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A review on *Pentapetes phoenicea* (dupurmoni): Chemical constituents, pharmacological activities and toxicology study

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ABSTRACT

Technological advancements are bringing attention to herbs used in ethnopharmaceuticals, sparking interest in plants with medicinal properties. *Pentapetes phoenicea* has been traditionally used for treating conditions like swelling, inflamed glands and snake bite. Some of its phyto-constituents that possess anti-oxidant, anti-cancer, mucilaginous, anti-inflammatory, and thermogenic qualities are flavonoids, alkaloids, saponins and steroids. *P. phoenicea* is a relatively less familiar plant that has yet to gain significant recognition in therapeutic applications. Only a few studies have explored its pharmacological activities, leaving researchers with limited empirical

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knowledge about its potential health benefits. Despite this, the plant possesses several promising constituents for inducing various healing effects. This review aims to present a comprehensive overview of *P. phoenicea*, encompassing its botanical description, traditional uses, chemical composition, and pharmacological properties. This work compiles existing data obtained through an extensive literature review of peer-reviewed journals from reputable scientific sources, aiming to serve as a valuable resource for guiding future research on the plant's therapeutic potential in advancing human health.

Keywords: *Pentapetes phoenicea*, phytochemical analysis, pharmacological activities, toxicity, snake bite

INTRODUCTION

Historically, drug discovery has benefited greatly from the use of natural products[1]. As of 2008, more than 100 natural product-derived compounds—predominantly derived from plant and microbial sources—were undergoing clinical studies[2]. Nevertheless, natural product-based drug development has significant challenges and hence for a couple of decades, the pharmaceutical industry has been concentrating on synthetic chemical libraries. However, its unsatisfying result has revitalized natural product-based drug discovery again despite its complexities[3]. The re-emergence is receiving attention since medications for various pharmacological purposes are being developed, ranging from drugs for cancer, and infectious diseases to neuropharmacological and metabolic disorders, cardiovascular diseases, and so on[1,2]. In such a scenario, numerous technological advancements are being made to facilitate effective natural-based drugs[1]. Thanks to these improvements, many of the herbs utilized for ethnopharmaceutical purposes are now coming to attention[4]. *Pentapetes phoenicea*, an upright, somewhat woody plant from the Malvaceae family fits this description. In Hindi, it is frequently referred to as "Dopahariya", and in English, "scarlet mallow" or "midday flower"[5,6]. *P. phoenicea* is a native of a large area of tropical South Asia, from northern Australia and the Philippines to Sri Lanka and India. It is widespread and naturalized, growing alongside roadways, in wastelands close to settlements, in dumping grounds, and in swampy locations throughout the drier regions of India[7]. *P. phoenicea* can reach a height of 1.5 m and can be grown during the rainy season after a month of flowering and ten days of fruiting[8]. Ethnologically the herb has been utilized therapeutically for an extensive variety. In India, the plant's leaves were made into a decoction that was consumed to treat inflamed glands[6]. Also, in

China and Annam, the root is used as an emollient. Several pharmacologically active constituents including flavonoids, tannins, saponins, phenols, steroids, and so on have been reported in *P. phoenicea*[7]. This review focuses on the pharmacognostical, phytochemical, and pharmacological aspects of the plant.

Morphology and anatomy of the plant

P. phoenicea grows on moist land as a weed of the rice fields and is also grown as an ornamental plant. It is an annual herb with an erect branched stem[9]. Regarding the pharmacognostical properties of the plant, there is only one study available. According to the authors, the study might be used as a foundation for standardizing, collecting, and identifying the plant. The leaves were discovered to be green, simple, 4 to 15 cm long, hastate, lanceolate, or oblong, with a crenate margin, and peltate. Anisocytic stomata, cuticle, a significant amount of rhomboidal calcium oxalate crystals, sclerenchymatous cells, collenchymatous cells, and a single layer of palisade cells were observed during a microscopic examination of the leaf. The researchers also reported that the flowers were umbrella-shaped, had five persistent sepals, and were peltate. The flowers also had superior ovaries and were reported to have twisted shapes. *P. phoenicea* produces subglobose, capsule-shaped fruits with dotted, subglobose seeds. The root measures around 2-3 mm in thickness, is light brown in color, conical to cylindrical, and has branches[8].

Phytoconstituents of different parts of *P. phoenicea*

Alkaloids

Alkaloids are naturally occurring toxic amines produced by plants as a defense mechanism, affecting systems like the immune, reproductive, digestive, and central nervous systems[10]. Despite their toxicity, they serve as important medicinal lead compounds due to their basic properties and solubility behavior, which support membrane interaction[11]. Alkaloids constitute approximately 20% of plant secondary metabolites and exhibit antibacterial, antiviral, insecticidal, and antimetastatic properties[12,13]. Some, like rutaecarpine, piperine, and harmine, have been used as antiplatelet agents[14]. Rasouli et al. highlighted the antidiabetic potential of plant-derived alkaloids and emphasized the need for further *in vitro* and *in vivo* studies to confirm their long-term efficacy[15].

Alkaloids can be categorized as true alkaloids, protoalkaloids and pseudoalkaloids from a structural point of view based on their molecular precursor, structures, and origins or based on the biological pathways used to obtain the molecule[16].

Phenolics

Phenolics are the most abundant secondary metabolites in plants and are present throughout their metabolic processes[17]. They are synthesized via the pentose phosphate and shikimic acid pathways through phenylpropanoid metabolism[18]. Structurally, phenolics contain one or more aromatic rings with hydroxyl groups and are classified into various groups such as phenolic acids, flavonoids, tannins, stilbenes, curcuminoids, coumarins, lignans, and quinones based on their ring structures and linkages[19]. Their antioxidant activity is attributed to their ability to stabilize phenoxyl radicals through delocalization of unpaired electrons[17].

Coumarin, a benzopyran-2-one (chromen-2-one) compound, is found in the leaves, stem, and roots of *P. phoenicea*[7]. Coumarins exhibit a wide range of pharmacological activities, including anti-inflammatory, anticoagulant, antibacterial, antifungal, antiviral, anticancer, antihypertensive, antituberculous, anticonvulsant, antiadipogenic, antihyperglycemic, antioxidant, and neuroprotective effects[20]. They have been extensively investigated for their anticancer potential[21].

Anthocyanins, a class of flavonoids, are known for their roles in plant pigmentation and human health. Studies suggest their protective effects against cancer, hyperlipidemia, and cardiovascular diseases[21]. They are the primary water-soluble pigments in plants, accumulating in vacuoles across various plant tissues, especially in leaves, stems, and roots[22-24]. Additionally, anthocyanins contribute to plant defense by disrupting insect camouflage, mimicking protective structures, and helping plants blend into their surroundings[25].

Tannins are widely occurring secondary metabolites in plants, composed of water-soluble flavonoid polymers that precipitate proteins[26,27]. They are classified into condensed tannins (common in vascular plants) and hydrolyzable tannins (mainly in dicotyledons)[27,45]. Tannins protect plants by inactivating insect digestive enzymes like trypsin and chymotrypsin[28], and possibly through the production of reactive oxygen species causing toxicity in insects[29].

Flavonoids are plant polyphenols with a structure consisting of two benzene rings and one heterocyclic ring[30]. Shen et al. classify them into seven subclasses, including flavonols, flavones, isoflavones, and others[31]. Luteolin (3,4,5,7-tetrahydroxy flavone) exhibits anticancer properties, while nobiletin has shown antioxidant and anti-inflammatory effects in mice[32,33]. Most flavonoids act as antioxidants through radical-scavenging activity[34].

Steroid

Phytosteroids are plant-derived metabolites that bind to steroid receptors in humans and animals, modulating receptor-mediated signaling pathways[35]. When combined with sugars, they form glycosides such as steroidal saponins, glycoalkaloids, and cardiac glycosides, known for their wide range of pharmacological properties, including anticancer, antimicrobial, hepatoprotective, and cardiotonic effects[36]. Structurally, steroids have a tetracyclic cyclopentanoperhydrophenanthrene skeleton with various methyl and alkyl substitutions contributing to their diversity[37]. Based on structural and taxonomic traits, plant steroids are classified into seven main groups: withanolides, steroidal saponins, brassinosteroids, phytosterols, steroidal alkaloids, mammalian steroidal hormones, and cardiac glycosides[38]. Cardiac glycosides are well-known for inhibiting sodium channels and have been clinically used to treat atrial arrhythmias and heart failure[39]. Traditionally, they have been used as emetics, diuretics, and heart tonics, and are listed in pharmacopeias such as the Danish, Chinese, German, and Indian[40,41]. Compounds like digitoxin, ouabain, digoxin, and bufalin show anticancer activity by inducing immunogenic cell death, and have potential for treating conditions like cystic fibrosis, ischemic stroke, and neurodegenerative diseases[39,42].

