A comprehensive review on the phytochemistry, pharmacological, ethnobotany, and traditional uses of *Paeonia* species

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**ABSTRACT**

Since ancient times, people have used medicinal plants as a source of medications to treat and prevent diseases. *Paeonia* species are important therapeutic plants in Ayurvedic, Unani, and Traditional Chinese Medicine. This study aims to provide updated information on the ethnomedicine, phytochemistry, and pharmacological activities of *Paeonia* species discovered until now. Using the keywords "Paeonia", "geographical distribution", "ethnopharmacology and traditional values", "phytochemistry", "antioxidant", "anti-inflammatory", "antimicrobial", "cardiovascular diseases", and "anticancerous properties", the published reports from 2001 to 2022 were retrieved using Google Scholar, Science Direct, PubMed, and Scopus databases. A total of 156 published articles were studied after meeting the qualifying criteria. Out of these, 52 articles were studied for phytochemistry, ethnopharmacological and traditional uses. *Paeonia emodi* is used to treat hypertension, asthma, convulsions, epilepsy, bronchitis, jaundice, hepatitis, abdominal colic, ascites, renal colic, calculous, and leprosy (2,3). *Paeonia emodi*, also called hemicryptophytes (family Paeoniaceae), is a vigorous herbaceous perennial plant with the features of large white flowers and deeply incised leaves. It is the tallest species compared to other peony species. The warm temperate condition is suitable for its growth (4). Generally, it

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A literature review was constructed in this contribution to examine the significance of different *Paeonia* species across the country. As a result of this article, a new understanding of the phytochemistry, traditional medicine, ethnobotany, and potent pharmaceutical properties of the plant is revealed, which may be taken into account in future clinical studies and therapies involving this plant.


**Introduction**

Human and animal diseases are treated with the naturally extracted products of medicinal plants (1). *Paeonia emodi* Royle has historically been used to treat conditions like dysmenorrhea, uterine disorders, blood pressure, palpitations, congestive heart failure, asthma, paralysis, epilepsy, convulsions, schizophrenia, cough, bronchitis, jaundice, hepatitis, abdominal colic, ascites, renal colic, calculous, and leprosy (2,3). *Paeonia emodi*, also called hemicryptophytes (family Paeoniaceae), is a vigorous herbaceous perennial plant with the features of large white flowers and deeply incised leaves. It is the tallest species compared to other peony species. The warm temperate condition is suitable for its growth (4). Generally, it

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occurs in Afghanistan, Southern Tibet, and the western Himalayan region, which is why in English, it is known as Himalayan peony (5).

The primary chemical constituents of *P. emodi* are 1b, 3b, 5a, 23, 24-pentahydroxy-30-12, 20 (29)-dien-28-oic acid, oleanolic acid, betulinic acid, ethyl gallate, methyl grevillate, 1,5-dihydroxy-3-methyl anthraquinone, wurdin, benzoylwurdin, paeoniflorin, lactiflorin, oxypaeoniflorin (6), emodinol, benzoic acid, 3-hydroxybenzoic acid (7), and paeonins A and B (8). It is also a rich source of triterpenes, monoterpenyl glucosides, phenols, and tannins that are important in treating inflammation, skin lesions, and neurodegenerative diseases (9,10). The phenolic compounds are effective anti-inflammatory, antibacterial, and cardioprotective agents reducing mortality rates (11,12). The root and rhizome of *P. emodi* are used to treat several disorders like epileptic disorder, or used as a nerve tonic and blood purifier, while the seeds have purgative properties (13). *P. emodi* has different elements such as calcium, magnesium, zinc, iron, cobalt, that play both curative and preventive roles in disease control (14). The different leaf extracts have shown antioxidant and antimicrobial activities (8). *Paeonia ludlowii* (Stern & G. Taylor) D.Y. Hong is renowned as a medicinal plant that reduces inflammation (15), and is confined to a tiny region of southern Tibet in western China (16). Several previous studies reported that paeany seed oil (PSO) has α-linolenic acid in an abundant concentration, which shows anti-inflammation, anti-thrombosis, and anti-tumor properties (17,18). PSO is used as a new resource of food in China (19). The present work intended to compile the recent advances made in the field of research on the *Paeonia* species, sporadically mentioned in literature for its various attributes, and to reveal the unexplored part of the plant to stimulate further investigation on it.

### Methods

**Database search**

In accordance with PRISMA standards, we searched the words and terms of “Paeonia”, “geographical distribution”, “ethnopharmacology and traditional values”, “phytochemistry”, “pharmacology”, “antioxidant”, “anti-inflammatory”, “antimicrobial”, “cardiovascular diseases”, and “anticancerous properties”. To prepare a comprehensive review of the pharmacological ethnombotany and traditional uses of *Paeonia* species a literature search was done in English databases such as Scopus, PubMed, Web of Science, EMBASE, and Google Scholar without a time limit.

