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REVIEW

Valeriana jatamansi: An herbaceous plant with multiple medicinal uses

Arun K. Jugran[1] | Sandeep Rawat[2] | Indra D. Bhatt[2] | Ranbeer S. Rawal[2]

[1] G. B. Pant National Institute of Himalayan Environment and Sustainable Development, Garhwal Regional Centre, Srinagar, Uttarakhand, India

[2] Centre for Biodiversity Conservation and Management (CBCM), G. B. Pant National Institute of Himalayan Environment and Sustainable Development, Kosi-Katarmal, Almora, Uttarakhand, India

Correspondence
Dr Arun Kumar Jugran, G. B. Pant National Institute of Himalayan Environment and Sustainable Development, Garhwal Regional Center, Srinagar-246 174, Uttarakhand, India.
Email: arunjugran@gbpihed.nic.in

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Valeriana jatamansi Jones (Family: Caprifoliaceae), a high value medicinal plant, was distributed in many countries of Asia. The species possesses important valepotriates and is a good source of flavones or flavone glycosides, lignans, sesquiterpenoids or sesquiterpenoid glycoside, bakkenolide type sesquiterpenoids, phenolic compounds, terpinoids, etc. The use of the species in traditional and modern medicines is well known. For instance, *V. jatamansi* is very important for its insect repelling and antihelmethic properties. Similarly, sedative, neurotoxic, cytotoxic, antidepressant, antioxidant, and antimicrobial activities of the species in various ailments in the indigenous system of medicine, particularly in Asia, are reported. This review focuses on the detailed phytochemical composition, medicinal uses, and pharmacological properties of *V. jatamansi* along with analysis of botanical errors in published literature and reproducibility of the biomedical researches on this multipurpose herbaceous species.

KEYWORDS

botanical errors, pharmacological properties, phytochemistry, reproducibility, *Valeriana jatamansi*

1 | INTRODUCTION

Valeriana jatamansi Jones (synonymous *V. wallichii* DC.; common name Indian valerian or Tagar) is an important medicinal plant that belongs to family Caprifoliaceae (initially, it was a saparate family Valerianaceae; APG, 2009). It is a small perennial herb native to Himalaya and distributed from Afghanistan to southwest China, India, Nepal, Bhutan, and Myanmar at an altitude of 1,000 to 3,000 m asl (Jugran et al., 2013; Jugran, Bhatt, Rawal, Nandi, & Pande, 2013; Polunin & Stainton, 1987). The species reproduces through sexual (seeds) and asexual (rhizome) means (Khajuria, Verma, & Sharma, 2011). It is used for various medicinal purposes in the Indian, British, and Chinese Pharmacopoeia. Valerenic acid and valepotriates isolated from the species are often used for drug preparation (Bhatt et al., 2012; Singh, Gupta, Singh, & Kaul, 2006). The species has also been reported as a psychopharmacological agent and a natural source of valepotriates (Mishra, 2004). The presence of valerenic acid and valerinone in *V. jatamansi* is a source of drug valerian. Among the top selling herbal supplements, the drug valerian ranks eighth place (Blumenthal, 2001). The naturally occurring valepotriates/iridoids are the most active ingredient of this species, which possesses various activities such as antibacterial, anticancer, anticoagulant, antifungal, anti-inflammatory, antioxidative, antiprotozoal, hepatoprotective, and neuroprotective (Dinda, Chowdhury, & Mohanta, 2009). *V. jatamansi* has long history of uses and mentioned as a medicine in the Rigveda, Charka Samhita, and modern medicine system. The species is used for its aromatic, stimulant, carminative, and antispasmodic activity. As an ingredient, the species is used in the preparation of 39 Ayurvedic formulations (Prakash, 1999; Rawat & Vashistha, 2011). Species is also used in the treatment of epilepsy, hysteria, and urinary troubles (Sharma, 2003; Singh & Ali, 1998). The dry roots of *V. jatamansi* are used to remove foul odor of mouth caused by tooth trouble (http//www.sdpi.org.com). Crushed leaves of the plant are rubbed in forehead in extreme headache (Bhattacharjee, 2008; Chevallier, 1999). Dry rhizomes are used in perfumes, blackening of hair, and as incense (Bhattacharjee, 2008). The roots are employed for the treatment of head and eye troubles, diseases related to blood, liver, spleen, kidney ulcers, wounds, cardiac debility, dry cough, asthma, chronic fever, and intermittent fever (Awan, 1990; Prakash, 1999). Furthermore, the species is known to cure obesity, skin diseases, anxiety, insanity, failing reflexes, hysteria, neurosis, sciatica, tranquilizer, emmenagogue, and snake poisoning (Baquar, 1989; Nadkarni, 1976). Diuretic (Said,

1970) and hepatoprotective properties (Awan, 1990) of the species are also reported. The whole plant is used for nervous debility, as a hypnotic and in the treatment of spastic disorders. Clinical and animal studies have proved its use in the central nervous system depression (Marder et al., 2003). Essential oil and extract of the species are used in flavor, pharmaceutical, and fragrance industries especially for flavoring tobacco, honey, and beer (Sah, Mathela, & Chopra, 2010a). Several herbal preparations of the plant have been reported to use traditionally in treatment of diarrhea (Awan, 1990), gastrospasms (Kapoor, 1990), and hypertension (Chevallier, 1996). In Nepal, decoction of the drug has been reported to be given to mothers after parturition, probably as a sedative (Sah et al., 2010a). The species is considerably well known for its traditional use in inflammatory conditions such as scorpion stings and jaundice (Nadkarni, 1976). *V. jatamansi* also demonstrated activity against acetylcholinesterase (Wang et al., 2011; Wang et al., 2014) and played important role in learning, memory, Alzheimer's disease, and Parkinson's disease (Goodman & Soliman, 1991; Heese, Low, & Inoue, 2006). The increasing global acceptance of complementary and alternative medicine is the major reason for the increasing demand of the species. *V. jatamansi* is one among the 178 traded medicinal plants, which has been traded in high volumes over 100 MT/year (Rawat & Vashistha, 2011; Sharma, Shanker, Tyagi, Singh, & ChV, 2008).

The major challenge in the botanical research is to maintain scientific rigor and effective communication (avoiding ambiguity and error). However, in recent years, this issue has become ever more common in ethnopharmacology due to the increase in the number of studies published on the medicinal properties of the plants. For example, Rivera et al. (2014) explored problems and impacts of ambiguous or erroneous use of botanical scientific nomenclature in ethnopharmacological studies suggested approaches to reduce frequency, and impact of such errors and found that these problems are consistent even with several reputed journals. Likewise, in modern era, generally new findings in a biomedical research are published in a peer reviewed journal where it contributed in the advancement of the science which can be measured by work quality and citation. Once a research article published, research and findings should be replicated. However, in many instances, the data, methodology, and results cannot be replicated because of shortcoming in conceptualization of hypothesis, experiment and study design execution, and analysis and fabrication of research. Therefore, is it essential to check the research quality and highlight the gaps in the research performed on *V. jatamansi*. This will help to identify accurate raw material and bring therapeutic agent to any medical practice. Therefore, the present review attempted to (a) describe the researches regarding the pharmacological attributes of *V. jatamansi*, (b) list and describe the major phytochemicals extracted from the species, (c) identify the major botanical errors in the published research, and (d) authenticity and accuracy of the biomedical researches published on this herb. This will help to identify the gap area and open avenue for future research prospects in *V. jatamansi*.

2 | METHOD

Systematic literature survey was conducted for information collection. Various scientific search engines, such as PubMed, Google Scholar, NCBI, Ingenta, Agricola, Science-Direct, Mendeley, Scopus, Springer Link and JSTOR, were used to download the information published in journals; conference papers; electronic books; scientific reports of international, regional, and national organizations; and research thesis to carry out a systematic and comprehensive literature search. The keywords, such as *V. jatamansi*, *Valeriana wallichii*, Indian valerian, Tagar, and Muskbala, were used to explore the relevant articles. Literature was also searched by consultation in some reputed libraries of the Himalayan region for enhancing the scientific database of the species. The results were then cross referenced to generate maximum number of publications available in the species, and a total number of 165 references (150 references cited in the main text + 15 references cited only in the Supplementary Tables) were used in this review (during the time span of 1961–2017).

Chemicals structures of some of the most important active constituents and compounds present in essential oil were prepared with the help of the freely available software "Instant J Chem" (version 6.2.1, Chem-Axon). The taxonomic and nomenclatural accuracy was assessed by following the standard methodology of Rivera et al. (2014) with modification (Table S1). Five different types of common errors in botanical studies were assessed in present review along with other observation for *V. jatamansi* as highlighted by Rivera et al. (2014) (Table S1). Name and taxonomic description of the species was assessed from most authentic database (www.theplantlist.org [TPL]), and regional flora and accuracy in the scientific nomenclature and errors was assessed. In order to analyze the gaps and way forward, among the 165 articles (excluding book chapters cited in the study), 116 articles used in this study were assessed. Comparative assessment of botanical errors in the published articles was made to analyze all papers exactly with the same methodology.

Similarly, in order to address the issue of none reproducibility, undermining the scientific credibility, relevance, and sustainability of the research process used in pharmacological studies on *V. jatamansi*, several factors were monitored using Mullane, Enna, Piette, and Williams (2015) with minor modifications. Although, this approach was suggested to publish the quality paper in biomedical journals, it is modified and used for already published biomedical research on *V. jatamansi* (Table S2). Various parameters such as errors in experimental design, hypothesis conceptualization, statistical analysis, and data analysis; investigator biases and errors; validation of reagents including cells and antibodies; and scientific fraud were assessed in the present study. This approach will definitely help to determine the potential and quality of already published ethanopharmacological, pharmacological, and biomedical studies on *V. jatamansi*. It will also be helpful to improve the future biomedical research and encourage researchers to perform quality research to improve the transparency and accuracy of data reporting via the use of checklists of "best practice" that aid in validating the methodologies and reagents used in data generation along with highlighting the shortcomings and gap area in already published researches on *V. jatamansi* (Table S2).

3 | PHYTOCHEMISTRY

The major chemical constituents from roots and rhizomes of *V. jatamansi* are valepotriates (Becker & Chavadeoi, 1985), flavonoids

and flavone glycosides (Marder et al., 2003; Thies, 1968), lignans (Lin et al., 2010), sesquiterpenoids (Willis, Bone, & Morgan, 2000), bakkenoloids type sesquiterpenoids (Xu, Yang, et al., 2011), phenolics (Bhatt et al., 2012), essential oils (Bhatt et al., 2012; Bos et al., 1997; Sati, Chanotiya, & Mathela, 2005; Verma et al., 2011; Verma, Padalia, & Chauhan, 2013), and other phytochemicals. A summary of all the phytochemical constituents present in *V. jatamansi* has been shown, and chemical structure of major compounds extracted from the species is given (Figures 1 and 2; Table S3). The details of each group of compounds are summarized below.