Triterpenoids

Triterpenoids are structurally varied chemical molecules with an essential backbone that can be changed in various ways, allowing the synthesis of over 20,000 naturally existing triterpenoid variations[43]. Triterpenoids can be found in nature either in their free form or as saponins[44]. Triterpenoid saponins exhibit a variety of biological actions, which resulted in research into the synthesis and efforts to increase natural source yields[45]. The therapeutic activities of triterpenoids include anticancer (cytotoxic and cytostatic activity), anti-inflammatory, herbicidal activity, antiulcerogenic, antimicrobial, and antiviral activity, as well as triterpenoids, show analgesic properties[45,46].

Carbohydrates

Carbohydrates are the primary organic compounds produced by photosynthesis and serve as the foundation for the synthesis of the majority of the other organic substances in woody plants. Most organic compounds found in nature are presumably carbohydrate-based[47]. The crucial carbohydrates are polysaccharides (starch and cellulose) oligosaccharides (raffinose and sucrose), and monosaccharides (hexoses and pentoses)[48]. The primary component of

plant cell walls, cellulose, is the most prevalent carbohydrate in the kingdom of plants. Carbohydrates play a crucial role in plants as essential energy sources, skeletons of carbon for organic molecules, and storage materials[49]. Similarly, polysaccharides serve an indispensable role in many different aspects of a plant's life cycle, including the construction of physical structures, the storage of energy, participation in metabolic processes, signaling, and defense responses[50].

Gums and mucilage

Gums and mucilage are both plant hydrocolloids, which gives them a few characteristics in common[51]. Due to its bioavailability and widespread use by humans since antiquity, plant gums are among the most significant gums. The primary characteristics that make them suitable for many applications are their high stability, emulsification action, viscosity, surface-active activity, and adhesive properties[51]. Gums and mucilage provide several benefits for the pharmaceutical sector, including fewer adverse effects, improved patient tolerance, biodegradability, biocompatibility, and non-toxicity, are inexpensive to produce, are not irritating to the eyes or skin, and do not create allergies in people[51-52]. However, many drawbacks prevent these materials from being used widely. To list a few are the microbial contamination and the amount of hydration that is often arduous to control[53]. Detailed information on the phytochemical analysis and the preclinical and clinical studies related to the phytoconstituents of *P. phoenicea* is presented in Table 1 and Table 2.

Table 1. Phytochemical analysis of *P. phoenicea*

Constituents	Extraction Solvent	Probable Type (Based on extraction solvent)	Plant Parts	Probable Pharmacological Activity
Coumarins	Petroleum ether Chloroform Acetone Methanol Distilled water	Trans O-hydroxycinnamic acid, psoralen, angelicin, bergapten, isopimpinellin, imperatorin, isoimperatorin, furanocoumarins[54,55]	Leaves Stem Roots	Anti-cancer Anti-tuberculosis Anticoagulant Anti-fungal
Alkaloids	Petroleum ether Chloroform Acetone Methanol	Isoboldine, boldine, laurolitsine,isocorydine,N-methyllaurotetanine, laurotetanine, reticuline coclaurine, N-methylcoclaurine[56]	Leaves Stem Roots	Antidiabetic Anticancer Anti-inflammatory Neurodegenerative disorders Antitussive Expectorant
Carotenoids	Petroleum ether	Lycopene, β-carotene, α-carotene, δ-carotene, 9-cis-β-carotene, 15-cis-β-carotene, 13-cis-β-carotene[57]	Leaves Stem	Antioxidant Anti-cancer Anti-tumor Anti-atherosclerotic[58,61]
Flavonoids	Acetone Methanol	Quercetin, kaempferol, patuletin, quercetagetin, luteolin and quercetagetin 5-methyl ether, aglycones of isoflavones, flavanones, methylated flavones, and flavonols[59,60]	Leaves Stem Roots	Cerebroprotective; Anxiolytic; Anti-cancer; Antioxidant Cholesterol-lowering activity Anti-bacterial Anti-inflammatory Anti-nociceptive Antihistamine Antifungal Anti-viral [(61)]
Saponins	Distilled water	Momordicatin, Sessiloside and chiisanoside, Eleutherosides B, E and K, Syngrin, Resveratrol, Yuccaloeside A-I[62-64]	Leaves Stem Roots	Anti-cholesterol effect on animal Cytostatic effects against cancerous cells
Steroids	Petroleum ether Chloroform Methanol Distilled water Hexane Ethyl acetate	Brassinosteroid, Bufadienolides, Cardenolides, Ecdysteroids[65-71]	Leaves Roots Stem	Hepatoprotective Anticancer Antimicrobial Antifungal Anti-inflammatory Cardiotonic activities
Phenolics	Petroleum ether Chloroform Acetone Methanol Distilled water	Coumarins[72]	Leaves Roots Stem	Antioxidants

Triterpenoids	Acetone Methanol Distilled water		Leaves Roots Stem	Anti-inflammatory Herbicidal activity Antiulcerogenic Antimicrobial
Anthocyanins	Distilled water	malvidin-3-glucoside, cyanidin-3-glucoside, pelargonidin-3-glucoside, cyanidin-3-O-rutinoside, delphinidin-3-O-glucoside, delphinidin-3-O-rutinoside[73-74]	Roots Stem	Anti-cancer Protective effects against hyperlipidemia Cardiovascular disease
Anthocyanidines	Methanol Distilled water	Delphinidin, Cyanidin[74]	Leaves Roots Stem	Anti-cancer
Anthracene glycosides	Methanol Distilled water	Rhein emodin [(75)]		
Cardiac glycosides	Methanol	Thevetosides, neriifolin, acetylneriifolin and acetylperuvoside[76]		Anti-tumor
	Distilled water	Anivirzel		
Tannins	Methanol Distilled water	Geraniin, Isoterchebin, Tellimagrandin I, Pedunculagin, Gemin D, Rugosin E, Cornusiin A[77]	Leaves Roots Stem	Antiulcerant Vasorelaxant Hypotensive Antioxidant Antimicrobial Antiviral
Carbohydrates	Distilled water	Mannitol, Sorbitol, Dulcitol, Xylitol, Arabitol, Fructose, Sorbose, Galactose, Mannose, Glucose, Arabinose, Xylose, Ribose, Rhamnose, Fucose, Galacturonic acid[78]	Leaves Roots Stem	

Table 2. Preclinical and clinical studies of phytoconstituents of *P. phoenicea*

Constituents	Probable Stage
Coumarins	**Preclinical studies** *in vitro* experiments using 8-hydroxy psoralen showed improvement in hepatocellular carcinoma through antioxidant activity and proliferation suppression[79].
	Clinical studies Patients with small cell and non-small cell lung cancer, colon cancer, head and neck cancer, and pancreatic cancer were assessed in a phase III trial. Warfarin and chemotherapy were administered to the patients, or only chemotherapy. When compared to patients with non-small-cell lung cancer, it was discovered that warfarin is associated with enhanced survival in patients with small-cell lung cancer who are receiving chemotherapy (p=0.018)[10].
Alkaloids	**Preclinical studies** Boldine relaxes smooth muscle in vitro in the rat ileum at doses between 10^{-5} and 10^{-4} M. This effect is at least partially mediated by anticholinergic effects[80].
	Clinical studies In a study of 553 patients (aged 18-75) with colorectal adenoma who had undergone total polypectomy, berberine (0.3 g twice daily) was given for two years starting six months post-surgery. The treatment reduced adenoma recurrence with no significant side effects, apart from mild constipation[81].
Carotenoids	**Preclinical studies** 1.Lycopene and β-carotene cause inhibition of cell proliferation; cell cycle arrest in different phases, and induction of apoptosis in MCF-7, MDA-MB-231, and MDA-MB-235 cell lines (*in vitro*) regarding breast cancer at 10μM concentration. 2.β-carotene reduced the number of skin tumors in female SKH·h–1 mice (*in vivo*) at a 3.3 mg dose.
	Clinical studies 1.At a dose of 7 mg, lycopene improves endothelial (vascular) function in patients with CVD. 2.In Finnish men, a high serum content of β-carotene was linked to a lower risk of prostate cancer[58].
Flavonoids	**Preclinical studies** 1.Quercetin lowers the amount of TNF-, IL-1, and IL-6 produced by the macrophage RAW 264.7 cell line. 2.Quercetin acts on the hCBMCs cell line of mast cells to lower histamine, leukotrienes, and PGD2.
	Clinical studies Quercetin at 500 mg, daily for 8 weeks in 50 women improved clinical symptoms, disease activity, hs-TNFα, and health assessment questionnaire in women with rheumatoid arthritis when used as supplements[82].

