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Dillenia indica in the Era of Sustainable Bioprospecting: Integrating Phytochemistry, Green Extraction, Genetic Diversity, and Biomedical Applications

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Abstract

Dillenia indica, or Elephant apple, is a traditional medicinal and food plant that has undergone additional scientific investigations in the field of sustainable bioprospecting. The current review summarizes knowledge on the phytochemistry of *D. indica*, focusing on important bioactive constituents (flavonoids, phenolic compounds, triterpenoids, and tannins) that contribute to its antioxidant, anti-inflammatory, and antidiabetic properties, as well as its antimicrobial and anticancer effects. Emerging green extraction methods (including ultrasound-assisted, microwave-assisted, enzyme-assisted, and supercritical fluid methods) are highlighted for improving extraction efficiency while mitigating environmental impacts and reducing solvent toxicity. Preclinical pharmacological evidence and mechanistic insight will be used to evaluate the biomedical potential of *D. indica*. Genetic diversity, molecular markers, and control of biosynthetic pathways are also discussed, and opportunities for breeding and genetic improvement of D. indica to enhance phytochemical yield, stress resistance, and sustainable farming are outlined. The use of omics technology with conservation breeding strategies is being proposed as a strategy for achieving consistent quality, scalable production, and long-term sustainability of *D. indica*. This multidisciplinary framework provides a basis for developing *D. indica* into a model plant species for eco-friendly drug discovery, nutraceutical development, and sustainable agro-biotechnological applications.

1. INTRODUCTION

Medicinal plants are used as a major part of healthcare globally, and approximately 80% of the world's population relies on medicinal plants for their primary healthcare needs (Wijesekera, 2017). An increase in interest in using natural medicines is being driven by an increasing number of people that want safer medicines and increases in antimicrobial resistance, increasing prevalence of metabolic conditions and the global trend towards more green holistic sustainable development across industries including development technology and therapeutic development for different types of medical disorders, particularly metabolic disorders, antimicrobial resistance and many other disorders (Abdallah *et al*., 2023). Within this environment, *Dillenia indica* L., offers great promise as a candidate for sustainable bioprospecting due to its multiple functional applications, presence of bioactive compounds, ethnomedicinal use for several medical disorders and growing number of applications in plant-based medicine, functional food etc. This plant, which has a widespread distribution in India, Nepal, Bangladesh, Sri Lanka, Bhutan, Malaysia, and Thailand, has reported traditional use in treating gastrointestinal conditions, fever, inflammation, diabetes, infections, and reproductive issues, among various other conditions of comparable significance. The plant's fruit has been utilized as a food, pickle, and functional food. The bark and leaf of this plant are used in traditional Ayurvedic medicines as well as in tribal medicines since long (Kumar *et al*., 2018). However, in recent studies, especially in the last decade, a variety of new potential applications have been identified. In studies conducted on *D. indica*, a larger variety of secondary metabolite classes and biological activities have been discovered compared to those established in existing literature, which include: betulinic acid, stigmasterol, quercetin, luteolin, kaempferol, n-hydroxybenzoic acid, hydroxycinnamic acid derivatives, naphthoquinones, proanthocyanidins, saponins, and polysaccharides (Singh & Saha, 2018). The variety of phytochemicals detected in *D. indica* has continued to rise with the advancement in technology such as LC-MS/MS, GC-MS metabolomics, and HPTLC, among others, including NMR analysis (Gandhi & Mehta, 2013). Coupled with the use of these new technologies, over time, there has been increasing utilisation by researchers of green methodologies for extraction in phytochemicals. These include ultrasound-assisted extraction, supercritical CO2 extraction, hydrotropic extraction, and deep eutectic solvent extraction, among others, as ecologically friendly alternatives to conventional solvent extraction methodologies for phytochemical extraction. These methods increase the efficiency of *D. indica* extraction and reduce energy consumption and the amount of chemicals utilized, aligning with SDG-12 Responsible Consumption and Production and SDG-13 Climate Action. Improvement in biotechnology continues to add increased value to the species *D. indica*. Thus, the development of various nanoparticle formulations exhibiting antibacterial, anti-cancer, and antioxidant activity was enabled by using environmentally sound technologies in the manufacture of nanoparticles from plant extracts. (Gupta *et al*. (2024). By incorporating biomolecules from *D. indica* into microcapsules, functional meals, and smart delivery systems, this species can create new opportunities for a range of industrial purposes (Bora *et al.,* 2025). Notwithstanding the achievements, there are still several challenges to overcome before the commercial value of *D. indica* and its biomolecules can be realized. Many of the chemical pathways within the plant have not yet been investigated, and therefore many molecules that may possess therapeutic properties have yet to be identified; *D. indica* is currently under threat in its natural environment; limited clinical trial experience has been completed on the use of *D. indica*-based therapies; and a very few bioavailability studies have been conducted. Moreover, *D. indica* has not yet been classified as a standardized phytopharmaceutical despite its potency for broader therapeutic uses. The main objective of this review would be to provide a new perspective on how *Dillenia indica* can be explored for bioprospecting with a focus on developing new industries at the intersection of traditional knowledge and modern advancements.

