

Review Article

The therapeutic potential of Delonix Regia: An updated review

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Abstract

Delonix regia is a species of flowering plant in the pea family (Fabaceae) and subfamily Caesalpinioideae. It is distributed in Madagascar, India, Africa, and Northern Australia. This review article is a summary of significant scientific literature on *D. regia* from several research databases. The review has revealed that *D. regia* is rich in alkaloids, flavonoids, steroids, tannins, and phenolic compounds, all of which contribute to a variety of biological properties such as anti-inflammatory, antimicrobial, antidiabetic, wound-healing, hepatoprotective, and antioxidant effects. Most previous reviews on the plant merely provided general phytochemical overviews. In contrast, the present review is focused on the specific phytoconstituents of different parts of the plant (flowers, leaves, bark, seeds, and roots), and these phytoconstituents were correlated with experimentally validated therapeutic outcomes reported in scientific studies. The review highlighted the unique therapeutic potential of *D. regia* and identified the research gaps, such as limited clinical validation and lack of extract standardization, while proposing directions for future studies. These insights underscore the potential of the plant for use as a source of phytotherapeutic agents.

Keywords: *Delonix regia*, Royal Tree, Antioxidant, Anti-inflammatory, Antimicrobial, Wound healing

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INTRODUCTION

Complementary medicine and traditional healthcare systems in most regions of the world consider medicinal plants as essential parts of treatment [1]. For thousands of years, these plants have found applications in folk medicine for treatment of a wide range of diseases, and natural products of such plants have been considered the foundation for the discovery and development of modern pharmaceuticals [2-4]. These plants are considered a treasure trove of classical knowledge that has produced numerous flavors in traditions of medical treatments such as Traditional Indian and Chinese Medicines,

and Arabic-Islamic Medicine. The utilization of this classical knowledge has continued to this day, especially in the development of modern medicines [3]. The World Health Organization (WHO) estimates that 80 percent of the world population uses herbal medicine as the main source of healthcare. This has come as a result of rising concerns over the toxicity and side effects of modern allopathic medications [3,5]. Since plants naturally produce bioactive compounds in their metabolism, phytotherapy has become a promising area for addressing health problems in the world and for developing new therapeutic agents [5].

The etymology of the general name *Delonix* may

be linked directly to its Greek origins, specifically the terms *Delos*, which means *apparent*, and *onyx*, which means *claws*. The visible and characteristically curled petals of the flowers are responsible for this common name. The term *regia* is based on the Latin word *regis*, which denotes royalty, regality and magnificence. The plants belonging to the *Delonix* family are mainly evergreen plants characterized by open, expansive, and umbrella-shaped canopies. These plants are commonly referred to as flame plants [6].

Delonix regia (*D. regia*) is a species of flowering plant in the pea family *Fabaceae*, and subfamily *Caesalpinioideae*. It is a yellow-brown colored, medium-sized ornamental tree that is usually located in parks and gardens in tropical areas such as Taiwan, Vietnam, Malaysia, India, and the central region of South America [7,8].

The plant species is popularly referred to as 'Royal', 'Flame tree', 'Flamboyant', 'Gulmohar', 'Shima', 'Sunkesula', 'Chura', 'Radha', 'Gold mohur', 'Peacock flower', and 'Gulmohr', an indication of regional and national differences in nomenclature. The growth of this tree is dependent on the presence of light, as it exhibits weakened development in shaded environments. It grows in regions with both abundant and limited precipitation. Deciduous plants are predominantly found in regions with prolonged and well-defined dry seasons [6,9].

Delonix regia is a tree that grows to a height of 10–15 meters, with a girth of up to 2 meters. It has bipinnate, alternate, light green, feathery leaves, and roughly 10-25 pairs of pinnae, each having 12-40 pairs of small leaflets. Towards the tip of the twig, 15-30 cm-long, laterally-borne corymbs are present. Each corymb has loosely arranged, slightly fragrant and orange-red flowers that cover the tree from April to June. The petals, ranging from 5 to 6.5 cm in length and 2 to 3 cm in width, are broadly spoon-shaped [9,10].