4 | VALEPOTRIATES

Valepotriates are important plant secondary metabolites of the family Caprifoliaceae (earlier Valerianaceae), contain various acyloxy group linkages to the valepotriate nucleus, and exhibit significant biological activities. In the recent years, considerable progress has been made in the search of novel valepotriates compounds, and 145 valepotriates compounds have been reported from *V. jatamansi*. The composition of valepotriates varies significantly among different plant parts, habitats, place of collection, etc. (Chen et al., 2002). The valepotriates were first isolated in 1966 from *V. jatamansi* (Thies & Funke, 1966). Valepotriates are among the main compounds of this herb include valtrate (**1**), acevaltrate (**2**), and didrovaltrate (**3**). Valepotriates isolated from *V. jatamansi* hydrolyze rapidly and metabolize in gastrointestinal tract to yield the breakdown products baldrinal (**4**), homobaldrinal (**5**), decyl baldrinal (**6**), and valtroxal (**7**), consisting of an unsaturated version of ring skeleton (Schneider & Willems, 1982; Thies, 1968). Dihydrovaltrate (**8**) was also isolated from the rhizome of the species (Bounthanh, Bergmann, Beck, Hagg-Berrurier, & Anton, 1981). Similarly, isovalterate (**9**) and homovalterate (**10**) were extracted from the roots of *V. jatamansi* (Finner, David, & Thies, 1984; Tang, Liu, & Yu, 2003). Chen, Qin, and Zheng (2000) studied the levels of valepotriate, dihydrovalepotriate (**11**), and acetyl-valepotriate (**12**) from *V. jatamansi* and found that major iridoids from the species contain didrovaltrate (**3**) and valepotriates derivatives (0.5–9.0%), mainly valepotriates, isovalepotriate (**13**), acetoxyvalepotriate (**14**), and isovalemxyhydroxy-dihydrovatrate (**15**) (Table S3). Lin et al. (2009) identified 13 acylated iridoids, namely, jatamanvaltrates A–M (**16**–**28**) from whole plant. Two new iridoids, jatamanvaltrates N (**29**) and O (**30**), were also extracted from the roots of *V. jatamansi* (Xu, Guo, Fang, Li, & Guo, 2012). Similarly, Wang et al. (2014) reported the occcurance of two iridoids, jatamanvaltrates P (**31**) and Q (**32**), along with three known iridoids, valtrate (**1**), rupesin B (**33**), and chlorovaltrate (**34**) from the roots and rhizomes of *V. jatamansi*. Three new iridoids, namely, valeriandoids A (**35**), B (**36**), and C (**37**) have been isolated from the roots of this species (Xu et al., 2011). Recently, three new iridoids jatamanvaltrate R (**38**), jatamanvaltrate S (**39**), and jatamanin Q (**40**) were isolated from the roots of *V. jatamansi* (Dong et al., 2015). Thirteen new iridoids Jatamanins A–M (**41**–**53**) were also extracted from whole plants (Lin et al., 2010). Likewise, three new iridoids, jatamanins N (**54**), O (**55**), and P (**56**), were isolated from the roots of this herb (Li, Wu, Li, Li, & Li, 2013). Xu et al. (2012) has isolated three new natural iridoids including valeriandoids D–F (**57**–**59**). Wang et al. (2008) isolated valeriotetrates B (**60**) and C (**61**), 8-methylvalepotriate (**62**), and 1, 5-dihydroxy-3, 8-epoxyvalechlorine A (**63**) from the roots of *V. jatamansi*. Jatadoids A (**64**) and B (**65**) were isolated from the roots of *V. jatamansi* (Xu et al., 2012). Three new iridoids, jatairidoids A (**66**), B (**67**), and C (**68**) from the roots of *V. jatamansi* were also reported (Xu et al., 2012). Yu et al. (2006) isolated a new tetracester known as valeriotetraester (**69**) from the roots of this herb. Recently, three new minor valepotriate isomers were isolated and identified as jatamanvalterates Z1 (**70**), Z2 (**71**), and Z3 (**72**) from whole plant of this species (Lin et al., 2017). In addition, 10 new valepotriates, jatamanvaltrates P (**31**), Q (**32**), R (**38**), S (**39**), T–Y (**73**–**78**), and nardostachin (**79**), have been isolated from the whole plant of *V. jatamansi* (Lin et al., 2015). Besides 3,5-diene and 3-monoene valepotriates, one new 3,7-diene valepotriate [jatamanvaltrate P (**31**), five new 4,7-diene valepotriates (jatamanvaltrates Q (**32**), R (**38**), S (**39**), T (**73**), and U (**74**), two new 4,6-diene valepotriates (jatamanvaltrates V (**75**) and W (**76**), and two new 3-monoene valepotriates with p-hydroxycinnamyloxy at C-7 (jatamanvaltrates X (**77**) Y (**78**), and valepotriate nardostachin (**79**)] have been characterized (Lin, Chen, et al., 2015). Fifteen chlorinated valepotriates isolated from the whole plants of *V. jatamansi* include chlorovaltrates A–O (**80**–**94**). Six known analogues, namely, (1S,3R,5R,7S,8S,9S)-3,8-epoxy-1,5-dihydroxyvalechlorine (**95**), volvaltrate B (**96**), rupesin B (**33**), chlorovaltrate (**34**), (1S,3R,5R,7S,8S,9S)-3,8-epoxy-1-*O*-ethyl-5-hydroxyvalechlorine (**97**), and (1R,3R,5R,7S,8S,9S)-3,8-epoxy-1-*O*-ethyl-5-hydroxyvalechlorine (**98**) were also extracted from this species (Lin et al., 2013). The structure of three new decomposition products of valepotriates, valtrals A–C (**99**–**101**) isolated from ethanol extract of the whole plants of *V. jatamansi*, was studied using spectroscopic methods (Lin et al., 2015). More recently, five new iridoids, named as chlorovaltrate P–T (**102**–**106**), along with six known analogues, (4β,8β)-8-methoxy-3-methoxy-10-methylene-2,9-dioxatricyclo[4.3.1.$0^{3,7}$]decan-4-ol (**107**), chlorovaltrate A (**80**), (1*R*,3*R*,5*R*,7*S*,8*R*,9*S*)-3,8-epoxy-1-*O*-ethyl-5-hydroxyvalechlorine (**108**), 8-methoxy-4-acetoxy-3-chlormethyl-10-methylen-2,9-dioxatricyclo[4.3.1.$0^{3,7}$] decan (**109**), (1*S*,3*R*,5*R*,7*S*,8*R*,9*S*)-3,8-epoxy-1-*O*-ethyl-5-hydroxyvalechlorine (**110**), and (1*R*,3*R*,5*R*,7*S*,8*R*,9*S*)-3,8-epoxy-1-*O*-methyl-5-hydroxyvalechlorine (**111**) were isolated from the roots of *V. jatamansi* (Wang et al., 2017). Valerjatadoids A–B (**112**–**113**) were also reported from the roots and rhizomes of this herb (Yang et al., 2015). Similarly, 1-homoacevaltrate (**114**), 1-homoisoacevaltrate (**115**), 10-acetoxy-1-homovalterate hydrin (**116**), 10-acetoxy-1-acevalterate hydrin (**117**), and 11-homohydroxyl dihydrovalterate (**118**) have been isolated from the root and rhizome of *V. jatamansi* (Tang, Liu, & Yu, 2002) while Yu et al. (2005) identified valeriotriates A (**119**) and B (**120**) from the roots of this herb. Likewise, Chen, Yu, Huang, Lv, and Gui (2005), isolated 11-methoxyviburtinal (**121**), prinsepiol-4-*O*-β-D-glucoside (**122**), coniferin (**123**), and hexacosanic acid (**124**) from the roots of *V. jatamansi*. In addition, a valepotriate known as valeriotetrate A (**125**) was also detected and quantified from the roots of this herb (Yu et al., 2006). Two valepotriates, namely, volvatrate A (**126**) (Wang et al., 2009; Li et al., 2013) and jatamandoid A (**127**) (Xu et al., 2012) were isolated from the roots of *V. jatamansi* whereas patriscabrol (**128**) from the whole plant of this species (Lin et al., 2010). Several valepotriate compounds and their analogues, namely, acetovaltrate (**129**), 8, 11-

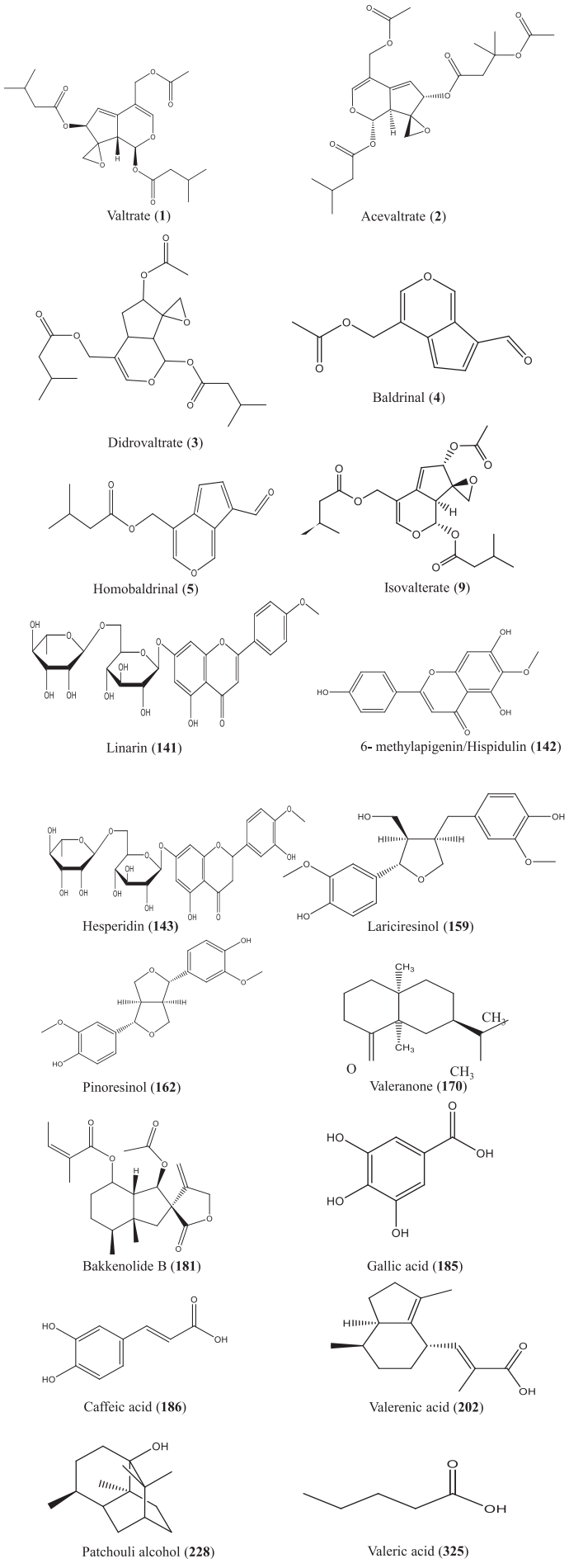

FIGURE 1 Major active constituents in *Valeriana jatamansi*

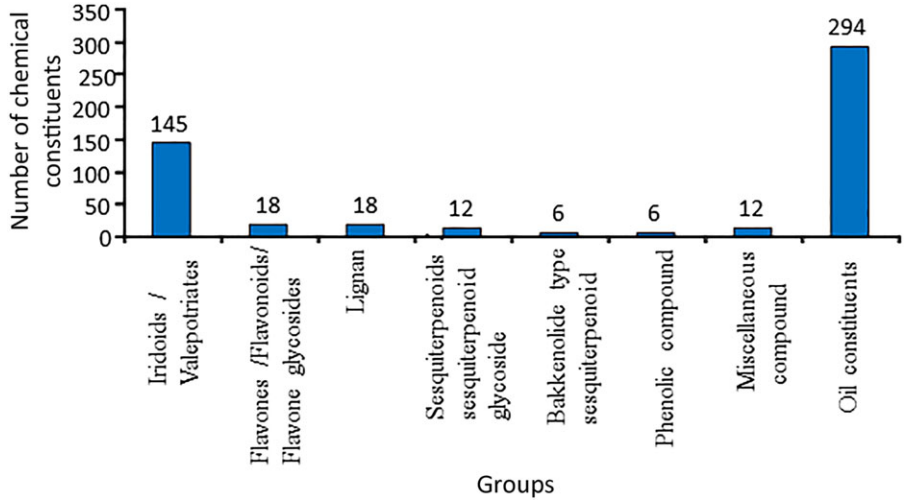

FIGURE 2 Major active constituents groups in *Valeriana jatamansi* [Colour figure can be viewed at wileyonlinelibrary.com]

desoidodidrovaltrate (**130**), desoxidodidrovaltrate (**131**), isovaltrate isovaleroyloxyhydrin (**132**), 1,5-dihydroxy-3,8-epoxyvalechlorine (**133**), rupesin E (**134**), didrovaltrate acetoxy hydrin (**135**), 10-acetoxyvaltrathydrin (**136**), isovaleroxyhydroxy-didrovaltrate (IVHD-valtrate) (**137**), 5-hydroxydidrovaltrate (**138**), (3S,4R,5S,7S,8S,9S)-3,8-epoxyoctahydro-4,8-dimethylcyclopenta[*c*]pyran-7-ol (**139**), (3S,4S,5S,7S,8S,9S)-3,8-epoxy-7-hydroxy-4,8-dimethylperhydrocyclopenta[*c*]-pyran (**140**), 4,7-dimethyloctahydrocyclopenta[*c*]pyran (**141**), hexahydro-6-hydroxy-7-(hydroxymethyl)-4-methylene cyclopenta[*c*]pyran-1(3*H*)-one (**142**), (4β,8β)-8-methoxy-3-methoxy-10-methylene-2,9-dioxatricyclo[4.3.1.$0^{3,7}$]decan-4-ol (**143**), isovalerate isovaleroxyhydrin (**144**), and homoisovaltrate (**145**) were also studied. Furthermore, significantly higher valepotriates content was reported in the rhizome of *V. jatamansi* growing in different conditions during January, October, and November months (Singh et al., 2010).