2. Morphological and Botanical Description of *Dillenia indica*

According to Rahman (2022), *Dillenia Indica* L. is an extremely unique tree that is an evergreen, has large, ridged leaves, and a very different type of fruit (Dilleniaceae). When growing naturally, the tree is between 8 and 15 meters tall, but if it is given optimal growing conditions, it can be much taller (Desanayaka *et al.,* 2022). Its trunk has a generally thick and straight appearance and becomes covered with irregularly peeling greyish-brown bark with age. Its main branches are horizontal, bearing large alternate leaves along their length (Cowen, 1952). The leaves are either oblong or oval-shaped and have a tough leathery texture and great glossiness, with prominent parallel veins, which extend from the midrib toward the leaf margin. According to Shome *et. al.,* (1979) strong venation was selected because strong venation provides a quick way for the tree to transport water from one place to another, and the tree has structural integrity; this is particularly important in regions with warm and moist environmental conditions (high humidity and seasonal monsoons). The tree is characterised by producing large, attractive flowers which may be single or grow on clusters. The flowers of this tree are typically white, have fleshy petals with a very pleasant fragrance, and produce many bright yellow stamens surrounding a mulitlobed stigma located at the centre of the flower (Endress, 1997). It generally flowers in the early morning hours to correspond with the activity of its various pollinators. Honey bees, beetles and nocturnal insects serve as the primary pollinators for the species *Dillenia indica*. These animals produce reproductive, viable fruit and seeds for this species in all its geographic ranges where it occurs (Rizzo *et al*., 2019). *Dillenia indica* normally produces large, rounded fruits in case reproduction occurs since this is characteristic of this species. The fruits comprise of several fleshy, rounded carpel bodies that grow in the form of concentric circles around each fruit's hollow center (Petit *et al*. 2024). The fruit's average diameter measures up to 8 cm to 15 cm. The outer layer remains green/yellow until the fruit has completely matured at which period it is hardened into a solid, heavy, and dense wood-like carpel. Inside *Dillenia* *indica* carpels, there exists a cavity composed of many light brown wedge-shaped seeds surrounded by a pulp with a sour taste. The jelly-like pulp helps in dispersing the seeds by means of water or through consumption by animals because it retains moisture there inside.

Figure 1. Showing the morphological view of *Dillenia indica*

The distribution of *D. indica* is extensive throughout the Tropical/Subtropical areas of Southeast Asia. It is a Native Species of India, Nepal, Bangladesh, Sri Lanka, and Bhutan, extending from these countries into Myanmar, Thailand, Malaysia, and Indonesia (Rahman, 2022). In Nature, this species does best in Warm and Humid climates where average annual Precipitation is between 1500-3500 mm. The species can be found naturally growing along the banks of rivers and lakes, at the edges of forests, in the valleys (moist valley), and at the edges of Wetlands, where the soil is rich in organic matter and has a high capacity of retaining moisture (Venugopal & Liangkuwang, 2007). The species is also Flood Tolerant, allowing it to occupy riparian zones more effectively compared to other Species of Forest Plants. However, the species is Drought Sensitive and grows best in areas that are consistently accessible to water (Glenz *et al*., 2006; Haq and colleagues (2023) indicate that *Dillenia indica (D. indica)* is ecologically important to maintain forest biodiversity because it is consumed by a variety of organisms such as birds (e.g. hummingbirds), bats, and many different types of mammals. These organisms will aid in seed dispersal and help *D. indica* to have a successful regeneration. Due to its adaptive nature and ecological importance, *D. indica* is now being recognized by more people as an important species for future sustainable bioprospecting and promotion of agroforestry. *D. indica* has a large distribution (across a wide range of eco-geographical areas) and can withstand and recover from fluctuations in climate, making it a valuable resource for future agriculture that is climate resilient, conservation planning, and green biotechnological applications.

Ethnobotanical importance

In traditional food and medicine, the jelly-like pulp of the fruit *D. indica* is utilized during the production of food and medicine in traditional herbal medicine. Moreover, the species *Dillenia indica* has cultural, historical, and ethnobotanical significance to the people of South and Southeast Asia because it serves as a food and medicine. The people of Northeast India, Assam, Tripura, and certain areas along the Himalayan foothills use the fruit from this tree in a food way. The fruit is eaten regularly in curries, pickles, chutneys and is made as a fermented food product (Chakraborty *et al.,* 2025). Because of its high acid pulp, it has long been viewed as good for digestion. It has been given to individuals as a treatment for constipation, dyspepsia, and irregularities in bowel movements. Multiple Indigenous medicine systems state that the decocted fruit is recommended for individuals with Diabetes, respiratory congestion, and inflammatory diseases (Saikia *et al*., 2023).The leaves are used topically on open wounds, ulcers and swollen areas due to arthritis. They have also been used in infusion form to reduce elevated body temperature (fever) and to help in the healing of the body from ailments of the skin. The bark (which is high in tannins) is used to treat diarrhea, microbial infections and gastric ulcers (Kviecinski *et al.,* 2017). According to Khatun and Sen. (2025), the tribal medicine men of Assam, Meghalaya, and some areas of Bangladesh use roots from the plant for treating snakebites, fatigue, urinary problems, etc., as evidence of how historically these tribes have used the plant in a holistic way. The historical ways that tribal cultures have used plants have provided information that has led to modern scientific studies on the pharmacology of these plants and identified the active ingredients in plants that have medicinal benefits.

