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Compressive Review on Plant Profile, Ethnomedicinal Uses, Phytochemistry and Pharmacology of *Paeonia emodi* Royle (Himalayan Paeony)

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Members of the genus Paeonia, which contains well-known ornamentals as well as traditional medicinal plants with a history reaching back over 1500 years, may be found all throughout the Northern Hemisphere. Many of these ethnomedicinal properties have been studied in animal models. It has been listed as a critically endangered plant species. *P. emodi* has been shown to have antioxidant, nephroprotective, lipoxygenase inhibitory, cognition and oxidative stress release, cytotoxic, anti-inflammatory, antiepileptic, anticonvulsant, haemaglutination, alphachymotrypsin inhibitory, hepatoprotective, hepatic chromes, and pharmacokinetics of carbamazepine expression. spas Data was acquired from unpublished theses (India, China, Pakistan, and Nepal) and numerous published research articles related to pharmacology, phytochemistry, and other activities using certain keywords. The pertinent information about medicinal uses, taxonomic/common names, parts used, collection and recognition source, authentication, voucher specimen number, plant extracts and their characterization, isolation and characterization of phytochemicals, methods of study (in silico, in vivo, or in vitro), model organism used, dose and time, minimal active concentration, bioactive compound(s), mechanism of action on single or multiple targets, and toxicological information. Triterpenoids, monoterpenoids, phenolics, and tannins are among the natural substances produced by the species. The purpose of this study was to collect broad

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traditional medicinal uses, phytochemistry, pharmacology, and toxicological data on P. emodi. This work also emphasises taxonomic validity, experimental design quality, and weaknesses in previously published Himalayan paeony material, which may help researchers plan for future research.

Keywords: Paeonia emodi Royle; traditional medicinal plants; pharmacology; phytochemistry; toxicological.

1. INTRODUCTION

Medicinal plants have been utilised to treat and cure many ailments since prehistoric times. Because of their safety and security, these medicinal herbs are given first priority in Indian healthcare systems such as Ayurveda, Siddha, and Unani. The literature from Rigveda, 1500-400 BC, provides attestable proof of these medicinal herbs' curative usage [1]. Since ancient times, India has been a rich store of medicinal plants, and these plants have been utilised for therapeutic purposes for centuries. Worldwide, 480,000 plant species have been found, with 28,187 of them being employed for medicinal purposes [2, 3]. In India, there are around 9,500 plant species of therapeutic use [4]. Himalaya is well recognised for its diverse medicinal and fragrant plant variety. Because of its distinctive geographical configuration, topography, and undulant environment, climatic conditions vary along with altitudinal gradients, resulting in a wide biological habitat spanning from tropical forest, grassland, and alpine meadows with enormous and diverse natural resources. Unfortunately, certain natural resources, notably medicinal plants, are being used in an incorrect manner. In recent years, there has been a surge in interest in the use of medicinal and aromatic plants as pharmaceuticals, herbal medicines, flavouring, fragrances and cosmetics, and other natural goods [5, 6]. Western Himalayan medicinal plants provide alternative treatments with enormous potential. It not only offers impoverished people with access to and inexpensive medicine; it may also produce cash and jobs for developing nations [7]. Paeonia is a single genus in the Paeoniaceae family, with around 35 species found primarily in warm-temperate areas of Europe and Asia [8]. Paeonia species, which have a cage-like pinane structure, are a major source of monoterpene chemicals [9, 10]. Many bioactive chemicals from various species have been found, including monoterpene glycosides, triterpenoids, phenols, and tannins [11]. Underground tubers are used to treat neurological disorders, uterine illnesses, colic, bilious obstructions, dropsy, epilepsy, convulsions, and hysteria [12]. The dried flowers are used to treat gastric problems [13]. The whole plant is used to cure vomiting, cholera, TB, and eye disorders. The seeds have purgative and emetic properties [14]. *P. emodi* tender shoots are cooked and consumed as a vegetable. Several compounds extracted from Paeonia species have sedative and anti-inflammatory properties and are used to inhibit neuromuscular junctions [15]. The Himalayan paeony (Paeonia emodi Royle, Paeoniaceae) is known colloquially as the "Queen of Herbs." It is found in the Himalayan areas of Northern Pakistan, China, North-West India, and West Nepal, with an altitude range of 2200 to 3200 metres [16]. It grows naturally in loamy-moist soil with cold climatic conditions and is grown in temperate regions across the world. Flowering takes place throughout the months of April and May. This species has been considered to be one of the most beneficial medicinal herbs for the treatment of a variety of ailments [17]. Its roots (rhizomes) are widely marketed in herbal marketplaces across the world. Because of its great therapeutic value and clandestine commerce, this species faces serious challenges to its survival [18]. As previously described in research, it is a well-known wild edible plant with a wide range of traditional therapeutic purposes. Various components of this plant are used to cure a variety of diseases [19]. The family Paeoniaceae is sometimes known as the Ranunculaceae, and it consists of 33 genera that are mostly found in the mild temperate regions of Europe, Asia, and North-Western America. They are perennial herbs or shrubby plants that can grow up to 2 m tall and are rooted in strong rootstocks [20]. The Himalayan peony has been referenced by several writers under various scientific names, but according to the most recent criteria [21, 22]. There can only be one recognised scientific name for a plant, and the others are classified as synonyms. *P. emodi* Wall, P. anomala var. emodi, *P. emodi* f. glabrata, *P. emodi* var. glabrata, *P. emodi* subs. Sterniana are the plant's synonyms. *P. emodi* is classified as Kingdom: Plantae, Division:

