

Research Article



Integrative Phytochemical Profiling, GC-MS Characterization, *In Silico* Prediction, and Multi-Target Molecular Docking Reveal the Wound-Healing Potential of *Pavonia zeylonica* (L.)

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ABSTRACT

Pavonia zeylonica is traditionally used for the treatment of wounds, cuts, abrasions, and inflammatory skin disorders, and this study aimed to evaluate its phytochemical composition, antioxidant potential, bioactive constituents, pharmacokinetic properties, and wound-healing activity through *in vitro* and *in silico* approaches. Leaf extracts were prepared successively using petroleum ether, ethanol, and water by Soxhlet extraction and subjected to preliminary phytochemical screening, estimation of total phenolics, flavonoids, and tannins, DPPH radical scavenging assay, GC-MS analysis, ADME/T prediction, and molecular docking studies against COX-2, VEGFR, FGFR, and EGFR proteins. The ethanolic leaf extract showed the highest phenolic, flavonoid, and tannin contents and exhibited strong antioxidant activity with an IC₅₀ value of 21.72 ± 0.6 µg/mL. GC-MS analysis identified 33 phytocompounds, among which Ethyl-α-D-glucopyranoside and γ-sitosterol were predominant. ADME/T analysis indicated favourable pharmacokinetic and low-toxicity profiles for the identified compounds. Molecular docking studies revealed strong binding affinities of γ-sitosterol toward wound-healing target proteins, suggesting its role in inflammation control, angiogenesis, and tissue regeneration. These findings support the therapeutic potential of *P. zeylonica* as a promising natural source for wound-healing drug development.

Keywords: Wound healing, γ-sitosterol, GC-MS analysis, Antioxidant Activity, Molecular docking.

INTRODUCTION

A wound is generally defined as the disruption or loss of the normal anatomic and functional continuity of living tissues. Wound healing is a dynamic and multifactorial biological process aimed at restoring tissue integrity through a series of overlapping stages: haemostasis, inflammation, proliferation, and remodelling¹. When any of these stages are impaired, wound healing becomes delayed or incomplete, resulting in chronic wounds². Chronic wounds, such as diabetic foot ulcers, venous leg ulcers, and pressure ulcers, are typically trapped in a persistent inflammatory state with inadequate angiogenesis, poor granulation, and insufficient oxygenation, leading to delayed closure and frequent infections³. Chronic wounds continue to pose a serious global health and economic challenge. Reports from the World Health Organization (WHO) and other wound-care studies highlight that millions of people are affected each year, especially older adults and individuals with diabetes. These conditions often lead to prolonged pain, reduced quality of life, and increased healthcare expenses⁴. In Europe, chronic wounds account for a notable share of healthcare spending, estimated at around 1- 2% of national budgets. In the United States, over 5 million individuals experience non-healing wounds each year⁵. In many developing countries, the financial burden of treatment is often difficult to manage, and wound conditions are further complicated by a higher risk of infection⁶. Studies from Europe indicate that diabetic foot ulcers are a leading cause of lower-limb amputations, accounting for nearly 85% of

cases⁷. In regions such as sub-Saharan Africa and South Asia, chronic wounds affect approximately 1-2% of the population at some point in their lives⁸.

A wide range of therapeutic agents has been developed, and several others are still being explored, highlighting the complex nature of wound healing⁹; (WHO, 2024). Pharmacological approaches include growth factor-based treatments such as becalpermin and epidermal growth factor formulations, which promote fibroblast activity and support angiogenesis¹⁰. Enzymatic agents, including collagenase and papain- urea, are commonly used to aid in debridement. In addition, antimicrobial preparations like silver sulfadiazine, mupirocin and povidone-iodine are widely applied to manage infection and reduce inflammation¹¹. Although effective, these therapies are often expensive, can induce cytotoxicity or allergic reactions, and may contribute to antimicrobial resistance¹². Additionally, most synthetic drugs act via single-target mechanisms, limiting their ability to address the multifaceted nature of wound healing involving oxidative stress, inflammation, and tissue remodeling¹³. Plant-based medicines provide a safe, affordable, and multi-targeted approach¹⁴. Phytochemicals such as flavonoids, phenolics, tannins, alkaloids, and saponins demonstrate strong antioxidant, anti-inflammatory, antimicrobial, and collagen-promoting properties¹⁵. These compounds act synergistically to modulate oxidative stress, suppress excessive inflammation, stimulate fibroblast proliferation, and promote angiogenesis, key processes in effective tissue repair (WHO, 2024). Moreover, herbal remedies are less



likely to cause adverse effects and are particularly valuable in low-resource settings¹⁶.

According to WHO (2024), nearly 80% of the global population depends on traditional medicine for primary healthcare needs¹⁷. In many developing countries such as China and India, they are use plants-based medicines for managing wounds, burns, and skin infections is a long-standing tradition¹⁸. Medicinal herbs help maintain a moist wound environment, promote tissue granulation, and accelerate epithelialization. The growing evidence supporting their pharmacological efficacy has shifted global research interest toward validating traditional knowledge and discovering novel phytotherapeutics for wound care¹⁵. Traditional medicine continues to play an important role in accessible healthcare and also provides valuable insights for modern drug discovery. Medicinal plants are rich in bioactive secondary metabolites, many of which demonstrate antioxidant, anti-inflammatory, and tissue-regenerative properties¹⁹. Among the plants traditionally used for wound-healing, *Pavonia zeylonica* (L.) Cav., (family Malvaceae) has attracted due to its ethnomedicinal importance, diverse phytochemical profile, and potential biological activities. This species is widely distributed in tropical and subtropical regions and has long been used by rural and tribal communities to manage wounds, inflammation, and skin infections²⁰. In southern India, *Pavonia zeylonica* is used in traditional systems such as Ayurvedic, Siddha, and Unani medicine, and is also employed by indigenous communities including the Kurumba, Irula, Toda, and Paniya tribes of the Nilgiris in Tamil Nadu. These groups typically prepare leaf pastes or decoctions, which are applied topically to treat cuts, ulcers, and boils²¹. Similar uses have been documented in countries such as Sri Lanka, Bangladesh, as well as parts of Africa and South America, underscoring the broader cultural relevance to its traditional applications, with leaf extracts showing anti-inflammatory, analgesic, and antioxidant activities²². Pharmacological studies further support the plant's traditional use, indicating anti-inflammatory, analgesic, and antioxidant properties in leaf extracts²³.

To validate its traditional uses scientifically, advanced analytical and computational approaches such as Gas Chromatography- Mass Spectrometry (GC-MS), ADMET profiling, and molecular docking are increasingly applied²⁴. ADMET analysis- covering absorption, distribution, metabolism, excretion, and toxicity helps assess drug-likeness and pharmacokinetic properties, providing insights into safety, bioavailability, and metabolic stability²⁵. Such computational modelling provides early insight into a compound's therapeutic potential and toxicity before experimental or clinical validation²⁶. Molecular docking analysis provides insights into the interaction between phytocompounds and key wound-healing target proteins²⁷. Simulating ligand- receptor binding, docking studies help predict the potential of these compounds to modulate inflammatory responses, enhance angiogenesis, and stimulate collagen synthesis, fundamental processes that collectively promote tissue regeneration²⁸.

The present investigation represents the first comprehensive study integrating phytochemical profiling, antioxidant evaluation, GC-MS characterization, ADMET prediction, and multi-target molecular docking analysis of *Pavonia zeylonica* leaf extracts for wound healing applications. Notably, 33 phytoconstituents were identified through GC-MS analysis, including ethyl α -D-glucopyranoside and γ -sitosterol, which are reported for the first time in this species. Furthermore, this study is the first to evaluate the multi-target interaction of major phytocompounds against key wound healing proteins (COX-2, VEGFR, FGFR and EGFR), highlighting γ -sitosterol as a promising multi- mechanistic modulator. The integrative *in silico* and phytochemical validation provides a scientific basis for the traditional use of *P. zeylonica* and proposes it as a potential source of novel wound-healing therapeutics.

MATERIALS AND METHODS

Collection and identification of plant materials

The plant *Pavonia zeylonica* L. was collected from Thirumalayam Palayam Village, Coimbatore, Tamil Nadu, India (Fig. 1). Fresh leaves were collected between January and May 2023. The taxonomic identification of the plant was verified and authenticated by comparison with the Gamble herbarium-type specimen at the Botanical Survey of India, Southern Circle, Tamil Nadu, India (BSI/SRC/5/23/2023-24/Tech-96). To remove dirt and debris, the plant samples were washed thoroughly with running tap water and rinsed two to three times with distilled water. The cleaned samples were cut into small pieces and air-dried at room temperature. The dried materials, finely ground using a mechanical grinder, yielded a powder stored at 4°C until further use.