Several reviews have summarized the phytochemistry and pharmacology of *D. regia* [9,11,12]. However, most of these reviews are essentially broad overviews lacking systematic differentiation between plant parts or analysis of mechanistic links to therapeutic outcomes. The novelty of the present review lies in the organization of phytochemical data for each part of the plant (flowers, leaves, bark, seeds, and roots). It also connects the bioactive constituents to the pharmacological effects of the plant. Finally, it identifies research gaps and possible future directions to move with respect to clinical

applications.

Distribution of phytochemical constituents in parts of *D. regia*

The bright ornamental flowers of *D. regia* are cultivated in the tropical and subtropical regions of the world [13]. In addition to its aesthetic importance, this plant has also received a significant amount of scientific interest due to its complex phytochemical profile, which may potentially have enormous medical and therapeutic benefits. This part of the review is aimed at describing a broad spectrum of bioactive compounds in various parts of the plant. It also analyzes the essence of the phytochemical compounds present in the plant.

Flowers

The biochemistry of *D. regia* flowers is complicated. It provides a wide range of compounds for executing multiple biological processes. On the molecular scale, these complex structures are full of an impressive array of biologically active compounds, which are important for plant survival and reproduction [14]. Table 1 shows the various phytoconstituents found in the flower of *D. regia*.

Anthocyanins are one of the most significant flavonoid compounds, which are considered the main source of the red coloration found in flowers. These water-soluble pigments are accumulated in the petal vacuoles. The intensity of the color is subject to pH and the presence of co-pigments as well as metal ions. Thus, the flowers are red when the environment is acidic, but turn purple or blue when under alkaline conditions [15,16]. Carotenoids also add yellow and red colors to flowers, and protect flower tissues against light-induced damage [17,18]. Other important compounds of the flowers are phenolic glycosides, tannins, alkaloids, saponins, and steroids, in addition to essential oils [14,19,20].

Leaves

A high abundance of secondary metabolites was identified through analysis of the phytochemical constituents of the leaves. Alkaloids, flavonoids, proteins, amino acids, carbohydrates, diterpenes, and steroids have been detected, indicating the biochemical richness of the leaves [13,25]. These components provide the leaf extract of the plant with its pharmacological properties. All the identified phytoconstituents are summarized in Table 2. Various proportions of hydrolysable and condensed tannins, which have defensive roles in the plant, have also been reported, indicating

promising therapeutic effects [26,27]. The presence of a diverse range of saponin glycosides indicates that the leaves have enhanced herbivore repulsion. Not only do terpenoids (especially monoterpenes and sesquiterpenes) give plants their aromatic properties, but they also have fundamental ecological functions in plant-insect interactions [14,28]. These phytochemicals aid in protecting the plant against predators.

Bark

The chemical structure of the bark tissue of *D. regia* is complicated. This fulfils two purposes:

protection and transport. The bark contains a lot of alkaloids and it serves as an effective chemical repellent against herbivores and pathogens [14,31,32]. It also contains procyanidins, which are associated with the structural stability and antioxidant properties of the bark. Beta-sitosterol is also central in membrane structure and regulation of cell signaling [33,34]. One of the components that has potential application in the pharmaceutical industry is lupeol, which has significant anti-inflammatory and anticancer effects [14]. Table 3 shows an overview of the various phytoconstituents found in the bark of *D. regia*.

Table 1: Phytoconstituents of *D. regia* flowers

Chemical components	Active ingredients	Reference
Flavonols	Quercetin 3-O-robinobioside, Quercetin trihexoside, Quercetin 3-O-(rutinoside, galactoside, or glucoside); Cyanidin 3-(β -D-rutinoside, β -D-glucoside, or gentiobioside); Kaempferol, Isorhamnetin rhamnosyl hexosides; and Quercetin.	[9,12,21,22]
Phenolic acids	Gallic acid, protocatechuic acid, 2-hydroxy 5-[3, 4, 5 trihydroxyphenyl) carbonyl oxy] benzoic acid	[23]
Glucoside	12, 15-Dihydroxy-chol-8-en-24-oic-acid-3-oxy-6'-acetyl-glucoside and sodium, potassium adduct of 12, 15-dihydroxy-5-chol-9-en-24-oic-acid-3-oxy-rhamnosyl-rhamnoside, Stigmasten-diol-3-O-glucoside.	[12]
Carotene hydrocarbons	Phytoene, phytofluene, β -carotene, pigment X, C-carotene, γ -carotene, prolycopene, neolycopene, lycopene.	[13]
Ketocarotenoid	Astaxanthin	[13]
Anthocyanins	Peonidin-3-O-glucoside and petunidin-3-O-acetyl-glucoside, as well as a range of organic acids such as α -ketoglutaric acid, oxaloacetic acid, pyruvic acid, and glyoxylic acid and the carotenoid zeaxanthin.	[13,24]