Fig. 1. Photographs of the *P. emodi* in the field

Magnoliophyta, Subdivision: Spermatophytina, Class: Magnoliopsida, Order: Saxifragales, Family: Paeoniaceae, Genus: Paeonia, Species: Paeonia emodi or P. emodi. Paeonia emodi Wall. ex Royle is the scientific name for this plant. *P. emodi* is also known as paeony rose, himalayan paeony (English), undsalib, pamekh, ood-salib (Urdu), pawin, chandayra, ud-salap (Hindi), mamekh, mamaikh (Pashto, Hindko, Gojri and Kalasha), chandra (Sanskrit), bhoi (Marathi) [23]. Therefore, in this study, the ethno pharmacological review of *P. emodi* was carried out aimed at providing a detailed précis of the botany, ethnomedicinal uses, pharmacological activities and chemical composition of the species.

2. RESEARCH METHODOLOGY

P. emodi data was obtained using a variety of search engines, including PubMed, Scopus, Google Scholar, Medline, Web of Science, Google Scholar, and Science Direct. For scanning the literature, indicators such as Paeonia emodi, Himalayan paeony, ethnopharmacology, ethnobotany, traditional applications, phytochemistry, and toxicity were used. The right taxonomic names and synonyms, on the other hand, were confirmed utilising databases. Ethnomedicinal uses were downloaded and cross-checked from several universities and research institutions in India, China, Pakistan, and Nepal. In addition, 1200 research publications on ethnopharmacological/ ethnobotanical applications published in prestigious journals throughout the world were evaluated. Chem Depict, a scientifically acknowledged tool, was used to draw the chemical structures of bioactive substances. The databases mentioned above were used to compile detailed information on P. emodi's taxonomic validity (correct taxonomic names, common names, distribution, identification, Herbarium, etc.), ethnopharmacology (part used, traditional uses, preparation and administration, etc.), pharmacology (extract preparation, dosage, duration, model organism, clinical trials, etc.), and phytochemistry (bioactive compounds, extraction, separation, isolation, structural elucidation, etc). (in vitro, in vivo etc).

