properties. It contains bioactive compounds such as flavonoids, tannins, saponins, phenolic acids, alkaloids, and glycosides, which contribute to its pharmacological effects [82].

Antioxidant Activity

Acacia auriculiformis exhibits potent antioxidant activity in in vitro and in vivo studies. Leaf, bark, and pod extracts effectively scavenge reactive oxygen species (ROS) such as superoxide anions, hydroxyl radicals, and nitric oxide [83, 84]. These extracts also inhibit lipid peroxidation in cell membranes and increase the levels of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) [85].

Mechanism of Action

- Hydrogen/electron donation: Flavonoids and phenolic compounds donate hydrogen atoms or electrons to neutralize free radicals [86].
- Metal chelation: Polyphenols chelate redox-active metals like Fe^{2+} and Cu^{2+} , preventing ROS formation [87].
- Activation of endogenous antioxidants: Extracts upregulate SOD, CAT, and GPx, enhancing cellular defense mechanisms [87].
- Inhibition of lipid peroxidation: Prevents oxidative degradation of lipids in cell membranes, maintaining cellular integrity [87].

Anti-inflammatory Activity

The anti-inflammatory activity of *A. auriculiformis* has been demonstrated using carrageenan-induced paw edema, formalin-induced paw edema, and xylene-induced ear edema models [88, 89]. Both aqueous and methanolic extracts reduce swelling, infiltration of inflammatory cells, and production of inflammatory mediators.

Mechanism of Action

- Inhibition of prostaglandin synthesis: Flavonoids and tannins inhibit COX-1 and COX-2 enzymes, reducing prostaglandin-mediated inflammation [90].
- Suppression of NF- κ B pathway: Downregulates pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6, limiting inflammatory responses [91].
- Lysosomal stabilization: Protects lysosomal membranes in inflammatory cells, preventing release of proteolytic enzymes [92].
- Modulation of nitric oxide production: Inhibits inducible nitric oxide synthase (iNOS), reducing nitric oxide-mediated tissue damage [92].

Analgesic Activity

Extracts of *A. auriculiformis* exhibit significant analgesic effects in chemical nociception models like acetic acid-induced writhing, formalin-induced pain, and thermal nociception (hot plate test) [93, 94].

Mechanism of Action

- Peripheral analgesia: Inhibition of prostaglandin synthesis at the peripheral nociceptor level reduces pain sensation [95].
- Central analgesia: Interaction with opioid receptors in the CNS modulates pain perception [96].
- Reduction of nociceptor sensitization: Anti-inflammatory activity reduces peripheral sensitization of nociceptors [97].
- Inhibition of excitatory neurotransmitters: Suppresses release of substance P and glutamate involved in pain signaling [97].

Immunomodulatory Activity

The plant shows immune-enhancing properties, including stimulation of lymphocyte proliferation, macrophage activity, and cytokine production [98, 99]. Extracts improve humoral and cell-mediated immunity, making them useful in traditional treatment of infections.



Mechanism of Action

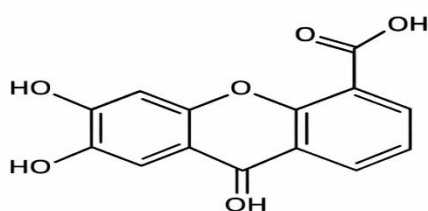
- Activation of phagocytic cells: Enhances macrophage activity and antigen presentation [100].
- Cytokine modulation: Upregulates IL-2, IFN- γ , and TNF- α , promoting adaptive immune responses [101].
- Saponins and tannins: Act as immunostimulants, enhancing both humoral and cell-mediated immunity [100].
- Signal transduction pathways: Flavonoids regulate MAPK and JAK-STAT pathways, balancing immune responses [102]

Antimicrobial Activity

Acacia auriculiformis exhibits broad-spectrum antimicrobial effects against Gram-positive and Gram-negative bacteria, fungi, and yeasts [103,104]. Extracts disrupt microbial cell walls and inhibit enzymatic activity.