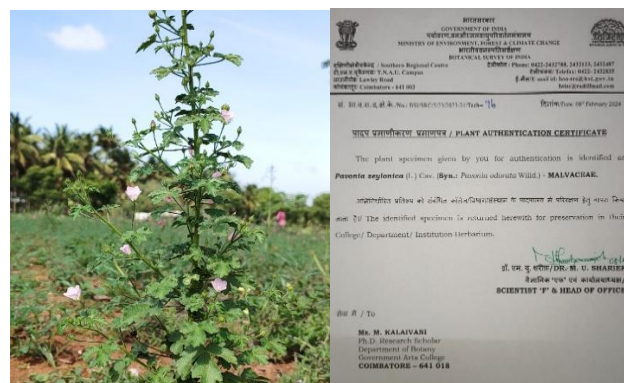


Figure 1: Monograph of the whole plant of *P. zeylonica* L. and an authenticated certificate

Extraction preparation

Approximately 50 g of powdered plant material underwent extraction with organic solvents in increasing order of polarity, beginning with petroleum ether, followed by ethanol and hot water. A Soxhlet extraction method facilitated this process. The thimble was air-dried before each extraction with the following solvent. For the aqueous extraction, a solvent-to-plant material ratio of 3:1 (v/w) was maintained to ensure efficient extraction of water-soluble compounds. Finally, the material was macerated with hot

water and stirred continuously for 24 hours, and the water extract was filtered using Whatman No. 1 filter paper. The solvents were evaporated with a rotary vacuum evaporator, and the condensed extracts were dried in hot air. The dried extracts were kept at 20°C and used for biochemical estimation.

Phytochemical Studies

Preliminary Phytochemical Screening

The petroleum ether, ethanol, and aqueous extracts of the plant material were subjected to preliminary phytochemical screening to identify the presence of major classes of secondary metabolites, following standard procedures²⁹. Qualitative tests were performed to detect compounds such as alkaloids, flavonoids, tannins, saponins, glycosides, steroids, terpenoids, and phenolic compounds. For alkaloids, Mayer's and Wagner's tests were used, in which the formation of a precipitate indicated the presence of alkaloids. Flavonoids were detected using the Shinoda test and alkaline reagent test, based on the development of a red or yellow colouration. Tannins were confirmed by the ferric chloride test, which produces a blue-black or greenish colouration, whereas saponins were identified by their ability to produce stable froth upon vigorous shaking with water. Glycosides underwent evaluation using Keller-Killiani and Borntrager's tests, with positive results indicated by distinct colour changes after reaction with specific reagents. Steroids and terpenoids showed characteristic colour development in the Liebermann-Burchard and Salkowski tests. Phenolic compounds produced green, blue, or purple coloration in the ferric chloride test, confirming their presence. All analyses included three independent trials to ensure consistency, and observations were recorded systematically for further interpretation.

Quantitative biochemical analysis

Major secondary metabolites, including total phenolics, tannins, and flavonoids were quantified using standard colorimetric assays. Total phenolic content followed the Folin-Ciocalteu method³⁰. Briefly, a measured volume of plant extract reacted with Folin-Ciocalteu reagent, after which sodium carbonate solution was added. Following incubation, the development of a blue colour was recorded at 765 nm using a spectrophotometer. Gallic acid served as the standard, and results were expressed as mg of gallic acid equivalents per gram of extract (mg GAE/g). Tannin content was estimated according to Siddhuraju and Manian³¹. The plant extract reacted with vanillin-HCl reagent under controlled conditions, leading to the formation of a red colour. Absorbance was measured at 500nm, with catechin used as the reference standard. The results were expressed as mg catechin equivalents per gram of extract (mg CE/g). Flavonoid content was determined using the aluminium chloride colorimetric method described by Zhishen et al.³². The extract was treated with aluminium chloride solution and allowed to react at room temperature for 30 minutes. The appearance of a yellow colour indicated the presence of flavonoids, and absorbance was measured at 510 nm.

Quercetin was used as the standard, and values were expressed as mg quercetin equivalent per gram of extract (mg QE/g).

In vitro antioxidant activity

DPPH (2,2- diphenyl-1-picrylhydrazyl) Scavenging Activity

The extract's antioxidant activity was evaluated in terms of hydrogen-donating or radical scavenging capacity using the stable radical DPPH, as per Blois's method³³. Sample extracts were obtained in various amounts and reduced to 100 μ L with methanol. The aliquots of samples and standards (BHA, BHT, & Rutin) were then vigorously shaken in around 5 mL of a 0.1 mM methanolic DPPH solution. To generate the negative control, 100 μ L of methanol was mixed with 5 mL of a 0.1 mM methanol solution of DPPH. The tubes were left to stand for 20 minutes at 27°C. The sample's absorbance was measured at 517 nm against the blank (methanol). The samples' radical scavenging activity was represented as IC₅₀, which is the concentration required to block 50% of the DPPH concentration.

Gas Chromatography mass spectrum (GC-MS)

GC-MS analysis of the two collected fraction extracts was performed using a Clarus 600 gas chromatograph equipped with a Clarus 600C mass spectrometer (PerkinElmer, USA). The GC-MS study was carried out at DRDO-Bharathiar University, Centre for Life Sciences, Coimbatore, Tamil Nadu, India. Elite-5 MS (5% biphenyl 95% dimethylpolysiloxane, 30 m $\times$ 0.25 mm ID $\times$ 250 μ m df) and the components were separated using helium as the carrier gas at a constant flow rate of 1 mL/min. The injector temperature was set to 260°C during the chromatographic run. A 1 μ L extract sample was inserted into the apparatus. The oven temperature was initially held at 60°C for 2 min, then increased at a rate of 10°C per minute until it reached 300°C, where it was maintained for 6 min. The mass detector conditions were as follows: transfer line temperature of 240°C; ion source temperature of 240°C; and ionisation mode electron impact at 70 eV, a scan time of 0.2s and a scan of 0.1s. Fragments ranged from 40 to 600 Da. The spectra of the components were compared with the database of known components stored in the GC-MS NIST (2008) library³⁴.

ADME and Drug-likeness prediction

Experimental evaluation of the Absorption, Distribution, Metabolism, and Excretion (ADME) properties was assessed by Swiss ADME. The Swiss Institute of Bioinformatics (SIB) website was accessed in a web browser that displays the submission page of Swiss ADME. The simplified molecular-input line-entry system (SMILES) was retrieved from the PubChem database, pasted into the computational input zone, and found on the right side of the submission page. The program was processed, and the ADME, physiochemistry, drug-likeness, pharmacokinetics and medicinal chemistry properties were estimated. Drug-likeness was assessed using Lipinski's rule, the Ghose filter, MDDR-like rules, and the Veber rule. According to Lipinski's



rule, “drug-like” if it has Log P ≤ 5 , molecular weight (M.W.) ≤ 500 , several hydrogen bond acceptors (HBAs) ≤ 10 , and several hydrogen bond donors (HBDs) ≤ 5 . Lipinski’s rule of five was applied to select probable ligands. The Ghose filter determines drug-likeness based on values of log P (-0.4 to 5.6); molar refractivity (40–130); molecular weight (160–480); number of atoms (20–70); and TPSA ≤ 140 . According to MDDR-like rules, drug-like molecules should have several rings ≥ 3 ; several Ridge Bonds ≥ 18 and several Rotatable Bonds ≥ 6 . According to the Verber rule, drug-like compounds have a rotatable bond count ≤ 10 and TPSA ≤ 140 . This criterion was used to determine the likely ligands.^[35] Mol inspiration has provided valuable support to the online chemistry community in calculating key molecular properties to predict bioactivity scores for critical drug targets, including GPCR ligands, kinase inhibitors, ion channel modulators, and nuclear receptors (Ertl 2000). To estimate the molecular characteristics of the selected compounds, the Mol inspiration program was used^{34,36}.

Toxicity prediction

For predicting the toxicity behaviour of the researched phytochemicals, the AdmetSAR prediction tool is applied. Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) is a pharmacokinetic property detection method that primarily evaluates the ADMET properties of ligands in the human body. AdmetSAR predicted human intestinal absorption (HIA), blood-brain barrier (BBB) penetration, Caco-2 permeability, carcinogenicity, cytochrome P450 solubility, cytochrome P (CYP) inhibitory promiscuity, human ether-a-go-go related gene inhibition, acute toxicity, Tetrahymena pyriformis and Ame’s toxicity in fish³⁴.

Molecular docking

Molecular docking studies were carried out using AutoDock 4.2 software following the protocol described by [Morris et al., 2009] with minor modifications. The three-dimensional crystal structure of the target protein COX2 (PDB ID: 6COX), VEGFR (2VPF), FGFR (1E0O), and EGF (1JL9) were obtained from the Protein Data Bank (PDB). Prior to docking, each protein structure underwent refinement, including the removal of crystallographic water molecules, heteroatoms, and co-crystallized ligands. Polar hydrogen atoms were added, and Kollman charges were assigned to all amino acid residues using AutoDock Tools (ADT, version 1.5.6). The processed receptor structure was then saved in PDBQT format for docking experiments. The selected ligands were phytoconstituents obtained from GC-MS analysis of the plant extract. The molecular structures of the identified compounds were retrieved from the PubChem database in SDF format and converted into PDB format using Open Babel software (version 2.3.1). The ligands were subjected to optimisation and energy minimisation, followed by the addition of Gasteiger charges and torsional flexibility assignment using ADT (version 1.5.6). Finally, the ligands were saved in PDBQT format. The docking grid was generated by covering the active site residues of the protein, with grid box dimensions set at (X $\times$ Y $\times$ Z Å) and

spacing of 0.375 Å. Docking runs were performed using the Lamarckian Genetic Algorithm (LGA) with the following parameters: population size= 150, maximum number of energy evaluations = 2,500,000, and maximum number of generations= 27,000. Each ligand was docked with 100 independent runs to explore possible binding conformations. The resulting docking log (DLG) files were analysed, and the best docking pose for each ligand was selected based on the lowest binding energy and favourable binding orientation. The receptor–ligand interactions, including hydrogen bonds, hydrophobic interactions, and π – π stacking, were visualised using Discovery Studio Visualizer (BIOVIA, version 2021) and PyMOL (version 2.5.0). The reference standard (e.g., quercetin or cisplatin) was docked using the same procedure to validate the docking protocol³⁴.