Table 2: Phytoconstituents of *D. regia* leaves

Chemical components	Active ingredients	References
Flavonoids	Kaempferol derivatives • Kaempferol-3-rhamnoside • Kaempferol-3-glucoside • Kaempferol-3-rutinoside • Kaempferol-3-neohesperidoside Quercetin derivatives • Quercetin-3-rhamnoside • Quercetin-3-rutinoside • Quercetin-3-glucoside	[9,29]
Tannin	Prodelphinidin (PD) Propelargonidin (PP)	[30]
Triterpenoidal saponin	Lupeol	[12]
Sterols	β -Sitosterol	[12]
Others	• L-Azetidine-2-carboxylic acid • Proline with free OH group • Phytol • Oleanoic acid • Coumarin 7,8-dihydro-7-hydroxy-6-methoxy-8-oxo • Scopoletin • Squalene • Vitamin E • Protocatechuic • Salicylic acid	[12,30]

Table 3: Phytoconstituents of *D. regia* bark

Chemical components	Active ingredients	References
Polyphenols	Proanthocyanidin	[14,30,35]
Tannins	Propelargonidin, procyanidin	
Alkaloids	Indole, isoquinoline	
Sterols	β -Sitosterol, stigmasterol	
Triterpenoidal saponins	Lupeol, epilupeol	
Flavonoids	Leucocyanidin	
Pigments	Carotene, auroxanthin	
Other compounds	p-Methoxybenzaldehyde	
	Hydrocarbons	
	Phytotoxins	
	Proline with a free OH group	
	Gallic acid	

Table 4: Phytoconstituents of seeds of *D. regia*

Chemical component	Active Ingredients	References
Fatty acids	Linoleic acid, malvalic acid (7-(2-octacyclopropen-1-yl) heptanoic acid), sterculic acid (8-(2-octacyclopropen-1-yl) octanoic acid), myristic acid, palmitic acid, stearic acid, oleic acid, omega-3, omega-6 polyunsaturated.	[14]
Amino acids	<i>Trans</i> -3-hydroxy-L-proline, γ -methyleneglutamic acid, γ -methyleneglutamine.	[41]
Hydrocarbons		[12]
Sterols	Stigmasterol, sitosterol, phytol, ergost-4-en-3-one, ergost-5-en-3-ol.	[12]
Carbohydrates and proteins	Galactomannan, crude protein.	[12]
Tannins	Propelargonidin, procyanidin.	[12]

Seeds

The seeds contain a fortified composition of bioactive compounds, which are necessary for plant reproduction and survival. The proteins found within the seeds contain balanced amino acids, which provide the nutrients required for the growth of the plant [36,37]. In addition, the fatty acids present are necessary, particularly the omega-3 or omega-6 polyunsaturated fatty acids, as they act as energy storage and vital components of the membrane structure [38,39]. The energy stored in complicated polysaccharides, e.g., galactomannan, is vital for providing moisture in the seeds. The seeds also contain protease inhibitors, which are involved in defense mechanisms that help to guard seed proteins against early destruction and pathogens [14]. The other phytochemicals found in the seeds are flavonoids, fixed oils, fats, steroids, triterpenoids, and carbohydrates [40]. Table 4 shows the different phytochemicals present in the seeds of *D. regia*.

Roots

The roots of *D. regia* contain several bioactive compounds comprised of alkaloids, saponins, flavonoids, and steroids. Furthermore, the roots

are abundant in secondary metabolites such as tannins, sterols, phenols, cardiac glycosides, and terpenoids [42]. The roots also contain proteins, lectins, fatty acids, and free amino acids [13].