2.1 Botany and Taxonomy

The Himalayan peony is a diploid nothospecies with ten chromosomes (2n=10) that resulted from the hybridization of P. lactiflora and P. mairei [24]. The life cycle of the plant *P. emodi* begins in mid-February and ends in August-September. This huge kind of perennial herbaceous peony has hairless stems 60-150 cm tall, enormous deep-cut leaves 30-60 cm long, and up to fifteen hairless, lanceolate pointed leaflets or lobes 14 cm long. The stems may have two to four buds, not all of which mature into 8-12cm diameter blooms in May or June. Each bloom is subtended by three to six bracts that resemble leaves. The persistent sepals are typically round and convex-concave, with a pointed tip. Five to ten white elliptical petals are inverted egg-shaped, 4½×2½ cm long, and wrap numerous stamens consisting of 1½–2 cm long filaments capped by yolk yellow anthers. A narrow ring-shaped disc encircles the very base of one, occasionally two, pale yellow carpels, which are generally coated in felty hairs. This grows into a 2–312 cm densely hairy or hairless follicle containing numerous roundish seeds that are crimson at first but become brownish black if viable in August or

September [25]. The foliar epidermis is made up of irregularly shaped epidermal cells with undulating walls that may be seen under a microscope. The length and breadth of an adaxial epidermis cell are 71.5m and 73.5m, respectively, whereas the length and width of an abaxial epidermal cell are 88.5m and 76m (width). The stomata are usually anomocytic in nature, with various lengths and widths [26]. The fruit is an oval follicle containing lobose black seeds. In polar perspective, pollens are tricolporate, monad, and round, but in equatorial view, pollens are perprolate. The polar diameter is 38.14m (polar view), 30.87m (equatorial view), the P/E ratio is 1.23m, the colpi length is 12.3m, the breadth is 15.83m, and the exine thickness is 2.5m [27].

2.2 Phytochemistry

The principal phytochemicals described in *P. emodi* in the literature include phenolics, monoterpenes, triterpenes, steroids, and a variety of organic acids. Phenolics were thought to be useful in the treatment of cancer, cardiovascular disease, diabetes, and epilepsy [28-30]. Monoterpenes have been found to have antipruritic, anti-inflammatory, analgesic, and anaesthetic properties [31-33]. Approximately 4000 known triterpenes found in *P. emodi* were employed in various medications [34, 35], whereas steroids were recognised for bronchodilation and anticancer activity [36]. Several forms of phenolics have been identified in earlier investigations, include paeonol, eugenol, carvacrol, thymol, trans-myrtanol, cis-myrtanol, carvacrol methyl ether, hydroxybenzoic acid, gallic acid, methyl grevillate, ethyl gallate, methyl gallate, benzoic acid, 4-hydroxy benzoic acid, oligostil Paeonins A, B, and C, wurdin (Boron nitride), benzoyl wurdin (Dibenzoyl peroxide), oxypaeoniflorin, paeoniflorin, lactiflorin, tricyclene, -thujene, -pinene, sabinene, -pinene, myrcene, p-cymene Previous research has found that the quality and amount of plant-based phytochemicals can vary depending on the environment in which the medicinal plant grows, the growth circumstances, harvesting and extraction processes, and processing methods. [37].

2.3 Occurrence and Distribution

It is found mostly in North West India, Northern Pakistan, Eastern Afghanistan, China, and West Nepal [38]. It is only known from one location in China [39]. In India, it is found in the North-West Himalayas, from Kashmir to the Garhwal-Kumaon areas of Uttarakhand [40, 41], at elevations ranging from 1800m asl to 3000m asl [42]. *P. emodi* lives in deciduous woods of numerous oak species and Quercus floribunda, primarily on south-facing slopes. In general, the plant thrives in damp deciduous mixed woodland with Quercus species.

2.4 Ethnopharmacology

Because of its broad therapeutic profile, *P. emodi* is frequently employed in indigenous and traditional systems of medicine. The fleshy roots are used to treat uterine disorders, biliousness, dropsy, and neurological ailments; they are especially recommended for youngsters as a blood cleanser. Excessive dosages result in headaches, blurred vision, and vomiting. The seeds have emetic and cathartic properties. Diarrhea is treated by an infusion of dried flowers [43]. The rhizome of *P. emodi* has been used to treat headaches, stomach spasms, hysteria, and as a nervine tonic. It is a component of an important formulation in Unani pharmacopoeia that is extensively used for the treatment of urinary incontinence [44]. Peony has also been used in different cardiovascular and respiratory illnesses including palpitations, high blood pressure, congestive heart failure and atherosclerosis [45].