Statistical analysis

Each experiment was replicated three times (n=3), and results were expressed in mean $\pm$ SD. The statistical analysis was carried out using one-way ANOVA, and the difference was estimated by Tukey’s multiple comparison tests using software ($p < 0.05$). The graphical representation was performed using GraphPad Prism 5.0 software.

RESULT AND DISCUSSION

Phytochemical analysis:

The type of solvent utilized in the extraction procedure has a significant impact on the successful evaluation of phytocompounds from plant material. The present research on the various solvent leaf extracts of *P. zeylonica* has revealed the presence of alkaloids, flavonoids, steroids, terpenoids, anthraquinone, anthocyanin, proteins, phenolics, carbohydrates, saponins, lignin, tannins, cardiac glycosides, glycoside tests, coumarins, and volatile oils. (Fig 2) The preliminary phytochemical screening of *P. zeylonica* leaf extracts revealed the existence of several beneficial chemicals. The ethanolic extract had the richest phytochemical profile, with strong reactions for alkaloids, flavonoids, steroids, phenolics, proteins, carbohydrates, tannins, cardiac glycosides, anthraquinones, and volatile oils. In contrast, the aqueous extract contained all the compounds except coumarins. The petroleum ether extract showed minimal activity toward alkaloids, flavonoids, and cardiac glycosides, and no detectable steroids, terpenoids, anthocyanins, lignin glycosides, coumarins, or volatile oils. In contrast, all plant extracts indicated the presence of flavonoids, tannins, phenols, proteins, anthraquinones, and cardiac glycosides. These observations align with earlier findings reported by Leon et al.³⁷, which highlight the potential role of plant-derived alkaloids in anaesthetic applications. The detection of tannins in the test plant suggests possible roles in managing cardiac conditions, inflammation, coagulation disorders, as well as gastrointestinal issues such as diarrhoea and dysentery³⁸. The presence of phenols and other phenolic compounds further indicates potential antibacterial activity, in agreement with earlier findings³⁹. Anthraquinones and



carbohydrates appeared more prominent in the ethanol and aqueous extracts, suggesting that these solvents effectively extract both structural components and energy-related molecules⁴⁰. Saponins and cardiac glycosides, found in higher amounts in the aqueous extract, are well known for their anti-inflammatory, immunomodulatory, and cardioprotective effects⁴¹. Additionally, members of the Malvaceae family are recognized for their rich phenolic content, including phenolic acids, flavonoids, coumarins, and triterpenes⁴².

Figure 2: Estimation of Preliminary Phytochemical screening of *P. zeylonica* leaf extracts

Phytochemicals	LEAF		
	PE	ET	WA
Alkaloids	3	3	2
Flavonoids	3	3	2
Steroids	0	2	0
Terpenoids	0	0	0
Antraquinone	1	3	3
Anthocyanin	0	0	0
Proteins	1	2	1
Phenolic	1	3	1
Carbohydrates	1	3	3
Saponins	2	0	3
Lignin	0	0	0
Tannins	1	2	0
Cardiac glycoside	2	2	3
Glycoside's test	0	0	0
Coumarins	0	0	2
Volatile oils	0	3	0

0 (Absent)- Light yellow, 1 (Low) – Light pale green, 2 (Moderate) – Green, 3 (High)- Dark green

Recent studies report that the ethanol leaf extract of the same plant contains a wide range of phytoconstituents, including alkaloids, flavonoids, coumarins, phenols, quinone, gum and mucilage, fixed oils, and lipids^{43,44}. Within the genus, *Pavonia odorata* and *Pavonia cancellata* predominantly contain flavonoids, terpenoids, and glycosides, while phytochemical analysis of *Pavonia glazioviana* has confirmed the presence of phenolics, flavonoids, tannins, coumarins, alkaloids, steroids, and triterpenes⁴⁵. Similarly, related members of the Malvaceae family, such as *Hibiscus rosa-sinensis* and *Sida cordifolia*, also possess flavonoids, phenolics, and saponins, though often in comparatively lower amount in lower amounts⁴⁶. These observations support earlier phytochemical reports on the *Pavonia* genus, indicating clear chemotaxonomic similarities among species^{45,47}.

In the present study, the leaf extract of *P. zeylonica* showed a strong positive response for a wide range of phytochemicals, with ethanol proving to be the most effective solvent for extracting both polar and semi-polar compounds. This finding highlights the plant's potential for therapeutic applications, particularly in antioxidant, anti-inflammatory, and wound-healing contexts, and provides biochemical support for its traditional use⁴⁸. Based on these findings, the phytochemical profile observed here suggests that *P. zeylonica* possesses a comparatively rich composition, indicating promising pharmacological potential relative to related species within the genus and family.

Secondary metabolites activity

Quantitative analysis of *P. zeylonica* leaf extracts demonstrated significant variation in phenolic, flavonoid, and tannin contents depending on the extraction solvent used (Table 1). Among the three extracts evaluated, the ethanol extract contained the highest levels of total phenolics (169.88 ± 2.07 mg GAE/100 mg), flavonoids (27.92 ± 0.07 mg RE/100 mg), and tannins (150.43 ± 2.95 mg GAE/100 mg). The aqueous extract showed moderate concentrations of phenolics (107.28 ± 0.87 mg GAE/100 mg) and tannins (93.28 ± 1.42 mg GAE/100 mg), while its flavonoid content was comparatively low (3.90 ± 0.45 mg RE/100 mg). In contrast, the petroleum ether extract yielded the lowest levels of all three metabolites (TPC: 13.68 ± 0.42 ; TFC: 6.53 ± 0.14 ; TTC: 9.86 ± 0.91 mg/100mg). Although the solvent was applied in the order petroleum ether → ethanol → aqueous, the efficiency of secondary metabolite extraction followed the order ethanol > aqueous > petroleum ether, highlighting the influence of solvent polarity on phytochemical recovery. Numerous bioactive secondary metabolites have been reported from members of the Malvaceae family^{49,50}, with phenolics, flavonoids, and tannins being the most prominent classes. Phenolic compounds are of particular pharmaceutical interest due to their well-documented antioxidant and anti-inflammatory activities. In a comparable study,^[51] reported total phenolic and flavonoid contents of 44.28 ± 1.79 mg EAG g⁻¹ and 33.68 ± 0.76 mg EAG g⁻¹, respectively, in the ethanol extract of *P. glazioviana*. In comparison, the ethanol extract of *P. zeylonica* in the present study exhibited substantially higher phenolic content. Similar investigations on other Malvaceae species, such as *Sidastrum micranthum* and *Sida rhombifolia*, reported lower phenolic levels of 38.22 ± 0.43 and 39.37 ± 2.54 mg EAG g⁻¹, respectively⁵². High concentrations of phenolic and flavonoid compounds have also been reported in *Malva parviflora* stems. Flavonoids are widely recognized for their diverse biological activities, including antioxidant, anti-inflammatory, and anticancer effects. Several *in vitro* and *in vivo* studies have demonstrated their promising anticancer potential⁵³, while anti-inflammatory activity has also been extensively documented⁵⁴. Aly et al.⁵⁵ quantified the total phenolic and flavonoid contents of flavonoid-rich fractions from *Glycyrrhiza glabra* and *Sophora japonica*, reporting TPC values of 71.61 ± 3.23 and 70.29 ± 1.04 µg GAE/mg and TFC values of 46.99 ± 2.57 and 49.91 ± 2.36 µg QE/mg, respectively. The health benefits of flavonoids have been further associated with reduced risk of cardiovascular disorders and anti-inflammatory conditions⁵⁶. Phenolic acids identified in several Malvaceae species have also exhibited notable cytotoxic and anti-carcinogenic activities⁵⁷. Phenolic and flavonoid compounds function as primary antioxidants by scavenging reactive species such as hydroxyl, superoxide, and lipid peroxyl radicals⁵⁸. Tannins, another important class of secondary metabolites abundant in medicinal plants, contribute significantly to antioxidant and anti-inflammatory effects and play a role in accelerating wound healing processes⁵⁹. Compared with other species of

the genus *Pavonia*, including *P. glazioviana* and *P. speiniode*, *P. zeylonica* exhibited higher secondary metabolite content in the present study. These findings are consistent with

available literature and indicate that *P. zeylonica* leaves represent a particularly rich source of bioactive phytochemicals.

