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Review Article

A Review on Botanical Description, Phytoconstituents, and Biological Activity of *Drypetes Roxburghii*

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ABSTRACT

The aim of this review is to discuss the distribution, botanical description, phytochemistry, and biological activity of Drypetes roxburghii. Electronic databases such as Scopus, Science direct, PubMed, Bentham were explored using scientific name Drypetes roxburghii and Putranjiva roxburghii. The results of the literature review shed light on following facet: Drypetes roxburghii syn. Putranjiva roxburghii is an important Indian medicinal plant belonging to family Euphorbiaceae, is distributed wildly and is cultivated throughout the tropical India, Sri Lanka, Java, Pakistan, Nepal, Thailand, Vietnam, West Himalayas, Bangladesh, Borneo, China Southeast, Laos, Malaya, Maluku. Various parts of the plants have been explored for the presence for several medicinally important phytoconstituents such as isopropyl isothiocyanate, Friedlein, putrone, putranjivadione, and many more. The plant has been scientifically reported to have anti-inflammatory, anti-oxidant, analgesic, anti-pyretic, anti-microbial, cytotoxic, anti-platelet, anti-thrombotic and anti-epileptic activity. This review shed light on all these aspects related to Drypetes roxburghii.

INTRODUCTION

Drypetes roxburghii (Wall.) Hurusawa, syn. *Putranjiva roxburghii* is an important Indian medicinal plant belonging to family Euphorbiaceae, is distributed wildly, and is cultivated throughout the tropical India (Khare, 2008).It is distributed in evergreen forest, scrub jungles, aside river banks from the coastal plains up to 800-1000 m(Auroville virtual Herbarium). *Drypetes roxburghii* Wall, also known as child's amulet tree or child-life tree, is a widespread plant in India. *Putranjiva roxburghii* has sparked debate due to its misleading naming and supposed ability to bear male children. The concept of changing a baby's sex after conception is recorded in ancient Ayurvedic writings (Vidhya and Nishteswar, 2015). However, no such quality or action is attributed to or related with Putranjiva in Ayurveda or any other old traditional medicine source (Gupta, 2016). The various parts of the plants have great medicinal importance in Indian traditional system as a remedy for catarrh, skin disease, fever, cold, rheumatism, sterility, filarial disease, artharlgia, swollen throat, spermatogenic, as an aphrodisiac, optic lavage, laxative etc (Wansi *et al.*, 2016)
This review aims to provide in-depth information about every aspect related to *Drypetes.roxburghii.*

DISTRIBUTION

It is widely distributed in India, Sri Lanka, Himalayas, Indo-China, Java, Moluccas, Lesser Sunda Islands, East New Guinea (Rao *et al*., 2022). Pakistan, Nepal, Thailand, Vietnam, West Himalayas, Bangladesh, Borneo, China Southeast, Laos, Malaya, Maluku (eFloraofindia, 2011). United States of America, Zimbabwe (Hurus, 1954). In India, it is distributed throughout tropical region. In Maharashtra (Pune, Raigad, Ratnagiri, Sindhudurg, Thane); Karnataka: (Belgaum, Chikmagalur, N. Kanara); Kerala (Idukki, Malapuram, Palakkad,

Thrissur, Alappuzha); Tamil Nadu (All districts); Western Assam (India Biodiversity Portal) Throughout the tropical India (Khare, 2008).

BOTANICAL DESCRIPTION

Tree: *Drypetes roxburghii*trees are up to 20 m high with dark grey bark, pendent branches, terete, brown to blackish, slender branchlets(India Biodiversity Portal).

Leaves:

Leaves of *Drypetes roxburghii* are 8-12 cm in length and 2.5-3 cm in width. It is simple, alternate, distichous, dark green-colored on upper surface and pale on lower surface; coriaceous and glabrous on both sides; Petiole5-7 mm in length, almost glabrous, pubescent, slender; lamina is elliptic-oblong to elliptic-ovate; The shape of blade is lanceolate; apex is acute or slightly acuminate with blunt/retuse tip; base is obliquely cuneate; margin serrate or serrulate, dark green, shining, glabrous; reticulate venation with flat or prominent midrib (India Biodiversity Portal; Auroville virtual herbarium, 2015).