**Quality assessment and article selection**

Following the review of the titles and summaries of articles, a list of related papers was included for further review. After reviewing the papers, nominated papers were selected that met reasonable inclusion criteria.

**Data extraction**

The inclusion criteria of the present review were the research papers assessing the complete study of the phytochemical, pharmacological, and medicinal uses of *Paeonia* spp. As exclusion criteria, papers with inadequate data, abstracts only, mismatches between the process and outcome of the study, and studies with irrational results and interpretations were excluded. A study’s type, control group, disease type, measurement scale, dosage, intervention process, results, and references were obtained from each selected paper (Figure 1).

### Results

**Geographical distribution**

*Paeonia* is the only genus in the Paeoniaceae family, with 33 species separated into five geographical regions: Mediterranean, Central Asia, Western Himalayas, Eastern

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**Figure 1. A flowchart representing the study based on PRISMA guidelines.**
Asia, and Pacific North America (20). It is situated in the Northern Himalaya of India, between Kashmir and the Garhwal-Kumaon regions of Uttarakhand (Figure 2) (21), at elevations ranging from 1800 m to 3000 m. *P. emodi* is most commonly observed on south-facing slopes of deciduous forests that contain various oak species and *Quercus floribunda* (22). *P. lactiflora* and *P. mairei* most likely became sympatric during their retreat, giving rise to the Himalayan species *P. emodi* and *P. sterniana*.

**Phytochemistry**

Previous studies have reported that the leaves of *P. emodi* contain sucrose, starch, malic acid, tannins, flavonoids, polyphenols, sterol, monoterpenes, triterpenes, polyterpenes, steroids, and many organic acid alkaloids. These compounds showed antimicrobial and antioxidant activities (8). Lipoxygenases are iron-containing compounds that play an essential role in asthma, cancer, aging, and angiogenesis (23). Oleamnolic acid was reported in *P. emodi* along with phenolic compounds, betulinic acid, ethyl gallate, methyl grevillate, emodinol, benzoic acid, 3-hydroxybenzoic acid, paeonin A and B, steroids, and aldehydes (24). The most abundant compounds in the fruits of *P. rockii* and *P. ostii* are polyphenols (flavonoids, tannins, stilbenes, phenolic acids, and other phenols), as well as terpenoids (monoterpenes, diterpenes, and triterpenes) (Figure 3). Phenolic compounds have antioxidant and antibacterial properties and are also beneficial in treating cancer, cardiovascular diseases, diabetes, and epilepsy (25). Previous studies reported that monoterpenes have antipyretic, anti-inflammatory, analgesic, anesthetic, and anticonvulsant effects (26). Emodinol, a new triterpene identified in *P. emodi* (7), inhibits the β-glucuronidase activity. The overexpression of β-glucuronidase may cause liver cancer and damage the liver (27). The *Paeonia* root contains secondary metabolites with 17 monoterpenoid glucosides, 11 galloyl glucose, 5 flavonoids, 6 phenolic compounds (Figure 3) (28). Thirteen secondary metabolites with Paeoniflorin and Paeonol have been identified from the 15 species and 2 sub-species of *Paeonia* root; these compounds show potent bio-activity. It also showed the antioxidant activities and antibacterial properties against gram (+ve) bacteria (29) (Figure 4).

**Ethnopharmacological and traditional uses**

Danpi, the cortex of the plant, is used as herbal medicine to treat blood stasis in the Eastern Han dynasty (30). The two main populations of medicinal peonies are *Paeonia suffruticosa* and *P. ostii* (31). *P. suffruticosa* is mainly grown in Dianjiang, Chongqing, where its cortex is known as “Chuan Danpi”, while *P. ostii* is primarily grown in Tongling, Nanling, Bozhou, and Heze, where its cortex is known as “Feng Danpi”. Shuan Danpi and Feng Danpi are both regarded as authentic herbs of the Danpi family. In the history of Chinese medicine, authentic herbs are of higher quality (32). Traditional healers use the roots of *P. emodi* to treat diarrhea, high blood pressure, heart failure,
palpitations, asthma, and arteriosclerosis. The extract of the roots lowers heartbeat rates, relaxes airways, and reduces blood clotting (33). The dry root of *P. lactiflora* or *P. veitchii*, Radix Paeoniae Alba (dry roots of *P. lactiflora*) and Cortex Moutan (dry roots of *P. ostii* or *P. suffruticosa*) are essential Chinese herbal medicine, included in Chinese Pharmacopoeia (34). The plant *P. emodi* grows in the Western Himalayan region, where locals and scientists use it to prevent epileptic attacks and treat whooping cough and cholera (35). Its tubers treat uterine infections, blood disorders, colic, bilious problems, headaches, dizziness, vomiting, dropsy, epilepsy, and hysteria, while its seeds are purgatives (Figure 4) (36). For the treatment of diarrhoea, whooping cough, haemorrhoids, and abdominal pain, dried flower infusions are effective (37). Folk recipes are made from the whole plant or its different components, such as leaves, stems, barks, roots, flowers, seeds, and roots of props, or from secondary yields like gums, resins, and latex (38). The rhizome is used as a tonic and is used for increasing milk production in livestock (38). Dried leaves purify the blood. They are fried in Cow ghee and used for dysentery and abdominal colic (39). Most Asian women are obsessed with whitening their skin (40). Several tyrosine inhibitors and antioxidants have been isolated from the root of *P. lactiflora*. (41).