3. Phytochemical and Bioactive potential of *Dillenia indica*

The complexity of *Dillenia indica's* phytochemistry has recently been better understood thanks to the development of sophisticated analytical techniques (Doan *et al.* 2023). The advantage afforded by being able to analyze spectroscopically and chromatographically for all the components offered by the plant *Dillenia indica* has enabled a better and more comprehensive understanding of its chemistry, which enabled the identification of various biologically active compounds with immense value in developing new drugs, nutraceuticals, and various uses of *Dillenia indica* (Ebrahim *et al.* 2024). Whilst earlier studies primarily focused on the identification of flavonoid, phenolic acid, terpenoid, and tannin constituents of *Dillenia indica* (Gogoi *et al*. 2025), in the past 10 years extensive research using several advanced techniques, including LC–MS/MS, GC–MS, UHPLC, FTIR, HPTLC, 1D and 2D NMR spectroscopy have allowed researchers to identify many more chemical constituents than previously identified. These advanced techniques have led not only to the identification of the major bioactive constituents of *Dillenia indica* but also to the identification of a much larger number of minor or previously unreported phytochemicals, contributing to the diversity of the pharmacological profile of the plant. Phytochemicals from *D. indica's* parts (fruit, bark, leaves) represent a vast majority of all Flavonoids available (Harborne 1989). Commonly detected flavonoidic phytochemicals include myricetin, quercetin, kaempferol, apigenin, luteolin, epicatechin, catechin. Aside from its antioxidant and anti-diabetic effects, flavonoids also possess an anti-inflammatory property because it has the capability to either donate a hydrogen atom or chelate a metal ion, which will result in the reduction of free radicals due to its interaction with enzymes involved in carbohydrate metabolism and inflammation. (Shamshudin *et al.* 2022).

Another large group of metabolites in *D. indica* are those of phenolic acids. Examples of these compounds include ae, syringic acid, and gallic acid. The reliable identification of these phenolic acid compounds in *D. indica* was achieved with LC-Mass Spectrometry and HPLC (Datta *et al*., 2018). For example, one such contribution to *D. indica's* ability to scavenge free radicals is the contribution of several free radical scavenging activities (Saleem *et al.,* 2022). Their multifunctional biological properties are attributed to their ability to bind to free radicals, regulate the expression of genes associated with oxidative stress, and prevent lipid peroxidation (Rao & Zheng, 2025). An adequate amount of hydrolyzable tannins and ellagic acid derivatives in addition to the phenolic content, within the pulp of fruits adding to its overall astringent and therapeutic effects (Yang & Liu, 2014). Within the group of triterpenes and terpenoids, betulinic acid, oleanolic acid, ursolic acid, lupeol, and several other derivatives of amyrin have been repeatedly demonstrated by different authors through phytochemical analysis (Parvez *et al.,* 2018). More importantly, the phycochemical components described above serve as a biochemical basis upon which many of the plant's pharmacologic properties are based-particularly for the anticancer, anti-inflammatory, and antimicrobial properties attributed to plants. One illustrative example is betulinic acid, which can induce cancer cell apoptosis by its ability to modulate mitochondrial pathways. Ursolic and oleanolic acids have anti-inflammatory and antidiabetic activity; they regulate nuclear factor pathways such as NF-kappa B, PI3K/Akt, and PPAR-gamma. The fruit and bark of *D. indica* are also rich in steroid compounds, including β-sitosterol, stigmasterol, and campesterol. *D. indica* is a very valuable source for supplement and food product development with an emphasis on boosting cardiovascular health benefits because it is a plant sterol with demonstrated lipid-lowering properties (Uttu *et al.,* 2023). According to pharmacological analysis, *D. indica's* cholesterol-lowering impact results from competitive reduction of the gastrointestinal tract's absorption of cholesterol (Bruckert *et al*., 2003).

Dillenia indica, a source of an evergreen plant from Southeast Asia, has in recent times been in consideration for its different uses and benefits as an herbal medicine. Recent research into *Dillenia indica* involves the metabolite compounds present in the plant with potential application as an herbal medicine. The different metabolites include naphthoquinones, comprised of dilleniin and iso-dilleniin. *D. indica* has small levels of naphthoquinones, but these compounds possess strong biological properties in cytotoxic and antibacterial effects. The naphthoquinones have the structural properties that enable interaction with the redox systems inside cells. The interactions provide the inhibition of microbial growth, as well as the inhibition of the cancerous cell signalling pathways. Naphthoquinones from *D. indica* have been identified as interesting leads for the discovery of new drugs based on their rare skeleton type. Polysaccharides and pectins from *D. indica* fruits enhance its nutritional and medicinal value. Fruit pulp with mucilaginous properties contains pectin polysaccharides like xyloglucans, arabinogalactans, and rhamnogalacturons and shows gastro-protective and prebiotic action and thus immunomodulation. Pulp polysaccharides may prove useful in improving gastrointestinal functions, overcoming gut microbial populations, and can be explored further for augmentation in therapy and management of metabolic disorders. Phytol, squalenes, furfural compounds, fatty acids with larger atomic numbers, alkanes, and various alcohols are some volatile and semi-volatile components, as revealed via GC-MS analysis (Gupta *et al.,* 2020). These act cumulatively on enhancing aroma and various antimicrobial properties and developing cosmetic properties associated with *Dillenia indica* (Rahman, 2022). FTIR profiling supports the existence of functional groups indicative of phenolic hydroxyls, carbonyls, aliphatic chains and glycosidic bonds; demonstrating the complexity of the chemical composition of the plant (Fu *et al.,* 2015). Currently, *Dillenia indica* should be seen as an integrated chemical system as opposed to simply a source of isolated active metabolites. Some synergistic action of these compounds may provide an explanation for the high performance associated with the traditional use of *Dillenia indica*. Recent developments in the characterization of this plant's chemistry support its relevance in fields such as pharmacognosy, drug development and recent advancements in nutraceuticals.

