



# A Green Anticancer Approach on Acanthaceae

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**Abstract:** Medicinal plants play an important role in the development of new drugs both for humans and animals which act as a potential material for maintaining health. Almost 3/4<sup>th</sup> of the herbal medicines used worldwide are discovered from local medicinal plants. Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. According to WHO in 2020 nearly 10 million deaths are reported worldwide due to cancer. Many people seek alternative complementary methods of cancer treatment because of high death rate and serious side effects of chemotherapy and radiation therapy. Herbal medicine has become a very safe, non toxic and easily available source of cancer treating compounds. Some plant species belonging to Acanthaceae are useful for treatment of cancer. These species with active anticancer activity due to phytochemicals have to be investigated for future to improve cancer therapy.

**Keywords:** Cancer, Acanthaceae, herbal medicines, metastasis, apoptosis

Cancer is a generic term for a large group of diseases that can affect any part of the body and is one of the most common leading causes of death worldwide. According to WHO, cancer is a serious health problem in all populations. The global response to cancer has been uneven and inequitable. In 2020, one in five people globally will face a cancer diagnosis during their life time. Chemotherapy, radiation therapy, immunotherapy, stem cell therapy etc. are commonly recommended to overcome the disease. But most of them prefer traditional medicines due to its safety, efficacy and cost effectiveness. Traditional herbs are effective for the treatment of cancer and have less toxic side effects (Rajeshkumar et al., 2015).

Plant species belonging to family

Acanthaceae have abundant medicinal properties and are rich source of phytochemicals. For instance, among the many anticancer medicinal plants, *Andrographis paniculata*, *Justicia gendarussa*, *Justicia adhatoda*, *Acanthus ilicifolius*, *Avicennia alba*, *Avicennia marina*, *Barleria prionitis*, *Odontonema strictum*, *Rhinacanthus nasutus*, *Thunbergia grandiflora*, *T. laurifolia* etc. of Acanthaceae have been used traditionally for the anticancer properties of their active ingredients.

## 1. Anticancer plants in Acanthaceae

### 1.1. *Acanthus* L.

*A. ilicifolius* is commonly known as 'Sea holly', 'Chullikandal', 'Harikusa', 'Holly mangrove', 'Nivagur' etc. This plant is a mangrove with spiny holly leaves. It contains wide

range of secondary metabolites and has traditional usage in Indian and Chinese system of medicine. Mangrove survives in the most hostile environment with fluctuating tidal and saline regime. Hence, these plants are considered to be rich sources of steroids, triterpenoids, saponins, flavonoids, alkaloids and tannins. Traditionally, the plant has been used for dyspepsia, paralysis, asthma, headache, rheumatism and skin diseases (Singh & Aeri, 2013). Several classes of polyphenolic compounds such as phenolics, flavonoids and tannins contribute to plant defense mechanism in resisting pathogenic microorganisms (Vani et al., 2018).

**Anticancer activities:** The plant extract prevents DNA alterations in a transplantable ehrlich ascites carcinoma bearing murine model (Chakraborty et al., 2007). The administration of *A. ilicifolius* reduces viable tumour cell count and brought about a marked increase in mean survival of tumour bearing hosts, suggesting the tumour combating efficacy of the extract under investigation. Anticancer efficacy of root tissue and callus of *A. ilicifolius* is evident on Benzo (A) Pyrene induced pulmonary carcinoma in *Mus musculus* (Singh & Kathiresan, 2013). The plant is potent to have chemoprotective, antimutagenic, antioxidant and anticancer effects against Benzo (a) Pyrene induced albino rat. Moreover, the plant is found to be a natural preventive source of pulmonary carcinoma. Anticancer activity of leaf and root extracts of *A. ilicifolius* reveals that the ethyl acetate extract reduces cellular viability in MCF-7 and PA-1 cells (Smitha et al., 2014).

## 1.2. *Andrographis* Wall. ex Nees

*A. paniculata* is an important medicinal

plant and widely used around the world. It is also known as 'Indigenous king of bitter' and uses as a traditional herbal medicine in India, Bangladesh, China, Hong Kong, Pakistan, Philippines, Malaysia, Indonesia and Thailand. The plant is ethnobotanically used for the treatment of snake bite, bug bite, diabetes, dysentery, fever and malaria.