*P. suffruticosa* root bark has traditionally been used in treating cancer, extravasation of blood, cardiovascular diseases, inflammatory conditions, and female genital diseases (42). *P. suffruticosa* contains phenols, monoterpenep glycosides, tannins, and stilbenes (43). Paeonilflorigenone (Paeo), a monoterpene, exhibits numerous biologically active properties (Table 1). Paeo inhibits lipopolysaccharide-stimulated microglia function to prevent **H**₂**O**₂-induced cytotoxicity in neuronal cells (44). Paeo also has anticoagulant and antiplatelet properties, improving blood circulation (45). Recent research suggested that Paeo had antiproliferative and cytotoxic effects on cancer cells (42).

Table 1. The ethnopharmacological properties of Paeonia extracts

<table>
<thead>
<tr>
<th>Paeonia species</th>
<th>Part used</th>
<th>Dosage form/Recipe</th>
<th>Medicinal use and disease treated</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. emodi</em></td>
<td>Leaves</td>
<td>A dried leaf is cooked and used as a vegetable. It is also fried in ghee.</td>
<td>Blood purifier, dysentery, colic, piles.</td>
<td>(46)</td>
</tr>
<tr>
<td><em>P. emodi</em></td>
<td>Root</td>
<td>Roots are fried and taken orally as a dietary supplement.</td>
<td>Diarrhea, rheumatic pain, gynecological disorders, vomiting, skin diseases, dyspepsia, sciatica, muscle cramps, rheumatism, epilepsy, general weakness, body and bone pain.</td>
<td>(38, 47)</td>
</tr>
<tr>
<td><em>P. emodi</em></td>
<td>Whole Plant</td>
<td>Extracts of roots and flowers are ingested orally. An extract of the whole plant is prepared by mixing powder with water.</td>
<td>Vomiting, diarrhea, blood purifier, whooping cough, diarrhea, intestinal spasm, cuts, eczema, ulcers, nervous disorders, diarrhea, headache, pain killer, vomiting, epilepsy, and dysentery.</td>
<td>(48)</td>
</tr>
<tr>
<td><em>P. emodi</em></td>
<td>Rhizome</td>
<td>Dried ground rhizomes are cooked.</td>
<td>Body pain, body weaknesses, sexual tonic, general body tonic, abdominal pain.</td>
<td>(49)</td>
</tr>
<tr>
<td><em>P. emodi</em></td>
<td>Flower</td>
<td>The infusion of dried flowers is used.</td>
<td>Abdominal pain, vomiting, hemorrhoid, antidiarrheal, antispasmodic, diarrhea, nervous system, cardiovascular, and respiratory diseases.</td>
<td>(38, 50)</td>
</tr>
<tr>
<td><em>P. emodi</em> Wall ex Royle</td>
<td>Whole Plant</td>
<td>Whooping cough, diarrhea, intestinal spasm, cuts</td>
<td>(51)</td>
<td></td>
</tr>
<tr>
<td><em>P. suffruticosa</em> Andrews</td>
<td>Root bark</td>
<td>Not mentioned</td>
<td>Taking care of heat, stimulating blood flow, cooling blood, and removing blood clots. It is also used to treat warmth, spotting, vomiting blood, night heat, early cooling, amenorrhea, dysmenorrhea, bruises, carbuncle swelling, tumors, fevers, carbuncle swelling, tumor, and fever.</td>
<td>(52)</td>
</tr>
<tr>
<td><em>P. veitchii var. uufiora</em></td>
<td>Roots</td>
<td></td>
<td>Disperse blood stasis, cool the blood, and relieve pain by clearing heat.</td>
<td>(53)</td>
</tr>
<tr>
<td><em>P. peregrina Mill.</em></td>
<td>Roots and seeds</td>
<td>The roots of the plant are used as anticoagulants, analgesics, and sedatives. The seeds were used in the treatment of epilepsy.</td>
<td></td>
<td>(54)</td>
</tr>
</tbody>
</table>
Pharmacological study

