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Review

Botany, ethnomedicines, phytochemistry and pharmacology of Himalayan paeony (*Paeonia emodi* Royle.)

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ABSTRACT

Ethnopharmacological relevance: Himalayan paeony (*Paeonia emodi* Royle.) is an important species used to treat various diseases. This study aimed to compile the detailed traditional medicinal uses, phytochemistry, pharmacology and toxicological investigations on *P. emodi*. This study also highlights taxonomic validity, quality of experimental designs and shortcomings in previously reported information on Himalayan paeony.

Methods: The data was extracted from unpublished theses (Pakistan, China, India and Nepal), and different published research articles confined to pharmacology, phytochemistry and antimicrobial activities using different databases through specific keywords. The relevant information regarding medicinal uses, taxonomic/common names, part used, collection and identification source, authentication, voucher specimen number, plant extracts and their characterization, isolation and identification of phytochemicals, methods of study in silico, in vivo or in vitro, model organism used, dose and duration, minimal active concentration, zone of inhibition (antimicrobial study), bioactive compound(s), mechanism of action on single or multiple targets, and toxicological information.

Results: P. emodi is reported for diverse medicinal uses with pharmacological properties like antioxidant, nephroprotective, lipoxygenase inhibitory, cognition and oxidative stress release, cytotoxic, anti-inflammatory, antiepileptic, anticonvulsant, haemaglutination, alpha-chymotrypsin inhibitory, hepatoprotective, hepatic chromes and pharmacokinetics of carbamazepine expression, β-glucuronidase inhibitory, spasmolytic and spasmogenic, and airway relaxant. Data confined to its taxonomic validity, shows 10% studies with correct taxonomic name while 90% studies with incorrect taxonomic, pharmacopeial and common names. The literature reviewed, shows lack of collection source (11 reports), without proper source of identification (15 reports), 33 studies without voucher specimen number, 26 reports lack information on authentic herbarium submission and most of the studies (90%) without validation of taxonomic names using recognized databases. In reported methods, 67% studies without characterization of extracts, 25% lack proper dose, 40% without duration and 31% reports lack information on proper controls. Similarly, only 18% studies reports active compound(s) responsible for pharmacological activities, 14% studies show minimal active concentration, only 2.5% studies report mechanism of action on target while none of the reports mentioned *in silico* approach.

Conclusion: P. emodi is endemic to Himalayan region (Pakistan, China, India and Nepal) with diverse traditional therapeutic uses. Majority of reviewed studies showed confusion in its taxonomic validity, incomplete methodologies and ambiguous findings. Keeping in view the immense uses of *P. emodi* in various traditional medicinal systems, holistic pharmacological approaches in combination with reverse pharmacology, system biology, and

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"omics" technologies are recommended to improve the quality of research which leads to natural drug discovery development at global perspectives.

1. Introduction

The Himalayan paeony (*Paeonia emodi* Royle.) is commonly called "the queen of herbs". It is commonly distributed in Himalayan regions of Northern Pakistan, China, North-West India and West Nepal with altitudinal range of 2200–3200 m (Ali et al., 2011). It naturally grows in loamy-moist soil with cool climatic conditions and cultivated in temperate parts of the world. The Himalayan paeony is known with different names like 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), dhandharu (Garhwali).

This species is one of the most useful medicinal plant reported for treatment of various diseases (Misra et al., 2008). Its roots (rhizomes) are frequently traded in herbal markets of various countries. Due to its high medicinal value and illegal trade, this species is facing severe threats towards its sustainability (Sevim et al., 2013). This species is endemic to Himalayan region (Rawat et al., 2010; Fazal et al., 2012; Wang, 2013). It is well known wild edible plant with diverse traditional medicinal uses as reported in previous studies (Samant and Dhar, 1997; Nautiyal and Kaechele, 2007; Rawat et al., 2010; Bisht et al., 2013). Different parts of this species are used to treat various ailments (Wang, 2013). In literature, numerous studies are published on phytochemical, pharmacological and antimicrobial activities while at the same time some problems exist regarding its taxonomic validity, ambiguous methodologies, incomplete information about its pharmacological activities in relation to its active constituents and traditional medicinal uses, authenticity of previous published data and repetition of similar findings.

