



## REVIEW

### Isolated Phytochemicals and Biological Activities of *Dendrophthoe falcata*: A Review

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Received: 17 January 2023;

Accepted: 15 March 2023;

Published online: 30 March 2023;

AJC-21176

*Dendrophthoe falcata* is one of the hemiparasitic plants that belong to the mistletoe family Loranthaceae. Since ancient times, *Dendrophthoe falcata* extracts have been recognized for their medicinal importance and many of them have been used as traditional remedies for treatment of ailments like ulcers, impotence, asthma and wounds. As a result, the significance of this plant inspired us to conduct a literature review on the biochemical significance of its isolated phytochemicals. So, in the present review, an inclusive account of phytochemicals and biological activities of leaf, stem and fruit extracts of *D. falcata* are included in view of the many related recent findings.

**Keywords:** Phytochemicals, Biological activities, *Dendrophthoe falcata*.

## INTRODUCTION

Since the dawn of the civilization, plants have been used to maintain health and treat disease. In modern times too, plants are not only one of the most significant sources for drug development but it is also estimated that a majority of the world's population still relies on the herbal medicines for primary health care [1,2]. The extracts of plants used in traditional systems of medicine like Ayurveda and oriental medicines have been evaluated for their efficacy against certain diseases to form a valuable source of therapeutic agents [3,4]. To our best of knowledge, several physiologic impacts of phytonutrients remain unknown.

*Dendrophthoe falcata* (synonymous with *Loranthus falcatus*), is a hemi-parasitic, evergreen shrub widely spread across the forests of Bangladesh, India, Sri Lanka, Myanmar, Malaysia, China, etc. It is a stem parasite that grows on the branches of trees commonly such as teak, eucalyptus, neem, mango, guava, apple, etc. It belongs to family *Loranthaceae* and is one among the 20 known species of genus *Dendrophthoe*. It is commonly called the Indian mistletoe in English and *Banda* in Hindi [5].

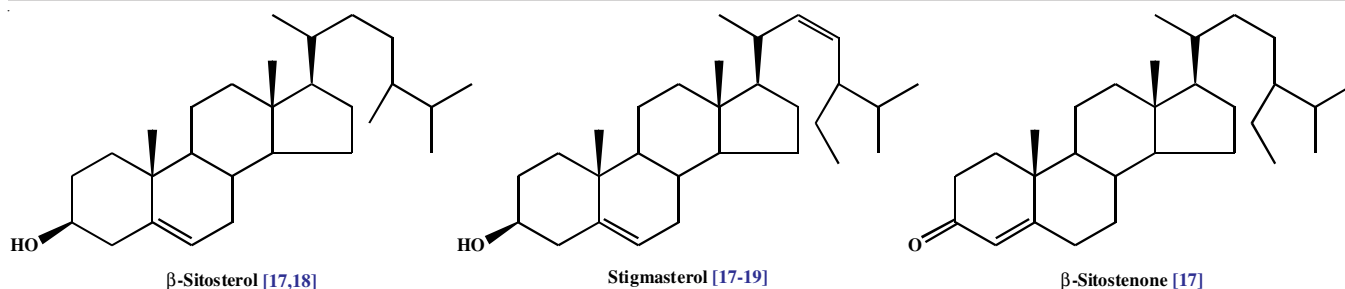
*Dendrophthoe falcata* is used in the traditional medicine systems for treatment of ailments like ulcers, impotence, asthma

and wounds [6]. Its leaf paste is applied to boils on the skin for extracting pus [7]. Forest inhabiting tribals of western India use *D. falcata* as an antifertility agent [8] and also traditionally used for the treatment of pulmonary tuberculosis [9,10]. The medicinal properties of *D. falcata* are known to be influenced by the host plant [11]. It is used to treat cognitive functions when grown on *Calotropis gigantea*, impotence when grown on *Tamarindus indicus* and paralysis when grown on *Shorea robusta* [12].

In this review, a comprehensive account of phytochemicals and biological activities of leaf, stem and fruit extracts of *D. falcata* are included in view of the many related recent findings.

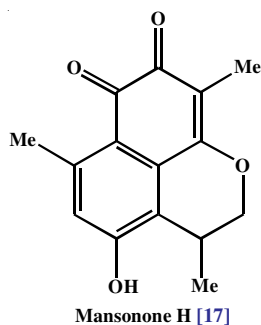
**Phytochemicals isolated from *Dendrophthoe falcata*:** The leaf, stem and fruit extracts of *Dendrophthoe falcata* have been investigated using various spectral and separation techniques for identification of the phytochemicals present. These can be broadly characterized as steroids, sesquiterpenoids, triterpenoids of oleanane, lupane and ursane series, flavonoids, hydrocarbons, carboxylic acids, phenols and tannins, glycosides, esters, alcohols, triglycerides and enzymes.

**Steroids:** Steroids are known for their antibacterial activity associated with membrane lipids [13]. Stigmasterol is reported

Fig. 1. Isolated steroids from *D. falcata*

to be a strong antioxidant and an antibacterial agent against the multidrug resistant mycobacteria [14,15]. β-Sitostenone is reported to be a metabolic intermediate [16]. Three steroids viz. β-sitosterol [17,18], stigmasterol [17-19] and β-sitostenone [17] (Fig. 1) have been reported from the stem part of *D. falcata*.

**Sesquiterpenoids:** Sesquiterpenoids having 1,2-naphthaquinone structure are called mansonones. Mansonones are secondary plant metabolites known to possess antifungal, antibacterial and antifeedant activities [20]. They are known to have widespread uses in traditional Asian medicine [21]. There is only one report of sesquiterpenoid, namely, mansononeH [17] (Fig. 2) isolated from stem of *D. falcata*.

Fig. 2. Representative structure of mansonone H from *D. falcata*

**Pentacyclic triterpenoids:** Pentacyclic triterpenoids have a broad range of biological activities like anti-inflammatory, anticarcinogenic, antidiabetic, hepatoprotective, antimicrobial, antimycotic, analgesic and immunomodulatory [22]. Oleanane, ursane and lupane (Figs. 3-5) are some of the commonly known classes isolated from *D. falcata*. According to reports, triterpenoids exhibit antimycobacterial activity against *M. tuberculosis* [23].