Phytochemical distribution as a function of plant parts

Delonix regia is a well-known plant utilized in folk medicine, and its pharmacological properties are numerous. In this section, the therapeutic benefits of the *D. regia* plant are explained, as well as the way these benefits may be utilized for curing several health disorders.

Anti-inflammatory effect

Anti-inflammatory action is one of the most remarkable therapeutic qualities of *D. regia*. This property is attributable to the presence of large amounts of flavonoids and triterpenes in the plant. Inflammatory processes are controlled by flavonoids and triterpenes, which are biologically active substances. Some of the major pathways involved in the regulation of inflammation entail the inhibition of proinflammatory cytokines such as TNF- α , IL-1 β , IL-6 and IL-12. *Delonix regia* also modulates the expressions of toll-like receptor 4 (TLR4), nuclear factor kappa B (NF-K65), and

myeloid differentiation primary response gene 88 (MyD88) and the inflammatory enzyme cyclooxygenase-2 (COX-2). Another pathway involved in the regulation of inflammation is control of the activity of inducible nitric oxide synthase (iNOS), which leads to reduced production of prostaglandins and reactive nitrogen species. The apigenin and quercetin derivatives of flavonoids contribute to the inhibition of the COX enzymes. They are complemented by triterpenes, which stabilize the cell membrane and reduce the permeability of the vascular walls (Figure 1). Studies in animal models have demonstrated the remarkable anti-inflammatory potential of *D. regia* extracts, which may justify the traditional use of the plant for therapeutic applications in human disorders such as arthritis, asthma, and inflammatory bowel disease [14,43,44].

Delonix regia leaf powder has been used for reduction of inflammation. In a 2012 study, the anti-inflammatory property of *D. regia* was evaluated using rat paw edema and cotton pellet granuloma models [45]. The ethanolic extract produced a significant anti-inflammatory effect at a dose of 400 mg/kg body weight, when compared to the standard drug indomethacin, which was used at a dose of 10 mg/kg body weight. In addition, methanol extract of *D. regia* leaves and stems, which contain flavonoids, alkaloids, and phenols, was found to have significant anti-inflammatory effects (membrane-stabilization up to 47.77 %). The extract also displayed superior antioxidant properties in DPPH, FRAP, and TAC assays, when compared to the standard drug indomethacin [46]. Furthermore, in a study conducted by Kurup and

Tiwari [47], it was found that the methanol extract of the bark, which is abundant in alkaloids and flavonoids, produced a high level of anti-inflammatory effect. It was established that the different components found in the crude extract played synergistic roles in improving the anti-inflammatory effect, as the *in vivo* study showed that the extract had great anti-inflammatory potential at a dose of 400 mg/kg body weight.

Antioxidant activity

Delonix regia has high antioxidant activity, which is mainly due to its richness in flavonoids and phenolic compounds. These phytochemicals, e.g., quercetin, kaempferol derivatives, gallic acid, and protocatechuic acid, confer anti-oxidative properties on *D. regia* against reactive oxygen species (ROS), reduce oxidative stress, and protect cellular components through electron donation, metal ion chelation, and neutralization of free radicals. Methanol extracts of the leaves, flowers and stems of *Delonix regia* have shown high degrees of radical scavenging properties in different *in vitro* tests involving DPPH, hydroxyl, and nitric oxide radicals. It is worth noting that the leaf and flower extracts were more effective antioxidants than standard antioxidants such as BHA and BHT, with leaf extract having the highest reducing power in some of the assays. These extracts were also very effective in inhibiting lipid peroxidation, especially in neural tissues. Moreover, the antioxidant activity of *D. regia* was comparable to that of the well-established antioxidants such as ascorbic acid and quercetin.