Mechanism of Action

- Cell wall disruption: Tannins and phenolics bind to bacterial cell walls, causing leakage of intracellular contents [105].



Quercetin

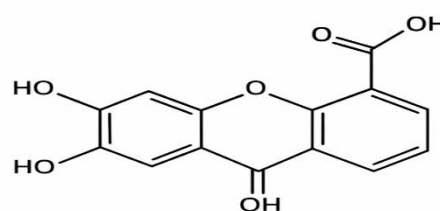
- Enzyme inactivation: Inhibits microbial enzymes essential for replication and metabolism [106].
- Metal ion chelation: Polyphenols chelate essential metal ions, impairing microbial growth [107].
- Biofilm inhibition: Reduces microbial adherence and biofilm formation, enhancing susceptibility [107]

Phytochemical Profile of *Acacia auriculiformis*

Acacia auriculiformis is a fast-growing leguminous tree widely recognized for its medicinal, ecological, and industrial applications. Phytochemical investigations of its leaves, bark, seeds, and flowers have revealed a rich array of secondary metabolites, which are responsible for its therapeutic properties [108].

Flavonoids

Flavonoids are a major class of polyphenolic compounds present in leaves and bark, including quercetin, kaempferol, catechin, and their glycosides [109, 110].



Kaempferol

• Pharmacological roles

Antioxidant activity: Flavonoids neutralize reactive oxygen species (ROS), inhibit lipid peroxidation, and chelate metal ions [111].

Anti-inflammatory effect: They suppress inflammatory mediators such as prostaglandins and cytokines (IL-1, TNF- α) and inhibit cyclooxygenase (COX) and lipoxygenase (LOX) pathways [110].



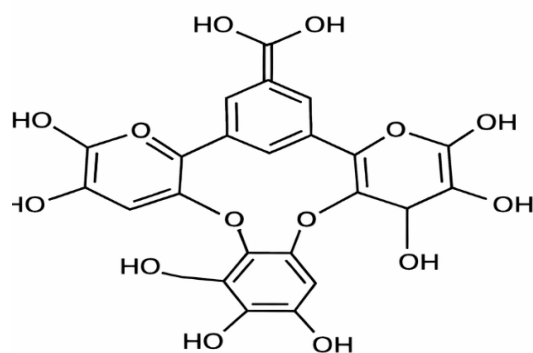
Immunomodulation: Flavonoids enhance macrophage activation and stimulate adaptive immunity [111]

Mechanism of action:

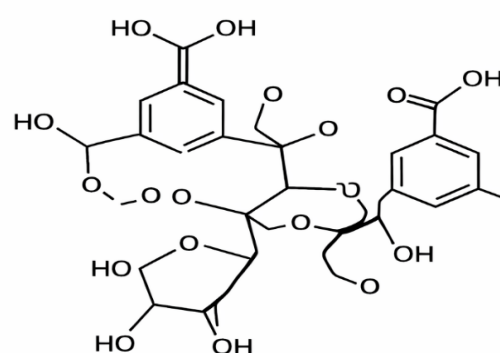
Flavonoids act through free radical scavenging, enzyme inhibition, and modulation of signaling pathways like NF- κ B and MAPK, which control inflammatory responses and oxidative stress [109–111].

Tannins

Both hydrolyzable and condensed tannins are abundant in the bark and leaves [112].



Ellagitannin



Gallotannin

Pharmacological roles:

Astringent and antimicrobial: Tannins bind to microbial cell walls and precipitate proteins, inhibiting microbial growth [113].

Antioxidant and anti-inflammatory: They scavenge free radicals, reduce oxidative damage, and downregulate inflammatory mediators [112, 113].

Wound healing: Tannins promote tissue repair by precipitating proteins and forming a protective layer on wounds [113].