**Pentacyclic triterpenoids of oleanane series:** Nine compounds belonging to oleanane class of pentacyclic triterpenoids have been isolated from extracts of *D. falcata*. These include β-amyirin [19], β-acetylamyirin [18,19], oleanolic acid [17,19], 3β-acetoxy-1β-(2-hydroxy-2-propoxy)-11α-hydroxy-olean-12-ene [24], 3β-acetoxy-11α-ethoxy-1β-hydroxy-olean-12-ene [24], 3β-acetoxy-1β-hydroxy-11α-methoxy-olean-12-ene [24], 3β-acetoxy-1β,11α-dihydroxy-olean-12-ene [24], acetate of oleanolic acid [19], methyl ester acetate of oleanolic acid [19].

**Pentacyclic triterpenoids of lupane series:** The pentacyclic triterpenoids of lupane series isolated from *D. falcata* include lupeol [25], betulinic acid [17], 3β-acetoxy-lup-20(29)-

ene [24], 30-nor-lup-3β-acetoxy-20-one [24] and (20S)-3β-acetoxy-lupan-29-oic acid [24].

**Pentacyclic triterpenoids of ursane series:** The pentacyclic triterpenoids of ursane series isolated from *D. falcata* include 3β-acetoxy-1β, 11α-dihydroxy-urs-12-ene [6,24] and 3β-acetoxy-urs-12-ene-11-one [6,24].

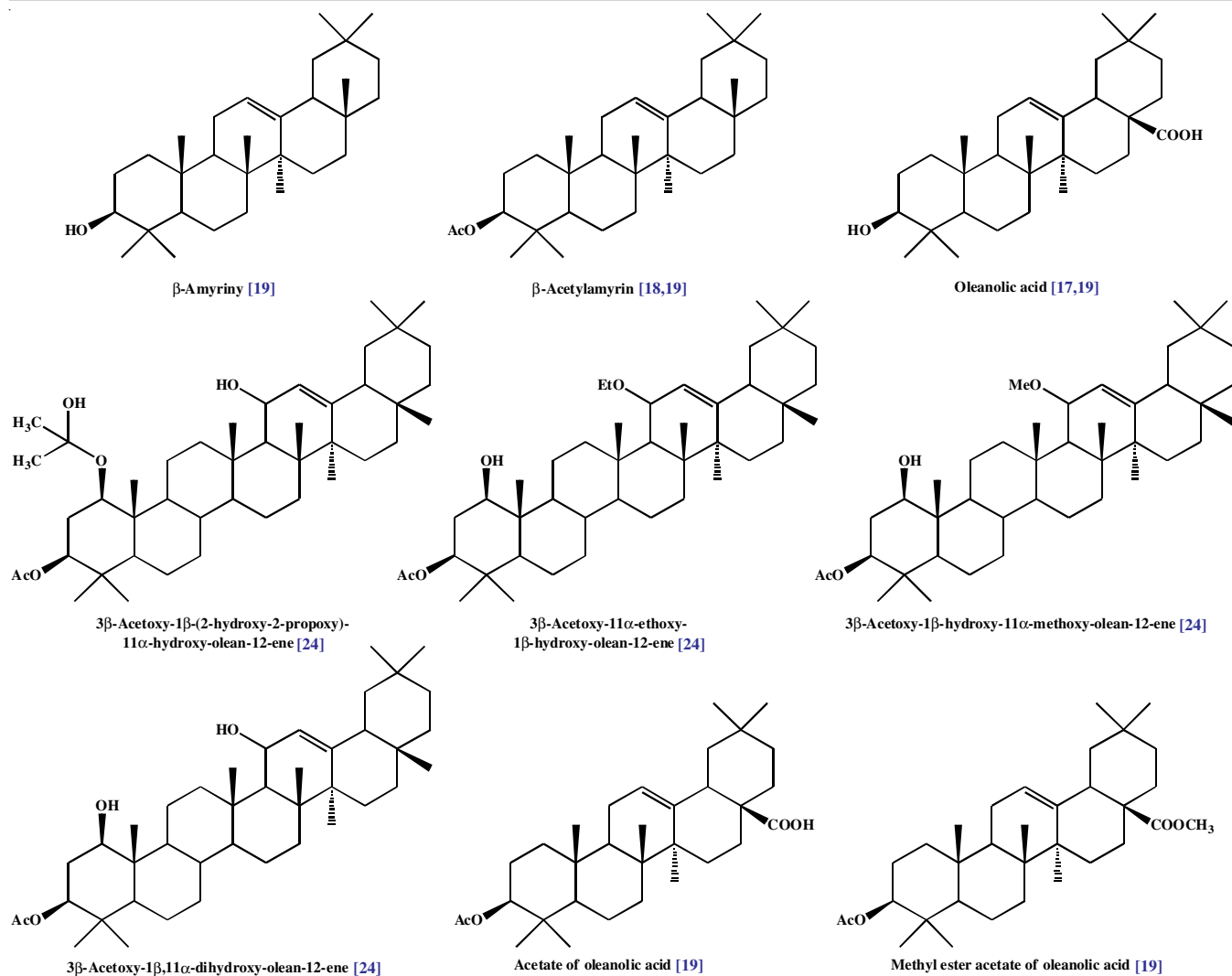
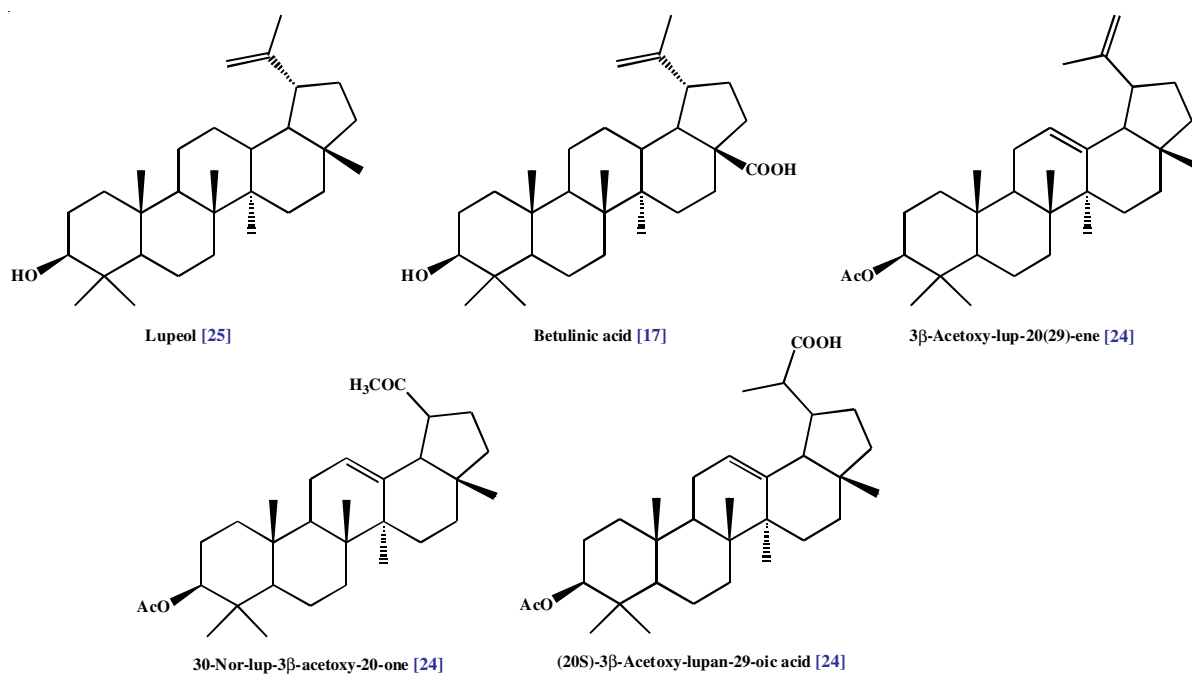
**Flavonoids:** Secondary metabolites in plants like flavonoids, are known to be responsible for a wide variety of pharmacological activities like antioxidative, hepatoprotective, anti-inflammatory and anticancer activity along with free radical scavenging capacity and ability to induce human protective enzymes. In plants they regulate growth factors and assist in the defense system against biotic and abiotic stress [26]. The flavonoids isolated from *D. falcata* include quercetin [24,27], quercetin [27], myricetin [27], leucocyanidin [28], catechin [27,28], kaempferol [27] and 7-hydroxy-4',5,6-trimethoxy flavone [17] (Fig. 6).