**Anticancer activities:** Extracts of *A. paniculata* reduce the risk of cancer due to the presence of flavonoids. The aerial part of the plant is most commonly using in medicines because of the presence of diterpenoids, diterpene glycosides, lactones, flavonoids and flavonoid glycosides in the extracts. Leaves have many phytochemical constituents like phenols, tannins, alkaloids, saponins, flavonoids and reducing sugars. These phytochemicals actively involved in the medicinal uses for treating various diseases. The plant has been reported to have a broad range of pharmacological effects including anticancer, anti-diarrheal, anti-hepatitis, anti-HIV, anti-hyperglycemic, anti-inflammatory, anti-microbial, anti-malarial, antioxidant, cardiovascular, cytotoxic, hepatoprotective, immunostimulatory and sexual dysfunctions (Sadhana et al., 2020). The in vitro anticancer activities of different solvent derived extracts of *A. paniculata* leaves are against different human cancer cell lines, neuroblastoma (IMR-32) and human colon (HT-29) (Rajeshkumar et al., 2015). Andrographolide exhibits both direct and indirect effects on cancer cells by inhibiting proliferation of cancer cells, cell cycle arrests or cell differentiation that enhancing body's own immune system against cancer cells and inducing apoptosis and necrosis of diseased cells (Hossain et al., 2014). The presence of

various chemical constituents in the aerial parts of *A. paniculata* is andrographolide which is diterpene lactone, colourless, crystalline and bitter in taste (Nyeem et al., 2017). Ethanol extract of *A. paniculata* contains 2.13 ppm neoandrographolide and shows an inhibitory effect in MCF-7 cells with higher doses (Sholihah et al., 2019).

### 1.3. *Avicennia* L.

*A. alba* is also known as 'Api Api Putih', and considers as the iconic tree of the mangrove forest. The height may be up to 20 m and bearing the salt excreting leaves in presence of salt glands. The tree develops pneumatophores that protrude out of the soil allowing root respiration in the anaerobic muddy soil. *A. marina* is commonly known as 'Grey mangrove' or 'Cheru uppatty'. They are generally 10-4 m long and have light gray or whitish bark with stiff, brittle and thin flakes. Their leaves are thick, glossy and bright green on the upper side and gray or silvery white with small hairs on the lower side. The pneumatophores can grow up to 20 cm (Baishya et al., 2020).

**Anticancer activities:** Polyisoprenoids from *A. alba* show anticancer activity (Llian et al., 2019). Isoprenoids as well as polyisoprenoids identified from the leaves and roots of the mangrove which possesses various pharmacological activities including anticancer and anti-inflammatory. Bioactive compounds in leaf extract exhibit in vitro anticancer potential against MCF-7 and Hela cell lines (Eswaraiah et al., 2020). It could be used as a potential alternative for the development of bioactive leads in the treatment of cancer. The leaves of plants include flavonoids, steroids, saponins

and tannins; whereas in roots, flavonoids and steroids / triterpenoid compounds are present (Rahmania et al., 2018). *A. marina* plant extracts show anticancer and antiproliferative activity (Albinhassan et al., 2021). The hexane extract of leaves is helpful for anticancer drug development due to the presence of highest phenolic and flavonoid contents. Polyphenol rich leaf extracts induce apoptosis in human breast and liver cancer cells (Huang et al., 2016).

### 1.4. *Barleria* L.

*B. prionitis* is commonly known as 'Yellow nail dye', 'Chemmulli', 'Manjakanakambaram', 'Shemmuli', 'Vennkurinjiveru' etc. It is an indigenous herb of Southern Asia and some regions of Africa. The various parts including leaf, flower, stem, seed, shoot and root are with therapeutic effects against numerous disorders including cough, fever, jaundice, asthma, severe pain and cut wound (Banerjee et al., 2021).

**Anticancer activities:** *B. prionitis* leaf ethanol extract shows anticancer and antimicrobial potential. The anticancer effect against lung cancer cell line, breast cancer cell line, breast metastatic cell line, colon cancer cell line and lung metastatic cell line is statistically significant at particular concentration (Panchal et al., 2018). Assessment of stem ethanol extract potential to kill pathogenic microbial strains and in vitro inhibitory effect on human cancer cell lines is prominent (Panchal et al., 2021). Several bioactive compounds isolated from *Barleria* species, such as iridoids, phenolics, flavonoids, terpenoids, phytosterols and phenylethanoid glycosides possess various biological properties of medicinal importance.

Moreover, both extracts and bioactive compounds from *Barleria* have demonstrated several biological activities including antioxidant, antibacterial, antifungal, antiinflammatory and anticancer properties and the ability to synthesize silver nanoparticles (Gangaram et al., 2022).