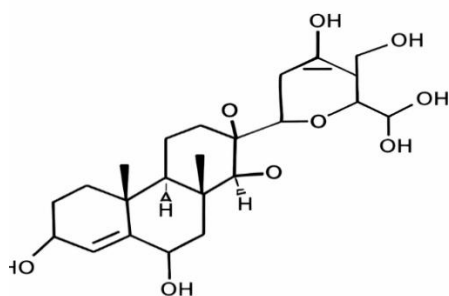
• **Mechanism of action:** Tannins exert effects via protein complexation, membrane stabilization, and free radical scavenging, leading to reduced microbial proliferation and inflammation [112, 113].

Tannins are a group of naturally occurring high-molecular-weight polyphenolic compounds widely distributed in the plant kingdom. They are characterized by their ability to precipitate proteins, alkaloids, and other macromolecules. In medicinal plants, tannins play a crucial role in defense mechanisms and contribute significantly to various pharmacological activities. *Acacia auriculiformis* is particularly rich in tannins, especially in its bark, making it an important tannin-yielding plant of medicinal and industrial significance.

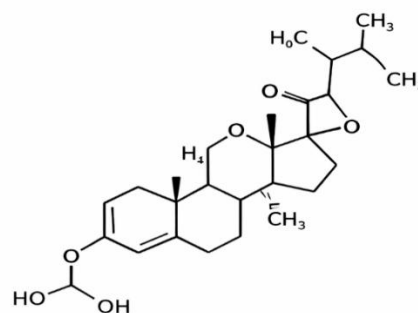
Saponins

Saponins are found in leaves, seeds, and flowers [114]. Saponins are a diverse group of naturally occurring glycosidic compounds widely distributed in higher plants. Chemically, saponins consist of a lipophilic aglycone (sapogenin) linked to one or more hydrophilic sugar moieties, which impart their characteristic soap-like foaming property when shaken with water. Due to their amphiphilic nature, saponins exhibit a wide range of biological and pharmacological activities. *Acacia auriculiformis* has been reported to contain appreciable amounts of saponins, contributing significantly to its medicinal value.

Saponins



Triterpenoid Saponin



Steroidal Saponin

• Pharmacological roles:

Immunostimulatory: Saponins activate macrophages, dendritic cells, and natural killer cells, enhancing both innate and adaptive immunity [115].

Anti-inflammatory and cholesterol-lowering: They reduce pro-inflammatory cytokines and modulate lipid metabolism [114, 115].

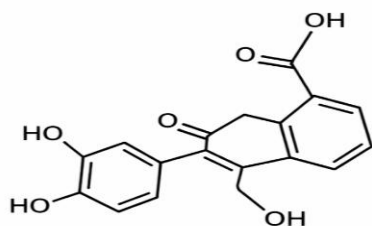
• Mechanism of action:

Saponins enhance phagocytosis, stimulate cytokine production, and form complexes with cholesterol,

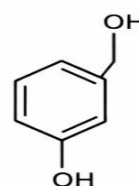
which also aids in reducing inflammation and enhancing immune defense [114, 115].

Phenolic Compounds

Phenolic compounds, including gallic acid, catechin, and tannic acid, are abundant in leaves and bark [116]. Phenolic compounds constitute one of the most important classes of secondary metabolites in plants and are characterized by the presence of one or more hydroxyl groups attached to an aromatic ring. These compounds play a vital role in plant defense mechanisms and contribute significantly to the therapeutic properties of medicinal plants.



Triterpenoid Saponin



Simple Phenol

• Pharmacological roles:

Antioxidant activity: Phenolics neutralize ROS, prevent DNA and lipid oxidation, and maintain cellular redox balance [117].

Antimicrobial activity: They disrupt microbial membranes and inhibit growth [116].

Anti-inflammatory: Phenolics inhibit COX and LOX enzymes and modulate inflammatory signaling pathways [116, 117].

• Mechanism of action:

Phenolics act primarily via hydrogen donation to free radicals, metal chelation, and modulation of NF-κB



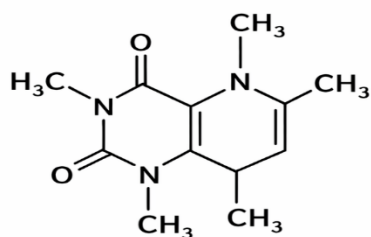
and MAPK signaling, reducing oxidative stress and inflammation [116, 117].