4. Sustainable Extraction techniques for *Dillenia indica*

Focusing on sustainable bioprospecting has led to an increased focus on environmentally friendly and energy-efficient extraction processes that are able to maintain the quality of thermally unstable biological active ingredients. As a result, with increasing interest in the phytochemical composition of *Dillenia indica*, the scientific community has been using more "green" extraction processes as replacements for traditional extraction with solvents. In spite of the high efficacy of traditional extraction techniques, they generally consume a greater amount of solvent than necessary and create a much greater ecological burden due to prolonged heating and use of solvents. For this reason, scientists all over the world have been implementing novel extraction techniques that include green chemistry concepts and lessen their environmental impact. One of the most used extraction technologies is based on acoustic cavitation, a process by which ultrasonic sound waves create, grow and collapse micro-bubbles in the extraction medium, called ultrasound-assisted extraction. This bubble implosion creates areas of very high pressure and temperature that result in the damaging of cell walls and increased solvent diffusion of plant phytochemicals to the extraction solvent. In *D. indica*, this method has been efficient for the extraction of flavonoids, phenolic compounds and some triterpenoids. Compared to traditional methods, it is faster and less damaging for heat-sensitive compounds. It results in higher yields compared to the standard maceration method, especially when producing bioactive extracts from fruit pulp and leaves.

Dillenia indica (Banna *et al.,* 2023) is another instance where microwave-assisted extraction is used as a sustainable technique for extraction. While using microwave-Assisted Extraction (MAE) in this technique, it is faster because of how quickly it heats both solvent and plant materials using microwaves, resulting in cell destruction and hence increased mass transfer of materials from plant extracts into solvents. Heating plant materials using microwaves is better since these microwaves can directly interact with molecules in plant materials, heating them really fast without destroying them because they do not have time to degrade (Hu *et al*., 2021). Research shows that using MAE can improve isolation methods for phenolic, sterols, triterpenoids, and maintaining purity and reducing isolation time (Singh & Saha, 2018). In addition, using MAE with either water or hydroalcoholic solvents in this technique is a good thing since it gives room to scale up this isolation technique in Pharmaceutical/Nutraceutical technology for increased production of pharmaceutical/nutraceutical compounds (Sarkar *et al.,* 2023). Further, enzyme-Assisted Extraction is a technique that attracts a lot of attention because it is used in isolation to increase isolation yield for intracellular metabolite. Additionally, a cell wall of a plant cell contains compounds such as cellulose, hemicellulose, pectin, and complex carbohydrates. Therefore, using available enzymes such as cellulase, hemicellulases, and pectinases would be ideal in this technique to increase isolation yield of intracellular metabolite. Furthermore, an increased amount of flavonoids, pectin, and polysaccharides in addition to increased isolation of phenolics of *D. indica* fruits and leaves using an enzyme-assisted technique of isolation, have been successfully achieved (Maled *et al* 2024). EAE technique consumes less energy, less solvent, and mild processing. Additionally, EAE is safer and more environmentally friendly in contrast to methodology isolation that utilizes high temperatures. Moreover, EAE preserves better structure and purity with higher biological value relative to methods using high temperatures during isolation processing because it utilizes mild processing methods (Kumar *et al* 2023). The usage of Deep Eutectic Solvents, a latest 'green' technology and a new solvent in place of conventional organic solvents to be used in isolating bioactive compounds from medicinal plants, gained popularity in recent years because they can easily replace conventional solvents in these isolations using a small percentage of them because they function really well in this technique when used in a small composition in combination with other components from plant extracts in a solvent mix meant for medicinal/nutraceutical isolation technology as a solvent in this isolations technique because these solvents can function better in dissolving these compounds without using all these components because of their higher boiling point in combination with other constituents in this mix given their boiling point other than completely using them because they are very cheap when in small proportions in combination with other elements in a mix meant for this isolations technique because these elements or compounds can interact really well in dissolving these medicinal/nutraceutical isolates without using all these elements in a mix because they have a higher boiling point than this small mix composition given their boiling point because of safety concerns and cost-effectiveness in this isolations technique using Deep Eutectic Solvents are produced through a mixture of two natural compounds such as urea, organic acids, sugar, and choline chloride. The compounds are linked through a hydrogen bond to forge a biodegradable liquid solvent with excellent dissolving properties. The application of Deep Eutectic Solvents on *Dillenia indica* extracted excellent extraction rates of phenolic acids, flavonoids, and tannins (Bora *et al* 2025) because they are polar and enable selective extraction with a non-toxic and biodegradable nature that supports global sustainability efforts. Moreover, given that food-grade natural deep eutectic solvents have ingredients made from plants, these types of solvents are the safest and most eco-friendly for use within the food, cosmetic, and pharmaceutical industries as the utilization of these solvents is highly necessary for global sustainability efforts related to safety within any given application (Silva *et al.,* 2021).