Table 1: Total Phenolic, Flavonoids and Tannin Content of *P. zeylonica* leaf extracts

Plant extracts	Total Phenolic (GAE mg/100 mg)	Total Flavonoids (RE mg/ 100 mg)	Total Tannins (GAE mg/100 mg)
Petroleum ether	13.86 ± 0.42	6.53 ± 0.14	9.86 ± 0.91
Ethanol	169.88 ± 2.07	27.92 ± 0.07	150.43 ± 2.95
Aqueous	107.28 ± 0.87	3.9 ± 0.45	93.28 ± 1.42

Result is shown as mean ± SD of triplicate analyses (n=3), Statistical analysis was performed for TPC, TFC and TTC using One-way ANOVA, and difference were considered highly significantly at p<0.001 according to Tukey's HSD test. GAE- Gallica acid Equivalents; RE- Rutin.

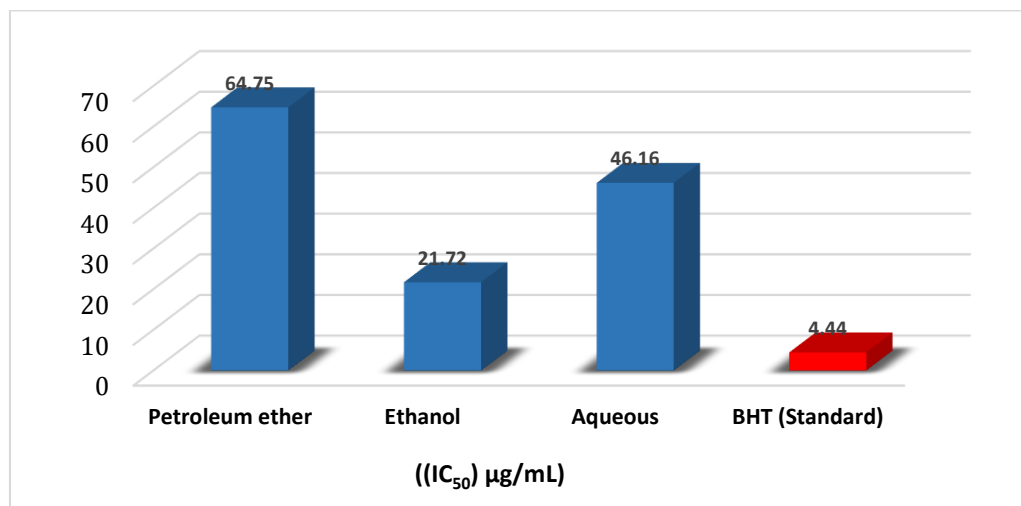
In vitro antioxidant activity

DPPH (2,2- diphenyl-1-picrylhydrazyl) Scavenging Activity

A single analytical method cannot comprehensively qualify all antioxidants and radical species present in complex biological matrices. According to Nguyen et al.⁶⁰, *in vitro* antioxidant assays are broadly classified into two major categories. One category involves hydrogen atom transfer-based reactions to evaluate the free radical scavenging ability of test samples⁶¹. Among these, the DPPH assay is one of the most commonly employed methods for assessing the antioxidant potential of plant extracts⁶². This method is reliable and is based on the reduction of the stable DPPH free radical to a non-radical form by electron-or hydrogen-donating antioxidants present in the extract^{63,58}. The scavenging activity results in a measurable decrease in absorbance due to decolorization of the DPPH solution,

which is directly proportional to the concentration and effectiveness of the antioxidant compounds⁶⁴. The second category of assays operates through single- electron transfer mechanisms, typically involving metal iron radical species⁶⁵. In the present study, the DPPH radical scavenging activity of *P. zeylonica* leaf extracts prepared using different solvents was evaluated (Fig. 3). The ethanol extract exhibited the strongest antioxidant activity (IC₅₀ = 21.72 ± 0.6 µg/mL), followed by the aqueous extract (46.16 ± 1.9 µg/mL) and petroleum ether extract (64.75 ± 3.5 µg/mL), suggesting that polar solvents enhance the extraction of compounds with greater radical scavenging capacity. Butylated hydroxytoluene, used as a standard antioxidant, showed superior activity compared to all plant extracts. Almost, the inhibitory potential against DPPH radicals decreased in the order of ethanol > aqueous > petroleum ether extracts.

Figure 3: DPPH of analysis of antioxidant activity of different solvents of *P. zeylonica* leaf extract



DPPH- analysis of different extracts at a concentration of (50, 100, 15, 200, and 250µg/mL). IC50 values were calculated from the concentration-response curve. BHT- Butylated hydroxytoluene. Results are shown as the mean ± SD of triplicate (n=3).

Similar findings were reported in earlier studies on *P. zeylonica* root extracts, where ethanol fractions rich in phenolics and flavonoids demonstrated the highest antioxidant activity²². The pronounced antioxidant activity of the ethanolic leaf extract indicates a high content of bioactive compounds such as phenolics, flavonoids, and

tannins, which are known for their reducing and free radical scavenging properties. Comparable results have been reported for the ethanolic leaf extracts of *Hibiscus-rosa-sinensis*, which showed significant antioxidant and wound-healing activities with an acceptable safety profile⁶⁶. Since oxidative stress plays a key role in inflammation, tissue

injury, arthritis, and delayed wound healing⁵⁹, the strong antioxidant activity observed in *P. zeylonica* leaves provides scientific support for their traditional use in anti-inflammatory, wound healing, and analgesic applications. Furthermore, comparison with earlier reports on root extracts suggests that the leaves may represent an even richer source of bioactive constituents responsible for these therapeutic effects.

Gas Chromatography-Mass Spectrometry (GC-MS) Analysis

Gas chromatography-mass spectrometry (GC-MS) is a powerful analytical technique widely used for the identification of volatile and semi-volatile compounds, including long- and branched-chain hydrocarbons, organic acids, alcohols, esters, and related phytoconstituents. In the present study, GC-MS analysis of the ethanolic leaf extract of *P. zeylonica* led to the identification of multiple chemical constituents. The GC-MS chromatogram revealed 33 distinct peaks, indicating the presence of 33 compounds in the ethanolic extract (Fig. 4). The detected compounds were

identified based on their retention times and mass spectral data. Phytoconstituents are primarily responsible for the therapeutic potential of medicinal plants, and therefore, plant-derived extracts represent valuable sources of nutraceutical and pharmacologically active compounds. Phenolic and flavonoid constituents, in particular, are known to contribute significantly to antioxidant, antibacterial, anticancer, anti-inflammatory and antidiabetic activities. The identified compounds in *P. zeylonica* leaf extract, along with their retention time (RT), molecular formula (MF), molecular weight (MW), and peak area percentage, are presented in Table 2. The major compounds detected included glyceraldehyde, dihydroxyacetone, 1,2-cyclopentanedione, glycerin, 2,4-dihydroxy-2,5-dimethyl-3(2H)-furan-3-one, pyrrolidinone derivatives, D-alanine derivatives, 5-hydroxymethylfurfural, heptanoic acid derivatives, pentanoic acid esters, sucrose, salicylamide, 2,4-di-tert-butylphenol, fatty acids and their esters (n-hexadecanoic acid, octadecanoic acid, and their derivatives), campesterol, and γ -sitosterol.