5 | FLAVONES AND FLAVONOID GLYCOSIDES

Few flavonoids and flavonoid glycosides, namely, linarin (**146**), linarin-isovalerianate (**147**), linarin-2-*O*-methylbutyrate (**148**), 6-methylapigenin/hispidulin (**149**), hesperetin-7-*O*-β-rutinoside [2S(-) hesperidin (**150**)], and acacetin-7-O + rutinoside (**151**) have been isolated from the roots of *V. jatamansi* (Glaser, Schultheis, Moll, Hazra, & Holzgrabe, 2015; Marder et al., 2003; Thies, 1968). Two new flavone glycosides, acacetin 7-*O*-β-sophoroside (**152**) and acacetin 7-*O*-(600-*O*-a-L-rhamnopyranosyl)-β-sophoroside (**153**) were also isolated from the rhizomes and roots of *V. jatamansi* (Tang et al., 2003). Similarly, kaempferol 3-*O*-β-rutinoside (**154**), rutin (**155**), kaempferol 3-*O*-β-D-glucopyranoside (**156**), quercetin 3-*O*-β-D-glucopyranoside (**157**), kaempferol (**158**), and quercetin (**159**) were also reported from the roots and rhizomes of this herb (Tang et al., 2003). Daucosterol (**160**) and trans-caffeic acid (**161**) were identified from rhizomes and roots of *V. jatamansi* (El-Mousallamy, Hawas, & Hussein, 2000; Jares, Tettamanzi, & Pomilio, 1990; Morishita et al., 1987; Tang et al., 2003; Zheng, Tang, Lou, & Zhi, 2000). Two other flavonoids, namely, acacetin 7-*O*-β-D-glucopyranoside (**162**) and apigenin 7-*O*-β-D-glucopyranoside (**163**), have been isolated from rhizomes and roots of the *V. jatamansi* (Bennini, Chulia, Kaouadji, & Thomasson, 1992; Itokawa, Suto, & Takeya, 1981; Tang et al., 2003; Thies, 1968).

6 | LIGNANS

Five lignan compounds, namely, massoniresinol-4′-*O*-β-D-glucoside (**164**), berchemol-4′-*O*-β-D-glucoside (**165**), pinoresinol-4,4′-di-*O*-β-D-glucoside (**166**), 8-hydroxypinoresinol-4′-*O*-β-D-glucoside (**167**), and pinoresinol-4-*O*-β-D-glucoside (**168**) were isolated from the roots and rhizome of *V. jatamansi* (Navarrete, Avula, & Choi, 2006). Few other lignans such as lariciresinol (**169**), pinsepiol (**170**), syringaresinol (**171**), pinoresinol (**172**), monomethylpinoresinol (**173**), cyclo-olivil (**174**), 5′-hydroxypinoresinol (**175**), massoniresinol (**176**), berchemol (**177**), and 4,4′,9,7′-tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan (**178**) were also identified from the whole plant of this herb (Lin et al., 2010). A new lignan compound known as (+)-9′-isovaleroxylariciresinol (**179**) is isolated from *V. jatamansi* (Lin et al., 2010). Podophyllotoxin (**180**) and 4′-demethylpodophyllotoxin (**181**) are the compounds for the first time isolated from *V. jatamansi* (Glaser et al., 2015).

7 | MAJOR SESQUITERPENOIDS AND SESQUITERPENOID GLYCOSIDES

A compound known as jatamansone (Valerenone) (**182**) has been isolated from *V. jatamansi* (Arora & Arora, 1963). Three sesquiterpenoids compounds, namely, valerianannoids A–C (**183**–**185**) have been isolated from *V. jatamansi* (Ming, Yu, Yang, & He, 1997). Three sesquiterpenoids hydroxyvalerenic acid (**186**), acetoxyvalerenic acid (**187**), and valerenic acid (**188**) were isolated from the roots and rhizome of *V. jatamansi* (Navarrete et al., 2006). Recently, three new sesquiterpenoids, namely, valerianannoids D (**189**), valerianannoids E (**190**), and clovane-2β-isovaleroxy-9α-ol (**191**) were isolated from the roots of *V. jatamansi*, and their structure were elucidated using spectroscopic methods (Dong et al., 2015). Comprative assessment of the NMR data of valerianannoids D (**189**) with those of the known compound valerianannoids C (**185**) revealed that they are structural analogues; however, the only difference was the AcO group at C-2

position in valerianananoid C (**185**), which was replaced by a feruloyl group in valerianananoids D (**189**). More recently, a sesquiterpenoid glycoside named as valerianananoid F (**192**) was isolated from the roots of *V. jatamansi*, and its structure has been elucidated using spectroscopic methods (Tan et al., 2016). Similarly, a new secoiridoid glycoside compound named as isopatrinioside (**193**) has been isolated from the roots of *V. jatamansi* (Tan et al., 2016).

8 | BAKKENOLLIDE TYPE SESQUITERPENOIDS

Four bakkenollide type sesquiterpenoids named as valerilactones A (**194**) and B (**195**) and two known analogues bakkenollides B (**196**) and H (**197**) have been isolated from the roots of *V. jatamansi* (Xu, Yang, et al., 2011). Two other bakkenollide type sesquiterpenoids extracted from whole plant of this species were 4-hydroxy-8-methoxy-3-methyl-10-methylene-2, 9-dioxatricyclo (4, 3, 1, 03, 7)-decane (**198**) and longiflorone (**199**) (Lin et al., 2010).

9 | PHENOLIC COMPOUNDS

Six phenolic compounds, namely, gallic acid (**200**), catechin (**201**), hydroxybenzoic acid (**202**), caffeic acid (**203**), chlorogenic acid (**204**) and *p*-coumaric acid (**205**) have been quantified from aerial and root portions of *V. jatamansi* and suggested that except gallic acid (**200**), all the phenolic constituents were significantly influenced by the growing condition (wild and planted) and plant portions (Bhatt et al., 2012; Jugran et al., 2016).

10 | MISCELLANEOUS COMPOUNDS

There are several other compounds such as trans-*p*-coumaric acid (**206**), β-sitosterol (**207**), behenic acid (**208**), nonadecyl alcohol (**209**), decursidin (**210**), decursitin B (**211**), decursitin A (**212**), 3′(S)-acetoxy-4′(R)-angeloyloxy-3′,4′-dihydroxanthyletin (**213**), dibutyl phthalate (**214**), cinnamic acid bornyl ester derivatives (**215**), bornyl caffeate (**216**), and villoside aglycone (**217**) were also reported from *V. jatamansi*.

11 | ESSENTIAL OIL COMPOSITION

Essential oils comprise an important part of *V. jatamansi*. Over 290 compounds have been identified from the essential oils of *V. jatamansi*, mainly including monoterpenes and sesquiterpenes (Table S4). Studies on rhizome and root oil of this herb has shown the representation of large number of compounds such as valerenic acid (**188**); isovaleric acid (**218**); valeranone (**219**); 1-pinene (**220**); camphene (**221**); α-santalene (**222**); ar-curcumene (**223**); xanthorrhizol (**224**); α-terpineol (**225**); bornyl isovalerate (**226**); maaliol (**227**); valtrate (**1**); didrovaltrate (**3**); patchouli alcohol (**228**); 8-acetoxy patchouli alcohol (**229**); and α, β, and γ-patchoulene (**230**–**232**) (Arora & Arora, 1963; Bos et al., 1996; Kapoor, 1990; Keochanthala-Bounthanh, Haag- Berrurier, Beck, & Anton, 1993; Nadkarni, 1976; Sati et al., 2005). Besides, leaf and root oil of *V. jatamansi* analyzed by GC and GC/MS demonstrated the presence of 20–23 compounds (Sati et al., 2005). Maaliol (**227**) and 3-methylvaleric acid (**233**) were the major constituents of the leaf oil; however, maaliol (**227**) and β-gurjunene (**234**) was recorded maximum in root oil (Sati et al., 2005).

Bos et al. (1997) detected unidentified sesquiterpene hydrocarbon, α-santalene (**222**), ar-curcumene (**223**), and xanthorrhizol (**224**) in the root and rhizome oil of *V. jatamansi* of European origin whereas patchouli alcohol (**228**) was the main component in case of Nepalese and commercially available roots material, except one sample. Likewise, wild growing populations of *V. jatamansi* displayed higher patchouli alcohol (**228**), maaliol (**227**), isovaleric acid (**218**), and viridiflorol (**235**) in rhizome oils, and α-bulnesene (**236**), α-guaiene (**237**), bornyl acetate (**238**), 7-epi-α-selinene (**239**), γ-patchoulene (**232**), and β-elemene (**240**) relatively higher in root oils of all studied populations (Verma et al., 2011). Agnihotri, Wakode, and Ali (2011), observed mainly sesquiterpenes such as carotol (**241**), germacrene B (**242**), cis-β-farnesene (**243**), α-humulene (**244**), and humulene epoxide-II (**245**) in the oil extracted from the whole plant of *V. jatamansi*. Nine significant compounds were detected in the oil extracted from the fresh roots of 16 accessions of *V. jatamansi* (Sundaresan et al., 2012). Chemotype-1, comprises maaliol (**227**) as the major compound, followed by β-gurjunene (**234**), viridiflorol (**235**), (E)-caryophyllene (**246**), and α-santalene (**222**). The chemotype-2 was dominated by patchouli alcohol (**228**), followed by α-bulnesene (**236**), viridiflorol (**235**), and α-patchoulene (**230**). Chemotype-3 found to contain patchouli alcohol (**228**) and maaliol (**227**) as major compounds, followed by α-bulnesene (**236**).

In another experiment, 27 compounds were identified in the roots oil of *V. jatamansi* including patchoulol (**247**), α-bulnesene (**236**), isovaleric acid (**218**), α-guaiene (**237**), and 3-methylvaleric acid (**233**) as the major compounds using GC–MS (Thusoo et al., 2014). Raina and Negi (2015) studied 21 compounds in the oil isolated from roots of *V. jatamansi* by GC and GC–MS. Patchouli alcohol (**228**), maaliol (**227**), seychellene (**248**), calarene-β-gurjunene (**249**), and α-santalene (**222**) were identified as major compounds. Other compounds present were bornyl acetate (**238**), α-guaiene (**237**), α-bulnesene/delta-guaiene (**236**), 7-epi-α-selinene (**222**), kessane (**250**), spathulenol (**251**), viridiflorol (**235**), α-patchoulene (**230**), and β-patchoulene (**231**).