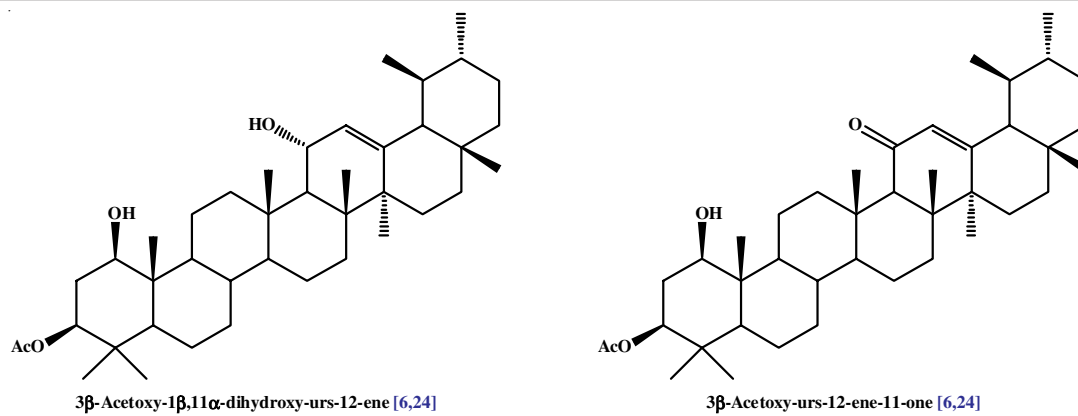
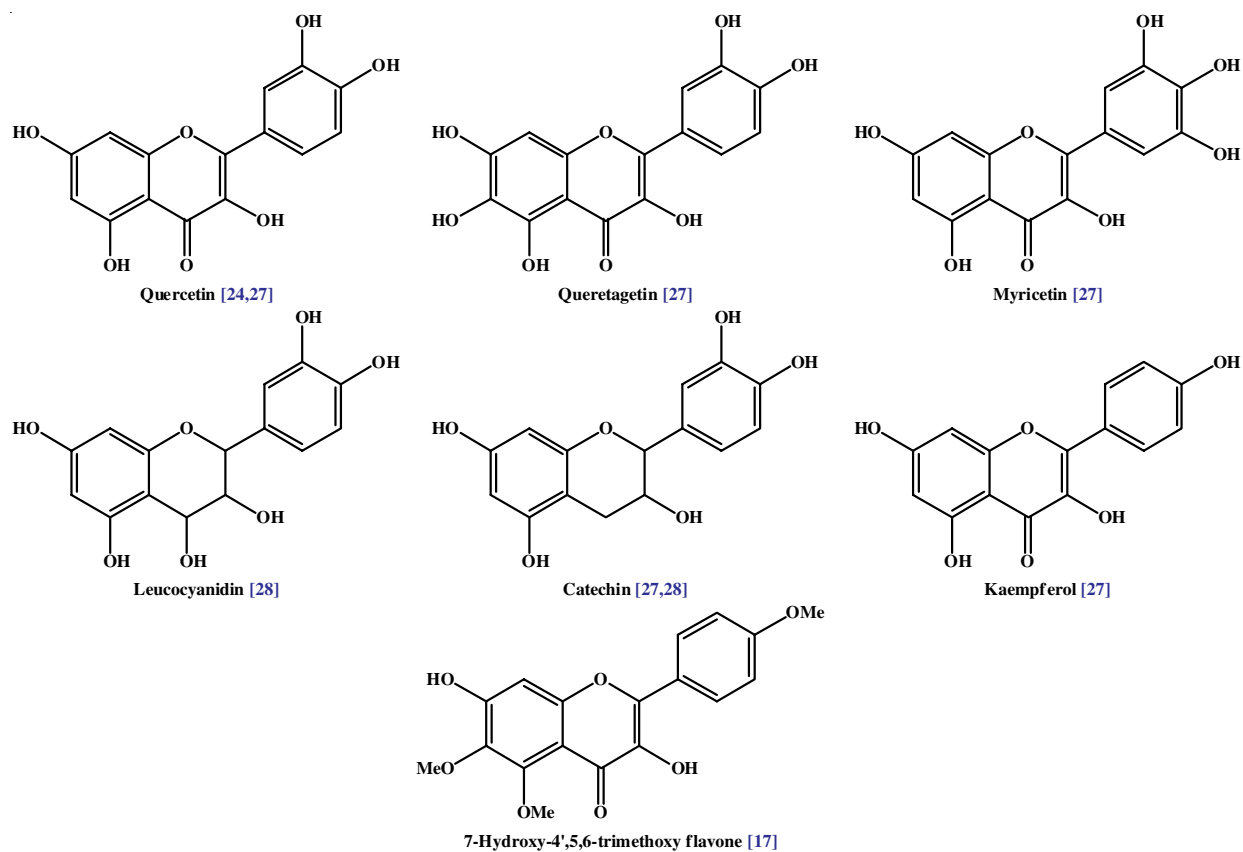
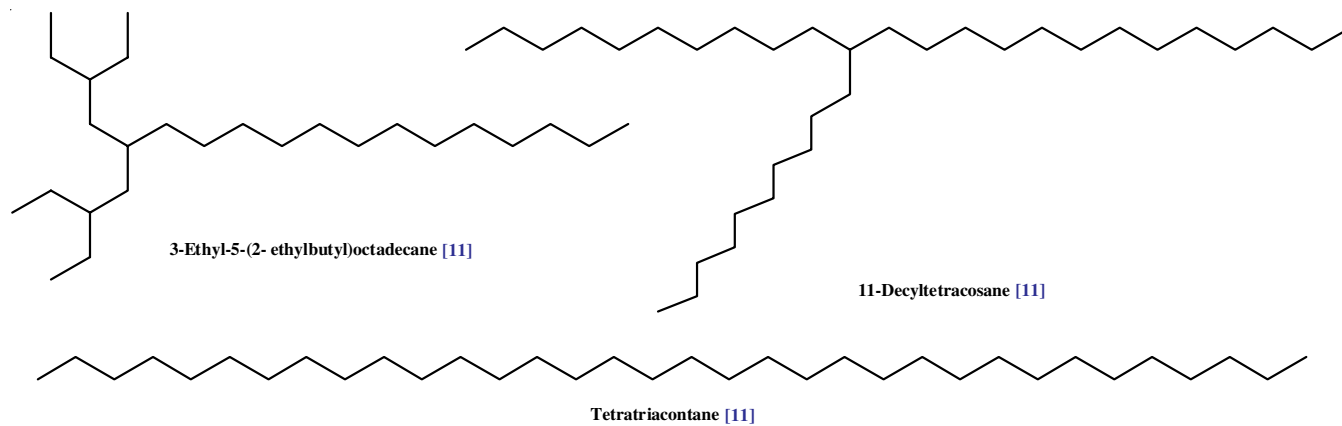
**Hydrocarbons:** Phytochemicals containing only carbon and hydrogen reported from *D. falcata* are 3-ethyl-5-(2-ethyl-butyl)octadecane [11] which has anti-inflammatory and antioxidant properties [29], 11-decyltetracosane [11] which is known to have anticancer activity [30] and tetratriacontane [11], which is reported to exhibit growth inhibition on the cancerous cells [31] (Fig. 7).