Saponins	**Preclinical studies** 1.*In vitro*, pancreatic lipase activity was decreased by sessiloside and chiisanoside. Additionally, adding the saponin-rich fraction to a high-fat diet prevented mice from gaining weight. 2.Momordicatin was reported to suppress 100% of the growth of parasites in vitro at doses as low as 0.4 mg/L. When momordicatin dosages of 10 mg/kg were administered to hamsters, no parasites were found in vivo[62]. 3.Steroid saponins showed strong cytotoxic effects and induced apoptosis in a dose-dependent manner. In an in vivo study, oral administration of diosgenin to T739 mice with LA795 lung adenocarcinoma reduced tumor growth by 33.94%. Histological analysis (HE staining) revealed tissue changes in the liver and lungs, and TUNEL assay confirmed increased tumor cell apoptosis compared to controls[83].
	Clinical studies Overweight subjects who were given saponin extract had a significant reduction in daily fat consumption, as measured by the ratio of fat-reported energy intake/total energy expenditure (fat-REI/TEE) compared to those who received a placebo (fat-REI/TEE 0.26±0.02 vs. 0.30±0.01, respectively; p=0.032)[84].
Steroids	**Preclinical studies** 1.Rats' paw volumes were significantly reduced by steroids at various doses. When ethanolic extract was compared to the reference standard Diclofenac sodium at a concentration of 300 mg/mL, it demonstrated strong efficacy[85]. 2.Steroids demonstrated anticancer efficacy on MGC-803 cells in vitro. They also activated caspase-3 and caused S phase arrest in MGC-803 cells, which may have been caused by up-regulating the ratio of Bax to Bcl-2 and down-regulating mutant p53[86].
	Clinical studies In a 20-year follow-up, Stenkvist found that breast cancer patients using digitalis had a significantly lower mortality rate (6%) compared to non-users (34%) (p=0.002). Supporting this, Goldin and Safa's retrospective analysis of 127 cancer patients showed only one cancer-related death among those who had taken digitalis[86].
Phenolics	**Preclinical studies** The methanol extract demonstrated strong antioxidant activity, effectively scavenging $ABTS^{\bullet+}$ and DPPH• radicals with ID_{50} values of 8.6 µg/mL and 21.5 µg/mL, respectively. Its activity was dose-dependent, with notable $ABTS^{\bullet+}$ reduction at 25.0 µg/mL. LC-MS/MS analysis linked this effect to the presence of flavonoids. The ORAC assay further confirmed its antiradical potential by measuring the inhibition of fluorescein oxidation by peroxyl radicals[72].
	Clinical studies The *in vivo* antioxidant potential of phenolic extracts was evaluated in clinical trials involving healthy individuals, including basketball players and postmenopausal women. A low-polyphenol diet for two weeks influenced the immune status of athletes during training. While the exact biological impact is unclear, these changes may help reduce the long-term risk of diseases like cancer and cardiovascular conditions[73].

Triterpenoids	**Preclinical studies** 1.Triterpenoids showed significant antitumor activity against Ehrlich ascites carcinoma in both *in vivo* and *in vitro* studies. Treatment increased the infected mice's lifespan, RBC hemoglobin levels, and total cell count, while reducing viable and nonviable tumor cells and liver enzymes (SGOT, SGPT, ALP). Their anticancer effect is likely due to the triterpene nucleus containing an active hydrogen adjacent to a carbonyl group, enabling free radical neutralization[87]. 2.By lowering a variety of inflammatory cytokines, triterpenoids show promise as an anti-inflammatory agent in RAW264.7 cells treated with lipopolysaccharide (LPS). Additionally, in mice treated with TPA, it reduced pathogenic damage and suppressed skin inflammation. It is possible that the anti-inflammatory effects stem from the suppression of NF-kB and MAPK phosphorylation[88].
	Clinical studies Triterpenoid formulations showed promising results in early clinical trials. In patients with astrocytomas, a crude chloroform/methanol extract reduced urinary cysteinyl-LT levels and peritumoral brain edema. A 7-day treatment in malignant glioma patients significantly reduced perifocal edema, though tumor size remained unchanged (66) (72). It is suggested that 5-LO inhibition has pharmacological relevance for patients with brain tumors who have elevated LT biosynthesis[89].
Anthocyanins	**Preclinical studies** 1.Cyanidin-3-glucoside inhibits tumor growth in MDA-MB-453 cells-inoculated nude mice by doing active apoptosis involving caspase-3 cleavage and DNA fragmentation through Bcl-2 and Bax pathway[90]. 2.Long-term dietary intake of plant-derived anthocyanins in male Wistar rats reduced the heart's susceptibility to ischemia-reperfusion injury both ex vivo and in vivo. This protective effect is likely linked to enhanced endogenous antioxidant defenses in the myocardium[91]. 3.In high-fat diet-fed C57BL/6 mice, anthocyanins like Cyanidin3-glucoside and related compounds reduced elevated glucose and triglyceride levels, with no change in cholesterol. The effect may involve regulation of hepatic lipid metabolism[92].
	Phase 0 human clinical trial Male and female OSCC cancer patients (N=38)≥21 years of age of any race or ethnicity with newly diagnosed, untreated, biopsy-confirmed OSCC (oral squamous cell carcinomas) of any stage; cyanidin-3-rutinoside and cyanidin-3- xylosylrutinoside significantly reduced the expression of prosurvival genes (AURKA, BIRC5, EGFR) and proinflammatory genes (NFKB1, PTGS2)[93].
Anthocyanidines	**Preclinical studies** Delphinidin (30–240mM; 48h) treatment of human colon cancer HCT116 cells suppressed the NF-KB pathway, resulting in G2/M-phase arrest and apoptosis[94].
Anthracene glycosides	N/A

Cardiac glycosides	**Preclinical studies** 1.Neriifolin suppressed the tumor growth by increasing DNA damage and apoptosis through CHOP-C/EBP-α (C/EBP homologous protein- CCAAT enhancer binding protein alpha) signaling axis of ERS (endoplasmic reticulum stress) in prostate cancers in nude mice[95]. 2.Neriifolin inhibited the proliferation of HepG2 cells markedly in a dose and time-dependent manner [(0–8 µg/ml) of neriifolin for 12, 24, 48, and 72 h] without significantly reducing the viability of normal Chang human liver cells. Mechanism: reduced viability of HepG2 cells, induced S and G2/M phase arrests of the cell cycle, and stimulated apoptosis of Also, induced activation of caspase-3, -8, and -9, and up-regulated expression of Fas and FasL proteins[96].
	Phase I clinical trial Anivirzel inhibits the FGF-2 in prostate cancer cells in time and dose-dependent manner to induce cell death. The results of the phase I clinical trials were promising and can safely be administered intramuscularly by up to 1.2 mL/m2/day[97].
Tannins	**Preclinical studies** Ellagitannin pedunculagin showed strong inhibition of lipid peroxidation in rat liver mitochondria. Tannins like geraniin also effectively prevented lipid peroxidation in mouse eye lens cell membranes. Additionally, tannins demonstrated antibacterial activity against various gastrointestinal pathogens. Ellagitannins showed potent inhibition of *Candida albicans, Campylobacter jejuni,* and *Staphylococcus* species. Hydrolyzable tannins such as tellimagrandins I and II, pedunculagin, geraniin, and isoterchebin exhibited strong antioxidant activity in the DPPH assay[98].
Carbohydrates	N/A
Gums and mucilage	N/A

Pharmacological activities

Cerebroprotective effects

Global cerebral ischemia is one of the leading causes of disability and mortality worldwide, which is also a significant financial drain on medical care[99]. Global cerebral ischemia alludes to a reduction in the amount of cerebral blood flowing through the entire brain[100]. Generally, days or months after the initial trauma, it causes neuronal degeneration and occasionally the patient's death[101]. Even though reperfusion reinstates cerebral blood flow, it also causes an increase in reactive oxygen species, cerebral edema, and hemorrhage, as well as a drop in nitric oxide[6,102]. After global cerebral ischemia, there is a significant chance of getting Alzheimer's disease or vascular dementia[102].