Pandian and Nagarajan (2015) detected 76 compounds including isovaleric acid (**218**), 3-methylvaleric acid (**233**), and seychellene (**248**) as major compounds from hydro distilled oil of *V. jatamansi*. Similarly, 98 and 76 compounds were identified in the supercritical CO_2 fluid extracts extracted at 100 and 200 bar pressure using GC–MS. The major compounds identified were cis-adamantane-2-carboxylic acid (**252**), 4-hydroxy (**253**), isovaleric acid (**218**), β-bisabolol (**254**), and bornyl isovalerate (**220**), from the *V. jatamansi* extract at 200 and 100 bar pressure, respectively. Other major compounds present in the supercritical fluid extracts were β-methasone valerate (**255**), valeranone (**219**), benzyl isovalerate (**256**), nerolidol (**257**), 3-methylvaleric acid (**233**), and geranyl isovalerate (**258**), and these were either absent or present in trace amount in the hydrodistilled essential oil.

GC and GC–MS analysis of the essential oil extracted from wild and planted material of *V. jatamansi* revealed the presence of 20 compounds (Bhatt et al., 2012). V. jatamansi Highest amount of patchouli

alcohol (**228**) was recorded in the samples of planted source than wild. Other major compounds detected in both the samples (wild and planted) were seychellene (**248**), α-guaiene (**237**), and α-humulene (**238**), whereas δ-guaiene (**259**) was isolated only from wild individuals. Other oil compounds (**260**–**511**) reported from *V. jatamansi* using GC and GC–MS analysis are presented (Table S4). Moreover, studies on seasonal variation in essential oil in the rhizomes of *V. jatamansi* in different conditions have revealed that essential oil yield was significantly higher during May month (Singh et al., 2010).

12 | MEDICINAL USES AND PHARMACOLOGY PROPERTIES

Various uses and pharmacological properties of *V. jatamansi* are reported (Table 1; Figure 3). The medicinal uses and pharmacological activities ascribed to *V. jatamansi* are mentioned below.

12.1 | Stress relaxant and neuroprotective effects

Various compounds isolated from *V. jatamansi* shown varying degree of effects to reduce stress and nervous disorders. Plant extract of this herb has been found to attenuate stress, anxiety, and depression (Bhattacharya, Jana, Debnath, & Sur, 2007). The species also found beneficial for cerebro-spinal system, hypochondriasis, insomnia, migraines, nervous unrest, nervous tension, neuralgia, and neuroasthemia (Cionga, 1961). The extract showed the depressed central nervous system activity in mice by oral administration (You et al., 2012). The valiracyl possessed a pronounced neurotropic effect (Dunaev, Trzhetsinskii, Tishkin, Fursa, & Linenko, 1987), suppressed the orientation reflex of animals, decreased a spontaneous and caffeine-stimulated motor activity, potentiated and prolonged the action of barbiturates, significantly reduced aggressiveness of animals, decreased sensitivity to the contraction effects of corasol and thiosemicarbazide, and produced the antihypoxic and mild myorelaxant actions (Dunaev et al., 1987). The neurotropic effects of valiracyl were found related to the increased level of the gamma-aminobutyric acid (GABA) inhibition mediator and decreased intensity of bioenergetic processes in the brain (Dunaev et al., 1987). The effect of chlorophyll and aqueous extract examined on ischemia and reperfusion-induced cerebral injury markedly attenuated in terms of decreased infarct size, increase in short term memory, motor coordination, and lateral push response (Rehni, Pantlya, Richa, & Singh, 2007).

Valepotriate, jatamanvaltrate N (**29**) from the roots of *V. jatamansi*, exhibited weak neuroprotective activities (Xu, Guo, Fang, et al., 2012). Jatamanvalterate P (**31**) is a novel iridoid ester isolated from *V. jatamansi* traditionally used for treatment of nervous disorder (Yang et al., 2017). Jatamanvaltrate G (**22**), chlorovaltrate (**34**), valeriandoids A (**35**), valeriandoids C (**37**), 1,5-dihydroxy-3,8-epoxyvalechlorine (**63**), valeriotriate B (**120**), and jatamandoid A (**127**) isolated from this herb demonstrated moderate neuroprotective activities whereas valerilactones A (**196**), valerilactones B (**195**), and Bakkenolide-H (**197**) displayed strong neuroprotective activity against 1-methyl-4-phenylpyridinium (MPP^+)-induced neuronal cell death in dopaminergic neuroblastoma SH-SY5Y cells (Xu, Zhao, et al., 2011). Another *in vitro* study demonstrated that the jatamanvaltrate G (**22**), valeriotriate B (**120**), and jatamandoid A (**127**) isolated from *V. jatamansi*, jatamandoid A (**127**) displayed maximum neuroprotective activity whereas valeriotriate B (**120**) and jatamanvaltrate G (**22**) exhibited moderate effects (Xu, Guo, Guo, et al., 2012). Jatamanvaltrate H (**23**); jatadoids A (**64**); jatairidoids A (**66**), B (**67**), and C (**68**) isolated from *V. jatamansi* also exhibited moderate neuroprotective property against MPP^+-induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells (Xu, Guo, Xie, et al., 2012; Xu, Li, Guo, et al., 2012). Moreover, bakkenollides, valerilactones A (**194**), valerilactones B (**195**), and bakkenollide-H (**197**) extracted from the roots of *V. jatamansi* showed potent neuroprotective effects against MPP^+-induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells (Xu et al., 2011). Administration of Wistar Albino rats with 20 and 40 mg/kg valeric acid i.p. significantly decrease escape latency and retention transfer latency, as compared with intracerebroventricular-streptozotocin group (Vishwakarma, Goyal, Gupta, & Dhar, 2016). Likewise, isopatrinioside (**193**) isolated from *V. jatamansi* revealed moderate neuroprotective effects against $CoCl_2$-induced neuronal cell death in PC12 cells (Tan et al., 2016).

Valeric acid (**325**) isolated from *V. jatamansi* possesses similar structure to the neurotransmitter GABA and act as an NMDA-receptor antagonist by displaying the neuroprotective effect through amelioration of intracerebroventricular streptozotocin induced neurodegeneration in Wistar rats (Vishwakarma et al., 2016). Valeric acid (**325**) was isolated from dichloromethane extract of coarsely powdered rhizomes of *V. jatamansi* and characterized using Fourier-transform infrared spectroscopy. Picrotoxin (2 mg/kg) was used as GABA-A antagonist. Intracerebroventricular administration of streptozotocin significantly enhanced escape latency, retention transfer latency in treated rats as compared with control. Administration with *V. jatamansi* extract (100 and 200 mg/kg) and valeric acid (20 and 40 mg/kg) significantly decreased the escape latency and retention transfer latency than intracerebroventricular-streptozotocin group, thereby suggesting the significant GABAergic effect of valeric acid (**325**) in amelioration of experimental dementia.

Oxidative stress and inflammation are among contributing factors for dopaminergic neurodegeneration in Parkinson's disease. Parkinson's disease induced mice supplemented orally with varying extract doses of *V. jatamansi* significantly recuperated the altered behavioral test scores, striatal dopamine levels, mid brain TH^+ cell count and TH protein levels, increased GFAP expression and the histopathological changes. In addition, decrease in the level of antioxidants and increase in the level of reactive oxygen species, lipid peroxidation, and inflammatory cytokines were also significantly reduced which clearly indicated the potential of the species to mitigate oxidative stress and inflammatory damage in Parkinson's disease.

12.2 | Sedative and tranquillizing effect

V. jatamansi is reported to be effective in treating various sleeping disorders in human. Valerenic acids and iridoid glycosides from *V. jatamansi* are responsible for sedative activity. Clinical trials on *V. jatamansi* have confirmed that root extract reduces sleep latency

TABLE 1 Major pharmacological activities of *Valeriana jatamansi* extract

S. no.	Activity	Plant part	Extract/compound	Model/system	Formulation/dosage	Result	Reference
1	Neuroprotective effects	Rhizome	Lypholized extract	SH-SY5Y neuroblastoma cells	Powdered material with 50% methanol kept for 24 hr and filtered. The filtrate was lyophilized and used	The IC_{50} value of the extract was 2.21 mg/ml. In MPP^+ treated cells 0.5 mg and 1 mg/ml dose exhibit significant improvement in cell viability, whereas after 8 and 16-hr post MPP^+ treatment, the effect was significant at 1 mg/ml concentration. Significant protective effect of the extract (1 mg/ml) in tunicamycin-treated cells was observed only at 0 hr.	Sridharan, Kumar, Jeepipalli, & Sadras, 2014
	Neurodegeneration	Root	Extract in dichloromethane	Wistar Albino rats	Extract 100 and 200 mg/kg, p.o. (suspended in 1% CMC solution)	Both extract doses significantly decreased the escape latency and retention transfer latency, as compared with intracerebroventricular-streptozotocin group. Administration of picrotoxin significantly reversed the effects produced by plant extract and valeric acid in intracerebroventricular-streptozotocin treated rats.	Vishwakarma et al., 2016
2	Acute and chronic toxicity	Rhizome	Hydroethanolic extract	Swiss albino mice	Acute toxicity: p.o. was administered orally with 2000 mg/kg body weight. Chronic toxicity p.o. administered with three different doses 200, 600, and 1,800 mg/kg/body weight/day	No sign of abnormality, morbidity, or mortality was recorded in acute toxicity assay. However, significant differences in the loss of auditory startle, aggressiveness (control > treated), nasal discharge, and dyspnea were recorded in treated and control groups in chronic toxicity. At necropsy, tracheitis was observed in three cases. Photoactometer test displays dose-dependent increase in sedative property.	Joseph et al., 2016
	Acute toxicity	Roots and rhizomes	Dichloromethane extract/essential oil	LACA mice	Three fixed doses of 25, 200, and 2,000 mg/kg	Oral administration of oil (10–2,000 mg/kg) did not produce toxic effect or lethality. Toxic effect and mortality was detected in mice up to 2,000 mg/kg, p.o. dose of extract during 48 hr of observation period.	Sah, Mathela, & Chopra, 2012
	Acute and subchronic toxicity	Root and rhizome	Iridoids rich fraction (IRFV)	Adult mice	Single dose p.o. 3,200 mg/kg body weight. In the subchronic toxicity study p.o. was administered with low (240 mg/kg body weight), middle (960 mg/kg body weight), and high doses (1,200 mg/kg body weight)	No significant difference detected in the body weight. The maximum tolerated dose of IRFV was 3,200 mg/kg. In the subchronic toxicity study, the daily single oral doses did not result in death nor affected the general behavior. No significant differences were observed in the hematological and blood biochemical parameters, and no abnormality of other organs were recorded. The lethal dose with 50% mortality rate (LD_{50}) on mice was over 2,000 mg/kg body weight.	Xu et al., 2015
3	Gastrointestinal and cardiovascular disorders	Rhizome	Crude extract and its fractions	Rabbit, Guinea pigs and Sprague–Dawley rats	P.o. 0.1–3.0 mg/ml	Crude extract cause relaxation in spontaneous contractions in rabbit jejunum preparation. Test against high K^+ (80 mM)-induced contractions it produced weak inhibitory effect, whereas caused complete relaxation of the contractions induced by low K^+ (20 mM). Intravenous administration of crude extract produced fall in arterial blood pressure in normotensive anaesthetized rats. In rabbit aortic preparations, plant extract caused a selective and glibenclamide-sensitive relaxation of low K^+ (20 mM)-induced contractions.	Gilani et al., 2005

(Continues)

TABLE 1 (Continued)