D. indica is also being researched as a prospective new method for extraction due to the prospect of supercritical carbon dioxide extraction offered by Gandhi and Mehta in 2013. This new method uses carbon dioxide in a state that is considered 'supercritical', meaning it is liquid but displays attributes of both a liquid and a gas-like substance, as well as a liquid solvate or solvent (Gandhi & Mehta, 2013). Supercritical carbon dioxide extraction is highly successful in taking out non-polar triterpenoids, sterols, and volatile components from bark, fruits, and leaves with high efficacy (Chemat *et al.,* 2019). Supercritical carbon dioxide extraction also creates highly concentrated remedies and leaves no destructive residue from the solvent, making it a very useful method for uses requiring high purity, as seen with remedies and functional food products (Shi, *et al*., 2005). The selectivity of extraction can be enhanced by modifying the extraction conditions such as pressure and temperature, or by using very small amounts of co-solvents (such as ethanol) to extract slightly polar constituents (Young *et al.,* 2010). The environmentally friendly nature of supercritical CO2 extraction, together with its ability to produce large quantities and be scaled up to meet future industrial demand, makes this extraction method one of the most promising candidates for the commercialisation of *D. indica*. Extracting compounds found in the medicinal plant *D. indica* by using pressurised hot water, (also known as hydrothermal extraction), has mostly been applied to identify and extract only the water-soluble compounds from the plant, such as polysaccharides, tannins and certain phenolic compounds (Mohanta *et al,* 2024). When water is heated under pressure, its properties (specifically, dielectric constant) change and the chemical characteristics of water make it a more efficient solvent to extract the desired compound(s) that would typically require a solvent of the organic nature (Flórez *et al*, 2015). Hydrothermal extraction technology is capable of producing clean extracts (solvent residues do not exist in the final extract) with lower environmental costs and eliminates the risk of introducing toxic solvents into the environment. These "green" extraction strategies represent the ongoing shift towards sustainable practices associated with the extraction of substances from FWPs (natural products derived from plants). Each of these technologies offers specific benefits based on the type of metabolites that are targeted, and collectively, they create opportunities for the sustainable development of *D. indica* and continued demand for plant-derived therapeutic products, functional food products and green bioproducts through environmentally sensitive, economically viable and scientifically sound methods of extraction.

5. Pharmacological Activities of *Dillenia indica*

Because of the large number of active components contained in the various plant tissues and products, combined with the rich tradition of ethnopharmacology associated with *Dillenia indica,* there has been much research effort to investigate the pharmacology of this species. As a result of laboratory and animal studies conducted during 2023, scientific research has confirmed that many aspects of *D. indica* are valid and that they support the traditional medicinal uses of this species, and that there is scientific evidence for potential mechanisms of action of the components of this plant (Aswathy *et al.* 2021). Numerous plant tissues including fruit, stem bark, leaf, and mucilaginous seed pulp possess pharmaceutical activity. The bioactive components that occur in various plant tissues, particularly in high concentrations, have demonstrated substantial biological activity across various physiological systems and are thought to work together to provide the effects described. Evidence from modern scientific studies suggests that *D. indica* has multiple benefits and is capable of having multiple biological actions, including but not limited to antioxidant, antidiabetic, anticancer, anti-inflammatory, antimicrobial, hepatoprotective, nephroprotective, gastroprotective, cardioprotective, neuroprotective, immunomodulatory, and wound-healing (Sharma *et al.,* 2016). The medicinal uses of *Dillenia indica* have existed for centuries and it has demonstrated a wide variety of pharmacological activities including being an antioxidant (Abdille *et al.* 2005; Akter *et al*. 2022). Chronic conditions like diabetes, heart disease, cancer, and neurological diseases are believed to be caused by oxidative stress.

Empirical data shows that *D. indica* has a strong capacity to scavenge free radicals, particularly when a fruit or leaf extract is used. Antioxidant activities are largely attributed to the phenolic acids (e.g., gallic, protocatechuic, ferulic, and caffeic acids), flavonoids (quercetin, luteolin, and kaempferol), and donating electrons or hydrogen atoms to neutralise reactive oxygen species, inhibit lipid peroxidation, and stabilise free radicals (Mohanty & Jena 2017, Fu *et al.* 2015). Furthermore, by promoting the synthesis of superoxide dismutase, catalase, glutathione peroxidase, and heme oxygenase-1, *D. indica* extracts can strengthen the body's natural antioxidant defense mechanism (Alam *et al*. 2020). An increased level of activity of Nrf2/HO-1 is observed in cells treated with *D. indica* extracts because these extracts work by triggering the cell's detoxification function in order to shield it from oxidative stress (Song *et al.,* 2025). The role of Nrf2 in triggering this pathway is critical since this activation leads to restoring redox balance, reducing oxidative stress, and shielding the cell against damage under oxidative stress.