Flower

Flowering season is from March through May. Flowers are dioeciuous. (eFloraofindia, 2011)
Male flowers are yellow, sessile, arranged in rounded axillary clusters on the main or on short axillary branches, glabrous pedicels (1.5-2mm long), 3-5 tepals: oblong, ciliate, obtuse, imbricate; 2-4 stamens (1.5-2 mm long), ovate anthers, thick filament with more or less connate towards base
Female flowers solitary or in 2-3 axil; puberulous pedicel (up to 15 mm long), lanceolate bracts, 5-6 tepals: unequal, oblong, puberulous without ciliate, superior ovary (3 x 2.5 mm), globose, tomentose, 3-celled with 2 ovules in each cell; 3 styles, spreading, tomentose, connate below into broad fleshy stigma; glandular, crescent-shaped stigma.(Kumar *et al*., 2019; Dar *et al*., 2018)

Fruits

Fruits are rounded drupe or oval-ellipsoid, 1.3 – 2 cm long, with a single seed crustaceous. Yellowish when ripe. (Kumar *et al*., 2019; Dar *et al*., 2018)

PHYTOCONSTITUENTS OF DRYPETES ROXBURGHII

Multiple secondary metabolites and biomolecules have been extracted from various vegetative sections of this plant, and their structures have been characterized. The Drypetes roxburghii species mentioned in the literature has terpenoid chemicals and mustard oils as its primary ingredients. Flavonoids and glycosides were also among the most abundant chemical groups in this species.[13] Table 1 contains phytoconstituents isolated from various parts of *Drypetes roxburghii.*

Table 1: Phytoconstituents present in various parts of Drypetes roxburghii

S. No	Part of the plant	Name of phytoconstituents	Reference
1	Seed	Isopropyl isothiocyanate	(Kala and Khan, 2020)
		1. Palmitic acid 2. Hexadecanoic acid 3. 9-octadecanoic acid 4. Linoleic acid ethyl ester 5. Ethyl oleate 6. Octadecanoic acid 7. Bis(2-ethylhexyl) phthalate	(Emasushan and Britto, 2018)
		8. N-propyl heptyl ether 9. 5-ethyl hydantoin 10. Octadec-9-enoic acid 11. 1,2-Benzene dicarboxylic acid	(Kala *et al*., 2020)
2	Bark	1. Friedlein 2. methylputranjate 3. Putrone 4. putranjivadione 5. roxburghonic acid 6. roxburghonol	(Mishra *et al*., 2019)a
3	Twigs	1. 2,4 dihydroxy-5-(hydroxymethyl) benzoic acid 2. L-quebrachitol	(Mishra *et al*., 2019)b
4	Whole plant	Friedelane-3,7-dione (Putranjivadione)	(Sengupta *et al*., 1968)
5	Fruit peel	1. Cyclohexanol 2. 5-methyl-2-(1-methylethenyl) 3. 6-Octen-1-ol, 3,7-dimethyl- 4. Geraniol 5. (1R,2S,5R)-2-(2-Hydroxy-2-propanyl)-5-methylcyclohexanol	(Hasan *et al*., 2019)

		6. 2,6-Octadiene, 2,6-dimethyl- 7. p-Menthane-3,8-diol, cis-1,3, trans-1,4 8. 2,6-Octadien-1-ol, 3,7-dimethyl-, acetate 9. 13-Docosenamide	
6	Leaves	1. Putralone, a novel 10α-hydroxy-25 nor D: A friedo-olean-9(11)-en-3 one 2. 3β-acetoxy-cycloart-24-en-23-one 3. Adian-5-en-3β,29-diol 4. 3β-acetoxy-adian-5-ene 5. Putrol 6. Putrone 7. Putranjivadione 8. Roxburghonic acids 9. Friedelin 10. Friedlan-3α-ol 11. Oleanic acid 12. Erthrodiol	(Mukharjee *et al*., 2012)
7	Bark	1. 3'-O-methylellagic acid 4-O-α-rhamnopyranoside 2. Putranoside-D 3. Putranoside-A 4. Putranoside-A methyl ester	(Kumar *et al*., 2014)
9	Seed kernels	1. Isopropyl isothiocyanate 2. Sec-butyl isothiocyanate 3. Phenyl isothiocyanate	(Puntambekar, 1950)
		1. 2-Methylbutyl isothiocyanate	(Kjaer *et al*., 1962)