Alkaloids

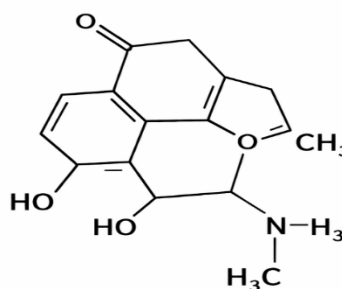
Alkaloids are present in minor quantities in leaves and bark [118]. Alkaloids are a diverse group of naturally occurring nitrogen-containing organic compounds that exhibit significant physiological and pharmacological effects in humans and animals. They

are typically basic in nature and often possess heterocyclic nitrogen atoms. Alkaloids play an important role in plant defense mechanisms and are widely recognized for their potent biological activities. Although *Acacia auriculiformis* is more prominently known for its tannin and phenolic content, phytochemical studies have reported the presence of alkaloids in its bark and leaves, contributing to its overall pharmacological profile.

Alkaloids



Caffeine



Morphine

• Pharmacological roles:

Analgesic: Alkaloids interact with central and peripheral nervous system receptors to alleviate pain [118].

Antimicrobial and cytotoxic effects: Alkaloids inhibit microbial growth and exhibit potential anti-cancer properties [118].

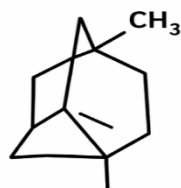
• Mechanism of action:

Alkaloids act through binding to neurotransmitter receptors, modulating ion channels, and inhibiting microbial enzymes, producing analgesic, antimicrobial, and cytoprotective effects [118].

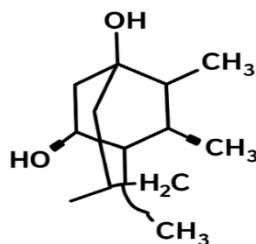
Terpenoids

Terpenoids, present in smaller amounts, are found in leaves and bark [119]. Terpenoids, also known as isoprenoids, constitute one of the largest and most diverse classes of plant secondary metabolites. They are biosynthesized from five-carbon isoprene units and occur in plants as volatile oils, resins, and pigments. Terpenoids play an essential role in plant growth, defense, and ecological interactions. In medicinal plants, terpenoids are widely recognized for their broad spectrum of pharmacological activities. Phytochemical investigations have reported the presence of terpenoids in the bark and leaves of *Acacia auriculiformis*, contributing to its medicinal significance.

Terpenoids



Pinene



Menthol

- **Pharmacological roles:**

Anti-inflammatory: Terpenoids inhibit pro-inflammatory mediators and enzymes [119].

Antimicrobial and anticancer: They disrupt microbial membranes and induce apoptosis in cancer cells [119].

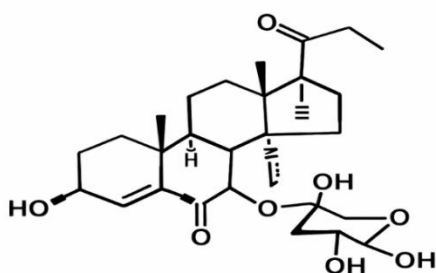
- **Mechanism of action:**

Terpenoids modulate enzyme activity, cell signaling pathways, and membrane integrity, contributing to their broad therapeutic effects [119].

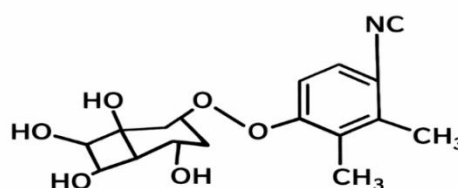
Glycosides

Glycosides, including cardiac glycosides, are detected in leaves and seeds [120]. Glycosides are an important class of naturally occurring secondary metabolites widely distributed in medicinal plants. Chemically, glycosides consist of a sugar moiety (glycone) linked to a non-sugar moiety (aglycone or genin) through glycosidic linkage. The pharmacological activity of glycosides largely depends on the nature of the aglycone, while the sugar part influences solubility, absorption, and bioavailability. Phytochemical investigations have confirmed the presence of glycosides in the bark and leaves of *Acacia auriculiformis*, contributing significantly to its therapeutic potential.