In literature, some researchers formulated the guidelines and set criteria to write reviews on particular species (Chan et al., 2012; Uzuner et al., 2012; Rivera et al., 2014). In such type of guidelines, the reviews on particular species must include (i) correct and valid taxonomic names, (ii) collection site and source, (iii) morphology and physiological notes, (iv) standard extraction and isolation methods, (v) identification and characterization of bioactive compounds, (vi) extract, dosage and duration in model organisms, (vii) in vivo or in vitro applications, (viii) action mechanism on single or multiple targets and (ix) clinical trials etc. Such kind of guidelines can improve the quality and authenticity of natural drug development using medicinal plants like *P. emodi*. Keeping in view the significance of above mentioned criteria, the present study aims to critically review and compile the data about traditional uses, phytochemistry, pharmacology, antimicrobial potential, taxonomic validity and to highlight the research gaps, ambiguities and deficiencies in previous literature published on *P. emodi* (Uzuner et al., 2012; Chan et al., 2012; Rivera et al., 2014).

2. Botany and taxonomy

P. emodi is commonly known as Himalayan paeony, belongs to family Paeoniaceae and endemic to Himalayan region (Haq et al., 2011). It is generally up to 70 cm tall shrub with glabrous stem, oblong lanceolate leaves with glabrous surface (Misra et al., 2008). In microscopy, the foliar epidermis consists of irregular shaped epidermal cell with undulating walls. The size of adaxial epidermal cell is 71.5 μm (length) and 73.5 μm (width) while abaxial epidermal cell is 88.5 μm (length) and 76 μm (width). The stomata are mostly anomocytic type with varying size in length and width (Shazia, 2012). Flowers are white in colour and terminal or axillary arranged on shoots. Flowers are mostly bracteates with sub orbicular sepals and obovate petals. Fruit is ovoid follicle with lobose black colored seeds. Pollens are tricolporate, monad and circular shape in polar view while perprolate in equatorial view (Fig. 1). Polar diameter is 38.14 μm (polar view), 30.87 μm (equatorial view), P/E ratio 1.23 μm, colpi length 12.3 μm, width 15.83 μm and exine thickness 2.5 μm (Ahmed, 2008).

3. Methodology

Data on *P. emodi* was compiled using various search engines i-e, PubMed, Scopus, Google Scholar, Medline, Web of Science, Google scholar, Science Direct. Indicators like *Paeonia emodi,* Himalayan paeony, ethnopharmacology, ethnobotany, traditional uses, phytochemistry and toxicology were applied for searching the literature. However, the correct taxonomic names and synonyms were verified using databases; (www.theplantlist.org). Ethnomedicinal uses were downloaded and cross checked from accessible unpublished theses of different universities and research institutes of Pakistan (http://eprints.hec.gov.pk/), India (http://shodhganga.inflibnet.ac.in), China (http://www.cnki.net) and Nepal (http://tribhuvan-university.edu.np/tu-central-library-tucl). In addition to this, 1200 research articles published on ethnopharmacological/ethnobotanical uses in various journals of repute across the world were also reviewed. Chemical structures of bioactive compounds were drawn using scientifically accepted program ChemDraw. The above mentioned databases were used to compile detailed information on *P. emodi* about its 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), phytochemistry (bioactive compounds, extraction, separation, isolation, structural elucidation etc), various biological activities (strain used, dosage, zone of inhibition, positive and negative control etc), clinical trials (in vitro, in vivo etc).

4. Ethnopharmacology

P. emodi is well known traditional medicine and traded herbal drug. Different plant parts especially roots of *P. emodi* is used for the treatment of different diseases throughout the world. In literature, roots were most frequently used plant parts (90 reports), followed by leaves (18 reports), tuber and seeds (13 and 10 repots) (Fig. 1: Supplementary data). Powder (34 reports) was most frequently reported method of administration and preparation followed by decoction (15 reports), extracts (09 reports) (Fig. 2: Supplementary data). Table 1 presents the detailed information about the use of *P. emodi* for treatment of various diseases. The frequently treated diseases were epilepsy (28 reports) followed by skeletal disorders (28 reports) and blood purification (19 reports).

5. Phytochemistry

In literature, major phytochemicals reported in *P. emodi* includes phenolics, monoterpenes, triterpenes, steroids and variety of organic acids (Table 2). Phenolics were considered to be beneficial in treating cancers, cardiovascular diseases, diabetes, and epilepsy (Rio et al., 2013; Acosta-Estrada et al., 2014; Helal et al., 2015). Monoterpenes were reported to be used as antipruritic, anti-inflammatory, analgesic and anesthetic (Xu et al., 2005; Chen et al., 2008; Takaishi et al., 2014). About 4000 known triterpenes reported in *P. emodi* were used in different drugs (Patočka, 2003; Qu et al., 2017), while steroids were