BIOLOGICAL ACTIVITIES

Anti-platelet and anti-thrombotic activity

Isothiocyanate from *Drypetes roxburghii* seeds has been reported to exert significant anti-platelet and anti-thrombotic activity. Kala *et al*, 2020 isolated and characterized isopropyl isothiocyanate (IPI) from the seeds of *Drypetes roxburghii* and evaluated its anti-platelet and anti-thrombotic activity using in-vivo, ex-vivo and in-vitro experimental model. From various doses selected the dose 30 and 40 mg/kg BW was found to be potent. The test drug was able to inhibit platelet aggregation, increased clot lysis, prolonged clotting time, prothrombin time and activated thromboplastic time. Administration of IPI reduced the length of thrombus induced by intravenous carrageenan administration. The histopathological analysis of lungs after collagen and epinephrine induced pulmonary thromboembolism revealed that IPI reduced vascular and peri-vascular area thrombosis, hemorrhage and congestion. (Kala and Khan *et al.,* 2020)

The study was further extended, by preparing IPI loaded vesicles with chitosan and assessing its anti-platelet and anti-thrombotic activity. The result demonstrated that IPI chitosan vesicles showed significant anti-platelet and anti-thrombotic activity compared to pure IPI and IPI vesicles. (Kala *et al*., 2022)

Anti-epileptic activity:

A study reported anti-epileptic activity of ethanolic extract of *Drypetes roxburghii* seeds. The study involved the GC-MS analysis of ethanolic crude extract of *Drypetes roxburghii* seeds *and* assessment of anti-epileptic activity using Pentylenetetrazol (PTZ) induced seizures and Maximal electroshock seizures (MES). The anti-epileptic activity of the extract was attributed to presence of 5-ethyl hydantoin in the extract. (Kala *et al.,* 2020)

Cytotoxic activity

The methanolic extract of seed of *Drypetes roxburghii* was evaluated for cytotoxic activity using brine shrimp lethality assay at concentration 1, 10, 100, and 1000 µg/ml. The extract was able to exert cytotoxic effect on brine shrimp at dose 100, and 1000 µg/ml. The maximum effect was shown by dose 1000 µg/ml with 72% mortality. The LC_{50} of the extract was found to be 427.74 µg/ml. (Sudha and Sarath., 2019)

Nayaka S., *et al,* 2020 synthesized silver nanoparticle using aqueous extract of seeds of *Drypetes roxburghii* and assessed anti-cancer activity against human breast cancer cell line. The nanoparticles at concentration 12.5 – 200 µg/µl reduced % viability of the human breast cancer cell line cells with an IC50 of 72.32 µg/ml. (Nayaka *et al.,* 2020)

Methanolic extract of leaves of *Drypetes roxburghii* was evaluated for cytotoxic activity using MTT assay using L929 fibroblast cells over 6.25 – 100 µg/ml concentration and LC50 value was recorded as 211.776 µg/ml. (Raghvendra *et al.,* 2010)

Anti-inflammatory activity and anti-oxidant

Anti-inflammatory activity, anti-oxidant, and analgesic activity of *Drypetes roxburghii* has been studied extensively. Anti-inflammatory of various parts of leaves and stem of *Drypetes roxburghii* was studied against carrageenan-induced paw edema, croton oil induced ear edema, anus edema. The crude extract at 250 and 500 mg/kg in carrageenan-induced paw edema, p.o; 1.25, 2.5, and 5 mg/ear against croton-oil induced ear edema, and 800 mg/kg in anus edema significantly reduced the inflammation. (Khobragade., 2013 and Reanmongkol *et al.,* 2009). Kaushik et al, 2011 isolated a triterpenoidal compounds from leaf of *Drypetes roxburghii* and assessed its anti-inflammatory activity against carrageenan and dextran induced inflammation in rats. The isolated compound at dose 50 mg/kg BW significantly reduced inflammation compared to control group. (Kaushik *et al*, 2011)