S. no.	Activity	Plant part	Extract/compound	Model/system	Formulation/dosage	Result	Reference
4	Sedative and tranquillizing effect	Roots and rhizomes	Dried fractions	Adult male Wistar rats/adult male Swiss mice	6-Methylapigenin (MA) and 2S(-)-hesperidin (HN) dissolved by the sequential addition of 10% di methyl sulfoxide, 10% ethanol, and 80% saline	Intraperitoneal administration of HN at a dose of 2 mg/kg increased the sleeping time. This HN hypnotic action was potentiated by the addition of 1 mg/kg MA at the anxiolytic dose.	Marder et al., 2003
	Primary insomnia	Rhizomes	Dry powdered material	Human	4 g powdered material with milk	Significantly ($p < 0.001$) improve sleep initiation (76%), sleep duration (55.17%), disturbed sleep (69.58%), and disturbances in routine work (73.95%).	Toolika, Bhat, & Shetty, 2015
5	Anxiety	Whole plant	Ethanolic extract	Male, Sprague–Dawley rats	Low (0.015 g/ml), medium (0.030 g/ml), and high (0.045 g/ml) extracts doses p.o.	Expression of Elk-1, Ets-1, Apaf-1, Bax, and Bcl-2 genes were up-regulated in the model group. But the abnormal gene expressions were adjusted in the other groups, which suggest the important role of the species in regulating the abnormal apoptosis-related gene expression.	Yan et al., 2011
6	Antidepressant effect	Roots and rhizomes	Dichloromethane extract	Mouse	P.o. 10, 20, and 40 mg/kg extract	Extract (40 mg/kg) significantly inhibited the immobility period. Similarly, chronic administration of 20 and 40 mg/kg extract significantly reduced the immobility period and significantly ($p < 0.05$) increased norepinephrine and dopamine level in mouse forebrain.	Sah et al., 2011
7	Antispasmolytic and blood pressure lowering activity	Rhizome	Crude extract	Rabbits and Guinea Pig	Crude extract p.o. 0.1–3.0 mg/ml	The crude extract caused inhibition of spontaneous contractions of isolated rabbit jejunum preparations. The spasmolytic effect was dose dependent, mediated at the dose range of 0.1–3.0 mg/ml with a median effective concentration (EC_{50}) of 0.60 ± 0.06.	
8	Antinociceptive effect	Roots and rhizome	Dichloromethane extract/essential oil	LACA mice	P.o. 20, 40, and 80 mg/kg	Dose-dependent inhibition of acetic acid induced writhes was observed and the effect being significant at 80 mg/kg. The reduction (37.8%) in the writhing response was with 80 mg/kg. Essential oil at doses 40 and 80 mg/kg produced significant reduction (28.2% and 47.9%, respectively) in writhing. A time dependent increase in tail flick latency at 80 mg/kg. Essential oil (20 mg/kg, p.o.) potentiated the antinociceptive action of asprin.	Sah et al., 2012
9	Antidiarrheal and bronchodilatory activities	Rhizomes	Crude extract	Mice and Guinea-pig	P.o. 300 and 600 mg/kg	Crude extract caused inhibition of castor oil-induced diarrhea in mice at 300–600 mg/kg. In guinea-pig trachea, 0.03–3.0 mg/ml doses relaxed the low K^+ (25 mM)-induced contractions, with a mild effect on the contractions induced by high K^+ (80 mM).	Khan & Gilani, 2012

(Continues)

TABLE 1 (Continued)

S. no.	Activity	Plant part	Extract/compound	Model/system	Formulation/dosage	Result	Reference
10	Anti-inflammatory activity	Rhizomes	Aqueous and methanolic extract	Adult male Sprague–Dawley rats	P.o. 100, 150, and 200 mg/kg of aqueous and methanolic extracts	Significant ($p < 0.05$) anti-inflammatory effect was exhibited by aqueous and methanolic extracts at different doses (100, 150, and 200 mg/kg) as compared with control in the carrageenan induced paw edema.	Subhan et al., 2007
	Topical anti-inflammatory activity	Whole plant	Hydrodistilled oil	Swiss albino mice	Oil in 20 µl acetone, applied on the edema induced ear for 30 min.	The essential oil exhibited significant ($p < 0.05$) activity as compared with standard drug	Agnihotri et al., 2011
11	Analgesic activity		Extract and essential oil	LACA mice	P.o. 20, 40, and 80 mg/kg in acetic acid induced writhing	Extract produced dose-dependent inhibition of acetic acid induced writhing in mice being significant at 40 and 80 mg/kg doses. Percent reduction in writhing response was 29.8% and 54.3%, respectively, at 40 and 80 mg/kg. Similarly, 40 and 80 mg/kg doses of essential oil produced significant reduction in writhing response, that is, 31.1% and 50%, respectively.	Sah et al., 2010b
12	Constipation	Fresh leaves	Crude extract	Guinea pigs	Extract solubilized in distilled water	In the ileum, the extract caused a concentration-dependent contractile effect at 3–10 mg/ml. The efficacy of the stimulant effect was 8.0 ± 1.5%, 24.7 ± 1.5%, and 36.8 ± 3.2% at the concentrations of 3, 5, and 10 mg/ml, respectively, when compared with ACh maximum response.	Khan & Gilani, 2011
13	Reverses liver cirrhosis and tissue hyperproliferative response	Rhizome	Hydroalcoholic extract	Wistar rats	Drugs extract 800 mg/kg body weight, p.o. suspended in 1% gumacacia daily	The animals treated with the drug extract demonstrated signs of improvement from liver cirrhosis.	Prasad et al., 2010
14	Anti-HCV activity	Roots	Water, chloroform, and methanol extracts	Huh-7.5 cells infected with J6/JFH chimeric HCV strain	The methanolic subfractions F1, F2, F3, and F4 at 100, 200, 400, 600, and 800 µg/ml concentrations.	Methanolic extract showed reduction in HCV replication. Significant viral inhibition was noted only in F4 fraction. Intrinsic fluorescence assay of purified HCV RNA-dependent RNA polymerase NS5B in the presence of F4 resulted in sharp quenching of intrinsic fluorescence with increasing amount of plant extract.	Ganta et al., 2017
15	Regulation of lipid metabolism	Rhizome	Iridoids rich fraction (IRFV)	Hyperlipidemia rat model	P.o. 7.5, 15, and 30 mg/kg/day	Three different dosages slow down the weight gain, reduce TG contents and increase HDL-C contents. All three dosages significantly increase the ApoA5 and PPAR-α protein expression and decrease the SREBP-1c protein expression. Whereas the LXR-α protein expression decreased in low- and high-dose groups. Pathological observation of liver tissue exhibited that IRFV improve cell degeneration to a certain extent.	Zhu et al., 2016

(Continues)

TABLE 1 (Continued)

S. no.	Activity	Plant part	Extract/compound	Model/system	Formulation/dosage	Result	Reference
16	Adeptogenic activity	Roots	Aqueous lyophilized root extract	Cold-hypoxia-restraint (C-H-R) animal model of Sprague–Dawley inbred male rats	P.o. 50, 100, 200, or 500 mg/kg body weight	Single oral dose of 200 mg/kg provided maximum adeptogenic activity. In a single dose overnight study, the extract, provided about 27.91% resistance to C-H-R induced hypothermia by delaying fall in Trec 23°C and a faster recovery by 14.46% to Trec 37°C. Maximal effective dose (200 mg/kg) administration as a single dose per day exhibited more or less similar adaptogenic activity to control.	Sharma et al., 2012
17	Enzyme inhibition activity	Leaves	Crude extract and subsequent fractions	*In vitro* assay	n-hexane, chloroform, ethyl acetate, *n*-butanol, and aqueous fractions	100 µg/ml crude extracts displayed (73%) inhibition and the IC_{50} values were 68 µg/ml. The chloroform fraction exhibited highest inhibition (76%) with IC_{50} as 61 µg/ml. The crude extract showed 82% inhibition against utyrylcholinesterase and the IC_{50} was 89 µg/ml. Ethylacetate fraction exhibited highest inhibition (86%) with the IC_{50} value of 58 µg/ml. The crude extracts showed significant inhibition against α-glucosidase enzyme. Their percent inhibition were 69% whereas the IC_{50} values were 89 µg/ml. The *n*-butanol fraction also displayed significant activity (71% inhibition) with the IC_{50} value of 71 µg/ml.	Khuda et al., 2014
18	Antioxidant activity	Roots	Essential oil, methanolic, chloroform, and aqueous extract	DPPH and chelation power on ferrous ions	15 g powdered material in 75 ml of each solvent, stirred and filtered. The filtrate was collected and dried, and solid thus obtained after evaporation of each of the solvents was labeled and stored for further use.	Methanolic extract exhibited most potent antioxidant potential (IC_{50} values 78 ± 2.9 µg/ml), followed by aqueous extract (IC_{50} values 154 ± 4.6 µg/ml). Essential oil displayed poor radical scavenging activity (IC_{50} values 876 ± 12.8 µg/ml). Methanolic extract possesses good chelation activity (76%) followed by aqueous extracts (43%) and essential oil (31%) at 100 µg/ml concentration whereas chloroform extract showed poor chelation activity (12%).	Thusoo et al., 2014
		Rhizomes	Oil and extract	DPPH, superoxide radical scavenging activity, hydroxyl radical scavenging activity, reducing power antioxidant activity	0.3 ml of hydro distilled oil, CO_2 extract at 100 and 200 bar	In all assay, the essential oil, supercritical fluid extract at 100 bar, and supercritical fluid extract at 200 bar on antioxidant activity linearly increased with increasing concentration from 0.2 to 1.0 mg.	Pandian & Nagarajan, 2015
		Root	*In vitro* assay	ABTS, DPPH, and FRAP, assay	10 g of sample was loaded per cell filled with water at a pressure of 1,500 psi. Cell was rinsed and solvent was purged from cell with N_2 gas through depressurization. The solvent was lyophilized and extract was stored in dark at 4°C until use.	Aqueous extract exhibited potent antioxidant activity of 543 ± 4.9, 234 ± 4.3, and 301.8 ± 2.14 mg of trolox/g extract when analyzed by DPPH, ABTS, and FRAP assay, respectively.	Sharma et al., 2012

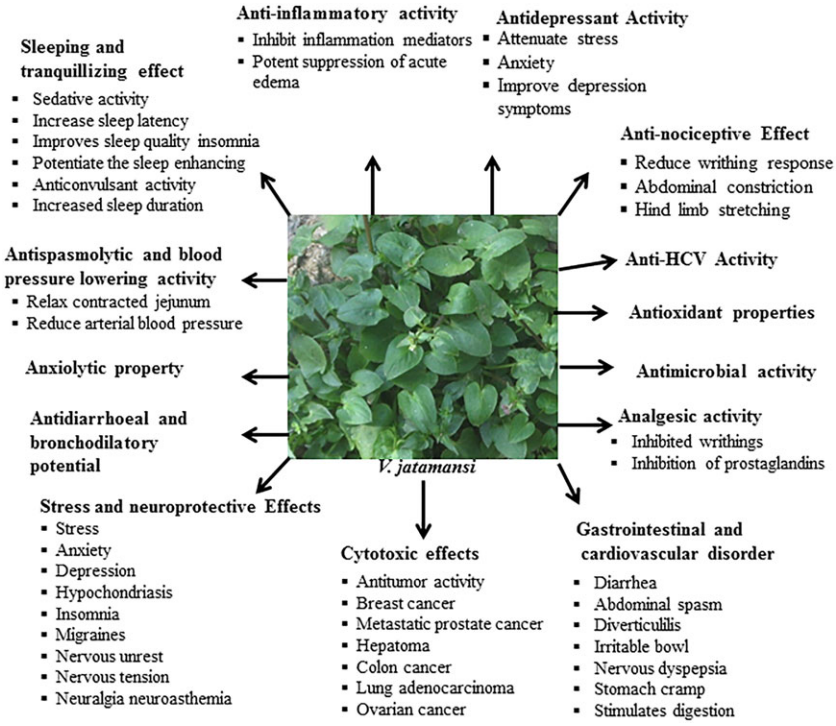

FIGURE 3 Pharmacological properties of *Valeriana jatamansi* [Colour figure can be viewed at wileyonlinelibrary.com]

