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Research Article

A Clinical Investigation of Acalypha Wilkesiana's Possible Heart-Protecting Effects: Combining Network Pharmacology With In Vivo Research

Hrutik Sunil Jaiswal*, Aditi Jyotishi, Karna Khavane

Dr. Vedprakash Patil College of Pharmacy, Chh. Sambhajinagar.

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ABSTRACT

Acalypha wilkesiana's hydroalcoholic Extract shows a broad spectrum, a multiple-protective cardiac protector against myocardial lesions caused by doxorubicin. Extracts structural and functional degradation of the heart through regulation of oxidative stress, inflammatory mediators, apoptosis regulators, and electrophysiological parameters. Histological storage, normalization of enzymes, and hemodynamic recovery confirms efficiency at the physiological level. The integration of network pharmacology and molecular mooring shows that biologically active major components target central cardiac alarm paths containing PI3K/AKT, NF-ux, and estrogen receptors, thus confirming the extracted polyfuma pharmacologic diet. In particular, components such as quercetin, chorrazine, and campferol have preferred drug profiles and biological activities, further improving their role in observed cardioprotective effects. Overall, the findings provide strong preclinical support for Acalypha wilkesiana as a phytopharmaceutical option for the treatment of chemotherapy-induced cardiotoxicity. Future research should focus on thorough pharmacokinetic and safety profiles, formulation uniformity, and clinical validation. Given its promising effectiveness and safety profile, AW extract has the potential to be integrated into cardio-oncology therapy regimens as a supplemental or adjunct intervention.

INTRODUCTION

Copperleaf is a remarkable plant which has leaves that are more colorful than many flowers. It grows as a spreading evergreen shrub with upright branches that tend to originate near the base. It can get up to 10 ft tall with a similar spread. Alternately arranged leaves are elliptic to oval, toothed, 5-8 in long and multi-colored. The flowers are small and inconspicuous, in 4-8 in long, somewhat drooping, green racemes often

***Corresponding Author:** Hrutik Sunil Jaiswal
Address: *Dr. Vedprakash Patil College of Pharmacy, Chh. Sambhajinagar.*
Email ✉: hrutikjaiswal@gmail.com

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hidden in the foliage. Many cultivars are available with different leaf forms and colors.[1] Acalypha wilkesiana 'Marginata' has coppery-green leaves with pink or crimson margins. 'Macrophylla' has larger leaves, variegated with bronze, cream, yellow and red. The leaves of 'Musaica' are mottled with orange and red. 'Godseffiana' has narrow, drooping leaves with cream colored margins. Copperleaf is native to Fiji and neighboring South Pacific islands, widely cultivated in India. A much-branched monoecious shrub up to 4.5 m. Young shoots tomentose, later puberulous. Petioles (1-) 2-5 (-9) cm long. Leaf-blade broadly ovate, 5-17 (-25) x 5-13 cm, shortly obtusely or acutely acuminate, rounded-cuneate to cordate, crenate-serrate, 7-11-nerved from the base,[2] sparingly pubescent above and beneath at first, especially along the midrib and main veins, later subglabrescent, often copper- or bronze-coloured, sometimes white- or pink-margined (var. marginata Mill.) or variegated. Stipules subulate, 1-1.5 cm long. Inflorescences axillary, solitary, unisexual, spicate; the males up to 7 cm long, fairly dense-flowered, with a pubescent axis and lanceolate bracts c. 1 mm long; the females up to 12 cm long, lax-flowered, with a puberulous axis; female bracts 7-13-partite, the median lobe broadly ovate and accrescent to 5 mm long and 3 mm wide, the laterals smaller and narrower, 1-flowered. Male flowers sessile; buds tetragonal, pubescent. Female flowers sessile; sepals 3-4, ovate-lanceolate, 1 mm long, acute; ovary subglobose-trilobate, 1 mm diam, densely pubescent; styles united at the base, (5-) 7-9 mm long, laciniate, yellowish-or greenish-white, occasionally reddish. Fruits trilobate, 1.5-2 mm long, 4 mm diam., smooth, pubescent[3].



Figure 1: ***Acalypha wilkesiana Müll.Arg***

Acalypha wilkesiana is a phytochemically rich plant containing a diverse range of bioactive constituents that contribute to its wide spectrum of therapeutic activities. Its leaves are known to possess flavonoids such as quercetin, kaempferol, rutin, apigenin, luteolin, orientin, and catechin, which offer strong antioxidant, anti-inflammatory, and antidiabetic effects[4]. The presence of hydrolyzable tannins like geraniin, corilagin, gallic acid, and ellagic acid supports its antimicrobial, hepatoprotective, and antioxidant properties. Additionally, phenolic acids such as caffeic, chlorogenic, and syringic acids contribute to its cytoprotective action. The plant also contains triterpenoids and sterols, including β-sitosterol, stigmasterol, squalene, ursolic acid, and oleanolic acid, which exhibit lipid-lowering, anticancer, and anti-inflammatory potential [5]. Alkaloids, saponins, cardiac glycosides, and anthraquinones are also present, each contributing to its immunomodulatory, analgesic, and cardiotonic effects. GC-MS analyses have revealed further compounds like acetaldehyde, ethyl gallate, cyclopropyl carbinol, and hexadecanoic acid, which are associated with antimicrobial and insecticidal activities. Furthermore, proximate and elemental analysis has confirmed the presence of essential vitamins (C, E, A, B-complex) and minerals (potassium, sodium, calcium, magnesium, zinc), supporting its nutritional