A study in 2016 established the cerebroprotective effect of *P. phoenicea* in global ischemia-induced rats[6]. Global cerebral ischemia leads to further complications through oxidative stress by altering the antioxidant enzymes[103]. The antioxidant enzymes include catalase, glutathione reductase, glutathione peroxidase, glutathione-S-transferase, glutathione, and superoxide dismutase. The level of malondialdehyde and H_2O_2 was found to be increased in the ischemic brains. H_2O_2 causes neuronal injury by impairing mitochondrial function.

P. phoenicea attenuated these issues by reducing malondialdehyde and increasing catalase, and superoxide dismutase which respectively catalyze the decomposition of H_2O_2 and act as a major antioxidant. The rats treated with *P. phoenicea* also showed an increased level of antioxidant enzymes including glutathione, glutathione reductase, glutathione peroxidase, and glutathione-S-transferase.

Furthermore, the gel electrophoresis result concluded a high protein content in the experimental groups, treated with *P. phoenicea*. They also showed a more than two-fold decrease in brain water content, cerebral infarct size, as well as neuronal loss, although a significant decrease in brain weight was reported[6]. This cerebroprotective effect confirmed the presence of flavonoids like rutin and quercetin in *P. phoenicea*[104].

Neuropharmacological activity

P. phoenicea's traditional usage in psychological diseases is well recognized. Therefore, its effect on the central nervous system is analyzed in a recent study. Triterpenoids, tannins, flavonoids, alkaloids, phenolics, and glycosides were all identified through qualitative analysis of the methanolic and aqueous extract. Also, the *in-vivo* neuropharmacological activity was assessed on both albino mice and rats. Studies reveal dose-dependent decline in spontaneous motility, locomotor activity, and an increase in the length of induced sleep, prominently in the methanolic extract. Also, a reduction in exploratory behavior was reported in the elevated plus maze, evasion test, Y-maze, and hole board apparatus. Suppression of aggressiveness and moderate anticonvulsant activity were also demonstrated, supporting the GABAnergic activity of the plant extract[104].

Antiradical effects

Free radicals are found to be directly linked to causing several life-threatening diseases including atherosclerosis, cancer, diabetes, and so on[105]. Any molecular entity capable of independent existence that has an unpaired electron in an atomic orbital is referred to as a free radical[106]. Numerous processes result in the formation of these free radicals, which damage the DNA, proteins, lipids, and carbohydrates in the nucleus as well as other cell membranes[107]. An experiment by Sharma and colleagues established the free radical scavenging activity of *P. phoenicea* leaves. In the study, the extract was subjected to multiple fractionations and found that the crude hydroalcoholic extract's capacity to scavenge free radicals was lower than that of the ethyl acetate fraction and the aqueous fraction. The study suggests that the fraction contains flavonoids and tannins[108].

Anti-diabetic effects

The experiment by Sharma and colleagues also proved the α-amylase inhibitory activity of the leaves of *P. phoenicea*. This study examined the potential of a plant extract to prevent the *in vitro* hydrolysis of starch. The pancreatic amylase inhibitory effects of the ethyl acetate fraction gradually increased in a dose-dependent manner. The aqueous fraction initially showed a dose-dependent response, however, at higher doses, its inhibitory effect plateaued. Contrarily, as compared to the other fractions, the crude hydroalcoholic extract lacked any appreciable inhibitory potential. The ethyl acetate and aqueous portions of the plant extract appear to have the strongest inhibitory effects on starch breakdown, according to these results. The study suggests that saponins may be present and may be the cause of the observed antidiabetic, lipid-lowering, and cholesterol-lowering effects[109]. However, according to their later investigation, the hydro-alcoholic extract of *P. phoenicea* showed effective blood glucose-lowering action in streptozotocin-induced hyperglycemic rats. And here they concluded that the presence of sterols, flavonoids, terpenoids, and tannins is associated with the exerting effect[109]. Starch, glycogen, and other oligosaccharides have their 1, 4-glucosidic linkages hydrolyzed by α-amylase into simple and easily absorbable sugars. By reducing the glucose uptake from the starch, α-amylase inhibition in the human digestive tract has been suggested to be useful in treating diabetes[110]. The currently available drugs that work in such a way include acarbose, miglitol, and voglibose[111]. Nevertheless, adverse effects of these drugs including lactic acidosis, liver problems, and diarrhea have been reported[112].

Acaricidal activity

Many of the acaricides are organothiophosphate chemicals that are used to kill mites and ticks[113]. Previously, fish oil, kerosene oil, cotton-seed oil, etc. were used as acaricide[114]. However, the introduction of synthetic acaricides changed the scenario despite having the potential to affect the agricultural environment and cause acaricide resistance[114]. Hence, nowadays the application of plant extract as acaricide is at the peak of interest as multiple studies have shown the strong activity of several plant extracts[115-120]. Furthermore, the study by Chungsamarnyart et al. established both the acute and delayed acaricidal effect of *Pentapetes phoenicia* when combined with *Calotropis procera* and *Calotropis gigantea* respectively. Combining *Calotropis procera* and *Calotropis gigantea* with *Pentapetes phoenicia* significantly boosted the acaricidal effects. This finding suggests that *Pentapetes phoenicia*, when combined with certain plant extracts, exhibits enhanced tick-killing properties[121].

Toxicology study

The brine shrimp lethality bioassay is used as a screening tool to test an indication of anticancer, cytotoxicity, antimicrobial, pesticidal, antiviral, and other pharmacological activities of different extracts, and pure compounds[122]. Sharma and colleagues performed the brine shrimp lethality test to examine the biosafety of the *Pentapetes phoenicia* extracts. A stock solution was prepared by dissolving several plant extracts, including those derived from hexane, chloroform, and ethyl acetate, in pure dimethyl sulfoxide. Following the preparation of the stock solution, a handful number of *Artemia salina* larvae (a species of brine shrimp) were placed and incubated for 24 hours at a temperature between 25°C and 27°C under light.

It was discovered that up to a maximum dose level of 600 µg/mL, none of the *Pentapetes phoenicia* extracts were toxic. Moreover, with an LC_{50} of 659.8 µg/mL, the chloroform extract appeared to be moderately toxic. Hence, the study indicates that *Pentapetes phoenicia* can be taken safely following the claims stated traditionally[5].

METHODOLOGY

To ensure a reliable and thorough literature review on *P. phoenicea*, several steps were followed. First, we tried to conduct a comprehensive search of peer-reviewed journal articles using keywords such as *P. phoenicea*, phytochemical analysis, pharmacological activities, and therapeutic applications. Websites like Google Scholar, PubMed, ResearchGate, ScienceDirect, and related pharmaceutical journals were among the sources. Non-reviewed reports and conference abstracts were not taken into account. Additionally, the literature search did not include non-English journals. Besides, references from the selected articles were scanned to locate further relevant studies. The manuscript was written using Microsoft Word 2016 on an HP ProBook 450 G5, and tables were created in Word. This review compiles critical information regarding the pharmacognostic properties, phytochemical composition, therapeutic potential, reported biological activities, ethnopharmaceutical uses and toxicity of *Pentapetes phoenicea*.

RESULTS and DISCUSSION

Despite being a relatively less familiar plant, *P. phoenicea* has been traditionally used in various systems of medicine for treating various ailments such as fever, snake bite, headache, rheumatic swelling, and hair lice in a limited scale. The plant has been reported to possess phytochemicals such as flavonoids, alkaloids, saponins, tannins, and steroids that may be responsible

for its pharmacological activities. Only a few studies have demonstrated that plant extracts can exhibit antipyretic, astringent, carminative, detoxicant, anti-cancer, emollient, mucilaginous, anti-inflammatory, and thermogenic properties. However, the scientific evidence supporting the efficacy and safety of *P. phoenicea* remains limited and unsatisfactory, largely due to a lack of rigorousness and diversity of research. For instance, toxicological reports in pregnancy and for neonates are still not examined. Therefore, more studies are needed to validate the ethno-medicinal uses of the plant and to explore its potential as a source of novel drugs for human health. To compensate for the dearth of the meticulousness of studies, we have also incorporated theoretical and empirical data of phytochemical constituents of *P. phoenicea* even when the researchers used different plants. Because the same constituent will remain a potential candidate for the same therapeutic effects. Therefore, the researchers would get diverse concepts and justified grounds to execute several types of research to explore the numerous pharmacological activities of plants. Such studies can facilitate the discovery of new therapeutic activity of *P. phoenicea*. Alongside, the rigorous studies will enhance the possibility of getting novel compounds in the future, and such compounds will enrich some disease management system.