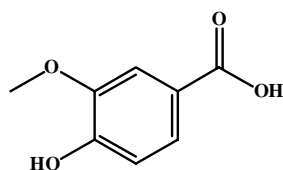
**Carboxylic acids:** 4-Hydroxy-3-methoxybenzoic acid or vanillic acid, a derivative of benzoic acid and a widely used flavouring agent, is reported to possess antioxidant activity [32]. Vanillic acid has been reported to be isolated from *D. falcata* [17] (Fig. 8).

**Phenols and tannins:** Polyphenolic substances found in plants, called tannins, have been linked to improved glucose regulation and prevention of type 2 diabetes. These have also shown potential for the discovery of new hypoglycemic agents [33]. From the extract of *D. falcata*, the few tannins isolated are ellagic acid [27], chebulinic acid [27] and gallic acid [27,34] (Fig. 9).

**Esters:** Phthalic acid esters are widely used commercially as plasticizers, have been isolated from natural sources, thus suggesting their biosynthesis in nature. These are known to exhibit allelopathic, antimicrobial, insecticidal activity and help manage biotic and abiotic stress in the organisms [35]. The Phthalic acid esters isolated from *D. falcata* are di-*iso*-octylphthalate [17], di-pentylphthalate [36] and hex-3-yl *isobutyl*-phthalate [36]. Other esters isolated are methyl ester of hexadecanoic acid [36], methyl ester of 14-oxononadec-10-enoic acid [36], methyl ester of 6-octadecenoic acid [36] and methyl

Fig. 3. Representative structure of pentacyclic triterpenoids of Oleanane series from *D. falcata*Fig. 4. Representative structure of pentacyclic triterpenoids of lupane series from *D. falcata*

Fig. 5. Representative structure of pentacyclic triterpenoids of ursane series from *D. falcata*Fig. 6. Representative structure of flavonoids isolated from *D. falcata*Fig. 7. Representative structure of some hydrocarbons isolated from *D. falcata*



4-Hydroxy-3-methoxybenzoic acid [17]

Fig. 8. Structure of vanillic acid isolated from *D. falcata*

ester of 3,5-dicyclohexyl-4-hydroxybenzoic acid [36] (Fig. 10).

**Alcohols:** Long chain fatty alcohols isolated from plants are reported to have antibacterial activity [37]. They also are known to have potential substitute for commercial insecticides [38]. To date, only one fatty alcohol is isolated from *D. falcata*, namely, nonadecane-1-ol [17] (Fig. 11).