and improves sleep quality and, therefore, considered useful in treating anxiety and insomnia (Leathwood & Chauffard, 1983). Pharmacological screening of valerenal and some other components showed that the sedative action can be attributed to essential oil and valepotriates fractions (Hendricks, Geertsma, & Th M Malingre, 1981; Wagner, Jurcic, & Schaette, 1980). Reports also indicated that baldrinal (**4**), homobaldrinal (**5**), decyl baldrinal (**6**), and valtroxal (**7**) are partially responsible for sedative activity as they get well absorbed and significantly decreased mortality in mice (Schneider & Willems, 1982). In addition, valerenic acid (**188**) inhibits the enzyme system responsible for central catabolism of GABA (Riedel, Hänsel, & Ehrke, 1982), and the valerian extract releases [3*H*] GABA by reversal of the GABA carrier, which is Na^+ dependent and Ca^{++}-independent (Santos et al., 1994). This increase in [3*H*] GABA release appears to be independent from Na^+-K^+-ATPase activity and the membrane potential. The evaluation of commercially available root extract of this species exhibited pronounced sedative properties in the mice with respect to a reduction in motility and an increase in the thiopental sleeping time (Leuschner, Müller, & Rudman, 1993). A direct comparison with diazepam and chlorpromazine has revealed a moderate sedative activity for the tested extract (Leuschner et al., 1993). Flavanone glycoside 2S(-)hesperidin (**150**) isolated from *V. jatamansi* was observed to potentiate the sleep enhancing properties (Marder et al., 2003). *In vivo* experiments on 6-methylapigenin (**149**) and hesperidin (**150**) on rat exhibited sleep enhancing properties (Marder et al., 2003). Flavonoid glycosides such as linarin (**146**) and hesperidin (**150**) have been reported sedative and anticonvulsant agents likely to interact with $GABA_A$ receptors (Fernandez, Wasowski, Paladini, & Marder, 2004). Similarly, valerenic acid (**188**) was observed to possess anticonvulsant properties (Hiller & Zetler, 1996). Valerenic acid (**188**) supplementation to mice also exhibited a decrease in locomotor activity. It was found that valerenic acid (**188**) decreases the breakdown of GABA in the brain and acts as $GABA_A$ receptor substrate resulting in its sedative and anxiolytic actions (Houghton, 1999). Another study on *V. jatamansi* has established that flavonoids might be responsible for sleep enhancing properties (Sharma, Chandola, Singh, & Basisht, 2007).

Adult male Sprague–Dawley rats treated with varying extract doses (100–300 mg/kg) of *V. jatamansi* studied for sleep–wake profile and EEG delta activity demonstrated that sleep latency and nonrapid eye movement sleep delta activity were significantly decreased after extract treatment (300 mg/kg). However, extract at 200 and 300 mg doses significantly decreased the duration of wake state. The levels of neurotransmitters and metabolites were significantly decreased in the cortex and brainstem region after 2 hr of extract (200 mg/kg) treatment. The study concluded that the root extract significantly declined sleep latency, enhanced duration of total sleep, NREM sleep, and decreased duration of wakefulness in treated group, which ultimately improve sleep quality and modulates brain monoamine level in rats (Sahu et al., 2012).

12.3 | Cytotoxic effects

Various compound especially valepotriates isolated from *V. jatamansi* have shown varying degree of counteracting effects on the growth and proliferation of cancer cells. Yang et al. (2017) reported that jatamanvalterate P (**31**) demonstrated concentration dependent inhibition of growth and proliferation of MCF-7 and triple negative breast cancer cell lines (MDA-MB-231, MDA-MB-453, and MDA-MB-468) and lower cytotoxicity to human breast epithelial cells (MCF-10A) using *in vitro* and *in vitro* methods. Furthermore, the treatment of jatamanvaltrate P (**31**) with triple negative breast cancer induces G2/M-phase arrest and G0/G1-phase arrest in MCF-7 cells. Molecular mechanism analysis showed that jatamanvalterate P (**31**) enhances the cleavage of PARP and caspases, which ultimately reduced the expression of Cyclin B1, Cyclin D1, and Cdc-2. It was observed that autophagy inhibition by 3-methylapigenin cotreatment undermined

jatamanvaltrate P-induced cell death. However, in case of MDA-MB-231 xenografts, jatamanvaltrate P (**31**) exhibited a potential antitumor effect (Yang et al., 2017).

Lin et al. (2013) reported the moderate cytotoxic effects of rupesin B (**33**), chlorovaltrate (**34**), and chlorovaltrates K–N (**90**–**92**) against lung adenocarcinoma (A 549), metastatic prostate cancer (PC-3M), colon cancer (HCT-8), and hepatoma (Bel 7402) cell lines with IC_{50} values of 0.89–9.76 μM. Another report showed that jatamanvaltrate P (**31**), jatamanvaltrate X (**77**), and nardostachin (**79**) isolated from whole plants of *V. jatamansi* displayed stronger cytotoxic activity against PC-3M cells (Lin, Chen, et al., 2015). Similarly, various compounds such as valtrate (**1**) and didrovaltrate (**3**) (Keochanthala-Bounthanh et al., 1993), volvaltrate B (**96**) (Lin et al., 2010), jatamanvaltrates P (**31**), Q (**32**), R (**38**), S (**39**), and T-Y (**73**–**78**) (Lin, Fu, et al., 2015) exhibited cytotoxic activity against different cell lines in *in vivo* experimentation. Moreover, lignan compound (+)-9′-isovaleroxylariciresinol (**179**) isolated from *V. jatamansi* possess significant *in vitro* cytotoxic activity against PC-3M and HCT-8 cell lines, with IC_{50} values of 8.1 and 5.3 μM, respectively (Lin et al., 2010).

Three decomposition products of valepotriates, namely, valtrals A (**99**), B (**100**), and C (**101**) demonstrated selective cytotoxicity against metastatic prostate cancer (PC-3M) and colon cancer (HCT-8) cell lines (Lin, Fu, et al., 2015). Lin et al. (2009) determined cytotoxic activity of jatamanvaltrates A–M (**16**–**28**), together with nine known valepotriates (e.g., valtrate (**1**), acevaltrate (**2**), didrovaltrate (**3**), valeriotetrate A (**125**), valeriotriate B (**60**), didrovaltrate acetoxy hydrin (**135**), 10-acetoxyvaltrathydrin (**136**), IVHD-valtrate (**137**), and 5-hydroxydidrovaltrate (**138**) on lung adenocarcinoma (A549), metastatic prostate cancer (PC-3M), colon cancer (HCT-8), and hepatoma (Bel7402) cell lines. Compounds valtrate (**1**), acevaltrate (**2**), didrovaltrate acetoxy hydrin (**135**), IVHD-valtrate (**137**), and 5-hydroxydidrovaltrate (**138**) displayed activity against all tested cell lines (IC_{50}:1.0–7.4 μM). Acevaltrate (**2**) was found to be the most active compound against the A549, PC-3M, HCT-8, and Bel7402 cell lines, respectively. Except jatamanvalterate C (**18**), jatamanvaltrate E (**20**), and 10-acetoxyvaltrathydrin (**136**), all remaining compounds exhibited cytotoxicity against the PC-3M cell line (IC_{50}: 1.4–6.3 μM).

IVHD-valtrate (**137**) isolated from *V. jatamansi* is reported to prevent the growth and proliferation of A2780 and OVCAR-3 ovarian cancer cell lines in a dose-dependent manner; however, relatively low cytotoxic properties against immortalize nontumorigenic human ovarian surface epithelial cells (IOSE-144) lines were exhibited (Lin et al., 2013). The administration of IVHD-valtrate (**137**) induces apoptosis and arrests the ovarian cancer cells in the G2/M phase. The molecular mechanisms of IVHD-valtrate (**137**) showed that it modulate the expression of numerous molecules by enhancing (p53, Rb, p21, and p27) and reducing (Mdm2, E2F1, Cyclin B1, Cdc25C, and Cdc2) their level. It was also observed to down-regulate the proportion of Bcl-2/Bax and Bcl-2/Bad and enhance the cleavage of PARP and caspases, which indicated its potential as a therapeutic agent for ovarian cancer and for development of novel chemotherapeutic compounds (Li et al., 2013). Recently, three new minor valepotriate isomers, jatamanvaltrates Z1 (**70**), Z2 (**71**), and Z3 (**72**) extracted from *V. jatamansi*, displayed moderate cytotoxicity against the lung adenocarcinoma (A549), metastatic prostate cancer (PC-3M), colon cancer (HCT-8), and hepatoma (Bel7402) cell lines with IC_{50} values of 2.8–8.3 μM (Lin et al., 2017).

Acute and chronic oral toxicity of hydroethanolic extract of *V. jatamansi* rhizome was assessed in Swiss albino mice (Joseph, Puthallath, & Rao, 2016). Acute oral toxic dose (2,000 mg/kg body weight) was evaluated by limit test. Chronic oral toxicity study was performed with three varying doses (200, 600, and 1,800 mg/kg/body weight/day). In case of acute toxicity analysis, no signs of abnormality, morbidity, or mortality were recorded during the study period. Treated and control groups exhibited significant differences in loss of auditory startle, aggressiveness (control > treated), nasal discharge, and dyspnoea. Furthermore, photoacetometer test showed dose-dependent increase in sedative property. Thus, ethanolic extract of *V. jatamansi* did not exhibit any toxicity on single oral dose or chronic doses administration in healthy animals.

12.4 | Gastrointestinal and cardiovascular disorder

V. jatamansi is used for treating different gastrointestinal disorder such as diarrhea, abdominal spasm, diverticulilis, irritable bowl, nervous dyspepsia, and stomach cramp and for stimulating digestion (Houghton, 1999). The extract of the species was used for lowering blood pressure and strengthening and palpitations of the heart (Morazzoni & Bombardelli, 1995). Gilani, Khan, Jabeena, Subhan, and Ghafar (2005) demonstrated that this herb possesses antispasmodic and hypotensive effects, which possibly mediated through K-ATP channel activation, and supports its use in gastrointestinal and cardiovascular disorder. The mechanism of iridoid isolated from *V. jatamansi* treating irritable bowel syndrome was investigated in male Sprague–Dawley rats. The control groups were administered with fluoxetine (2.5 mg/kg, positive control) or distilled water (negative control). It was observed that in model group, 5-HT content in colon and serum increased significantly but decreased significantly in hypothalamic region. In three iridoid-treated groups, the content of 5-HT in colon and serum decreased but increased in hypothalamic whereas no markable change was detected in 5-HIAA. The value of 5-HT/5-HIAA also reduced in colon and serum. The mechanism of iridoid from *V. jatamansi* treating irritable bowel syndrome may be related to the regulatory effect to the levels of 5-HT from gastrointestinal to central nervous system (Yan, Zhang, Pan, & Zuo, 2011).

12.5 | Anxiolytic property

6-Methylapigenin (**149**) isolated from *V. jatamansi* as a new flavonoid compound is a benzodiazepine binding site ligand and exhibited anxiolytic property. 6-Methylapigenin (**149**) functioned as a competitive ligand for the brain $GABA_A$ receptors (Wasowski, Marder, Viola, Medina, & Paladini, 2002). Shi et al. (2014) investigated the anxiolytic effects of valtrate (**1**) in rats by oral administration with different doses followed by subsequent exposure to open field test and elevated plus maze. Valtrate (**1**) exhibited the anxiolytic effect in rats by increasing the time and entry percentage into the open arms in the elevated plus maze and the number of central entries in the open field test. Furthermore, it significantly reduces the corticosterone level in the rat serum,

which clearly suggests the anxiolytic activity of valtrate (**1**) in behavioral models possibly mediated via the function of hypothalamus–pituitary–adrenal axis (Shi et al., 2014). Gene chip technology was used to investigate the gene expression difference among apoptosis-related genes in normal rats, anxiety model rats, and rats administred with *V. jatamansi* extract. The expression of Elk-1, Ets-1, Apaf-1, Bax, and Bcl-2 genes were up-regulated in the model group as compared with normal group, whereas gene expression was recorded abnormal in the other groups. These results indicated that the species can play important role in regulating the abnormal apoptosis-related gene expression in the anxiety rat model (Yan et al., 2011). The anxiolytic properties of compound *V. jatamansi* were also studied in mice (You et al., 2012).