STATEMENT OF ETHICS

This study does not require any ethical permission.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Conceptualization, RT, SA, FA; writing original draft, SA, SMN, RSH, OBAB, TRFAS, IJP; review and editing, RT, SMB.

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REFERENCES

1. Atanasov AG, Zotchev SB, Dirsch VM, the International Natural Product Sciences Taskforce, Supuran CT. Natural products in drug discovery: advances and opportunities. Nat Rev Drug Discov, 2021;20(3):200-216. Doi: 10.1038/s41573-020-00114-z

2. Harvey AL. Natural products in drug discovery. Drug Discov Today, 2008;13(19-20):894-901. Doi: 10.1016/j.drudis.2008.07.004

3. Atanasov AG, Waltenberger B, Pferschy-Wenzig E, Linder T, Wawrosch C, Uhrin P, et al. Discovery and resupply of pharmacologically active plant-derived natural products: a review. Biotechnology advances, 2015;33(8):1582-1614. Doi: 10.1016/j.biotechadv.2015.08.001

4. Patwardhan B. Ethnopharmacology and drug discovery. J Ethnopharmacol, 2005;100(1-2):50-52. Doi: 10.1016/j.jep.2005.06.006

5. Sharma N, Gupta PC, Singh A, Rao, CV. Brine shrimp bioassay of *Pentapetes phoenicea* Linn. and *Ipomoea carnea* Jacq. leaves. Der Pharmacia Lettre, 2013;5(1):162-167.

6. Sravanthi KN, Rao NR. Cerebroprotective activity of *Pentapetes phoenicea* on global cerebral ischemia in rats. Indian J Pharmacol. 2016;48(6):694-700. Doi: 10.4103/0253-7613.194849

7. Yawalikar N, Bhowal M, Rudra J. Preliminary phytochemical analysis of *Pentapetes phoenicea* L. IOSR J Pharm Biol Sci, 2014;9(6):36-39. Doi: 10.9790/3008-09633639

8. Sharma N, Gupta P, Gupta, Singh A, Rao CV. Pharmacognostical, phytochemical investigations and HPTLC fingerprinting of *Pentapetes phoenicea* L. leaves. Indian J Nat Prod Resour, 2014;5(2):158-163. Doi: 10.56042/ijnpr.v5i2.1934

9. Yawalikar N, Bhowal M, Rudra J. Effect of Chemical and physical factors on seed germination of *Pentapetes phoenıcea* L. Indian J Fundam Appl Life Sci, 2012;2(1):200-206. Doi: 10.5897/AJB12.485

10. Mohan VR, Tresina PS, Daffodil ED. Antinutritional factors in legume seeds: characteristics and determination. Encycl Food Health, 2016;211-220. Doi: 10.1016/B978-0-12-384947-2.00036-2

11. Heinrich M, Mah J, Amirkia V. Alkaloids used as medicines: structural phytochemistry meets biodiversity—an update and forward look. Molecules, 2021;26(7):1836. Doi: 10.3390/molecules26071836

12. Kaur R, Arora S. Alkaloids-important therapeutic secondary metabolites of plant origin. J Crit Rev, 2015;2(3):1-8.

13. Qiu S, Sun H, Zhang AH, Xu HY, Yan GL, Han Y, et al. Natural alkaloids: basic aspects, biological roles, and future perspectives. Chin J Nat Med, 2014;12(6):401-406. Doi: 10.1016/S1875-5364(14)60063-7

14. Ain QU, Khan H, Mubarak MS, Pervaiz A. Plant alkaloids as antiplatelet agent: drugs of the future in the light of recent developments. Front Pharmacol, 2016;22(7):292. Doi: 10.3389/fphar.2016.00292

15. Rasouli H, Yarani R, Pociot F, Popović-Djordjević J. Anti-diabetic potential of plant alkaloids: revisiting current findings and future perspectives. Pharmacol Res, 2020;155:104723. Doi: 10.1016/j.phrs.2020.104723

16. Dey P, Kundu A, Kumar A, Gupta M, Lee BM, Bhakta T, et al. In: Silva AS, Nabavi SF, Saeedi M, Nabavi SM, editors. Analysis of alkaloids (indole alkaloids, isoquinoline alkaloids, tropane alkaloids) [Internet]. Elsevier; 2020. p. 505-567. Available from: https://doi.org/10.1016/B978-0-12-816455-6.00015-9. [Mar 30, 2020].

17. Babbar N, Oberoi HS, Sandhu SK, Bhargav VK. Influence of different solvents in extraction of phenolic compounds from vegetable residues and their evaluation as natural sources of antioxidants. J Food Sci Technol, 2014;51(10):2568-2575. Doi: 10.1007/s13197-012-0810-8

18. Randhir R, Lin Y, Shetty K. Stimulation of phenolics, antioxidant and antimicrobial activities in dark germinated mung bean sprouts in response to peptide and phytochemical elicitors. Process Biochem, 2004;39(5):637-646. Doi: 10.1016/S0032-9592(03)00197-3

19. Huang W, Cai Y, Zhang Y. Natural phenolic compounds from medicinal herbs and dietary plants: potential use for cancer prevention. Nutr Cancer, 2009;62(1):1-20. Doi: 10.1080/01635580903191585

20. Sharifi-Rad J, Cruz-Martins N, López-Jornet P, Lopez EP, Harun N, Yeskaliyeva B, et al. Natural coumarins: exploring the pharmacological complexity and underlying molecular mechanisms. Oxid Med Cell Longev, 2021;2021(1):6492346. Doi: 10.1155/2021/6492346

21. Teresa SDP, Ballesta MTS. Anthocyanins: from plant to health. Phytochem Rev, 2008;7 (2):281-299. Doi: 10.1007/s11101-007-9074-0

22. Mazza G, Cacace JE, Kay CD. Methods of analysis for anthocyanins in plants and biological fluids. J AOAC Int, 2004;87(1):129-145. Doi: 10.1093/jaoac/87.1.129

23. Landi M, Tattini M, Gould KS. Multiple functional roles of anthocyanins in plant-environment interactions. Environ Exp Bot, 2015;119:4-17. Doi: 10.1016/j.envexpbot.2015.05.012

24. Chalker-Scott L. Environmental significance of anthocyanins in plant stress responses. Photochem Photobiol, 1999;70(1):1-9. Doi: 10.1111/j.1751-1097.1999.tb01944.x

25. Lev-Yadun S, Gould KS. Role of anthocyanins in plant defence. In: Winefield C, Davies K, Gould K, editors. Anthocyanins. New York, NY: Springer; 2008. p. 22-28. Available from: https://link.springer.com/chapter/10.1007/978-0-387-77335-3_2. [Jan 1, 2008].