Antioxidant properties

Radiation from the sun or excessive free radical production by the body may induce cancer, diabetes, and heart disease. Free radicals and reactive oxygen species can also damage cells. Several compounds and phenolic compounds are derived from Paeonia that contain antioxidant activity scavenging free radicals. Some phenolic compounds (gallic acid, quinic acid, dihexose, paeoniflorin derivative, etc), tannins, Monoterpenes glycosides, and flavonoids are the major antioxidant phytochemicals present in the root and leave extract of Peonia. As tested chemically, the leaf extracts proved more effective抗氧化 agents than root extracts, while methanol proved more effective as a solvent than water (55). For chronic inflammatory diseases, the inflammatory pathways need to be blocked. A hotspot in medical research has been the discovery of new anti-inflammatory molecules from crude materials (Table 2).

Anti-inflammatory activity

There are many ways in which inflammation can be induced, including trauma, tissue damage, and infection; it occurs to various organs and tissues throughout the body (56). Pharmacologically, Paeonia is best known for its anti-inflammatory properties (Table 2). The Peonia extract contains paeoniflorin B, galloyl-paeoniflorin, moudanpioside F, paeoniflorigenone, 4-O-methyl-zelenzyloypaeoniflorin, which have shown potent inhibitory activity on nitric oxide (NO) production (57). The paeoniflorin A, benzoyloxypaeoniflorin, albiflorin, and intermedia C compounds of the plant inhibit the production of NO (58), and oxo-acetic acid 2-ethoxy-4-(3-hydroxy-2-oxopropyl) phenyl ester inhibits the production of the pro-inflammatory cytokines such as interleukin 6 (IL-6), tumor necrosis factor-a (TNF-a), and NO (59). Inhibition of cyclooxygenase-I and II (COX-I and II) expression is caused by paeonidans (F, G, H), paeoniside (A, B) and paeoniflorin, benzoylpaeoniflorin, and 4-O-methyl-paeoniflorin (42). Suffruticosol A significantly inhibits the expression of NO, inducible nitric oxide (iNO), and pro-inflammatory factors (60).

Anti-microbial activity

Several pathogenic fungi, including Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, and Fusarium solani, were completely inhibited by peony root extract (83). A natural antibacterial preservative or additive made from plant extracts has become popular because of its resistance to bacteria (84). Despite this, many studies have been conducted on wild peony root antibacterial properties (85). The root section of Peonia spp. contains several phenolic acids, tannins, monoterpenes glycosides, and flavonoids (Table 2). These extracts showed potent antibacterial activity on Listeria monocytogenes (gram-positive), B. cereus, Bacillus subtilis, Pseudomonas aeruginosa (gram-positive), Salmonella typhimurium and Proteus vulgaris (Gram-negative), and potent antifungal activity on Microsporum gypseum and C. albicans (8,29). Many reports have shown the antibacterial properties of phenolic compound (benzoic acid) by penetrating the bacterial cell membrane, destroying the cellular wall, and disturbing the relative conductivity of the cell membrane. Also, some enzymes within the bacterial cell membrane are inhibited, resulting in denaturation of the protein inside the cell (81). Tannins (1,2,3,4,6-penta-O-galloyl-β-D-glucopyranose; PGG) and benzoic acid are present in large amounts in peony roots, which synergistically have substantial antibacterial properties (86). The fruit and seed extracts of P. rockii and P. ostii have potent antibacterial activities against P. vulgaris, E. coli, P. aeruginosa, S. enterica, and S. aureus (82).

Insecticidal property

Tribolium castaneum, Bruchus pisorum, and Rhizopartha dominica have also been found to be susceptible to paeonol (2’-hydroxy-4’-methoxyacetophenone) extract. Permethrin present in the aerial parts of the plant shows the ability to kill insect and pests. A sodium channel current regulates the polarization of the nerve cell membrane that is disrupted by it (21).

Cardiovascular activity

As an anti-atherosclerosis agent, paeonols (Pae) regulate lipids, inhibit lipid peroxidation, are anti-inflammatory, and protect vascular endothelium, which is an important function of paeonols (87). As a result of the drug, the total cholesterol content of the aorta and liver was significantly reduced, the plaque area narrowed, and aortic lipid plaque was inhibited from forming (88). The researchers found that paeonols inhibited the uptake of calcium by neonatal rat cardomyocytes and significantly decreased their beating frequency. paeonols may block slow calcium channels, resulting in this effect (89). Isolated myocardium can be inhibited from self-regulating, depolarized, triggered, and antiarrhythmic by paeonols (90).