Ethanolic extract of the seeds of *Drypetes roxburghii* along with *Coscinium fenestratum and Narcostachys jatamansi dc* (dose 0.5 and 1.0 mg/ml) were studied for their anti-oxidant potential using 1,1- diphenyl-2-picryl hydrazyl (DPPH) free radical scavenging assay, hydroxyl radical scavenging assay and Ferric (Fe) reducing assay. *Drypetes roxburghii* was found to have highest hydroxyl radical scavenging activity; moderate DPPH free radicle scavenging activity and Fe reducing activity. The anti-oxidant activity of *Drypetes roxburghii*was attributed to presence of flavonoids and phenolics in it (Chinmaya *et al.,* 2009).

Similarly, the ethanolic extract of stem and leaves of *Drypetes roxburghii* was found to have potent anti-oxidant comparable to that of ascorbic acid when assessed in-vitro anti-oxidant activity using DPPH and H_2O_2 model (Khobragade., 2013).

In another study, anti-oxidant activity of the ethanolic extracts of *Drypetes roxburghii* leaves was assessed using DPPH assay. The DPPH scavenging activity of the extract was compared with ascorbic acid and the IC50 value was found to be 87.80. The extract was reported to be rich cardiac glycosides, flavonoids, phenol, proteins, carbohydrates, and saponins which may be responsible for its anti-oxidant activity (Arvind *et al*., 2021).

Analgesic and anti-pyretic activity

Ether extract from the leaves of *Drypetes roxburghii* were assessed for its analgesic potential using writhing reflex, hot plate, and formalin tests and for evaluation of anti-pyretic activity yeast-induced pyrexia model in rats was used. The extract reported to decrease the writhing count and the effect at dose 400 mg/kg BW was comparable to that of standard aspirin. In formalin test, the test extract at 400 mg/kg decreased the licking activity associated with the late phase. However, the test extract does not exert protective effect against hot plate test induced pain. The author concluded that presence of flavonoids in the extract may be responsible for its analgesic and anti-pyretic activity (Reanmongkol *et al.,* 2009).

In another study, the seeds of *Drypetes roxburghii*were assessed for its analgesic activity by evaluating tail-flick latency using tail-flick analgesiometer. The extract significantly prolonged tail-latency time at 60, 90, 120, 150 minutes compared to normal control group. The study indicated that presence of flavonoids, alkaloids, saponins, and alkaloids in the extract may be responsible for analgesic activity (Sudharshan *et al.,* 2009)

Anti-microbial activity:

Nayaka S., *et al,* 2020 synthesized silver nanoparticle using aqueous extract of seeds of *Drypetes roxburghii* and assessed its anti-bacterial activity. The synthesized nanoparticles were found to have anti-bacterial property against *Staphylococcus aureus, Streptococcus pneumonia and Enterococcus faecalis*.(Nayaka *et al*., 2020)

The isolated flavonoids fraction of leaves of *Drypetes roxburghii* was evaluated for anti-bacterial properties against *Escherichia Coli, Salmonella typhimurium* and *Pseudomonas aeroginosa* and anti-fungal properties against *Apergillus fumigates, Apergillusniger* and *Microporumgypseum*. The flavonoids fraction was found to be active against E. *Coli, S. Typhimurium, P. Aeroginosa*. However, the zone of inhibition was lesser as compared to standard streptomycin (Bijekar *et al.,* 2015)

The methanolic extract of *Drypetes roxburghii* showed maximum activity against *A.flavus* followed by *A.niger*and *A.nidulans*. The extract was also found to be active against worms at concentration 5 mg/ml. It also exhibited 100% mortality of larvae of *Aedes aegypti* at dose 2.5 and 5 mg/ml (Sudharshan *et al.,* 2009)