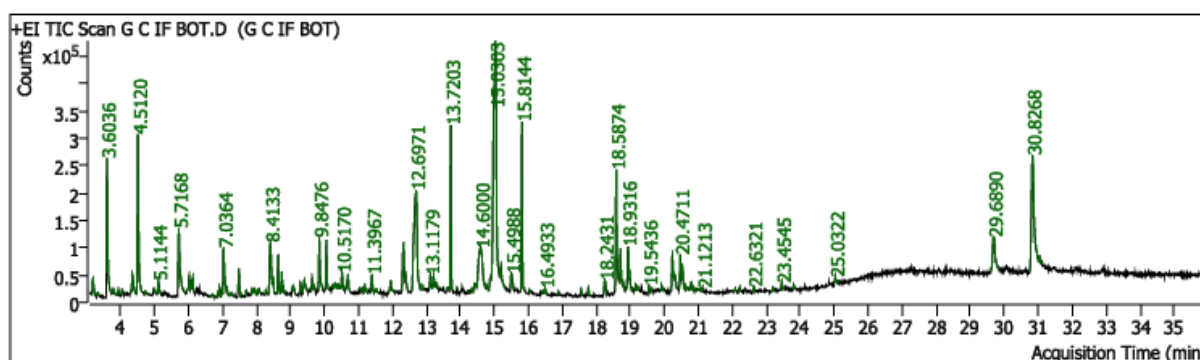


Figure 4: GC-MS chromatogram of the ethanol leaf extract of *Pavonia zeylonica*

Table 2: GC-MS analysis of ethanolic leaf extracts of *Pavonia zeylonica*

S. No	R/ Time	Compound Name	Peak Area %	Molecular Formula	Molecular weight	Uses
1.	3.6036	Glyceraldehyde	4.74	C ₃ H ₆ O ₃	90.8	Anti-sickling, Anticancer, Anti-fibrotic, Glucose stabilization in blood, AGE- induced inflammatory signaling.
2.	4.5120	Dihydroxyacetone	5.40	C ₃ H ₆ O ₃	90.8	Antifungal, Vitiligo camouflage, Photoprotection, Anticancer formulations, Cellular stress.
3.	5.1144	1,2-Cyclopentanedione	0.57	C ₅ H ₆ O ₂	98.1	Anti-inflammatory, Antioxidant, Metabolic modulation, Antimicrobial, Redox-sensitive protein probe.
4.	5.7168	Glycerin	3.37	C ₃ H ₈ O ₃	92.9	Skin hydration, Dry eye, IOP- reduction, Laxative, Antiseptic (dental), Cryoprotection, Pharmaceutical base.
5.	6.0228	2,4-Dihydroxy-2,5-dimethyl-3(2H)-furan-3-one	0.62	C ₆ H ₈ O ₄	144.12	Antioxidant/NADH-OX inhibitor, Antibacterial, Antibiofilm activity, Anti-microbial coatings.
6.	7.0364	-Pyrrolidinone, 1-methyl-	2.57	C ₅ H ₉ NO	99.13	Bone regeneration, Anti-atherosclerosis, Anti-inflammation and Immunomodulation in myeloma.
7.	7.4858	D-Alanine, N-propargyloxycarbonyl-, isohexyl ester	0.83	C ₁₃ H ₂₁ NO ₄	255.31	Not Activity Reported

8.	8.0786	Cyclobutane, 1,2-diethyl-	0.27	C ₈ H ₁₆	112.21	Cancer & Fibrosis, Diabetes, NASH (liver Fibrosis), Antibacterial activity, Broad pharmacology.
9.	.4133	Dihydroxyacetone	2.82	C ₃ H ₆ O ₃	90.8	Antifungal, Vitiligo camouflage, Photoprotection, Anticancer formulations, Cellular stress.
10.	9.8476	5-Hydroxymethylfurfural	1.88	C ₆ H ₆ O ₃	126.11	Sickle cell treatment, Inflammation & cytokines, Antioxidant & Cardio protection, Neuroprotection, Anti-microbial.
11.	10.5170	Heptanoic acid, 6-oxo-	0.67	C ₇ H ₁₂ O ₃	144.17	HDAC6 inhibitor, moderate antiproliferative, Enhances chemotherapy efficacy, Induces apoptosis.
12.	11.3967	Pentanoic acid, propyl ester	0.64	C ₈ H ₁₆ O ₂	144.21	Not used medicinally but finds extensive use in the food, fragrance and cosmetic industries.
13.	12.3242	2,3,4,4-Tetramethyl-pentane-1,3-diol	2.13	C ₉ H ₂₀ O ₂	160.25	Used in aroma formulations for food, cosmetics personal care, mid Anti- inflammatory role.
14.	12.6971	Sucrose	10.11	C ₁₂ H ₂₂ O ₁₁	342.3	Medicinal uses of sucrose, specifically as an analgesic for infants during minor painful.
15.	13.1179	Salicylamide	0.60	C ₇ H ₇ NO ₂	137.44	Analgesia, Antipyretic, Cardiovascular, Melanin stimulation.
16.	13.7203	2,4-Di-tert-butylphenol	4.18	C ₁₄ H ₂₂ O	206.32	Acne- related skin inflammation, Anti-TB, Anticancer, Antifungal, Antioxidant/ Neuroprotection, Anti-pyrogenic/Endocrine disruption.
17.	14.6000	3-Deoxy-d-mannonic lactone	5.64	C ₆ H ₁₀ O ₅	162.14	Bacterial infections, Inflammation/Oxidative stress, Chronic metabolic diseases.
18.	15.0303	Ethyl. alpha. -d-glucopyranoside	23.51	C ₈ H ₁₆ O ₆	208.21	Anticancer potential, Drug Solubility enhancement, Antioxidant/Anti-inflammatory, Enzyme substrate research.
19.	15.4988	1,2,3,4-Tetrahydro-1-naphthalenethiol, S-trimethylsilyl-	0.85	C ₁₃ H ₂₀ SSi	236.45	Not activity reported
20.	15.8144	Dodecyl acrylate	4.21	C ₁₅ H ₂₈ O ₂	240.38	Antimicrobial, Anticancer and Irritation risks.
21.	16.4933	Tetradecanoic acid	0.30	C ₁₄ H ₂₈ O ₂	228.37	Anti-inflammatory/ Analgesic, Antimicrobial/Antifungal, Anti- Virulence in Pseudomonas, Antitubercular, Antioxidant & Neuroactive.
22.	18.2431	1,2-Benzenedicarboxylic acid, butyl 2-ethylhexyl ester	0.66	C ₂₀ H ₃₀ O ₄	334.4	Endocrine disruption, Neurological impact, Metabolic dysfunction, Cardio-hepatonephrotoxicity, Carcinogenic concerns, Genotoxic& Immunotoxin effects.
23.	18.5874	n-Hexadecanoic acid	4.55	C ₁₆ H ₃₂ O ₂	256.42	Anti-inflammatory, Anticancer, Antifungal/Antibiofilm, Oxidative/Pro-inflammatory, Cancer progression, Metabolic modulation.
24.	18.9316	Hexadecanoic acid, ethyl ester	2.21	C ₁₈ H ₃₆ O ₂	284.5	Anti-inflammatory, Antioxidant, Antibacterial/Antifungal, Anticancer.
25.	19.5436	Heptadecanoic acid	0.21	C ₁₇ H ₃₄ O ₂	270.5	Anticancer (Pancreas, lung), Breast cancer cytotoxicity, Human disease biomarker, Anti-inflammatory signaling.
26.	19.9165	9,12-Octadecadienoic acid, methyl ester	0.19	C ₁₉ H ₃₄ O ₂	294.5	Anti- inflammatory, Antioxidant, Antimicrobial/Antifungal, Anticancer, Antidiarrheal/ Anti-arthritis, Biomarker in psoriasis.
27.	20.4711	Octadecanoic acid	1.07	C ₁₈ H ₃₆ O ₂	284.5	Anti-inflammatory, Anticancer, Neuroprotection, Cardiovascular risk improvement, Improved insulin responses.
28.	21.1213	2,6,6,10-Tetramethyl-undeca-8,10-diene-3,7-dione	0.28	C ₁₅ H ₂₄ O ₂	236.35	Anticancer, Anti-inflammatory, Analgesic, molecular targets, Antitumor activity (Breast cancer).

29.	22.6321	Allyl 3,4-epoxy-6-methylcyclohexanecarboxylate (isomer 2)	0.19	C ₁₁ H ₁₆ O ₃	196.24	Not activity reported
30.	23.4545	Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl)ethyl ester	0.24	C ₁₉ H ₃₃ O ₄	330.5	Pharmaceutical excipient, Antimicrobial (mild), Topics skincare, drug delivery, Precursor to bioactive lipids.
31.	25.0322	Octadecanoic acid, 2,3-dihydroxypropyl ester	0.28	C ₂₁ H ₄₂ O ₄	358.6	Antibacterial, Antifungal activity, wound healing, Dermatological uses, Lipids- Based drug delivery, Neuroprotective and metabolic roles.
32.	29.6890	Campesterol	2.84	C ₂₈ H ₄₈ O	400.7	Cholesterol-lowering, Anti-inflammatory (rodent arthritis models), Antioxidant/ Hepatoprotective, Anti-angiogenic, Chemo preventive (lung, breast cancer), Metabolic/Antidiabetic.
33.	30.8268	γ-sitosterol	11.20	C ₂₉ H ₅₀ O	414.7	Antioxidant (Neurological protection), Anti-inflammatory, Cancer prevention (Apoptosis induction), Metabolic syndrome/Diabetes, Antimicrobial uses.
			100			

Previous reports on the ethanolic leaf extracts of *P. zeylonica* revealed the presence of 15 phytochemical compounds belonging to this genus. Major constituents such as hexadecanoic acid, 3-tetradecyn-1-ol, ethane-1,1-diethoxy, and phytol were previously reported by Divya et

al.⁴³. In contrast, in the present study, we identified several compounds, including glyceraldehyde, ethyl-α-D-glucopyranoside, and γ-sitosterol, which are reported in *P. zeylonica*. The structures of the major phytocompounds are presented in Fig. 5.