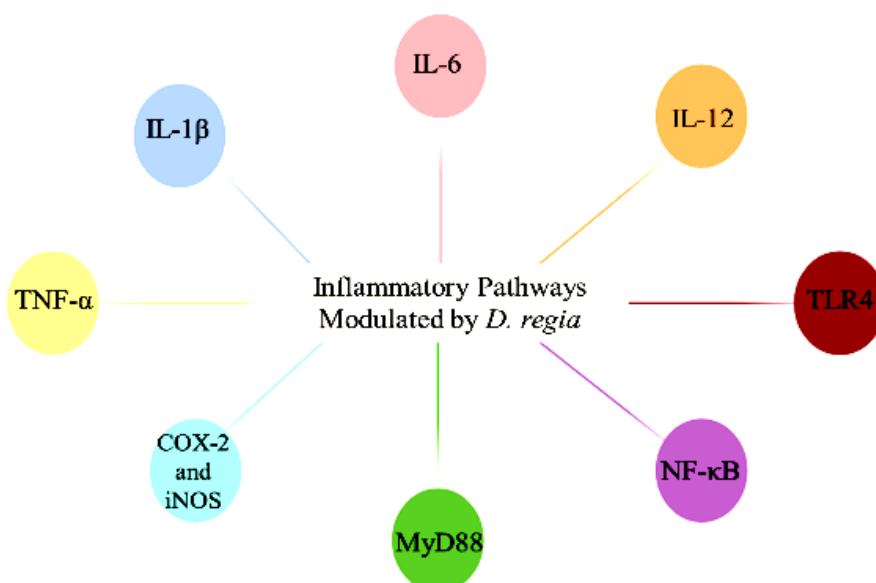


Figure 1: The anti-inflammatory effects of *D. regia*

This was evident in the low IC₅₀ values, which are consistent with its therapeutic potential in the management of oxidative stress-related diseases such as neurodegenerative diseases, cardiovascular diseases and some cancers [30].

In a study, Ebada *et al* [48] investigated the *in vitro* antioxidant, anticancer and antibacterial activities of isolated polysaccharides and pigments from *D. regia* flowers. The results obtained confirmed the presence of anthocyanins and carbohydrates, which contribute to these potential activities. Another study [49] using the 2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid (ABTS) radical scavenging assay, demonstrated the antioxidant properties of extracts of *D. regia* leaves and flowers. The authors found that the optimum antioxidant activity of the leaf extract (IC₅₀ = 22.50 µg/mL) was higher than that of the flower extract (IC₅₀ = 24.88 µg/mL).

Antimicrobial activity

Dolenix regia pigment extract (DRPE) and extracts of the leaves, stems, roots, bark, and flowers of *D. regia* produced good antibacterial performance against diverse Gram-positive bacteria (*Staphylococcus aureus*, *Enterococcus faecalis*, and *Listeria monocytogenes*) and Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella Typhimurium*) [42,48,50]. The antibacterial activity of these extracts was determined using agar well diffusion technique, in addition to minimum inhibitory concentration (MIC). The results obtained suggest a wide-range antimicrobial action of *D. Regia*. In addition, the antifungal effects of leaf and bark extracts were found to be effective against a wide range of fungi such as *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Microsporum canis*, *Candida albicans*, *Aspergillus otrasae*, *Aspergillus niger* and *Fusarium solani* [51]. The antimicrobial properties of *D. regia* are attributed to its chemical constituents, i.e., alkaloids, phenolic compounds, anthocyanins, and flavonoids, as well as other secondary metabolites. It is necessary to add that the sterol derivatives containing 2-hydroxyl group (e.g., 2-sitosterol, hordinine and others) have also been reported to be bioactive antimicrobial agents, in the context of bacterial cell membrane disruption and inhibition of protein synthesis. An example is tannic acid, a phenolic acid that exerts anti-pathogenic effects through protein precipitation. The aggregate effect of the phytoconstituents justifies the historical importance of *D. regia* in the treatment of infectious diseases and underscores its potential in supplying new

antibacterial agents, especially in the face of growing antimicrobial resistance [14,52].