value[6]. Ethnomedicinally, *Acalypha wilkesiana* has been traditionally employed for treating various ailments across Africa, Asia, and the Pacific Islands. It is widely used for managing skin infections, boils, and eczema through topical applications, and for treating gastrointestinal conditions such as dysentery, ulcers, and diarrhea using leaf decoctions[7]. The plant is also used for blood sugar control in diabetic individuals and for its hepatoprotective effects in cases of toxin-induced liver damage. Its analgesic and anti-inflammatory properties support its use in treating fever, arthritis, and general body pain. The plant is traditionally consumed for cardiovascular health, with scientific validation showing its efficacy in lowering blood cholesterol and regulating blood pressure. It is also used for wound healing, oral hygiene (as a chewing stick), and as an antiemetic agent. Moreover, due to its insecticidal properties, *Acalypha wilkesiana* oil is applied in traditional grain preservation and pest control[8].

1. Scope of Work

Despite the broad ethnopharmacological relevance of *Acalypha wilkesiana* in managing cardiovascular conditions, inflammatory disorders, and oxidative stress, there remains a substantial scientific gap concerning its cardioprotective potential, particularly in relation to chemotherapy-induced cardiotoxicity[9]. Traditionally utilized for blood pressure regulation, lipid profile modulation, and general cardiac support, *A. wilkesiana* is phytochemically rich in flavonoids (quercetin, kaempferol, catechin), hydrolyzable tannins (geraniin, corilagin), triterpenoids (ursolic and oleanolic acids), and phenolic acids, all known for their potent antioxidant, anti-inflammatory, and cytoprotective actions[10]. While several studies have validated its antidiabetic, hepatoprotective, and antimicrobial properties, and a few have explored its in vitro antioxidant and anti-inflammatory activities, there is a conspicuous lack of integrative studies assessing its cardioprotective efficacy in established in vivo models such as doxorubicin-induced cardiotoxicity[11]. Moreover, its bioactive constituents have not been systematically examined for their interaction with molecular targets involved in oxidative myocardial injury, mitochondrial dysfunction, and inflammatory cascades—key mechanisms in anthracycline-induced cardiotoxicity[12]. Network pharmacology, in tandem with in vivo validation, remains unexplored in this context for *A. wilkesiana*. Thus, there exists a compelling need to bridge this gap by employing a systems pharmacology approach coupled with in vivo evaluation to unravel the cardioprotective mechanisms, multi-target interactions, and therapeutic potential of *A. wilkesiana*, paving the way for its development as a safe, plant-based adjunct in cardioprotection, particularly for patients undergoing chemotherapy[13].

2. Experiment And Results

3.1 Collection and authentication of plant Material

The Leaves of the plant *Acalypha wilkesiana* Müll.Arg was collected from Nashik District, Maharashtra, India in July 2024. The botanist performed authentication of the plant at Sandip University, Nashik, India, and prepared the herbarium of the plant deposited at Sandip University, Nashik, India (Voucher specimen no SUN2024/07/09)

3.2 Extraction

A total of 1000 g of dried leaf powder was extracted by maceration in a hydroalcoholic solvent system (70:30 v/v) with intermittent

stirring at 25 ± 2°C for three days[14]. The extract was then filtered through a sterile cotton plug using a Buchner funnel. The solvent was removed under reduced pressure using a rotary evaporator, resulting in 34.94 g of crude hydroalcoholic extract. This extract was subsequently used for the evaluation of cardioprotective activity[15].

Yield of Extract – 3.49 %

3.3 Pharmacological Investigation

Electrocardiographic parameter

The effect of *Acalypha wilkesiana* leaves hydroalcoholic extract on cardiac electrophysiology in doxorubicin induced cardiotoxicty are summarized.