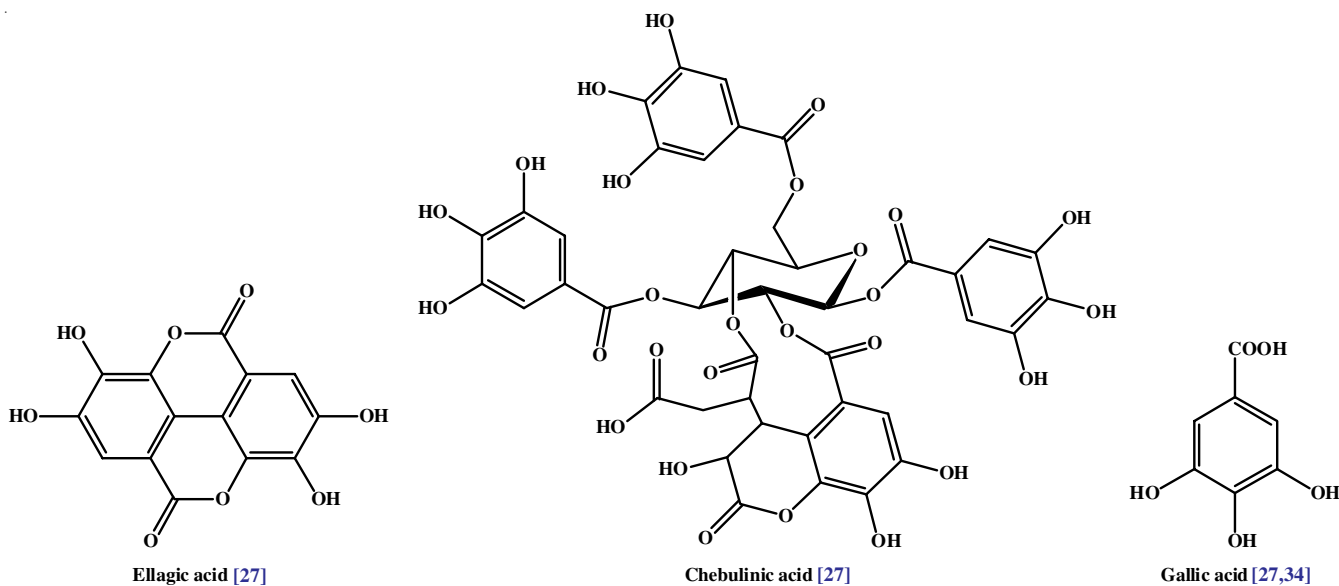


Fig. 9. Representative structure of some phenols and tannins isolated from *D. falcata*

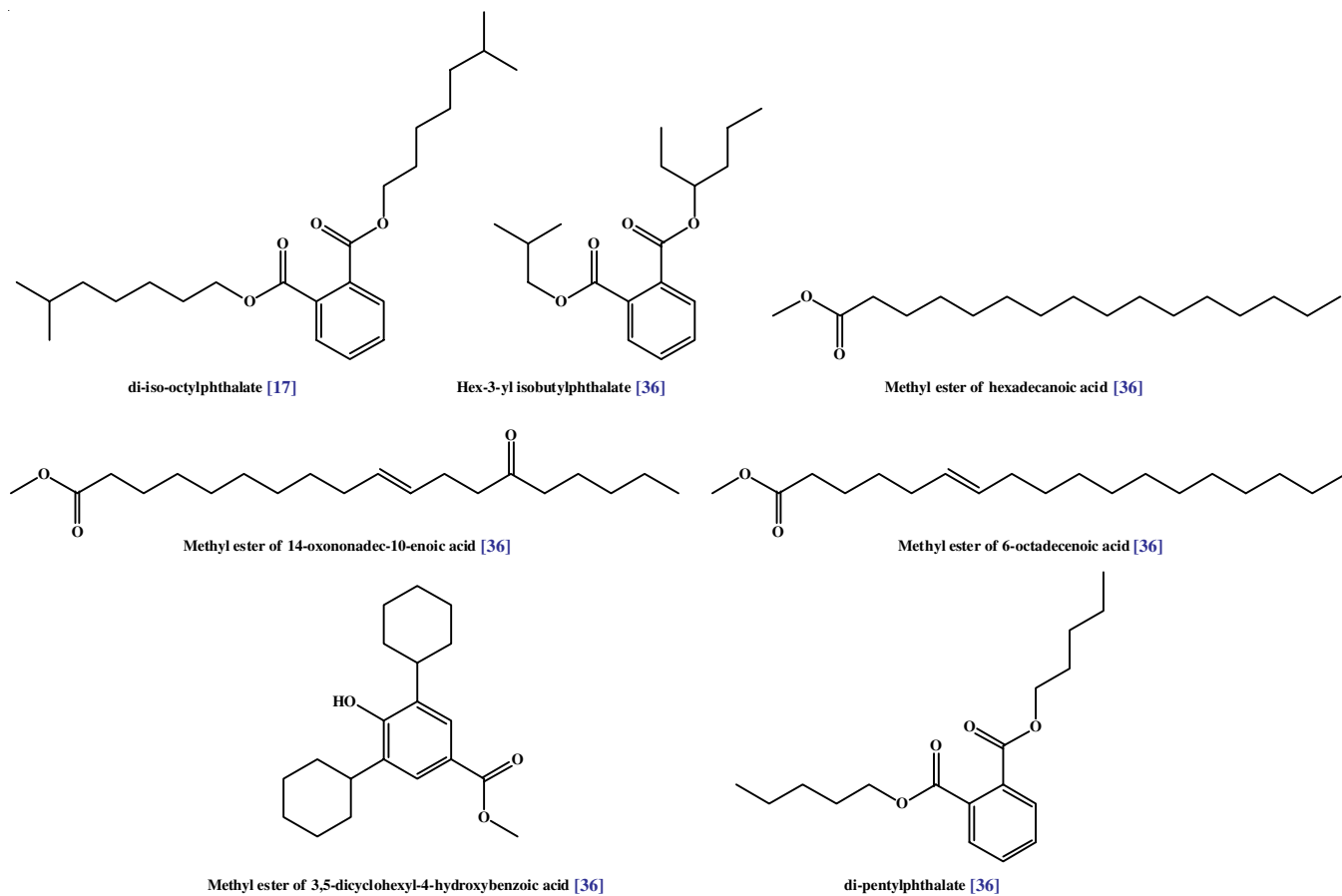
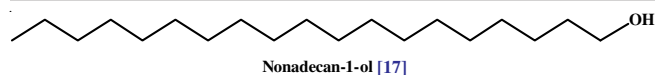