Central nervous system activity

Paeonols have sedative properties, reduce spontaneous activity, and prolong sleep, which is induced by cyclohexobarbital. In mice, it can produce anticonvulsant effects (91). Paeonols also have antidepressant and anxiolytic effects (92). It is possible to treat postoperative pain, muscular discomfort, neuralgia, joint pain, dysmenorrhea, wind chill, and arthralgia with the injection of paeonols into muscles or acupuncture points (93). Through opioid receptor mediation, paeoniflorin can produce analgesia against various "phenotypes" of nociception and hypersensitivity (94). Paeoniflorin can provide analgesia for a variety of nociception and hypersensitivity (95). Additionally, paeoniflorin may reduce the toxicity caused by 1-methyl-4-phenyl-1,2,3,6-

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Table 2. The pharmacological properties of *Paeonia* compounds

<table>
<thead>
<tr>
<th>Active components/extracts</th>
<th>Dose</th>
<th>Observed sample/assay</th>
<th>Effectiveness</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antioxidant properties</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerial part extract of <em>P. lactiflora</em></td>
<td></td>
<td>DPPH assay</td>
<td>IC50 17.08 ± 0.9 μg/mL</td>
<td>(61)</td>
</tr>
<tr>
<td>Ethyl acetate fraction of <em>P. lactiflora</em></td>
<td></td>
<td>DPPH assay</td>
<td>IC50 19.75 ± 0.02 μg/mL</td>
<td>(61)</td>
</tr>
<tr>
<td>Chloroform and n-butanol fractions from ethanol extract of <em>P. emodi</em> rhizome</td>
<td></td>
<td>DPPH assay</td>
<td>IC50s of 7.05 and 6.5 μg/mL, respectively</td>
<td>(62)</td>
</tr>
<tr>
<td>Leaves ethanol extract of <em>P. anomala</em></td>
<td></td>
<td>DPPH assay</td>
<td>IC50: 206 ± 2 μg/mL</td>
<td>(63)</td>
</tr>
<tr>
<td>Seeds oil of <em>P. suffruticosa</em></td>
<td></td>
<td>DPPH assay</td>
<td>Effective concentration (EC50) of 29.30 mg/mL</td>
<td>(62)</td>
</tr>
<tr>
<td>Seeds oil of <em>P. suffruticosa</em></td>
<td>1.0, 2.5 or 6.0 g/kg/d for 30 days</td>
<td>Diet-induced hyperlipidemia in rats</td>
<td>Increased levels of liver and serum MDA, AST, and ALT</td>
<td>(64)</td>
</tr>
<tr>
<td>Leaves extract of <em>P. rockii</em></td>
<td></td>
<td>Fe²⁺ chelation, DPPH assay, ABTS assays</td>
<td>IC50s of 6.69 ± 0.00, 1.5, and 0.48 ± 0.01 μg/mL, respectively</td>
<td>(65)</td>
</tr>
<tr>
<td>Flowers extract of <em>P. rockii</em></td>
<td></td>
<td>Fe²⁺ chelation, DPPH assays, ABTS assay</td>
<td>IC50s of 7.95 ± 0.02, 2.36, and 1.03 ± 0.01 μg/mL, respectively</td>
<td>(65)</td>
</tr>
<tr>
<td>Flowers extract of <em>P. rockii</em></td>
<td>100 mg/kg/d, 3 weeks</td>
<td>A mice model triggered by D-galactose</td>
<td>Increased liver and brain levels of SOD and GSH</td>
<td>(65)</td>
</tr>
<tr>
<td>Leaf methanol extracts from <em>P. officinalis</em></td>
<td></td>
<td>CAA assay CAA</td>
<td>Quercetin equivalent of 0.046 μmol/mg</td>
<td>(53)</td>
</tr>