In another study methanolic extract of leaves of *Drypetes roxburghii* (250-100 mg/ml) was evaluated for antimicrobial screening against *Escherichia coli, Staphylococcus aureus*, *Aspergillus niger* and *Candida albicans*. Among all the strains mentioned above, *Aspergillus niger* found to be the most sensitive one.(Sudha and Sarath., 2019)

Larvicidal activity:

The larvicidal activity of Ag nanoparticles fabricated from Drypetes roxburghii was assessed in a study. A total of twenty-five larvae in different stages of development (second, third, and fourth instar) belonging to the species *Anopheles stephensi* and *Culex quinquefasciatus* were individually placed into distinct glass beakers. These beakers contained deionized water as well as a solution containing silver nanoparticles (Ag NP), which was carefully dispersed to ensure the nanoparticles were evenly distributed and maintained at the desired concentration. The observation of mortality occurred within a 24-hour period subsequent to exposure. The larvae were determined to be deceased upon observation of their lack of response to needle stimulation at the

cervical region, as well as their inability to ascend to the surface within a reasonable temporal interval. Throughout the experimental trials, the larvae were subjected to a deprivation of sustenance, wherein no nutritional provisions were administered. The experiments were conducted in a manner consistent with scientific rigor, ensuring that the results obtained were reliable and reproducible. Specifically, the experiments were replicated a total of four times to validate the findings and confirm their robustness. A control group was established, consisting solely of distilled water, in order to investigate the inherent mortality rate of mosquito larvae during the designated experimental timeframe. The findings indicate a noteworthy mortality rate even when exposed to nanoparticle concentrations that are considered to be insufficient. The conducted toxicity assessment on the non-target organism revealed an absence of deleterious effects throughout the duration of the study (Haldar *et al.,* 2013).

Radioprotective activity

The radioprotective activity of the ethanolic extract derived from the seeds of Drypetes roxburghii Wall was investigated in a study involving mice. The evaluation of this activity was conducted through a 30-day survival study, followed by the assessment of antioxidant biochemical assays. The administration of a pretreatment dosage of 400 mg/kg of the ethanolic extract derived from Drypetes roxburghii Wall exhibited a notable delay in the initiation of mortality and a subsequent increase in the survival rate, reaching up to 40% when compared to the control group subjected to irradiation. An observed elevation in the in-vivo lipid peroxidation (LPO) activity was noted within the irradiation control group, which was subsequently mitigated by the administration of the extract treatment. The observed findings indicate a notable elevation in the activities of glutathione-S-transferase (GST), reduced glutathione (GSH), superoxide dismutase (SOD), glutathione peroxidase (GSHPx), and glutathione reductase (GR) within the extract group when compared to the irradiation control group. An observed phenomenon of notable magnitude was the reduction in oxidative stress resulting from exposure to radiation in an in-vitro setting. This reduction was specifically observed in the group that received treatment with an extract, targeting the mitochondrial fraction. The administration of the extract also demonstrated concentration-dependent in-vitro free-radical scavenging activity as observed in various assays including DPPH, ABTS, Total Antioxidant Capacity, and H2O2. The results indicate that the administration of 400 mg/kg of the ethanolic extract derived from the seeds of Drypetes roxburghii Wall. exhibits significant radioprotective properties (Shastry *et al.,* 2014).