2.5 Reported Pharmacological Activities of *P. emodi*

The crude extracts as well as pure compounds obtained from *P. emodi* have been used to establish the local and traditional claims and to search for novel activities. The different compounds obtained from *P. emodi* possess a number of biological activities which have been reported from time to time.

2.5.1 Anti-inflammatory activity

Ahmad et al. [46] studied the root extract of *P. emodi* containing polysaccharides showed significant anti-inflammatory activity during *in vivo* experiments in male albino rats. It is suggested that *P. emodi* should be checked to determine the anti-inflammatory potential during *in vitro* studies [46].

2.5.2 Lipoxygenase inhibitory activity

Lipoxygenase enzymes are responsible for the production of chemicals in humans and other

animals such as leukotrienes, hepoxylines, and lipoxins. While such chemicals have been linked to a variety of illnesses including bronchial asthma, inflammation, and tumour angiogenesis. Plant-based extracts, on the other hand, might be used to suppress lipoxygenase. According to the literature [47, 48], *P. emodi* leaves and fruit extracts suppress the formation of lipoxygenase. Riaz et al. [49] found paeoninol and paeonin C in Himalayan Paeony as natural compounds that block lipoxygenase production. However, in the aforementioned research, plant-based extracts were neither analytically defined nor assessed for in vivo experiments.

2.5.3 Nephroprotective and Antihyperlipidimic activity

Nephropathy is a typical consequence of major illnesses such as diabetes that can lead to morbidity and death, whereas hyperlipidemia is a primary cause of oxidative stress, a lack of antioxidant defence, diabetes, and nephropathy. Previously, several researchers researched fruit extracts to treat nephropathy, and it was discovered that this plant significantly reduced glucose levels up to normal range [50]. While the preceding investigations were lacking in screening for particular or active chemicals and lacked information on their mechanism of action [51-54],

2.5.4 Hepatoprotective and α- chymotrypsin inhibitory activities

The liver is an essential organ that performs a variety of activities in the digestive system as well as detoxification of xenobiotic compounds generated in the body. *P. emodi* methanolic and ethanolic extracts have been examined for their hepatoprotective properties [55, 56]. According to Raish et al. [57], *P. emodi* extract significantly decreased the expression of hepatic cytochrome P450 (CYP3A2 and CYP2C11). Riaz et al. [49] investigated emodinol's inhibitory effect in -glucuronidase, whereas Nawaz et al. [58] discovered that triterpenoids isolated from the root of Himalayan paeony can likewise inhibit -glucuronidase. It has been discovered that inhibiting -glucuronidase can prevent liver and spleen enlargement. Alpha-chymotrypsin is an enzyme responsible for synthesis of proteins such as serine which is involved in replication of HCV. The ethyl acetate extract of *P. emodi* containing alpha-chymotrypsin having inhibition capability up to 91% [59].

2.5.5 Antiepileptic and anticonvulsant activities

Epilepsy is a neurological illness that is mostly caused by psychological, physical, and social actions. Regarding P. emodi's traditional usage, a number of publications reported this species being used for epilepsy therapy because to its antiepileptic and anticonvulsant action [60-62].

2.6 GI Activities

Previous research has shown that various components of *P. emodi* are utilised to treat a variety of gastrointestinal ailments. According to several investigations, the aerial sections of Himalayan Paeony exhibit potential spasmolytic and spasmogenic actions [63].

2.7 Potential Cardioprotective and Mutagenic Properties

P. emodi has also been examined in the literature for cardiovascular and airway relaxant actions [45], cardioprotective and antihyperlipidemic potentials [64, 65], cardioprotective potential [66], and anti-mutagenic potential [67].

2.7.1 Antimicrobial properties

Previous research has shown that several plant components of *P. emodi* exhibit antimicrobial, antibacterial, and antifungal properties [68-75].

2.7.2 Cancer-fighting properties

Tantry et al. [76] investigated the cytotoxic effects of identified chemicals from *P. emodi* roots chloroform-ethyl acetate extract against human cancer cell lines A549, HL-60, HCT116, and ZR-75-30 [76].