### 1.5. *Justicia* L.

*J. adhatoda* is a widespread plant throughout the tropical regions of Southeast Asia and commonly known as 'Vasaka' or 'Malabar nut'. The species is a perennial, evergreen and highly branched shrub with unpleasant smell and bitter taste. It has opposite ascending branches with white, pink or purple flowers. It is a highly valuable ayurvedic medicinal plant used to treat cold, cough, asthma and tuberculosis. The major alkaloids of the plant, vasicine and vasicinone, have been found to be biologically active and are the area under discussion of many chemical compounds and pharmacological studies. *J. gendarussa* is commonly known as 'Black adusa'. The species is a shade loving, quick growing, evergreen shrub found throughout India and also in all Asian countries like Malaysia, Indonesia, Sri Lanka and Bangladesh.

**Anticancer activities:** *J. adathoda* shows in vivo anticancer activity against dal cell lines (Jiju, 2019). It has potent phytochemical, antimicrobial and antiinflammatory activity. The qualitative analysis of the extracts from the leaf sample of *J. adathoda* reveals the presence of tannins, saponin, flavonoids, steroid, lipids, amino acids and terpenoids. The active compounds such as amino acids, flavonoids, alkaloids and lipids have antiinflammatory activity and can be considered as a resource for

a potential anticancer agent. A compound "vasicine" isolated from n-butanol fraction is found potent in inhibiting proliferation of prostate cancer cells (Battoo et al., 2017). *J. adhatoda* leaf extract showed a potential anticancer effect in MCF-7 cells (Kumar et al., 2022).

Phytochemical screening of *J. gendarussa* plant extracts show higher yield of phenolic and flavonoid content (Ramees et al., 2019). *Jendarussa* crude extracts exhibit cytotoxicity against human cancer cell lines (Ayob et al., 2013). The leaf extracts have potential cytotoxic activity on human cancer cell lines particularly BxPC-3 cells. Usually, the plant is used in traditional medicinal practice for chronic rheumatism, inflammations, bronchitis, vaginal discharges, dyspepsia, eye diseases and fever.

### 1.6. *Odontonema* Nees

*O. strictum* is commonly known as 'Fire spike', 'Cardinal guard' and 'Scarlet flame', native to semi-forested areas in Central America. Fire spike is attractive evergreen shrub with sparse stiff branches that grow mostly straight up to about 6 feet tall. It has shiny dark green leaves with wavy margins and long pointed tips. The leaves are oblong and arranged opposite each other on the stem. From late summer through winter, fire spike produces abundant 9-12 m upright panicles of brilliant red tubular flowers. The individual flowers are about an inch long and two lipped.

**Anticancer activities:** The silver nanoparticles isolated from *O. strictum* leaf extract show antioxidant activity (Luhata et al., 2022). Their antioxidant properties in the management of

oxidative stress are found in several acute and chronic pathological processes such as hypertension, cancer, diabetes and neurodegenerative diseases (Luhata et al., 2016). A qualitative phytochemical screening of the extracts obtained from the leaves of *O. strictum* indicates the presence of flavonoids, saponins, glycosides, tannins, steroids and terpenoids (Luhata & Usuki, 2021).

### 1.7. *Rhinacanthus* Nees

*R. nasutus* is commonly known as 'Snake jasmine', 'Dainty sprus', 'Nagamulla' or 'Kaurasago'. It is a small slender shrub growing to a height of about 0.6 to 1.2 m with sparsely branched club shaped fruit and four seeds. The whole plant is widely used in traditional medicinal practices for the treatment of diverse disease conditions. Medicinal preparations of the plant in the form of decoctions and herbal tea have been given internally to the people for the treatment of hepatitis, diabetes and hypertension; while the external application in the form of paste has been used by the people who suffer from psoriasis, eczema, ringworm as well as inflammation. Traditionally seeds, roots and leaves of the plant have been used against scabies, eczema and various skin conditions. Leaves are used for prickly heat as well as scurf and roots are being boiled along with milk which is used as an aphrodisiac (Brimson et al., 2020).