12.6 | Antidepressant activity

Depressive disorder is a common affliction; however, therapeutic agents are currently available for treating depression. The rate of success in depressed patients is about 65–70%, but serious side effect may limit treatment strategies (Keith & Mathews, 1993). Bhattacharya et al. (2007) described a method for clinical study on *V. jatamansi* extract to attenuate stress, anxiety, and improvement in the symptoms of depression. It was observed that *V. jatamansi* extract significantly reduced locomotor activity at 200 mg/kg in the tail suspension test and has a negative functional interaction with antidepressant-like effects. The methanolic and aqueous ethanolic extracts of *V. jatamansi* have indicated that antidepressant-like action of this plant was not contingent upon its terpenoids (Subhan, Karim, Gilani, & Sewell, 2010). However, a considerable degree of antilocomotor activity was reported at the higher doses of terpenoids in tail swim test or forced swim test (Subhan et al., 2010). Sah, Mathela, and Chopra (2011) reported the antidepressant effect of dichloromethane extract of *V. jatmansi* patchouli alcohol chemotype in albino Laca mice using forced swim test. Acute toxicity was determined by treating the mice with varying extract doses (10, 20, and 40 mg/kg, p.o.). Single extract dose (40 mg/kg) administration in mice significantly ($p < 0.05$) inhibited the immobility period. Meanwhile, the chronic extract doses (20 and 40 mg/kg) significantly reduced the immobility period and increased the levels of norepinephrine and dopamine in mouse forebrain, which clearly demonstrated antidepressant effect of *V. jatamansi*.

12.7 | Antispasmolytic and blood pressure lowering activity

Gilani et al. (2005) reported the antispasmolytic and blood pressure lowering effects of crude extract of *V. jatamansi* rhizome and its fractions. Test against high K^+ (80 mM)-induced contractions produced weak inhibitory effect but completely relaxed the contractions induced by low K^+ (20 mM). In guinea pig ileum, the plant extract produced similar results as in rabbit jejunum. Furthermore, blood pressure lowering effect of the *V. jatamansi* extract (10–100 mg/kg i.p. administered) in rats showed a dose-dependent fall in mean arterial blood pressure in normotensive anaesthetized rats. Study concluded that the valeranone (**219**) isolated from the species possess hypotensive activity (Arora & Arora, 1963), which might be responsible for lowering blood pressure effect of *V. jatamansi*. Valepotriates [valtrate (**1**) and didrovaltrate (**3**)] of the species also reported to exert spasmolytic effect (Wagner et al., 1980). The commercial mixture of valepotriates was found effective as compared with the same dose of standard papaverine (Gilani et al., 2005). Antispasmodic and blood pressure lowering activities of the root portion of *V. jatamansi* revealed that these activities might be mediated through activation of K^+ (ATP) channel thereby justified its use in gastrointestinal and cardiovascular disorders (Gilani et al., 2005).

12.8 | Anti-inflammatory activity

Khuda, Iqbal, Khan, Zakiullah, and Shah (2013) reported the anti-inflamatory effect of the crude leaves extract of *V. jatamansi* using *in vivo* and *in vitro* assays. Leaves of *V. jatamansi* were extracted in methanol, filtrated and obtained crude extract, dissolved in water, and then sequentially partitioned with various solvents. Methanolic extract topical formulation (cream) of the species were screened for anti-inflammatory activity using carrageenan-induced hind paw edema test and its effect on the acute and chronic phase inflammation models in male Wistar rats. Methanolic extract and its fractions were also investigated for *in vitro* anti-inflammatory activity using lipoxygenase inhibition assay. Leaves of *V. jatamansi* showed substantial *in vitro* anti-inflammatory activity than the standard carrageenan. This activity was present in ethyl acetate fraction during *in vitro* screening (IC_{50}: 76) as compared with that of standard (IC_{50}: 6.11). These results demonstrated that the ethyl acetate fraction of the crude extract of *V. jatamansi* can be used for the isolation of new anti-inflammatory lead compounds. Other studies also reported the anti-inflammatory activity of methanolic and ethanolic extract of this species (Subhan, Karim, & Ibrar, 2007) and known to inhibit inflammation mediators such as histamine, serotonin, prostaglandins, and bradykinins (Vinegar, Schreiber, & Hugo, 1969). In another study, adult male Sprague–Dawley rats administered with aqueous and methanolic extracts (100, 150, and 200 mg/kg, p.o.) of *V. jatamansi* exhibited significant ($p < 0.05$) anti-inflammatory effect as compared with control, which was comparable with the reference drug aspirin (Subhan et al., 2007). Agnihotri et al. (2011) reported the suppression of xylene induced topical anti-inflammation by essential oil obtained from whole plant of *V. jatamansi*. It was found that topical application of essential oil to the mouse ear resulted to potent suppression of acute edema induced by xylene, which clearly suggested the topical anti-inflammatory effect of this herb is comparable with standard drug diclofenac.

12.9 | Hepatoprotective and tissue hyperproliferative response

Liver cirrhosis is developed in response to hepatocellular injury generally caused by chronic viral hepatitis, alcohol abuse, nonalcoholic steatohepatitis, inborn errors of metabolism, parasitemia, and a variety of chemical and toxic substances. It is the end stage of liver fibrosis, which ultimately caused shrinkage of the liver, portal hypertension, and liver failure (Torok, 2008; Le Bousse-Kerdiles, Martyre, & Samson, 2008). Prasad et al. (2010) provide evidences indicating the effect of

the dried rhizome extract of *V. jatamansi* in an animal model of liver cirrhosis and on cell proliferation. Oral administration of extracts of this herb in the thioacetamide induced liver cirrhosis partially reverse the elevated levels of alkaline phosphatase, γ-glutamyl transferase, and other biochemical markers of hepatic injury as well as the drug-metabolizing enzymes. Histopathological screening of the hepatic tissue supports the therapeutic effect of the extract, which was confirmed by biochemical changes. The extract was also found to reduce hepatic cell proliferation in rats injected with thioacetamide.

12.10 | Anticholinesterase activity

Search for potent anticholinesterase inhibitors is an area of research interest in modern era. Anticholinesterase activities against the butyrylcholinesterase and acetylcholinesterase enzymes are considered to be related to the prognosis of cognitive diseases. Acetylcholinesterase, butyrylcholinesterase, and alpha-glucosidase inhibiting activities of crude extract of *V. jatamansi* and its fractions were found to possess considerable activity against cholinesterase (Khuda, Iqbal, Khan, Zakiullah, & Khan, 2014). Likewise, chloroform fractions of this herb displayed significant activity against acetylcholinesterase (IC_{50}: 61 μg/ml) whereas ethyl acetate fractions exhibited significant activity against butyrylcholinesterase enzymes (IC_{50}: 58 μg/ml). These results demonstrated the potential therapeutic role of *V. jatamansi* for discovery of new lead compounds for curing cognitive dysfunctions such as Alzheimer's disease. Dong et al. (2015) showed that several compounds such as jatamanvaltrates R–S (**38**–**39**), jatamanin Q (**40**), volvaltrate B (**96**), valeriananoids D–E (**189**–**190**), clovane-2β-isovaleroxy-9α-ol (**191**), valeriananoids A–C(**183**–**185**), valeriotetrate A (**125**), valeriotetrate B (**60**), 8, 11-desoidodidrovaltrate (**130**), rupesin E (**134**), and (3S,4R,5S,7S,8S,9S)-3,8-ethoxy-7-hydroxy-4,8-dimethylperhydrocyclopenta[c]pyran (**140**) isolated from *V. jatamansi* showed acetylcholine esterase activity inhibition ratio of less than 10% at the concentration of 50 μM whereas the positive control (tacrine) displayed an inhibition rate of 47.6% at 0.33 μM.

12.11 | Antioxidant properties

V. jatamansi possess enormous antioxidant properties and can be considered as a natural source of antioxidants. For example, Kalim, Bhattacharya, Banerjee, and Chattopadhyay (2010) analyzed the antioxidant activity in the root extracts of *V. jatamansi* using different assays (DPPH free radical scavenging, hydroxyl radical [OH] scavenging, peroxynitrite scavenging activity, nonenzymatic superoxide radical scavenging activity, and nitric oxide scavenging activity) demonstrated that the species possess enormous antioxidant activity (IC_{50} values for scavenging DPPH: 86.61; ABTS: 21.26; OH: 37.92, O_2:78.35; and $ONOO^-$: 943.12 μg/ml). Likewise, antioxidant activity of essential oil and methanol extracts (Thusoo et al., 2014), essential oil and supercritical CO_2 fluid extracts (Pandian & Nagarajan, 2015), and aerial and root portions extract of *V. jatamansi* were also reported (Jugran et al., 2016). Bhatt et al. (2012) evaluated the antioxidant potential of extract and essential oil of wild and planted individuals of *V. jatamansi* using different *in vitro* methods and observed that root samples from planted individuals possess significantly higher ($p < 0.05$) antioxidant activity (ABTS: 4.87 mg/g; FRAP: 10.18 mg/g ascorbic acid equivalent dry weight). Whereas antioxidant activity estimated using DPPH was higher in case of wild source. Comparative assessment revealed that essential oil exhibited stronger antioxidant activity than methanol extract (Rawat et al., 2017). Moreover, several molecular markers (intersimple sequence repeats markers) were also identified to be associated with the antioxidant activity of *V. jatamansi* measured by ABTS, DPPH, and FRAP assay, and their use in identification and breeding of quality plants was envisaged (Jugran, Bhatt, et al., 2013; Jugran et al., 2015). Likewise, enhanced antioxidant activity of mycorrhiza treated plants of *V. jatamansi* is also reported (Jugran, Bhatt, & Rawal, 2015).

12.12 | Antimicrobial activity

Antibacterial and antifungal activity of *V. jatamansi* have been reported against large number of pathogenic bacteria and fungal pathogens (Girgune, Jain, & Garg, 1980; Suri & Thind, 1978; Thind & Suri, 1979). Antimicrobial activity in different solvents system (methanol, chloroform, hexane, and water) was found more effective than positive control (Ampicillin and Erythromycin; Sati, Khulbe, & Joshi, 2011). Antimicrobial (antifungal and antibacterial) activity of *V. jatamansi* aerial portion extract in chloroform fraction showed notable activity against *Staphylococcus aureus* whereas hexane fraction exhibited higher activity against *Bacillus subtilus* (Khuda, Iqbal, Zakiullah, & Nasir, 2012). However, hexane fraction was found to be the potent inhibitor of *Microsporum canis*, chloroform, and water fraction against *Microsporum canis* and *Aspergillus flavus*. Likewise, essential oil of *V. jatamansi* exhibited potential antimicrobial activity against *Bacillus pumilus*, *S. aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans* (Agnihotri et al., 2011). Babu, Verma, and Mathur (2015) detected the potent antimicrobial activity of hydroalcoholic extracts against *Micrococcus luteus*, *E. coli*, *E. coli* mutans, *Salmonella abony*, *Lactobacillus plantarum*, and *S. epidermidis*. However, hydroalcholic and hexane extracts of this species displayed high antibacterial activity against multidrug resistant *S. aureus* and *Pseudomonas aeruginosa*. Only hydroalcoholic extract of the species showed potent antifungal activity against *Aspergillus niger* (Babu et al., 2015). Antimicrobial potential of root material of *V. jatamansi* extracted in five different solvents, namely, water, methanol, ethanol, acetone, and hexane showed that ethanolic extract of *V. jatamansi* possess maximum activity against all studied bacterial strains except *Bacillus subtilis*. Furthermore, extracts in all the solvents were also found to inhibit the growth of *E. coli*. Whereas three fungal strains, namely, *Aspergillus flavus*, *Aspergillus fumigatus*, and *Candida albicans* displayed sensitivity. Likewise *Aspergillus fumigatus* was found sensitive against hexane extract of the species at high concentration. However, methanolic extract of the species was found much effective against bacterial strains (Rawat et al., 2017).