Fig. 10. Representative structure of esters isolated from *D. falcata*

Fig. 11. Structure of nonadecan-1-ol isolated from *D. falcata*

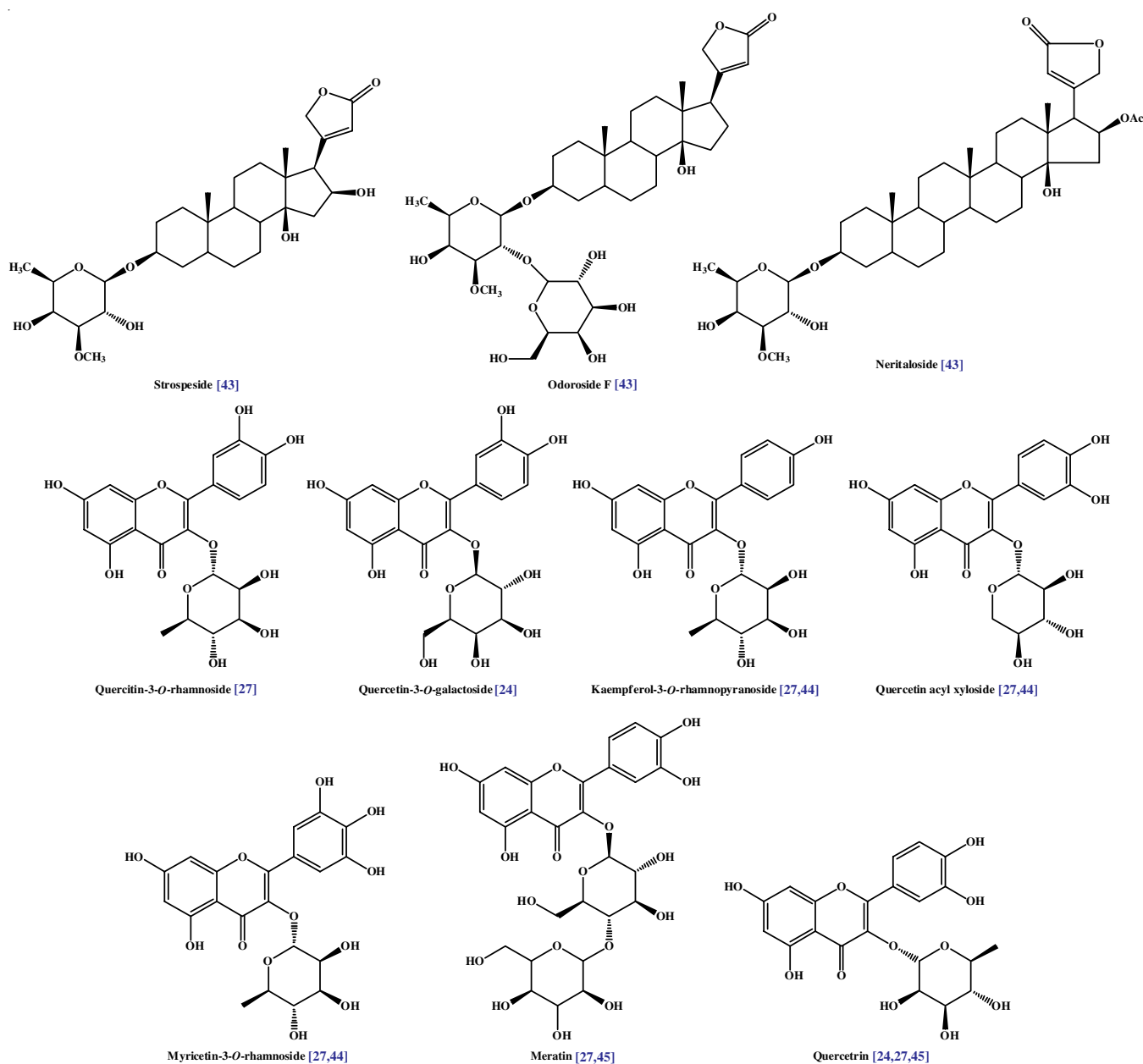
**Glycosides:** Strosposide, odoroside and neritaloside are cardiac glycosides, which are known to be used for treatment of congestive heart failure [39]. Saponins, triterpene or glycosides are widely distributed in plants and known to have been investigated for the development of new natural medicines and to establish the efficacy of traditional herbal medicines. Saponins exhibit significant anti-inflammatory, antipyretic, antiallergic and anticancer properties [40,41]. It has been reported that the glycosidic residue is important in determining the biological activity of compounds isolated from natural sources.

The *O*-glycoside derivatives of flavonoids like quercetin and other flavonoids are known to have better biological activities

[42] due to the glycosidic moiety. The glycosides isolated from *D. falcata* are strosposide [43], odoroside F [43], neritaloside [43], quercetin-3-*O*-rhamnoside [27], quercetin-3-*O*-galactoside [24], kaempferol-3-*O*-rhamnopyranoside [27,44], quercetin acyl xyloside [27,44], myricetin-3-*O*-rhamnoside [27,44], meratin [27,45] and quercetrin [24,27,46] (Fig. 12).

**Triglycerides:** Medium chain triglycerides like tricaproin (TCN) are known to inhibit oncogenic histone deacetylases, which are important in chromatin remodelling and oncogenic behaviour of cells, thereby retarding growth of cancer cells [47]. Tricaproin is reported to be isolated from *D. falcata* [36] (Fig. 13).

**Enzymes:** Enzymes isolated from plant materials are known to have widespread industrial applications. These are not only useful in avoiding hazardous materials and optimizing production, but they are also helpful in cleaving specific bonds for

Fig. 12. Structure of some glycosides isolated from *D. falcata*

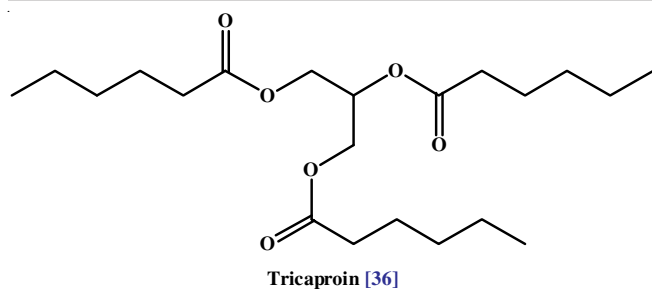


Fig. 13. Structure of tricaproin isolated from *D. falcata*

the release of bioactive molecules [48]. There are five reported enzymes isolated from *D. falcata*, namely, phosphatase enzyme [49-51], hexokinase enzyme [49-51], threonine dehydratase [52,53], glucan phosphatase [52,53] and  $\alpha$ -glucan phosphorylase [52].

**Minerals:** The few minerals isolated from *D. falcata* are calcium, iron, magnesium, phosphorus, zinc, etc. [54].

**Biological activities:** A number of studies report that the several biological activities exhibited by the extracts of *D. falcata*, which include antioxidant, antibiofilm, anxiolytic, cytotoxic, antidiabetic, antifungal, thrombolytic, *in vivo* antitumor, hepatoprotective, antihyperlipidemic and immunostimulatory activities.