26. Hussain G, Huang J, Rasul A, Anwar H, Imran A, Maqbool J, et al. Putative roles of plant-derived Tannins in neurodegenerative and neuropsychiatry disorders: an updated review. Molecules, 2019;24(12):2213. Doi: 10.3390/molecules24122213

27. Bernays EA, Driver GC, Bilgener M. Herbivores and plant tannins, 1989;19:263-302. Doi: 10.1016/S0065-2504(08)60160-9

28. Ahmad MF, Ahmad FA, Alsayegh AA, Zeyaullah Md, AlShahrani AM, Muzammil K, et al. Pesticides impacts on human health and the environment with their mechanisms of action and possible countermeasures. Heliyon, 2024;10(7):e29128. Doi: 10.1016/j.heliyon.2024.e29128

29. Barbehenn RV, Constabel CP. Tannins in plant-herbivore interactions. Phytochemistry, 2011;72(13):1551-1565. Doi: 10.1016/j.phytochem.2011.01.040

30. Biela M, Rimarčík J, Senajová E, Kleinová A, Klein E. Antioxidant action of deprotonated flavonoids: thermodynamics of sequential proton-loss electron-transfer. Phytochemistry, 2020;180:112528. Doi: 10.1016/j.phytochem.2020.112528

31. Shen N, Wang T, Gan Q, Liu S, Wang L, Jin B. Plant flavonoids: classification, distribution, biosynthesis, and antioxidant activity. Food Chem, 2022;383:132531. Doi: 10.1016/j.foodchem.2022.132531

32. Liu Y, Yang Q, Li S, Luo L, Liu H, Li X, et al. Luteolin attenuates angiotensin II-induced renal damage in apolipoprotein e-deficient mice. Mol Med Rep, 2020;23(2):157. Doi: 10.3892/mmr.2020.11796

33. Murakami A, Nakamura Y, Torikai K, Tanaka T, Koshiba T, Koshimizu K, et al. Inhibitory effect of citrus nobiletin on phorbol ester-induced skin inflammation, oxidative stress, and tumor promotion in mice. Cancer Res, 2000;60(18):5059-5066. Doi: 10.1158/0008-5472.CAN-00-1290

34. Bors W, Heller W, Michel C, Saran M. Flavonoids as antioxidants: determination of radical-scavenging efficiencies. Methods Enzymol, 1990;186:343-355. Doi: 10.1016/0076-6879(90)86128-i

35. Dean M, Murphy BT, Burdette JE. Phytosteroids beyond estrogens: regulators of reproductive and endocrine function in natural products. Mol Cell Endocrinol, 2017;442:98-105. Doi: 10.1016/j.mce.2016.12.013

36. Patra JK, Shukla AC, Das G. Advances in pharmaceutical biotechnology recent progress and future applications: recent progress and future applications [Internet]. Singapore: Springer Nature; 2020 [Jan 30, 2020]. Available from: https://link.springer.com/book/10.1007/978-981-15-2195-9

37. Gunaherath KB, Gunatilaka L. Plant steroids: occurrence, biological significance and their analysis. In: Robert A. Meyers, editors. Encyclopedia of analytical chemistry: applications, theory and instrumentation [Internet]. John Wiley & Sons, Ltd; 2014. p. 1-26. Available from: https://onlinelibrary.wiley.com/doi/10.1002/9780470027318.a9931. [Sep 18, 2020].

38. Kreis W, Müller-Uri F. Biochemistry of sterols, cardiac glycosides, brassinosteroids, phytoecdysteroids and steroid saponins. In: Michael Wink, editor. Annual plant reviews volume 40: biochemistry of plant secondary metabolism [Internet]. Wiley Online Books; 2018. p. 304-363. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/9781119312994.apr0428. [Sep 24, 2024].

39. Prassas I, Diamandis EP. Novel therapeutic applications of cardiac glycosides. Nat Rev Drug Discov, 2008;7(11):926-935. Doi: 10.1038/nrd2682

40. Kelly RA. Cardiac glycosides and congestive heart failure. Am J Cardiol, 1990;65(10):10E-16E. Doi: 10.1016/0002-9149(90)90245-v

41. Patel S. Plant-derived cardiac glycosides: role in heart ailments and cancer management. Biomed Pharmacother Biomedecine Pharmacother, 2016;84:1036-1041. Doi: 10.1016/j.biopha.2016.10.030

42. Kepp O, Menger L, Vacchelli E, Adjemian S, Martins I, Ma Y, et al. Anticancer activity of cardiac glycosides. Oncoimmunology, 2012;1(9):1640-1642. Doi: 10.4161/onci.21684

43. Petronelli A, Pannitteri G, Testa U. Triterpenoids as new promising anticancer drugs. Anticancer Drugs, 2009;20(10):880-892. Doi: 10.4161/onci.21684

44. Mahato SB, Nandy AK, Roy G. Triterpenoids. Phytochemistry, 1992;31(7):2199-2149. Doi: 10.1016/0031-9422(92)83257-y

45. Lambert E, Faizal A, Geelen D. Modulation of triterpene saponin production: *in vitro* cultures, elicitation, and metabolic engineering. Appl Biochem Biotechnol, 2011;164(2):220-237. Doi: 10.1007/s12010-010-9129-3

46. Dzubak P, Hajduch M, Vydra D, Hustova A, Kvasnica M, Biedermann D, et al. Pharmacological activities of natural triterpenoids and their therapeutic implications. Nat Prod Rep, 2006;23(3):394-411. Doi: 10.1039/b515312n

47. Likens GE. Inland waters and limnology. In: Thomas Mehner, Klement Tockner, editors. Encyclopedia of inland waters [Internet]. Elsevier; 2009. p. 5-10. Available from: https://www.sciencedirect.com/referencework/9780128220412/encyclopedia-of-inland-waters. [Jan 13, 2009].

48. Venugopala KN, Rashmi V, Odhav B. Review on natural coumarin lead compounds for their pharmacological activity. BioMed Research International, 2013;2013(1):963248. Doi: 10.1155/2013/963248

49. Trouvelot S, Héloir MC, Poinssot B, Gauthier A, Paris F, Guillier C, et al. Carbohydrates in plant immunity and plant protection: roles and potential application as foliar sprays. Front Plant Sci, 2014;5:592. Doi: 10.3389/fpls.2014.00592

50. Kongala SI, Kondreddy A. A review on plant and pathogen derived carbohydrates, oligosaccharides and their role in plant's immunity. Carbohydr Polym Technol Appl, 2023;6:100330. Doi: 10.1016/j.carpta.2023.100330

51. Amiri MS, Mohammadzadeh V, Yazdi MET, Barani M, Rahdar A, Kyzas GZ. Plant-based gums and mucilages applications in pharmacology and nanomedicine: a review. Mol Basel Switz, 2021;26(6):1770. Doi: 10.3390/molecules26061770

52. Deogade UM, Deshmukh VN, Sakarkar DM. Natural gums and mucilage's in NDDS: applications and recent approaches. Int J PharmTech Res, 2012;4(2):799-814.

53. Barani M, Torkzadeh-Mahani M, Mirzaei M, Nematollahi MH. Comprehensive evaluation of gene expression in negative and positive trigger-based targeting niosomes in HEK-293 cell line. Iran J Pharm Res IJPR, 2020;19(1):166-180. Doi: 10.22037/ijpr.2019.112058.13507

54. Skalicka-Woźniak K, Głowniak K. Pressurized liquid extraction of coumarins from fruits of *Heracleum leskowii* with application of solvents with different polarity under increasing temperature. Molecules, 2012;17(4):4133-4141. Doi: 10.3390/molecules17044133

55. Bourgaud F, Poutaraud A. Extraction of coumarins from plant material (Leguminosae). Phytochem Anal, 1994;5:127-132. Doi: 10.1002/pca.2800050308

56. Torres-Vega J, Gómez-Alonso S, Pérez-Navarro J, Pastene-Navarrete E. Green extraction of alkaloids and polyphenols from *Peumus boldus* leaves with natural deep eutectic solvents and profiling by HPLC-PDA-IT-MS/MS and HPLC-QTOF-MS/MS. Plants Basel Switz, 2020;9(2):242. Doi: 10.3390/plants9020242

57. Kultys E, Kurek MA. Green extraction of carotenoids from fruit and vegetable Byproducts: A Review. Molecules, 2022;27(2):518. Doi: 10.3390/molecules27020518

58. Milani A, Basirnejad M, Shahbazi S, Bolhassani A. Carotenoids: biochemistry, pharmacology and treatment. Br J Pharmacol, 2017;174(11):1290-1324. Doi: 10.1111/bph.13625

59. Munhoz V, Longhini R, Souza J, Zequi J, Leite Mello E, Lopes G, et al. Extraction of flavonoids from *Tagetes patula*: process optimization and screening for biological activity. Rev Bras Farmacogn, 2014;24(5):576-583. Doi: 10.1016/j.bjp.2014.10.001

60. Chaves JO, de Souza MC, da Silva LC, Lachos-Perez D, Torres-Mayanga PC, Machado AP da F, et al. Extraction of flavonoids From natural sources using modern techniques. Front Chem, 2020;8:507887. Doi: 10.3389/fchem.2020.507887

61. Ekalu A, Habila JD. Flavonoids: isolation, characterization, and health benefits. Beni-Suef Univ J, Basic Appl Sci, 2020;9:45. Doi: 10.1186/s43088-020-00065-9