2.8 Parkinson's Disease (PD)

Jalgaonkar et al. [77] investigated P. emodi's neuroprotective impact in a 6-hydroxy dopamine-induced Parkinson's disease (PD) model. Because of its potential to lower oxidative stress, the ethanolic extract demonstrated neuroprotective effect against 6-hydroxy dopamine-induced Parkinson's disease in rats.

2.9 Safety and Toxicology

For the last decade, there has been increasing interest in herbal dugs all over the world, but the safety of herbal treatments has been repeatedly

questioned. There are currently misconceptions and prejudices about the safety of herbal treatment [78-80]. Based on the literature research, only a little amount of investigation has been done on the toxicity of P. emodi. Ismail et al. [41] investigated the cytotoxicity of this plant species on brine shrimps (Artemia salina) and discovered that the ethanolic extract was non-toxic. Similarly, Zargar et al. [54] reported that hydroalcoholic and aqueous plant extracts did not induce mortality up to 2000mg/Kg body weight and were therefore deemed safe. There are several causes of adverse outcomes with herbal medications, which can be classified as direct or indirect. The inherent toxicity of some herbs at regular therapeutic dosage or in overdose is the direct cause. A regularity framework for herbal medications might provide customers more assurance. However, the regulation and definition of herbal medications range greatly among nations. To ensure the quality and safety of herbal medicines, the World Health Organization should propose global unified planning, which includes global management standards and quality standards, a radical source of herbs, seeds and seedling breeding, planting, harvesting, and storage, rational procedures, manufacturing, and quality standards. Furthermore, a safety guarantee system constituted of rational clinical practise and risk monitoring should be built to increase the safety of herbal medicine and to play a more essential role in human health maintenance.

3. PERSPECTIVES FOR THE FUTURE

In future research, more detailed information on the pharmacological activities of P. emodi, particularly antiepileptic activities using correct taxonomic validation, effective extraction techniques, the role of synergism and mechanism of action of compounds on single or multiple targets, and toxicology should be considered. More research is needed in the future to ensure proper plant identification, better methodology, and a systematic approach to extraction, characterisation, and isolation utilising analytical techniques such as GC-MS, NMR, LC-MS, and HPLC. Some of the significant future prospects include proper dosage duration, mechanism of action on single or multiple targets, responsible active chemicals, chemical structure elucidation in connection to their pharmacological effects, and relationship to their folk traditional usage. The taxonomic validity should include detailed information on the correct taxonomic name, validation from Herbaria, source of identification, deposit of voucher specimen in recognised herbarium, use of online databases such as The Plant List:(TPL) (theplantlist.org), source of plant collection, place, time, season, and morphological as well as physiological notes. Similarly, while dealing with *P. emodi* trade samples, keep in mind the commercial source, store, business name, its location, brand name, postharvest treatment, quality control assurance utilising DNA barcoding, and herbal processing. In addition to this advanced technique such as system biology coupled with metabolomics may be apply for further determination of mechanism of action on targets [81]. It is suggested that the pharmacological activities should be directly linked with folk uses mentioned in ancient literature [82, 83].

4. CONCLUSION

P. emodi is indigenous to the western Himalayas and has been utilised in traditional medicine in many regions of the world. P. emodi's various therapeutic effects have been proven by a large number of phytochemical and pharmacological research conducted over the last 62 years. This is the first complete and critical examination of traditional medicinal usage, phytochemistry, pharmacology, toxicology, and botanical identification. There is a lot of room for the plant to be tested further for dropsy, Parkinson's, and other neurological illnesses. Because oxidation of LDL causes its buildup in the plasma and limits its removal by the liver, the plant can also be used to treat hyperlipidemia. The oxidative alteration of APO A-1 causes the conversion of normal HDL to dysfunctional HDL, hence impeding reverse cholesterol transfer. Because it is the least utilised species in the genus, phytochemical screening can also be used to investigate novel chemical entities found in the plant. In the future, it is advised that extensive clinical studies be conducted to scientifically show the efficacy of medications made from the various sections of P. emodi. *P. emodi* should be investigated further for green manufacture of nanomedicine for biotechnological and nuetro-pharmaceutical applications. Validation of potential synergistic or antagonistic effects of extracts and isolated substances is also required.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

NOTE

The study highlights the efficacy of "traditional medicine" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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