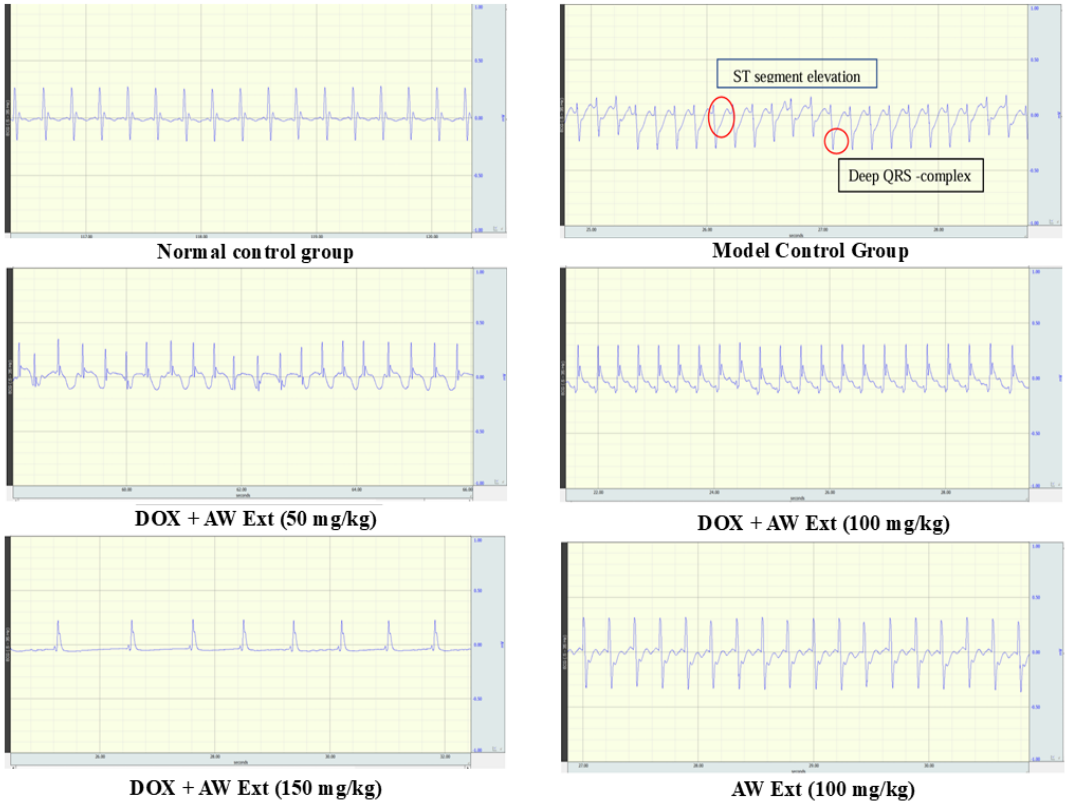


Figure 2: Photograph showing the changes in the rat ECG wave front

Effect of *Acalypha wilkesiana* leaves hydroalcoholic extract (AW) on changes in ST height in doxorubicin induced cardiotoxicity in rats

The analysis of variance (ANOVA) revealed no statistically significant differences in ST segment height among the six experimental groups ($F(5,30) = 0.569$, $P = 0.7231$), indicating that treatment with hydroalcoholic extract of Acalypha wilkesiana (AW), standard drug, or doxorubicin alone did not lead to significant alterations in ST segment height compared to the control. The R^2 value was 0.08662, suggesting a very low proportion of variance in ST height explained by the treatment groups[16]. Bartlett's test for homogeneity of variances showed a statistically significant result (Bartlett's statistic = 13.04, P = 0.023), suggesting that there were unequal variances across the groups, although this heterogeneity did not translate into significant group differences in the ANOVA. The Brown-Forsythe test result was not

reported, further confirming the primary ANOVA findings remain inconclusive regarding treatment effects on this ECG parameter. Dunnett's multiple comparisons test was employed to compare the treatment groups with the control group. The results revealed that none of the treatment groups—including the PERSE (AW Ext) treated group—showed a statistically significant difference in ST segment height compared to the control group. The mean difference between the control and the AW-treated group was −0.00055 (95% CI: −0.00762 to 0.00652), with an adjusted P value of 0.9997, indicating a nonsignificant change. Similarly, comparisons with other groups—Column B (mean diff. = 0.00246, P = 0.8218), Column C (mean diff. = 0.00311, P = 0.6598), Column D (mean diff. = 0.00088, P = 0.9972), and Column E (mean diff. = 0.00064, P = 0.9994)—also did not yield significant differences[17]. These findings confirm that the ST segment height remained unchanged across all experimental groups, further supporting the earlier ANOVA conclusion that the treatments, including AW extract, had no significant impact on this ECG parameter in the doxorubicin-induced cardiotoxicity model[18].

3. CONCLUSION

In conclusion, *Acalypha wilkesiana* hydroalcoholic extract demonstrates a broad-spectrum, multi-targeted cardioprotective effect against doxorubicin-induced myocardial injury. Through modulation of oxidative stress, inflammatory mediators, apoptotic regulators, and electrophysiological parameters, the extract mitigates structural and functional cardiac deterioration. Histological preservation, enzyme normalization, and restoration of hemodynamics substantiate its efficacy at the physiological level. The integration of network pharmacology and molecular docking reveals that key bioactive constituents target central cardiac signaling pathways—including PI3K/Akt, NF-κB, and estrogen receptor pathways—thus validating the extract's polypharmacological mode of action. Particularly, constituents such as Quercetin, Corilagin, and Kaempferol exhibit favorable drug-likeness and bioactivity profiles, further reinforcing their role in the observed cardioprotective effect. Collectively, the findings provide robust preclinical evidence for *Acalypha wilkesiana* as a potential phytopharmaceutical candidate in the management of chemotherapy-induced cardiotoxicity. Future directions should include detailed pharmacokinetic and safety profiling, formulation standardization, and clinical validation. Given its favorable efficacy and safety profile, AW extract holds promise for integration into cardio-oncology therapeutic protocols as a complementary or adjunct intervention.

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