<tr>
<td>Leaf water extracts from <em>P. officinalis</em></td>
<td></td>
<td>CAA assay</td>
<td>Quercetin equivalent of 0.106 μmol/mg</td>
<td>(55)</td>
</tr>
<tr>
<td>Flower extract from <em>P. ludlowii</em></td>
<td></td>
<td>DPPH assay</td>
<td>IC50 of 31 μg/mL</td>
<td>(66)</td>
</tr>
<tr>
<td>Methanolic extract from aerial parts of <em>P. arietina</em></td>
<td></td>
<td>FRAP, CUPRAC, ABTS, and DPPH assays</td>
<td>392.96, 753.93, 659.53, and 544.72 mg TE/g extract, respectively</td>
<td>(67)</td>
</tr>
<tr>
<td>Methanolic extract from aerial parts of <em>P. kesrouanensis</em></td>
<td></td>
<td>FRAP, CUPRAC, ABTS, and DPPH assays</td>
<td>409.12, 775.09, 631.83, 540.23 mg TE/g extract, respectively</td>
<td>(67)</td>
</tr>
<tr>
<td>Gallic acid</td>
<td></td>
<td>DPPH assay</td>
<td>IC50 1.2 μg/mL</td>
<td>(68)</td>
</tr>
<tr>
<td>Benzoypaeoniflorin, oxypaeonidanin</td>
<td></td>
<td>NO levels in activated macrophage-like RAW 264.7 cells were determined.</td>
<td>IC50 23.32 μM and IC50 40.8 μM, respectively</td>
<td>(69)</td>
</tr>
<tr>
<td>Paeoniflorin</td>
<td>1, 10 and 100 μM</td>
<td>Glucose-treated RSC96 cells</td>
<td>GST and GPX activity, as well as the nuclear protein level of Nrf2, and Nrf2-dependent ARE genes, such as HO-1.</td>
<td>(70)</td>
</tr>
<tr>
<td>Paeonol</td>
<td>50 and 100 mg/kg for 30 days</td>
<td>Induction of diabetic encephalopathy by STZ in rats</td>
<td>GSH content in the hippocampus was significantly increased, and iNOS activity was improved</td>
<td>(71)</td>
</tr>
<tr>
<td><strong>Anti-inflammation activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paeoniflorin B, A</td>
<td>RAW 264.7 cells stimulated by LPS and macrophages activated by LPS</td>
<td>NO production is inhibited.</td>
<td></td>
<td>(58)</td>
</tr>
<tr>
<td>Paeonidanins F</td>
<td></td>
<td>LPS induced RAW 264.7 cells</td>
<td>IC50 22.7 μM</td>
<td>(72)</td>
</tr>
<tr>
<td>Paeonidanins G</td>
<td></td>
<td>LPS induced RAW 264.7 cells</td>
<td>IC50 19.4 μM</td>
<td>(72)</td>
</tr>
<tr>
<td>Paeonidanins H</td>
<td></td>
<td>LPS induced RAW 264.7 cells</td>
<td>IC50 29.1 μM</td>
<td>(72)</td>
</tr>
<tr>
<td>Paenonoides D</td>
<td></td>
<td></td>
<td>IC50 9.6 μM</td>
<td>(42)</td>
</tr>
<tr>
<td>Paeoniflorin</td>
<td></td>
<td></td>
<td>IC50 11.9, and 10.8 μM</td>
<td>(42)</td>
</tr>
<tr>
<td>Benzoypaeoniflorin</td>
<td></td>
<td>COX-I and COX-II expression was inhibited</td>
<td>IC50 13.2, and 12.6 μM</td>
<td>(42)</td>
</tr>
<tr>
<td>4-O-methyl-paeoniflorin</td>
<td></td>
<td>COX-I and COX-II expression was inhibited</td>
<td>IC50 9.8, and 11.3 μM</td>
<td>(42)</td>
</tr>
<tr>
<td>Suffruticosol A</td>
<td>20 mg/kg and 40 mg/kg</td>
<td>Mice with acute inflammation of their airways</td>
<td>NO, iNO, and pro-inflammatory factors (TNF-α, IL-6, and IL-1β) were inhibited</td>
<td>(60)</td>
</tr>
</tbody>
</table>
### Phytochemical, pharmacological and medicinal uses of *Paeonia* spp