62. Cheok CY, Salman HAK, Sulaiman R. Extraction and quantification of saponins: a review. Food Res Int, 2014;59:16-40. Doi: 10.1016/j.foodres.2014.01.057

63. Han C, Hui Q, Wang Y. Hypoglycaemic activity of saponin fraction extracted from *Momordica charantia* in PEG/salt aqueous two-phase systems. Nat Prod Res, 2008;22(13):1112-1119. Doi: 10.1080/14786410802079675

64. Jang H, Kim WJ, Lee SU, Kim M, Park MH, Song S, et al. Optimization of chiisanoside and chiisanogenin isolation from *Eleutherococcus sessiliflorus* (Rupr. & Maxim.) leaves for industrial application: a pilot study. Ind Crops Prod, 2022;185:115099. Doi: 10.1016/j.indcrop.2022.115099

65. Pettit GR, Kasturi TR. Steroids and related natural products. 63. 17-beta-acetoxy-4-oxa-2-androstene. J Med Chem, 1970;13(6):1244-1245. Doi: 10.1021/jm00300a060

66. Li J, Zhang Y, Lin Y, Wang X, Fang L, Geng Y, et al. Preparative separation and purification of bufadienolides from ChanSu by high-speed counter-current chromatography combined with preparative HPLC. Quím Nova, 2013;36(5):686-690. Doi: 10.1590/S0100-40422013000500013

67. Siddiqui BS, Sultana R, Begum S, Zia A, Suria A. Cardenolides from the methanolic extract of *Nerium oleander* leaves possessing central nervous system depressant activity in mice. J Nat Prod, 1997;60(6):540-544. Doi: 10.1021/np960679d

68. Tofighi Z, Moradi-Afrapoli F, Ebrahimi SN, Goodarzi S, Hadjiakhoondi A, Neuburger M, et al. Securigenin glycosides as hypoglycemic principles of *Securigera securidaca* seeds. J Nat Med, 2017;71(1):272-280. Doi: 10.1007/s11418-016-1060-7

69. Caspi E, Lewis DO. Progesterone: its possible role in the biosynthesis of cardenolides in *Digitalis lanata*. Science, 1967;156(3774):519-520. Doi: 10.1126/science.156.3774.519

70. McKinney DA, Strand MR, Brown MR. Evaluation of ecdysteroid antisera for a competitive enzyme immunoassay and of extraction procedures for the measurement of mosquito ecdysteroids. Gen Comp Endocrinol, 253:60-69. Doi: 10.1016/j.ygcen.2017.08.028

71. Dinan L, Harmatha J, Lafont R. Chromatographic procedures for the isolation of plant steroids. J Chromatogr A, 2001;935(1-2):105-123. Doi: 10.1016/s0021-9673(01)00992-x

72. Fernandez-Panchon MS, Villano D, Troncoso AM, Garcia-Parrilla MC. Antioxidant activity of phenolic compounds: from *in vitro* results to *in vivo* evidence. Crit Rev Food Sci Nutr, 2008;48(7):649-671. Doi: 10.1080/10408390701761845

73. Tena N, Asuero AG. Up-to-date analysis of the extraction methods for anthocyanins: principles of the techniques, optimization, technical progress, and industrial application. Antioxid Basel Switz, 2022;11(2):286. Doi: 10.3390/antiox11020286

74. Azman EM, Charalampopoulos D, Chatzifragkou A. Acetic acid buffer as extraction medium for free and bound phenolics from dried blackcurrant (*Ribes nigrum* L.) skins. J Food Sci, 2020;85(11):3745-3755. Doi: 10.1111/1750-3841.15466

75. Panichayupakaranant P, Sakunpak A, Sakunphueak A. Quantitative HPLC determination and extraction of anthraquinones in *Senna alata* leaves. J Chromatogr Sci, 2009;47(3):197-200. Doi: 10.1093/chromsci/47.3.197

76. Balderas-López J, Barbonetti S, Pineda-Rosas EL, Tavares-Carvalho JC, Navarrete A. Cardiac glycosides from *Cascabela thevetioides* by HPLC-MS analysis. Rev Bras Farmacogn, 2019;29(4):441-444. Doi: 10.1016/j.bjp.2019.04.008

77. Romani A, Ieri F, Turchetti B, Mulinacci N, Vincieri FF, Buzzini P. Analysis of condensed and hydrolysable tannins from commercial plant extracts. J Pharm Biomed Anal, 2006;41(2):415-420. Doi: 10.1016/j.jpba.2005.11.031

78. Johnson KM, Sieburth JMcN. Dissolved carbohydrates in seawater. I, A precise spectrophotometric analysis for monosaccharides. Mar Chem, 1977;5:1-13. Doi: 10.1016/0304-4203(77)90011-1

79. Khursheed A, Jain V. Medicinal research progress of natural coumarin and its derivatives. Nat Prod J, 2021;11(5):648-662. Doi: 10.2174/2210315510999201102201552

80. Speisky H, Cassels BK. Boldo and boldine: an emerging case of natural drug development. Pharmacol Res, 1994;29(1):1-12. Doi: 10.1016/1043-6618(94)80093-6

81. Olofinsan K, Abrahamse H, George BP. Therapeutic role of alkaloids and alkaloid derivatives in cancer management. Molecules, 2023;28(14):5578. Doi: 10.3390/molecules28145578

82. Ferraz CR, Carvalho TT, Manchope MF, Artero NA, Rasquel-Oliveira FS, Fattori V, et al. Therapeutic potential of flavonoids in pain and inflammation: mechanisms of action, pre-clinical and clinical data, and pharmaceutical development. Molecules, 2020;25(3):762. Doi: 10.3390/molecules25030762

83. Raju J, Rao CV. Diosgenin, a steroid saponin constituent of yams and fenugreek: emerging evidence for applications in medicine. In: Rasooli I, editor. Bioactive compounds in phytomedicine [Internet]. InTech; 2012. p. 125-142. Available from: http://www.intechopen.com/books/bioactive-compounds-in-phytomedicine/diosgenin-a-steroid-saponin-constituent-of-yams-and-fenugreek-emerging-evidence-for-applications-in-. [Jan 18, 2012].

84. Chevassus H, Gaillard J, Farret A, Costa F, Gabillaud I, Mas E, et al. A fenugreek seed extract selectively reduces spontaneous fat intake in overweight subjects. Eur J Clin Pharmacol, 2010;66(5):449-455. Doi: 10.1007/s00228-009-0770-0

85. Saleem TM, Azeem AK, Dilip C, Sankar C, Prasanth NV, Duraisami R. Anti-inflammatory activity of the leaf extacts of *Gendarussa vulgaris* Nees. Asian Pac J Trop Biomed, 2011;1(2):147-149. Doi: 10.1016/S2221-1691(11)60014-2

86. Mijatovic T, van Quaquebeke E, Delest B, Debeir O, Darro F, Kiss R. Cardiotonic steroids on the road to anti-cancer therapy. Biochim Biophys Acta, 2007;1776(1):32-57. Doi: 10.1016/j.bbcan.2007.06.002

87. Ray SD, Dewanjee S. Isolation of a new triterpene derivative and *in vitro* and *in vivo* anticancer activity of ethanolic extract from root bark of *Zizyphus nummularia* Aubrev. Nat Prod Res, 2015;29(16):1529-1536. Doi: 10.1080/14786419.2014.983921

88. Chen M, Qin Y, Ma H, Zheng X, Zhou R, Sun S, et al. Downregulating NF-κB signaling pathway with triterpenoids for attenuating inflammation: *in vitro* and *in vivo* studies. Food Funct, 2019;10(8):5080-5090. Doi: 10.1039/c9fo00561g

89. Safayhi H, Sailer ER. Anti-inflammatory actions of pentacyclic triterpenes. Planta Med, 1997;63(6):487-493. Doi: 10.1055/s-2006-957748

90. Cho E, Chung EY, Jang H, Hong O, Chae HS, Jeong YJ et al. Anti-cancer effect of cyanidin-3-glucoside from mulberry via caspase-3 cleavage and DNA fragmentation *in vitro* and *in vivo*. Anticancer Agents Med Chem, 2017;17(11):1519-1525. Doi: 10.2174/1871520617666170327152026