Hepatoprotective activity

The protective benefits of ethanol extracts of *D. regia* flower and its composition against carbon tetrachloride-induced hepatic cell damage have been assessed. Analyses of data from histopathological studies and serum levels of hepatic enzymes showed that ethyl acetate extract had a strong protective effect, which was exceeded by those of ethanol and n-hexane extracts. The observed effect was attributed to flavonoids. HepG2, a fatal liver cancer cell line, has been tested to determine the defensive effect of composites, especially flavonoids, sterols, and triterpenes (from ethanolic extract). A higher level of defensive effectiveness was demonstrated when compared to doxorubicin. An ethanolic extract from *D. regia* was shown to have significant hepatoprotective effect in a study conducted by Viswanathan *et al* [30]. In a study by Anil Kumar *et al* [53], it was found that ethanol extract of *D. regia* leaves produced hepatoprotective activity against acetaminophen-induced liver toxicity in rats, which significantly reduced the high serum levels of SGOT, SGPT, SALP, and bilirubin [54]. It has been reported that methanol extract of aerial portion of *D. regia* (400 mg/kg) exerted hepatoprotective action against CCl₄-induced hepatotoxicity in Wistar rats, and also significantly decreased serum levels of AST, ALT, ALP, albumin, total protein and bilirubin, thereby demonstrating its potential hepatoprotective effect. Moreover, an ethanol extract of the flowers showed great hepatoprotective effect against CCl₄-induced liver damage in rats. This may be attributed to the free radical-scavenging capacity of the flavonoid-rich fraction [55].

Elhassaneen *et al* [56] investigated the hepatoprotective effect of *D. regia* seed powder (DRSP) against CCl₄-induced liver injury in rats. The extract (DRSP) had significant effects on the parameters of serum lipid profile, liver functional parameters, and histopathological changes. These findings justify the use of DRSP for preventing and controlling hepatotoxicity. The findings also contribute to the benefits of diet modification and supplementation with DRSPs in the treatment of chemical-related poisoning of the liver, e.g., CCl₄ poisoning.

Wound healing effect

Several studies have established that *D. regia* is an effective extract for wound healing. The study by Modi *et al* [12] indicated that aqueous extracts

of *D. regia* flower were significantly more active in wound healing when compared to the ethanolic extract or conventional povidone-iodine ointment (5 %). This was evident in a higher degree of wound contraction, higher tensile strength and lower content of hydroxyproline, and reduced epithelialization time. The wound-healing effects of 70 % ethanol and aqueous extracts of *D. regia* flower were compared using incision wound model, excision wound model, and dead space wound model [57]. It was found that the presence of flavonoids was responsible for the wound-healing activity of the extract. The study by Lima *et al* [58] revealed that galactomannan extracted from the seeds of *D. regia* had strong anti-inflammatory and wound-healing effects in mice. It increased wound healing through decreases in oxidative stress and levels of pro-inflammatory cytokines (IL-1 2 and IL-6), and upregulation of growth factor expressions and collagen deposition.

Vasodilatory, cardioprotective, and anti-diabetic effects

A study by Wang *et al* [8] showed that the mortality of a mouse model of isoproterenol (ISO)-induced cardiac injury and hypertrophy was decreased by *D. regia* leaf extract (DRLE) at a dose of 400 mg/kg/day. The extract (DRLE) exhibited cardioprotective effects by promoting vasodilation. Moreover, DRLE administration led to decreased serum levels of creatine phosphokinase, LDH, GOT, and TNF-alpha, along with increases in nitric oxide levels in ISO-

injured mice. In the *in vitro* study, DRLE induced a dose-dependent vasodilatory effect on porcine coronary arteries. It has been reported that methanol extract of aerial parts of *D. regia* exhibited antidiabetic effects. This was attributed to the antioxidant and α -amylase inhibitory effects of phenolic and flavonoid compounds present in the extract. In streptozotocin–nicotinamide-induced diabetic models, oral administration of the extract improved glucose tolerance, leading to dose-dependent reduction in hyperglycemia, as well as improvements in hematological and biochemical parameters, and restoration of oxidative stress markers such as SOD, CAT, and H_2O_2 . The maximum hypoglycemic effect was observed at a dose of 500 mg/kg, with efficacy comparable to that of glibenclamide. Comet assay studies demonstrated strong genoprotective potential, with the highest effect at a dose of 100 μ g/mL. Collectively, these findings demonstrate that the methanol extract of the aerial part of *D. regia* exhibited hypoglycemic and antidiabetic activities [59]. The use of ethanol leaf extract of *D. regia* (1000 mg/kg) showed a strong anti-diabetic effect on alloxan-induced type-2 diabetic rats. The extract significantly reduced levels of fasting blood glucose, total cholesterol, triglycerides, SGPT, SGOT and serum creatinine ($p < 0.001$). It also increased HDL concentration, thereby reducing LDL levels. These findings show the potential of *D. regia* as a natural drug in the management of diabetes and other related metabolic syndromes [60].