Glycosides



Digoxin



Amygdalin

- **Pharmacological roles:**

Cytoprotective and antioxidant effects: Glycosides protect cells from oxidative damage and improve cellular health [120].

Cardiovascular modulation: Some glycosides may influence heart function and circulation [120].

- **Mechanism of action:**

Glycosides exert effects through ion channel modulation, enzyme inhibition, and antioxidant

activity, supporting both cardioprotective and cellular defense mechanisms.

Conclusion and Future Perspectives

Acacia auriculiformis has emerged as a highly valuable medicinal plant owing to its broad spectrum of pharmacological activities and rich phytochemical profile. Extensive experimental studies have demonstrated its potent antioxidant, antimicrobial, anti-inflammatory, analgesic, antidiabetic, hepatoprotective, anticancer, wound-healing, anthelmintic, immunomodulatory, and gastroprotective properties. These diverse biological activities are primarily attributed to the presence of bioactive constituents such as flavonoids, polyphenols, tannins, saponins, and phenolic acids, which act through multiple biochemical and molecular pathways. The antioxidant potential of *A. auriculiformis* plays a central role in mitigating oxidative stress, which is a key underlying factor in the pathogenesis of chronic diseases including diabetes mellitus, cardiovascular disorders, cancer, and neurodegenerative conditions. Its anti-inflammatory and analgesic effects further strengthen its therapeutic relevance in inflammatory and pain-related disorders by inhibiting the synthesis of inflammatory mediators and modulating enzymatic pathways. Additionally, its antimicrobial and wound-healing activities validate its traditional use in the treatment of infections and skin ailments. Preclinical toxicological studies suggest that *Acacia auriculiformis* exhibits a favorable safety profile when administered at therapeutic doses, with no significant adverse effects observed in acute and subacute toxicity models. Although most pharmacological evidence is based on in vitro and animal studies, the cumulative findings strongly support the traditional medicinal claims and highlight the plant's potential as a promising source of novel phytotherapeutic agents. Therefore, *Acacia auriculiformis* holds considerable promise for further pharmaceutical development and integration into modern medicine as a natural, multi-target therapeutic agent. Despite the substantial progress in understanding the pharmacological properties of *Acacia auriculiformis*, several areas require further scientific exploration to fully realize its therapeutic potential. Future research should prioritize the

isolation, purification, and structural characterization of individual bioactive compounds responsible for specific pharmacological actions. Such studies will aid in identifying lead molecules with defined mechanisms of action and improved therapeutic specificity. In-depth mechanistic studies at the molecular and cellular levels are essential to elucidate signaling pathways involved in its antioxidant, anti-inflammatory, antidiabetic, and anticancer effects. Additionally, comprehensive pharmacokinetic and bioavailability studies are required to understand absorption, distribution, metabolism, and excretion patterns of its active constituents, which are critical for dose optimization and formulation development. Another important future direction involves conducting well-designed clinical trials to validate preclinical findings and establish safety, efficacy, and therapeutic dosage in human subjects. Standardization of plant extracts, quality control, and batch-to-batch consistency must be ensured to meet regulatory requirements for herbal drug development. Furthermore, exploration of advanced drug delivery systems, such as nano formulations and synergistic polyherbal combinations, may enhance bioavailability and therapeutic outcomes. Overall, continued interdisciplinary research integrating pharmacology, phytochemistry, toxicology, and clinical sciences will be essential to translate *Acacia auriculiformis* from traditional medicine into evidence-based clinical applications. Such efforts could ultimately lead to the development of safe, effective, and affordable plant-derived therapeutic agents for the management of various chronic and infectious diseases.

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