DNA topoisomerases IB inhibitory activity

The activity of Type I DNA topoisomerase was evaluated through the observation of reduced mobility of the relaxed isomers of supercoiled pBS (SK+) DNA, also known as pBluescript (SK+), in a 1.2% agarose gel. The relaxation assay was performed in accordance with previously established protocols utilizing LdTOP1LS. LdTOP1LS was subjected to serial dilution in the relaxation buffer, which consisted of a composition of 25 mM Tris-HCl (pH 7.5), 5% glycerol, 0.5 mM DTT, 10 mM MgCl2, 50 mM KCl, 25 mM EDTA, and 150 µg/mL BSA. Additionally, supercoiled plasmid PBS (SK+) DNA was employed in the assay, with approximately 85-95% of the DNA being negatively supercoiled, while the remaining portion consisted of nicked circles. In all experimental investigations, the DNA and buffer mixture underwent a controlled elevation in temperature to 37°C prior to the introduction of enzymes. The reactions were expeditiously halted through the utilization of a stop solution and maintained at a low temperature by placing them in an ice bath. The gels underwent staining with ethidium bromide (EtBr) at a concentration of 0.5 µg/mL. Subsequently, the fluorescence emitted by the supercoiled monomer DNA band was measured using Gel Doc 2000 equipment, which was operated under UV illumination. The quantification of fluorescence was performed through integration, utilizing the Bio-Rad Quantity One Software. The isolated compound demonstrated significant inhibitory activity against DNA topoisomerase IB (Kumar *et al.,* 2014).

Adulticidal activity

In a study adulticidal effectiveness and repellent capabilities of crude and ethyl acetate extracts derived from fully developed fruits of Drypetes roxburghii (Wall.) Hurus was evaluated. The study focused on evaluating the impact of these extracts on adult specimens of *Culex quinquefasciatus* and *Anopheles stephensi*, employing established protocols for accurate analysis. In both mosquito species, it was observed that the mortality rate exhibited a gradual increase as the concentrations of ethyl acetate extract were elevated. The LC50 and LC90 values of the ethyl acetate extract were determined to be 109.62 ppm and 189.01 ppm, respectively, for *Culex quinquefasciatus* in the adulticidal bioassay. Similarly, for *Anopheles stephensi*, the LC50 and LC90 values were found to be 95.41 ppm and 181.96 ppm, respectively. *Anopheles stephensi* exhibited a higher susceptibility towards the ethyl acetate extract compared to *Culex quinquefasciatus*. Both the crude and ethyl acetate extracts exhibited noteworthy potentiality in terms of repellency. The application of an ethyl acetate extract with a concentration of 99% resulted in complete protection, reaching 100%, against the biting activity exhibited by both mosquito species for a duration of 120 minutes (Mallick and Chandra., 2015).

Anti-plasmodial activity

The investigation focused on assessing the anti-plasmodial activity of a triterpene and triterpenoid compound isolated from Drypetes roxburghii. This was accomplished by employing an in vitro assay that measured the activity of parasite-specific lactate dehydrogenase (pLDH). The IC50 values obtained from the experiment indicate that friedlein (2.40 ± 0.70) and roxburghonol (4.10 ± 1.7 µg/ml) exhibit superior anti-plasmodial activity compared to the other isolated triterpenes. However, their potency falls short when compared to chloroquine (0.023 ± 0.002 µg/ml), which demonstrates a significantly higher efficacy against the chloroquine-sensitive Plasmodium falciparum (3D7) strain (Mishra *et al*., 2021).

Cytogenetic activity

Swiss albino mice in the weaning stage were subjected to oral administration of Putranjiva roxburghii leaf extract at varying dosages of 0.5, 1.0, or 2.0 g/kg body weight per day, over a period of seven consecutive days. The findings of the study revealed that the application of the leaf extract exhibited a noteworthy capacity to provoke chromosomal alterations that disrupt the process of mitosis in cells found within the bone marrow. However, it is worth noting that there was no observed alteration in the occurrence of structural abnormalities within the metaphase chromosomes. The hypothesis suggests that the administered extract may have potentially disrupted the normal functioning of spindle proteins and other associated proteins, thereby leading to the occurrence of polyploidy, aneuploidy, and c-mitosis (Awasthy *et al*., 2000).

CONCLUSION

The review contained detailed information on *Drypetes roxburghii* and shed light on its medicinal importance. There is lots of scope of research on the plant related to isolation of its phytoconstituents and determination of its medicinal value. As the herbal medicine is gaining massive momentum among the majority of the population, *Drypetes roxburghii* among other medicinal plant can be studied extensively to be included as a potent herbal medicines and combination.

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