The antidiabetic and antioxidant properties in the plant go parallel to each other, and research in both aspects mainly focuses on the pharmacological properties of *Dillenia indica* (Saiful & Armania, 2014). Conventional healers have been using the fruit to treat diabetic patients for a very long time, and recent studies have proved this conventional treatment to be very effective. The preclinical model demonstrates a decrease in glucose tolerance and an increment in insulin sensitivity due to the ingestion of this fruit extract (Talukdar *et al.,* 2012). Moreover, this antidiabetic property can be attributed to the inhibition of various carbohydrate-splitting enzymes by these flavonoids, including amylases and glucosidases, which decelerate glucose absorption in the body. Moreover, modulation of the PI3k/Akt pathway in *D. indica* by quercetin and betulinic acid accelerates insulin function and boosts β-cells of the pancreas (Camaya *et al.,* 2022). In animal models with diabetes, it was observed that extracts of *D. indica* can boost glucose uptake in muscle cells (GLUT4) and lower beta-cell apoptosis and pancreatic oxidative stress (Khanum, 2021). Moreover, the polysaccharides present within the fruit mucilage of *D. indica* will form a gel-like structure in the stomach and intestines. That means all the sugar present in the fruit would not be degraded till the next meal. Altogether, these several mechanisms provide evidence for developing *D. indica* as an adjunct antihyperglycemic therapy.

In various in vitro studies, the bark, leaves, and fruit extracts of *Dillenia indica* showed significant cytotoxic activities against various cancer cell lines such as those inducing breast, cervical, lung, liver, and colon cancers. The antibeamer properties of this tree thus form a major area of the current study. The cytotoxic activities of this plant are due to the occurrence of triterpenoids such as betulinic acid, lupeol, oleanolic acid, and phytochemicals obtained from its leaves, fruit, and flowers, along with certain naphthoquinones Studies on these agents demonstrate that they have anticancer effects through manifold affecting pathways on cancerous cell survival including apoptosis, angiogenesis, and inhibiting cell growth/proliferation and also altering the way in which tumor cells respond to external signals. An example is betulinic acid which acts to induce apoptosis by activating the activation of caspases-3 and 9. In addition to causing apoptosis through caspases activation, it causes a disruption of electrical potential across mitochondria and thus enables the release of cytochrome C from mitochondria to cytosol (programmed cell death). Flavonoids isolated from this plant have also been shown to inhibit either the PI3K/Akt and NF-κB signaling pathways, which are normally hyperactivated in cancer cells and as a result could potentially interfere with the efficacy of these agents as therapeutic interventions for cancer (Liu *et al*., 2020). Another physiological effect attributed to *Dillenia indica* is its anti-inflammatory effects as a result of its ability to eliminate pro-inflammatory agents (Yeshwante, *et al.,* 2009). Inflammation is one of the common symptoms found in various chronic and acute conditions. Besides the above-mentioned effects, extracts from *Dillenia indica* also showed inhibition of nitric oxide, prostaglandins, and cytokine secretion, including TNF-α, IL-1β and IL-6 (Malleshappa, *et al*., 2018). These effects may also be linked to suppression of COX-2 and INOS and inhibiting NF-κB. Moreover, the effects of terpenoids like oleanolic and ursolic acid involve membrane stabilization, which reduces the accumulation of inflammatory cells in tissues damaged or injured. For this reason, phytotherapy from Dillenia indica has traditionally been utilized for treating arthritis, fever and pain.

Dillenia indica exhibits strong antimicrobial action. The extracts of fruit, bark, and leaves were found to inhibit various pathogenic bacteria and fungi, such as Staphylococcus aureus, Escherichia coli or Pseudomonas aeruginosa, Candida albicans, and several dermatophytes (Singh & Saha, 2018). The way their active components exert an antimicrobial effect is the synergistic mechanism that involves phenolic acids, flavonoids, tannins, and other volatile chemicals inhibiting microbial cell wall integrity, synthesis of nucleic acid, and its capacity for quorum sensing, thus interfering with communication with one another (Bouyahya *et al.,* 2022). Highly redox active naphthoquinones from the plant can cause microbial cells to die due to localized oxidative stress. Therefore, the broad spectrum of antimicrobial activity provided by *D. indica* increases its potential to act as a natural preservative and provide therapeutic treatment for infectious diseases (Klotz *et al.,* 2014). Additionally, chemical-induced liver injury from various experimental models has been used to demonstrate the protective effects of *D. indica* on the liver. Padhya *et al*. (2008) describe the ability of the extract from the *D.indica* plants to protect the hepatocyte (liver) cells from oxidative stress and to stabilise the cell membranes and also provides for an increased ability of the liver to detoxify itself. (Sen *et al.,* 2018) have depicted evidence for the benefits of several different variants of *D. indica* contain and especially in terms of being able to protect the liver from multiple types of injury caused by carbon tetrachloride (CCl_4). Paracetamol damages the liver through its production of reactive oxygen species, while alcohol does so through its production of lipid peroxides. The antioxidant activity exhibited by *D. indica* provides evidence for *D. indica's* role as a protector of the cell membrane from damage due to lipid peroxides. A recent investigation by Azelle and colleagues supports the view that *D. indica* extracts may hold promise as a protective agent for the liver, as they have the potential to modulate detoxification enzymes. (2025). Laboratory studies indicate that *D. indica* extracts provide similar renal protection from oxidative stress, toxins, and diabetes-related complications. (Kaur *et al*.2018). *D. indica* extracts can reduce urea, creatinine and uric acid concentrations in serum while increasing antioxidant enzyme levels in kidney tissue. *D. indica* flavonoids provide glomerular protection by reducing the degree of inflammation and facilitating normal tubular cell function. (Khanum 2021).