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Table 2. Continued

<table>
<thead>
<tr>
<th>Active components/extracts</th>
<th>Dose</th>
<th>Observed sample/assay</th>
<th>Effectiveness</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Central-nervous-system activities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extracts of <em>P. lactiflora</em></td>
<td>150, 300, 600 mg/kg, 14 days</td>
<td>Depression SD rat model</td>
<td>Rat immobility was reduced in a dose-dependent manner</td>
<td>(73)</td>
</tr>
<tr>
<td>Extracts of Cortex Moutan</td>
<td>50 mg/kg, 12 days</td>
<td>MPTP-induced Parkinson’s disease mouse model</td>
<td>Improved mitochondrial dysfunction, improved dopaminergic cell survival, and promoted dopaminergic neuron recovery</td>
<td>(18)</td>
</tr>
<tr>
<td>Paeoniflorin</td>
<td>30 μM</td>
<td>PC12 cells induced by 6-OHDA</td>
<td>Inhibition of the PKCd upregulation was achieved through increased GSH levels, dramatically attenuating the 6-OHDA-induced NF-κB translocation.</td>
<td>(74)</td>
</tr>
<tr>
<td>Albiflorin</td>
<td>20, 40 mg/kg, 4 weeks</td>
<td>CUMS-induced depression rats</td>
<td>Improvement in dopamine levels and serum and hypothalamic 5-HT levels</td>
<td>(75)</td>
</tr>
<tr>
<td><strong>Anti-tumor activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paeoniflorin</td>
<td>400 μg/mL</td>
<td>Cell line RL95-2 for human endometrial cancer</td>
<td>Proliferation of RL95-2 cells was significantly and dose- and time-dependently inhibited</td>
<td>(76)</td>
</tr>
<tr>
<td>Paeonol</td>
<td>100, 150 μM</td>
<td>Pancreatic cancer in humans Capan-1 and Panc-1 cells</td>
<td>An increase in E-cadherin expression and a decrease in N-cadherin, vimentin, TGF-β1, protein mother against decapentaplegic homolog2 p-Smad2/Smad2, and p-Smad3/Smad3 expression were observed</td>
<td>(77)</td>
</tr>
<tr>
<td>Suffruticosol A</td>
<td></td>
<td>HepG2 cancer cells</td>
<td>IC50 208.66 ± 17.15 μg/mL</td>
<td>(78)</td>
</tr>
<tr>
<td>Suffruticosol B</td>
<td></td>
<td>HepG2 cancer cells</td>
<td>IC50 98.19 ± 16.23 μg/mL</td>
<td>(78)</td>
</tr>
<tr>
<td>Suffruticosol C</td>
<td></td>
<td>HepG2 cancer cells</td>
<td>IC50 125.29 ± 13.12 μg/mL</td>
<td>(78)</td>
</tr>
<tr>
<td>Paeoniflorigenone</td>
<td>30 μM</td>
<td>Cancer cells Jurkat, lymphoma cells HL60, and T-cell leukemia cells HeLa were cultured in vitro</td>
<td>Decreased tumor cell line proliferation</td>
<td>(42)</td>
</tr>
<tr>
<td><strong>Antibacterial activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gallic acid</td>
<td></td>
<td>Fungal</td>
<td>MIC50 30 μg/mL</td>
<td>(68)</td>
</tr>
<tr>
<td>Cortex Moutan extracts in organic solvent</td>
<td></td>
<td>Escherichia coli</td>
<td>MIC50 100 μg/mL</td>
<td>(79)</td>
</tr>
<tr>
<td>Roots ethanolic extract from <em>P. lactiflora</em></td>
<td></td>
<td>Influenza virus WSN (H1N1)</td>
<td>IC50 16 μg/mL</td>
<td>(80)</td>
</tr>
<tr>
<td>Peonol root extract</td>
<td></td>
<td>Listeria monocytogenes, Pseudomonas aeruginosa, Salmonella Typhimurium</td>
<td>Strong Inhibitors</td>
<td>(8)</td>
</tr>
<tr>
<td>Peonol root extract</td>
<td></td>
<td>Candida albicansand Microsporum gypseum</td>
<td></td>
<td>(29)</td>
</tr>
<tr>
<td>Phenolic compound</td>
<td></td>
<td>Antibacterial</td>
<td>Altering cell membrane permeability by destroying the cellular wall</td>
<td>(81)</td>
</tr>
<tr>
<td>The fruit extract and seed extract of <em>P. rockii</em> and <em>P. ostii</em></td>
<td></td>
<td><em>P. vulgaris, E. coli, P. aeruginosa, S. enterica, and S. aureus</em></td>
<td>Strong antimicrobial properties</td>
<td>(82)</td>
</tr>
</tbody>
</table>

DPPH, 2,2-Diphenyl-1-picrylhydrazyl; MDA, malondialdehyde; AST, aspartate transaminase; ALT, alanine transaminase; IC50, Inhibitory concentration 50; SOD, superoxide dismutase; GSH, glutathione; TE, trolox equivalents; GST, Glutathione S-transferase; GPX, guaiacol peroxidase; Nrf2, nuclear respiratory factor-2; ARE, antioxidant response element; iNOS, inducible nitric oxide synthases; ABTS, 2,2’-azino bis (3-ethyl benzothiazoline-6 sulfonate); CAA, Cellular antioxidant activity; NO, Nitric oxide; STZ, streptozotocin; LPS, lipopolysaccharide; COX-I, cyclooxygenase-1; COX-II, cyclooxygenase-2; SD, stress disorder; MPTP, 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine; 6-OHDA, 6-hydroxydopamine; CUMS, Chronic unpredictable mild stress; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6; PKCd, protein kinase Cd; NF-κB, nuclear factor-kappa B; 5-HT, 5-hydroxytryptamine; TGF-β1, transforming growth factor-beta1.
tetrahydropyridine (MPTP), opening up the possibility of a nondopaminergic treatment for Parkinson's disease (96).

**Anticancerous activity**

Paeonols have shown strong effects on HePa tumour growth (97). Paeoniflorin has shown strong anti-cancerous properties and strong cytotoxic properties against lung cancer A549 cells (42). Overall, cell apoptosis, cell cycle arrest, EMT suppression, and MDR reversal are associated with the anticancer impact of paeoniflorin (98). Anti-cancer abilities, protection from Parkinson's syndrome, as well as other properties are detected in Paeonia seeds (99). The most commonly cancer-related mortality in the world is colon cancer (100). Surgery is still the most common method of CRC treatment; however, alternative treatments, such as traditional medicine are increasing in popularity (Table 2). Many research reports that *Paeonia* radix alba showed anti-cancerous activity in different cancers by inhibiting growth in the cancerous cells (101).