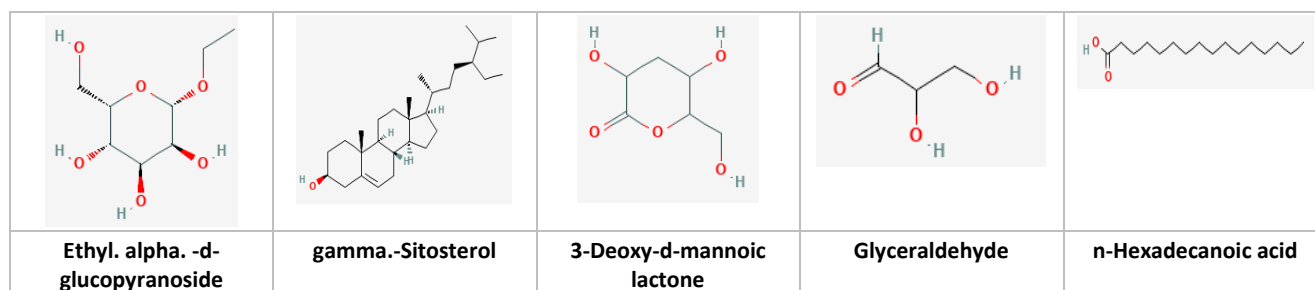


Figure 5: Chemical structures of major phytocompounds identified by GC-MS analysis

GC-MS analysis of the methanolic leaf extract of *Abutilon pannosum* revealed multiple peaks, with n-hexadecanoic acid showing the highest peak area (13.38%) at a retention time of 25.47 min⁶⁷. In comparison, in the present study, we identified n-hexadecanoic acid as a major compound with a peak area of 4.55% at a retention time of 18.58 min. Several compounds identified in the present investigation, including n-hexadecanoic acid, octadecanoic acid, hexadecanoic acid ethyl ester, tetradecanoic acid, glyceraldehyde, campesterol, 9,12-octadecadienoic acid methyl ester, heptadecanoic acid, glycerin, salicylamide, and heptanoic acid, have also been reported in *Pavonia urens*⁶⁸. Additionally, GC-MS profiling of the ethanolic leaf extracts of *Eugenia punicifolia* (Malvaceae family) revealed the presence of phytochemical compounds⁶⁹, while dodecyl acrylate has been reported in *Chromolaena odorata*⁷⁰. Earlier GC-MS studies on the methanolic leaf extract of *P. zeylonica* identified 11 phytochemical compounds⁴⁰. Furthermore, Manivannan et al.⁷¹ reported nine compounds in the chloroform extract and four major compounds in the ethyl acetate extract of *Pavonia odorata* roots.

In the present study, we identified compounds including pentadecanoic acid derivatives, campesterol, and α- and β-

sitosterols, which have been previously associated with antioxidant, anticancer, and cholesterol-lowering activities. Among the detected constituents, ethyl-α-D-glucopyranoside exhibited the highest peak area (23.51%) and has been reported to possess anticancer potential, antioxidant and anti-inflammatory properties and applications in drug solubility enhancement and enzyme substrate studies⁷². γ-sitosterol (11.20%) is known for its antioxidant, neuroprotective, anti-inflammatory, anticancer, and antimicrobial activities⁷³. Other bioactive compounds such as 3-deoxy-D-mannonic lactone (5.64%), glyceraldehyde (4.74%), and n-hexadecanoic acid (4.55%) have been reported to exhibit activities including anti-inflammatory, anticancer, antifungal, metabolic regulatory, and oxidative stress-modulating effects^{74, 75, 76}. The genus *Pavonia*, one of the largest genera within the Malvaceae sensu lato family, has been widely reported to exhibit diverse biological activities across its species⁷⁷. To date, approximately 169 phytochemical compounds have been isolated and identified from various species of the genus *Pavonia*, highlighting its rich phytochemical diversity and therapeutic potential. The GC-MS analysis carried out in the present study indicates that the ethanolic leaf extract of *P. zeylonica* contains a diverse range of bioactive

phytoconstituents. These findings support its traditional medicinal value and suggest its promising potential for future therapeutic and nutraceutical applications.

Pharmacological evaluation

Based on the GC-MS analysis, the five most abundant phytochemical compounds identified in the ethanolic leaf extract of *P. zeylonica* were selected for further evaluation of their drug-likeness and pharmacokinetic behavior using in silico ADMET prediction. The assessment was performed using the SwissADME web tool. The physicochemical properties of the selected phytoconstituents, including molecular weight (MW), hydrogen-bond donors (HBD), hydrogen-bond acceptors (HBA), topological polar surface area (TPSA), lipophilicity (Log P), water solubility (Log S), and pharmacokinetic parameters influencing ADME behaviour, are summarized in Table 3. The chemical structures of the selected compounds were converted into canonical SMILES format and submitted to SwissADME to predict their drug-likeness properties according to Lipinski's rule of five. According to this rule, orally active drug candidates should exhibit HBD ≤ 5 , HBA ≤ 10 , molecular weight ≤ 500 Da, Log P ≤ 5 , and TPSA ≤ 140 Å (Ivanovic et al. 2020). The predicted drug-likeness results are presented in Tables 3 and 4. All selected compounds showed no violations of Lipinski's rule, indicating favourable drug-likeness. SwissADME predictions, which consider molecular properties such as lipophilicity, solubility, molecular weight, hydrogen bonding, and membrane permeability, further support their potential bioavailability³⁴. TPSA was identified as a key factor influencing intestinal absorption, with values above 140 Å generally associated with poor absorption. Lipophilicity also plays an important role in determining oral bioavailability.

Pharmacokinetic behaviour was further evaluated using the BOILED-Egg model to predict human intestinal absorption (HIA) and blood-brain barrier (BBB) permeability (Fig. 6). Molecule 5 (n-hexadecenoic acid) was located in the yolk region, indicating a high probability of BBB penetration and P-glycoprotein non-substrate behaviour (PGP-). Molecules 1 (ethyl- α -D-glucopyranoside), 3 (3-deoxy-D-mannoic lactone), and 4 (glyceraldehyde) were positioned in the white region, suggesting good gastrointestinal adsorption;

however, Molecule 1 was predicted as a PGP+ substrate, while Molecules 3 and 4 were identified as PGP-. Molecule 2 (γ -sitosterol) fell outside the model, indicating poor absorption and low BBB permeability. Considering these results, Molecules 1, 3 and 4, while Molecule 5 may exhibit good oral bioavailability, while Molecule 5 may be suitable for central nervous system applications. Molecule 2 may require structural optimization to improve its pharmacokinetic profile. Although these findings provide useful preliminary insights, experimental validation remains essential, as promising compounds may not always translate successfully in clinical studies⁷⁸.

Boiled-Egg overview for brain access and intestinal absorption of major compounds identified from ethanol extract from *P. zeylonica* leaves. Molecule 1- Glyceraldehyde, Molecule 2- 3-Deoxy-d-mannoic lactone, Molecule 3- Ethyl.alpha.-d- glucopyranoside, Molecule 4- n-Hexadecanoic acid and Molecule 5- γ -sitosterol.

ADMET Studies

A comprehensive evaluation of pharmacokinetic properties is essential during the early stages of drug design and development. This assessment includes the analysis of absorption, distribution, metabolism, and excretion (ADME) parameters, which play a crucial role in determining the therapeutic success of drug candidates. Understanding the pharmacological basis of traditional medicinal plants is particularly important for translating their therapeutic potential into modern drug development. However, experimental evaluation of ADME properties through in vivo studies is often time-consuming and costly, making in silico prediction approaches valuable alternatives. Lipinski's rule of five (RO5) is a widely accepted guideline used to predict the drug-likeness and pharmacokinetic suitability of bioactive compounds, including plant-derived phytoconstituents⁷⁰.

In the present study, ADMET properties of the five isolated compounds from *P. zeylonica* were predicted using the SwissADME platform. Most of the analysed compounds showed moderate solubility within the acceptable range. All compounds exhibited positive human intestinal adsorption, indicating good potential for oral uptake (Tables 3-4).

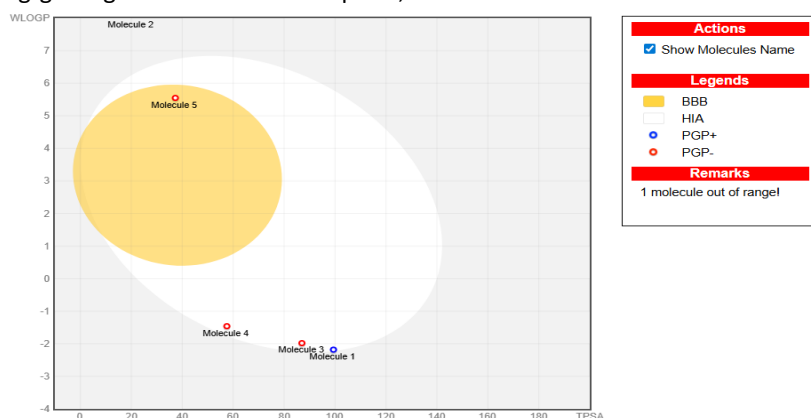


Figure 6: BOILED-Egg model showing gastrointestinal absorption and BBB permeability

Table 3: Physiochemical properties and Pharmacokinetics evaluation parameters of selected compounds