The bioactivity of *Dillenia indica* in protecting the stomach lining from damage is a basic intervention that has recently been scientifically documented. *D. indica* contains a high pectin and mucilage concentration in its fruit pulp. Such compounds form a "Slime Layer" or "slimy" coat on the stomach lining and aid in ulcers healing and alleviating irritation by ulcers (Sachan *et al*. 2017), with other extracts from the *D. indica* plant controlling gastric acid secretion, mildly inhibiting Helicobacter species growth, and stimulating mucus production. Hence, all these factors make way for support for the use of *D. indica* in curing ailments concerning acidity, indigestion, and/or stomach discomfort in earlier years. There is sufficient evidence to prove *D. indica* can work in a direct manner on the cardiovascular system by lowering the quantities of total cholesterol, triglycerides, and low-density lipoprotein (LDL) but raising concentrations of high-density lipoprotein (HDL) in humans (Khan *et al*. 2019). The presence of sterols in plants such as β-sitosterol and Stigmasterol has allowed *D. indica* to lower existing cholera levels in humans by reducing absorption in the intestine. Moreover, antioxidant and anti-inflammatory properties in *D. indica* protect cardiac tissues in bodies from oxidative damage, ischemic damage, and inflammatory responses in bodies (Wang *et al*. 2019). Although research concerning this topic can be considered less studied in comparison with other research, sufficient explanation can be drawn in this research to unfold circumstances under which *Dillenia indica* can be used in controlling neurodegenerative ailments. Neurotoxic compounds create an oxidative burst in neurons, reduce acetylcholinesterase in decomposing acetylcholine molecules, and initiate an inflammatory response in bodies (Mohd *et al*. 2020). The research adds to existing augment knowledge in *Dillenia indica* research concerning efficacy and tradition in using *Dillenia indica* in clearing headaches in bodies. Open wounds can heal faster due to the capability of *Dillenia indica* in reducing inflammation, oxidative responses produced by reactive molecules in bodies, and bacteria. As explained in a research conducted by Ghiulai *et al.* in 2020, using topically diluted concentrations of extracts in *Dillenia indica* in bodies injured with *Dillenia indica* indicated faster recoveries, an increase in production of collagens in bodies, and skin regeneration in bodies. As explained in a research above, it shows in a pathological manner a larger quantity of fibroblast and blood vessels were increased in bodies when in contrast to using a control product. In earlier research, immune-modulatory effects have been demonstrated in *Dillenia indica* because of increased macrophage function in phagocytosis, increased function of macrophages in ingestion, and stimulation of lymphocyte proliferation (Singh & Saha 2018). Based on this information, *Dillenia indica* is a plant with immune-modulatory effects because of which it demonstrates an immune system-stimulating effect, not only on the innate immune system but also on physiological functions concerning the adaptive immune system because of the availability of both polysaccharides and phenolic compounds in *Dillenia indica* (Saikia *et al*. 2023). *Dillenia indica* is a plant with multiple modes of action and multiple pharmacological activities. Its wide pharmacology shows that this plant possesses a way in which it manifests effects concerning immuno-modulatory functions because of functions concerning oxidative stress, regulation, anti-inflammatory effects, functions concerning mitochondrial stabilization, and cellular signaling because of which *Dillenia indica* possesses multiple capabilities in order to function in terms of developing natural medicines because of which it will facilitate green technology in biomedicine.