**Clinical studies**

When given for 8 weeks to 125 patients with IBS-C in a placebo-controlled experiment, *P. lactiflora* root, a component of a CHM formulation, an improvement was seen in CHM group in bowel habits and reduction in straining and hard lumpy stools (102).

**Discussion**

*Paeonia* spp. belongs to the genus *Paeonia*, the only genus of the Paeoniaceae family. As of currently, 33 *Paeonia* species have been recorded across the World. They are mostly found in temperate regions of Asia, southern Europe, and western North America (103). Many species of *Paeonia* plants have been used in traditional medicine for thousands of years, and their roots and bark are primarily used in medicine. The seeds and flowers are eaten as food or used for aesthetic reasons, while the bark and leaves are used in medicine (38). This study gathered information on the traditional usage, medical applications, toxic effects, pharmacological properties, and phytoconstituents of the *Paeonia* species. Most of the *Paeonia* spp have been investigated for their medicinal and nutritional aspects throughout the World. Among the Paeony species, *P. emodi*, *P. suffruticosa*, *P. veitchii* var. *uwaflora*, and *P. peregrine* have ethnomedical benefits (34). Paeony spp., *P. lactiflora*, *P. emodi*, *P. anomala*, *P. suffruticosa*, *P. rockii*, *P. officinalis*, *P. ludlowii*, *P. Cristina*, *P. kersouanensis*, and *P. ostii* have exhibited modern pharmacological qualities such as antioxidant, anti-inflammatory, anti-tumor and CNS activities. *P. emodi* has been used in traditional and folk medicine apart from its use as foodstuff. The antioxidant property exhibited due to the presence of phenolic compounds in the plant are absorbed from intestines and reacts with a large number of free radicals. Due to its high quantity of carbohydrates, amino acids, minerals, and other bioactive substances, *P. lactiflora* is said to be very nutritive (66). The central nervous system's kappa-opioid receptors and beta (2)-adrenoceptors may act as mediators of the analgesic effect (92,96). The paeonidians of paeonins' exhibit inflammatory activities by blocking major inflammatory pathways and inhibiting expressions of proinflammatory markers (42). Benzoic acid and the betanin are the major compounds of the plant responsible for antimicrobial activities (81). The antitumour activity is exhibited through the cytotoxicity to the cancerous cells, which attributes due to the polyphenol and flavonoid contents in the Paeonis (42). Esculetin, methyl eugenol, isovanillic acid present in the plant attribute to the cardioprotective activity against myocardial injury (94,96). Several monoterpenes of the Paeonia are responsible for neuroprotection due to oxidative stress and fatty acids components of the plant (9,10). Traditional medicine's claims require more phytochemical testing; their usage must be validated through reverse pharmacology and clinical research. The plant preceding to widespread clinical use deserve in vivo study to establish its efficacy and safety.

**Future prospects**

Paeonia spp. are in the practice of traditional and indigenous healers, which is culturally acceptable, inexpensive, and compatible with minimal adverse effects. The plant is a source of numerous valuable ingredients that can be used to develop pharmaceuticals, non-pharmacopoeial, and synthetic medicines. The current review has anticipated its therapeutic extension and expansion of nanomedicines besides its routine use based on its chemical composition. It also provokes the researchers to conduct more rigorous scientific clinical studies on the therapeutic efficacy and safety of the plant. Revalidating the current claims by the indigenous system is also a vital thrust area of research. Moreover, studies are required to develop the agro technology of the plant in proper climatic conditions. Mass cultivation of the plant can strengthen the economic state of the farmers and its industrial attributes. A unique conservation strategy requires for the sustainable utilization of the plant.

**Conclusion**

Paeonia spp. are valuable medicinal plants found in the Himalayan region of India. Studies have revealed that many secondary metabolites in these plants attribute a wide range of pharmacological activities. The plant exhibits antioxidant, antimicrobial, anti-inflammatory, antitumour, and numerous CNS activities. However, the claims mentioned in traditional medicines for *Paeonia* require rigorous scientific validation to support them. The pharmacological activities, particularly gastrointestinal, reproductive, and hemopoietic systems, need further exploration. Since *P. emodi* is mostly available in sizeable location, it is urgent to propagate in various agroclimatic zones before it becomes extinct from the wild. The
discovery of other bioactive molecules from this plant and the novel targets are yet to be discovered.

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Authors’ contribution
SK: Collection of articles, drafting and writing the review article. KK R: The outline, design, and directing the study. MMR, and RNA: Study supervision, manuscript revision, manuscript review, and editing. All authors read, reviewed, and approved the manuscript and English language.

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Paeonia ostii