S. No	Ligand	Canonical SMILES	Molecular weight	Heavy Atoms	Aromatic heavy atoms	H- bond Acceptors	H- bond Donors	Log S	Log P	TPSA (Å²)
1.	Glyceraldehyde	<chem>C(C(=O)O)O</chem>	90.8	6	0	3	2	Highly soluble	0.19	57.53
2.	3-Deoxy-d-mannonic lactone	<chem>C1C(C(OC(=O)C1O)CO)O</chem>	162.14	11	0	5	3	Very soluble	0.72	86.99
3.	Ethyl. alpha. -d-glucopyranoside	<chem>CCO[C@@H]1[C@H]([C@H]([C@@H]([C@@H](O1)CO)O)O)O</chem>	208.21	14	0	6	4	Highly soluble	0.50	99.38
4.	n-Hexadecanoic acid	<chem>CCCCCCCCCCCCCCCC(=O)O</chem>	256.42	18	0	2	1	Moderately soluble	3.85	37.30
5.	γ-sitosterol	<chem>CC[C@@H](CC[C@@H](C)[C@H]1CC[C@@H]2[C@@]1(CC[C@H]3[C@H]2CC=C4[C@@]3(CC[C@@H](C4)O)C)C(C)C</chem>	414.7	30	0	1	1	Poorly Soluble	5.07	20.23

Table 4: ADME/T- predicted absorbance properties of *P. zeylonica* compounds

S. No	Ligand	G1 Absorption	BBB Permeant	Blood Brain Barrier	Human Intestinal Absorption	CaCo-2 permeability	P- glyco protein Substrate	P-glyco Protein Inhibitor	Renal Organic Cation Transporter
1.	Glyceraldehyde	High	No	BBB+	HIA+	Caco2-	Non- Substrate	Non- Inhibitor	Non- Inhibitor
2.	3-Deoxy-d-mannonic lactone	High	No	BBB+	HIA+	Caco2-	Non- Substrate	Non- Inhibitor	Non- Inhibitor
3.	Ethyl. alpha. -d-glucopyranoside	High	No	BBB-	HIA-	Caco2-	Non- Substrate	Non- Inhibitor	Non- Inhibitor
4.	n-Hexadecanoic acid	High	Yes	BBB+	HIA+	Caco2+	Non- Substrate	Non- Inhibitor	Non- Inhibitor
5.	γ-sitosterol	Low	No	BBB+	HIA+	Caco2+	Substrate	Non- Inhibitor	Non- Inhibitor

Table 5: ADMET-predicted distribution and metabolism properties

S. No	Ligand	Subcellular Localization	CYP450 2C9 Substrate	CYP450 2D6 Substrate	CYP450 3A4 Substrate	CYP450 1A2 Inhibitor	CYP450 2C9 Inhibitor	CYP450 2D6 Inhibitor	CYP450 2C19 Inhibitor	CYP450 3A4 Inhibitor	CYP Inhibitory Promiscuity
1.	Glyceraldehyde	Mitochondria	Non- Sub	Non- Sub	Non- Sub	Non	Non	Non	Non	Non	Low
2	3-Deoxy-d-mannonic lactone	Mitochondria	Non- Sub	Non- Sub	Non- Sub	Non	Non	Non	Non	Non	Low
3.	Ethyl. alpha. -d-glucopyranoside	Mitochondria	Non- Sub	Non- Sub	Non- Sub	Non	Non	Non	Non	Non	Low
4.	n-Hexadecanoic acid	Mitochondria	Non- Sub	Non- Sub	Non- Sub	Inhibitor	Non	Non	Non	Non	Low
5.	γ-sitosterol	Lysosome	Non- Sub	Non- Sub	Substrate	Non	Non	Non	Non	Non	Low

Table 6: ADMET - predicted toxicity for *P. zeylonica* bioactive compounds

S. No	Ligand	Human Ether-a-go-go-related gene inhibitor	AMES toxicity	Carcinogens	Fish-toxicity	Tetra-Hymena pyriformis toxicity	Honey Bee Toxicity	Biodegradation	Acute Oral Toxicity	Carcinogenicity (3 classes)
1.	Glyceraldehyde	Weak Inhibitor	Non- AMES toxic	Non- Carcinogens	Low-FHMT	Low- TPT	High- HBT	Ready-Biodegradable	III	Non- required
2.	3-Deoxy-d-mannonic lactone	Weak Inhibitor	Non- AMES toxic	Non- Carcinogens	Low-FHMT	Low- TPT	High- HBT	Ready-Biodegradable	III	Non- required
3.	Ethyl. alpha. -d-glucopyranoside	Weak Inhibitor	Non- AMES toxic	Non- Carcinogens	Low-FHMT	Low- TPT	High- HBT	Ready-Biodegradable	IV	Non- required
4.	n-Hexadecanoic acid	Weak Inhibitor	Non- AMES toxic	Non- Carcinogens	High -FHMT	High- TPT	High- HBT	Not Ready - Biodegradable	IV	Non- required
5.	γ-sitosterol	Weak Inhibitor	Non- AMES toxic	Non- Carcinogens	High -FHMT	High- TPT	High- HBT	Not Ready - Biodegradable	I	Non- required



The permeability results from the (BBB) and Caco-2 models suggest that these compounds can cross biological membranes effectively. Similar trends have been reported for plant-derived compounds in earlier studies³⁵. As gastrointestinal absorption is an important factor for oral bioavailability, the compliance of these compounds with Lipinski's rule further supports their absorption potential⁷⁹. The compounds were predicted to be non-inhibitors of the renal organic cation transporter (ROCT), and P-glycoprotein, which is known to influence drug efflux and bioavailability. In addition, all compounds were predicted to be non-substrates and non-inhibitors of Cytochrome P450 (CYP450) enzymes, indicating metabolic stability and a lower risk of drug-drug interactions. (Table 5). Similar observations have been reported in previous studies on phytochemicals⁸⁰.

Toxicity analysis using the ProTox-II platform showed that all five compounds were non-carcinogenic, non-mutagenic, and non-toxic. They also showed negative AMES test results and acceptable LD₅₀ values (Table 6). These results are consistent with earlier reports describing favourable safety profiles of plant-based compounds⁸¹. Nevertheless, excluding compounds solely based on Lipinski's rule may result in the loss of potentially active candidates. Therefore, it is important to consider a balance between pharmacokinetic properties, efficacy, and safety during drug development^{82, 83}. Taken together, the in silico ADMET profiling suggests that these compounds possess acceptable pharmacokinetic properties, safety, and bioavailability. Molecular docking further aids in predicting ligand-protein interactions and helps in prioritizing compounds for subsequent experimental validation.

Molecular docking

The molecular docking study was conducted to evaluate the interactions of five phytochemicals-ethyl α -D-glucopyranoside, γ -sitosterol, 3-deoxy-D-mannonic lactone, glyceraldehyde, and n-hexadecanoic acid with wound healing-related protein targets, namely COX-2 (6COX), VEGFR (2VPF), FGFR (1E0O), and EGFR (1JL9). Docking simulations were performed using AutoDock 4.2, and binding affinities were expressed as negative binding energy values (kcal/mol), where more negative values indicate stronger ligand-protein interactions⁸⁴. The docking results presented in Table 7 show that γ -sitosterol exhibited the highest binding affinities across all selected protein targets, with values ranging from -6.6 to -8.5 kcal/mol, indicating its potential as a multi-target compound in wound healing. The strongest interaction was observed with COX-2 (-8.5 kcal/mol), suggesting a significant role in modulating inflammatory response during wound repair. Ethyl α -D-glucopyranoside showed moderate binding affinities, with the highest interaction also noted for COX-2 (-6.9 kcal/mol), followed by slightly lower affinities towards VEGFR, FGFR, and EGFR. Similarly, 3-deoxy-D-mannonic lactone displayed moderate interactions, with a preference for COX-2 (-6.5 kcal/mol), indicating possible involvement in inflammation-related pathways. In comparison, glyceraldehyde and n-hexadecanoic acid showed lower binding affinities across all targets. However, their ability to interact with the active sites suggests that they may contribute in a supportive or synergistic manner. As shown in Fig. 7, COX-2 appeared to be the most responsive target, followed by VEGFR, FGFR, and EGFR.

Table 7: Molecular docking binding affinity of *P. zeylonica* Ethanol leaf extracts compounds

Proteins	Ethyl. Alpha. -d- glucopyranoside	γ -sitosterol	3-Deoxy-d-mannonic lactone	glyceraldehyde	n-Hexadecanoic acid
COX2	-6.9	-8.5	-6.5	-4.6	-6.2
2VPF	-5.1	-7.9	-5.0	-3.9	-3.7
1E0O	-5.4	-8.3	-5.5	-3.9	-4.8
1JL9	-5.0	-6.6	-5.4	-4.2	-4.5

This pattern indicates that the selected compounds may primarily act through anti-inflammatory mechanisms, while also supporting angiogenesis and tissue regeneration via interactions with growth factor receptors.