6. Nutraceutical and Pharmacological Applications

Dillenia indica is becoming a popular choice in the fields of medicine and biomedicine for its ability to produce many bioactive compounds. Bioactive compounds present in this plant include flavonoids, phenolics, saponins and triterpenoids. Much research has shown the antioxidant properties of *Dillenia indica*, including its ability to protect the body from oxidative stress related to chronic disease (e.g. diabetes, cardiovascular disease) and some types of dementia. Moreover, research work has proved the anti-inflammatory properties of *Dillenia indica* in different animal models, and it is evident that this plant possesses efficacy in dealing with diseases which cause tissue damage, such as rheumatoid arthritis and inflammatory bowel diseases, by acting on the pathways of inflammation (Nahar *et al.,* 2025). The application of *D. indica* in natural medicine for infectious diseases gets added because of the plethora of antimicrobial actions possessed by this plant against both bacteria and fungi because of rising cases of antibiotic resistance (Bora *et al.,* 2023). Recently conducted studies have proved that *D. indica* possesses anti-cancer agents, which include cell growth inhibition and apoptosis. Moreover, because of recent developments in medicine and pharmaceutical innovations in present-day civilization, *D. indica* has gathered significance in this genre of medical research. The combination of both & traditional and modern medical knowledge with new technology progresses greatly in ameliorating the application of *D. indica* in present-day health circles with successfully derived methods (Ghiulai *et al.,* 2020). Moreover, when referring to developments in medicine with emerging new technology, when considering dealing with diseases in a population with new medical methods, including indigenous medical practices. It is an important step towards improving our health, controlling infectious diseases, and achieving a better life.

7. Genetic diversity:

The variety of DNA sequences between individuals of a given species is a key component of genetic variation. For instance, within populations (such as within a single variety) or between populations (for example, between two different varieties), there is considerable variation in the DNA sequence that can be used during plant breeding. Genetic diversity is critical for successful breeding programs because it creates a reservoir of potential genetic traits that can be used to improve existing breeds. Without such a reservoir of genetic resources, it would be impossible to improve such traits as yield, quality, resistance to disease, and tolerance of stress (Salgotra & Chauhan 2023). Plant genetic resources such as cultivated varieties, wild relatives, and landraces contain valuable alleles that plant breeders can utilize to create new and better crops. The utilization of these resources assists plant breeders in responding to the challenges posed by climate change and changes in pest populations and/or diseases. Plant breeders are also able to introduce new traits to increase the resilience of their crops through the utilization of broad genetic diversity. This is essential for sustainable agricultural production and for assuring that there will be sufficient food available to meet the needs of people living on earth in the future. The narrowing of the genetic base of plants as a result of modern plant breeding (particularly with regard to some intensively selected high-yielding varieties) can result in the loss of genetic diversity in crops and could restrict future breeding improvements. Thus, the preservation of genetically diverse seed stock and the application of advanced tools such as molecular markers and genomic selection are becoming more commonly incorporated into breeding efforts to evaluate and manage genetic variation. (Fu *et al*., 2015).

8. Genetic diversity in crop improvement strategies

Plant breeding requires genetic diversity to attain the degree of variability needed for adequate selection and genetic enhancement. Breeding success ultimately depends on having access to adequate amounts of diverse allelic combinations that govern important agronomic traits, notably yield, quality, maturity, ability to resist biotic and abiotic challenges, and so forth. The bigger the genetic base of the plant, the more opportunity there are for breeders to identify superior genotypes and create new varieties with desirable traits through hybridization; thus, making breeding programs more effective and sustainable source (Govindaraj et al., 2015).

In light of climate change, genetic diversity is increasingly important in providing crop breeders with the genetic resources necessary to create drought-, heat-, salinity-, emerging pest- and disease-resistant crop varieties. Additional sources of genetic diversity, such as wild relatives and landraces, provide novel alleles that are important for enhancing long-term crop resilience and food security, and are often absent in modern cultivars (Salgotra & Chauhan 2023). In contrast, reduced genetic diversity due to intensive selection and monoculture practices can create genetic vulnerability, thus putting greater risk on the potential for widespread failure in a crop. As such, plant genetic diversity should be preserved and utilized using modern tools (in particular, molecular markers and genomic selection) to ensure sustained genetic improvement and future crop enhancement (Brown, 2016).

9. Conclusion

Dillenia indica is an important plant for sustainable bioprospecting because it has an extensive list of traditional uses, extensive scientific literature concerning the presence of valuable phytochemicals and an increasing number of studies demonstrating its biomedical value. The phytochemistry of *D. indica*, which includes phytochemicals such as triterpenoids, flavonoids, polyphenols and other classes of bioactive compounds, accounts for the potential of this species to be used therapeutically for many of the same reasons as other plants in the same families (for example, as an anti-inflammatory, anti-diabetic, antioxidant, and antimicrobial). Therefore, *D. indica* may be a significant natural resource for the development of health products. The use of green extraction technologies is increasingly important in extracting the bioactive properties from *D. indica* while reducing the environmental impact. Therefore, eco-friendly extraction methods, such as solventless or low-solvent methods and energy-efficient processes, improve extraction yield and stability as well as align research into phytochemicals with principles of sustainability (i.e., circular bioeconomy). In biomedical terms, the sustainable harvest of phytochemicals from *D. indica* supports the development of plant-based therapeutics, nutraceuticals, and functional foods. Additionally, when biomedical advances are coupled with responsible harvesting, increased use of these products will not threaten either biodiversity or the health of an ecosystem. In summary, the future research of *Dillenia indica* involves incorporating traditionally used plant medicine into a modern straight-forward system based on sustainable development principles. Future studies should include international standards for green extraction methods, development of extended pharmacological testing, and development of conservation strategies for *D. indica's* genetic resources, and establish equitable access and sharing of benefits. These combined efforts can help *D. indica* make a significant contribution to sustainable development, conserving global biodiversity, and encouraging innovation in global health.

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Data Availability

"Data will be available on demand."