**Anticancer activities:** The phytochemical analysis of *R. nasutus* reveals the presence of alkaloids, phenols, saponins, flavonoids, tannins, steroids and terpenoids. The aqueous extract possesses a higher concentration of phenolic compounds and flavonoids. The anticancer activity of *R. nasutus* is significant in

pharmacology (Nirmala & Savitha, 2021). *R. nasutus*, a Chinese medicinal herb, is rich in carotenoids and possesses vital biological activities such as anti-cancer. Carotenoids reduce the risk of cancer and cardiovascular diseases. Utilization of microemulsions from *R. nasutus* helps to improve carotenoid bioavailability (Ho et al., 2016). The leaf extracts exhibit cytotoxic activity against oral human carcinoma (KB), human breast cancer (MCF-7) and lung cancer (NCI-H187) cell lines (Boonyaketguson et al., 2018).

### 1.8. *Thunbergia* Retz.

*T. grandiflora* is also known as 'Blue *Thunbergia*' or 'Bengal clock vine'. It is native to India, southern China and Myanmar. It thrives predominantly on tropical and subtropical regions, and the habitat preference is exhibited by its morphological characteristics. The species has the medicinal properties such as antibacterial, antifungal, antidiabetic, antipyretic, antiinflammatory, anthelmintic, antioxidant, antinociceptive, antidrug, antidote, antimutagenic, detoxifying, cytotoxic and hepatoprotective activities; hence, it can be considered as potential alternative herbal medicine to treat different types of diseases (Sultana et al., 2015).

*T. laurifolia* is commonly known as 'Blue trumpet vine' or 'Laurel clock vine', a popular ornamental vine in the tropics. Leaves are heart shaped with a pointed tip and slightly serrated leaf margin. Flowers are attractive with pale purplish blue petals and a yellow throat. In Thailand, the leaves of *T. laurifolia* are believed to have detoxifying effects. They are used as an antidote for poisons and drugs including the treatment of drug addiction. It has reported to

have antioxidant, antidiabetic, antiinflammatory and antipyretic properties (Chan et al., 2011).

**Anticancer activities:** *T. grandiflora* is the agent of in vivo acute toxicity and anticancer and antioxidant properties (Thorat & Jain, 2020). The plant extracts inhibit lung cancer effectively (Jain, 2020). The extract contains phenolic acid, flavonoid, kaempferol and quercetin. It's presence indicates the significant antioxidant, antidiabetic, antimicrobial and hepatoprotective activities which give the plant a great potential and supporting the use of the plant as a source of natural raw material for phytopharmaceutical preparations (Ibrahim et al., 2017).

Radical intermediate generation and cell cycle arrest by an aqueous extract of *T. laurifolia* detected in human breast cancer cells (Jetawattana et al., 2015). The plant possesses antioxidant, antiinflammatory and anticancer activities (Wonkchalee et al., 2012). *T. laurifolia* leaf extract increases the levels of antioxidant enzymes and protects human cell lines in vitro against cadmium (Junsi et al., 2020). The aqueous extract of leaves significantly increases antioxidant enzyme activities in human embryonic kidney and human liver cells; and significantly decreases malondialdehyde levels in vitro. Crude dried extract of *T. laurifolia* leaves can protect against Cd induced oxidative stress in cells possibly due to its antioxidant

properties. Cytotoxicity of *T. laurifolia* crude extracts investigated in L929, BHK (21) C13, HepG2 and Caco-2 cell lines (Oonsivila et al., 2008).

Two novel iridoid glucosides of 8-epi-grandifloric acid and 3'-O- $\beta$ -glucopyranosylstilbericoside have been isolated from *T. laurifolia* leaves along with seven known compounds of grandifloric acid, benzyl  $\beta$ -glucopyranoside, benzyl  $\beta$ -(2'-O- $\beta$ -glucopyranosyl) glucopyranoside, 6-C-glucopyranosyl apigenin, 6,8-di-Cglucopyranosyl apigenin, (E)-2-hexenyl- $\beta$ -glucopyranoside and hexanol- $\beta$ -glucopyranoside. Leaves and flowers have been found to contain other bioactive phenolic constituents including delphinidin-3, 5-di-O- $\beta$ -D-glucopyranoside, apigenin, apigenin-7-O- $\beta$ -D-glucopyranoside and chlorogenic acid. A phenolic profiling of water extract of leaves shows the presence of apigenin and apigenin glucosides, as well as phenolic acids of caffeic, gallic and protocatechuic (Chan et al., 2011).

## 2. Outlook

The purpose of this review is to brief the plants' literature survey via internet sources and to explain various anticancer plants belonging to the family Acanthaceae. Plant species belonging to the family Acanthaceae have abundant source of anticancer compounds. It is beneficial for drug industry to find out this compounds.

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