12.13 | Other biological properties

V. jatamansi is used in the preparation of polyherbal combination of anti-wrinkle cream (Ravichandran, Bhardwaz, & Kolhapure, 2005) and forms

ingredient of herbal antidepressant formulation Sumenta (Prakash, 1999). Didrovaltrate (**3**) present in *V. jatamansi* is reported to inhibit alternative synthesis in the complement system of the serum and its possible use in some autoimmune diseases (Baibado, 2011; Houghton, 1999). The radioprotective property of the hesperidin (**150**) extracted from the roots of this herb evaluated against γ irradiation stimulated severe DNA damage. Results demonstrated that hesperidin (**150**) at the concentration of 16.38 μM was most effective in rendering radioprotection (Katoch, Kaushik, Kumar, Agrawal, & Misra, 2012).

The effect of the total flavonoids extracted from *V. jatamansi* was evaluated on transforming growth factor (TGF)-beta signaling pathway in hepatocarcinoma 22-bearing mice by examining difference in gene expression chart using the gene chip technology. Results showed that in TGF-beta signaling pathway, the expression of seven genes were significantly regulated in the other three groups as compared with model group. Among them, the expression of Cul1, E2f5, Myc, and Smad7 genes was up-regulated, whereas the expression of Comp, Smad1, and Thbs4 genes was down-regulated. It was found that the total flavonoids from this species can regulate the abnormal gene expression in TGF-beta signaling pathway in hepatocarcinoma 22-bearing mice (Zhang et al., 2012).

Larvicidal and adulticidal activity of the root extract of *V. jatamansi* was reported against different mosquito species (Dua et al., 2008). *In vitro* anthelmentic activity of the rhizome of *V. jatamansi* against adult Indian earthworms (*Pheretima posthuma*) has been detected (Potdar, Lole, & Patil, 2011). Furthermore, methanol and chloroform extracts of *V. jatamansi* showed enormous activity against *Leishmania donovani* and *Leishmania major* and exerted beneficial effects against leshmania disease (Ghosh et al., 2011). Valerianannoids B (**180**) isolated from the species exhibited moderate *in vitro* antirotovirus activity (Ming et al., 1997). Furthermore, preliminary reports on analgesic activity (Sah, Mathela, & Chopra, 2010b), antidiarrheal and bronchodilatory activity (Khan & Gilani, 2012), antinociceptive effect (Sah et al., 2010b), constipation (Khan & Gilani, 2011), anti-HCV (Hepatitis C virus) activity (Ganta, Mandal, Debnath, Hazra, and Chaubey (2017), lipid metabolism regulatory activity (Zhu et al. 2016), and adeptogenic activity (Sharma, Kirar, Meena, Suryakumar, & Misra, 2012) of *V. jatamansi* are also reported.

13 | SYSTEMATIC ANALYSIS OF BOTANICAL ERRORS AND INACCURACY

Of the 116 articles published in various journals used in this review were devoted to plant sciences (with the scientific name usually appearing in the title). Of these, 26 published studies were for bioactive constituents, medical plant catalogue, or review and also used scientific name of the plants (Table 2). Thus, all the articles reviewed were 107 (92.24%) in the present study referred to one or more citation of scientific names. Among these, 61 (52.59%) were free from any nomenclature or taxonomic errors (Table 3). A total of ninety (77.59%) articles used appropriate scientific plant names. One hundred six (91.38%) articles used an appropriate style and differentiate scientific names from other text (Table 4). A sixth category was also analyzed that includes names not erroneous but in some respect inappropriate (Table 5). Of these, 43 (37.07%) articles used names and reflecting taxonomies that are not currently "accepted" by modern regional floras and databases (Table 6). Fifty (43.10%) articles comprises the species name (*V. jatamansi*) presently accepted in the title whereas 33 articles (28.45%) contain synonyms (*V. wallichii*) in the title. However, 22

TABLE 3 Articles failing to provide evidence of which plants were studied (i.e., failings to provide details of voucher specimens seen) or to provide sufficient evidences of identity of specimens studied by failing to establish how these specimens were identified

Subject	No. of scientific plant	Inaccurate voucher details (%)	No. of details how specimens identified (%)
Specific plant monograph	One	38.89	37.78
Medicinal plant catalogues, studies on active constituents, market of medicinal plant	Multiple	2.92	6.77

TABLE 4 Articles failing to provide any scientific plant name of the specimen used

Subject	No. of scientific plant	Articles concerning plants (%)	Without any scientific plant name (%)
Specific plant monograph	One	77.58	1.72
Medicinal plant catalogues, studies on active constituents, market of medicinal plant	Multiple	18.10	6.03

TABLE 5 Articles using inappropriate name (synonyms) in the title (although this cannot be considered as errors)

Subject	Species name (presently accepted) in the title (%)	Synonyms in the title (%)	Paper with no species name in title (%)
Single species	42.24	25.86	4.31
Multispecies	0.86	2.59	14.66

TABLE 2 Scale and nature of issues found in papers reviewed

Subject	No scientific plant name each paper species	Articles	% Total	With correct botanical nomenclature	With incorrect botanical nomenclature	With no scientific name at least in part
Specific plant monograph	One	90	77.58	76	14	N/A
Medicinal plant catalogues, studies on active constituents, market of medicinal plant	Multiple	26	22.42	16	10	N/A
Articles not referring to plants	None	N/A	N/A	N/A	N/A	N/A
Totals		116	100	92	24	N/A

TABLE 6 Articles using scientific plants name appropriately and using name and reflecting taxonomies that is not being accepted currently

Subject	Using scientific plant names appropriately (%)	Using a style appropriate to formally differentiate scientific names from other text (%)	A sixth category is also analyzed, which includes names not erroneous but in some respect inappropriate (%)	Using names and reflecting taxonomies that are not currently "accepted" by modern regional floras and databases (%)
Single species	64.66	74.14	32.76	28.45
Multi species	12.93	17.24	6.90	8.62

articles have no species name in their titles. Of these, 14 (12.07%) articles were dealing with other species except *V. jatamansi* whereas 15 articles deals with many species including *V. jatamansi* and 20 (17.24%) articles with the market potential, ayurveda, active constituents, and diseases treated. Based on these results, it can be clarily observed that studies on *V. jatamansi* suffer from many errors, which are needed to be corrected for reducing ambiguity in future research on *V. jatamansi*. This review on botanical inaccuracy of *V. jatamansi* identifies a series of key steps needed to address the taxonomic errors and inaccuracies, which can be replicated on the review of the other species to obtain such information.

14 | QUALITY ASSESSMENT OF BIOMEDICAL RESEARCH

Quality of the biomedical studies performed on *V. jatamansi* was also analyzed in six major catagories, namely, poor (0–10), average (11–15), good (16–20), better (21–25), excellent (26–30), and outstanding (31 above) based on the questions addressed in the research articles (Table 7). Question wise evaluation of each articles revealed that out of 51 articles analyzed only in three (5.88%) studies the source(s), passage number, and population doubling time (PDL) of cell lines were mentained. Similarly, in two (3.92%) studies, the selectivity of antibodies and/or interference RNA has been validated, and their source was clearly indicated. In three (5.88%) studies, the method of anesthesia was properly described. However, none of the study clearly stated about the criteria used for excluding any data from analysis. Here, it is recommended that exclusion of any data from a study should be heighlighted in future studies to obtain reproducibility and authenticity of the study. In four (7.84%) studies, western blots were shown describing appropriate loading controls for each western blot, replication of data, quantification, and the results of a statistical analysis. In a single study (1.96%), polymerase chain reaction and reverse transcription polymerase chain reaction were included following Minimum information necessary for evaluating qPCR experiments (MIQUE) guidelines. Furthermore, there were several major questions such as where the limitations of the current study or alternative interpretations of the findings clearly stated (37.25%), conflict of interest statement (41.18%); human tissues, fluids, or cells used in the study (39.22%); and cell lines authenticated by the author or vendor (29.41%) needed special attentions by the authors, reviewers, editors and publishers. Article wise analysis revealed that the studies were fall under average (3.92%), good (15.69%), better (43.14%), excellent (35.29%), and outstanding (1.96%) categories. Based on these results, it is suggested that the author should enhance the planning and execution of their research to address all major questions highlighted in this study to attain maximum score (outstanding). Furthermore, all gaps/questions with lower score need to be addressed on the basis of priority. This will enhance the reproducibility and authenticity of the researches for better understanding the potential of the species. This will provide future research direction so that the potential of the species can be harnesses in right prospective.

15 | FUTURE PROSPECTIVES

This review presents the comprehensive view about the phytochemical constituents, ethnopharmacological activities, botanical errors, and quality assessment of biomedical research published on *V. jatamansi*. This species has widely been used in traditional and modern medicine particularly as a sedative, flavoring, and fragrance agent. Although several studies have been conducted on *V. jatamansi* but there is a need to isolate new compounds from this species along with their particular biological activity. Botanical errors, taxonomic accuracy, and reproducibility of the biomedical research on *V. jatamansi* revealed that the researchers need to pay especial attention when dealing with the botanical and biomedical studies of any species. Various pharmacological studies on *V. jatamansi* revealed its potential in the treatment of different diseases such as stress, diarrhea, nervous disorders, and gastrointestinal disorders. However, validation of these studies by long-term clinical trials is lacking. Also, effectiveness of the extract largely

TABLE 7 Pharmacological studies (n = 51) analyzed for the standards of biomedical studies in species reviewed

S. no.	Question number	Categories	Total studies	Percentage (%)
1	0 to 10	Poor	0	0.00
2	11 to 15	Average	2	3.92
3	16 to 20	Good	8	15.69
4	21 to 25	Better	22	43.14
5	26 to 30	Excellent	18	35.29
6	31 above	Outstanding	1	1.96
		Total	51	100

dependent on quantitative value of active constituent(s) thus may be affected by chemotypic variation. As the species is largely been used as a polyherbal combination in preparation of different drugs and it is difficult to attribute a particular medicinal action being solely due to *V. jatamansi* component of the drug, therefore, it would be important to determine bioguided separation activity for identification of component specific action. Furthermore, isolation of most effective compounds and development of analytical tools of various *in vitro* and *in vivo* studies may bring numerous opportunities to further unravel the potential bioactivities of the species. Also, *in silico* molecular docking techniques may play important role in identification/designing of most effective molecules. These effective molecules may be synthesized from its analogues available in higher quantity in the plants to reduce the pressure in their natural habitat. Moreover, research on multilocational sampling to identify the active constituents will open up opportunity to discover new chemotypes as promising source of drugs. As the pharmacological studies on *V. jatamansi* suggested that the species have potential to act as a drug source for various disorders. Therefore, more clinical studies on this species and its compound will be crucial to ensure its safety and potential in modern medicines. Besides its traditional medicinal uses, several preliminary reports on other biological properties, for example, analgesic, antidiarrheal, bronchodilatory, antinociceptive, anti-HCV, and lipid metabolism regulatory activity have been recently identified. These studies provide a lead towards new biological application of *V. jatamansi* for future drug discovery. Series of the key questions designed for botanical errors assessment will help to solve botanical ambiguities and errors in *V. jatamansi*. This will help in proper authentication of material. However, journals need to reinforce their policies on accurate and validated name of a texa. Evaluation of biomedical research published on *V. jatamansi* will help the authors to draw clear, logical, and unambiguous conclusion along with providing a new checklist for analyzing already published research. Finding from this review will promote many types of research into identifying the active constituents and their mechanism of action. However, more research is needed in the area of pharmacokinetics and toxicity to give further information on the clinical use control the quality of this herb. This will provide authentic datasets especially on the long-term clinical use of the herb and new drug research and development, work on toxicity, and other unexplored area highlighted in the study.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ORCID

Arun K. Jugran https://orcid.org/0000-0003-3294-2847
Sandeep Rawat https://orcid.org/0000-0001-7991-2878

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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