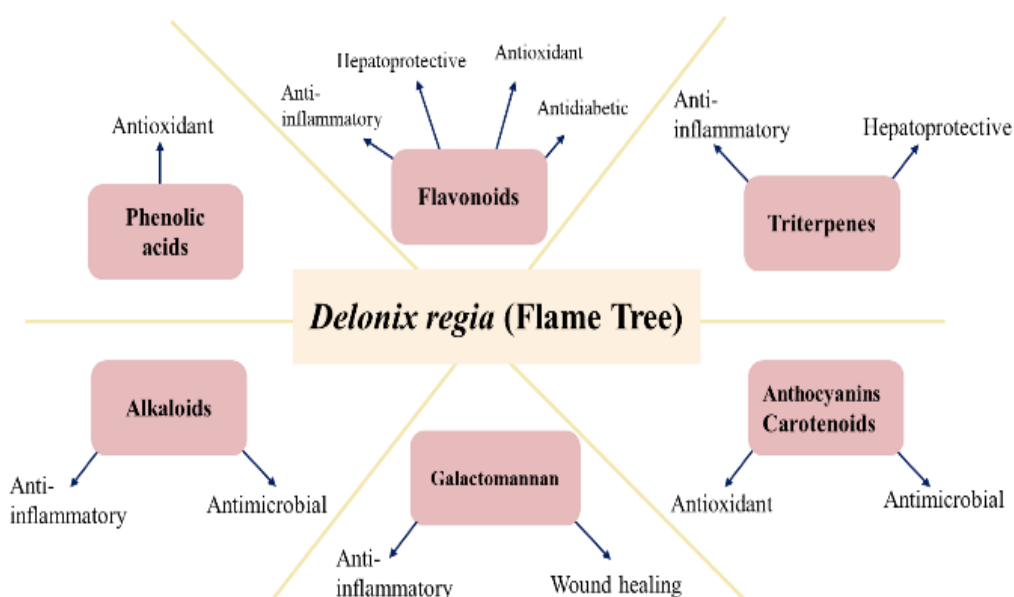


Figure 2: Phytochemicals of *D. regia* and their pharmacological properties. The central node represents *D. regia* (Flame Tree), surrounded by major classes of phytochemicals (pink boxes), each connected to the experimentally validated pharmacological effects. The diagram highlights the multidimensional therapeutic potential of the plant

Conclusion and future directions

Delonix regia is admired as an ornamental plant, and it has also gained increased attention as a source of a wide range of phytochemicals such as alkaloids, flavonoids, steroids, tannins, and phenolic compounds. It has been proposed that the structural complexity and synergistic interactions among these compounds underline its wide-range of biological effects. All parts of the plant (flowers, leaves, bark, and seeds) contain different sets of bioactive constituents which account for its reported antioxidant, anti-inflammatory, antimicrobial, wound-healing, hepatoprotective and antidiabetic effects. Even with this promising potential, the available scientific knowledge remains limited as a result of variations in methodology involving non-standardization of extraction methods, small number of studies conducted *in vivo*, and very limited clinical validation. Therefore, future studies should focus on:

- Standardization of extracts to ensure reproducibility of pharmacological effects when the biological activity is examined *in vitro* or *in vivo*.
- Focused on the mechanisms of action of the bioactive components so as to clarify molecular pathways and structure–activity relationships.
- Evaluation of the safety of the extracts so as to validate their usage in traditional medicine and to determine clinical doses.
- Investigation of the pharmacokinetics and bioavailability of the medicinal herb, which is essential for the determination of the potential of using the plant extract or derived products in clinical applications.
- Use of clinical trials to validate the observed efficacy in humans. This will act as a linker between laboratory findings and therapeutic applications.

It is expected that if these future directions are focused on, *D. regia* could advance from a traditionally valued plant into a precisely validated source of phototherapeutics, thereby supporting the integration of folk medicine with pharmaceutical medicine.

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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