**Antioxidant activity:** Rafe *et al.* [25] tested the efficacy of petroleum ether, dichloromethane, chloroform and aqueous fractions of the methanolic extract of the leaves of *D. falcata*. The antioxidant activities of these fractions were compared to that of ASA (L-ascorbic acid) using DPPH (2,2-diphenyl-1-picrylhydrazyl) assay. The  $IC_{50}$  activities of the fractions exhibit the significant antioxidant activity in leaf extracts of *D. falcata*.

Dashora *et al.* [55] conducted a study to evaluate the antioxidant activity of the methanolic and aqueous extract of stem part of *D. falcata* using the nitric oxide scavenging assay. A method reported by Prieto *et al.* [56] was used to measure the total antioxidant activity with ascorbic acid as reference. The results obtained indicated substantial free radical scavenging and antioxidant activity, thus supporting the use of *D. falcata* extract as a potent natural antioxidant with therapeutic use in antiaging and oxidative stress related degenerative diseases.

Atun *et al.* [57] identified the total phenolic and flavonoid content of *n*-hexane, chloroform and ethyl acetate fractions of the ethanol extract of stem bark of *D. falcata*. For the quantitative analysis of phenolic content, the Folin-Ciocalteu reagent was used with gallic acid as reference [58], whereas the quantitative analysis of flavonoid content was done using Liu method [59] having rutin as reference. The ethyl acetate fraction showed the highest phenolic content (2079.2 GAE/g) and highest flavonoid content (980.0 RE/g). The antioxidant activity of the fractions was tested by DPPH method using ascorbic acid as positive control [60]. The ethyl acetate and chloroform fraction showed the highest antioxidant activity.

**Thrombolytic activity:** The methanolic extract of the leaves of *D. falcata* upon further separation into petroleum ether, dichloromethane, chloroform and aqueous fractions using Kupchan method [61] was tested for thrombolytic activity [25]. The highest thrombolytic activity of 43.50% was demon-

strated by the petroleum ether extract while the other extracts showed mild activity. This study may be helpful in identifying cardioprotective drugs from the natural sources.

***In vivo* antitumor activity:** Kodithala *et al.* [62] evaluated the *in vivo* anticancer potential of the methanolic extract of leaf of *D. falcata*. The antitumor activity was studied by comparative study of tumor volume, Hb content, RBC and WBC differential count in the sacrificed mice. Survival time and increased life span were calculated from the remaining mice. The 100 mg/kg of methanolic extract (G-4) showed significant antitumor activity comparable to the standard drug used with survival time ( $34.20 \pm 0.87$ ), life span (73.95), tumor volume ( $2.24 \pm 0.26$ ) and hemoglobin ( $16.82 \pm 0.29$ ), RBC ( $11.84 \pm 0.15$ ), WBC ( $9.48 \pm 0.35$ ), lymphocytes ( $62.44 \pm 2.5$ ).

Dashora *et al.* [63] in a similar study evaluated the antitumor activity of ethanolic and aqueous extracts of *D. falcata* at doses of 200 and 400 mg/kg of body weight orally comparing with that of standard drug cisplatin (3.5 mg/kg). The study showed a significant decrease in tumor volume and increase in life span of EAC tumor bearing mice, without any visible signs of toxicity while maintaining the haematological profile. This being a criterion for evaluating the efficacy of anticancer drugs, demonstrated the potential of *D. falcata* in tumor treatment.

**Hepatoprotective activity:** *D. falcata* extracts are known to have widespread use as traditional remedies and hence, its effect on the hepatic tissue as a health risk was evaluated by Pattanayak & Priyashree [64] by studying the hepatoprotective effect of the ethanolic and aqueous extracts of the leaves of *D. falcata*. The biochemical study involved carbon tetrachloride-induced hepatotoxicity in Wistar albino rats which elevated the levels of AST, ALT, alkaline phosphatase (ALP) and total bilirubin (TB) alongside reducing the levels of proteins (TP) and bilirubin (ALB). These changes indicated the hepatocellular damage and biliary obstruction. The rats injected with 400 mg/kg of ethanolic extract of leaves of *D. falcata* showed a decrease in the elevated levels of AST, ALT, ALP and TB. A significant increase in reduced levels of TP and ALB in comparison to the control group was also observed. The results were comparable to that of the standard drug silymarin. Acute toxicity studies using up to 2000 mg/kg of ethanolic and aqueous extract showed no mortality and so the leaf extract can be considered safe.

**Antihyperlipidemic activity:** Tenpe *et al.* [65] investigated the lipid lowering activity of *D. falcata* in high fat diet Swiss Albino mice. 300 mg/kg of body weight per day of the plant extract (70% ethanol extract) was administered orally for 42 days along with a high fat diet. The study showed a significant decrease in total cholesterol and high-density triglyceride lipoprotein when compared with hyperlipidemic control, thus suggesting significant antihyperlipidemic activity in the plant extract.

**Antidiabetic activity:** Diabetes mellitus is characterized by hyperglycemia and glycosuria due to lack of insulin that maybe treated by use of insulin and hypoglycemics. Obatomi *et al.* [66] reported a significant antidiabetic activity in the streptozotocin-induced diabetes in Wistar albino rats in the

aqueous leaf extract of the African mistletoe, *Loranthus bengwensis*. The infusions significantly reduced serum glucose levels in both diabetic and non-diabetic rats. It is also reported that the antidiabetic activity to be highly dependent on the species of the host plant.

Osadebe *et al.* [67] evaluated the hypoglycaemic and antihyperglycemic activities of methanolic leaf extract of the Eastern Nigerian species of the African mistletoe on alloxan-induced diabetic rats to find the results statistically comparable to the drug glibenclamide as positive control.

Anarthe *et al.* [68] investigated the cytoprotective and oral hypoglycemic effect of *D. falcata*, growing on *Mangifera indica*, in alloxan-induced diabetic rats. At 200 mg/kg, the methanolic extract of the stem part exhibited significant antidiabetic activity with reduced blood glucose levels ( $p < 0.01$ ), cytoprotective activity ( $p < 0.05$ ), reduced the elevated levels of triglycerides ( $p < 0.05$ ) and blood cholesterol ( $p < 0.01$ ) and improved the alloxan-induced reduction in blood protein levels ( $p < 0.01$ ). The study rationalized the potential for *D. falcata* to emerge as a remedy for treatment of diabetes mellitus.