These observations are in line with earlier reports. Vadivel et al.²⁷ documented notable docking interactions of compounds *Tamarindus indica* bark with FGFR-2 (-8.3 kcal/mol) and VEGF (-4.4 kcal/mol). Similarly, Samesh et al.⁸³ demonstrated that bioactive metabolites from plants belonging to the Malvaceae family exhibited high binding affinities towards EGFR kinase, with scores of -10.4, -10.2, and -10.1 kcal/mol. Mokhtar et al.⁷⁰ reported that COX-2 showed the most stable binding interactions with major compounds from *Chromolaena odorata*, emphasizing the role of hydrophobic interactions in protein-ligand binding. During the inflammatory phase of wound healing, inhibition of COX-2 activity has been shown to reduce inflammation

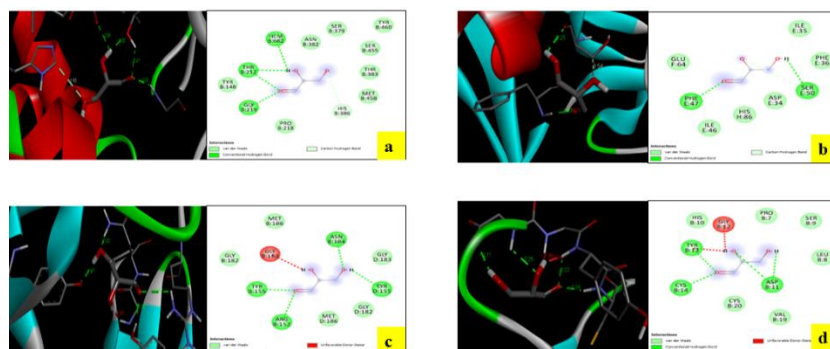
and promote dermal reconstruction and scar formation⁸⁵. VEGF interactions, with reported binding energies ranging from -5.7 to -7.8 kcal/mol in *Tridax procumbens* compounds, have been associated with enhanced collagen deposition, angiogenesis, and epithelialization⁸⁶. EGFR is known to activate several signalling pathways essential for wound repair, and its role in promoting healing has been demonstrated in both animal models and clinical studies^{87,88}. High EGFR binding affinities ranging from -9.7 to -7.0 kcal/mol have been reported in earlier studies, often exceeding those of co-crystallised ligands⁸⁹. In the present study, docking results (Figure 7; Table 7) show γ -sitosterol as the most promising compound, showing strong binding across multiple targets. Its high affinity towards COX-2, along with moderate interactions with VEGFR, FGFR, and EGFR, suggests a multi-target mode of action involving inflammation control, angiogenesis, and tissue



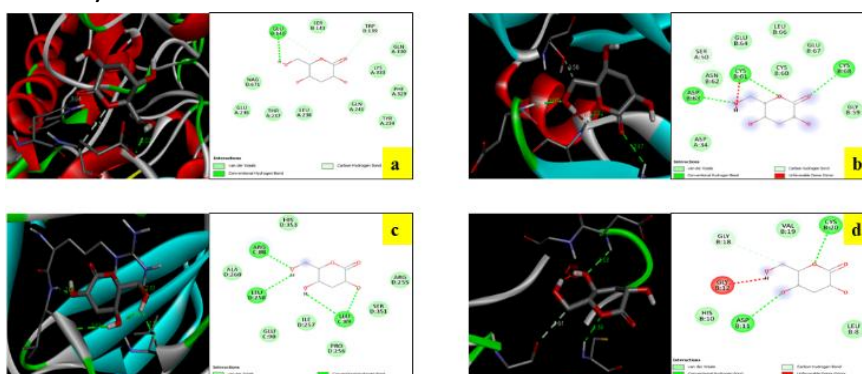
regeneration. Taken together, these findings support the wound-healing potential of ethanolic extract *P. zeylonica*. However, further experimental studies are required to

confirm these results and to understand the underlying mechanisms better.

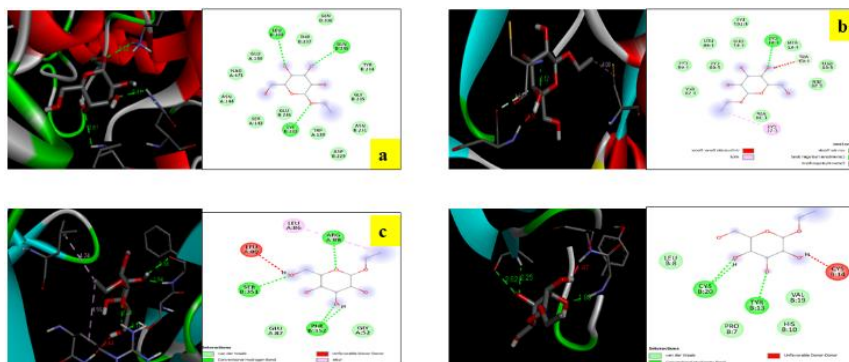
Figure 7: Molecular docking interactions of selected compounds with wound-healing proteins.



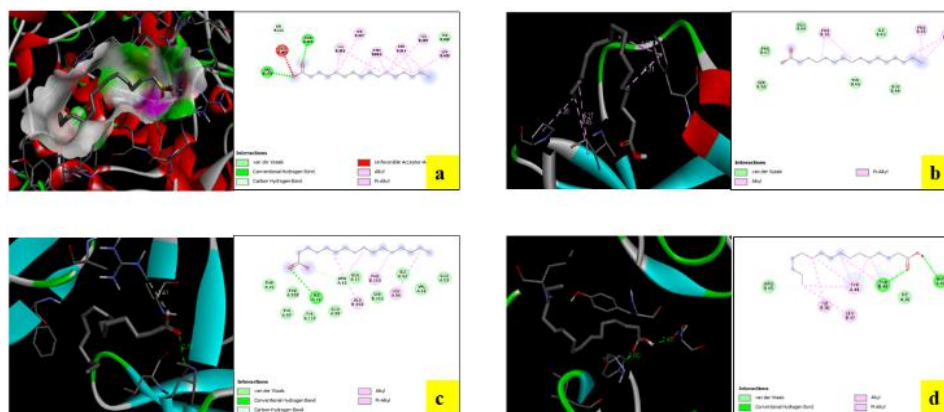
Molecular docking interaction of the selected compounds glyceraldehyde with target proteins represented in 2D and 3D structure: a) COX-2; b) VEGFR; c) FGFR and d) EGFR



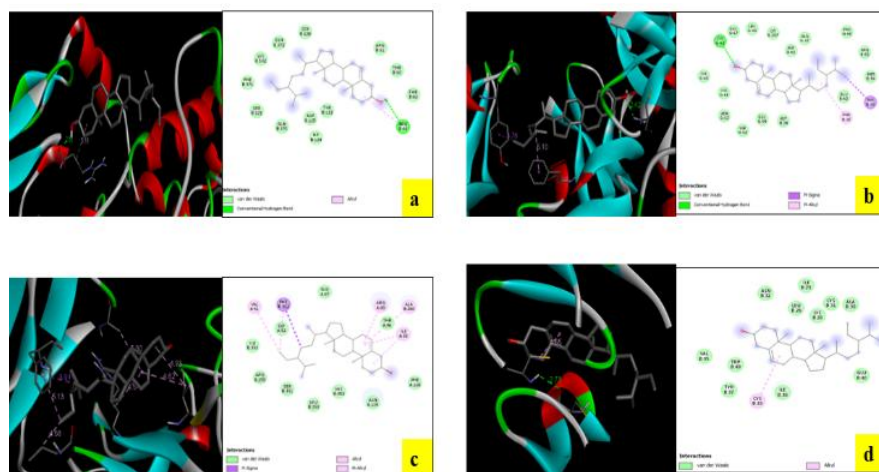
Molecular docking interaction of the selected compounds 3-Deoxy-d-mannonic lactone with target proteins represented in 2D and 3D structure: a) COX-2; b) VEGFR; c) FGFR and d) EGFR



Molecular docking interaction of the selected compounds Ethyl. Alpha. -d- glucopyranoside with target proteins represented in 2D and 3D structure: a) COX-2; b) VEGFR; c) FGFR and d) EGFR



Molecular docking interaction of the selected compounds n-Hexadecanoic acid with target proteins represented in 2D and 3D structure: a) COX-2; b) VEGFR; c) FGFR and d) EGFR



Molecular docking interaction of the selected compounds .gamma.- Sitosterol with target proteins represented in 2D and 3D structure: a) COX-2; b) VEGFR; c) FGFR and d) EGFR

CONCLUSION

The present study demonstrated that the ethanolic leaf extract of *Pavonia zeylonica* possesses significant antioxidant potential and contains several bioactive phytochemicals identified through GC-MS analysis. Among the identified compounds, γ -sitosterol exhibited strong molecular interactions with wound-healing target proteins including COX-2, VEGFR, FGFR, and EGFR, suggesting its possible role in inflammation regulation, angiogenesis, and tissue regeneration. The integrated phytochemical, antioxidant, ADMET, and molecular docking analyses provide scientific support for the traditional medicinal use of *Pavonia zeylonica* in wound management. Overall, the study highlighted the relevance of this medicinal plant as a promising natural candidate for future wound-healing therapeutics and Phytoformulation research.

Abbreviation: COX-2- Cyclooxygenase-2, VEGFR- Vascular Endothelial Growth Factor, FGFR- Fibroblast Growth Factor Receptor, EGFR- Epidermal Growth Factor Receptor.

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