91. Toufektsian M, de Lorgeril M, Nagy N, Salen P, Donati MB, Giordano L, et al. Chronic dietary intake of plant-derived anthocyanins protects the rat heart against ischemia-reperfusion injury. J Nutr, 2008;138(4):747-752. Doi: 10.1093/jn/138.4.747

92. Wu T, Yu Z, Tang Q, Song H, Gao Z, Chen W, et al. Honeysuckle anthocyanin supplementation prevents diet-induced obesity in C57BL/6 mice. Food Funct, 2013;4(11):1654-1661. Doi: 10.1039/c3fo60251f

93. Thomas JK, Uhrig LK, Dennis KP, Casto BC, Warner BM, Clinton SK, et al. Suppression of proinflammatory and prosurvival biomarkers in oral cancer patients consuming a black raspberry phytochemical rich troche. Cancer Prev Res, 2016;9(2):159-171. Doi: 10.1158/1940-6207.CAPR-15-0187

94. Yun J, Afaq F, Khan N, Mukhtar H. Delphinidin, an anthocyanidin in pigmented fruits and vegetables, induces apoptosis and cell cycle arrest in human colon cancer HCT116 cells. Mol Carcinog, 2009;48(3):260-270. Doi: 10.1002/mc.20477

95. Zhao W, Li G, Zhang Q, Chen M, He L, Wu Z, et al. Cardiac glycoside neriifolin exerts anti-cancer activity in prostate cancer cells by attenuating DNA damage repair through endoplasmic reticulum stress. Biochem Pharmacol, 2023;209:115453. Doi: 10.1016/j.bcp.2023.115453

96. Zhao Q, Guo Y, Feng B, Li L, Huang C, Jiao B. Neriifolin from seeds of *Cerbera manghas* L. induces cell cycle arrest and apoptosis in human hepatocellular carcinoma HepG2 cells. Fitoterapia, 2011;82(5):735-741. Doi: 10.1016/j.fitote.2011.03.004

97. Reddy D, Kumavath R, Barh D, Azevedo V, Ghosh P. Anticancer and antiviral properties of cardiac glycosides: a review to explore the mechanism of actions. Molecules, 2020;25(16):3596. Doi: 10.3390/molecules25163596

98. Sieniawska E. Activities of tannins—from *in vitro* studies to clinical trials. Nat Prod Commun, 2015;10(11):1877-1884. Doi: 10.1177/1934578X1501001118

99. León-Moreno LC, Castañeda-Arellano R, Rivas-Carrillo JD, Dueñas-Jiménez SH. Challenges and improvements of developing an ischemia mouse model through bilateral common carotid artery occlusion. J Stroke Cerebrovasc Dis Off J Natl Stroke Assoc, 2020;29(5):104773. Doi: 10.1016/j.jstrokecerebrovasdis.2020.104773

100. Harukuni I, Bhardwaj A. Mechanisms of brain injury after global cerebral ischemia. Neurol Clin, 2006;24(1):1-21. Doi: 10.1016/j.ncl.2005.10.004

101. Khoshnam SE, Winlow W, Farzaneh M, Farbood Y, Moghaddam HF. Pathogenic mechanisms following ischemic stroke. Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol, 2017;38(7):1167-1186. Doi: 10.1007/s10072-017-2938-1

102. Khan S, Yuldasheva NY, Batten TFC, Pickles AR, Kellett KAB, Saha S. Tau pathology and neurochemical changes associated with memory dysfunction in an optimised murine model of global cerebral ischaemia—a potential model for vascular dementia? Neurochem Int, 2018;118:134-144. Doi: 10.1016/j.neuint.2018.04.004

103. Chan PH. Role of oxidants in ischemic brain damage. Stroke, 1996;27(6):1124-1129. Doi: 10.1161/01.STR.27.6.1124

104. Sravanthi KN. Neuropharmacological evaluation of *Pentapetes phoenicea* Linn. extracts. Int J Green Pharm IJGP, 2015;9(4):257-266. Doi: 10.22377/ijgp.v9i4.596

105. Florence TIM. The role of free radicals in disease. J Ophthalmol, 1995;23(1):3-7. Doi: 10.1111/j.1442-9071.1995.tb01638.x

106. Singh R, Devi S, Gollen R. Role of free radical in atherosclerosis, diabetes and dyslipidaemia: larger-than-life. Diabetes Metab Res Rev, 2015;31(2):113-126. Doi: 10.1002/dmrr.2558

107. Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: impact on human health. Pharmacogn Rev, 2010;4(8):118-126. Doi: 10.4103/0973-7847.70902

108. Sharma N, Gupta PC, Rao CV. *In-vitro* antiradical and inhibitory potential of *Pentapetes phoenicea* Linn. Leaves against digestive enzymes related to diabetes. JOPR, 2013;6(5):569-572. Doi: 10.1016/j.jopr.2013.04.034

109. Sharma N, Gupta PC, Rao CV. Therapeutic hypoglycemic potential of *Pentapetes phoenicea* L. in experimentally induced hyperglycemic rats. Pak J Biol Sci, 2014;17(5):709-714. Doi: 10.3923/pjbs.2014.709.714

110. Hara Y, Honda M. The inhibition of α-amylase by tea polyphenols. Agric Biol Chem, 1990;54(8):1939-1945. Doi: 10.1271/bbb1961.54.1939

111. Agarwal P. Alpha-amylase inhibition can treat diabetes mellitus. Res Rev J Med Health Sci, 2016;5(4):1-8.

112. Coles TM, Dryden MW. Insecticide/acaricide resistance in fleas and ticks infesting dogs and cats. Parasit Vectors, 2014;7(8). Doi: 10.1186/1756-3305-7-8

113. Durden LA, Mullen GR. Introduction. In: Mullen GR, Durden LA. Medical and veterinary entomology [Internet]. Academic Press; 2018. p. 1-16. Available from: https://shop.elsevier.com/books/medical-and-veterinary-entomology/mullen/978-0-12-814043-7. [Oct 2, 2019].

114. Mohler JR. Texas or tick fever and its prevention [Internet]. Washington: Government Printing Office; 1906 [Sep 24, 2024]. Available from: https://digital.library.unt.edu/ark:/67531/metadc87422/

115. Chungsamarnyart N, Jiwajinda S, Jansawan W, Kaewsuwan U, Buranasilpin P. Effective plant crude-extracts on the tick (*Boophilus miscroplus*) I. larvicidal action. Agric Nat Resour, 1988;22(5):37-41.

116. Adenubi OT. Fasina FO, MicGaw LJ, Elof JN, Naidoo V. Plant extracts to control ticks of veterinary and medical importance: a review. S Afr J Bot, 2016;105:178-193. Doi: 10.1016/j.sajb.2016.03.010

117. Chungsamarnyart N, Jiwajinda S, Jansawan W. Effects of plant crude-extracts on the cattle tick (*Boophilus microplus*) insecticidal action I. Agric Nat Resour, 1990;24(5):28-31.

118. Chungsamarnyart N, Jiwajinda S, Ratanagreetakul C, Jansawan W. Practical extraction of sugar apple seeds against tropical cattle ticks. Agric Nat Resour, 1991;25(5):101-105.

119. Chungsamarnyart N, Jiwajinda S, Jansawan W. Acaricidal effect of plant crude-extracts on tropical cattle ticks (*Boophilus microplus*). Kasetsart Journal: Natural Science (Thailand), 1991;25(5):90-100. Doi: https://agris.fao.org/search/en/providers/122623/records/647227c177fd37171a730b97

120. Salman M, Abbas RZ, Israr M, Abbas A, Mehmood K, Khan MK, et al. Repellent and acaricidal activity of essential oils and their components against *Rhipicephalus ticks* in cattle. Vet Parasitol, 2020;283:109178. Doi: 10.1016/j.vetpar.2020.109178

121. Chungsamarnyart N, Ratanakreetakul C, Jansawan W. Acaricidal activity of the combination of plant crude-extracts to tropical cattle ticks. Agric Nat Resour, 1994;28(4):649-660.

122. Bastos MLA, Lima MRF, Conserva LM, Andrade VS, Rocha EMM, Lemos RPL. Studies on the antimicrobial activity and brine shrimp toxicity of *Zeyheria tuberculosa* (Vell.) Bur. (Bignoniaceae) extracts and their main constituents. Ann Clin Microbiol Antimicrob, 2009;8:16. Doi: 10.1186/1476-0711-8-16