Channabasava [69] evaluated *D. falcata* for *in vitro* anti-diabetic activity using aqueous and methanolic extracts. These were observed to strongly inhibit important diabetic enzymes, namely,  $\alpha$ -amylase,  $\alpha$ -glucosidase,  $\beta$ -glucosidase and sucrase. An enzyme-starch system [70] was used to evaluate the effect of the extracts on  $\alpha$ -amylase, an enzyme responsible for hydrolyzing dietary starch into maltose which further breaks down to glucose for absorption. In animals and human beings,  $\alpha$ -amylases are the important for starch assimilation and their inhibitors maybe of value as therapeutic agents [71]. A significant correlation was observed between the inhibitory activities of  $\alpha$ -amylase,  $\alpha$ - and  $\beta$ -glucosidase and sucrase and aqueous and methanolic extracts of *D. falcata*.

Gallagher *et al.* [72] also studied the effect of aqueous and methanolic extracts of *D. falcata* on *in vitro* glucose movement. The aqueous extract decreased glucose movement by 46.04% while methanol extract reduced it by 63.13%. They also explained this on the basis of ability of phytochemicals to increase the glucose transport and metabolism in muscles or/and to stimulate insulin secretion.

**Antifungal activity:** In an attempt to study the potential of higher plants as a source of fungicides against phytopathogenic fungi, Samuel & Chaudhary [73] conducted a study to investigate the fungitoxic activity of leaf extract of *D. falcata*. The antifungal activity was tested against 12 phytopathogens *viz.* *Pythium debaryanum*, *Aspergillus niger*, *Alternaria alternata*, *Aspergillus fumigatus*, *Colletotrichum falcatum*, *Curvularia lunata*, *Fusarium moniliforme*, *Helminthosporium oryzae*, *Phytophthora infestans*, *Fusarium udum*, *Pyricularia oryzae* and *Rhizoctonia solani*. The methanolic extract exhibited the higher fungitoxic activity than the aqueous extract against *Alternaria alternata*, *Aspergillus fumigates*, *Aspergillus niger*, *Helminthosporium oryzae*, *Fusarium moniliforme*, *Fusarium udum* and *Pyricularia oryzae*. Both extracts showed the lowest inhibition for *Rhizoctonia solani*.

Being natural, the extracts are eco-friendly, non-phyto-toxic and show strong antifungal activity. Thus, the potential

for commercial formulations for protection of crops against diseases needs to be explored.

**Antibiofilm activity:** Ramesh *et al.* [11] assessed the traditional claim that the leaf extract of *D. falcata* possesses the antibiofilm and antiquorum sensing activities. Bacteria exhibit biofilm formation as a resistance mechanism against environmental stress. Biofilms are resistant to the most antimicrobial activities and thus, are important in management of human pathogenic diseases. At concentrations 300-500  $\mu\text{g/mL}$ , the leaf extract of *D. falcata* showed the pronounced effect on inhibition of biofilm formation. The presence of terpenoids in the leaf extract maybe correlated to this activity.

**Cytotoxic activity:** Rafe *et al.* [25] evaluated the potential cytotoxic activity of the methanolic extract of the leaves of *D. falcata* using brine shrimp lethality bioassay. Vincristine sulphate was used as control and significant activity of  $\text{IC}_{50}$  value of 4.477  $\mu\text{g/mL}$  was demonstrated by the crude methanolic extract. Kodithala *et al.* [62] investigated the methanolic extract of the leaves of *D. falcata* for *in vitro* and *in vivo* anticancer studies. The study involved comparison with standard drug 5-flourouracil.

**Anxiolytic activity:** Benzodiazepines are the commonly used treatment for anxiety disorders but their use may also cause problematic sedation, memory problems and other symptoms. A variety of potential medicines for treatment of anxiety disorders revealed in herbal psychopharmacology the anxiolytic and motor coordination activity of aqueous and methanolic extracts of leaves of *D. falcata* were studied by Aryal & Khan [74] in Swiss Albino mice. The elevated plus maze (EPM) and light/dark box (LDB) test were used to evaluate anxiolytic effect while motor incoordination activity was assessed by Rota-rod test. The study showed significant increase in time spent in open arm in EPM, thus indicating reduction of anxiety. Like-wise a decrease in time spent in dark box indicated anxiolytic activity. In the Rota-rod test, the methanol extract caused significant decrease in time spent on rotating rod indicating muscle relaxant activity. The study thus showed the potential use of *D. falcata* for treating anxiety disorders.

**Immunostimulatory activity:** Michael *et al.* [75] investigated the immunostimulatory activity of polysaccharide fraction of *D. falcata* on fish immunity. Groups of experimental fish *Oreochromis nilochitus* were fed with diet supplemented with low, medium and high doses of polysaccharide fraction of *D. falcata*. The fish were tested for non-specific immunological parameters, immune related gene expression and disease protection after every feeding regimen for one week. Pathogen challenge studies were done using gram negative bacteria *Aeromonas hydrophila*, commonly found in fresh waters. The treated fish exhibited significant enhancement of lysozyme activity which is one of the prevalent bactericidal enzymes and first line of defense against bacterial infections. Serum antiprotease, that inhibits the bacterial that break down host tissue, also showed increased activity. Decrease in percentage mortality and increase in percent survival was also observed as compared to control group. The study thus enhanced the innate immune mechanisms in fish fed on diet supplemented with the polysaccharide extract.



## Conclusion

In this review, we have presented information on the chemicals isolated from the extracts of leaf, stem and fruit of *Dendrophthoe falcata*. These have been categorized as steroids, sesquiterpenoids, pentacyclic triterpenoids of oleanane, ursane and lupane series, flavonoids, hydrocarbons, carboxylic acids, phenols and tannins, esters, long chain alcohols, glycosides (cardiac, flavonoids and saponins), triglycerides and enzymes, based on their structure and functional groups. The detailed reports of the biological activities exhibited by the extracts of *D. falcata* are also discussed. These studies not only justify the extensive use of *D. falcata* in traditional and folk medicine systems for a wide range of ailments but also substantiate further research of the pharmaceutical potential of its phytochemicals.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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